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First Total Synthesis of (+)-Varitriol†

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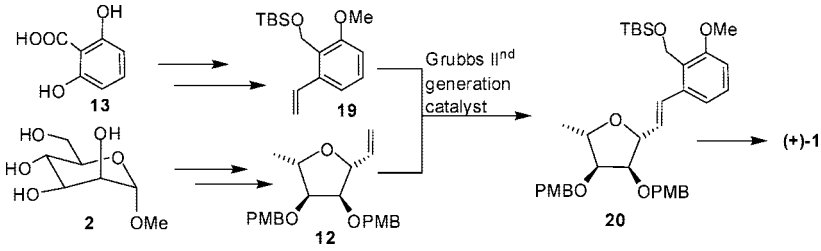

A highly stereoselective total synthesis of (+)-varitriol, an antitumor natural product, has been achieved for the first time from commercially available methyl α,D-mannopyranoside and 2,6-dihydroxybenzoic acid.

Introduction

Marine-derived biologically active natural products continue to be a source of potential therapeutic compounds as well as motivation to develop new synthetic strategies for their construction.[1] Recently, Barrero and co-workers reported the isolation and structure elucidation of (+)-varitriol (**1**) from marine strain (named M75-2) of the fungus *Emericella varicolor*, isolated from a sponge collected in Venezuelan waters of the Caribbean Sea.[2a] This naturally occurring substance was found to exhibit potent cytotoxicities toward a variety of cancer cell lines. Strikingly, (+)-varitriol demonstrated a more than 100-fold increased potency (over the mean toxicity) toward the RXF 393 (renal cancer, $GI_{50} = 1.63 \times 10^{-7}$ M), T-47D (breast cancer, $GI_{50} = 2.10 \times 10^{-7}$ M), and SNB-75 (CNS cancer, $GI_{50} = 2.44 \times 10^{-7}$ M) cell lines and lower potency against the DU-145 (prostate cancer, $GI_{50} = 1.10 \times 10^{-6}$ M), HL-60 (TB) (leukemia, $GI_{50} = 2.52 \times 10^{-5}$ M), CCRFCEM (leukemia, $GI_{50} = 2.60 \times 10^{-5}$ M), OVCAR-5 (ovarian cancer, $GI_{50} = 6.82 \times 10^{-5}$ M), SNB-19 (CNS cancer, $GI_{50} = 9.13 \times 10^{-5}$ M), and COLO 205 (colon cancer, $GI_{50} = 9.59 \times 10^{-5}$ M) cell lines tested within the 60 cell line panel of the National Cancer Institute (NCI).[2] This array of interesting biological properties has attracted an immense synthetic interest directed toward the varitriols and their analogues.

Recently, Clemens et al.[3a] and subsequently the Taylor group[3b] have achieved the total synthesis of unnatural (−)-varitriol. In their studies, both groups utilized D-(−)-ribose to construct the furanoside portion of (−)-varitriol and argued that the synthesis of the natural isomer might be possible from expensive L-(+)-ribose. Furthermore, synthetic analogues of (+)-varitriol and their cytotoxicity have also been reported.[4] Thus, the impressive biological activity, novel structural features, and lack of literature report toward the total synthesis of (+)-varitriol encouraged us to undertake the total synthesis of this interesting natural product. Herein, we report the first total synthesis of natural (+)-varitriol.

The retrosynthetic strategy for (+)-varitriol (**1**) is delineated in Scheme 1. We envisaged that **1** could be elaborated from the aromatic and carbohydrate portions **15a** and **5a**, respectively, by utilizing the cross metathesis strategy. The fragment **5a**, which contains all of the four required stereocenters of the natural product, could in turn be prepared from the key intermediate **5** by replacing iodide at C6 with hydride and inversion of configuration at C4 followed by Wittig olefination at C2′. Aromatic part **15a** could be obtained from triflate **15**[11,12] by Stille coupling.

Results and Discussion

The synthesis of stereochemically pure tetrasubstituted tetrahydrofuran (THF) subunit **5** was initiated from the

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(1) Bugni, T. S.; Richards, B.; Bhoite, L.; Cimbora, D.; Harper, M. K.; Ireland, C. M. *J. Nat. Prod.* **2008**, *71*, 1095–1098, and references therein.

(2) (a) Malmstrom, J.; Christophersen, C.; Barrero, A. F.; Oltra, J. E.; Justicia, J.; Rosales, A. *J. Nat. Prod.* **2002**, *65*, 364–367. (b) Mayer, A. M. S.; Gustafson, K. R. *Eur. J. Cancer* **2004**, *40*, 2676–2704.

(3) (a) Clemens, R. T.; Jennings, M. P. *Chem. Commun.* **2006**, 2720–2721. (b) McAllister, G. D.; Robinson, J. E.; Taylor, R. J. K. *Tetrahedron* **2007**, *63*, 12123–12130.

(4) Nagarapu, L.; Paparaju, V.; Satyender, A. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 2351–2354.

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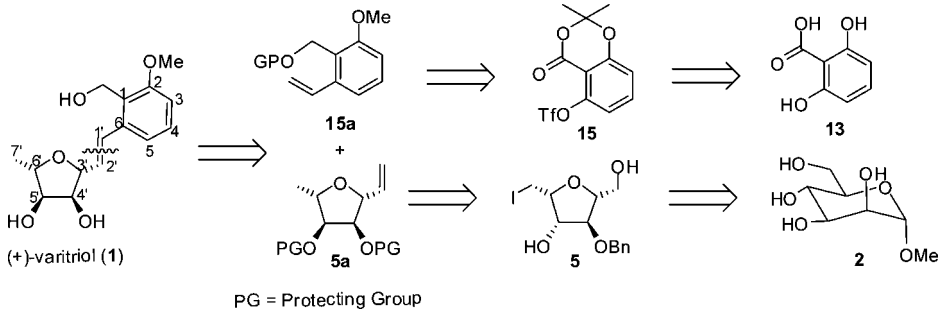
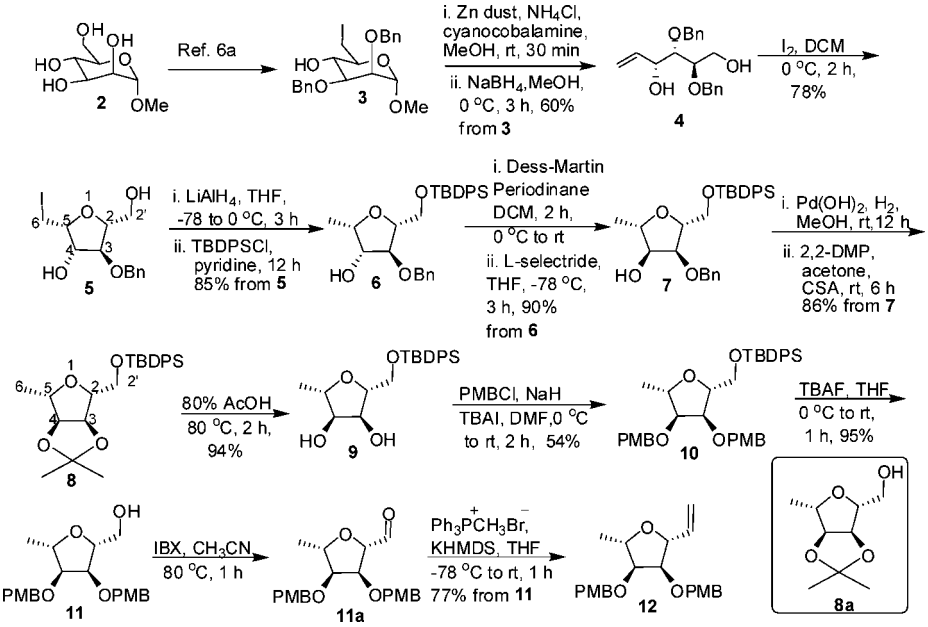
SCHEME 1. Retrosynthetic Strategy



SCHEME 2. Synthesis of Furanoside 12



commercially available methyl α,D-mannopyranoside **2** as shown in Scheme 2. The terminal allylic alcohol **4** was obtained in 60% yield by reductive zinc dust opening[5] of methyl 6-deoxy-6-iodo-2,3-di-*O*-benzyl-α,D-mannopyranoside **3**[6a,b] followed by sodium borohydride reduction. The iodocyclization of the chromatographically pure terminal allylic alcohol **4** involving the participation of secondary benzyl-protected oxygen in cyclization followed by debenzylation furnished 4,5-*cis* tetrasubstituted THF **5** with very high diastereoselectivity (>99:1).[6a,c−e] Here, the selectivity may be attributed to the formation of iodine−π complex at the *re* face of the double bond in the most favorable acyclic conformation[7] of allylic alcohol **4a** while the *si* face approach of the I_2 across the double bond is completely blocked by the benzyloxy group (Figure 1).

$LiAlH_4$ reduction of **5** followed by selective silyl protection of the primary alcohol furnished α-*C*-furanoside **6**. At this stage, among the four stereocenters in **6** three of them have the required stereochemistry as present in the (+)-varitriol while C4 has the opposite one. Thus, the inversion of C4-OH group in α-*C*-furanoside **6** was achieved to provide the isomeric compound **7** by first exposing **6** to Dess−Martin periodinane and subsequent reduction of the resulting crude ketone with different hydride reagents.[8] Here, it is worth to mention that the L-selectride which showed overall best result in terms of selectivity (>99:1) as well as yield (90%) (Table 1, entry 4, see Supporting Information) compared to other hydride reagents screened for this reaction, is the reagent of choice.

The cleavage of benzyl ether in **7** with H_2 in the presence of $Pd(OH)_2$ and acetonation[9] of the resulting *syn* diol with 2,2-dimethoxypropane (DMP) and catalytic amount of camphor-

(5) (a) Kleban, M.; Kautz, U.; Greul, J.; Hilgers, P.; Kugler, R.; Dong, H.-Q.; Jäger, V. *Synthesis* **2000**, 1027–1033. (b) Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1979**, *62*, 1990–2016.

(6) (a) Kumar, V.; Gauniyal, H. M.; Shaw, A. K. *Tetrahedron: Asymmetry* **2007**, *18*, 2069–2078. (b) Sletten, E. M.; Liotta, L. J. *J. Org. Chem.* **2006**, *71*, 1335–1343. (c) Bew, S. P.; Knight, D. W.; Middleton, R. J. *Tetrahedron Lett.* **2000**, *41*, 4453–4456. (d) Chamberlin, A. R.; Mulholland, R. L., Jr.; Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 672–677. (e) Reitz et. al. reported haloetherification of D-arabinose-derived 1,2,3,4,-tetrabenzyloxy hex-5-ene with NBS or Br_2 to obtain a mixture of 2,3-*cis*/*trans* tetrasubstituted THF (*cis*:*trans* ratio 87:13 with NBS and 90:10 with Br_2); see:(f) Reitz, A. B.; Nortey, S. O.; Maryanoff, B. E.; Liotta, D.; Monahan, R., III. *J. Org. Chem.* **1987**, *52*, 4191–4202.

(7) For conformations of acyclic molecules, see:Hoffmann, R. W. *Angew. Chem. Int. Ed.* **2000**, *39*, 2054–2070, and references therein.

(8) See Supporting Information.

(9) Acetonide protection on compound **8** was necessary because conversion of compound **6** to compound **7** was diastereoselective. The diastereomeric mixture of **7** obtained from $NaBH_4$ or CBS reduction of intermediate ketone derived from **6** could not be separated by column chromatography due to their close R_f values (NMR of column purified sample showed mixture of two diastereoisomers). Though, L-selectride reduction of the ketone was highly diastereoselective as it was evident from NMR spectra of **7** showing only one isomer (see supporting information), even then we preferred to perform acetonization of the resulting diol obtained after debenzylation of **7** in order to purify the desired *cis*-diol completely.

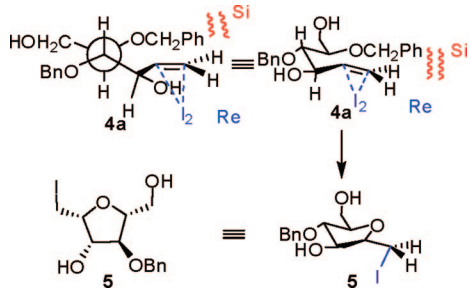


FIGURE 1. Proposed mechanism[6] for the formation of THF **5**.

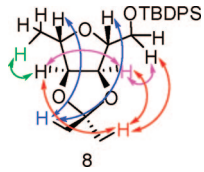


FIGURE 2. NOESY correlations for compound **8**.

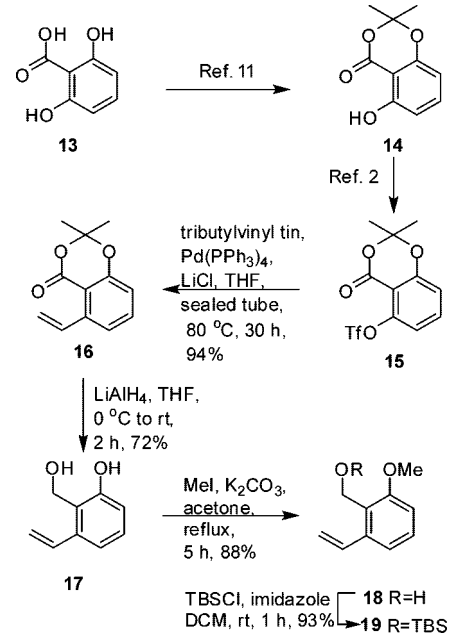
sulfonic acid (CSA) in acetone delivered the acetonide **8** in 86% yield as a single diastereoisomer. The stereochemistry of compound **8** was confirmed on the basis of its NOESY spectrum. The significant NOESY correlations are shown in Figure 2. The H-6 showed the NOESY correlation with H-4 which is *syn* to H-3. The H-3 showed the NOESY correlation with H-2′. The proton of the β methyl of acetonide ring showed NOESY correlation with H-2 and H-5, while the α methyl proton showed NOESY with H-3, H-4, and H-2′. All these correlations confirmed the stereochemistry of **8**.

The cleavage of silyl ether in **8** with TBAF in THF furnished alcohol **8a**. The oxidation of **8a** with IBX in acetonitrile[10] and Wittig olefination of the resulting labile aldehyde to obtain the desired vinylic furanoside was very sluggish, perhaps owing to the highly volatile nature of aldehyde[3a] and vinylic furanoside. To overcome this problem, we decided to replace acetonide protection with an appropriate protecting group. Accordingly, the acidic hydrolysis of **8** with 80% AcOH and protection of the resulting *syn* diol **9** as their PMB ethers afforded **10** in 54% yield. Now preparation of desired vinyl furanoside **12** became possible from **10**. Thus, the silyl ether deprotection of **10** to obtain the primary alcohol **11**, and its oxidation with IBX in acetonitrile[10] followed by Wittig olefination of the aldehyde intermediate in succession afforded olefin **12** in 77% from **11**(Scheme 2).

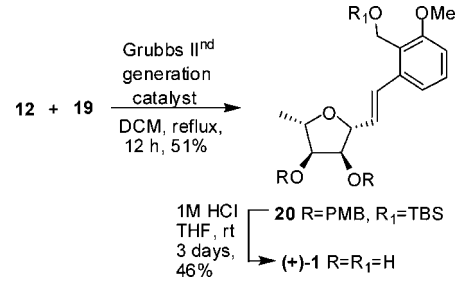
With the furanoside part in hand, our next attempt was focused toward the construction of aromatic portion **19**. Its synthesis was started from commercially available phenolic acid **13** involving a series of reactions as depicted in Scheme 3. Stille coupling of tributylvinyl tin (TBVT) with triflate **15**[11,12] in the presence of tetrakis(triphenylphosphine)palladium(0) and lithium chloride in a sealed tube[13] at 80 °C afforded compound **16**. The compound **16** on $LiAlH_4$ reduction[14] gave diol **17**. Its methylation followed by silyl protection furnished **19** (Scheme 3).

Having synthesized the two building blocks **12** and **19**, the next step was to link them together to obtain the fully protected natural product **20**. The removal of all the protecting groups in

SCHEME 3. Synthesis of Styrene 19



SCHEME 4. Synthesis of (+)-1



20 should then furnish the target molecule **1**. Thus, the cross metathesis[15] of **12** and **19** in presence of Grubbs' second-generation catalyst (5 mol %) generated the fully protected varitriol **20**. Attempted deprotection of PMB ethers of **20** by adopting standard procedures (DDQ, 10% TFA/DCM, 5% TFA/DCM, 2% TFA/DCM) ended with complex mixture of products. Fortunately, prolonged exposure of **20** to 1 M HCl in THF at room temperature (~ 35 °C) for 3 days afforded the natural product (+)-varitriol **1** in 46% yield (Scheme 4).[16]

Conclusion

In summary, a highly convergent first total synthesis of antitumor natural product (+)-varitriol has been disclosed. Herein we have successfully constructed the carbohydrate subunit from inexpensive methyl α,D-mannopyranoside in place of highly expensive L-(+)-ribose. Other key features of the synthetic venture include a highly diastereoselective (>99%) iodocyclization reaction of **4** to deliver the key intermediate **5**, stereoselective L-selectride reduction of the ketone obtained from **6**, stille coupling of **15** with TBVT and an efficient cross metathesis. Further application of this strategy toward the synthesis of novel isomers of varitriol to evaluate their cytotoxicity is currently under progress and will be presented in due course.

(10) More, J. D.; Finney, N. S. *Org. Lett.* **2002**, *4*, 3001–3003.
(11) Hadfield, A.; Schweitzer, H.; Trova, M. P.; Green, K. *Synth. Commun.* **1994**, *24*, 1025–1028.
(12) Furstner, A.; Konetzki, I. *Tetrahedron* **1996**, *52*, 15071–15078.
(13) Han, Q.; Wiemer, D. F. *J. Am. Chem. Soc.* **1992**, *114*, 7692–7697.
(14) Bajwa, N.; Jennings, M. P. *J. Org. Chem.* **2006**, *71*, 3646–3649.
(15) Chatterjee, A. K.; Choi, T.-L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360–11370, and references therein.
(16) See Supporting Information for detailed comparative ^1H and ^{13}C NMR of synthetic (+)-varitriol and natural (+)-varitriol.

Experimental Section

Compound 4. To a stirred suspension of zinc dust (3.39 g, 51.84 mmol) and NH_4Cl (2.77 g, 51.79 mmol) in methanol (90 mL) was added cyanocobalamine (25 mg, 0.015 mmol). Compound **3** (2.50 g, 5.17 mmol) in methanol was added to the suspension after 10 min. After the completion of reaction (TLC control, 30 min), the reaction mixture was passed through a Celite bed. The resulting filtrate was evaporated to dryness under reduced pressure to give a residue that was dissolved in ethyl acetate (100 mL). It was washed with a mixture of brine and water (1:1 v/v, 20 mL each). The organic layer was separated, dried (Na_2SO_4), and concentrated under reduced pressure to give clear oil (1.70 g). The oil without further purification was taken in methanol (25 mL) and reduced with $NaBH_4$ (294 mg, 7.77 mmol) at 0 °C. After completion of reaction (TLC control, 2 h), 10 mL of acetone was added to neutralize excess $NaBH_4$. The solvent was then concentrated to dryness to give the residue that was dissolved in ethyl acetate (15 mL) and was washed with water and brine. The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure to obtain clear oil which on column purification yielded **4** (1.02 g, 60% from **3**) as a colorless oil. Eluent for column chromatography: EtOAc/hexane (9/41, v/v); $[\alpha]^{28}_D = +23.3$ (*c* 0.56 $CHCl_3$); R_f 0.42 (2/3 EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.28 (m, 10H, ArH), 5.99 (ddd, J = 4.9, 10.6, 17.2 Hz, 1H, H-5), 5.40 (dt, J = 1.6, 17.3 Hz, 1H, H-6a), 5.24 (dt, J = 1.5, 10.6 Hz, 1H, H-6b), 4.72−4.57 (m, 4H, 2 × CH_2Ph), 4.37 (brs, 1H, H-4), 3.87 (dd, J = 3.2, 12.1 Hz, 1H, H-1a), 3.75 (dd, J = 2.6, 14.5 Hz, 1H, H-1b), 3.69−3.67 (m, 2H, H-2, H-3,), 2.71 (brs, 0.7H, OH); ^{13}C NMR (50 MHz, $CDCl_3$ + CCl_4) δ 139.1 (=*C*H), 138.3 (ArqC), 138.2 (ArqC), 129.2 (ArC), 129.1 (ArC), 128.7 (ArC), 128.6 (ArC), 128.5 (ArC), 116.2 (=*C*H_2), 80.4 (CH), 80.0 (CH), 75.1 (CH_2), 72.9 (CH_2), 72.0 (CH), 60.9 (CH_2); IR (neat, cm^{-1}) 3467, 3393, 3093, 2934, 1652, 1515, 1457, 1219, 1097; mass (ESI-MS) *m*/*z* 328, found 351 $[M + Na]^+$, 311 $[M - OH]^+$; Elemental analysis for $C_{20}H_{24}O_4$: calcd C, 72.16; H, 7.42; found C, 72.16; H, 7.82.

Compound 5. To chilled solution of diol **4** (1.52 g, 4.63 mmol) in DCM (25 mL) was added iodine (1.77 g, 6.97 mmol) in four portions during 1 h. After stirring for an additional 1 h, 10% aqueous $Na_2S_2O_3$ (30 mL) was added to the reaction mixture and extracted with DCM (4 × 20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to obtain a residue that was subjected to column chromatography to afford compound **5** (1.32 g, 78%) as a white solid (mp 94−96 °C). Eluent for column chromatography: EtOAc/hexane (1/4, v/v); $[\alpha]^{28}_D = +62.8$ (*c* 0.50 $CHCl_3$); R_f 0.55 (1/1, EtOAc/hexane); ^{1}HNMR (300 MHz, $CDCl_3$ + CCl_4) δ 7.38−7.27 (m, 5H, ArH), 4.65 (d, J = 11.9 Hz, 1H, CH_2Ph), 4.54 (d, J = 11.9 Hz, 1H, CH_2Ph) 4.30−4.25 (m, 1H, H-5), 4.20 (brs, 1H, H-4), 4.14 (d, J = 1.9 Hz, 1H, H-2), 3.97 (d, J = 1.3 Hz, 1H, H-3), 3.83 (dd, J = 2.5, 11.7 Hz, 1H, H-2′a), 3.62 (dd, J = 1.9, 11.7 Hz, 1H, H-2′b), 3.36−3.24 (m, 2H, H-6); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4) δ 138.0 (ArqC), 129.2 (ArC), 128.6 (ArC), 128.3 (ArC), 87.1 (CH), 85.7 (CH), 83.4 (CH), 74.7 (CH), 72.6 (CH_2), 63.2 (CH_2), 0.6 (*C*H_2I); IR (KBr, cm^{-1}) 3516, 3377, 2919, 1649, 1516, 1461, 1085, 1025; mass (ESI-MS) *m*/*z* 364, found 387 $[M + Na]^+$, EI-HRMS: calcd for $C_{13}H_{18}O_4I$ $[M + H]^+$ 365.0250, measured 365.0251.

Compound 6. To a stirred solution of **5** (2.86 g, 7.86 mmol) in dry THF (50 mL) at −78 °C was added $LiAlH_4$ (358 mg, 9.43 mmol). The reaction mixture was then warmed to room temperature, and stirring was continued for 3 h. Ethyl acetate (∼30 mL) was added to quench the excess reducing agent. To this mixture, water was added and extracted with ethyl acetate (3 × 20 mL). The combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to give clear oil (1.90 g).

To the precooled (0 °C) solution of the above crude oil in pyridine (4 mL) was added TBDPSCl (2.25 mL, 8.65 mmol). The temperature of the reaction mixture was raised to room temperature. After 12 h, a saturated aqueous solution of NH_4Cl (15 mL) was added and the resulting solution was extracted with dichloromethane (4 × 20 mL). The combined organic phase was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography to furnish **6** (3.17 g, 85% from **5**) as a colorless oil. Eluent for column chromatography: EtOAc/hexane (3/47, v/v); $[\alpha]^{28}_D = +40.0$ (*c* 1.0 $CHCl_3$); R_f 0.49 (1/4 EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4) δ 7.76−7.65 (m, 4H, ArH), 7.47−7.31 (m, 11H, ArH), 4.67 (d, J = 11.9 Hz, 1H, CH_2Ph), 4.57 (d, J = 11.9 Hz, 1H, CH_2Ph), 4.19−4.16 (m, 1H, H-5), 4.08 (d, J = 1.2 Hz, 1H, H-3), 3.99 (d, J = 2.0 Hz, 1H, H-4), 3.94 (br s, 1H, H-2), 3.84 (dd, J = 2.6, 11.1 Hz, 1H, H-2′a), 3.63 (dd, J = 1.8, 11.2 Hz, 1H, H-2′b), 1.39 (d, J = 6.3 Hz, 3H, H-6), 1.08 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4) δ 138.5 (ArqC), 136.4 (ArC), 136.3 (ArC), 133.1 (ArqC), 132.7 (ArqC), 130.6 (ArC), 130.5 (ArC), 129.1 (ArC), 128.6 (ArC), 128.5 (ArC), 128.4 (ArC), 128.2 (ArC), 87.7 (CH), 84.7 (CH), 78.6 (CH), 76.1 (CH), 72.4 (CH_2), 65.4 (CH_2), 27.5 (3 × CH_3), 19.8 (qC), 14.1 (CH_3); IR (neat, cm^{-1}) 3439, 3065, 2932, 1650, 1515, 1460, 1102; mass (ESI-MS) *m*/*z* 476, found 499 $[M + Na]^+$; EI-HRMS: calcd for $C_{29}H_{35}O_4Si$ $[M - H]^+$ 475.2305, measured 475.2300.

Compound 7. Dess−Martin periodinane (134 mg, 0.32 mmol) was added to a solution of **6** (100 mg, 0.21 mmol) in dry dichloromethane (10 mL) at 0 °C. After stirring for 2 h, saturated solution of $NaHCO_3$ (15 mL) and 10% aqueous $Na_2S_2O_3$ (20 mL) were added successively and stirring was continued for another 1 h. The mixture was extracted with DCM (3 × 5 mL), washed with brine and dried (Na_2SO_4). The combined organic layer was concentrated under reduced pressure to give clear oil (101 mg).

To the above crude oil (101 mg) dissolved in dry THF at −78 °C (3 mL) was added L-selectride in THF (1.0 M sol, 0.32 mL, 0.32 mmol) and the reaction mixture was stirred at the same temperature for 3 h. An aqueous solution of NH_4Cl (5 mL) was added and the resulting mixture was extracted with ethyl acetate (3 × 5 mL). The combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure which on column chromatography gave **7** (90 mg, 90% from **6**) as a colorless oil. Eluent for column chromatography: EtOAc/hexane (3/47, v/v); R_f 0.48 (1/4 EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4) δ 7.67−7.61 (m, 4H, ArH), 7.41−7.25 (m, 11H, ArH), 4.65 (d, J = 11.6 Hz, 1H, CH_2Ph), 4.54 (d, J = 11.6 Hz, 1H, CH_2Ph), 4.02 (dd, J = 3.1, 5.9 Hz, 1H, H-3), 3.97 (dd, J = 3.5, 7.7 Hz, 1H, H-4), 3.77−3.71 (m, 1H, H-5), 3.64−3.59 (m, 3H, H-2, H-2′), 1.28 (d, J = 6.2 Hz, 3H, H-6), 1.06 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4) δ 137.7 (ArqC), 135.9 (ArC), 135.8 (ArC), 133.5 (ArqC), 133.3 (ArqC), 130.0 (ArC), 128.8 (ArC), 128.2 (ArC), 128.0 (ArC), 82.9 (CH), 79.6 (CH), 79.0 (CH), 76.4 (CH), 72.5 (CH_2), 64.3 (CH_2), 27.2 (3 × CH_3), 19.5 (qC), 18.6 (CH_3); IR (neat, cm^{-1}) 3439, 2929, 1629, 1108; mass (ESI-MS) *m*/*z* 476, found 494 $[M + NH_4]^+$; EI-HRMS: calcd for $C_{25}H_{27}O_4Si$ $[M - C_4H_9]^+$ 419.1679, measured 419.1678.

Compound 8. A catalytic amount of $Pd(OH)_2$ (∼20 mg) was added to a solution of **7** (100 mg, 0.21 mmol) in methanol (10 mL). A vacuum was created in a round bottomed flask containing the above reaction mixture with the help of pump and the mixture was stirred under H_2 in a balloon at 1 atm. After the completion of the reaction (TLC, 12 h) catalyst was removed by filtration, washed with methanol twice and the combined filtrate was concentrated to afford a compound (82 mg) as colorless oil which was immediately used for the next step.

To above colorless oil (82 mg, 0.21 mmol) in acetone (3 mL) was added 2,2-dimethoxypropane (0.03 mL, 0.25 mmol) followed by camphorsulfonic acid (24 mg, 0.11 mmol). After 6 h of stirring, the reaction mixture was concentrated under reduced pressure to a colorless oil which on column chromatographic purification gave the pure compound **8** (77 mg, 86% from **7**) as a colorless oil. Eluent for column chromatography: EtOAc/hexane (1/49, v/v); $[\alpha]^{28}_D = +8.72$ (*c* 1 $CHCl_3$); R_f 0.56 (1/9, EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64−7.59 (m, 4H, ArH), 7.34−7.27 (m, 6H, ArH), 4.64 (dd, J = 3.6, 6.6 Hz, 1H, H-3), 4.17 (t, J = 6.5 Hz, 1H, H-4), 3.96−3.89 (m, 2H, H-2, H-5), 3.70 (d, J = 4.0, Hz, 2H, H-2′), 1.45 (s, 3H, -C(CH_3)$_2$), 1.27 (s, 3H, -C(CH_3)$_2$), 1.22 (d, J = 6.3 Hz, 3H, H-6), 0.98 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 136.5 (ArC), 136.4 (ArC), 134.2 (ArqC), 134.0 (ArqC), 130.5 (ArC), 130.4 (ArC), 128.5 (ArC),

128.4 (ArC), 114.8 (qC), 86.9 (CH), 84.9 (CH), 83.0 (CH), 81.3 (CH), 65.1 (CH_2), 28.3 (CH_3), 27.6 (3 × CH_3), 26.4 (CH_3), 20.1 (qC), 19.9 (CH_3); IR (neat, cm^{-1}) 2931, 1628, 1430, 1216, 1110; mass (ESI-MS) *m/z* 426, found 444 $[M + NH_4]^+$; EI-HRMS: calcd for $C_{24}H_{31}O_4Si$ $[M - CH_3]^+$ 411.1992, measured 411.1991.

Compound 8a. To a stirred solution of **8** (238 mg, 0.56 mmol) in THF (5 mL) was added TBAF (0.75 mL, 1.0 M solution in THF) at 0 °C and left for stirring at room temperature. After 2 h, aqueous saturated solution of NH_4Cl (20 mL) was added and the resulting mixture was extracted with EtOAc (3 × 15 mL). The combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The residue obtained on column purification afforded **8a** (82 mg, 78%) as a colorless oil. Eluent for column chromatography: EtOAc/hexane (3/7, v/v); $[\alpha]^{28}_D = +10.0$ (*c* 0.1 $CHCl_3$); R_f 0.42 (1:1, EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$) δ 4.62 (dd, $J = 4.5$, 6.9 Hz, 1H, H-3), 4.23 (dd, $J = 5.2$, 6.9 Hz, 1H, H-4), 4.03−3.96 (m, 2H, H-2, H-5), 3.83 (dd, $J = 3.2$, 11.9 Hz, 1H, H-2′a), 3.68 (dd, $J = 4.2$, 11.8 Hz, 1H, H-2′b), 1.54 (s, 3H, -C(CH_3)$_2$), 1.34 (s, 3H, -C(CH_3)$_2$), 1.31 (d, $J = 6.4$ Hz, 3H, H-6); ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$) δ 115.3 (qC), 86.8 (CH), 84.8 (CH), 82.2 (CH), 81.2 (CH), 63.3 (CH_2), 28.1 (CH_3), 26.2 (CH_3), 19.5 (CH_3); IR (neat, cm^{-1}) 3447, 3018, 2929, 1215, 1078; mass (ESI-MS) *m/z* 188, found 144 $[M - C_3H_8]^+$; DART-HRMS: calcd for $C_9H_{17}O_4$ $[M + H]^+$ 189.1127, measured 189.1134.

Compound 9. Compound **8** (1.45 g, 3.40 mmol) was taken in 80% acetic acid (20 mL) and stirred for 2 h at 80 °C. After completion of reaction (TLC), the acidic solution was concentrated under reduced pressure to give a crude product which was purified by column chromatography to yield compound **9** (1.24 g, 94%) as a colorless oil. Eluent for column chromatography: EtOAc/hexane (1/3, v/v); $[\alpha]^{28}_D = +10.4$ (*c* 0.48, $CHCl_3$); R_f 0.5 (2:3 EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$) δ 7.61−7.56 (m, 4H, ArH), 7.32−7.25 (m, 6H, ArH), 4.07 (t, $J = 5.3$ Hz, 1H, H-3), 3.76−3.72 (m, 2H, H-2, H-5), 3.66 (t, $J = 3.1$, 3.9 Hz, 2H, H-2′), 3.61 (t, $J = 6.0$ Hz, 1H, H-4), 2.81 (brs, 2H, 2 × OH), 1.21 (d, $J = 6.2$ Hz, 3H, H-6), 0.98 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$) δ 136.1 (ArC), 136.0 (ArC), 133.6 (ArqC), 133.5 (ArqC), 130.2 (ArC), 130.1 (ArC) 128.2 (ArC), 128.1 (ArC), 84.5 (CH), 79.3 (CH), 77.2 (CH), 72.8 (CH), 64.7 (CH_2), 27.4 (3 × CH_3), 19.7 (qC), 19.2 (CH_3); IR (neat, cm^{-1}) 3430, 3020, 1517, 1216, 1105; mass (ESI-MS) *m/z* 386, found 404 $[M + NH_4]^+$; DART-HRMS: calcd for $C_{22}H_{34}NO_4Si$ $[M + NH_4]^+$ 404.2257, measured 404.2259.

Compound 10. To a solution of compound **9** (372 mg, 0.96 mmol) in DMF (5 mL) was added NaH (96 mg, 60% suspension in mineral oil) at 0 °C followed by addition of *p*-methoxybenzyl chloride (0.39 mL, 2.88 mmol) and TBAI (107 mg, 0.29 mmol) in succession. After 2 h, methanol was added to quench the excess reagent. The residue obtained after evaporation of the solvent was dissolved in ether and washed with water. The organic layer was separated and dried (Na_2SO_4) and concentrated under reduced pressure. The resulting crude product was purified by column chromatography to give compound **10** (325 mg, 54%) as a colorless oil. Eluent for column chromatography: EtOAc/hexane (3/22, v/v); $[\alpha]^{28}_D = -21.7$ (*c* 0.85 $CHCl_3$); R_f 0.46 (1:4 EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$) δ 7.69−7.63 (m, 4H, ArH), 7.44−7.35 (m, 6H, ArH), 7.28−7.22 (m, 4H, ArH), 6.85−6.81 (m, 4H, ArH), 4.62−4.41 (m, 4H, 2 × OCH_2Ar), 4.09−3.99 (m, 3H, H-2, H-3, H-5), 3.81 (s, 6H, 2 × OMe), 3.65 (d, $J = 3.6$ Hz, 2H, H-2′), 3.45 (dd, $J = 5.3$, 7.2 Hz, 1H, H-4), 1.26 (d, $J = 6.2$ Hz, 3H, H-6), 1.05 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$) δ 159.7 (ArqC), 159.6 (ArqC), 136.1 (ArC), 136.0 (ArC), 133.8 (ArqC), 133.6 (ArqC), 130.7 (ArqC), 130.6 (ArqC), 130.1 (ArC), 130.0 (ArC), 129.8 (ArC), 129.7 (ArC), 128.1 (ArC), 128.0 (ArC), 114.2 (ArC), 114.1 (ArC), 83.5 (CH), 83.2 (CH), 77.3 (CH), 76.7 (CH), 72.1 (CH_2), 71.8 (CH_2), 64.7 (CH_2), 55.4 (2 × CH_3), 27.3 (3 × CH_3), 19.7 (qC), 19.4 (CH_3); IR (neat, cm^{-1}) 3013, 2931, 1614, 1513, 1246, 1218, 1109, 1036; mass (ESI-MS) *m/z* 626, found 644 $[M + NH_4]^+$, 505 $[M - PMB]^+$; DART-HRMS: calcd for $C_{38}H_{50}NO_6Si$ $[M + NH_4]^+$ 644.3407, measured 644.3388.

Compound 11. TBAF (2.4 mL, 1.0 M sol in THF) was added to a solution of compound **10** (800 mg, 1.28 mmol) in THF at 0 °C and the reaction mixture was allowed to stir at room temperature for 1 h. A saturated solution of NH_4Cl was added to it and resulting solution was extracted with ethyl acetate (3 × 15 mL). The combined organic layer was dried (Na_2SO_4) and concentrated in vacuo to a residue which was purified by column chromatography to give pure compound **11** as a white solid material (470 mg, 95%), mp 84−86 °C. Eluent for column chromatography: EtOAc/hexane (2/3, v/v); $[\alpha]^{28}_D = -5.0$ (*c* 0.32 $CHCl_3$); R_f 0.32 (1:1 EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$) δ 7.22 (dd, $J = 3.3$, 8.6 Hz, 4H, ArH), 6.83 (d, $J = 8.6$ Hz, 4H, ArH), 4.55−4.41 (m, 4H, 2 × OCH_2Ar), 4.04 (t, $J = 6.2$ Hz, 1H, H-5), 3.99 (dd, $J = 3.5$, 7.0 Hz, 1H, H-2), 3.83 (t, $J = 5.3$ Hz, 1H, H-3), 3.78 (s, 6H, 2 × OCH_3), 3.68 (dd, $J = 3.3$, 11.9 Hz, 1H, H-2′a), 3.47 (dd, $J = 3.4$, 11.9 Hz, 1H, H-2′b), 3.37 (t, $J = 5.8$ Hz, 1H, H-4), 1.89 (brs, 1H, OH), 1.19 (d, $J = 6.3$ Hz, 3H, H-6); ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$) δ 160.0 (ArqC), 159.9 (ArqC), 130.7 (2 × ArqC), 130.1 (ArC), 130.0 (ArC), 114.4 (ArC), 114.3 (ArC), 83.2 (CH), 83.0 (CH), 77.9 (CH), 77.3 (CH), 72.4 (CH_2), 72.3 (CH_2), 63.2 (CH_2), 55.7 (2 × CH_3), 19.8 (CH_3); IR (KBr, cm^{-1}) 3460, 3109, 1597, 1216, 1036; mass (ESI-MS) *m/z* 388, found 406 $[M + NH_4]^+$; DART-HRMS: calcd for $C_{22}H_{32}NO_6$ $[M + NH_4]^+$ 406.2230, measured 406.2215.

Compound 12. To a solution of **11** (110 mg, 0.28 mmol) in acetonitrile (6 mL) was added IBX (238 mg, 0.85 mmol) and the reaction mixture was allowed to stir under reflux for 1 h. The resulting mixture was diluted with anhydrous ether, cooled to 0 °C and filtered through a Celite bed. The filtrate obtained was concentrated under reduced pressure to give crude labile aldehyde **11a** (106 mg) which was immediately used for next step without further purification.

To a suspension of methyltriphenylphosphonium bromide (740 mg, 2.07 mmol) in dry THF (6 mL) was added KHMDS (3.1 mL, 0.5 M in toluene) at −78 °C under argon atmosphere and the resulting mixture was stirred at −78 °C for 20 min. To this mixture at −78 °C was then added the solution of crude aldehyde **11a** (106 mg) in dry THF (2 mL) and the reaction mixture was allowed to stir at room temperature. After 1 h the reaction mixture was filtered through a Celite bed. The filtrate obtained was concentrated and dissolved in anhydrous ether to precipitate Ph_3PO. The organic layer was separated and concentrated to obtain a residue which on column chromatography yielded **12** (84 mg, 77% from **11**) as a colorless oil. Eluent for column chromatography: EtOAc/hexane (7/43, v/v); $[\alpha]^{28}_D = -20.8$ (*c* 0.24 $CHCl_3$); R_f 0.5 (1:4 EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$) δ 7.25−7.19 (m, 4H, ArH), 6.83 (d, $J = 8.4$ Hz, 4H, ArH), 5.76 (ddd, $J = 6.3$, 10.4, 16.9 Hz, 1H, H-2′), 5.32 (d, $J = 17.1$ Hz, 1H, H-2″a), 5.14 (d, $J = 10.4$ Hz, 1H, H-2”b), 4.55−4.34 (m, 5H, 2 × OCH_2Ar, H-2), 4.05 (quintet, $J = 6.2$ Hz, 1H, H-5), 3.79 (s, 6H, 2 × OCH_3), 3.61 (t, $J = 5.2$ Hz, 1H, H-3), 3.40 (t, $J = 5.8$ Hz, 1H, H-4), 1.22 (d, $J = 6.3$ Hz, 3H, H-6);^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$); δ 159.9 (2 × ArqC), 137.9 (=CH), 130.7 (ArqC), 130.6 (ArqC), 130.1 (ArC), 130.0 (ArC), 117.2 (=CH_2), 114.4 (ArC), 83.3 (CH), 82.6 (CH), 81.2 (CH), 77.8 (CH), 72.4 (CH_2), 72.2 (CH_2), 55.7 (2 × CH_3), 20.1 (CH_3); IR (Neat, cm^{-1}): 3018, 2927, 1613, 1513, 1216, 1125, 1036; mass (ESI-MS) *m/z* 384, found 402 $[M + NH_4]^+$; DART-HRMS: calcd for $C_{23}H_{32}NO_5$ $[M + NH_4]^+$ 402.2281, measured 402.2280.

Compound 16. A steel seal tube was charged with $Pd(PPh_3)_4$ (171 mg, 0.15 mmol), LiCl (488 mg, 11.51 mmol), tributylvinyltin (0.5 mL), triflate **15** (500 mg, 1.53 mmol) and THF (50 mL). The reaction mixture in the seal tube was flushed with nitrogen before the tube was sealed. The seal tube containing the reaction mixture was heated at 80 °C for 30 h. After being cooled to room temperature the reaction mixture was diluted with ether (50 mL) and washed with water twice. The organic phase was separated, dried (Na_2SO_4) and concentrated under reduced pressure to give colorless oil which on column purification afforded **16** as colorless oil (295 mg, 94%) as a colorless oil. Eluent for column chromatography: EtOAc/hexane (3/97, v/v); ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$) δ 7.73 (dd, $J = 10.9$, 17.4 Hz, 1H, H-5′), 7.45 (t, $J = 8.0$ Hz, 1H, H-7), 7.25 (d, $J = 8.0$ Hz, 1H, H-8), 6.86 (d, $J = 8.2$ Hz, 1H, H-6), 5.68 (dd, $J = 1.1$, 17.4 Hz, 1H, H-5″a), 5.41 (dd, $J = 1.2$, 10.9 Hz, 1H, H-5”b), 1.72 (s, 6H, 2 × CH_3); ^{13}C NMR (50 MHz, $CDCl_3 + CCl_4$) δ 160.2 (*C* = O), 157.2

(ArqC), 142.9 (ArqC), 135.9 (=CH), 135.5 (ArC), 121.8 (ArC), 118.2 (CH_2), 116.9 (ArC), 111.4 (qC), 105.5 (qC), 26.2 (2 × CH_3); IR (neat, cm^{-1}) 2923, 2361, 1726, 1635, 1575, 1267,1209, 1044; mass (ESI-MS) *m/z* 204, found 205 $[M + H]^+$; EI-HRMS: calcd for $C_{12}H_{12}O_3$ $[M]^+$ 204.0787, measured 204.0775.

Compound 17. $LiAlH_4$ (83 mg, 2.2 mmol) was added to a solution of compound **16** (300 mg, 1.47 mmol) in THF (20 mL) at −78 °C. The mixture was warmed to room temperature. After 2 h the reaction mixture was diluted with ethyl acetate (30 mL) and washed with water. The organic layer was separated, dried (Na_2SO_4) and concentrated under reduced pressure to a residue that was purified by column chromatography to give compound **17** (159 mg, 72%) as a colorless oil. Eluent for column chromatography: EtOAc/hexane (1/4, v/v); R_f 0.48 (2:3 EtOAc/ Hexane); ^1H NMR (300 MHz, $CDCl_3 + CCl_4$) δ 7.70 (brs, 0.7H, C1-OH), 7.11 (t, $J = 7.9$ Hz, 1H, H-5), 6.93 (d, $J = 7.6$ Hz, 1H, H-6), 6.84 (dd, $J = 10.9$, 17.2 Hz, 1H, H-3′), 6.75 (d, $J = 8.0$ Hz, 1H, H-4), 5.52 (dd, $J = 1.3$, 17.2 Hz, 1H, H-3"a), 5.29 (dd, $J = 1.2$, 10.8 Hz, 1H, H-3"b), 4.91 (s, 2H, H-2′), 2.02 (brs, 0.8 H, C2′-OH); ^{13}C NMR (50 MHz, $CDCl_3 + CCl_4$) δ 157.2 (ArqC), 138.4 (ArqC), 134.9 (=CH), 129.9 (ArC), 122.8 (ArqC), 119.5 (ArC), 118.4 (=CH_2), 116.9 (ArC), 60.7 (CH_2); IR (neat, cm^{-1}) 3401, 3019, 2924, 1579, 1461, 1268, 1217; mass (ESI-MS) *m/z* 150, found 174 $[M + H + Na]^+$, 133 $[M - OH]^+$; EI-HRMS: calcd for $C_9H_9O_2$ $[M - H]^+$ 149.0603, measured 149.0615.

Compound 18. vTo a stirred solution of **17** (100 mg, 0.67 mmol) in dry acetone (5 mL) was added anhydrous K_2CO_3 (185 mg, 1.34 mmol), methyl iodide (0.08 mL, 1.34 mmol) and the resulting mixture was allowed to reflux. After 6 h the reaction mixture was brought to room temperature and concentrated under reduced pressure to a residue that was dissolved in ethyl acetate (30 mL) and washed with water. The organic layer was collected, dried and concentrated under reduced pressure to an oil which was purified by column chromatography to give **18** (96 mg, 88%) as a colorless oil. Eluent for column chromatography: EtOAc/hexane (3/22, v/v); R_f 0.49 (3:7 EtOAc/hexane); ^1H NMR (300 MHz, $CDCl_3 + CCl_4$) δ 7.24−7.18 (m, 1H, H-4), 7.07 (dd, $J = 10.1$, 17.4 Hz, 2H, H-5, H-6′), 6.79 (d, $J = 8.1$ Hz, 1H, H-3), 5.63 (dd, $J = 1.3$, 17.4 Hz, 1H, H-6"a), 5.35 (dd, $J = 1.2$, 10.9 Hz, 1H, H-6"b), 4.75 (s, 2H, H-1′), 3.87 (s, 3H, OCH_3), 2.04 (brs, 0.8H, OH); ^{13}C NMR (50 MHz, $CDCl_3 + CCl_4$) δ 157.9 (ArqC), 138.7 (ArqC), 134.4 (=CH), 128.8 (ArC), 126.0 (ArqC), 119.0 (ArC), 117.4 (=CH_2), 109.6 (ArC), 56.7 (CH_2), 55.5 (CH_3); IR (neat, cm^{-1}) 3430, 3019, 2928, 1576, 1261, 1215, 1075; mass (ESI-MS) *m/z* 164, found 147 $[M - OH]^+$; EI-HRMS: calcd for $C_{10}H_{11}O_2$ $[M - H]^+$ 163.0759, measured 163.0764.

Compound 19. To a solution of **18** (35 mg, 0.21 mmol) in DCM (10 mL) was added imidazole (44 mg, 0.64 mmol), TBSCl (36 mg, 0.23 mmol) and then the mixture was allowed to stir at room temperature for 1 h. A saturated solution of NH_4Cl (15 mL) was added and the mixture was extracted with DCM (3 × 10 mL). The organic layer was separated, dried (Na_2SO_4) and evaporated under vacuo to give a residue that was purified by column chromatography to give 55 mg of compound **19** (93%) as a colorless oil. Eluent for column chromatography: EtOAc/hexane (1/49, v/v); R_f 0.58 (1:9, EtOAc/ Hexane); ^1H NMR (300 MHz, $CDCl_3 + CCl_4$) δ 7.37−7.25 (m, 3H, H-3, H-4, H-6′), 6.92 (d, $J = 8.0$ Hz, 1H, H-5), 5.82 (dd, $J = 1.5$, 17.5 Hz, 1H, H-6"a), 5.46 (dd, $J = 1.4$, 11.0 Hz, 1H, H-6"b), 4.96 (s, 2H, H-1′), 3.98 (s, 3H, OCH_3), 1.04 (s, 9H, $SiC(CH_3)_3$), 0.20 (s, 6H, $Si(CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3 + CCl_4$) δ 157.3 (ArqC), 139.8 (ArqC), 135.2 (=CH), 128.5 (ArC), 126.4 (ArqC), 118.5 (ArC), 115.9 (=CH_2), 109.8 (ArC), 55.9 (CH_2), 55.5 (CH_3), 26.1 (3 × CH_3), 18.5 (qC), −5.1 (2 × CH_3); IR (neat, cm^{-1}) 3010, 2932, 1577, 1468, 1256, 1217, 1068; mass (ESI-MS) *m/z* 278, found 279 $[M + H]^+$; EI-HRMS: calcd for $C_{15}H_{23}O_2Si$ $[M - CH_3]^+$ 263.1467; found 263.1468.

Compound 20. To a 50 mL two necked oven-dried round-bottom flask fitted with a reflux condenser and septum was added Grubbs II[nd] generation catalyst (15 mg, 0.018 mmol) under argon atmosphere. Dry degassed CH_2Cl_2 (10 mL) was then added to the above solution through a syringe and the solution was kept for stirring. Compounds **12** (60 mg, 0.16 mmol) and **19** (62 mg, 0.22 mmol) in DCM (2 mL each) were added simultaneously through a syringe to the stirring solution. The septum was replaced with a glass stopper while the stirring was continued. The solution was refluxed for 12 h. The temperature of the mixture was cooled slowly to room temperature. The organic solvent was evaporated under reduced pressure to give a black residue which was purified by column chromatography to give **20** as colorless oil (51 mg, 51%). Eluent for column chromatography: EtOAc/hexane (7/43, v/v); $[\alpha]^{28}_D = -13.3$ (*c* 0.85 $CHCl_3$); R_f 0.51 (1:4, EtOAc/ Hexane); ^1H NMR (300 MHz, $CDCl_3 + CCl_4$); δ 7.28−7.04 (m, 7H, 6 × ArH, H-1′), 6.87−6.76 (m, 5H, ArH), 6.07 (dd, $J = 6.6$, 15.8 Hz, 1H, H-2′), 4.79 (s, 2H, H-1"), 4.62−4.53 (m, 4H, 3 × C*H*Ar, H-3′), 4.45 (d, $J = 11.5$ Hz, 1H, C*H*Ar), 4.12 (t, $J = 6.2$ Hz, 1H, H-6′), 3.85−3.81 (m, 9H, 3 × OCH_3), 3.74 (t, $J = 5.3$ Hz, 1H, H-4′), 3.49 (t, $J = 5.9$ Hz, 1H, H-5′), 1.29 (d, $J = 6.2$ Hz, 3H, H-7′), 0.89 (s, 9H, $SiC(CH_3)_3$), 0.06 (s, 6H, $Si(CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$); δ 159.9 (2 × ArqC), 158.1 (ArqC), 139.4 (ArqC), 131.6 (ArC), 130.8 (ArqC), 130.6 (ArqC), 130.2 (ArqC), 130.1 (ArC), 130.0 (ArC), 129.1 (ArC), 127.2 (ArqC), 119.6 (=CH), 114.4 (ArC), 110.3 (=CH), 83.5 (CH), 82.9 (CH), 81.5 (CH), 77.8 (CH), 72.4 (CH_2), 72.2 (CH_2), 56.6 (CH_2), 56.1 (CH_3), 55.7 (CH_3), 55.6 (CH_3), 26.7 (3 × CH_3), 20.1 (CH_3), 19.1 (qC), −4.5 (2 × CH_3); IR (neat, cm^{-1}) 3010, 2929, 1611, 1582, 1464, 1250, 1219, 1040; mass (ESI-MS) *m/z* 634, found 652 $[M + NH_4]^+$; DART-HRMS: calcd for $C_{37}H_{50}O_7Si$ $[M]^+$ 634.3326, measured 634.3287.

Compound (+)-1. A solution of compound **20** (50 mg, 0.079 mmol) in THF (5 mL) was stirred with 1 M HCl (10 mL) for 3 days at room temperature. To this reaction mixture was added a saturated solution of $NaHCO_3$ and the resulting mixture was extracted with CH_2Cl_2 (6 × 5 mL). The combined organic layer was separated, dried over Na_2SO_4 and concentrated under reduced pressure to give oil which was purified by column chromatography to give (+)-varitriol (**1**) (10 mg, 46%) as a colorless oil. Eluent for column chromatography: acetone/DCM (3/7, v/v); $[\alpha]^{28}_D = +19.4$ (*c* 0.16 MeOH); R_f 0.3 (2:3, acetone/DCM); ^1H NMR (400 MHz, acetone-d_6); δ 7.21 (t, $J = 8.0$ Hz, 1H, H-4), 7.12 (d, $J = 13.6$ Hz, 1H, H-1′), 7.11 (d, $J = 8.1$ Hz, 1H, H-5), 6.88 (d, $J = 8.1$ Hz, 1H, H-3), 6.19 (dd, $J = 6.6$, 15.8 Hz, 1H, H-2′), 4.71 (s, 2H, OCH_2−C-1), 4.30−4.27 (m, 2H, H-3′, OH), 3.90 (t, $J = 5.6$ Hz, 1H, H-4′), 3.84−3.83 (m, 1H, H-6′), 3.81 (s, 3H, OCH_3), 3.68 (t, $J = 5.7$ Hz, 1H, H-5′), 2.95 (brs, 2H, OH), 1.26 (d, $J = 6.3$ Hz, 3H, H-7′); ^{13}C NMR (100 MHz, acetone-d_6) δ 158.9 (ArqC), 139.0 (ArqC), 132.5 (=CH), 129.4 (=CH), 129.3 (ArC), 127.9 (ArqC), 119.3 (ArC), 110.6 (ArC), 85.3 (CH), 80.0 (CH), 77.1 (CH), 76.5 (CH), 56.0 (O*C*H_3), 55.5 (CH_2), 19.5 (CH_3); IR (neat, cm^{-1}) 3380, 2925, 1592, 1218, 1088; EI-HRMS: calcd for $C_{15}H_{20}O_5$ $[M]^+$ 280.1311, measured 280.1300.

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Supporting Information Available: General experimental details, full characterization and copies of ^{1}HNMR and ^{13}CNMR spectra of compounds **4**−**12**, **16**−**20**, and **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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