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Organic & Biomolecular Chemistry
Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

Studies towards the Synthesis of Bielschowskysin. Construction of the Highly Functionalized Bicyclo[3.2.0]heptane Segment†

Anupam Jana,[a] Sujit Mondal[a] and Subrata Ghosh*[a]

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

A stereocontrolled approach for the construction of a highly functionalized bicyclo[3.2.0]heptane derivative embodying the bridged lactone present in the diterpene bielschowskysin is reported. The key step involves a stereoselective Cu (I)-catalyzed [2+2] photocycloaddition of a 1,6-diene embedded in a sugar derivative.

Introduction

Bielschowskysin **1**[1] (Figure 1) is a marine diterpene isolated from Caribbean gorgonian octocoral *Pseudopterogorgia kallos*. It exhibits antiplasmodium activity against *Plasmodium falciparum* and strong cyctotoxicity against human lung cancer and renal cancer cell lines.[1] It possesses a highly oxygenated unprecedented novel [9.3.0.0^{2,10}] tetradecane ring system with eleven stereocenters, six of which are arranged in a contiguous fashion on the periphery of the bicyclo[3.2.0]heptane unit. The unique structural feature along with strong bioactivity profile made bielschowskysin an attractive synthetic target. Several attempts[2] have recently been reported mainly for constructing the bicyclo[3.2.0]hepane segment. A major disadvantage in some of the reported approaches[2a,b] which were successful in the synthesis of bridged lactone will require an unfavorable aldol reaction at the bridge-head lactone enolate for addition of the C-12 substituent. As part of our continued interest[3] in intramolecular Cu (I)-catalyzed [2+2] photocycloaddition reaction in organic synthesis, we initiated a program towards the synthesis of bielschowskysin employing photocycladdition as the key step. Our synthetic plan is depicted in Scheme 1.

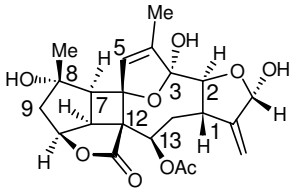

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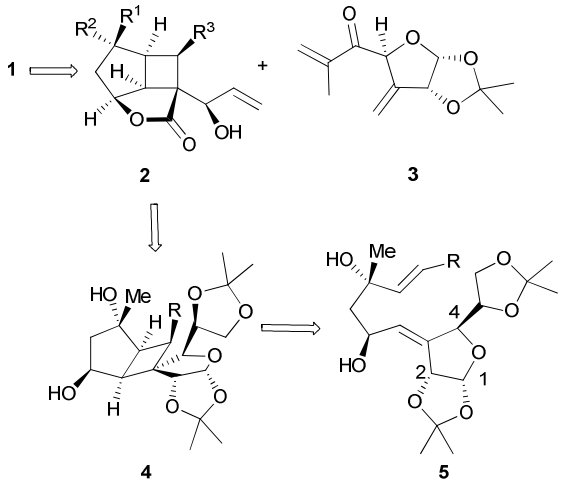
Figure 1. Structure of bielschowskysin.

Coupling of the prebuilt bicyclo[3.2.0] unit **2** with the fragment **3** was envisaged as a practical route to **1**. Thus our initial goal was to develop a route for the construction of the functionalized bicyclo[3.2.0]heptane derivative **2**. Compound **2** can in principle be derived from the cyclobutane derivative **4**. The C-1, C-2 sector of the glucose moiety in **4** is a latent carboxylic acid which can be employed to construct the lactone unit while C-4 oxygen of the sugar ring will provide the C-13 acetoxy group of **1**. Thus in the present approach the unfavorable aldol reaction at the bridge head lactone enolate can be avoided producing directly the lactone with the C-12 residue. Use of glucose will also provide the target in enantiomerically pure form. An intramolecular Cu (I)-catalyzed [2+2] photocycloddition[4] in the sugar embedded diene **5** will provide the bicyclo[3.2.0]heptane core with appropriately functionalized substituents for elaboration to **2**. Herein the results of this investigation[5] are described leading to the synthesis of the highly functionalized bicyclo[3.2.0]heptane core of bielschowskysin.



Scheme 1. Retrosynthetic analysis.

Results and Discussion

We initially paid attention to demonstrate the feasibility of this protocol for accessing the fragment **2**. We chose the diene **9** as the photosubstrate (Scheme 2). The diene **9** was prepared from the known[6] hydroxy-compound **6** as follows. Oxidation of **6** with Dess-Martin periodinane (DMP) provided the aldehyde **7** in excellent yield. Reaction of this aldehyde with 1-butenyl-4-magnesium bromide

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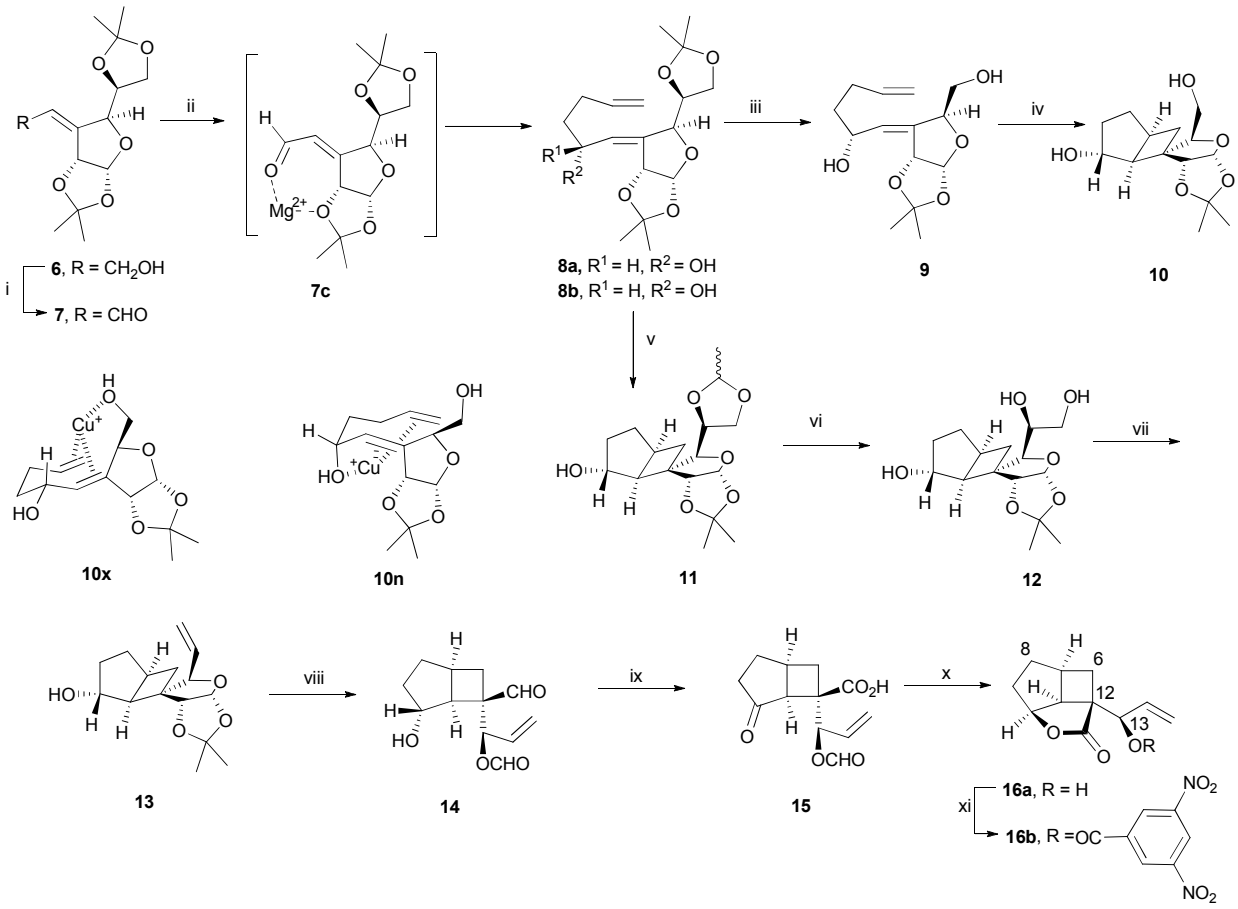

Scheme 2. Synthesis of bicyclo[3.2.0]heptane **16a**. Reagents and conditions: i) DMP, CH_2Cl_2, 0 °C, 1 h, 96%; ii) CH_2=$CHCH_2CH_2Br$, Mg, THF, 0 °C, 1 h, 65%; iii) (a) AcOH-H_2O (4:1), rt; (b) $NaIO_4$, THF-H_2O (2:1), 0 °C, 1.5 h; (c) $LiAlH_4$, Et_2O, 0 °C, 1.5 h, (70% in three steps); iv) hν, CuOTf, Et_2O, 2 h, 75%; v) hν, CuOTf, Et_2O, 3 h, 65%; vi) DDQ, CH_3CN-H_2O, 65 °C, 2 h, 88%; vii) (a) $NaIO_4$, THF-H_2O, 0 °C, 1.5 h; (b) Ph_3PCH_3Br, KHMDS, THF, -10 °C, 2 h, (65% in two steps); viii) (a) H_2SO_4, dioxane, 80 °C, 2 h; (b) $NaIO_4$, THF-H_2O (2:1), 0 °C, 1.5 h, (80% in two steps); (ix) Jones' reagent, acetone, 0 °C, 30 min, 88%; x) $NaBH_4$, MeOH, HCl, 0 °C to rt, 1.5 h, 91%; xi) 3,5-dinitrobezoyl chloride, CH_2Cl_2, Et_3N, DMAP, rt, 5 min, 71%.

provided a mixture of the dienes **8a** and **8b** in *ca.* 4:1 ratio in 82% yield. The pure dienes **8a** and **8b** were isolated by column chromatography in 65% and 17% yields respectively. The stereochemical assignment to the newly generated stereocenter in the major diastereoisomer **8a** is based on addition of the Grignard reagent to the carbonyl group of the Mg^{2+} chelated complex **7c.**[7] The assignment of stereochemistry was confirmed after its photocycloaddition to give the bicyclo[3.2.0]heptane derivative **10**. The 5,6-acetonide moiety in **8a** was then transformed to the hydroxy-methyl group to afford the diene **9** through a three-step protocol involving its selective deprotection[8]-periodate cleavage of the resulting vicinal diol followed by reduction of the aldehyde. Irradiation of a solution of the diene **9** in diethyl ether with a 450W Hanovia mercury vapor lamp through a water cooled quartz immersion well in presence of $2CuOTf.C_6H_6$ complex as catalyst for 3 h, afforded the cyclobutane derivative **10** in 75% yield. The presence of cyclobutane ring in the photoadduct **10** was indicated by shielding of one of the cyclobutane methylene hydrogens at δ 1.1 (dd, J = 6.5 and 13.3 Hz) over the other appearing as a multiplet at δ 2.11-a characteristic feature observed earlier in structurally analogous cyclobutane derivative.[3i] The relative stereochemistry of the newly generated stereocenters was assigned as follows. It is well established[9] that in ^{1}H NMR hydrogen α to the hydroxyl group in exo-2-hydroxy bicyclo[3.2.0]heptane derivatives appears as a doublet with J ≈ 4 Hz while in endo-2-hydroxy bicyclo[3.2.0]heptane derivatives it appears as a quartet with J ≈ 8 Hz. Comparison of the splitting pattern (doublet) with J = 4 Hz observed for the hydrogen α to the hydroxyl group in **10** with the above literature report indicated that it is an exo-2-hydroxy bicyclo[3.2.0]heptane derivative. Thus the hydrogen α to the hydroxyl group in **10** was assigned *anti* to the ring junction hydrogens. The exclusive formation of the adduct **10** can be attributed to cycloaddition occurring through the Cu(I)-complex **10x** rather than the sterically crowded Cu(I)-complex **10n** which would lead to the endo-2-hydroxy analogue of **10**. That the cycloaddition took place from the face *syn* to the hydroxymethyl moiety was in conformity[3i] with the formation of the adduct **18** from photocycloaddition of the structurally analogous diene **17** (Scheme 3).

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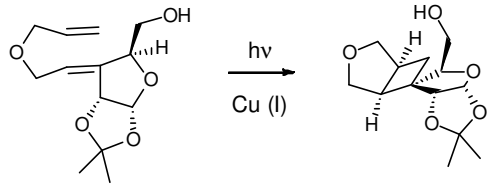
Photocycloaddition of the sterically crowded diene **8a** under identical condition was also found to give the cyclobutane derivative **11** in 65% yield. Compound **11** was obtained as a mixture of two diastereoisomers due to transformation[10] of the 5,6-acetonide moiety of **8a** to the acetal unit in **11** during photocycloaddition. The acetal moiety in **11** could be converted[11] to the triol **12** as a single diastereoisomer in 88% yield on treatment with catalytic amount of DDQ. This demonstrates that the photoadduct **11** was a diastereoisomeric mixture due to the presence of the C-5, C-6 acetal. The hydrogen α to the hydroxyl group in **12** also appeared as a doublet with J = 3.0 Hz confirming the stereochemical assignment.



17 **18**

Scheme 3. Reported [2+2] photocycloaddition of **17.**

The hydroxyl group on the five-membered ring in bicyclo[3.2.0]heptane derivative **10** or **12** has the stereochemistry opposite to that required for C-10 oxygen functionality of bielschowskysin **1**. It is obvious from the above investigation that photocycloaddition of the diene **8b** would provide the bicyclo[3.2.0]heptane derivative with the desired stereochemistry of the hydroxyl group required for the C-10 oxygen functionality in **1**. But the diene **8b** on attempted photocycloaddition under identical condition led to an intractable mixture from which no cyclobutane adduct could be isolated. Thus we decided to proceed for synthesis of the bicyclo[3.2.0]heptane derivative embodying the bridged lactone using the diol **12** and invert the stereochemistry of the hydroxyl group in a subsequent step.

Cleavge of the vicinal diol in **12** with $NaIO_4$ followed by Wittig olefination of the resulting aldehyde produced the alkene **13** in 65% overall yield. Compound **13** was then transformed to the hydroxy-aldehyde **14** in 80% yield on treatment with 4% aqueous H_2SO_4 followed by periodate cleavage of the resulting diol. At this stage inversion of the configuration of the hydroxyl group was required for lactonisation with the carboxylic acid to be generated during the subsequent steps. For this purpose an oxidation-reduction sequence was employed. Jones' oxidation of the hydroxy-aldehyde **14** provided the unstable keto-acid **15** which without purification was treated with sodium borohydride to afford directly the bridged γ-butyrolactone **16a** in 85% yield in two steps. The stereochemical assignment to **16a** was initially based on 2D NMR spectroscopy (COSY, NOESY and HSQC) (Figure 2). Finally this structural assignment to the lactone **16a** was confirmed by single crystal X-ray[12] (Figure 3) of its 3,5-dinitrobenzoate derivative **16b**. This route thus allows direct construction of the bicyclo[3.2.0]heptane unit **2** (R^1=R^2=R^3=H) embodying the bridged lactone with the C_{12} appendage having the stereodefined C_{13} hydroxyl group.

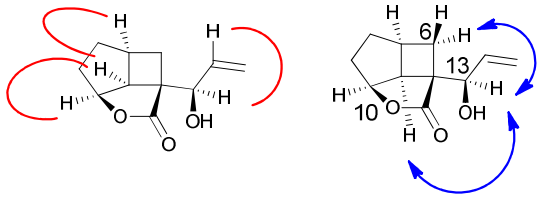


Figure 2. COSY ( ) and NOESY ( ) for **16a**

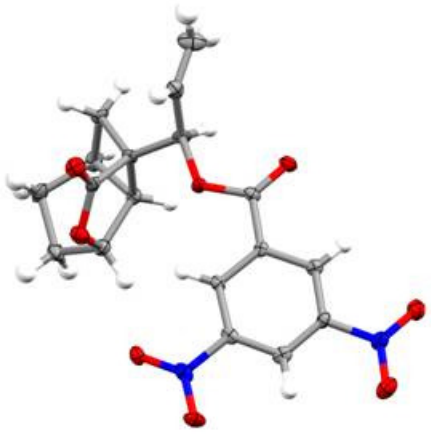


Figure 3. ORTEP diagram of compound **16b**.

After successfully demonstrating the strategy delineated in Scheme 1 for the construction of the model tricyclic lactone, we focussed on the construction of an analogue of **16a** having a substituent at C-6 (beilschowskysin numbering). The C-6, C-12 vicinal substituents will allow coupling with the fragment **3**. To this end the aldehyde **7** was allowed to react with the Grignard reagent prepared from (*E*)-6-bromohexa-1,3-diene[13] to afford the triene **19** in 75% yield as the major product (Scheme 4). The stereochemistry at the hydroxyl bearing stereocenter is based on analogy to the formation of **8a** from **7.** The compound **19** was then transformed to the trienol **20** through a three- step protocol involving selective deprotection of the 5,6-acetonide moiety-periodate cleavage of the liberated diol and $LiAlH_4$ reduction of the resulting aldehyde in 75% over all yield. Irradiation of **20** in diethyl ether in presence of copper (I) triflate provided an inseparable mixture of the cyclobutane derivative **21** along with its C_6-diastereoisomer in 65% yield in *ca*. 2:1 ratio. In the major diastereoisomer the C_{10}-H appeared at δ 4.65 as doublet of doublet with J = 3.5, 7.5 Hz. The J value (3.5 Hz) on comparison with J = 4 Hz observed for **10** confirmed the assignment of stereochemistry at the newly generated stereogenic centers of **21**. The assignment of stereochemistry at C-6 in the major isomer followed from its transformation to the tricyclic lactone **23** as detailed below. The mixture of **21** and its C-6 epimer was used for this transformation. Oxidation of the hydroxyl group in this mixture with DMP followed by Wittig olefination gave the divinyl compound **22** along with its C-6 diastereoisomer in 65% yield in two steps.

Transformation of this mixture to the lactone **23** and its C-6 epimer with the former predominating was achieved in 65% over all yield in four steps following a protocol similar to that used for the synthesis of the lactone **16a**. The stereochemical assignment

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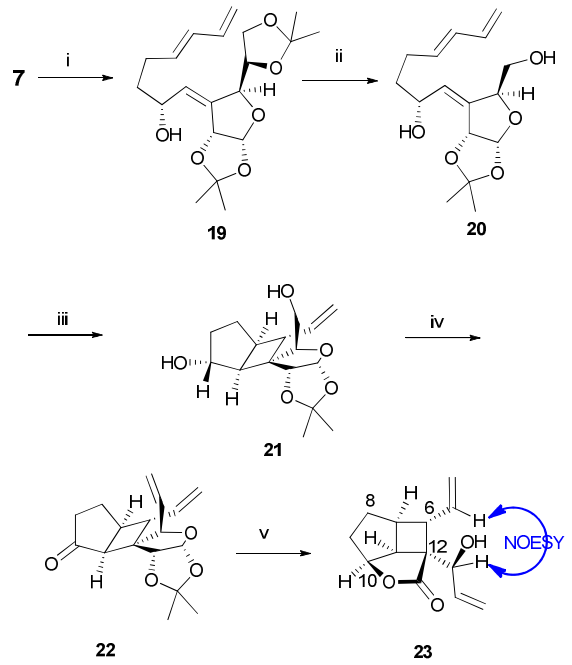
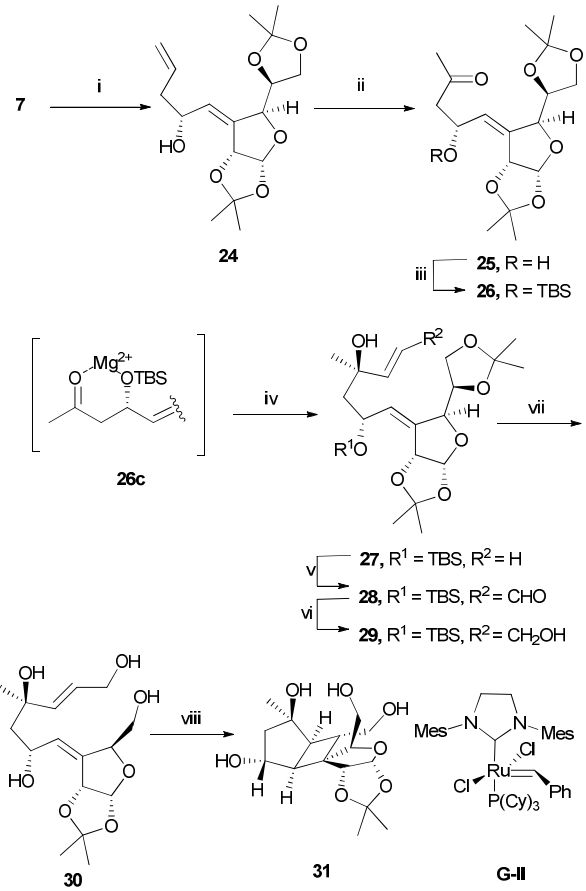
to the major lactone **23** was based on 2D NMR spectra. A strong correlation was observed between C-13 H and the methine of the C-6 vinyl in NOESY thus indicating a syn relationship of the C-6 vinyl and C-12 carbon appendage.



Scheme 4. Synthesis of Functionalized Bicyclo[3.2.0]heptane **23**. Reagents and conditions: i) (*E*)-6-bromohexa-1,3-diene, Mg, THF, 75%; ii) (a) AcOH-H_2O (4:1); (b) $NaIO_4$, THF-H_2O (2:1), 0 °C; (c) $LiAlH_4$, Et_2O, (75% in three steps); iii) hν, CuOTf, Et_2O, 65%; iv) (a) DMP, DCM; (b) Ph_3PCH_3Br, ^nBuLi, THF (65%); v) (a) 4% H_2SO_4, dioxane; (b) $NaIO_4$, THF-H_2O; (c) Jones' oxidation, acetone; (d) $NaBH_4$, MeOH, HCl, (65% in four steps).

The tricyclic lactone **23** obtained in this way lacks C-8 Me and OH groups of bielschowskysin. Thus we next focussed on developing a route for incorporation of C-8 functional groups. This required photocycloaddition of a diene with Me and OH groups. Synthesis of the diene and its subsequent transformation was accomplished in the following way (Scheme 5). Addition of allyl magnesium chloride to the aldehyde **7** afforded the hydroxy-compound **24** in 70% yield as the major diastereoisomer. The stereochemistry at the newly generated stereocenter is based on analogy to the formation of **8a** from **7**. The compound **24** was then transformed to the hydroxy-ketone **25** in 81% yield through Wacker process.[14] Addition of vinyl magnesium bromide to the silyl ether **26**, obtained on silylation of **25**, produced the carbinol **27** along with its minor diastereoisomer in *ca*. 7:1 ratio in 73% yield. The formation of the major diastereoisomer **27** may be attributed to addition of the nucleophile from the least hindered face of the β-silyloxy chelated[15] species **26c**. The hydroxy diene **27** was subjected to cross metathesis with crotonaldehyde in presence of Grubbs 2nd generation catalyst **G-II**. The cross metathesis product **28** was obtained in 79% yield as the only isolable product. Although a RCM path was expected, no RCM product was formed either during cross metathesis or even when the diene **27** was treated with **G-II** in the absence of crotonaldehyde. The failure of the diene **27** to undergo RCM may be attributed as follows. Steric factor plays an important role on the reactivity of alkene metathesis and chemoselective metathesis in substrates having more than one alkene can be achieved by increasing steric bulk around one of the alkene units.[16] It has been demonstrated[17] that in dienes, steric shielding of one of the alkene units by a bulky alkoxy group at the allylic position directs metathesis to take place on the alkene unit away from the bulky group. In the diene **27** shielding of the alkene attached to the sugar unit by the bulky *tert*-butyl dimethyl silyloxy group at the allylic position prohibits addition of the Ru-carbene formed from the terminal alkene inhibiting RCM. Thus only cross metathesis proceeds to produce **28**. Reduction of the aldehyde **28** with DIBAL-H gave the dihydroxy compound **29** in 90% yield. The diacetonide **29** was then transformed to the diene **30** through the standard protocol involving selective removal of the 5,6-acetonide moiety of the sugar unit-periodate cleavage of the resulting vicinal diol followed by hydride reduction of the generated aldehyde. Irradiation of an ethereal solution of the diene **30** in presence of CuOTf afforded the cycloadduct **31** as a viscous mass in 66% yield.



Scheme 5. Reagents and conditions: i) CH_2=$CHCH_2MgCl$, THF, 1 h, 70%; ii) $PdCl_2$, CuCl, O_2, DMF-H_2O, rt, 2 h, 81%; iii) TBSOTf, Lutidine, DCM, 0 °C- rt, 78%; iv) CH_2=$CHMgBr$, THF, 0 °C, 73%; v) crotonaldehyde, **G-II**, DCM, 3 h, 79%; vi) DIBAL-H, DCM, -78 °C, 2 h, 90%; vii) (a) AcOH-H_2O (4:1), 6 h, 65 °C, 72%; (b) $NaIO_4$, THF-H_2O (2:1); (c) $LiAlH_4$, Et_2O, (83% in two steps); viii) hν, CuOTf, Et_2O, 3 h, 66%.

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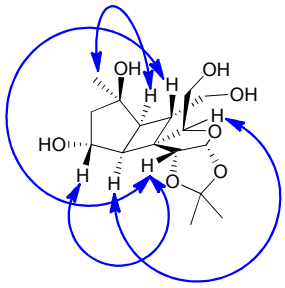
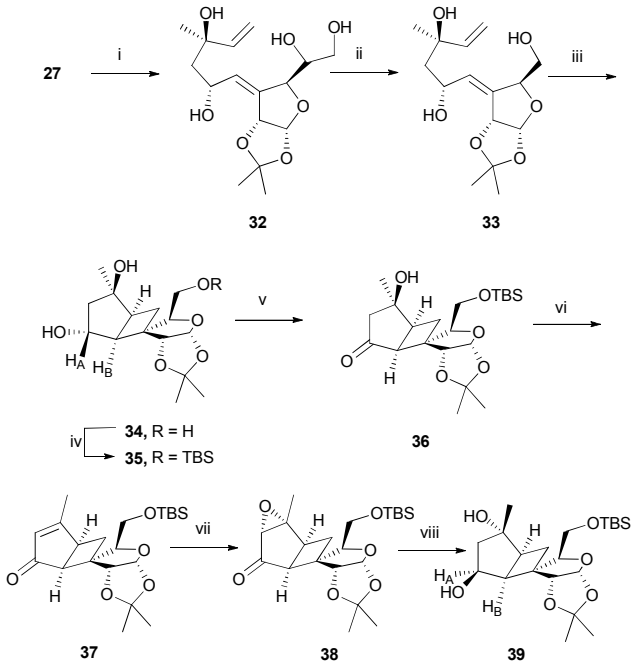


Figure 4. NOESY of compound **31.**

The assignment of stereochemistry to the phtoadduct was made by combination of the coupling constant of proton α to the hydroxyl group (J = 5 Hz) and 2D NMR (NOESY) spectrum (Figure 4). The five-membered ring in the bicyclo[3.2.0]hepane derivative **31** has the required C-8 and C-10 functional groups. However, they have the configuration opposite to that required for beilschowskysin. Further transformations to invert configuration at these centres could not be pursued due to insolubility of the adduct **31**. So we decided to prepare a simpler analogue of **31** (devoid of C-6 hydroxy-methyl group) to demonstrate how the stereochemistry could be inverted at the hrodoxyl bearing centres on the five membered ring.



Scheme 6. Reagents and conditions: i) (a) TBAF, DCM, 4 h; (b) AcOH-H_2O (4:1), 6 h, 65 °C, (83% in two steps); ii) (a) $NaIO_4$, THF-H_2O; (b) $LiAlH_4$, Et_2O, (72% in two steps); iii) hν, CuOTf, Et_2O, 78%; iv) TBSCl, DCM, Et_3N, DMAP, 4 h, 73%; v) DMP, DCM, 0 °C, 1 h, 90%; vi) Ac_2O, DMAP, Et_3N, rt, 5 h, 92%; vii) 30% H_2O_2, MeOH, 6 (N) NaOH, 0.5 h, 75%; viii) $LiAlH_4$, 1 h, Et_2O, 66%.

To this end the diene **27** on treatment with aqueous acetic acid at 65 °C led deprotection of the 5,6-acetonide unit in the sugar portion with concommitant desilylation to produce the tetrahydroxy compound **32** in 67% yield (Scheme 6). However, a two-step process involving sequential desilylation with TBAF followed by deprotection of the acetonide unit proceeded in much improved yield (83%). Periodate cleavage of the vicinal diol unit in **32** followed by $LiAlH_4$ reduction of the resulting aldehyde gave the triol **33** in 72% yield. With the diene ready in hand, it was irradiated in diethyl ether in the presence of CuOTf catalyst to afford the cyclobutane derivative **34** in 78% yield. The reaction was found to proceed with similar stereochemical outcome as evidenced by the coupling constant of the proton next to the silyloxy group of the silyl derivative **35**. Stereochemical assignment to **34** followed from its NOESY specrum (Figure 5).

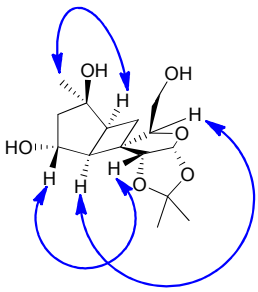


Figure 5. NOESY of compound **34.**

The five-membered ring in the bicyclo[3.2.0]hepane derivative **35** is fully functionalized. But C-8 and C-10 OH groups have the configuration opposite to that required for beilschowskysin. The inversion of configuration at these centers was achieved in the following way. The C-10 OH group in **35** was oxidized with DMP to afford the cyclopentanone derivative **36** in 90% yield. Treatment of **36** with Ac_2O-NEt_3 afforded the cyclopentenone **37** in excellent yield.

The enone **37** on reaction with alkaline H_2O_2 gave the oxirane **38** in 75% yield. As expected epoxidation took place from the least hindered convex face. Compound **38** on treatment with $LiAlH_4$ led to simultaneous reduction of the carbonyl group as well as the oxirane ring to produce the dihydroxy compound **39** in 66% yield. Comparison of the coupling constant ($J_{A,B}$ = 4 Hz) observed for H_A in **35** with that ($J_{A,B}$ = 7.5 Hz) observed for H_A in **39** confirmed that in the transformation of **35** to **39**, there is an inversion of configuration at C-10. The cross peak observed between C-7 H and C-8 CH_3 in NOESY spectrum of **35** was absent in the compound **39** (Figure 6) confirming inversion of configuration at C-8. The bicyclo[3.2.0]heptane derivative **39** have the desired configuration at C-8 and C-10 stereogenic centers for synthesis of beilschowskysin **1**. Trnsformation of **39** for the construction of the bridged lactone required removal of the acetonide unit. All attempts to deprotect the 1,2-acetonide of the glucose unit failed.

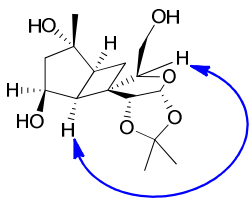


Figure 6. NOESY of compound **39.**

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Conclusion

We have developed a stereocontrolled route for the synthesis of a highly functionalized bicyclo[3.2.0]heptane derivative embodying the bridged lactone present in the diterpene bielschowskysin **1**. The attractive feature of this route is that it directly provides the bicyclo[3.2.0]heptane moiety with stereoselective generation of the C-12 quaternary center with stereodefined C-13 hydroxyl group through an intramolecular stereoselective Cu(I)-catalyzed [2+2] photocycloaddition of 1,6-diene embedded in a sugar derivative. CuOtf catalyzed [2+2] photocycloaddition strategy can be extended for the construction of bicyclo[3.2.0]heptane derivatives fully functionalized on the five membered ring.

Experimental

General experimental methods

All reactions were carried out under an atmosphere of argon. PE refers to the fraction of petroleum ether having bp 60-80 °C. EA refers to ethyl acetate. Column chromatography was carried out with silica gel (100-120 mesh). NMR spectra were recorded unless otherwise stated at 500 MHz for ^{1}H and 125 MHz for ^{13}C using residual chloroform as an internal standard. ^{13}C peaks assignment is based on DEPT experiment. Optical rotation values are given in 10^{-1} deg cm^2 g^{-1}. Melting points are uncorrected. High Resolution Mass spectra (HRMS) were measured in a QTOF I (quadrupole-hexapole-TOF) mass spectrometer with an orthogonal Z-spray-electrospray interface. Infrared spectra for liquids were recorded as thin film.

(Z)-2-((3aR,5S,6aR)-5-((R)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)acetaldehyde (7)

A solution of the alcohol **6** (3.0 g, 10.50 mmol) in dichloromethane (30 mL) and DMP (4.9 g, 11.54 mmol) was stirred at 0 °C for 1 h. The reaction mixture was quenched by $Na_2S_2O_3$ solution doped with $NaHCO_3$ and was stirred vigorously. After usual work up the residual mass was purified by column chromatography [PE-diethyl ether (5:1)] to give the compound **7** (2.86 g, 96%) as a viscous liquid; υ_{max} (neat) 2990, 1686 cm^{-1}; $[\alpha]_D^{23}$ +134.4 (*c* 2.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 10.07 (1H, d, *J* = 8.0 Hz), 6.40 (1H, m), 5.96 (1H, d, *J* = 4.0), 5.45 (1H, m), 4.78 (1H, m), 4.11 (1H, dd, *J* = 6.0, 8.3 Hz), 4.04-3.99 (2H, m), 1.49 (3H, s), 1.43 (3H, s), 1.42 (3H, s), 1.34 (3H, s); ^{13}C NMR ($CDCl_3$) δ 191.6 (CO), 160.3 (C), 127.0 (CH), 113.7 (C), 110.4 (C), 105.3 (OCHO), 80.8 (OCH), 78.2 (OCH), 76.9 (OCH), 67.1 (OCH_2), 27.5 (CH_3), 27.5 (CH_3), 26.8 (CH_3), 25.3 (CH_3); HRMS (ESI) *m/z* calcd for $C_{14}H_{20}O_6Na$ $(M+Na)^+$, 307.1158; found, 307.1157.

(R,Z)-1-((3aR,5S,6aR)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)hex-5-en-2-ol (8a) and *(S,Z)-1-((3aR,5S,6aR)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)hex-5-en-2-ol* (8b)

To the Grignard reagent [prepared from 4-bromo-1-butene (2.7 mL, 26.20 mmol) and magnesium (838 mg, 34.93 mmol)] cooled at 0 °C was added a solution of the aldehyde **7** (6.2 g, 21.83 mmol) in dry THF (20 mL). The reaction mixture was stirred for 1 h at 0 °C. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution (10 mL) and the precipitated solid was allowed to settle. The clear solution was decanted and concentrated to give a light yellow liquid which was chromatographed using PE-diethyl ether (5:1) as the eluent to afford the major diastereomer **8a** (4.8 g, 65%) as a light yellow oil; $[\alpha]_D^{25}$ +25.6 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.90-5.79 (3H, m), 5.22 (1H, d, *J* = 5.0 Hz), 5.04 (1H, dd, *J* = 1.0, 16.5 Hz), 4.98 (1H, dd, *J* = 1.0, 10.0 Hz), 4.66 (1H, d, *J* = 6.0 Hz), 4.45 (1H, q, *J* = 6.5), 4.05-3.98 (3H, m), 3.88 (1H, dd, *J* = 5.0, 7.5 Hz), 2.19-2.13 (2H, m), 1.79-1.73 (1H, m), 1.68-1.61 (1H, m), 1.48 (3H, s), 1.41 (3H, s), 1.38 (3H, s), 1.34 (3H, s); ^{13}C NMR ($CDCl_3$) δ 140.9 (C), 138.2 (CH), 131.8 (CH), 115.1 (CH_2), 112.8 (C), 110.0 (C), 105.1 (OCHO), 80.5 (OCH), 79.1 (OCH), 77.9 (OCH), 69.2 (OCH), 66.6 (OCH_2), 35.9 (CH_2), 29.8 (CH_2), 27.6 (CH_3), 27.5 (CH_3), 26.7 (CH_3), 25.8 (CH_3); HRMS (ESI) *m/z* calcd for $C_{18}H_{28}O_6Na$ $(M+Na)^+$, 363.1783; found, 363.1780 and **8b** (1.25 g, 17%) as a pale yellow liquid; $[\alpha]_D^{25}$ +106.9 (*c* 4.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89-5.80 (3H, m), 5.21-5.19 (1H, m), 5.05 (1H, dd, *J* = 1.0, 17.1 Hz), 4.98 (1H, d, *J* = 10.2 Hz), 4.60 (1H, d, *J* = 5.7 Hz), 4.51 (1H, q, *J* = 6.0), 4.06-3.87 (3H, m), 2.67 (1H, brs), 2.23-2.13 (2H, m), 1.74-1.66 (2H, m), 1.45 (3H, s), 1.41 (3H, s), 1.35 (3H, s), 1.33 (3H, s);^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9 (C), 138.5 (CH), 131.4 (CH), 115.0 (CH_2), 112.4 (C), 110.0 (C), 105.1 (OCHO), 80.1 (OCH), 78.8 (OCH), 77.7 (OCH), 69.6 (OCH), 66.8 (OCH_2), 36.3 (CH_2), 29.6 (CH2), 27.5 (2 CH_3), 26.7 (CH_3), 25.6 (CH_3); HRMS (ESI) *m/z* calcd for $C_{18}H_{28}O_6Na$ $(M+Na)^+$, 363.1783; found, 363.1784.

(R,Z)-1-((3aR,5S,6aR)-5-(Hydroxymethyl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)hex-5-en-2-ol (9)

Compound **8a** (2.4 g, 7.06 mmol) was treated with 80% aqueous acetic acid (8 mL) at room temperature for 10 h. After removing acetic acid the residual mass was purified by column chromatography [1:1 PE-EA] to provide the corresponding vicinal diol (1.8 g).

A solution of this diol (1.8 g, 5.99 mmol) in THF-H_2O (2:1) (20 mL) at 0 °C was stirred with $NaIO_4$ (1.93 g, 9.02 mmol) for 1.5 h. After usual workup the crude aldehyde (1.60 g) thus obtained was used for the next reaction without purification. A solution of the aldehyde (1.60 g. 5.97 mmol) in diethyl ether (30 mL) was added to a suspension of LAH (226 mg, 5.95 mmol) in diethyl ether (30 mL) at 0 °C. After stirring for 1.5 h, the reaction mixture was quenched by sequential addition of H_2O (0.2 mL), 15% NaOH solution (0.2 mL) and H_2O (0.6 mL). The reaction mixture was allowed to settle and filtered through sintered glass funnel. Removal of the solvent under reduced pressure followed by column chromatography (1:1 PE-EA) afforded the compound **9** (1.35 g, 70%) as colorless liquid; $[\alpha]_D^{25}$ +131.3 (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.92 (1H, d, *J* = 4.5 Hz), 5.87-5.79 (1H, m), 5.61 (1H, d, *J* = 8.0 Hz), 5.23 (1H, d, *J* = 4.0 Hz), 5.04 (1H, dd, *J*

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= 1.5, 17.5 Hz), 4.98 (1H, d, *J* = 10.0 Hz), 4.84 (1H, s), 4.46 (1H, q, *J* = 7.0 Hz), 3.80 (1H, dd, *J* = 3.0, 12.0 Hz), 3.59 (1H, dd, *J* = 4.5, 11.8 Hz), 2.19-2.07 (2H, m), 1.98 (2H, brs), 1.80-1.73 (1H, m), 1.67-1.60 (1H, m), 1.49 (3H, s), 1.40 (3H, s); ^{13}C NMR ($CDCl_3$) δ 140.1 (C), 138.1 (CH), 130.6 (CH), 115.2 (CH_2), 112.6 (C), 105.1 (OCHO), 81.2 (OCH), 78.9 (OCH), 69.0 (OCH), 64.5 (OCH_2), 35.8 (CH_2), 29.7 (CH_2), 27.7 (CH_3), 27.6 (CH_3); HRMS (ESI) *m/z* calcd for $C_{14}H_{22}O_5Na$ $(M+Na)^+$, 293.1365; found, 293.1366.

***(1S,3a'S,4R,5S,5'R,6R,6a'S)-5'-(Hydroxymethyl)-2',2'-dimethyldihydro-3a'H spiro[bicyclo[3.2.0]heptane-6,6'-furo[3,2-d][1,3]dioxol]-4-ol* (10)**

A solution of the diene **9** (500 mg, 1.85 mmol) in diethyl ether (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 $2CuOTf.C_6H_6$ (107 mg, 0.37 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 vapor lamp through a water cooled quartz immersion well for about 2 h. After completion (TLC), the reaction mixture was poured into ice cold ammonia solution (10 mL) in a separating funnel. The ether layer was separated, dried over Na_2SO_4 and concentrated in vacuum. The residual mass was purified through column chromatography [PE-EA (1:1)] as the eluent to afford the cyclobutane derivative **10** (374 mg, 75%). $[\alpha]_D^{25}$ +52.6 (*c* 1.2, $CHCl_3$); IR υ_{max} 3428, 2937, 1373, 1217 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.63 (1H, d, *J* = 3.5 Hz), 4.62 (1H, d, *J* = 4.0 Hz), 4.27 (1H, d, *J* = 3.0 Hz), 4.12-4.08 (1H, m), 3.97-3.88 (2H, m), 2.90-2.65 (2H, brs), 2.71 (1H, t, *J* = 7.5 Hz), 2.40 (1H, d, *J* = 7.0 Hz), 2.11 (2H, m), 2.02-1.97 (1H, m), 1.93-1.86 (2H, m), 1.48 (3H, s), 1.28 (3H, s) 1.1 (1H, dd, *J* = 6.5, 13.3 Hz); ^{13}C NMR ($CDCl_3$) δ 112.3 (C), 104.0 (OCHO), 86.1 (OCH), 83.6 (OCH), 74.7 (OCH), 61.7 (OCH_2), 49.3 (CH), 46.1 (C), 34.5 (CH), 33.6 (CH_2), 30.1 (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, 293.1365.

***(1S,3a'R,4R,5S,5'S,6R,6a'R)-2',2'-Dimethyl-5'-(2-methyl-1,3-dioxolan-4-yl)dihydro-3a'H-spiro[bicyclo[3.2.0]heptane-6,6'-furo[2,3-d][1,3]dioxol]-4-ol* (11)**

A solution of the diene **8a** (300 mg, 0.88 mmol) in diethyl ether (120 mL) was irradiated for 3 h in presence of $(CuOTf)_2.C_6H_6$ (51 mg, 0.18 mmol) according to the above procedure. Work up of the reaction mixture followed by column chromatography (PE-diethyl ether (4:1) as the eluent afforded the cyclobutane derivative **11** (180 mg, 65%) as a 1:1 diastereoisomeric mixture. $[\alpha]_D^{24}$ +58.2 (*c* 2.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) (for the mixture) δ 5.54-5.51 (1H, m), 5.13 (q, *J* = 4.6 Hz) and 5.03 (q, *J* = 4.8 Hz) (total 1H), 4.62 (1H, d, *J* = 3.5 Hz), 4.30-4.22 (2H, m), 4.01-3.81 (2H, m), 2.89-2.84 (1H, m), 2.65-2.62 (1H, m), 2.21-2.09 (2H, m), 2.05-1.95 (1H, m), 1.92-1.80 (3H, m), 1.65-1.53 (1H, m), 1.47 (3H, s), 1.39 (d, *J* = 4.8) and 1.34 (d, *J* = 4.8) (total 3H), 1.27 (3H, s), 1.18-1.10 (1H, m); ^{13}C NMR ($CDCl_3$) (for mixture) δ 112.2 (C), 111.0 (C), 103.8 (OCHO), 103.7 (OCHO), 102.4 (OCHO), 102.0 (OCHO), 86.5 (OCH), 86.3 (OCH), 83.1 (OCH), 82.5 (OCH), 76.6 (OCH), 74.9 (OCH), 74.5 (OCH), 73.5 (OCH), 69.9 (OCH_2), 69.3 (OCH_2), 50.1 (CH), 49.8 (CH), 46.9 (C), 46.8 (C), 34.9 (CH_2), 34.8 (CH_2), 33.7 (CH), 33.6 (CH), 30.0 (CH_2), 29.3 (CH_2), 28.0 (CH_2), 27.9 (CH_2), 27.1 (CH_3), 26.9 (CH_3), 26.6 (CH_3), 26.5 (CH_3), 20.0 (CH_3), 20.0 (CH_3); HRMS (ESI) *m/z* calcd for $C_{17}H_{26}O_6Na$ $(M+Na)^+$, 349.1627; found, 349.1629.

***(S)-1-((1S,3a'S,4R,5S,5'R,6R,6a'S)-4-Hydroxy-2',2'-dimethyldihydro-3a'H-spiro[bicyclo[3.2.0]heptane-6,6'-furo[3,2-d][1,3]dioxole]-5'-yl)ethane-1,2-diol* (12)**

To a stirred solution of the cyclobutane derivative **11** (200 mg, 0.64 mmol) in CH_3CN-H_2O (9:1) (10 mL) was added (DDQ) (15 mg, 0.66 mmol). After stirring the reaction mixture for 2 h at 65 °C it was cooled in ice bath. The reaction mixture was then quenched with slow addition of saturated $NaHCO_3$ solution (0.5 mL). The resulting mixture was concentrated in a rotary evaporator. The residual mass was diluted water, extracted with diethyl ether (3 X 10 mL), washed with brine. The organic extract was dried over anhydrous Na_2SO_4. The residual mass after removal of solvent was purified by column chromatography [PE-EA (1:1)] to afford the triol **12** (162 mg, 88%); υ_{max} (neat) 3370, 2957, 1217 cm^{-1}; $[\alpha]_D^{23}$ +15.5 (*c* 2.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.53 (1H, s), 4.63 (1H, d, *J* = 3.0), 4.30 (1H, d, *J* = 3.5), 4.12-4.10 (1H, m), 3.98-3.96 (1H, m), 3.91-3.85 (2H, m), 3.73 (1H, br s), 3.52 (2H, brs), 2.90-2.89 (1H, m), 2.77-2.75 (1H, m), 2.21-2.17 (1H, m), 2.05-2.03 (2H, m), 1.94-1.87 (2H, m), 1.48 (3H, s), 1.28 (3H, s), 1.13 (1H, dd, *J* = 6.0, 13.0); ^{13}C NMR ($CDCl_3$) δ 112.2 (C), 103.5 (OCHO), 86.2 (OCH), 81.7 (OCH), 75.0 (OCH), 70.9 (OCH), 65.5 (OCH_2), 50.0 (CH), 46.9 (C), 34.7 (CH), 33.9 (CH_2), 30.1 (CH_2), 28.2 (CH_2), 27.0 (CH_3), 26.5 (CH_3); HRMS (ESI) *m/z* calcd for $C_{15}H_{24}O_6Na$ $(M+Na)^+$, 323.1471; found, 323.1470.

***(1S,3a'R,4R,5S,5'R,6R,6a'R)-2',2'-Dimethyl-5'-vinyldihydro-3a'H-spiro[bicyclo[3.2.0]heptane-6,6'-furo[2,3-d][1,3]dioxol]-4-ol* (13)**

A solution of the triol **12** (200 mg, 0.67 mmol) in THF-H_2O (2:1) (4 mL) at 0 °C was stirred with $NaIO_4$ (285 mg, 1.33 mmol) for 1 h. After usual work up the crude aldehyde (170 mg) thus obtained was used for the next step. To a magnetically stirred suspension of methyltriphenylphosphonium bromide (790 mg, 2.21 mmol) in anhydrous THF (20 mL) at 0 °C under Ar atmosphere was added dropwise a solution of KHMDS (3.5 mL, 1.75 mmol, 0.5 M in toluene) and stirred for 10 min. A solution of the aldehyde (170 mg, 0.63 mmol) as obtained in THF (5 mL) was then added to the reaction mixture. After stirring for 2 h the reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution. Usual work up of the reaction mixture afforded after column chromatography (8:1 PE-diethyl ether) the cyclobutane derivative **13** (115 mg, 65%) as light yellow oil. $[\alpha]_D^{27}$ +65.8 (*c* 2.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.00 (1H, ddd, *J* = 6.4, 10.7, 17.1 Hz), 5.65 (1H, d, *J* = 3.5 Hz), 5.48 (1H, dt, *J* = 1.5, 17.2 Hz), 5.36 (1H, dt, *J* = 1.4, 10.6 Hz), 4.65 (1H, d, *J* = 4.1

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Hz), 4.43 (1H, d, *J* = 6.2 Hz), 4.32 (1H, d, *J* = 3.5 Hz), 2.63-2.57 (1H, m), 2.29 (1H, d, *J* = 6.8 Hz), 2.09-2.00 (2H, m), 1.94-1.83 (2H, m), 1.67 (1H, br s), 1.49 (3H, s), 1.49-1.42 (1H, m), 1.30 (3H, s), 1.08 (1H, dd, *J* = 6.3, 9.1 Hz); ^{13}C NMR ($CDCl_3$) δ 132.6 (CH), 119.2 (CH_2), 112.1 (C), 104.0 (OCHO), 85.5 (OCH), 83.7 (OCH), 75.0 (OCH), 49.3 (CH), 47.7 (C), 34.9 (CH_2), 33.2 (CH), 30.0 (CH_2), 28.0 (CH_2), 26.9 (CH_3), 26.5 (CH_3); HRMS (ESI) *m/z* calcd for $C_{15}H_{22}O_4Na$ (M+Na)$^+$, 289.1416; found, 289.1417.

***(R)-1-((1S,4R,5S,6R)-6-Formyl-4-hydroxybicyclo[3.2.0]heptan-6-yl)allyl formate* (14)**

To a solution of the alkene **13** (25 mg, 0.09 mmol) in dioxane (0.4 mL) 4% H_2SO_4 (0.4 mL) was added. The reaction mixture was heated at 80 °C for 2 h. After usual work up the residual mass was purified through column chromatography [PE-EA (2:3)] to afford the corresponding triol (18 mg).

A solution of this triol (18 mg, 0.08 mmol) in THF-H_2O (2:1) (0.5 mL) at 0 °C was treated with $NaIO_4$ (36 mg, 0.16 mmol). The reaction mixture was then stirred for 1 h 0 °C. On completion (TLC), the reaction mixture was extracted with diethyl ether (3 X 5 mL). The extract was washed with water, brine, dried over anhydrous Na_2SO_4. Removal of solvent afforded the compound **14** (16 mg, 80%) as yellow oil. υ_{max} (neat) 3418, 2949, 1732, 1714 cm^{-1}; $[\alpha]_D^{23}$ +44.9 (*c* 2.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 9.64 (1H, s), 8.13 (1H, s), 5.80 (1H, ddd, *J* = 17.0, 10.5, 6.5 Hz), 5.74 (1H, d, *J* = 7.5 Hz), 5.43 (1H, d, *J* = 17.0 Hz), 5.40 (1H, d, *J* = 10.0 Hz), 4.19 (1H, d, *J* = 4.0 Hz), 2.86-2.80 (1H, m), 2.65 (1H, *J* = 7.0 Hz), 2.14 (1H, dd, *J* = 6.5, 13.8 Hz), 1.95-1.72 (4H, m), 1.52 (1H, dd, *J* = 7.0, 12.0 Hz), 1.24-1.17 (1H, m); ^{13}C NMR ($CDCl_3$) δ 201.0 (CO), 160.1 (CO), 130.6 (CH), 121.4 (CH_2), 76.9 (OCH), 73.3 (OCH), 53.6 (CH), 52.2 (C), 33.9 (CH_2), 32.9 (CH), 29.9 (CH_2), 24.2 (CH_2); HRMS (ESI) *m/z* calcd for $C_{12}H_{16}O_4Na$ (M+Na)$^+$, 247.0946; found, 247.0947.

Synthesis of the lactone 16a

To a solution of the aldehyde **14** (18 mg, 0.08 mmol) in acetone (1 mL) at 0 °C, Jones' reagent was added dropwise till orange colour of the reagent persisted. After stirring for 30 min the reaction mixture was quenched by adding isopropanol (0.5 mL). On evaporation of solvents in vacuum, the residual mass was extracted with diethyl ether to afford the corresponding keto-acid **15** (18 mg). A solution of this crude acid (18mg, 0.07 mmol) in MeOH (0.5 mL) cooled to 0 °C, was reduced by adding $NaBH_4$ (5 mg, 0.13 mmol). On completion of the reaction (1.5 h) it was diluted with diethyl ether and quenched by adding 5% HCl (0.5 mL) at rt. After usual work up the crude compound was purified through column chromatography [PE-diethyl ether (4:1)] as eluent to afford the lactone **16a** (13.5 mg, 85%) as a light yellow oil; $[\alpha]_D^{27}$ –53.9 (*c* 0.56, $CHCl_3$); υ_{max} (neat) 3445, 2926, 1746 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.96 (1H, ddd, *J* = 6.5, 10.5, 17.0 Hz), 5.42 (1H, d, *J* = 17.5 Hz), 5.30 (1H, d, *J* = 10.5 Hz), 5.00 (1H, t, *J* = 5.0 Hz), 4.34 (1H, d, *J* = 6.0 Hz), 3.18 (1H, t, *J* = 7.5 Hz), 2.75 (1H, dd, *J* = 9.5, 11.0 Hz), 2.70-2.63 (1H, m), 2.27 (1H, dd, *J* = 6.5, 10.0 Hz), 2.20-2.13 (2H, m), 1.87-1.60 (2H, m), 1.27-1.24 (1H, m); ^{13}C NMR ($CDCl_3$) δ 181.1 (CO), 135.2 (CH), 118.3 (CH_2), 85.3 (OCH), 72.7 (CHO), 49.4 (C), 45.8 (CH), 36.3 (CH_2), 32.6 (CH), 32.3 (CH_2), 31.3 (CH_2); HRMS (ESI) *m/z* calcd for $C_{11}H_{14}O_3Na$ (M+Na)$^+$, 217.0841; found, 217.0842.

Synthesis of the lactone 16b

To a solution of lactone **16a** (7 mg, 0.04 mmol) in methylene chloride (1.5 mL) at 0 °C was added triethylamine (2 equiv, 0.01 mL, 0. 08 mmol), 3,5-dinitrobenzoyl chloride (2.0 equiv, 16 mg, 0.08 mmol), and DMAP (0.25 mg) sequentially. The reaction mixture was stirred at that temperature for 5 min, and then quenched with saturated aqueous sodium bicarbonate (0.1 mL). After usual work up followed by column chromatography [5:1 PE-ether] afforded the compound **16b** (10 mg, 71%) as a white solid which was recrystallized (Et_2O-CH_2Cl_2) to give colorless crystals, m.p. 162-164 °C. $[\alpha]_D^{28}$ –3.3 (*c* 0.56, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.26-9.08 (3H, m), 6.09 (1H, ddd, *J* = 7.5, 10.5, 17.0 Hz), 5.81 (1H, d, *J* = 7.5 Hz), 5.51 (1H, d, *J* = 17.1 Hz), 5.44 (1H, d, *J* = 10.2 Hz), 5.00 (1H, dd, *J* = 2.4, 6.3 Hz), 3.39 (1H, t, *J* = 7.2 Hz), 2.84-2.75 (1H, m), 2.64 (1H, dd, *J* = 9.6, 12.6 Hz), 2.36-2.20 (1H, m), 1.91 (1H, dd, *J* = 3.0, 12.6 Hz), 1.84-1.65 (2H, m), 1.30-1.22 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.0 (CO), 161.7 (CO), 149.0 (C), 133.7 (C), 130.3 (CH), 129.5 (CH), 127.0 (C), 122.8 (CH), 121.9 (CH_2), 84.9 (OCH), 78.0 (CHO), 48.8, (C), 46.6 (CH), 36.4 (CH_2), 33.5 (CH_2), 32.5 (CH), 31.0 (CH_2); HRMS (ESI) *m/z* calcd for $C_{18}H_{16}N_2O_8Na$ (M+Na)$^+$, 411.0804; found, 211.0805.

***(R,1Z,5Z)-1-((3aR,5S,6aR)-2,2-Dimethyl-5-(2,2-dimethyl-1,3-dioxolan-4-yl)furo[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)octa-5,7-dien-2-ol* (19)**

To the Grignard reagent [prepared from the reaction of (*E*)-6-bromohexa-1,3-diene (2.86 g, 17.76 mmol) with Mg (473 mg, 19.70 mmol)] at rt, a solution of the aldehyde **7** (2.80 g, 9.86 mmol) in dry THF (20 mL) was added. The reaction mixture was stirred for 1.5 h then quenched by saturated aqueous of NH_4Cl. The clear solution was decanted and concentrated. The residual mass was chromatographed by using PE-diethyl ether (5:1) as the eluent to afford the alcohol **19** (2.70 g, 75%) as a light yellow oil as the major diastereomer; $[\alpha]_D^{25}$ +84.4 (*c* 3.13, $CHCl_3$); IR ν_{max} 3480, 2988, 1373, 1067 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.28 (1H, ddd, *J* = 10.1, 10.2, 17.0 Hz), 6.09-6.00 (1H, m), 5.88-5.82 (1H, m), 5.82 (1H, d, *J* = 4.3 Hz), 5.76-5.69 (1H, m), 5.18 (1H, d, *J* = 2.9 Hz), 5.07 (1H, d, *J* = 16.8 Hz), 4.95 (1H, d, *J* = 10.0 Hz), 4.63 (1H, d, *J* = 5.4 Hz), 4.41 (1H, q, *J* = 6.8 Hz) 4.04–3.94 (2H, m), 3.86 (1H, dd, *J* = 4.5, 6.7 Hz), 2.51 (1H, brs), 2.18 (2H, d, *J* = 7.1 Hz), 1.81-1.53 (2H, m) 1.46 (3H, s), 1.39 (3H, s) 1.36 (3H, s) 1.32 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.8 (C), 137.1 (CH), 134.3 (CH), 131.8 (CH), 131.6 (CH), 115.4 (CH_2), 112.8 (C), 110.0 (C), 105.2 (OCHO), 80.4 (OCH), 79.0 (OCH), 77.8 (OCH), 69.1 (OCH), 66.6 (OCH_2), 36.1 (CH_2), 28.6 (CH_2), 27.7 (CH_3), 27.6 (CH_3), 26.7 (CH_3), 25.5 (CH_3); HRMS (ESI) *m/z* calcd for $C_{20}H_{30}O_6Na$ (M+Na)$^+$, 389.1940; found, 389.1943.

***(R,1Z,5E)-1-((3aR,5S,6aR)-5-(Hydroxymethyl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)octa-5,7-dien-2-ol* (20)**

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The triene **19** (1.0 g, 2.73 mmol) was treated with 80% aqueous acetic acid (3 mL) for 4 h at 50 ^{o}C. On completion of the reaction (TLC), acetic acid was removed under vacuum. Column chromatography of the residual mass with 1:1 PE-EA as the eluent gave the corrosponding triol (780 mg) as a viscous liquid.

A solution of this triol (780 mg, 2.39 mmol) in THF-H_2O (2:1) (20 mL) at 0 ^{o}C was stirred with $NaIO_4$ (767 mg, 3.58 mmol) for 1.5 h. Usual work up afforded the corresponding aldehyde (700 mg). This was used for the next step without further purification. A solution of the aldehyde (700 mg, 2.39 mmol) was added to a suspension of LAH (100 mg, 2.63 mmol) in diethyl ether (30 mL) at 0 ^{o}C. After stirring for 1.5 h, the reaction mixture was quenched with sequential addition of H_2O (0.1 mL), 15% NaOH solution (0.1 mL) and H_2O (0.3 mL). The reaction mixture was allowed to settle and filtered through sintered glass funnel. Removal of the solvent under reduced pressure followed by column chromatography [1:1PE-EA] afforded the compound **20** (600 mg, 75%) as colorless liquid; $[\alpha]_D^{25}$ +114.2 (*c* 2.25, $CHCl_3$); IR ν_{max} 3408, 2928, 1379, 1011 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.29 (1H, ddd, *J* = 10.2, 10.2, 16.9 Hz), 6.09-6.01 (1H, m), 5.89 (1H, d, *J* = 4.3 Hz), 5.72-5.63 (1H, m), 5.57 (1H, d, *J* = 7.9 Hz), 5.19 (1H, d, *J* = 4.3 Hz), 5.08 (1H, d, *J* = 16.8 Hz), 4.96 (1H, d, *J* = 10.2 Hz), 4.81 (1H, s), 4.42 (1H, q, *J* = 7.0 Hz) 3.78 (1H, dd, *J* = 2.8, 12.0 Hz), 3.57 (1H, dd, *J* = 4.6, 12.0 Hz), 3.10-3.40 (2H, brs), 2.21-2.16 (2H, m), 1.76-1.72 (2H, m), 1.48 (3H, s), 1.37 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.9 (C), 137.1 (CH), 134.2 (CH), 131.7 (CH), 130.4 (CH), 115.4 (CH_2), 112.6 (C), 105.1 (OCHO), 80.1 (OCH), 78.8 (OCH), 68.9 (OCH), 64.4 (OCH_2), 36.0 (CH_2), 28.5 (CH_2), 28.3 (CH_3), 27.6 (CH_3); HRMS (ESI) *m/z* calcd for $C_{16}H_{24}O_6Na$ (M+Na)$^+$, 319.1521; found, 319.1523.

(1S,3a'S,4R,5S,5'R,6R,6a'S,7S)-5'-(Hydroxymethyl)-2',2'-dimethyl-7-vinyldihydro-3a'H-spiro[bicyclo[3.2.0]heptane-6,6'-furo[2,3-d][1,3]dioxol]-4-ol **(21)**

Irradiation of the triene **20** (200 mg, 0.68 mmol) in diethyl ether (100 mL) in the presence of $(CuOTf)_2.C_6H_6$ (65 mg, 0.13 mmol) was accomplished following the procedure described for the preparation of the cyclobutane derivative **9** to afford after chromatography the cyclobutane derivative **21** (180 mg, 65%) along with its C-6 epimer in 2:1 ratio as a light yellow oil. $[\alpha]_D^{27}$ +90.66 (*c* 0.50 $CHCl_3$); IR ν_{max} 3428, 2938, 1373, 1051, 1645, 1217, 1051 cm^{-1}; ^{1}H NMR ($CDCl_3$) (for the mixture) δ 5.94-5.83 (1H, m), 5.74 (d, *J* = 3.5 Hz) and 5.49 (d, *J* = 3.5 Hz) (total 1H), 5.09-4.96 (3H, m), 4.72–4.71 (m) and 4.65 (dd, *J* = 3.5, 7.5 Hz) (total 1H), 4.47 (d, *J* = 3.5 Hz) and 4.38 (d, *J* = 3.0 Hz) (total 1H), 4.25-4.19 (1H, m), 4.13 (t, *J* = 5.0 Hz) and 4.00 (d, *J* = 4.5 Hz) (total 1H), 3.84-3.79 (1H, m), 3.11 (1H, t, *J* = 9.5 Hz), 2.91 (q, *J* = 7.5 Hz) and 2.76 (q, *J* = 7.5 Hz) (total 1H), 2.43 (d, *J* = 7.5 Hz) and 2.31 (d, *J* = 8.5 Hz) (total 1H), 2.38 (m) and 2.05-1.97 (m) 9 (total 2H), 1.90-1.75 (1H, m), 1.75-1.54 (2H, m), 1.52 (s) and1.50 (s) (total 3H), 1.32 (s) amd 1.30 (s) (total 3H); ^{13}C NMR ($CDCl_3$) (for the mixture) δ 137. (CH), 134.2 (CH), 119.2 (CH_2), 114.3 (CH_2), 112.2 (C), 111.9 (C), 104.3 (OCHO), 104.1 (OCHO), 87.4 (OCH), 85.9 (OCH), 83.7 (OCH), 81.8 (OCH), 75.2 (OCH), 75.1 (OCH), 61.6 (OCH_2), 61.3 (OCH_2), 51.6 (C), 51.5 (C), 47.8 (CH), 47.4 (CH), 39.2 (CH), 39.0 (CH), 37.1 (CH), 36.2 (CH_2), 35.5 (CH_2), 29.2 (CH_2), 26.8 (CH), 26.8 (CH_3), 26.5 (CH_3), 24.8 (CH_2); HRMS (ESI) *m/z* calcd for $C_{18}H_{24}O_6Na$ (M+Na)$^+$, 319.1521; found, 319.1521.

(1S,3a'S,5S,5'S,6R,6a'S,7S)-2',2-Dimethyl-5',7-divinyldihydro-3a'H-spiro[bicyclo[3.2.0]heptane-6,6'-furo[2,3-d][1,3]dioxol]-4-one **(22)**

A solution of the diol **21** (110 mg, 0.37 mmol) in dry dichloromethane (10 mL) and DMP (473 mg, 1.12 mmol) was stirred at rt for 2 h. It was quenched by addition of saturated $Na_2S_2O_3$ solution doped with $NaHCO_3$ (3 mL). The reaction mixture was then diluted with ether (10 mL) and vigorously stirred for 1.5 h at rt. Organic layer was separated and the aqueous layer was extracted with diethyl ether (2 X 10 mL). The combined organic extract was dried and concentrated to afford the corresponding keto-aldehyde (110 mg). Without further purification and characterization, this was used directly for Wittig reaction.

To a suspension of methyltriphenylphosphonium bromide (366 mg, 1.03 mmol) in anhydrous THF (10 mL) at 0 ^{o}C, *n*-BuLi (0.5 mL, 0.80 mmol, 1.6 M in hexane) was added drop wise and stirred for 30 min. A solution of the above aldehyde (100 mg, 0.34 mmol) in THF (5 mL) was then added to the reaction mixture and was stirred for 2 h. The reaction mixture was quenched by addition of water. After usual work up, the crude mass was purified through column chromatography [PE-diethyl ether (4:1)] to afford the divinyl compound **22** (70 mg, 65%) as light yellow oil; $[\alpha]_D^{26}$ -53.69 (*c* 2.5, $CHCl_3$); IR ν_{max} 2936, 1732, 1373, 1217 cm^{-1}; ^{1}H NMR ($CDCl_3$) (of the mixture of two diastereomers) δ 6.21 (ddd, *J* = 7.5, 10.1, 17.0) and 6.10 (ddd, *J* = 6.0, 10.8, 17.0 Hz) (total 1H), 6.00-5.90 (1H, m), 5.67 (d, *J* = 3.0 Hz) and 5.55 (d, *J* = 3.5 Hz) (total 1H), 5.51 (d, *J* = 17.0 Hz) and 5.41 (d, *J* = 17.0 Hz) (total 1H), 5.44 (d, *J* = 10.0 Hz) and 5.30 (d, *J* = 11.0 Hz) (total 1H), 5.20 (dd, *J* = 10 Hz) and 5.07 (d, *J* = 9.5 Hz) (total 1H), 5.12 (d, *J* = 17.0 Hz) and 5.05 (d, *J* = 17.5 Hz) (total 1H), 4.60-4.55 (m) and 4.28 (d, *J* = 3.5 Hz) (total 2H), 2.96 (q, *J* = 7.5 Hz) and 2.89 (dd, *J* = 2, 7.5 Hz) (total 1H), 3.19 (t, *J* = 9.5 Hz) and 2.70 -2.61 (m) (total 2H), 2.53 (d, *J* = 7.5 Hz) and 2.46 (d, *J* = 8.0 Hz) (total 1H), 2.41-2.36 (m) and 2.20-2.15 (m) (total 1H), 2.10 -1.97 (m) and 1.93 -1.89 (m) (total 1H), 1.70-1.64 (1H, m), 1.50 (s) and (s) (total 3H), 1.30 (s) and 1.27 (s) (total 3H); ^{13}C NMR ($CDCl_3$) (mixture of two diastereomers) δ 217.7 (CO), 217.3 (CO), 136.5 (CH), 133.6 (CH), 133.3 (CH), 132.1 (CH), 120.2 (CH_2), 120.1 (CH_2), 119.9 (CH_2), 115.5 (CH_2), 112.7 (C), 112.3 (C), 104.2 (OCHO), 103.9 (OCHO), 86.1 (OCH), 84.4 (OCH), 83.4 (OCH), 81.3 (OCH), 55.3 (C), 55.3 (C), 48.1 (CH), 45.2 (CH), 44.3 (CH), 40.4 (CH), 39.0 (CH), 38.8 (CH_2), 37.8 (CH_2), 34.8 (CH), 27.0 (CH_3), 26.8 (CH_3), 26.4 (CH_3), 26.4 (CH_3), 25.7 (CH_2), 22.2 (CH_2) ; HRMS (ESI) *m/z* calcd for $C_{17}H_{22}O_4Na$ (M+Na)$^+$, 313.1416; found, 313.1415.

Synthesis of the lactone 23

A solution of the diene **22** (16 mg, 0.06 mmol) in dioxane (0.2 mL) was heated with 4 N H_2SO_4 (0.2 mL) at 80 ^{o}C for 2 h. The reaction mixture, on cooling, was diluted with diethyl ether. After usual work up, the residual mass was purified through column

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chromatography [PE-EA (1:1)] to afford the corresponding vicinal diol (13 mg). Without further purification and characterization, this was used directly for the next step.

A solution of this diol (13 mg, 0.08 mmol) in THF-H_2O (2:1) (0.3 mL) at 0 ^oC was stirred with $NaIO_4$ (17 mg, 0.08 mmol) for 4 h. Usual workup of the reaction mixture afforded the corresponding aldehyde (12 mg) which was directly used for oxidation. A solution of this aldehyde (12 mg, 0.05 mmol) in acetone (0.5 mL) was oxidized with Jones' reagent at 0 ^oC. The reaction mixture after stirring for 1 h was quenched by isopropanol and worked up in the usual way to afford the corresponding keto-acid (11 mg).

To a solution of this keto-acid (11 mg, 0.04 mmol) in MeOH (0.5 mL) cooled to 0 ^oC, $NaBH_4$ (5 mg, 0.13 mmol) was added. After stirring for 1.5 h, the reaction mixture was diluted with diethyl ether (3 mL). To it 5% HCl (0.5 mL) was added and the mixture was stirred for 10 min. Usual work up and column chromatography [PE-diethyl ether (5:1)] as eluent afforded the lactone **23** (8 mg, 65%)**.** $[\alpha]_D^{26}$ -25.6 (*c* 0.27, $CHCl_3$); IR ν_{max} 3460, 2963, 1747, 1352, cm^{-1}; ^1H NMR ($CDCl_3$) (for the mixture) δ 6.19 (ddd, *J* = 8.0, 9.9, 17.5 Hz) and 6.12 (ddd, *J* = 6.0, 10.8, 17.0 Hz) (total 1H), 5.84-5.78 (1H, m), 5.39-5.11 (4H, m), 5.01 (t, *J* = 5.5 Hz for the major isomer) and 4.96 (t, *J* = 5.0 Hz for the minor isomer) (total 1H), 4.47 (d, *J* = 5.5 Hz for the major isomer), 4.38-4.34 (m, for the minor isomer) (total 1H), 3.49 (t, *J* = 7.5 Hz for the minor isomer) and 3.33 (t, *J* = 7.5 Hz for the major isomer) (total 1H), 3.17-2.66 (2H, m), 2.35-2.13 (3H, m), 1.89-1.62 (2H, m); ^{13}C NMR ($CDCl_3$) δ 179.3 (CO), 137.3 (CH), 135.6 (CH), 118.0 (CH_2), 117.4 (CH_2), 85.1 (OCH), 71.5 (CHO), 53.4,(C), 51.3 (CH), 44.1 (CH), 39.4 (CH), 36.0 (CH_2), 30.1 (CH_2); HRMS (ESI) *m/z* calcd for $C_{13}H_{16}O_3Na$ $(M+Na)^+$, 243.0997; found, 243.0994.

(R,Z)-1-((3aR,5S,6aR)-5-((S)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)pent-4-en-2-ol (24)

To a solution of the aldehyde **7** (2.0 g, 7.04 mmol) in dry THF (10 mL) at 0 ^oC was added allyl magnesium chloride (2.0 M solution in THF, 5.28 mL, 10.56 mmol) dropwise. The reaction mixture was stirred at that temperature for 1 h and quenched by addition of saturated aqueous NH_4Cl solution (2 mL). The precipitated solid was allowed to settle. The clear solution was decanted and concentrated to give **24** and its diastereoisomer (4:1) as a light yellow liquid which was chromatographed using PE-diethyl ether (5:1) as the eluent to afford the major diastereomer **24** (1.6 g, 70%) as a light yellow oil; $[\alpha]_D^{28}$ +114.6 (*c* 1.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.93-5.71(3H, m), 5.23-5.12 (3H, m), 4.68-4.66 (1H, m), 4.51 (1H, q, *J* = 6.6 Hz), 4.05-3.97 (2H, m), 3.91-3.82 (1H, m), 2.42-2.35 (2H, m), 1.50 (1H, brs), 1.49 (3H, s), 1.41 (3H, s), 1.38 (3H, s), 1.34 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.8 (C), 134.0 (CH), 131.3 (CH), 118.3 (CH_2), 112.8 (C), 110.0 (C), 105.3 (OCHO), 80.5 (OCH), 79.1 (OCH), 77.9 (OCH), 69.0 (OCH), 66.6 (OCH_2), 41.3 (CH_2), 27.7 (CH_3), 27.7 (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, 349.1624.

***(R,Z)-5-((3aR,5S,6aR)-5-((S)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)-4-hydroxypentan-2-one* (25)**

To a solution of CuCl (345 mg, 3.45 mmol) in 4 mL DMF-H_2O (3:1), $PdCl_2$ (41 mg, 0.23 mmol) was added. The reaction mixture was stirred at room-temperature and oxygen was bubbled. After 10 min, the solution of alkene **24** (750 mg, 2.30 mmol) in 2mL DMF-H_2O (3:1) was added and the resulting solution was allowed to stir for 2 h. On disappearance (TLC) of the starting material, DMF-H_2O was removed in vacuum. The residual mass was diluted with 50 mL diethyl ether and 5 mL water. The organic layer was separated, washed with water, brine and dried over anhydrous Na_2SO_4. Evaporation of solvent in vacuo and purification of the crude residue by column chromatography (1:1 Et_2O/PE) afforded the keto-methyl compound **25** (635 mg, 81%) as yellow oil; $[\alpha]_D^{26}$ +105.6 (*c* 1.0, $CHCl_3$); IR ν_{max} (film) 1713 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.86 (1H, td, *J* = 1.8, 7.8 Hz), 5.84 (1H, d, *J* = 4.5 Hz), 5.30-5.28 (1H, m), 4.95-4.92 (1H, m), 4.63 (1H, d, *J* = 6.3 Hz), 4.06-3.87 (3H, m), 2.90-2.79 (2H, m), 2.70-2.63 (1H, m), 2.20 (3H, s), 1.49 (3H, s), 1.41 (3H, s), 1.38 (3H, s), 1.33 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.6 (CO), 141.2 (C), 129.8 (CH), 112.8 (C), 110.0 (C), 105.2 (OCHO), 80.3 (OCH), 78.9 (OCH), 77.8 (OCH), 66.8 (OCH_2), 66.0 (OCH), 49.9 (CH_2), 31.1 (CH_3), 27.7 (CH_3), 27.6 (CH_3), 26.8 (CH_3), 25.6 (CH_3); HRMS (ESI) *m/z* calcd for $C_{17}H_{26}O_7Na$ $(M+Na)^+$, 365.1576; found, 365.1575.

(R,Z)-4-((tert-Butyldimethylsilyl)oxy)-5-((3aR,5S,6aR)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)pentan-2-one(26)

To a magnetically stirred solution of the alcohol **25** (3.2 g, 9.36 mmol) in CH_2Cl_2 (20 mL) 2,6-lutidine was added dropwise at 0 ^oC. After 5 min, tert-butyldimethylsilyl triflate (4.3 mL, 18.72 mmol) was added and the reaction mixture was stirred for 0.5 h. After completion of the reaction, the reaction mixture was quenched with water (2 mL) and was extracted with diethyl ether (3 x 30 mL). The combined extract was washed with brine and dried over anhydrous $NaSO_4$. Removal of solvent in vacuo followed by column chromatography [PE-diethyl ether (12:1)] afforded compound **26** (3.28 g, 78%) as a viscous light yellow oil. $[\alpha]_D^{29}$ +83.3 (*c* 4.5, $CHCl_3$); IR ν_{max} (film) 1712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.73-5.70 (2H, m), 5.14 (1H, d, *J* = 4.0 Hz), 4.89 (1H, q, *J* = 7.0 Hz), 4.53 (1H, d, *J* = 6.5 Hz), 3.92 (1H, dd, *J* = 6.0, 8.0 Hz), 3.86 (1H, q, *J* = 6.0 Hz), 3.82 (1H, dd, *J* = 5.5, 8.0 Hz), 2.70 (1H, dd, *J* = 7.5, 15.5 Hz), 2.46 (1H, dd, *J* = 6.0, 15.5 Hz), 2.08 (3H, s), 1.39 (3H, s), 1.34 (3H, s), 1.28 (3H, s), 1.24 (3H, s), 0.78 (9H, s), 0.01 (3H, s), -0.03 (3H, s); ^{13}C NMR ($CDCl_3$) δ 207.0 (CO), 138.2 (C), 130.9 (CH), 112.7 (C), 109.9 (C), 105.3 (OCHO), 79.6 (OCH), 78.4 (OCH), 77.8 (OCH), 67.5 (OCH), 66.8 (OCH_2), 51.8 (CH_2), 31.9 (CH_3), 27.6 (CH_3), 27.5 (CH_3), 26.9 (CH_3), 25.9 (three CH_3's of t-butyl group merged together), 25.6 (CH_3), 18.1 (C), -4.3 (CH_3), -5.1 (CH_3); HRMS (ESI) *m/z* calcd for $C_{23}H_{40}O_7SiNa$ $(M+Na)^+$, 479.2441; found, 479.243.

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***(3R,5R,Z)-5-((tert-Butyldimethylsilyl)oxy)-6-((3aR,5S,6aR)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)-3-methylhex-1-en-3-ol* (27)**

To a solution of the ketone **26** (4.5 g, 9.87 mmol) in dry THF (25 mL) at 0 ^{o}C was added dropwise vinyl magnesium bromide (1.0 M solution in THF, 14.8 mL, 14.80 mmol). The reaction mixture was stirred at that temperature for 1 h. The temperature of the reaction mixture was slowly raised to rt. The reaction mixture was quenched with saturated ammonium chloride solution (2 mL). The clear solution was decanted and concentrated to give **27** and its diastereo isomer (6:1) as a light yellow liquid. Chromatography of this mass with PE-diethyl ether (12:1) as the eluent afforded the alcohol **27** (2.70 g, 73%) as a light yellow oil as the major diastereomer; $[\alpha]_D^{28}$ +83.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.98-5.89 (2H, m), 5.80 (1H, d, *J* = 4.0 Hz), 5.42 (1H, dd, *J* = 1.0, 17.0 Hz), 5.18 (1H, dd, *J* = 1.5, 10.0 Hz), 4.96 (1H, d, *J* = 3.5), 4.81 (1H, dt, *J* = 2.0, 10.0 Hz), 4.56 (1H, d, *J* = 6.0 Hz), 4.40 (1H, s), 4.11-4.03 (1H, m), 3.99-3.94 (2H, m), 1.96 (1H, dd, *J* = 11.0, 14.0 Hz), 1.68 (1H, s), 1.49 (3H, s), 1.43 (3H, s), 1.38 (3H, s), 1.37 (3H, s), 1.26 (3H, s), 0.91 (9H, s), 0.14 (3H, s), 0.07 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.0 (CH), 136.7 (C), 131.9 (CH), 113.0 (C), 112.7 (CH_2), 109.9 (C), 105.1 (OCHO), 79.3 (OCH), 78.0 (OCH), 77.5 (OCH), 73.4 (C), 70.2 (OCH), 66.9 (OCH_2), 47.3 (CH_2), 29.9 (CH_3), 27.4 (CH_3), 27.3 (CH_3), 26.9 (CH_3), 26.0 (three CH_3's of t-butyl group merged together), 25.6 (CH_3), 17.8 (C), -3.6 (CH_3), -5.2 (CH_3); HRMS (ESI) *m/z* calcd for $C_{25}H_{44}O_7SiNa$ $(M+Na)^+$, 507.2754; found, 507.2752.

***(2E,4R,6R,7Z)-6-((tert-Butyldimethylsilyl)oxy)-7-((3aR,5S,6aR)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)-4-hydroxy-4-methylhept-2-enal* (28)**

To a degassed (on purging with argon) solution of compund **27** (830 mg, 1.72 mmol) in dry dichloromethane (30 mL) was added Grubbs 2nd generation catalyst **G II** (145 mg, 0.17 mmol) and crotonaldehyde (0.6 mL, 7.25 mmol) under Ar-atmosphere. After refluxing for 3 h, the reaction mixture was concentrated under vacou. Purification of the residue by column chromatography [PE-diethyl ehter (9:1)], afforded the conjugated aldehyde **28** (691 mg, 79%) as light yellow oil. $[\alpha]_D^{28}$ +50.6 (*c* 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (1H, d, *J* = 7.6 Hz), 6.91 (1H, d, *J* = 15.6 Hz), 6.46 (1H, dd, *J* = 8.0, 15.2Hz), 5.90 (1H, d, *J* = 8.4 Hz), 5.80 (1H, d, *J* = 4.0), 4.93 (1H, d, *J* = 4.4), 4.73 (1H, dt, *J* = 2.8, 10.8 Hz), 4.53 (1H, dd, *J* = 1.6, 6.4 Hz), 4.07-4.01 (1H, m), 3.99-3.90 (2H, m), 2.08 (1H, dd, *J* = 10.8, 14.4 Hz), 1.72 (1H, dd, *J* = 2.4, 14.4 Hz), 1.63 (1H, brs), 1.46 (3H, s), 1.42 (3H, s), 1.35 (9H, s), 0.91 (9H, s), 0.06 (3H, s), 0.05 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.3 (CO), 162.8 (CH), 137.6 (C), 131.4 (CH), 131.0 (CH), 112.9 (C), 110.0 (C), 105.2 (OCHO), 79.6 (OCH), 78.1 (OCH), 77.6 (OCH), 73.5 (C). 70.1 (OCH), 67.0 (OCH_2), 46.8 (CH_2), 29.2 (CH_3), 27.5 (CH_3), 27.4 (CH_3), 27.0 (CH_3), 26.0 (three CH_3's of t-butyl group merged together), 25.5 (CH_3), 17.8 (C), -3.6 (CH_3), -5.1 (CH_3); HRMS (ESI) *m/z* calcd for $C_{26}H_{44}O_8SiNa$ $(M+Na)^+$, 535.2703; found, 535.2701.

***(2E,4R,6R,7Z)-6-(tert-Butyldimethylsilyloxy)-7-((3aR,5S,6aR)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)-4-methylhept-2-ene-1,4-diol* (29)**

To a solution of the aldehyde **28** (1 g, 1.95 mmol) in dichloromethane (20 mL) at –78 ^{o}C was added DIBAL-H (6.5 mL, 9.75 mmol) and was stirred for 2 h at the same temperature. After completion of the reaction (TLC), it was quenched with addition of saturated Rochelle salt solution (13 mL) and was stirred vigorously at rt for 2 h. The aqueous phase was extracted with diethyl ether (4 × 20 mL) and the combined organic phases were washed with saturated aqueous NaCl (5 mL), dried with Na_2SO_4, filtered and evaporated to give a yellow oil. After column chrmatography of the crude mass using 7:1 diethyl ether/PE as the eluent afforded the diol **29** (900 mg, 90%) as viscous liquid. $[\alpha]_D^{29}$ +81.8 (*c* 3.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.02 (1H, td, *J* = 5.5, 15.5 Hz), 5.92 (1H, d, *J* = 8.5 Hz), 5.82-5.79 (2H, m), 4.94 (1H, d, *J* = 4.0 Hz), 4.85 (1H, t, *J* = 10.0), 4.56 (1H, d, *J* = 6.5), 4.35 (1H, s), 4.20 (1H, d, *J* = 5.5), 4.05-4.01 (1H, m), 3.96-3.93 (2H, m), 1.99 (1H, dd, *J* = 11.0, 14.5 Hz), 1.59 (1H, brs), 1.53-1.48 (2H, m), 1.48 (3H, s), 1.42 (3H, s), 1.39 (3H, s), 1.35 (3H, s), 1.27 (3H, s), 0.91 (9H, s), 0.13 (3H, s), 0.08 (3H, s); ^{13}C NMR ($CDCl_3$) δ 138.0 (CH), 136.9 (C), 132.5 (CH), 128.3 (CH), 112.8 (CH), 110.0 (C), 105.3 (OCHO), 79.7 (OCH), 78.3 (OCH), 77.7 (OCH), 72.9 (C). 70.1 (OCH), 66.9 (OCH_2), 63.3 (OCH_2), 47.9 (CH_2), 30.1 (CH_3), 27.7 (CH_3), 27.5 (CH_3), 27.0 (CH_3), 26.0 (three CH_3's of t-butyl group), 25.5 (CH_3), 17.9 (C), -3.5 (CH_3), -5.0 (CH_3); HRMS (ESI) *m/z* calcd for $C_{26}H_{46}O_8SiNa$ $(M+Na)^+$, 537.2859; found, 537.2856.

(2E,4R,6R,7Z)-7-((3aR,5S,6aR)-5-(Hydroxymethyl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)-4-methylhept-2-ene-1,4,6-triol (30)

Compound **29** (800 mg, 1.56 mmol) was treated with 80% aqueous acetic acid (4 mL) at 65 ^{o}C for 6 h. On disappearance (TLC) of the starting material acetic acid was removed in vacuum. The residual mass was purified by column chromatography [1:4 PE-EA] to provide the corresponding triol (403 mg, 72%). $[\alpha]_D^{27}$ +89.8 (*c* 1.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.83-5.74 (4H, m), 5.18 (1H, d, *J* = 4.2 Hz), 4.79-4.70 (3H, m), 4.10 (1H, d, *J* = 4.2 Hz), 4.09-4.70 (1H, m) 3.63-3.52 (4H, m), 1.90-1.68 (3H, m), 1.44 (3H, s), 1.36 (5H, s), 1.29 (3H, s) ; ^{13}C NMR (75 MHz, CD_3OD) δ 139.4 (C), 138.4 (CH), 132.1 (CH), 128.4 (CH), 113.6 (C), 106.7 (OCHO), 82.6 (OCH), 80.3 (OCH), 75.6 (OCH), 73.8 (C), 68.3 (OCH), 63.7 (OCH_2), 63.2 (OCH_2), 48.7 (CH_2), 29.7 (CH_3), 27.8 (CH_3), 27.8 (CH_3); HRMS (ESI) calcd for $C_{17}H_{28}O_8Na$ $(M+Na)^+$, 383.1682; found, 383.1685

The triol (110 mg, 0.31 mmol) in THF (2 mL) and water (1 mL) was cooled in ice-bath and $NaIO_4$ (100 mg, 0.47 mmol) was added to it. After stirring for 2 h, it was diluted with ethyl acetate. The reaction mixture was allowed to settle and filtered through sintered glass funnel. The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated. The residual mass was

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used for the next step without further purification. The crude aldehyde (95 mg) in diethyl ether (15 mL) was cooled to 0 °C and LAH (55 mg, 1.45 mmol) was added to it. On completion of the reaction the reaction mixture was quenched by sequential addition of H_2O (0.05 mL), 15% NaOH solution (0.1 mL) and H_2O (0.3 mL) followed by dilution with ethyl acetate. The clear solution was decanted, dried over anhydrous Na_2SO_4 and concentrated. Purification of the residual mass by column chromatography (1:4 PE-EA) afforded the tetraol **30** (84 mg, 83% in two steps) as a viscous liquid. $[\alpha]_D^{28}$ +72.17 (*c* 2.2, CH_3OH); ^1H NMR (300 MHz, $CDCl_3$) δ 5.94-5.75 (3H, m), 5.64-5.78 (1H, m), 5.22-5.20 (1H, m), 4.81 (1H, s), 4.71 (1H, dt, *J* = 3.0, 8.4 Hz) 4.19-4.14 (2H, m), 3.80 (1H, dd, *J* = 3.0, 12.0 Hz), 3.58 (1H, dd, *J* = 3.9, 12.0 Hz), 2.30 (3H, brs), 2.05-1.96 (1H, m), 1.74-1.64 (1H, m), 1.53(4H, s), 1.45 (3H, s), 1.35 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8 (C), 136.3 (CH), 129.5 (CH), 126.9 (CH), 111.7 (CH), 104.2 (OCHO), 80.2 (OCH), 77.8 (OCH), 72.1 (C). 66.6 (OCH), 63.2 (OCH_2), 62.0 (OCH_2), 46.1 (CH_2), 29.1 (CH_3), 26.7 (CH_3), 26.6 (CH_3); HRMS (ESI) calcd for $C_{16}H_{26}O_7Na$ $(M+Na)^+$, 353.1576; found, 353.1579.

***(1S,2R,3a'S,4R,5S,5'R,6R,6a'S,7S)-5',7-bis(Hydroxymethyl)-2,2',2'-trimethyldihydro-3a'H-spiro[bicyclo[3.2.0]heptane-6,6'-furo[2,3-d][1,3]dioxole]-2,4-diol* (31)**

Irradiation of the diene **30** (45 mg, 0.14 mmol) in diethyl ether (100 mL) in the presence of $(CuOTf)_2.C_6H_6$ (10 mg, 0.03 mmol) was accomplished to afford after chromatography (1:5 PE-EA) the cyclobutane derivative **31** (30 mg, 66%). $[\alpha]_D^{28}$ +17.8 (*c* 0.6, CH_3OH); ^1H NMR (300 MHz, CD_3OD) δ 5.72 (1H, d, *J* = 3.3 Hz), 4.64 (1H, d, *J* = 6.0 Hz), 4.58 (1H, brs), 4.47 (1H, d, *J* = 3.3 Hz), 4.18 (1H, dd, *J* = 4.2, 5.7 Hz), 3.91-3.89 (2H, m), 3.69-3.53 (3H, m), 2.38 (2H, t, *J* = 7.5 Hz), 2.34-2.25 (1H, m), 2.19 (1H, t, *J* = 7.8 Hz), 1.83 (1H, d, *J* = 14.1 Hz), 1.47 (3H, s), 1.40 (3H, s), 1.31 (3H, s), 1.25-1.18 (2H, m); ^{13}C NMR (75 MHz, CD_3OD) δ 111.9 (C), 104.2 (OCHO), 87.0 (OCH), 85.7 (OCH), 78.2 (C), 72.8 (OCH), 62.1 (OCH_2), 60.9 (OCH_2), 50.5 (C), 49.8 (CH), 47.6 (CH_2), 46.8 (CH), 43.0 (CH), 28.3 (CH_3), 25.8 (CH_3), 25.3 (CH_3); HRMS (ESI) *m/z* calcd for $C_{16}H_{26}O_7Na$ $(M+Na)^+$, 353.1576; found, 353.1575.

(2R,4R,Z)-1-((3aR,5S,6aR)-5-((S)-1,2-Dihydroxyethyl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)-4-methylhex-5-ene-2,4-diol (32)

To solution of the compound **27** (600 mg, 1.24 mmol) in dry dichloromethane (20 mL) under Ar atmosphere at 0 °C was added a solution of tetrabutylammonium fluoride in THF (2.5 mL, 2.50 mmol, 1M). After stirring for 4 h, the reaction mixture was quenched by water (1 mL) and extracted with ether (3 X 20 mL). The combined extract was washed with brine and dried over anhydrous Na_2SO_4. The residual mass on removal of the solvent in vaccuo was purified by column chromatography (PE-diethyl ehter 2:1) to afford the corresponding desilylated product (440 mg) as light yellow oil; $[\alpha]_D^{28}$ +117.8 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.95–5.82 (3H, m), 5.39 (1H, dd, *J* = 1.5, 17.1 Hz), 5.29–5.13 (2H, m), 4.69-4.60 (2H, m), 4.04-4.84 (4H, m), 3.25 (1H, brs), 1.98-1.93 (1H, m), 1.69-1.64 (1H, m), 1.46 (3H, s), 1.39 (3H, s), 1.37 (3H, s), 1.27 (3H, s), 1.24 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.0 (CH), 140.8 (C), 131.4 (CH), 113.0 (CH_2), 112.8 (C), 110.0 (C), 105.1 (OCHO), 80.4 (OCH), 78.9 (OCH), 77.7 (OCH), 73.7 (C), 68.0 (OCH), 66.7 (OCH_2), 46.5 (CH_2), 29.9 (CH_3), 27.7 (CH_3), 27.6 (CH_3), 26.7 (CH_3), 25.5 (CH_3); HRMS (ESI) *m/z* calcd for $C_{19}H_{30}O_6Na$ $(M+Na)^+$, 393.1889; found, 393.1886.

The desilylted product obtained as above (440 mg, 1.22 mmol) was treated with 80% aqueous acetic acid (2 mL). After stirring the reaction mixture for 6 h at 65 °C, acetic acid was removed in vacuo. The residual mass was purified by column chromatography using PE-EA (1:4) to afford the tetraol **32** (340 mg, 83%). $[\alpha]_D^{27}$ +99.6 (*c* 3.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.96–5.77 (4H, m), 5.36 (1H, dd, *J* = 1.5, 17.1 Hz), 5.17–5.13 (2H, m), 4.70-4.64 (2H, m), 4.15 (1H, brs), 3.65-3.62 (4H, m), 3.30 (1H, brs), 1.94 (1H, dd, *J* = 10.2, 14.4 Hz), 1.67 (1H, dd, *J* = 2.7, 14.4 Hz), 1.46 (3H, s), 1.38 (3H, s), 1.27 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.0 (CH), 140.0 (C), 131.0 (CH), 113.0 (CH_2), 112.9 (C), 105.1 (OCHO), 80.8 (OCH), 78.8 (OCH), 74.1 (C), 73.8 (OCH), 67.9 (OCH), 63.1 (OCH_2), 46.5 (CH_2), 29.5 (CH_3), 27.7 (CH_3), 27.6 (CH_3); HRMS (ESI) *m/z* calcd for $C_{16}H_{26}O_7Na$ $(M+Na)^+$, 353.1576; found, 353.1575.

***(2R,4R,Z)-1-((3aR,5S,6aR)-5-(Hydroxymethyl)-2,2-dimethylfuro[2,3-d][1,3]dioxol-6(3aH,5H,6aH)-ylidene)-4-methylhex-5-ene-2,4-diol* (33)**

A solution of the tetraol **32** (600 mg, 1.82 mmol) in THF-H_2O (2:1) (6 mL) at 0 °C was stirred with $NaIO_4$ (584 mg, 2.73 mmol) for 1.5 h. On full consumption of the starting material (TLC), the reaction mixture was diluted with ethyl acetate (50 mL). The clear solution was separated from precipitated solid by filtration. The organic layer was concentrated and the crude aldehyde (500 mg) thus obtained was used for the next reaction without purification. A solution of the aldehyde (500 mg. 1.68 mmol) in diethyl ether (20 mL) was added to a suspension of LAH (60 mg, 2.50 mmol) in diethyl ether (30 mL) at 0 °C. After stirring the reaction mixture for 1.5 h it was quenched with sequential addition of H_2O (0.06 mL), 15% NaOH solution (0.06 mL) and H_2O (0.18 mL). The reaction mixture was allowed to settle and filtered through sintered glass funnel. Removal of the solvent under reduced pressure followed by column chromatography [1:3 PE-EA] afforded the compound **33** (392 mg, 72%) as colorless liquid, $[\alpha]_D^{28}$ +96.5 (*c* 5.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 5.96–5.87 (2H, m), 5.58 (1H, d, *J* = 8.0 Hz), 5.36 (1H, d, *J* = 17.0 Hz), 5.20-5.13 (2H, m), 4.78 (1H, s), 4.67 (1H, t, *J* = 9.0 Hz), 4.08 (1H, brs), 3.76 (1H, d, *J* = 11.0 Hz), 3.62-3.48 (2H, m), 2.50 (1H, brs), 1.90 (1H, dd, *J* = 10.0, 15.0 Hz), 1.66 (1H, d, *J* = 14.0 Hz), 1.46 (3H, s), 1.38 (3H, s), 1.26 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.0 (CH), 139.9 (C), 130.1 (CH), 113.1 (CH_2), 112.7 (C), 105.1 (OCHO), 81.1 (OCH), 78.7 (OCH), 73.7 (C), 67.8 (OCH), 64.2 (OCH_2), 46.5 (CH_2), 29.7 (CH_3), 27.6 (CH_3), 27.6 (CH_3); HRMS (ESI) *m/z* calcd for $C_{15}H_{24}O_6Na$ $(M+Na)^+$, 323.1471; found, 323.1470.

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***(1S,2R,3a'S,4R,5S,5'R,6R,6a'S)-5'-(Hydroxymethyl)-2,2',2'-trimethyldihydro-3a'H-spiro[bicyclo[3.2.0]heptane-6,6'-furo[2,3-d][1,3]dioxole]-2,4-diol* (34)**

A solution of the diene **33** (400 mg, 1.33 mmol) in diethyl ether (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 $2CuOTf.C_6H_6$ (58 mg, 0.20 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 vapor lamp through a water cooled quartz immersion well for about 2 h. After completion (TLC), the reaction mixture was poured into ice cold ammonia solution (5 mL) in a separating funnel. The ether layer was separated, dried over Na_2SO_4 and concentrated in vacuum. The residual mass was purified through column chromatography [PE-EA (1:4)] as the eluent to afford the cyclobutane derivative **34** (312 mg, 78%). $[\alpha]_D^{25}$ +19.5 (*c* 1.6, CH_3OH); ^1H NMR (CD_3OD) δ 5.65 (1H, d, *J* = 3.0 Hz), 4.61 (1H, d, *J* = 5.5 Hz), 4.44 (1H, d, *J* = 3.5 Hz), 4.11 (1H, dd, *J* = 3.5, 7.5 Hz), 3.91 (1H, dd, *J* = 3.0, 11.5 Hz), 3.80 (1H, dd, *J* = 7.5, 11.5 Hz), 2.51-2.49 (1H, m), 2.43 (1H, q, *J* = 7.5 Hz), 2.30 (1H, dd, *J* = 5.5, 14.0 Hz), 1.86-1.81 (1H, m), 1.73 (1H, dd, *J* = 6.5, 13.5 Hz), 1.46 (3H, s), 1.40 (3H, s), 1.33-1.31 (5H, 3H of methyl group and two hydroxyl protons), 1.25-1.18 (2H, m); ^{13}C NMR (CD_3OD) δ 113.3 (C), 105.3 (OCHO), 87.2 (OCH), 84.8 (OCH), 80.0 (C), 74.0 (OCH), 62.1 (OCH_2), 50.2 (CH), 48.4 (CH_2), 47.3 (CH), 45.6 (CH), 30.0 (CH_3), 27.0 (CH_3), 26.6 (CH_3), 23.5 (CH_2); HRMS (ESI) *m/z* calcd for $C_{15}H_{24}O_6Na$ $(M+Na)^+$, 323.1471; found, 323.1470.

***(1S,2R,3a'S,4R,5S,5'R,6R,6a'S)-5'-(((tert-Butyldimethylsilyloxy)methyl)-2,2',2'-trimethyldihydro-3a'H-spiro[bicyclo[3.2.0]heptane-6,6'-furo[2,3-d][1,3]dioxole]-2,4-diol* (35)**

To a solution of the photoadduct **34** (400 mg, 1.33 mmol) in CH_2Cl_2 (10 mL) acooled to 0 °C, triethylamine (0.8 mL, 5.74 mmol), DMAP (16 mg, 0.13 mmol) and were added followed by t-butyldimethylsillyl chloride solution (50% in toluene, 0.6 mL, 1.99 mmol) dropwise. The reaction mixture was stirred for 4 h and then quenched with cold water (1.0 mL). The reaction mixture was diluted with diethyl ether, washed with brine and dried over andhydrous Na_2SO_4. Evaporation of the solvent followed by column chromatography [PE-diethyl ether (3:1)] of the residual mass afforded the compound **35** (40 mg, 73%) as a viscous yellowish liquid. $[\alpha]_D^{29}$ +38.4 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 5.64 (1H, d, *J* = 3.5 Hz), 4.71 (1H, t, *J* = 4.5 Hz), 4.41 (1H, d, *J* = 3.0 Hz), 4.11 (1H, t, *J* = 6.0 Hz), 3.90 (1H, dd, *J* = 5.0, 10.5 Hz), 3.87 (1H, dd, *J* = 7.0, 10.5 Hz), 2.57-2.50 (2H, m), 2.27 (1H, dd, *J* = 10.5, 14.0 Hz), 2.00-1.96 (1H, m), 1.88 (1H, dd, *J* = 3.0, 14.0 Hz), 1.80-1.77 (1H, m), 1.62 (2H, brs), 1.51 (3H, s), 1.45 (3H, s), 1.27 (3H, s), 0.91 (9H, s), 0.10 (6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 112.1 (C), 103.7 (OCHO), 86.6 (OCH), 82.2 (OCH), 78.6 (C), 74.1 (OCH), 61.9 (OCH_2), 50.4 (CH), 48.8 (CH_2), 46.8 (C), 44.7 (CH), 30.2 (CH_3), 27.0 (CH_3), 26.6 (CH_3), 26.0 (three CH_3's of t-butyl group merged together), 22.8 (CH_2), 18.4 (C), -5.2 (CH_3), -5.4 (CH_3); HRMS (ESI) *m/z* calcd for $C_{21}H_{38}O_6SiNa$ $(M+Na)^+$, 437.2336; found, 437.2335.

***(1S,2R,3a'S,5S,5'R,6R,6a'S)-5'-(((tert-Butyldimethylsilyl)oxy)methyl)-2-hydroxy-2,2',2'-trimethyldihydro-3a'H-spiro[bicyclo[3.2.0]heptane-6,6'-furo[2,3-d][1,3]dioxol]-4-one* (36)**

A solution of the alcohol **35** (100 mg, 0.24 mmol) in dichloromethane 10 mL and DMP (307 mg, 0.72 mmol) was stirred at 0 °C for 1 h. The reaction mixture was quenched by $Na_2S_2O_3$ solution doped with $NaHCO_3$ and was stirred vigorously for 0.5 h. The aqueous phase was extracted with diethyl ether (3 × 15 mL) and the combined organic phases were washed with brine, dried over anhydrous Na_2SO_4 and evaporated to dryness to give a pale yellow oil. It was purified by column chromatography [PE-diethyl ether (4:1)] to give the compound **36** (90 mg, 90%) as colorless oil. $[\alpha]_D^{28}$ -5.0 (*c* 1.7, $CHCl_3$); IR ν_{max} (film) 1728 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.62 (1H, d, *J* = 3.6 Hz), 4.35 (1H, d, *J* = 3.2 Hz), 4.22 (1H, dd, *J* = 4.4, 8.0 Hz), 3.98 (1H, dd, *J* = 4.8, 10.8 Hz), 3.85 (1H, dd, *J* = 8.4, 10.8 Hz), 3.07-2.97 (2H, m), 2.78 (1H, q, *J* = 8.4 Hz), 2.45-2.40 (1H, m), 2.30 (1H, ddd, *J* = 2.4, 9.2, 13.2 Hz), 2.05 (1H, dd, *J* = 7.2, 13.6Hz), 1.60 (1H, brs), 1.53 (3H, s), 1.27 (6H, s), 0.89 (9H, s), 0.10 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.9 (CO), 112.8 (C), 103.6 (OCHO), 85.9 (OCH), 81.2 (OCH), 74.3 (C), 61.3 (OCH_2), 51.8 (CH_2), 50.6(CH), 46.7 (C), 43.4 (CH), 28.4 (CH_3), 26.9 (CH_3), 26.4 (CH_3), 25.9 (three CH_3's of t-butyl group merged together), 23.8 (CH_2), 18.2 (C), -5.2 (CH_3), -5.5 (CH_3); HRMS (ESI) *m/z* calcd for $C_{21}H_{36}O_6SiNa$ $(M+H)^+$, 413.2354; found, 413.2357.

***(1S,3a'S,5S,5'R,6R,6a'S)-5'-(((tert-Butyldimethylsilyl)oxy)methyl)-2,2',2'-trimethyl-5',6a'-dihydro-3a'H-spiro[bicyclo[3.2.0]hept[2]ene-6,6'-furo[2,3-d][1,3]dioxol]-4-one* (37)**

To the solution of the compound **36** (50 mg, 0.14 mmol) in CH_2Cl_2 (10 mL), triethylamine (0.2 mL, 1.43 mmol), acetic anhydride (0.1 mL, 1.06 mmol), DMAP (2 mg) were sequentially added at rt. The resulting solution was stirred for 5 h. After completion of the reaction (TLC), it was quenched with water (1 mL) and diluted with diethyl ether (20 mL) and the aqueous layer was separated. The organic layer was washed thrice with water, once with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent in rotary evaporator followed by purification of the crude mass through column chromatography (5:1 PE/diethyl ether) provided the conjugate ketone **37** (88 mg, 92%) as light yellow oil. $[\alpha]_D^{28}$ +2.0 (*c* 3.8, $CHCl_3$); IR ν_{max} (film) 1697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.10 (1H, s), 5.56 (1H, d, *J* = 3.3 Hz), 4.33 (1H, dd, *J* = 5.1, 8.1 Hz), 4.27 (1H, d, *J* = 3.3 Hz), 4.02 (1H, dd, *J* = 5.1, 10.5 Hz), 3.82 (1H, dd, *J* = 8.1, 10.5 Hz), 3.27 (1H, d, *J* = 5.4 Hz), 3.09 (1H, ddd, *J* = 4.5, 4.8, 9.9 Hz), 2.55 (1H, dd, *J* = 9.6, 12.3 Hz), 2.12 (3H, s), 1.54 (3H, s), 1.37-1.33 (1H, m), 1.26 (3H, s), 0.90 (9H, s), 0.09 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.4 (CO), 178.0 (C), 133.0 (CH), 112.9 (C), 103.6 (OCHO), 86.8 (OCH), 80.8 (OCH), 62.2 (OCH_2), 48.6 (C), 48.0(CH), 40.2 (CH), 27.1 (CH_3), 27.0 (CH_3), 26.5 (CH_3), 26.0 (three CH_3's of t-butyl group merged together), 18.4 (C), 16.9

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(CH_2), -5.3 (CH_3), -5.5 (CH_3); HRMS (ESI) *m/z* calcd for $C_{21}H_{34}O_8SiNa$ $(M+Na)^+$, 417.2073; found, 417.2076.

***(1'S,2'R,3aS,4'R,5R,6R,6aS,6'S)-5-(((tert-Butyldimethylsilyl)oxy)methyl)-2,2,2'-trimethyldihydro-3aH-3'-oxaspiro[furo[2,3-d][1,3]dioxole-6,7'-tricyclo[4.2.0.02,4]octan]-5'-one* (38)**

Compound **37** (50 mg, 0.13 mmol) in methanol (0.5 mL) was stirred with 6 (N) NaOH solution (0.01 mL, 0.06 mmol) at 0 °C. Then, the reaction mixture was treated with 30% H_2O_2 solution (0.04 mL, 0.38 mmol) and sirring was continued for 0.5 h at 0 °C. After completion (TLC), methanol was removed in vacuo. Usual workup of the filtrate afforded the epoxide **38** (39 mg, 75%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.56 (1H, d, *J* = 3.3 Hz), 4.23-4.20 (2H, m), 4.98 (1H, dd, *J* =4.5, 10.8 Hz), 3.83 (1H, dd, *J* = 8.1, 10.8 Hz), 3.35 (1H, d, *J* = 0.9 Hz), 3.09-3.02 (1H, m), 2.97-2.94 (1H, m), 2.38 (1H, ddd, *J* = 2.7, 8.7, 12.3 Hz), 1.55 (3H, s), 1.54 (3H, s), 1.32 (4H, s), 0.90 (9H, s), 0.06 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.6 (CO), 113.0 (C), 103.3 (OCHO), 85.9 (OCH), 80.7 (OCH), 67.2 (C), 63.4 (OCH), 61.3 (OCH_2), 48.0(C), 46.1 (CH), 38.1 (CH), 27.0 (CH_3), 26.6 (CH_3), 26.1 (CH_3), 26.0 (three CH_3's of t-butyl group merged together), 18.3 (C), 13.7 (CH_2), -5.3 (CH_3), -5.4 (CH_3); HRMS (ESI) *m/z* calcd for $C_{21}H_{34}O_6SiNa$ $(M+Na)^+$, 433.2022; found, 433.2025.

***(1S,2S,3a'S,4S,5S,5'R,6R,6a'S)-5'-(((tert-butyldimethylsilyl)oxy)methyl)-2,2',2'-trimethyldihydro-3a'H-spiro[bicyclo[3.2.0]heptane-6,6'-furo[2,3-d][1,3]dioxole]-2,4-diol* (39)**

The epoxy-ketone **38** (50 mg, 0.12 mmol) in diethyl ether (15 mL) was cooled to 0 °C and LAH (14mg, 0.37 mmol) was added to it. As the reaction was completed (TLC), it was quenched by sequential addition of H_2O (0.02 mL), 15% NaOH solution (0.02 mL) and H_2O (0.06 mL). The reaction mixture was allowed to settle and filtered through sintered glass funnel.and worked up as usual. The crude residue was then purified through column chromatography to afford the diol **39** (33 mg, 66%) as a viscous liquid. $[\alpha]_D^{28}$ +28.8 (*c* 6.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.68 (1H, d, *J* = 3.3 Hz), 4.76-4.67 (1H, m), 4.57 (1H, d, *J* =3.3 Hz), 4.09 (1H, dd, *J* = 5.4, 5.7 Hz), 4.01 (1H, d, *J* = 5.4 Hz), 3.96-3.93(2H, m), 2.99 (1H, dt, *J* = 2.1, 7.5 Hz), 2.40 (1H, ddd, *J* = 1.5, 7.8, 15.9 Hz), 2.27-2.12 (2H, m), 2.02-1.94 (1H,m), 1.53 (3H, s), 1.33 (3H, s), 1.24 (4H, s), 0.90 (10H, s), 0.06 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 112.2 (C), 103.7 (OCHO), 86.1 (OCH), 83.1 (OCH), 79.1 (C), 73.5 (OCH), 61.8 (OCH_2), 47.6(CH_2), 46.3 (CH), 46.3(C), 43.7 (CH), 26.8 (CH_3), 26.7 (CH_2), 26.6 (CH_3), 26.0 (three CH_3's of t-butyl group merged together), 23.3 (CH_3), 18.4 (C), -5.1 (CH_3), -5.3 (CH_3); HRMS (ESI) *m/z* calcd for $C_{21}H_{38}O_6SiNa$ $(M+Na)^+$, 437.2336; found, 437.2339.

Acknowledgment.

Financial support from DST, Government of India through Grant Nos. SR/S1/OC-19/2011 and SR/S2/JCB-83/2011 is gratefully acknowledged. AJ and SM are thankful to CSIR for fellowships. We are grateful to DBT for Single crystal X-ray diffaractometer facility supported by the DBT-funded CEIB program (Project No. DBT/01/CEIB/11/V/13).

Notes and references

[a] *Department of Organic Chemistry, Indian Association for the Cultivation of Science Jadavpur, Kolkata 700 032, India*
**Corresponding author: ocsg@iacs.res.in*
*†Electronic Supplementary Information (ESI) available: Copies of NMR spectra for compounds, X-ray crystal data for compound **16b** (CCDC no. 902058). For ESI and crystallographic data in CIF or other electronic format See DOI: 10.1039/b000000x/*

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12. Crystallographic data for compounds **16b** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no CCDC 902058. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: +44 1223-336033. E-mail: deposit@ccdc.cam.ac.uk
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