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Carbocyclization of D-glucose: syntheses of gabosine I and streptol

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ABSTRACT

D-Glucose was differentially protected with a *trans*-diacetal at C-2,3, an ethoxymethyl ether at C-4, and a *tert*-butyldimethylsilyl ether at C-6, and then carbocyclized via a key Horner–Wadsworth–Emmons (HWE) olefination to give a versatile synthetic intermediate, enone **13**, which was readily transformed into gabosine I and streptol.

1. Introduction

Gabosines[1] belong to a family of unusual, hydroxylated cyclohexenones or hexanones that may be classified as pseudo- or carba-sugars.[2] Gabosines A–K were isolated in 1993 and have been shown to display interesting bioactivities, such as antibiotic,[1b] anticancer,[3] and DNA binding properties.[1c] A total of 14 gabosines have been identified since the first isolation of gabosine C and its crotonyl ester, COTC, from *Streptomyces* strains in 1974.[1a] Since then, 18 total syntheses have been described. Ten enantiospecific syntheses constructed the carbocyclic framework from carbohydrates using either an intramolecular nitrile oxide or nitrone cycloaddition,[4] a $SnCl_4$-promoted aldol-type cyclization of phenylsulfonyl enol silyl ether,[5] an intramolecular Nozaki–Hiyama–Kishi reaction,[6] a ring-closing alkene metathesis,[7] intramolecular Horner–Wadsworth–Emmons (HWE) olefination,[8] intramolecular direct aldol addition,[9] or iron-catalyzed aldol addition[10] as the key step. Three other enantiospecific syntheses, including our earlier endeavor,[11] employed (−)-quinic acid as the chiral starting material.[12,13] The remaining five constructions of gabosines involved a racemic norbornyl route,[14] a chemoenzymatic synthesis from iodobenzene,[15] an asymmetric Diels–Alder reaction of chiral sulfinylacrylate with 2-methoxyfuran,[16] enantioselective acetylation of hydoxyketals,[17] and enantioselective synthesis from [(*p*-tolylsulfinyl)methyl]-*p*-quinols[18] as the key strategies.

Gabosine I (**1**) is identical to valienone,[19] an intermediate for the biosynthesis of validamycin A (Fig. 1).[20] The corresponding reduction product of **1**, the α-allylic alcohol **3**, is known as valienol and also as (+)-streptol, is a plant-growth inhibitor.[21] Streptol (**3**) was isolated from a culture of *Streptomyces* and was shown to inhibit the growth of lettuce seedlings at a concentration above 13 ppm.[21a]

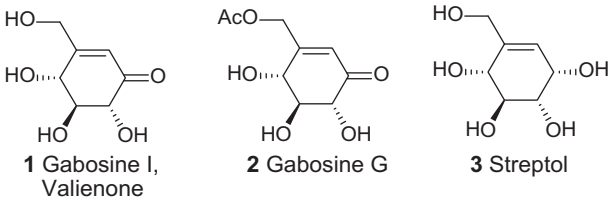

Fig. 1. Structures of gabosine I, G, and streptol.

Gabosine I (**1**) was firstly synthesized by Lubineau and Billault[6] in nine steps from tetra-*O*-benzyl-D-glucose employing an intramolecular Nozaki–Hiyama–Kishi reaction as the key step. Since tetra-*O*-benzyl-D-glucose was prepared from D-glucose in three steps, the total number of synthetic steps to **1** from D-glucose is therefore 12. A total synthesis of (+)-streptol (**3**) was accomplished by Mehta et al. from cyclopentadiene and benzoquinone as starting materials via a Diels–Alder and a retro-Diels–Alder strategy in 11 steps with 14% yield.[22]

Our present research is focused on facile construction of hydroxylated carbocycles from sugars, which was coined carbocyclization of carbohydrates. Our previous work already yielded gabosine I (**1**) and G (**2**) from α-D-gluconolactone via a Horner–Wadsworth–Emmons (HWE) olefination as the key step,

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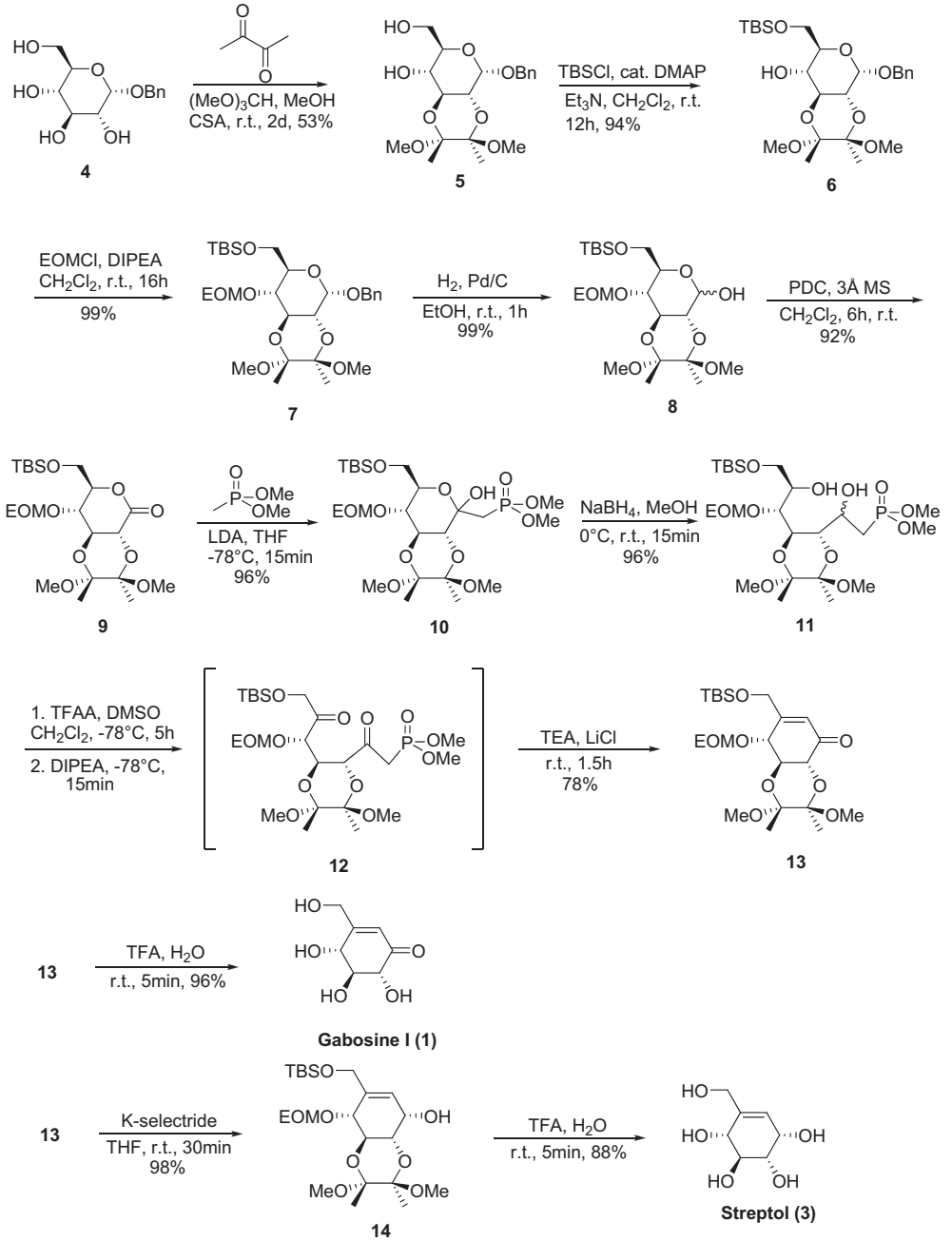
and established the absolute configuration of (−)-gabosine G (**2**).[8] In that synthesis, we employed a mixed acetal as the blocking group for the hydroxy function at C-1 and C-2. However, the mixed acetals were very acid sensitive and readily decomposed. We therefore searched for a robust alternative so that the carbocyclized enone could be stable enough to be elaborated into a variety of target molecules. Furthermore, differential protection of the hydroxyls is desirable as regioselective deprotection of the blocking group allows facile and selective functional group manipulation. With this in mind, we now report from D-glucose, efficient, and enantiospecific syntheses of gabosine I (**1**), streptol (**3**) using stable silyl ether, *trans*-diacetal, and ethoxymethyl (EOM) ether for the hydroxyl protection and an intramolecular HWE olefination[23,24] as the key carbocyclization step.

2. Results and discussion

The synthesis of gabosine I (**1**) from D-glucose is shown in Scheme 1. Commercially available benzyl α-D-glucopyranoside **4**[25] was transacetalized[26] with butadione and camphorsulfonic acid (CSA) at OH-2,3 to give, preponderantly, diacetal **5** in 53% yield. Differential protection was executed and the primary alcohol in diol **4** was selectively silylated with *tert*-butyldimethylsilyl chloride (TBSCl) and *N*,*N*-dimethylaminopyridine (DMAP) to give silyl ether **6** in 94% yield. Alkylation of the remaining free alcohol in **6** with ethoxymethyl (EOM) chloride in the presence of diisopropylethylamine (DIPEA) afforded an almost quantitative yield of the fully blocked benzyl glycoside **7**. Catalytic hydrogenolysis of the benzyl ether in **7** furnished lactol **8**, which was smoothly oxidized with pyridinium dichromate (PDC) to form lactone **9** in an excellent



Scheme 1. Syntheses of gabosine (**1**) and streptol (**3**).

yield. Nucleophilic addition of lithiated dimethyl methylphosphonate to the lactone carbonyl afforded phosphonate-lactol **10** in 96% yield.

Direct oxidation of lactol **10** to the corresponding diketone followed by HWE cyclization proved difficult, hence the hemiacetal was reduced by borohydride to give heptitol derivative **11** in an excellent yield. Several oxidation protocols were attempted and Swern oxidation[27] was found to be the most efficient for the production of diketone **12** and the subsequent intramolecular HWE olefination was effected in the same pot to give enone **13** in 78% overall yield. The olefination was better induced by triethylamine than by DIPEA. Since enone of this type is generally unstable in basic conditions, the addition of LiCl[28] was necessary for the HWE olefination because it shortened the reaction time.

Complete deprotection of enone **13** furnished gabosine I (**1**) in 96% yield. The *trans*-diacetal ring in **13** is the most stable protecting group in acidic conditions, so the hydrolysis conditions of trifluoroacetic acid (TFA) and H_2O in a ratio of 20:1 were adopted. Hence, gabosine I (**1**) was synthesized from benzyl glucopyranoside **4** in nine steps with 31% overall yield, identical in all respects to the one synthesized by us[8] previously. The overall yield (31%) of the present work is superior to our last synthesis (20.3%) and is the best overall yield for the preparation of gabosine I in the literature.[6] Since gabosine G was prepared in one step from **1**, this synthesis is also a formal synthesis of gabosine G (**2**).

For the synthesis of streptol, enone **13** was regio-selectively reduced by K-selectride to afford α-allylic alcohol **14** as the sole product in 98% yield. Complete deprotection of the blocking groups in **14** with aq TFA **12** gave streptol (**3**) in 88% yield. The spectral data (^{1}H, ^{13}C NMR) of streptol (**3**) are in accord with those in the literature.[22] Thus streptol (**3**) was synthesized from benzyl glucopyranoside **4** in 10 steps with 28% overall.

3. Conclusions

Since the chirality at the anomeric center was removed during the conversion of benzyl glycoside **7** into lactol **8**, we had also carried out a convenient synthesis of lactol **8** from a mixture of α-D and β-D-benzyl glucopyranoside.[25a] Thus the present synthesis of gabosine I (**1**) was achieved in 10 steps with 27% overall yield from D-glucose using an HWE olefination as the key step. This synthesis records a higher overall yield than our previous endeavor[8] (20.3%) and is the best overall yield for the preparation of gabosine I in the literature.[6] Since gabosine I can be converted into gabosine G in one step,[8] the present route is also a formal synthesis of gabosine G (**2**). On the other hand, a synthesis of streptol (**3**) was accomplished in 11 steps with 24% overall yield from D-glucose. Since the C-6 silyl ether and the C-4-EOM group in enone **13** could be selectively deprotected according to conditions, the facile construction of enone **13** provides opportunities for the syntheses of polyhydroxylated cyclohexenoid and cyclohexanoid natural products, such as the recently isolated ampleomins A–G.[29] It is also worthy that the **13** would be an attractive intermediate for elaboration into a wide variety of hydroxylated cyclohexenoid molecules of pharmaceutical interests.

4. Experimental section

4.1. General procedures

Melting points were measured with in Celsius degrees and were uncorrected. Optical rotations were operating at 589 nm. Infrared spectra (IR) were recorded as thin film on potassium bromide discs. Nuclear magnetic resonance (NMR) spectra were measured at 300.13 MHz (^{1}H), 400.13 MHz (^{1}H), 75.47 MHz (^{13}C) or at 100.13 MHz (^{13}C). All chemical shifts were recorded in parts per million relative to tetramethylsilane (δ=0.0). Spin–spin coupling constants (J value) recorded in hertz were measured directly from the spectra. All reactions were monitored by analytical thin-layer chromatography (TLC) on aluminum-precoated plates of silica gel with detection by spraying with 5% (w/v) dodecamolybdophosphoric acid in ethanol. Silica gel 60 (230–400 mesh) was used for flash chromatography. All reagents and solvents were general reagent grade unless otherwise stated. DMF was dried by magnesium sulfate and filtered. It was then freshly distilled under reduced pressure. THF was freshly distilled from Na/benzophenone ketyl under nitrogen. Dichloromethane was freshly distilled from P_2O_5 under nitrogen. Other reagents were purchased from commercial suppliers and were used without purification.

4.2. Synthesis

4.2.1. Diacetal ***5***. To a solution of benzyl glucoside **4** (1.05 g, 3.89 mmol) in dry MeOH (20 mL) were added 2,3-butanedione (0.44 mL, 5.06 mmol), trimethyl orthoformate (2.55 mL, 23.3 mmol), and (±)-10-camphorsulfonic acid (80 mg, 0.39 mmol). The reaction mixture was stirred for 48 h at room temperature under N_2. The reaction mixture was then treated with triethylamine (1 mL). Concentration of the solution followed by flash chromatography (*n*-hexane/EtOAc, 1:1) gave diacetal **5** (0.79 g, 53%) as a colorless oil: $[\alpha]_D^{20}$ −25.4 (*c* 0.43, $CHCl_3$); R_f 0.10 (*n*-hexane/EtOAc, 1:1); IR (thin film) 3406, 2994, 2927, 1456, 1376, 1207, 1135, 1039, 941, 884, 751 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (3H, s), 1.35 (3H, s), 3.23 (3H, s), 3.30 (3H, s), 3.60–3.64 (1H, m), 3.67–3.77 (4H, m), 4.08 (1H, t, J=9.8 Hz), 4.69 (1H, d, J=12.6 Hz), 4.75 (1H, d, J=12.6 Hz), 4.93 (1H, d, J=3.6 Hz), 7.28–7.41 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8, 17.9, 48.0, 48.1, 61.9, 68.3, 68.4, 69.5, 70.2, 72.2, 96.9, 99.6, 100.0, 127.8, 128.2, 128.4, 137.7; MS (ESI) *m*/*z* (relative intensity) 407 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{19}H_{28}O_8$ [M+Na]$^+$ 407.1676, found 407.1680.

4.2.2. Silyl ether ***6***. To a solution of diol **5** (232 mg, 0.61 mmol) in CH_2Cl_2 (5 mL) were added TBSCl (137 mg, 0.91 mmol), Et_3N (0.21 mL, 1.21 mmol), and DMAP (7.8 mg, 0.06 mmol). The mixture was stirred for 12 h at room temperature under N_2. The solution was diluted with EtOAc (10 mL). The resultant mixture was filtered through a pad of silica gel that was eluted with EtOAc. Concentration of the filtrate followed by flash chromatography (*n*-hexane/Et_2O, 3:1) gave silyl ether **6** (283 mg, 94%) as a colorless oil: $[\alpha]_D^{20}$ −27.4 (*c* 1.60, $CHCl_3$); R_f 0.17 (*n*-hexane/Et_2O, 3:1); IR (thin film) 3506, 2932, 1460, 1376, 1252, 1134, 1045, 885, 840, 779 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.07 (6H, 2s), 0.90 (9H, s), 1.34 (3H, s), 1.35 (3H, s), 3.24 (3H, s), 3.31 (3H, s), 3.59–3.76 (5H, m), 4.10 (1H, dd, J=10.1, 9.3 Hz), 4.70 (1H, d, J=12.5 Hz), 4.74 (1H, d, J=12.5 Hz), 4.90 (1H, d, J=3.6 Hz), 7.27–7.42 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.4, −5.3, 17.8, 18.0, 18.4, 26.0, 48.0, 48.0, 64.1, 68.2, 69.4, 69.8, 70.2, 71.5, 96.6, 99.5, 99.9, 127.7, 128.2, 128.3, 137.8; MS (ESI) *m*/*z* (relative intensity) 521 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{25}H_{42}O_8Si$ [M+Na]$^+$ 521.2541, found 521.2538.

4.2.3. Ethoxyl ether ***7***. To a solution of alcohol **6** (250 mg, 0.50 mmol) in dry CH_2Cl_2 (3.0 mL) was added DIEPA (0.27 mL, 1.51 mmol). Chloromethyl ethyl ether (EOMCl) (0.07 mL, 0.75 mmol) was added dropwise over 10 min at 0 °C. The mixture was stirred for 16 h at room temperature under N_2. The solution was diluted with EtOAc (10 mL). The resultant mixture was filtered through a pad of silica gel that was eluted with EtOAc. Concentration of the filtrate followed by flash chromatography (*n*-hexane/Et_2O, 5:1) gave ethoxyl ether **7** (276 mg, 99%) as a colorless oil: $[\alpha]_D^{20}$ +5.6 (*c* 0.96, $CHCl_3$); R_f 0.13 (*n*-hexane/Et_2O, 5:1); IR (thin film) 2933, 1461, 1375, 1253, 1134, 1042, 973, 839, 780 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.05 (6H, 2s), 0.89 (9H, s), 1.20 (3H, t, J=7.1 Hz), 1.29 (3H, s),

1.33 (3H, s), 3.22 (3H, s), 3.27 (3H, s), 3.58–3.73 (7H, m), 4.14 (1H, dd, J=9.9, 9.1 Hz), 4.69 (2H, s), 4.82 (1H, d, J=6.2 Hz), 4.86–4.89 (2H, m), 7.28–7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.3, −5.0, 15.2, 17.8, 18.0, 18.5, 26.1, 47.9, 48.0, 62.2, 64.0, 68.6, 69.3, 70.1, 72.4, 72.5, 96.0, 96.1, 99.5, 99.9, 127.6, 128.3, 128.4, 137.7; MS (ESI) m/z (relative intensity) 579 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{28}H_{48}O_9Si$ [M+Na]$^+$ 579.2960, found 579.2956.

*4.2.4. Lactol **8**.* To a solution of benzyl glucoside **7** (277 mg, 0.50 mmol) in ethanol (5.0 mL) was added 10% Pd-on-charcoal (20 mg). The mixture was stirred for 1 h at room temperature under an atmosphere of H_2 (balloon) and was then filtered. Concentration of the filtrate followed by flash chromatography (n-hexane/Et_2O, 1:1) gave lactol **8** (231 mg, 99%) as a colorless oil: $[\alpha]_D^{20}$ −35.6 (c 4.28, $CHCl_3$); R_f 0.23 (n-hexane/Et_2O, 1:1); IR (thin film) 3446, 2951, 2931, 2587, 1645, 1472, 1463, 1357, 1252, 1137, 1037 cm^{-1}; ^{1}H NMR (mixture of α and β isomer with ratio α/β=1:0.7) (400 MHz, $CDCl_3$) δ 0.03–0.06 (10.2H, m), 0.88 (15.3H, s), 1.19 (5.2H, t, J=7.0 Hz), 1.28–1.30 (10.2H, m), 3.24–3.28 (10.2H, m), 3.34–3.42 (1.7H, m), 3.58–3.89 (12.6H, m), 4.11 (1H, t, J=9.8 Hz), 4.76 (0.7H, d, J=7.8 Hz), 4.80–4.88 (3.4H, m), 5.19 (1H, d, J=3.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.3, −5.2, −5.0, 15.2, 17.7, 17.8, 17.9, 18.0, 18.6, 26.1, 47.9, 47.9, 48.1, 62.4, 62.6, 64.0, 64.1, 68.8, 69.4, 70.1, 71.8, 72.1, 72.5, 72.8, 77.0, 91.3, 94.6, 96.1, 96.1, 99.6, 100.0; MS (ESI) m/z (relative intensity) 489 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{21}H_{42}O_9Si$ [M+Na]$^+$ 489.2490, found 489.2507.

*4.2.5. Lactone **9**.* To a solution of lactol **8** (2.24 g, 4.8 mmol) in dry CH_2Cl_2 (5 mL) were added 3 Å molecular sieves (2 g) and PDC (2.16 g, 5.75 mmol). The mixture was stirred for 6 h and was diluted with diethyl ether (10 mL). The reaction mixture was filtered through a pad of silica gel topped with Celite. The residue was washed with EtOAc. The filtrate was concentrated under reduced pressure to give lactone **9** as a colorless oil (2.056 g, 92%). $[\alpha]_D^{20}$ −28.6 (c 2.76, $CHCl_3$); R_f 0.6 (hexane/EtOAc, 3:1), IR (thin film) 2953, 2931, 2896, 2858, 1773, 1645, 1463, 1379, 1257, 1236, 1214, 1141, 1115, 1036 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01 (3H, s), 0.04 (3H, s), 0.84 (9H, s), 1.15 (3H, t, J=7.2 Hz), 1.25 (3H, s), 1.33 (3H, s), 3.21 (3H, s), 3.23 (3H, s), 3.47–3.56 (1H, m), 3.47–3.64 (1H, m), 3.79 (2H, td, J=11.4, 1.7 Hz), 3.91–3.98 (1H, m), 4.16–4.20 (3H, m), 4.72 (1H, d, J=6.8 Hz), 4.88 (1H, d, J=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.8, −5.6, 14.8, 17.3, 17.4, 18.1, 25.7, 47.8, 48.4, 62.7, 63.6, 65.2, 68.4, 72.2, 82.1, 95.7, 98.6, 99.9, 167.6; MS (ESI) m/z (relative intensity) 487 ([M+Na]$^+$, 100), HRMS (ESI) calcd for $C_{21}H_{40}O_9Si$ [M+Na]$^+$ 487.2334, found 487.2338.

*4.2.6. Phosphonate **10**.* To a solution of diisopropylamine (0.12 mL, 1.19 mmol) in dry THF (2 mL) was added dropwise n-butyllithium in hexane (1.6 M solution, 0.743 mL, 1.19 mmol) at −78 °C under N_2. The reaction mixture was stirred for 30 min at −78 °C under N_2 and dimethyl methylphosphonate (0.07 mL, 0.59 mmol) was then added. The reaction mixture was stirred for a further 30 min at −78 °C and was added slowly to a solution of lactone **9** (138 mg, 0.30 mmol) in dry THF (2 mL) at −78 °C. Stirring was continued for an additional 1 h at the same temperature. The reaction was quenched with saturated aq NH_4Cl (1 mL) at −78 °C and was warmed to room temperature. The mixture was extracted with EtOAc (4×10 mL), the combined organic extracts were dried ($MgSO_4$) and filtered. Concentration of the filtrate followed by flash chromatography (n-hexane/EtOAc, 2:1) yielded phosphonate **10** (169 mg, 96%) as a colorless oil. $[\alpha]_D^{20}$ +55.6 (c 1.0, $CHCl_3$); R_f 0.5 (n-hexane/EtOAc, 1:1); IR (thin film) 2953, 2856, 1643, 1462, 1376, 1231, 1182, 1137, 1036 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.03 (6H, s), 0.88 (9H, s), 1.18 (3H, t, J=7.2 Hz), 1.29 (3H, s), 1.35 (3H, s), 1.92 (1H, dd, J=15.3, 18.3 Hz), 2.60 (1H, dd, J=15.6, 16.8 Hz), 3.22–3.34 (6H, m), 3.59–3.92 (11H, m), 4.17 (1H, t, J=9.9 Hz), 4.84 (1H, d, J=6 Hz), 4.88 (1H, d, J=6 Hz), 5.93 (1H, s, br); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.9, −4.7, 15.6, 18.3, 18.8, 26.4, 31.5, 33.3, 48.3, 48.4, 52.5, 52.6, 53.9, 53.9, 62.7,64.4, 70.3, 72.6, 72.8, 73.7, 95.7, 96.5, 99.7, 100.6; MS (ESI) m/z (relative intensity) 611 ([M+Na]$^+$, 100), HRMS (ESI) calcd for $C_{24}H_{49}O_{12}PSi$ [M+Na]$^+$ 611.2623, found 611.2603.

*4.2.7. Diol **11**.* To a solution of lactol **10** (1.43 g, 2.42 mmol) in MeOH (25 mL) was added $NaBH_4$ (0.31 g, 9.69 mmol) at room temperature. Stirring was continued for 0.5 h at the same temperature under N_2. The reaction was quenched with saturated aq NH_4Cl (15 mL). The mixture was extracted with EtOAc (4×30 mL). The combined organic extracts were dried, filtered, and the filtrate was concentrated. Flash chromatography (EtOAc) gave diol **11** (1.37 g, 96%) as a colorless oil. $[\alpha]_D^{20}$ −92.4 (c 2.97, $CHCl_3$); R_f 0.2 (EtOAc), IR (thin film) 3385, 2952, 2930, 2856, 1645, 1462, 1375, 1251, 1184, 1127, 1034 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (3H, s), 0.07 (3H, s), 0.89 (9H, s), 1.94 (3H, t, J=7.2 Hz), 1.28 (3H, s), 1.29 (3H, s), 1.87–2.03 (1H, m), 2.34–2.47 (1H, m), 3.20 (3H, s), 3.27 (3H, s), 3.48–3.57 (1H, m), 3.68–3.78 (8H, m), 3.80–3.88 (3H, m), 3.92–3.97 (1H, m), 4.26–4.32 (2H, m), 4.74–4.79 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.52, 14.8, 17.3, 17.4, 18.1, 25.7, 28.2, 29.6, 47.7, 47.9, 52.2, 52.3, 52.4, 63.2, 63.7, 63.8, 64.9, 64.9, 67.1, 69.8, 69.9, 70.9, 76.5, 76.6, 77.2, 96.1, 98.6, 98.7; MS (ESI) m/z (relative intensity) 613 ([M+Na]$^+$, 100), HRMS (ESI) calcd for $C_{24}H_{51}O_{12}PSi$ [M+Na]$^+$ 613.2780, found 613.2769.

*4.2.8. Enone **13**.* To a mixture of 3 Å molecular sieves (200 mg) and DMSO (0.23 mL, 3.2 mmol) in CH_2Cl_2 (2 mL) was added TFAA (0.27 mL, 1.91 mmol) dropwise at −78 °C with stirring. Stirring was continued for 0.5 h under N_2 at the same temperature. To the stirred mixture was added dropwise a solution of diol **11** (168 mg, 0.28 mmol) in CH_2Cl_2 (2 mL) and then the mixture was stirred for an additional 5 h at −78 °C. To the mixture was added DIEPA (1.1 mL, 6.37 mmol) dropwise with stirring and the stirring was continued for 15 min at −78 °C. The reaction mixture was removed from the cooling bath and allowed to warm to room temperature with stirring. To the mixture was added LiCl (27 mg, 0.64 mmol) and TEA (0.2 mL, 1.28 mmol). The mixture was stirred for 1.5 h at room temperature and then was filtered to get rid of 3 Å molecular sieves. The filtrate was concentrated and the residue was flash chromatographed (n-hexane/EtOAc, 8:1) to yield enone **13** (102 mg, 78%) as a yellowish oil. $[\alpha]_D^{20}$ −48.4 (c 0.80, $CHCl_3$); R_f 0.5 (n-hexane/EtOAc, 3:1); IR (thin film) 2930, 2856, 1700, 1632, 1471, 1378, 1257, 1135, 1040, 1016 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.07 (6H, s), 0.91 (9H, s), 1.24 (3H, t, J=7.2 Hz), 1.31 (3H, s), 1.40 (3H, s), 3.24 (3H, s), 3.29 (3H, s), 3.58–3.61 (1H, m), 3.72–3.75 (1H, m), 4.08 (1H, dd, J=8.7, 11.4 Hz), 4.26 (1H, d, J=11.4 Hz), 4.29 (1H, d, J=18 Hz), 4.59 (1H, d, J=9 Hz), 4.58 (1H, dd, J=1.8, 18 Hz), 4.79 (1H, d, J=6.6 Hz), 5.08 (1H, d, J=6.6 Hz), 6.26 (1H, d, J=2.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.0, −4.9, 15.7, 18.1, 18.2, 18.9, 26.4, 48.4, 49.0, 62.8, 64.9, 72.7, 74.6, 75.5, 97.3, 99.6, 100.6, 123.2, 162.1, 193.3; MS (ESI) m/z (relative intensity) 483 ([M+Na]$^+$, 100), HRMS (ESI) calcd for $C_{22}H_{40}O_8Si$ [M+Na]$^+$ 483.2385, found 483.2393.

4.2.9. Gabosine I. To enone **13** (70 mg, 0.16 mmol) was added TFA (2 mL) and H_2O (0.1 mL). The solution was stirred at room temperature for 5 min. Concentration of the solution followed by flash chromatography ($CHCl_3$/MeOH=8:1) yielded Gabosine I (**1**) (24 mg, 96%) as a colorless oil, identical in all respects to the one synthesized by us previously.[8]

*4.2.10. Allylic alcohol **14**.* To a solution of enone **13** (100 mg, 0.22 mmol) in THF (5 mL) was added K-selectride (1.0 M solution, 0.33 mL, 0.33 mmol) at 0 °C. Stirring was continued for 0.5 h at the same temperature. The excess of the hydride was quenched with methanol (0.1 mL). The reaction mixture was filtered through silica

gel and the residue was washed with EtOAc. Concentration of the solution followed by flash chromatography (*n*-hexane/EtOAc, 6:1) yielded allylic alcohol **14** (98 mg, 98%) as a colorless oil. $[\alpha]_D^{20}$ −30.4 (*c* 0.87, $CHCl_3$); R_f 0.4 (*n*-hexane/EtOAc, 3:1); IR (thin film) 2952, 2929, 2884, 2857, 1653, 1472, 1375, 1251, 1226, 1130, 1094, 1039, 1015 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.90 (9H, s), 1.21 (3H, t, *J*=7.2 Hz), 1.29 (3H, s), 1.32 (3H, s), 3.25 (3H, s), 3.26 (3H, s), 3.55–3.63 (2H, m), 3.66–3.74 (1H, m), 3.66–3.74 (1H, m) 4.12–4.33 (5H, m), 4.80 (1H, d, *J*=6.5 Hz), 5.01 (1H, d, *J*=6.5 Hz), 5.96 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.5, −5.3, 15.1, 17.6, 17.8, 18.3, 25.9, 47.8, 48.0, 62.6, 63.9, 64.7, 67.9, 69.6, 75.4, 96.2, 98.9, 99.5, 120.3, 142.5; MS (ESI) *m*/*z* (relative intensity) 485 ($[M+Na]^+$, 100), HRMS (ESI) calcd for $C_{22}H_{42}O_8Si$ $[M+Na]^+$ 485.2541, found 485.2543.

*4.2.11. Streptol (**3**).* To the allylic alcohol **14** (50 mg, 0.107 mmol) were added TFA (2 mL) and H_2O (0.1 mL). The solution was stirred at room temperature for 5 min. Concentration of the solution followed by flash chromatography ($CHCl_3$/MeOH=4:1) yielded streptol (**3**) (18 mg, 97%) as a colorless oil. $[\alpha]_D^{20}$ +95.6 (*c* 0.45, MeOH), lit.[22] $[\alpha]_D^{20}$ +91.8 (*c* 0.25, H_2O); R_f 0.2 ($CHCl_3$/MeOH=2:1); IR (thin film) 3336, 1676, 1435, 1384, 1203, 1133, 1057 cm^{-1}; ^1H NMR (400 MHz, methanol-d_4) δ 3.43 (1H, dd, *J*=4.2, 10.2 Hz), 3.71 (1H, dd, *J*=7.5, 10.2 Hz), 3.96 (1H, d, *J*=6.9 Hz), 4.2 (3H, m), 5.78–5.81 (1H, m); ^{13}C NMR (100 MHz, methanol-d_4) δ 62.1, 66.9, 71.9, 73.1, 73.3, 121.9, 143.3; MS (ESI) *m*/*z* (relative intensity) 199 ($[M+Na]^+$, 100), HRMS (ESI) calcd for $C_7H_{12}O_5$ $[M+Na]^+$ 199.0577, found 199.0574.

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Supplementary data

^1H NMR and ^{13}C NMR spectra for compounds **3**, **5**–**11**, **13**, and **14**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.06.028.

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