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Total synthesis of (+)-varitriol and (+)-6′-*epi*-varitriol

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ABSTRACT

Total synthesis of (+)-varitriol and its C6′-epimer have been achieved starting from commercially available D-(−)-ribose and *o*-anisic acid. The key steps involved are Corey Chaykovsky reaction, triethylamine mediated epimerization, and an olefin cross-metathesis.

1. Introduction

Natural products from marine sources continue to attract significant attention by both biologists and chemists due to their interesting biological properties and scarce availability for further elucidation toward their activities.[1] (+)-varitriol **1**, a novel low molecular weight natural product has been recently isolated from a marine derived strain of fungus *Emericella variecolor* by Malmstrom et al.[2] Though this compound did not inhibit growth of bacteria and yeast at 100 mg/mL concentration, it displayed significant cytotoxic activity against variety of tumor cell lines and showed increased potency toward renal, CNS, and breast cancer cell lines with GI_{50} values ranging from 1.63 to 2.44×10^{-7} M and lower potency toward leukemia, ovarian, and colon cell lines with GI_{50} values ranging from 2.52×10^{-5} to 9.59×10^{-5} M. As the mode of action of varitriol has not yet been established[3] it becomes necessary to further investigate and elucidate the mechanism of action by this molecule. This feature along with interesting preliminary biological property and simple structure have attracted several chemists to take up the total synthesis[4,5] and the analogue synthesis[6] of varitriol. The absolute structure of (+)-varitriol was initially determined after accomplishing the total synthesis of its enantiomer (−)-varitriol **1′** and later followed by the natural (+)-varitriol synthesis (Fig. 1).

The inaugural synthesis started with (−)-varitriol by Jennings and Clemens[4a] involving an olefin cross-metathesis and Suzuki–Miyaura reaction as key steps and was followed by Taylor[4b] group involving Horner–Wadsworth–Emmons (HWE) and Ramberg Backlund reactions.

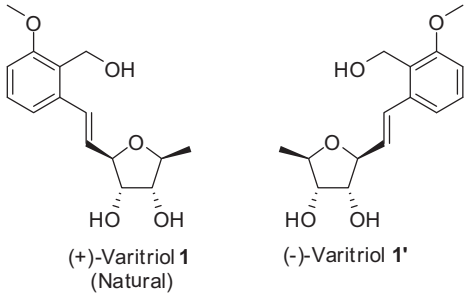

Fig. 1. Structures of natural and unnatural varitriols.

The first total synthesis of natural (+)-varitriol **1**, was achieved by Shaw and Kumar,[5a] utilizing olefin cross-metathesis to link the carbohydrate part obtained from methyl α,D-mannopyranoside and aromatic moiety prepared using Stille cross coupling reaction as key step. Several other publications have followed for the total synthesis of natural varitriol[5b–j] and their analogues.[6]

In continuation of our programme on total synthesis of recently isolated biologically active natural products,[7] here in we report our strategy for total synthesis of (+)-varitriol and its C6′-epimer. Our synthetic approach to (+)-varitriol relies on coupling of sugar olefin (carbohydrate part) **3** with appropriately derivatized styrene (aromatic part) **4** via an olefin cross-metathesis reaction to give intermediate **2**, which upon ester reduction and acetonide deprotection gives the target molecule (Scheme 1). While the sugar

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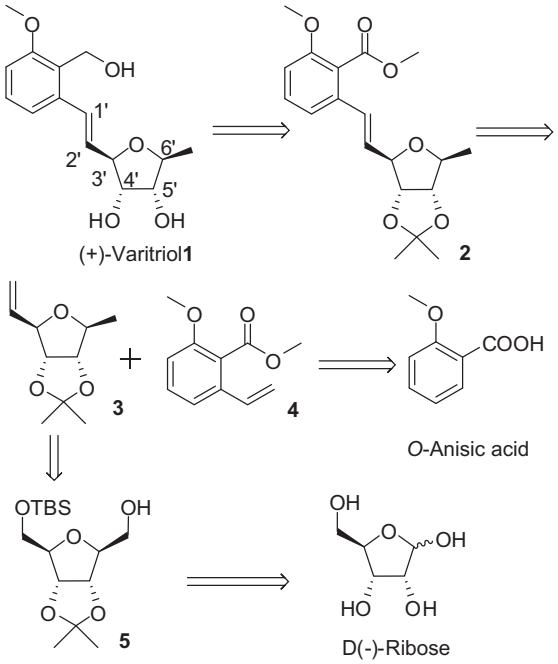
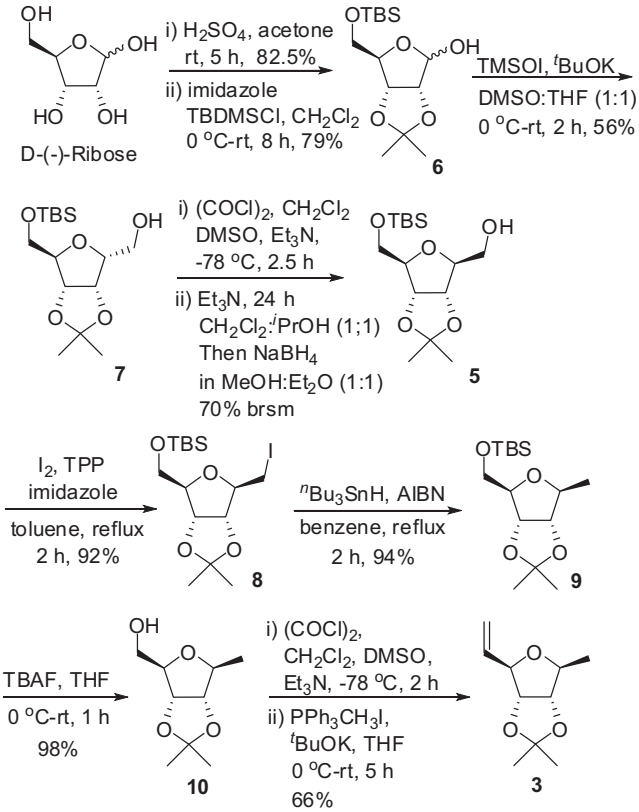
olefin **3** can be obtained from commercially available D(−)-ribose through sequence of reactions involving an epimerization, Corey Chaykovsky reaction etc., the aromatic part **4** is synthesized from commercially available *o*-anisic acid in four steps.



Scheme 1. Retrosynthesis for (+)-varitriol.

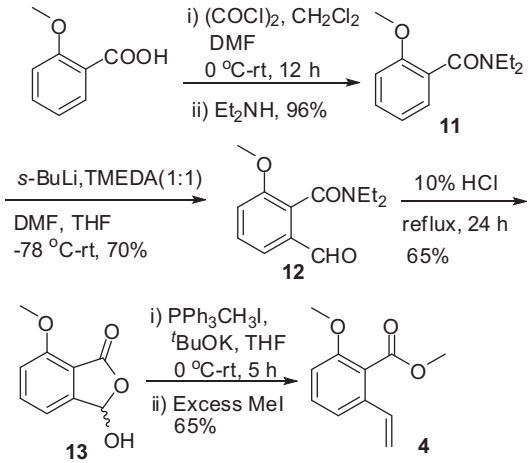


Scheme 2. Synthesis of **3**.

2. Results and discussion

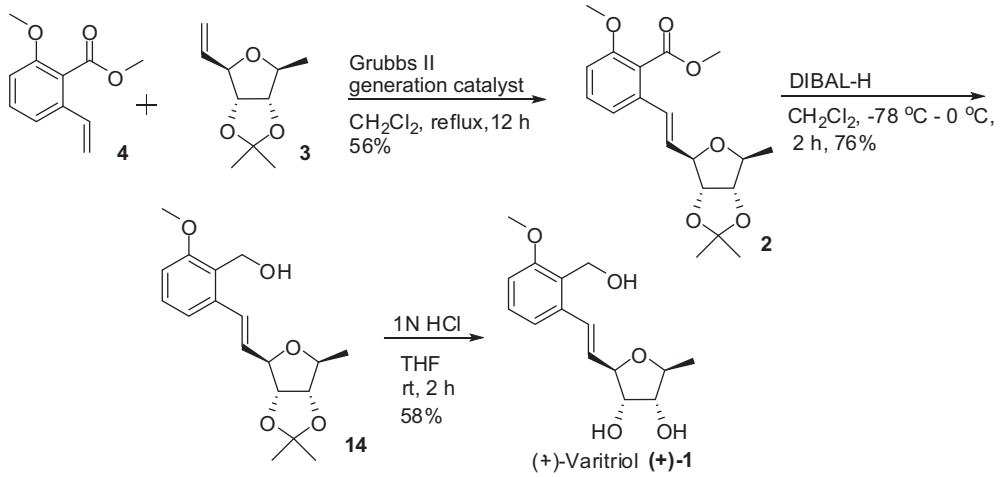
Synthesis of sugar olefin **3** started with D-(−)-ribose as shown in Scheme 2. D-(−)-Ribose was protected with isopropylidene and was followed by primary alcohol protection by *tert*-butyldimethylsilyl chloride to the corresponding *tert*-butyldimethylsilyl ether **6**.[8b] Corey Chaykovsky reaction[8] of lactol **6** with trimethylsulfoxonium iodide and potassium *tert*-butoxide in DMSO provided homologated alcohol **7**. While compound **7** can be directly utilized for total synthesis of 6′-*epi*-varitriol, epimerization of the newly generated carbinol group can lead to total synthesis of natural (+)-varitriol. The alcohol **7** upon oxidation under Swern conditions[9] provided aldehyde and was then exposed to several bases, such as DBU, K^{t}OBu, NaH, LDA, NaHMDS toward epimerization at α-center without any success as the reaction ended up either with starting material or undesired self Aldol product. Finally, epimerization[10] was achieved with triethylamine and was followed by reduction of aldehyde functionality with $NaBH_4$ in MeOH to give alcohol **5**.[11] The alcohol **5** was converted to corresponding iodide **8** upon treatment with I_2, TPP, and imidazole at reflux condition, and was further reduced to alkane **9** with ^{n}Bu$_3$SnH and AIBN.[12] Desilylation of **9** with TBAF provided primary alcohol **10**, which was oxidized to corresponding aldehyde under Swern condition and then subjected to one carbon Wittig homologation reaction with methyltriphenylphosphonium iodide and potassium *tert*-butoxide to provide the carbohydrate part (sugar olefin) **3** in 66% overall yield for last two steps (Scheme 2).

The synthetic strategy for aromatic part is given in Scheme 3. The commercially available *o*-anisic acid was converted to amide **11** on treatment with oxalyl chloride in presence of catalytic amount of DMF, followed by quenching with Et_2NH. *ortho* Formylation[13] with DMF in presence of ^{s}BuLi and TMEDA provided aryl aldehyde **12**, which on hydrolysis with 10% HCl gave lactone acetal **13**. The lactol **13** was subjected to one carbon Wittig olefination reaction using methyltriphenylphosphonium iodide and potassium *tert*-butoxide and then treated with excess of MeI to provide the aryl olefin **4** in 65% yield.



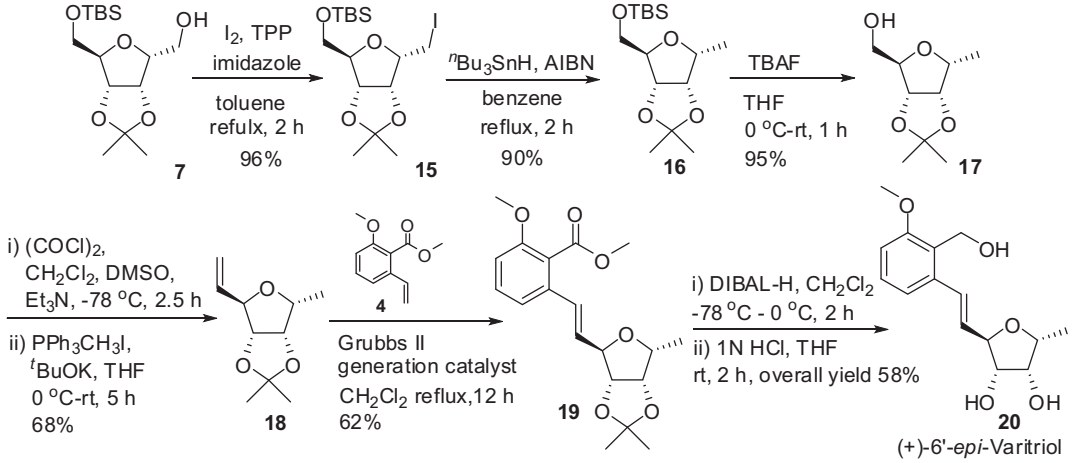
Scheme 3. Synthesis of **4**.

With the two key intermediates **3** and **4** in hand, the stage was set for coupling them toward total synthesis of (+)-varitriol (Scheme 4). Thus, treatment of **3** and **4** in presence of Grubbs' II generation catalyst[4a,5a,14] provided cross-coupled product **2**, which was subjected to reduction with DIBAL-H to provide alcohol **14**. Finally isopropylidene deprotection with 1 N HCl provided the natural product (+)-varitriol. The spectroscopic analytical data was found to be similar with that of the earlier synthesized product[5a] and isolated natural product.[2]



Scheme 4. Synthesis of (+)-varitriol.

With enough material of compound **7** in hand, we explored the total synthesis of 6′-*epi*-varitriol. Thus, iodination of alcohol **7** with I_2, TPP, and imidazole in toluene at reflux temperature furnished corresponding iodide **15** in good yield. The iodide **15** was reduced with $^{n}Bu_3SnH$ in presence of catalytic amount of AIBN to provide **16**. The compound **16** on desilylation with TBAF yielded the corresponding alcohol **17**. The alcohol **17** was oxidized to aldehyde under Swern conditions and subjected to one carbon Wittig olefination reaction with methyltriphenylphosphonium iodide and potassium *tert*-butoxide in THF to yield the olefin **18**. Further cross coupling of compound **18** with **4** using Grubbs II generation catalyst provided **19**. The ester **19** upon reduction with DIBAL-H followed by isopropylidene deprotection with 1 N HCl provided the (+)-6′-*epi*-varitriol (Scheme 5).



Scheme 5. Synthesis of 6′-*epi*-varitriol.

3. Conclusion

In summary, we have accomplished the total synthesis of natural (+)-varitriol and its 6′-epimer involving a convergent approach. The furanoside part was synthesized from readily available cheap material D(−)-ribose and the aromatic part was obtained from *o*-anisic acid. The key reactions include Grubbs' cross-metathesis reaction for coupling two fragments, a Corey Chaykovsky reaction for homologation of lactol system and an epimerization step to get the 2,5-*syn* geometry. This strategy can be further explored for the synthesis of other analogues to screen their biological activity and is being currently investigated in our laboratory.

4. Experimental

4.1. General

Column chromatography was performed using silica gel 60–120 mesh. All the solvents were dried and distilled prior to use. IR spectra were recorded on a Perkin–Elmer Infrared spectrophotometer as KBr wafers or neat or in $CHCl_3$ as a thin film. ^{1}H, ^{13}C NMR were recorded on a Bruker Avance 300 or Varian Unity 400 MHz or Varian Inova 500 MHz instrument using TMS as an internal standard. Mass spectra were recorded on Micromass VG 7070H mass spectrometer for EI, VG Autospec mass spectrometer for FABMS and micromass Quatro LC triple quadrupole mass spectrometer for ESI analysis. Syringe and septa techniques were used for moisture free reactions.

4.2. Procedures and analytical data

*4.2.1. (3aR,6R,6aR)-6-((tert-Butyldimethylsilyloxy)methyl)-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-ol (**6**).* To a stirred suspension of D-ribose (5.0 g, 33.3 mmol) in acetone (50 mL) was

added drop wise concd H_2SO_4 (0.3 mL) at room temperature and the reaction mixture was stirred at room temperature for 2.5 h. The mixture was neutralized with solid $NaHCO_3$ (10 g), filtered, and dried over anhydrous Na_2SO_4, the solvent was evaporated under reduced pressure to give crude material, which was purified by silica gel column chromatography (hexane/EtOAc 65:35) to afford acetonide protected lactol as colorless syrup (5.2 g, 82.5%). To this compound (5.2 g, 27.4 mmol, 1 equiv) in anhydrous CH_2Cl_2 (52 mL) was added imidazole (2.41 g, 35.5 mmol, 1.3 equiv) at a time at room temperature. The mixture was stirred at room temperature for 20 min after which the reaction mixture was cooled to 0 °C, and to this was added TBDMSCl (4.5 g, 30.1 mmol, 1.1 equiv) portion wise. The reaction mixture was allowed to warm to room temperature and stirred for 4 h. Water (40 mL) was added to the reaction mixture and the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2×30 mL). The combined organic layer was washed with brine (30 mL), and dried over anhydrous Na_2SO_4, solvent was removed under reduced pressure to give crude material, which was purified by column chromatography R_f: 0.90 (hexane/EtOAc, 95:5) to give **6** (6.6 g, 79% yield) as yellow oil; $[\alpha]_D^{20}$ −16.84 (*c* 1.36, $CHCl_3$); IR ν_{max} (KBr): 3360, 2936, 2860, 1471, 1261, 1068 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+CCl_4): δ 5.27 (d, *J*=11.9 Hz, 1H), 4.76 (d, *J*=11.7 Hz, 1H), 4.69 (d, *J*=5.9 Hz, 1H), 4.49 (d, *J*=6.0 Hz, 1H), 4.35 (br s, 1H), 3.79–3.71 (m, 2H), 1.47 (s, 3H), 1.31 (s, 3H), 0.92 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 112.0, 103.4, 87.6, 86.9, 81.7, 64.8, 26.4, 25.7, 24.9, 18.2, −5.6, −5.7; ESIMS: *m*/*z* 322 $[M+NH_4]^+$; HRESIMS: *m*/*z* 327.1589 $[M+Na]^+$ (calcd for $C_{14}H_{28}O_5NaSi$: *m*/*z* 327.1603).

*4.2.2. ((3aS,4R,6R,6aR)-6-((tert-Butyldimethylsilyloxy)methyl)-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (**7**).* To the mixture of trimethylsulfoxonium iodide (1.31 g, 5.96 mmol, 1.5 equiv) and potassium *tert*-butoxide (0.67 g, 5.96 mmol, 1.5 equiv) was added dry DMSO (10 mL) at 0 °C then reaction mixture was stirred at 0 °C for 30 min then at room temperature for an additional 30 min. To this reaction mixture was added compound **6** (1.2 g, 3.9 mmol, 1 equiv) in dry THF (10 mL) at 0 °C and the reaction mixture was stirred at 0 °C for 30 min and at room temperature for further 30 min. After complete consumption of starting material, the reaction mixture was quenched with saturated aq NH_4Cl (5 mL). The mixture was diluted with EtOAc (20 mL) and water (20 mL), organic layer was separated and the aqueous phase was extracted with EtOAc (2×15 mL). The combined organic layer was washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure to give crude material, which was purified by column chromatography R_f=0.50 (hexane/EtOAc, 85:15) to give **7** (0.71 g, 56%) as yellow oil; $[\alpha]_D^{20}$ −18.46 (*c* 0.52, $CHCl_3$); IR ν_{max} (Neat): 3475, 2933, 1466, 1256, 1079 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.84–4.77 (m, 2H), 4.21 (q, *J*=5.5, 9.6 Hz, 1H), 4.14 (t, *J*=3.4 Hz, 1H), 3.89–3.78 (m, 2H), 3.76–3.66 (m, 2H), 1.50 (s, 3H), 1.34 (s, 3H), 0.88 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 112.4, 84.2, 83.3, 82.1, 81.9, 64.9, 62.0, 26.1, 25.8, 24.5, 18.1, −5.5, −5.7; ESIMS: *m*/*z* 319 $[M+H]^+$; HRESIMS: *m*/*z* 341.1762 $[M+Na]^+$ (calcd for $C_{15}H_{30}O_5NaSi$: *m*/*z* 341.1760).

*4.2.3. ((3aS,4S,6R,6aR)-6-((tert-Butyldimethylsilyloxy)methyl)-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (**5**).* To the solution of dry DMSO (2.67 mL, 37.7 mmol, 4 equiv) in dry CH_2Cl_2 (10 mL) was added oxalyl chloride (1.65 mL, 18.8 mmol, 2 equiv) at −78 °C drop wise over 15 min and stirred for 20 min at the same temperature. To this mixture was added compound **7** (3.0 g, 9.4 mmol, 1 equiv) dissolved in dry CH_2Cl_2 (15 mL) added drop wise over 15 min at −78 °C and the reaction mixture was stirred at same temperature for 2 h. The reaction was quenched with Et_3N (7.85 mL, 56.6 mmol, 6 equiv) at −78 °C, and was allowed to warm to room temperature, to this water (30 mL) was added, organic layer was separated, aqueous layer was extracted with CH_2Cl_2 (2×30 mL), combined organic layer was washed with brine (30 mL), dried over anhydrous Na_2SO_4, solvent was removed under reduced pressure to give crude material, which was purified by flash column chromatography (hexane/EtOAc, 90:10) to give the aldehyde (2.6 g, 87.2%) as yellow oil, to this ^{i}PrOH, CH_2Cl_2 (50 mL, 60 mL), and Et_3N (3.6 mL, 26.2 mmol, 3.2 equiv) were added, after reaction mixture was stirred at room temperature for 24 h, reaction mixture was concentrated and to the reaction mixture diethyl ether and MeOH (60 mL, 60 mL) was added. The reaction mixture was cooled to 0 °C and to this was added $NaBH_4$ (0.63 g, 16.5 mmol, 2 equiv) in portion wise over 10 min. Solvent was removed under reduced pressure and diluted with water (20 mL) and EtOAc (20 mL). The organic layer was separated, aqueous layer was extracted with EtOAc (2×40 mL), combined organic layer was washed with brine, and dried over anhydrous Na_2SO_4, solvent was removed under reduced pressure to give crude material, which was purified by column chromatography R_f 0.55 (hexane/EtOAc, 90:10) to give **5** (1.05 g, 35%) as yellow oil (70% w.r.t. recovered starting material); $[\alpha]_D^{20}$ +10.89 (*c* 0.56, $CHCl_3$); IR ν_{max} (Neat): 3458, 2935, 2862, 1465, 1254, 1079 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.77–4.70 (m, 2H), 4.22–4.20 (m, 1H), 4.08–4.05 (m, 1H), 3.92–3.75 (m, 3H), 3.61 (t, *J*=9.6 Hz, 1H), 3.03 (d, *J*=9.6 Hz, 1H), 1.54 (s, 3H), 1.36 (s, 3H), 0.92 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 113.1, 85.5, 84.8, 82.7, 81.0, 63.8, 63.7, 27.5, 25.9, 25.5, 18.4, −5.5, −5.6; ESIMS: *m*/*z* 341 $[M+Na]^+$; HRESIMS: *m*/*z* 341.1762 $[M+Na]^+$ (calcd for $C_{15}H_{30}O_5NaSi$: *m*/*z* 341.1760).

*4.2.4. tert-Butyl(((3aR,4R,6R,6aR)-6-(iodomethyl)-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)dimethylsilane (**8**).* To the solution of compound **5** (1.0 g, 3.14 mmol, 1 equiv) in dry toluene (10 mL) was added imidazole (0.64 g, 9.41 mmol, 3 equiv), TPP (1.65 g, 6.29 mmol, 2 equiv) at room temperature followed by I_2 (1.76 g, 6.91 mmol, 2.2 equiv). Then reaction mixture was refluxed at 110 °C for 2 h. After complete conversion of starting material, mixture was allowed to cool to room temperature water (10 mL) was added to the reaction mixture and diluted with EtOAc (5 mL). The organic layer was separated; aqueous layer was extracted with EtOAc (2×10 mL). Combined organic layer was washed with hypo (15 mL) followed by brine (15 mL), dried over anhydrous Na_2SO_4, solvent was removed under reduced pressure to give crude material, which was purified by column chromatography R_f 0.90 (hexane/EtOAc, 95:5) to give **8** (1.24 g, 92%) as transparent syrup; $[\alpha]_D^{20}$ −3.17 (*c* 0.60, $CHCl_3$); IR ν_{max} (Neat): 2930, 1465, 1255, 1077, 837 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+CCl_4) : δ 4.63 (dd, *J*=3.0, 6.0 Hz, 1H), 4.41 (dd, *J*=3.8, 6.8 Hz, 1H), 4.09 (dd, *J*=3.0, 6.8 Hz, 1H), 4.03–3.98 (m, 1H), 3.71 (d, *J*=3.8 Hz, 2H), 3.19–3.30 (m, 2H), 1.52 (s, 3H), 1.34 (s, 3H), 0.92 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 113.5, 85.5, 85.1, 84.7, 82.4, 63.9, 27.3, 25.9, 25.4, 18.3, 6.7, −5.4, −5.6; ESIMS: *m*/*z* 429 $[M+H]^+$; HRESIMS: *m*/*z* 451.0765 $[M+Na]^+$ (calcd for $C_{15}H_{29}O_4NaSiI$: *m*/*z* 451.0777).

*4.2.5. tert-Butyldimethyl(((3aR,4R,6S,6aS)-2,2,6-trimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)silane (**9**).* To the solution of compound **8** (1.24 g, 2.89 mmol, 1 equiv) in dry benzene (15 mL), was added mixture of ^{n}Bu$_3$SnH (1.17 mL, 4.35 mmol, 1.5 equiv) and AIBN (0.023 g, 0.145 mmol, 5 mol %) in dry benzene slowly drop wise over 40 min at 80 °C. The reaction mixture was stirred at same temperature for another 1 h and was allowed to cool to room temperature and quenched with 10% aq KF solution (40 mL) and further stirred for 3–4 h. The organic layer was separated; aqueous layer was extracted with EtOAc (2×15 mL). The combined organic layer was washed with brine (15 mL), dried over anhydrous Na_2SO_4, solvent was removed under reduced pressure to give crude material, which was purified by column chromatography R_f 0.88 (hexane/EtOAc, 97:3) to give **9** (0.82 g, 94%) as light yellowish oil; $[\alpha]_D^{20}$

−2.66 (*c* 0.64, $CHCl_3$); IR ν_{max} (Neat): 2931, 1465, 1255, 1077 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+CCl_4): δ 4.58 (dd, *J*=3.8, 6.6 Hz, 1H), 4.14 (t, *J*=5.5 Hz, 1H), 3.94–3.89 (m, 2H), 3.75–3.65 (m, 2H), 1.50 (s, 3H), 1.31 (s, 3H), 1.27 (d, *J*=6.2 Hz, 3H), 0.91 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 113.9, 86.1, 84.4, 82.2, 80.6, 63.7, 27.5, 25.9, 25.5, 19.1, 18.3, −5.3, −5.4; ESIMS: *m*/*z* 325 $[M+Na]^+$; HRESIMS: *m*/*z* 325.1825 $[M+Na]^+$ (calcd for $C_{15}H_{30}O_4NaSi$: *m*/*z* 325.1811).

*4.2.6. ((3aR,4R,6S,6aS)-2,2,6-Trimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (**10**).* To the solution of compound **9** (0.82 g, 2.72 mmol, 1 equiv) in dry THF (10 mL) was added 1.0 M TBAF solution in THF (4.07 mL, 1.5 equiv) drop wise over 10 min at 0 °C. Then the reaction mixture was allowed to warm to room temperature while stirring for 2 h. After complete consumption of starting material, the reaction mixture was quenched with saturated aq NH_4Cl (5 mL), diluted with EtOAc (10 mL), water (10 mL). The organic layer was separated aqueous layer was extracted with EtOAc (2×10 mL). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, solvent was removed under reduced pressure to give crude material, which was purified by column chromatography R_f 0.20 (hexane/EtOAc, 60:40) to give **10** (0.5 g, 98%) as colorless oil; $[\alpha]_D^{20}$ +6.04 (*c* 0.48, $CHCl_3$); IR ν_{max} (Neat): 3450, 2982, 1378, 1212, 1076 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+CCl_4): δ 4.58 (dd, *J*=4.5, 6.8 Hz, 1H), 4.16 (dd, *J*=6.0, 7.6 Hz, 1H), 3.96–3.88 (m, 2H), 3.78 (d, *J*=12.1 Hz, 1H), 3.64–3.60 (br m, 1H), 1.89 (br s, 1H), 1.50 (s, 3H), 1.31 (s, 3H), 1.30 (d, *J*=5.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 114.7, 86.1, 84.2, 81.6, 80.5, 62.6, 27.3, 25.4, 18.8; ESIMS: *m*/*z* 186 $[M-H_2]^+$; HRESIMS: *m*/*z* 211.0954 $[M+Na]^+$ (calcd for $C_9H_{16}O_4Na$: *m*/*z* 211.0946).

*4.2.7. (3aS,4S,6R,6aR)-2,2,4-Trimethyl-6-vinyl-tetrahydrofuro[3,4-d][1,3]dioxole (**3**).* To the solution of dry DMSO (1.40 mL, 19.7 mmol, 4 equiv) in dry CH_2Cl_2 (10 mL) was added oxalyl chloride (0.86 mL, 9.89 mmol, 2 equiv) at −78 °C drop wise over 15 min and the reaction mixture was stirred for 20 min at same temperature. To this was added compound **10** (0.93 g, 4.94 mmol, 1 equiv) in dry CH_2Cl_2 (10 mL) drop wise over 15 min at −78 °C, and stirred at same temperature for 2 h. The reaction mixture was quenched with Et_3N (4.19 mL, 29.6 mmol, 6 equiv) at −78 °C, and was allowed to warm to room temperature and quenched with addition of water (15 mL). The organic layer was separated, aqueous layer was extracted with CH_2Cl_2 (2×20 mL), combined organic layer was washed with brine (20 mL), dried over anhydrous Na_2SO_4, solvent was removed under reduced pressure to give crude material, which was purified by flash column chromatography (hexane/EtOAc, 95:5) to give the aldehyde (0.7 g, 76%) as yellow oil. The above aldehyde in dry THF (3 mL) was added to the mixture of methyltriphenylphosphonium iodide (3.04 g, 7.52 mmol, 2 equiv) and potassium *tert*-butoxide (0.76 g, 6.78 mmol, 1.8 equiv) in dry THF, at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred at room temperature for 2 h. Reaction mixture was quenched with water (2 mL) and diluted with diethyl ether and hexane (1:1) (40 mL). The white precipitate formed, which was filtered off through a small pad of Celite and the filtrate was dried over anhydrous Na_2SO_4, solvent was removed under reduced pressure to give crude material, which was purified by column chromatography R_f 0.95 (hexane/EtOAc, 97:3) to give **3** (0.46 g, 65.7%) as light yellowish oil; $[\alpha]_D^{20}$ +8.59 (*c* 0.64, $CHCl_3$); IR ν_{max} (Neat): 2927, 1376, 1211, 1079 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.94–5.83 (m, 1H), 5.36 (dt, *J*=1.5, 17.4 Hz, 1H), 5.20 (dd, *J*=1.5, 10.6 Hz, 1H) 4.43 (dd, *J*=4.5, 6.8 Hz), 4.29–4.23 (m, 2H), 4.01–3.94 (m, 1H), 1.53 (s, 3H), 1.32, (s, 3H), 1.29 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.9, 117.3, 114.9, 86.1, 85.3, 84.9, 80.1, 27.3, 25.4, 18.9.

*4.2.8. N,N-Diethyl-2-methoxybenzamide (**11**).* To the solution of *o*-anisic acid (4.0 g, 26.3 mmol, 1 equiv) in dry CH_2Cl_2 was added DMF (1 mL, 13.2 mmol, 0.5 equiv) at room temperature to this oxalyl chloride (3.4 mL, 39.5 mmol, 1.5 equiv) was added at −10 °C drop wise over 10 min. Then reaction mixture was allowed to warm to room temperature and stirred at room temperature for 12 h Et_2NH (13.5 mL, 131.6 mmol, 5 equiv) was added to the reaction mixture at 0 °C over 20 min and the reaction mixture was stirred at 30 min at room temperature. The reaction mixture was concentrated under reduced pressure to give crude material, which was purified on column chromatography R_f 0.35 (hexane/EtOAc, 65:35) to give **11** (5.25 g, 96.5%) as yellowish oil; IR ν_{max} (Neat): 2978, 1627, 1431, 1243, 1018 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+CCl_4): δ 7.32 (dt, *J*=1.7, 7.4 Hz, 1H), 7.19 (dd, *J*=1.7, 7.4 Hz, 1H), 6.96 (dt, *J*=0.8, 7.4 Hz, 1H), 6.90 (d, *J*=8.3 Hz, 1H), 3.81 (s, 3H), 3.59–3.55 (m, 2H), 3.14 (q, *J*=7.2 Hz, 2H), 1.24 (t, *J*=7.2 Hz, 3H), 1.03 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.6, 155.1, 129.7, 127.3, 126.9, 120.6, 110.8, 55.4, 42.7, 38.7, 13.8, 12.8; ESIMS: *m*/*z* 230 $[M+Na]^+$; HRESIMS: *m*/*z* 208.1342 $[M+H]^+$ (calcd for $C_{12}H_{18}NO_2$: *m*/*z* 208.1337).

*4.2.9. N,N-Diethyl-2-formyl-6-methoxybenzamide (**12**).* To the solution of TMEDA (5.41 mL, 36.2 mmol, 1.5 equiv) in anhydrous THF was added 1.3 M ^{s}BuLi (27.9 mL, 1.5 equiv) drop wise at −78 °C, reaction mixture was stirred at −78 °C for 10 min, to this compound **11** (5.0 g, 24.2 mmol, 1 equiv) in dry THF was added drop wise over 20 min, and reaction mixture was stirred at same temperature over 2 h, after reaction mixture was quenched with DMF (7.5 mL, 96.6 mmol, 4 equiv) at −78 °C then allowed to warm to room temperature. After complete conversion of starting material, saturated NH_4Cl (15 mL), was added to the reaction mixture at 0 °C diluted with EtOAc and water (30 mL), organic layer was separated, aqueous layer was extracted with EtOAc (2×50 mL), combined organic layer was washed with brine (50 mL), dried over anhydrous Na_2SO_4, solvent was removed under reduced pressure to give crude material, which was purified by column chromatography R_f 0.30 (hexane/EtOAc, 60:40) to give **12** (4.0 g, 70.4%) as yellow oil; IR ν_{max} (Neat): 2977, 1700, 1630, 1469, 1269 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+CCl_4) : δ 9.94 (s, 1H), 7.50 (d, *J*=7.6 Hz, 1H), 7.42 (t, *J*=7.6 Hz, 1H), 7.12 (d, *J*=8.3 Hz, 1H), 3.86 (s, 3H), 3.75–3.64 (m, 1H), 3.56–3.47 (m, 1H), 3.09 (q, *J*=6.8 Hz, 2H), 1.29 (t, *J*=6.8 Hz, 3H), 1.01 (t, *J*=7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.2, 165.5, 155.2, 133.1, 129.6, 128.4, 120.9, 116.2, 55.6, 42.4, 38.6, 13.3, 12.2; ESIMS: *m*/*z* 236 $[M+H]^+$; HRESIMS: *m*/*z* 258.1111 $[M+Na]^+$ (calcd for $C_{13}H_{17}NO_3Na$: *m*/*z* 258.1106).

*4.2.10. 3-Hydroxy-7-methoxyisobenzofuran-1(3H)-one (**13**).* To the compound **12** (3.0 g), 10% HCl (40 mL) was added and the reaction mixture was heated at 100 °C for 24 h. After reaction mixture was allowed to cool to room temperature, the solvent was removed under reduced pressure to give crude material, which was purified by silica gel column chromatography R_f 0.95 (MeOH/$CHCl_3$, 95:5) to give **13** (1.5 g, 65.2%) as white fluffy solid; IR ν_{max} (KBr): 3355, 2969, 1732, 1605, 1487, 1044 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.75 (d, *J*=8.1 Hz, 1H), 7.63 (t, *J*=7.9 Hz, 1H), 7.11 (d, *J*=7.6 Hz, 1H), 7.01 (d, *J*=8.3 Hz, 1H), 6.41 (d, *J*=7.7 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 166.1, 157.5, 150.0, 136.8, 115.1, 113.3, 112.7, 96.6, 55.9; EIMS: *m*/*z* 180 $[M]^+$; HRESIMS: *m*/*z* 181.0505 $[M+H]^+$ (calcd for $C_9H_9O_4$: *m*/*z* 181.0500).

*4.2.11. Methyl 2-methoxy-6-vinylbenzoate (**4**).* To the mixture of methyltriphenylphosphonium iodide (16.8 g, 41.7 mmol, 5 equiv) and potassium *tert*-butoxide (4.5 g, 39.9 mmol, 4.8 equiv) was added dry THF (50 mL) at 0 °C and reaction mixture was allowed to warm to room temperature while stirring for 1 h. The reaction mixture was cooled to 0 °C and to this was added compound **13** (1.5 g, 8.33 mmol, 1 equiv) in dry THF (15 mL). The reaction mixture was allowed to warm to room temperature and further stirred for 5 h. To this reaction mixture methyl iodide (5.18 mL, 83.3 mmol,

10 equiv) was added at room temperature and further stirred for 12 h. Reaction mixture was quenched with water (2 mL) and diluted with diethyl ether and hexane (1:1) (40 mL). The white precipitate formed, which was filtered off through a small pad of Celite and the filtrate was dried over anhydrous Na_2SO_4, solvent was removed under reduced pressure to give crude material, which was purified by column chromatography R_f 0.85 (hexane/EtOAc, 95:5) to give **4** (1.05 g, 65.6%) as yellow oil; IR ν_{max} (Neat): 2950, 1731, 1573, 1468, 1269, 1072 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+CCl_4) : δ 7.28 (t, J=7.9 Hz, 1H), 7.12 (d, J=7.9 Hz, 1H), 6.79 (d, J=8.3 Hz, 1H), 6.63 (dd, J=10.9, 17.4 Hz, 1H), 5.70 (d, J=17.4 Hz, 1H), 5.31 (d, J=10.9 Hz, 1H), 3.89 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.3, 156.2, 136.1, 133.2, 130.3, 122.5, 117.4, 117.1, 109.9, 55.8, 52.2; EIMS: m/z 192 $[M]^+$; HRESIMS: m/z 193.0860 $[M+H]^+$ (calcd for $C_{11}H_{13}O_3$: m/z 193.0864).

*4.2.12. Methyl 2-methoxy-6-((E)-2-((3aR,4R,6S,6aS)-2,2,6-trimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)vinyl)benzoate (**2**).* To the degassed solution of compound **4** (0.313 g, 1.63 mmol, 1.5 equiv), and compound **3** (0.2 g, 1.09 mmol, 1 equiv) in dry CH_2Cl_2 (40 mL) was added Grubbs II generation catalyst (0.046 g, 0.054 mmol, 0.05 equiv) and the reaction mixture was refluxed for 12 h. The reaction mixture was concentrated under reduced pressure, purified by column chromatography R_f 0.40 (hexane/EtOAc, 90:10) to give **2** (0.211 g, 56%) as colorless liquid; $[\alpha]_D^{20}$ +29.82 (c 0.56, $CHCl_3$); IR ν_{max} (Neat): 2928, 1731, 1467, 1268, 1073 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (t, J=8.3 Hz, 1H), 7.12 (d, J=7.6 Hz, 1H), 6.82 (d, J=8.3 Hz, 1H), 6.65 (d, J=15.9 Hz, 1H), 6.22 (dd, J=6.0, 15.9 Hz, 1H), 4.51 (dd, J=4.5, 6.8, Hz, 1H), 4.44–4.40 (m, 1H), 4.32 (dd, J=4.5, 6.8 Hz, 1H), 4.08–3.99 (m, 1H), 3.91 (s, 3H), 3.82 (s, 3H), 1.56 (s, 3H), 1.34 (d, J=6.8 Hz, 3H), 1.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.2, 156.5, 135.3, 130.7, 130.4, 128.4, 122.9, 118.0, 114.9, 110.1, 86.2, 85.6, 84.5, 80.4, 55.9, 52.3, 27.3, 25.5, 19.1; ESIMS: m/z 371 $[M+Na]^+$; HRESIMS: m/z 371.1461 $[M+Na]^+$ (calcd for $C_{19}H_{24}O_6Na$: m/z 371.1470).

*4.2.13. (2-Methoxy-6-((E)-2-((3aR,4R,6S,6aS)-2,2,6-trimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)vinyl)phenyl)methanol (**14**).* To the solution of compound **2** (0.1 g, 0.25 mmol, 1 equiv) in dry CH_2Cl_2 (5 mL) was added 1.5 M DIBAL-H (0.48 mL) in toluene drop wise at −78 °C over 5 min, reaction mixture was stirred at same temperature for 2 h. The reaction mixture was quenched with saturated Na–K tartarate solution (5 mL) and was allowed to warm to room temperature while continuing stirring for 5 h. The organic layer was separated and aqueous layer was extracted with CH_2Cl_2 (2×5 mL), combined organic layer was washed with brine (5 mL), dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give crude material, which was purified by column chromatography R_f 0.40 (hexane/EtOAc, 65:35) to give **14** (0.07 g, 76%) as colorless oil; $[\alpha]_D^{20}$ +29.77 (c 0.44, $CHCl_3$); IR ν_{max} (Neat): 3451, 2926, 1578, 1465, 1261, 1078 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$+CCl_4): δ 7.18 (t, J=7.9 Hz, 1H), 7.05 (d, J=8.9 Hz, 1H), 7.02 (d, J=15.8 Hz, 1H), 6.77 (d, J=7.9 Hz, 1H), 6.12 (dd, J=5.9, 15.8 Hz, 1H), 4.74 (s, 2H), 4.49–4.48 (m, 1H), 4.41–4.39 (m, 1H), 4.28–4.26 (m, 1H), 4.02–3.96 (m, 1H), 3.87 (s, 3H), 1.55 (s, 3H), 1.35 (d, J=5.9 Hz, 3H), 1.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+CCl_4): δ 158.1, 137.7, 131.0, 129.2, 128.7, 126.8, 119.5, 115.0, 109.6, 86.4, 85.8, 84.7, 80.3, 56.8, 55.6, 27.6, 25.7, 19.2; ESIMS: m/z 343 $[M+Na]^+$; HRESIMS: m/z 343.1509 $[M+Na]^+$ (calcd for $C_{18}H_{24}O_5Na$: m/z 343.1521).

*4.2.14. (2R,3S,4R,5S,E)-2-(2-(Hydroxymethyl)-3-methoxystyryl)-5-methyl-tetrahydrofuran-3,4-diol ((+)-**1**).* To the solution of compound **14** (0.03 g, 0.094 mmol) in THF (3 mL) was added 1 N HCl (3 mL) and reaction mixture was stirred at room temperature for 3 h. After complete conversion of starting material, reaction mixture was quenched with solid $NaHCO_3$ (2.0 g), diluted with EtOAc, (5 mL) and the organic layer was separated. The aqueous layer was extracted with EtOAc (2×5 mL) and the combined organic layer was washed with brine (5 mL), dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to give crude product, which was purified by column chromatography R_f 0.30 (hexane/EtOAc, 20:80) to give (+)-**1** (0.015 g, 58%) as white solid; $[\alpha]_D^{20}$ +37.00 (c 0.4, MeOH); IR ν_{max} (KBr): 3378, 2924, 1464, 1260, 1090 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6): δ 7.22 (t, J=7.9 Hz, 1H), 7.15 (br s, 1H), 7.11 (d, J=5.5 Hz, 1H), 6.89 (d, J=8.1 Hz, 1H), 6.20 (dd, J=6.6, 15.9 Hz, 1H), 4.70 (br s, 2H), 4.30–4.27 (m, 1H), 3.92–3.88 (m, 1H), 3.85–3.78 (m, 1H), 3.82 (s, 3H), 3.70–3.67 (m, 1H), 1.26 (d, J=6.4 Hz, 3H); ^{13}C NMR (75 MHz, acetone-d_6+$CDCl_3$): δ 158.7, 138.7, 132.2, 129.2, 129.1, 127.6, 119.2, 110.4, 85.1, 79.9, 76.9, 76.2, 55.9, 55.5, 19.4; ESIMS: m/z 303 $[M+Na]^+$; HRESIMS: m/z 303.1231 $[M+Na]^+$ (calcd for $C_{17}H_{19}O_5Na$: m/z 303.1232).

*4.2.15. tert-Butyl(((3aR,4R,6S,6aR)-6-(iodomethyl)-2,2-dimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)dimethylsilane (**15**).* Similar procedure was followed as used earlier for the synthesis of **8** to yield **15** (96%) as light yellowish liquid; $[\alpha]_D^{20}$ −23.65 (c 0.96, $CHCl_3$); IR ν_{max} (Neat): 2932, 1256, 1125, 838 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$+CCl_4) : δ 4.80 (d, J=5.9 Hz, 1H), 4.72 (dd, J=3.6, 5.9 Hz, 1H), 4.39–4.34 (m, 1H), 4.06 (t, J=2.9 Hz, 1H), 3.70 (dq, J=2.9, 10.9, 13.8 Hz, 2H), 3.26 (t, J=7.9 Hz, 1H), 3.17 (dd, J=5.9, 8.9 Hz, 1H), 1.48 (s, 3H), 1.35 (s, 3H), 0.91 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 112.3, 84.7, 83.4, 83.3, 81.3, 65.1, 26.2, 25.8, 24.9, 18.1, 0.9, −5.6, −5.7; ESIMS: m/z 451 $[M+Na]^+$; HRESIMS: m/z 451.0756 $[M+Na]^+$ (calcd for $C_{15}H_{29}O_4NaSiI$: m/z 451.0777).

*4.2.16. tert-Butyldimethyl(((3aR,4R,6R,6aS)-2,2,6-trimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)silane (**16**).* Similar procedure was followed as used earlier for the synthesis of **9** to yield in **16** in 90% yield as colorless liquid; $[\alpha]_D^{20}$ −6.61 (c 0.56, $CHCl_3$); IR ν_{max} (Neat): 2934, 1375, 1257, 1087 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+CCl_4): δ 4.74 (d, J=6.0 Hz, 1H) 4.51 (dd, J=3.8, 6.0 Hz, 1H), 4.16–4.09 (m, 1H), 3.97 (t, J=3.8 Hz, 1H), 3.66 (d, J=3.8 Hz, 2H), 1.47 (s, 3H), 1.32 (s, 3H), 1.23 (d, J=6.8 Hz, 3H), 0.89 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 111.9, 84.0, 83.4, 82.7, 78.1, 64.6, 26.2, 25.7, 25.0, 18.0, 14.5, −5.6, −5.7; ESIMS: m/z 325 $[M+Na]^+$; HRESIMS: m/z 325.1819 $[M+Na]^+$ (calcd for $C_{15}H_{30}O_4NaSi$: m/z 325.1811).

*4.2.17. ((3aR,4R,6R,6aS)-2,2,6-Trimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (**17**).* Similar procedure was followed as used earlier for the synthesis of **10** to give **17** in 95% as colorless liquid; $[\alpha]_D^{20}$ +7.12 (c 0.52, $CHCl_3$); IR ν_{max} (Neat): 3445, 2937, 1378, 1210, 1033 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+CCl_4): δ 4.59–4.52 (m, 2H) 4.08–4.01 (m, 2H), 3.56 (d, J=6.0 Hz, 2H), 1.87 (br s, 1H), 1.49 (s, 3H), 1.32 (s, 3H), 1.28 (d, J=6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 112.4, 84.1, 82.7, 82.2, 76.6, 61.7, 26.2, 25.0, 14.1; ESIMS: m/z 186 $[M-H_2]^+$; HRESIMS: m/z 211.0951 $[M+Na]^+$ (calcd for $C_9H_{16}O_4Na$: m/z 211.0946).

*4.2.18. (3aS,4R,6R,6aR)-2,2,4-Trimethyl-6-vinyl-tetrahydrofuro[3,4-d][1,3]dioxole (**18**).* Similar procedure was followed as used earlier for the synthesis of **3** to give **18** in 68% yield as a yellowish liquid; $[\alpha]_D^{20}$ +24.11 (c 0.56, $CHCl_3$); IR ν_{max} (Neat): 2928, 1375, 1213, 1074 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+CCl_4): δ 5.80–5.69 (m, 1H), 5.28 (d, J=17.4 Hz, 1H), 5.16 (d, J=10.6 Hz, 1H), 4.59 (d, J=6.2 Hz, 1H), 4.50–4.47 (m, 2H), 3.93–3.86 (m, 1H) 1.49 (s, 3H), 1.31 (s, 3H), 1.29 (d, J=6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.1, 115.6, 111.9, 85.5, 83.4, 82.2, 75.9, 26.2, 25.2, 13.8.

*4.2.19. Methyl 2-methoxy-6-((E)-2-((3aR,4R,6R,6aS)-2,2,6-trimethyl-tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)vinyl)benzoate (**19**).* Similar

procedure was followed as used earlier for the synthesis of **2** to give **19** in 62% yield as sticky liquid; $[\alpha]_D^{20}$ +34.02 (*c* 1.12, $CHCl_3$); IR ν_{max} (Neat): 2931, 1731, 1468, 1268, 1069 cm^{-1}; ^1H NMR (500 MHz $CDCl_3$+CCl_4): δ 7.26 (t, *J*=7.9 Hz, 1H), 7.03 (d, *J*=7.9 Hz, 1H), 6.78 (d, *J*=8.9 Hz, 1H), 6.53 (d, *J*=15.8 Hz, 1H), 6.02 (dd, *J*=3.9, 15.8 Hz, 1H), 4.64 (d, *J*=5.9 Hz, 1H), 4.62 (br s, 1H), 4.51 (dd, *J*=3.9, 5.9 Hz, 1H), 3.96–3.92 (m, 1H), 3.88 (s, 3H), 3.83 (s, 3H), 1.50 (s, 3H), 1.32 (s, 3H), 1.31 (d, *J*=3.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.3, 156.4, 135.3, 130.5, 129.5, 127.6, 122.6, 117.9, 112.4, 110.1, 85.8, 83.4, 82.2, 76.4, 55.9, 52.3, 26.2, 25.1, 13.8; ESIMS: *m*/*z* 371 $[M+Na]^+$; HRESIMS: *m*/*z* 371.1462 $[M+Na]^+$ (calcd for $C_{19}H_{24}O_6Na$: *m*/*z* 371.1470).

*4.2.20. (2R,3S,4R,5R,E)-2-(2-(Hydroxymethyl)-3-methoxystyryl)-5-methyl-tetrahydrofuran-3,4-diol (**20**).* Compound **20** was prepared from **19** on reduction of ester moiety with DIBAL-H, following the similar procedure as given for the synthesis of **14**. Acetonide deprotection was achieved with 1 N HCl to give **20** as white solid with an overall yield of 58%; $[\alpha]_D^{20}$ +35.58 (*c* 0.52, MeOH); IR ν_{max} (KBr): 3440, 3306, 2970, 1580, 1471, 1259 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6): δ 7.22 (t, *J*=7.3 Hz, 1H), 7.13 (d, *J*=7.3 Hz, 1H), 7.07 (d, *J*=15.9 Hz, 1H), 6.88 (d, *J*=7.9 Hz, 1H), 6.20 (dd, *J*=6.5, 15.9 Hz, 1H), 4.72–4.70 (m, 2H), 4.33 (t, *J*=6.5 Hz, 1H), 4.24–4.18 (m, 1H), 4.07–3.99 (m, 2H), 3.82 (s, 3H), 1.21 (d, *J*=6.5 Hz, 3H); ^{13}C NMR (75 MHz, acetone-d_6): δ 159.9, 140.2, 134.2, 130.3, 129.9, 128.9, 120.4, 111.6, 84.1, 79.8, 78.1, 74.9, 57.1, 56.5, 16.6; ESIMS: *m*/*z* 303 $[M+Na]^+$; HRESIMS: *m*/*z* 303.1198 $[M+Na]^+$ (calcd for $C_{15}H_{20}O_5Na$: *m*/*z* 303.1208).

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Supplementary data

Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.12.008. These data include MOL files and InChIKeys of the most important compounds described in this article.

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