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Article

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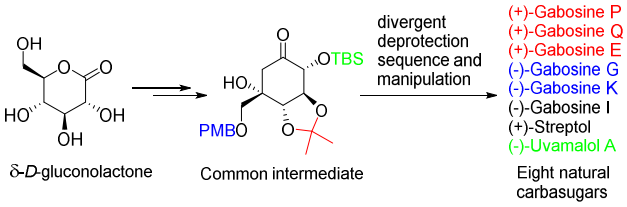


Abstract: A new diversity-oriented approach to C7-cyclitols, which possess a broad spectrum of biological activities, is developed. The key polyoxygenated intermediates with different *O*-protecting groups were accessed by an intramolecular aldol-cyclization of a diketone derived from δ-D-gluconolactone. The versatile intermediates can be easily transformed into structurally different carbasugars based on control of deprotection manipulation. The utility of the robust approach is illustrated by the first syntheses of (+)-gabosines P and Q, as well as the syntheses of several other gabosines and related analogues viz. (+)-gabosine E, (–)-gabosine G, (–)-gabosine I, (–)-gabosine K, (+)-streptol and (–)-uvamalol A. In addition, the absolute configuration of (–)-uvamalol A is assigned by its total synthesis.

Introduction

Many carbasugar-type natural products have a polyoxygenated methyl or hydroxymethyl cyclohexane as a common structural feature, and are known to have a diverse range of biological activities.[1] As a representative family of these C7-cyclitols, gabosines are a class of secondary metabolites isolated from several Streptomyces strains. They have been shown to display a wide range of interesting bioactivities such as antibiotic,[2] anticancer,[3] inhibition of cholesterol biosynthesis,[2] and DNA binding properties.[4] Some synthetic analogues of gabosines also present interesting and promising biological activities,[4a] and several derivatives have been described as very potent emerging antitumor agents due to their glutathione *S*-transferases (GST) inhibition activity.[5]

Although the term gabosines was first used in the literature in 1993,[2] the first isolation of gabosine member, KD16-U1 (identical to gabosine C, **1**), could be traced to the early 1970s.[6] After gabosines L, N and O (**2**-**4**) were reported in 2000,[4a] no new member was found within the next fifteen years. Very recently two new natural cyclitols, named gabosines P and Q (**5** and **6**), were isolated from the culture of *Streptomycetes* strain no. 8.[7] Structurally, **5** and **6** are the monoacylation derivatives of (+)-gabosine E (**7**)[2] at the different hydroxyl groups (Figure 1). Their absolute configurations were assigned by electronic circular dichroism (ECD). (+)-Gabosine P (**5**) exhibited significant α-glucosidase inhibitory activity with an IC_{50} values of 9.07 μM, which was over 70-fold stronger than that of clinical acarbose (IC_{50} = 663.28 μM), whereas (+)-gabosine Q (**6**), the acylation regioisomer of (+)-gabosine P, showed no obvious inhibitory activity.[7] (+)-Gabosine P is a potential leading compound in searching new drugs for the treatment of type 2 diabetes. Some other carbasugars isolated from natural sources, such as (+)-streptol (**8**)[8] and (–)-uvamalol A (**9**),[9] display also a structural pattern within the gabosine family.

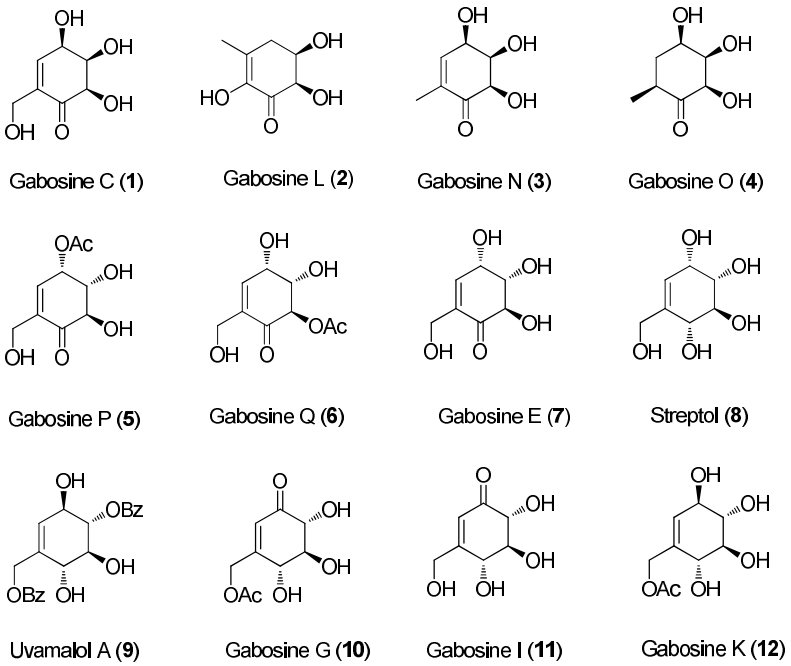


Figure 1. Several Representative Gabosines and Related Natural Carbasugars.

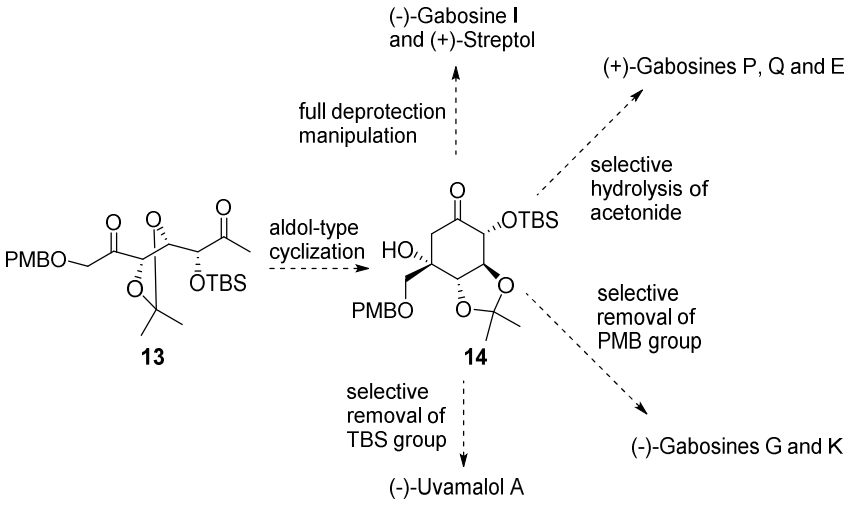
The gabosines and their natural analogues show high structural diversity due to differences in the unsaturation degree of the ring, the substituent positions, and the relative and absolute configuration of their stereogenic centers. More importantly, these structural alteration, including the change of the acetylation position (e.g. **5** vs **6**), may lead to the significant differences in biological activities. Their structural diversity and promising biological activities have motivated synthetic studies directed to these targets. Up to now, most of the gabosines have already been synthesized by various strageties.[10,11] However, the syntheses of (+)-gabosines P and Q have not been reported yet. Moreover, the synthesis strategies suitable for a large number of these compounds from common synthetic intermediates are rare hitherto.[11d,11h,12] Herein, we describe the first synthesis and absolute configuration confirmation of (+)-gabosine P and (+)-gabosine Q via a new diversity-oriented approach. Besides **5** and **6**, the generality versatility of our method can be validated by synthesizing several other representative gabosines and their

analogues including (+)-gabosine E (**7**),[2] (–)-gabosine G (**10**),[2] (–)-gabosine I (**11**),[2,13] (–)-gabosine K (**12**),[2] (+)-streptol (**8**)[8] and (–)-uvamalol A (**9**).[9]

Result and Discussion

Our divergent proposal for the synthesis of these gabosine-type cyclitols is shown in Scheme 1. Novel 1,5-diketone **13** with three different types of hydroxyl protecting groups is designed as the key cyclization precursor. The desired carbocyclic framework is constructed via an intramolecular aldol condensation of **13** to furnish common intermediate **14**, in which the OH protecting groups on the required position can be selectively removed for the subsequent modification. After reduction of the carbonyl group, selective cleavage of acetonide might open a rapid access to gabosines P, Q and E, whereas the removal of the PMB or TBS groups prior to isopropylidene acetal would favor the synthesis of (–)-gabosines G, K and (–)-uvamalol A respectively. In addition, complete deprotection of the intermediates in one step is feasible to produce (–)-gabosine I and (+)-streptol.

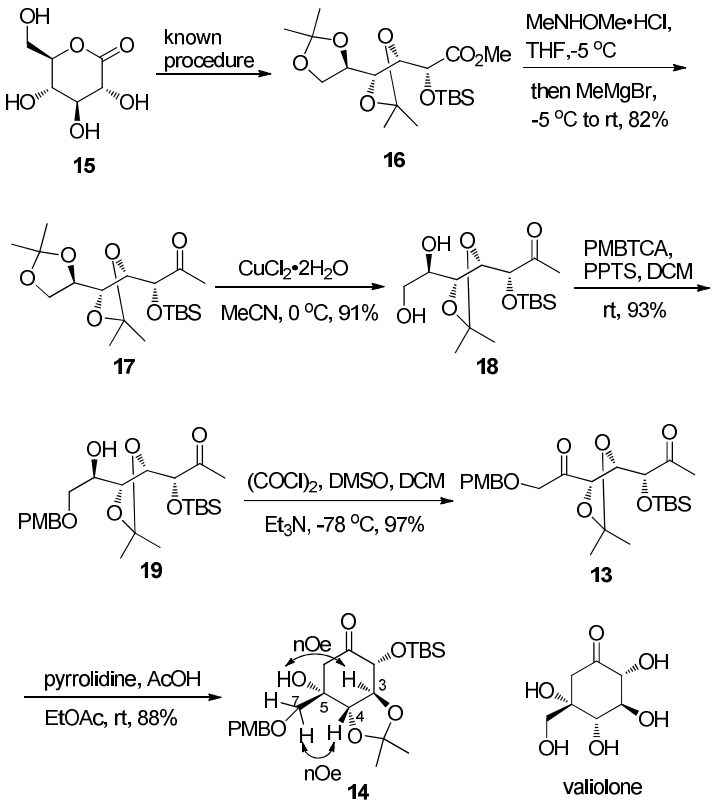
Scheme 1. Diversity-Oriented Strategy for the Syntheses of Gabosines and their Analogues.



The synthesis of 1,5-diketone **13** commenced from *D*-glucono-δ-lactone (**15**) (Scheme 2). According to the previously reported procedure, **15** was converted into the diisopropylidene derivative in high yield,[14] in which the free α-hydroxy group was subsequently protected as TBS ether to give the known derivative **16**.[15] Ester **16** was directly transformed into methyl ketone **17** by *in situ* formation of the Weinreb amide[16] followed by addition of MeMgBr (82% yield). The terminal isopropylidene acetal in **17** was selectively hydrolyzed to afford the diol **18**. After selective protection of primary hydroxyl group as PMB ether, the resulting secondary alcohol **19** was oxidized to the target diketone **13**. The key intramolecular aldol reaction of dione **13** was investigated next. Under the previous conditions for similar aldol-type cyclization (0.3 eq. *L*-proline in DMSO, room temperature, 6 days),[17] our reaction didn't work almost due to structural difference of the dione substrates. Even running the reaction with 1 equiv *L*-proline at 50 ^{o}C for 5 days, a poor yield of aldol product **14** was obtained (11%), along with considerable recovered starting material **13** (75%). Although employment of LDA as promoter led to a full consumption of **13**, cyclization product **14** was still obtained in low yield (19%).[18] Some other base-mediated reaction conditions, including KO*t*Bu,[19] NaH[20] and KHMDS,[21] also led to poor yields or failed to give results. Fortunately, when diketone **13** was treated with pyrrolidine and AcOH at room temperature, the aldol condensation proceeded smoothly to afford **14** in 88% yield.[22]

Although not important for the overall synthesis of the target molecules**,** the configuration of the tertiary hydroxy-bearing C-5 in **14** was assigned by NMR spectroscopic analysis. In its NOESY spectrum, HO-5 signal (δ = 2.33 ppm) correlated with H-3 signal (δ = 4.08 ppm), and H-7a signal (δ = 3.39 ppm) correlated with H-4 signal (δ = 3.94 ppm) respectively. It illustrates the α-configuration of C-5 hydroxyl group in the six-member ring. Namely, aldol product **14** is a hydroxyl-protected derivative of valiolone.[23]

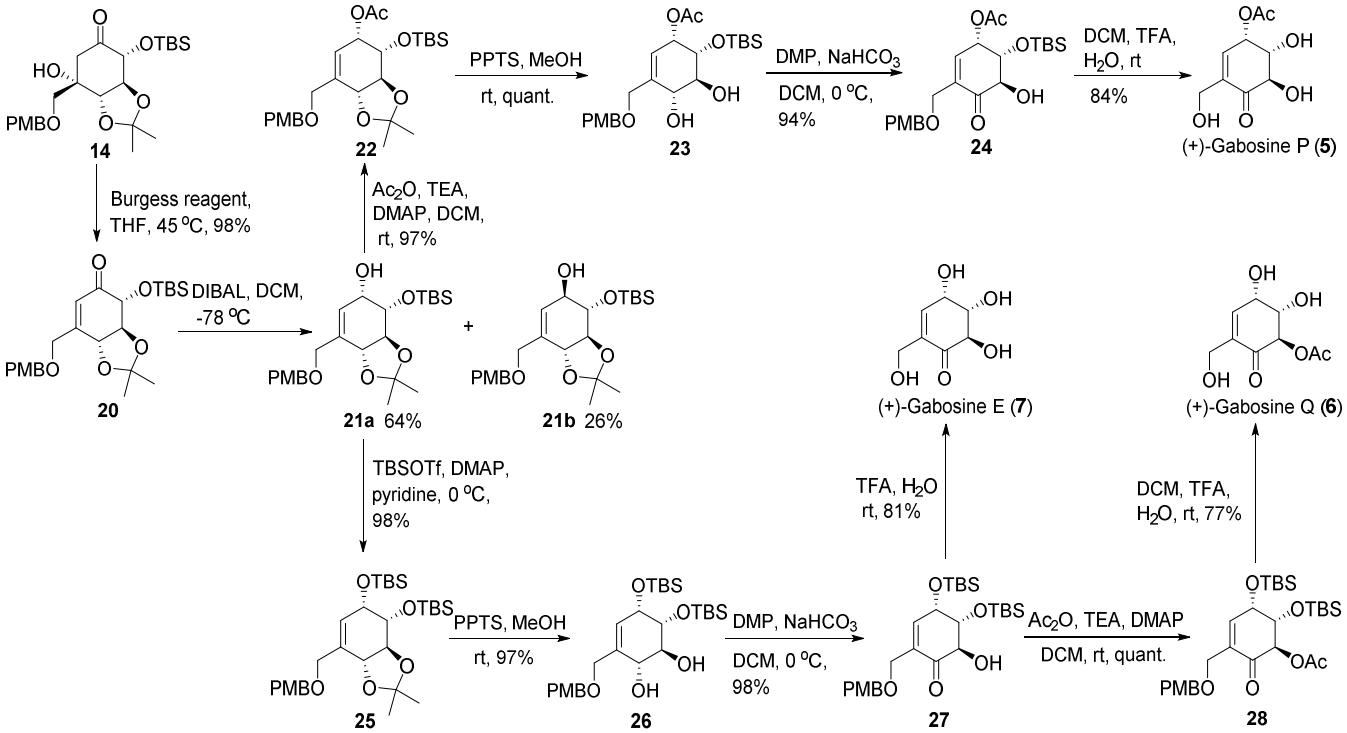
Scheme 2. Construction of Key Polyhydroxy Cyclic Intermediate **14**.



With the cyclic intermediate **14** in hand, we first aimed the syntheses of gabosines P, Q and E (Scheme 3). Elimination of the tertiary alcohol in **14** with Burgess reagent[24] furnished enone **20** in high yield. Selective 1,2-reduction of enone **20** with DIBAL produced a 2.4:1 mixture of diastereoisomeric alcohols **21a** and **21b**, respectively. The stereostructure of major α-alcohol **21a** was subsequently confirmed by its transformation into the natural products including streptol, gabosines P and Q. Thus, the desired isomer **21a** acetylated to give the corresponding acetate **22**, in which the isopropylidene blocking group was then removed with pyridine p-tolenesulfonate (PPTS) in MeOH to afford diol **23**. Chemoselective oxidation of the allyl alcohol functionality in diol **23** was smoothly achieved with the Dess-Martin periodinane to generate enone **24**. Finally, (+)-gabosine P (**5**) was easily obtained via simultaneous removal of PMB and TBS groups. In order to prepare (+)-gabosine Q, TBS was employed to mask the hydroxy group in **21a**.

Following the similar manipulation involving hydrolysis of the acetonide and oxidation of the allyl alcohol, the resulting bis-silyl ether **25** was transformed into enone **27**, which underwent acetylation of the remaining hydroxyl group to afford acetate **28**. **28** and **27** were separately subjected to acid-mediated cleavage of TBS and PMB groups to give (+)-gabosines Q (**6**) and E (**7**). The spectroscopic properties of the synthetic samples (the optical rotation, ^{1}H and ^{13}C NMR spectral data) were identical to those of the natural products.[7] The results validated the molecular structures and the absolute configuration of (+)-gabosines P and Q.

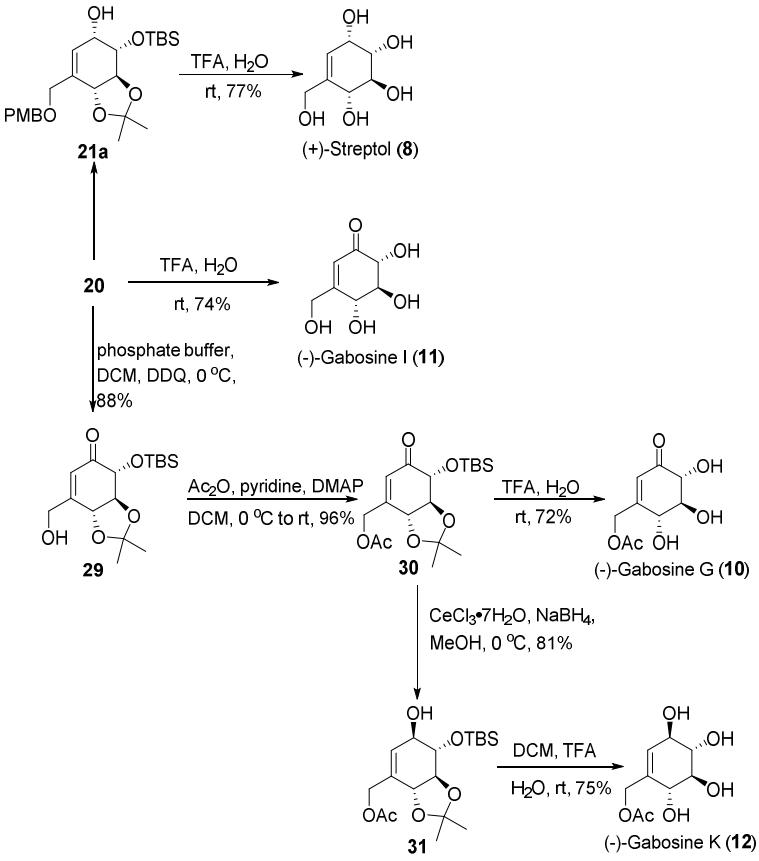
Scheme 3. Syntheses of (+)-Gabosines P, Q and E from **14**.



Next, we set out to utilize the above cyclic intermediates to synthesize other gabosine members by adjusting the deprotection sequence (Scheme 4). Most directly, for these protecting groups all are sensitive

to acid, the conversion of intermediates **20** and **21a** into (–)-gabosine I (**11**) and (+)-streptol (**8**) was easily achieved by a one-pot full deprotection respectively. On the other hand, the PMB group in **20** could be selectively removed with DDQ to give primary alcohol **29**, which was converted into the acetate **30** in high yield. Hydrolysis of acetonide and TBS groups gave (–)-gabosine G (**10**) by treatment with aqueous TFA. Luche reduction[25] of α,β-unsaturated ketone **30** exhibited inverse stereoselectivity to generate β-hydroxy isomer **31** as the major product (dr = 7.3:1), which underwent the acidic hydrolysis to afford (–)-gabosine K (**12**).

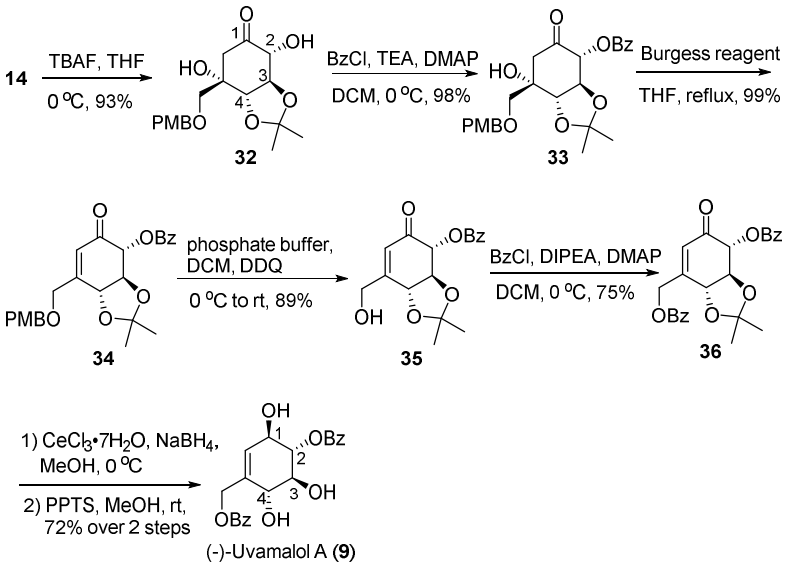
Scheme 4. Syntheses of (–)-Gabosines G, K, I and (+)-Streptol from **20**.



For the further illustration of the utility of this strategy, we turned our attention to the synthesis of (–)-uvamalol A (**9**). (–)-Uvamalol **A** was isolated from the roots of *Uvaria macrophylla*,[9] and its absolute

configuration was not identified. Up to date, there is only one synthesis of (±)-uvamalol **A** reported by the Sureshan group,[11i] and its enantioselective synthesis has not been reported yet. It is necessary to unmask the hydroxy functionality at C-2 prior to the rest for the conversion of the polyhydroxylated intermediates to (–)-uvamalol A. Although the treatment of **20** with TBAF failed to obtain the corresponding de-TBS product, the silyl group in **14** could be removed smoothly under the similar conditions to give α-hydroxyl ketone **32** (Scheme 5). After the benzoylation of the secondary hydroxyl group, the resulting compound **33** was transformed into dehydrated product **34** with Burgess reagent. Removal of PMB ether protecting group with DDQ gave primary alcohol **35**, which was subsequently converted into bis-benzoate **36**. Luche reduction of enone furnished an inseparable mixture of two diastereoisomers. Fortunately, the inseparable isomers were directly subjected to hydrolysis of isopropylidene group resulting in a mixture of deprotected products, which were easily separated on column chromatography to give (–)-uvamalol A (**9**) (72%) and 1-*epi*-uvamalol A (18%). To the best of our knowledge, this is the first synthesis of optically pure uvamalol A. All the spectral data including the optical rotation were found to match with the reported data,[9] and, hence, the absolute configuration of natural (–)-uvamalol **A** (**9**) could be confirmed to be (1*R*, 2*S*, 3*S*, 4*R*).

Scheme 5. Synthesis of (–)-Uvamalol A from **14**.



Conclusion

In summary, we have developed a general carbasugar synthesis strategy featuring employment of the polyoxygented aldol-cyclization products with different *O*-protecting groups as versatile intermediates, in which those masked hydroxyl groups can be selectively modified by control of deprotection to achieve syntheses of various C7-cyclitols. The utility of the robust approach has been demonstrated by the first syntheses of (+)-gabosines P and Q, as well as the syntheses of several other structurally different gabosines and related analogues viz. (+)-gabosine E, (–)-gabosine G, (–)-gabosine I, (–)-gabosine K, (+)-streptol and (–)-uvamalol A. In addition, the unknown absolute configuration of (–)-uvamalol A is established. Further exploitation of this strategy in the construction of other cyclohexa(e)noid natural products and their derivatives is in progress.

Experimental Section

General: Flash chromatography was performed using silica gel (200-300 mesh). Reactions were monitored by thin layer chromatography (TLC). Visualization was achieved under a UV lamp (254 nm), while Infrared (IR) spectra were recorded on a NEXUS 670 FT-IR (Fourier Transform Infrared) Spectrophotometer and are reported in wavenumbers (cm^{-1}). Optical rotations were measured on a polarimeter, and are reported as follows: $[\alpha]_D^T$ (*c*: g/100 mL, in solvent). ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz with TMS as the internal standard and were calibrated using residual undeuterated solvent as an internal reference ($CDCl_3$: ^1H NMR = 7.26, ^{13}C NMR = 77.16; CD_3OD: ^1H NMR = 3.31, ^{13}C NMR = 49.00). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants (*J*) are reported in Hertz (Hz). HRMS spectra were recorded on a LCMS-IT-TOF spectrometer, and methanol or dichloromethane was used to dissolve the sample. Solvents for reaction were distilled prior to use: dichloromethane (DCM), $PhCH_3$ and MeCN from CaH_2, tetrahydrofuran (THF) from Na. Methanol was distilled from magnesium, acetone from potassium carbonate, and other reagents were obtained from commercial suppliers unless otherwise stated.

Compound 17: To a solution of compound **16** (290 mg, 0.717 mmol) and MeNHOMe·HCl (87.5 mg, 0.897 mmol) in THF (7 mL) at –5 °C was added dropwise MeMgBr (3 M in THF, 1.44 mL, 4.30 mmol). The mixture was stirred at –5 °C for 90 min, and then allowed to warm slowly to room temperature in the low-temperature bath. The reaction was stirred for 14 h at room temperature before saturated aqueous NH_4Cl (1.5 mL) and EtOAc (5 mL) were slowly added. The phases were separated and the aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4,

filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 16:1) to give ketone **17** (228 mg, 82%) as a colorless crystalline solid. m.p. 51 – 52 ℃; $[\alpha]_D^{18}$ +73.5 (*c* 1.62, $CHCl_3$); IR (neat) ν_{max} 2931, 1719, 1375, 1254, 1149, 1074, 846 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.17 – 4.12 (m, 2H), 4.09 (d, *J* = 2.4 Hz, 1H), 4.04 – 3.92 (m, 2H), 3.78 (dd, *J* = 8.4, 6.8 Hz, 1H), 2.22 (s, 3H), 1.40 (s, 3H), 1.37 (s, 3H), 1.32 (s, 6H), 0.94 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.8, 110.4, 109.7, 82.4, 78.6, 77.4, 76.7, 68.3, 27.5, 27.1, 26.8, 26.4, 25.8, 25.2, 18.2, –4.7, –4.9; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{19}H_{36}NaO_6Si$ 411.2179; Found 411.2178.

Compound 18: $CuCl_2 \cdot 2H_2O$ (369 mg, 2.16 mmol) was added to the solution of compound **17** (840 mg, 2.16 mmol) in CH_3CN (4 mL) at 0 °C. The vigorously stirred mixture was kept at the same temperature for 45min. The reaction was quenched with saturated aqueous $NaHCO_3$ (1 mL). The mixture was filtered and the filtrate was extracted with EtOAc (3 × 10 mL). Then the organic phase was dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 8:1) to yield diol **18** (301 mg, 91%) as a white solid. m.p. 85 – 87 ℃; $[\alpha]_D^{19}$ +36.7 (*c* 1.31, $CHCl_3$); IR (neat) ν_{max} 3448, 2933, 2860, 1713, 1467, 1374, 1254, 1139, 1079, 930, 842, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.23 (d, *J* = 2.4 Hz, 1H), 4.16 (dd, *J* = 7.6, 2.8 Hz, 1H), 3.95 (t, *J* = 7.4 Hz, 1H), 3.81 (d, *J* = 10.8 Hz, 1H), 3.70 (dt, *J* = 12.8, 3.6 Hz, 1H), 3.61 (m, 1H), 3.36 (brs, 1H), 2.77 (brs, 1H), 2.22 (s, 3H), 1.39 (s, 3H), 1.33 (s, 3H), 0.93 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.3, 110.0, 81.7, 78.3, 76.2, 73.3, 64.3, 27.6, 27.3, 26.8, 25.9, 18.3, –4.8, –5.0; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{16}H_{32}NaO_6Si$ 371.1866; Found 371.1867.

Compound 19: To a solution of compound **18** (235 mg, 0.675 mmol) in DCM (6 mL) was added PPTS (17 mg, 0.0675 mmol) and PMBTCA (210 mg, 0.743 mmol). The mixture was stirred at room temperature for 2 h, and then evaporated under reduced pressure and purified by flash column chromatography (petroleum ether/EtOAc, 8:1) on silica gel to afford the desired product **19** (294 mg, 93%) as a slight yellow oil. $[\alpha]_D^{19}$ +43.0 (*c* 0.54, $CHCl_3$); IR (neat) ν_{max} 3447, 2932, 2859, 1714, 1613, 1514, 1465, 1372, 1302, 1250, 1137, 1077, 929, 881, 840, 779, 678 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 2H), 6.90 – 6.82 (m, 2H), 4.53 – 4.46 (m, 2H), 4.22 (dd, *J* = 7.2, 2.4 Hz, 1H), 4.16 (d, *J* = 2.8Hz, 1H), 4.01 (t, *J* = 7.8 Hz, 1H), 3.80 (s, 3H), 3.79 – 3.74 (m, 1H), 3.70 (dd, *J* = 9.6, 3.2 Hz, 1H), 3.51 (dd, *J* = 9.6, 6.0Hz, 1H), 2.51 (d, *J* = 4.4 Hz, 1H), 2.21 (s, 3H), 1.40 (s, 3H), 1.32 (s,3H), 0.94 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.9, 159.5, 130.0, 129.6, 114.0, 110.1, 81.9, 78.7, 75.5, 73.3, 72.6, 71.6, 55.4, 27.4, 27.3, 26.9, 25.9, 18.3, –4.7, –4.5; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{40}NaO_7Si$ 491.2441; Found 491.2439.

Compound 13: To a stirred solution of $(COCl)_2$ (106 μL, 1.21 mmol) in DCM (10 mL) was added DMSO (171 μL, 2.42 mmol) in DCM (0.2 mL) at –78 ℃ under argon. After 40 min, a solution of **19** (378 mg, 0.807 mmol) in DCM (2 mL) was slowly added dropwise to the reaction mixture at –78 ℃ under argon. After 60 min, Et_3N (675 μL, 4.84 mmol) was added dropwise to the above mixture. Then the mixture was allowed to warm slowly to room temperature by removing low-temperature reactor. The reaction mixture was poured into saturated $NaHCO_3$ solution, extracted with DCM (3 × 15 mL), dried over anhydrous Na_2SO_4. The evaporated residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 8:1) to give diketone **13** (365 mg, 97%) as a slight yellow oil. $[\alpha]_D^{19}$ +80.0 (*c* 0.17, $CHCl_3$);

IR (neat) ν_{max} 2932, 2858, 1732, 1613, 1514, 1465, 1379, 1302, 1251, 1138, 1093, 1037, 839, 780 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2H), 6.90 – 6.84 (m, 2H), 4.52 (s, 2H), 4.49 – 4.33 (m, 3H), 4.25 (dd, *J* = 7.6, 3.2 Hz, 1H), 4.13 (d, *J* = 3.2 Hz, 1H), 3.79 (s, 3H), 2.21 (s, 3H), 1.42 (s, 3H), 1.31 (s, 3H), 0.93 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.2, 206.2, 159.6, 129.9, 129.1, 114.0, 111.6, 79.8, 79.3, 78.2, 73.1, 72.4, 55.4, 27.2, 26.6, 25.8, 18.2, –4.8, –5.1; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{38}NaO_7Si$ 489.2284; Found 489.2280.

Compound 14: To a solution of **13** (1.58 g, 3.39 mmol) in EtOAc (35 mL) was added pyrrolidine (0.3 mL, 3.56 mmol) and AcOH (0.2 mL, 3.56 mmol) at room temperature under argon. After stirring for 30 h, the reaction was evaporated under reduced pressure and purified by flash column chromatography (petroleum ether/EtOAc, 8:1) on silica gel to afford **14** (1.39 g, 88%) as a colorless oil. $[\alpha]_D^{19}$ +4.3 (*c* 0.94, $CHCl_3$); IR (neat) ν_{max} 3455, 2932, 2857, 1733, 1612, 1514, 1466, 1376, 1296, 1249, 1176, 1116, 1024, 1002, 841, 781, 666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.21 (m, 2H), 6.91 – 6.85 (m, 2H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.26 (d, *J* = 10.8 Hz, 1H), 4.08 (dd, *J* = 11.0, 9.4 Hz, 1H), 3.94 (d, *J* = 9.6 Hz, 1H), 3.81 (s, 3H), 3.45 (d, *J* = 9.0 Hz, 1H), 3.39 (d, *J* = 9.0 Hz, 1H), 2.58 (s, 2H), 2.33 (s, 1H), 1.49 (s, 3H), 1.45 (s, 3H), 0.92 (s, 9H), 0.14 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6, 159.6, 129.8, 129.5, 114.0, 111.9, 79.2, 77.7, 77.4, 73.3, 73.0, 70.9, 55.4, 46.9, 27.4, 26.7, 25.9, 18.8, –4.6, –5.1; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{38}NaO_7Si$ 489.2284; Found 489.2278.

Compound 20: To a solution of **14** (573 mg, 1.22 mmol) in THF (12 mL) was added freshly prepared Burgess reagent (625 mg, 2.44 mmol) at room temperature under argon. Then the reaction mixture was stirred rapidly at 45 ℃ for 50 min, extracted with EtOAc (3 × 20mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 6:1)

to give **20** (540 mg, 98%) as a slight yellow oil. $[\alpha]_D^{18}$ –25.1 (*c* 0.90, $CHCl_3$); IR (neat) ν_{max} 2988, 2932, 2889, 2856, 1689, 1615, 1586, 1514, 1466, 1379, 1299, 1250, 1148, 1106, 1068, 1037, 967, 928, 890, 842, 781, 675 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.24 (m, 2H), 6.91 – 6.86 (m, 2H), 6.11 (q, *J* = 2.0 Hz, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), 4.51 (d, *J* = 11.6 Hz, 1H), 4.33 – 4.28 (m, 3H), 4.16 (d, *J* = 10.8 Hz, 1H), 3.81 (s, 3H), 3.82 – 3.77 (m, 1H), 1.47 (s, 3H), 1.44 (s, 3H), 0.94 (s, 9H), 0.19 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 159.6, 157.7, 129.7, 129.5, 123.1, 114.1, 112.6, 82.5, 78.3, 75.8, 73.0, 67.0, 55.4, 26.9, 26.6, 25.9, 18.8, –4.4, –5.1; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{36}NaO_6Si$ 471.2179; Found 471.2180.

Compound 21a: To a solution of **20** (238 mg, 0.531 mmol) in CH_2Cl_2 (10 mL) was added dropwise DIBAL-H (1.5 M in toluene, 0.71 mL, 1.06 mmol) at −78 °C under argon. After 30 min, saturated aqueous sodium potassium tartrate (10 mL) was added and the mixture was diluted with CH_2Cl_2 (5 mL). The reaction mixture was warmed to room temperature and kept still for 3 – 5 h until the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine (2 × 10 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 8:1) to yield compound **21a** (153 mg, 64%) and **21b** (62 mg, 26%) respectively.

21a: a colorless oil; $[\alpha]_D^{18}$ +21.4 (*c* 0.28, $CHCl_3$); IR (neat) ν_{max} 3528, 2931, 2857, 1613, 1513, 1465, 1377, 1296, 1249, 1169, 1088, 841, 781, 669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ7.29 – 7.26 (m, 2H), 6.89 – 6.85 (m, 2H), 5.78 (dd, *J* = 4.0, 2.4Hz, 1H), 4.51 (d, *J* = 11.2 Hz, 1H), 4.47 (d, *J* = 11.2 Hz, 1H),4.33 (t, *J* = 4.6 Hz, 1H), 4.19 (dd, *J* = 13.4, 1.4 Hz, 1H), 4.05 (d, *J* = 13.6 Hz, 1H), 4.01 (dd, *J* = 8.0, 1.2 Hz, 1H), 3.95 (dd, *J* = 10.8, 5.6 Hz, 1H), 3.80 (s, 3H), 3.73 (dd, *J* = 10.8, 8.4 Hz, 1H), 3.27 (s, 1H), 1.43 (s, 3H),

1.41 (s, 3H), 0.93 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 137.8, 130.4, 129.5, 123.2, 113.9, 112.1, 78.3, 77.0, 72.5, 71.3, 69.0, 68.3, 55.4, 27.0, 26.8, 25.9, 18.4, –4.3, –4.9; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{38}NaO_6Si$ 473.2335; Found 473.2338.

21b: a colorless oil; $[\alpha]_D^{18}$ –12.1 (*c* 0.34, $CHCl_3$); IR (neat) ν_{max} 3443, 2931, 2856, 1613, 1514, 1465, 1376, 1301, 1249, 1174, 1097, 841, 781, 668 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 2H), 6.90 – 6.84 (m, 2H), 5.58 (s, 1H), 4.51 (d, *J* = 11.6 Hz, 1H), 4.47 (d, *J* = 11.6 Hz, 1H), 4.29 (s, 1H), 4.20 – 4.12 (m, 2H), 4.05 (d, *J* = 14.4 Hz, 1H), 3.93 (dd, *J* = 10.6, 6.2 Hz, 1H), 3.80 (s, 3H), 3.51 (dd, *J* = 10.8, 8.8 Hz, 1H), 2.01 (d, *J* = 5.2 Hz, 1H), 1.42 (s, 3H), 1.40 (s, 3H), 0.92 (s, 9H), 0.14 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 136.2, 130.4, 129.5, 124.1, 113.9, 111.4, 80.3, 77.9, 77.7, 76.7, 72.4, 67.9, 55.4, 26.9, 26.7, 26.0, 18.4, –4.2, –4.7; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{38}NaO_6Si$ 473.2335; Found 473.2336.

Compound 22: To a stirred solution of **21a** (206 mg, 0.457 mmol) in CH_2Cl_2 (4.6 mL) was added Et_3N (191 µL, 1.37 mmol) and DMAP (5.6 mg, 0.0457 mmol) at room temperature. Then Ac_2O (129.6 µL, 1.37 mmol) was slowly added dropwise. The reaction was allowed to stir at room temperature for 4 h, extracted with CH_2Cl_2 (3 × 10 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 16:1) to give **22** (219 mg, 97%) as a colorless oil. $[\alpha]_D^{18}$ +78.9 (*c* 0.23, $CHCl_3$); IR (neat) ν_{max} 2932, 2896, 2857, 1743, 1613, 1586, 1514, 1466, 1373, 1301, 1246, 1173, 1102, 1031, 966, 938, 892, 862, 840, 783, 673 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 2H), 6.90 – 6.84 (m, 2H), 5.69 (t, *J* = 4.8 Hz, 1H), 5.57 (dd, *J* = 4.0, 2.2 Hz, 1H), 4.51 (d, *J* = 10.8 Hz, 1H), 4.47 (d, *J* = 11.2 Hz, 1H), 4.17 (dd, *J* = 14.0, 1.6 Hz, 1H), 4.08 (d, *J* = 14.0 Hz, 1H), 4.01 (dd, *J* = 10.8, 5.2 Hz, 1H), 3.99 – 3.95 (m, 1H), 3.80 (s, 3H), 3.77 (dd, *J* = 11,2, 8.4 Hz, 1H), 2.07 (s, 3H),

1.44 (s, 3H), 1.43 (s, 3H), 0.89 (s, 9H), 0.13 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 159.4, 140.1, 130.2, 129.5, 120.1, 113.9, 112.2, 78.5, 72.6, 70.5, 70.3, 68.0, 55.4, 26.9, 26.8, 25.8, 21.2, 18.6, –4.9, –4.9; HRMS (ESI - TOF) m/z $[M + H]^+$ calcd for $C_{26}H_{41}O_7Si$ 493.2622; Found 493.2625.

Compound 23: To a stirred solution of **22** (219 mg, 0.445 mmol) in MeOH (9 mL) was added PPTS (111 mg, 0.445 mmol) at room temperature. After stirring for 75 min, the reaction was evaporated under reduced pressure and purified by flash column chromatography (petroleum ether/EtOAc, 6:1) to afford diol **23** (201 mg, quant.) as a colorless oil. $[\alpha]_D^{19}$ +113.5 (*c* 0.83, $CHCl_3$); IR (neat) ν_{max} 3451, 2931, 2857, 1740, 1612, 1586, 1513, 1466, 1369, 1301, 1252, 1176, 1142, 1036, 941, 892, 838, 782, 674 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.20 (m, 2H), 6.92 – 6.81 (m, 2H), 5.78 (dd, *J* = 5.4, 1.4 Hz, 1H), 5.39 (t, *J* = 4.8 Hz, 1H), 4.49 (d, *J* = 11.2 Hz, 1H), 4.44 (d, *J* = 11.2 Hz, 1H), 4.22 (d, *J* = 12.8 Hz, 1H), 4.19 – 4.14 (m, 1H), 4.02 (d, *J* = 12.4 Hz, 1H), 3.91 (ddd, *J* = 9.8, 7.6, 2.0 Hz, 1H), 3.80 (s, 3H), 3.66 (dd, *J* = 9.8, 4.2 Hz, 1H), 2.99 (d, *J* = 4.4 Hz, 1H), 2.55 (d, *J* = 2.0 Hz, 1H), 2.04 (s, 3H), 0.89 (s, 9H), 0.12 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 159.5, 141.8, 129.9, 129.6, 120.6, 114.0, 73.5, 72.7, 72.4, 71.1, 69.9, 68.6, 55.4, 25.8, 21.2, 18.2, –4.6, –4.8; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{23}H_{36}NaO_7Si$ 475.2128; Found 475.2127.

Compound 24: To a suspension of the above diol **23** (152 mg, 0.336 mmol) and $NaHCO_3$ (30 mg, 0.353 mmol) in CH_2Cl_2 (17 mL) was added Dess-Martin periodinane (150 mg, 0.353 mmol). The resulting solution was stirred for 30 minutes at 0 ℃. The reaction mixture was quenched with saturated $Na_2S_2O_3$ solution, stirred until clarification, extracted with CH_2Cl_2 (3 × 20mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/ EtOAc, 8:1) to afford the product **24** (142 mg, 94%) as a colorless oil. $[\alpha]_D^{19}$ +155.5 (*c* 0.20, $CHCl_3$); IR (neat)

ν_{max} 3488, 2931, 2857, 1747, 1686, 1613, 1514, 1466, 1370, 1305, 1247, 1147, 1033, 938, 901, 838, 782, 670 cm^{-1}; ^1H NMR (400 MHz) δ 7.29 – 7.19 (m, 2H), 6.94 (dt, *J* = 6.0, 1.8 Hz, 1H), 6.91 – 6.85 (m, 2H), 5.68 (t, *J* = 5.0, 1H), 4.55 – 4.48 (m, 2H), 4.46 (dd, *J* = 10.4, 2.4 Hz, 1H), 4.24 ((dt, *J* = 14.8, 1.6 Hz, 1H), 4.17 (dd, *J* = 14.8, 1.6 Hz, 1H), 3.90 (dd, *J* = 10.0, 4.4 Hz, 1H), 3.81 (s, 3H), 3.27 (d, *J* = 2.4 Hz, 1H), 2.10 (s,3H), 0.89 (s, 9H), 0.14 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 170.2, 159.4, 138.7, 137.6, 129.6, 129.5, 113.9, 74.5, 73.1, 72.4, 67.4, 65.5, 55.3, 25.6, 20.8, 18.2, –4.7, –5.1; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{23}H_{34}NaO_7Si$ 473.1971; Found 473.1968.

(+)-Gabosine P (5): To a stirred solution of **24** (72 mg, 0.16 mmol) in CH_2Cl_2 (4.4 mL) was added TFA (0.74 mL) and H_2O (74 μL) at room temperature. The solution was stirred at room temperature for 24 h. Concentration of the solution followed by flash chromatography ($CHCl_3$/MeOH, 10:1) to yield (+)-**5** (29 mg, 84%) as a colorless oil. $[\alpha]_D^{17}$ +275.6 (*c* 0.27, MeOH) {lit.[7] $[\alpha]_D^{21}$ +106.9 (*c* 0.37, MeOH)}; IR (neat) ν_{max}3379, 2925, 1737, 1689, 1374, 1240, 1141, 1094, 1026, 941, 896 cm^{-1}; ^1H NMR (400 MHz, MeOD) δ 6.88 (dt, *J* = 5.4, 1.8 Hz, 1H), 5.67 (t, *J* = 4.6 Hz, 1H), 4.33 (d, *J* = 9.6 Hz, 1H), 4.26 – 4.19 (m, 2H), 3.98 (dd, *J* = 10.0, 4.0 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 198.8, 172.2, 142.3, 137.1, 75.5, 72.3, 69.8, 59.4, 20.7; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_9H_{12}NaO_6$ 239.0532; Found 239.0530.

Compound 25: To a stirred solution of **21a** (357 mg, 0.793 mmol) in pyridine (8 mL) was added DMAP (5 mg, 0.0396 mmol) and TBSOTf (0.55 mL, 2.38 mmol) at 0 °C under argon. After stirring for 5 min, the reaction was concentrated by rotary evaporation under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 20:1) to give **25** (438 mg, 98%) as a colorless oil. $[\alpha]_D^{18}$ +62.5 (*c* 0.20, $CHCl_3$); IR (neat) ν_{max} 2932, 2892, 2857, 1613, 1514, 1467, 1377, 1298, 1250,

1172, 1091, 1040, 967, 944, 907, 869, 836, 779, 669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 2H), 6.89 – 6.84 (m, 2H), 5.61 (dd, *J* = 4.4, 2.4 Hz, 1H), 4.52 – 4.46 (m, 2H), 4.32 – 4.28 (m, 1H), 4.17 (dd, *J* = 13.2, 1.2 Hz, 1H), 4.03 (d, *J* = 13.2 Hz, 1H), 3.93 (m, 1H), 3.89 – 3.83 (m, 2H), 3.81 (s, 3H), 1.44 (s, 3H), 1.43 (s, 3H), 0.93 (s,9H), 0.89 (s,9H), 0.12 (s, 3H), 0.11 (s,3H), 0.09 (s,3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 135.9, 130.6, 129.4, 125.5, 113.9, 111.6, 77.9, 77.7, 72.6, 72.4, 71.2, 68.5, 55.4, 27.0, 26.9, 26.3, 26.1, 18.9, 18.4, –4.0, –4.2, –4.2, –4.3; HRMS (ESI - TOF) m/z $[M + H]^+$ calcd for $C_{30}H_{53}O_6Si_2$ 565.3381; Found 565.3378.

Compound 26: To a solution of **25** (429 mg, 0.76 mmol) in MeOH (15 mL) was added PPTS (191 mg, 0.76 mmol) at room temperature. After stirring for 90 min, the reaction was evaporated under reduced pressure and purified by flash column chromatography (petroleum ether/EtOAc, 6:1) to give diol **26** (387 mg, 97%) as a colorless oil. $[\alpha]_D^{18}$ +73.1 (*c* 0.54, $CHCl_3$); IR (neat) ν_{max} 3445, 2954, 2931, 2890, 2857, 1613, 1586, 1514, 1467, 1389, 1361, 1300, 1251, 1174, 1135, 1092, 1037, 953, 900, 866, 835, 778, 710, 674 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 2H), 6.91 – 6.80 (m, 2H), 5.74 (dd, *J* = 5.0, 1.0 Hz, 1H), 4.51 – 4.43 (m, 2H), 4.23 – 4.20 (m, 2H), 4.10 (t, *J* = 6.0 Hz, 1H), 4.05 – 3.96 (m, 2H), 3.80 (s, 3H), 3.54 (dd, *J* = 9.0, 3.4 Hz, 1H), 2.83 (d, *J* = 5.2 Hz, 1H), 2.36 (d, *J* = 2.0 Hz, 1H), 0.92 (s, 9H), 0.88 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 137.9, 130.3, 129.5, 125.9, 114.0, 73.3, 72.9, 72.7, 72.5, 70.3, 68.1, 55.4, 26.1, 26.1, 18.4, 18.3, –3.7, –3.8, –4.3, –4.6; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{27}H_{48}NaO_6Si_2$ 547.2887; Found 547.2884.

Compound 27: To a stirred solution of diol **26** (235 mg, 0.448 mmol) and $NaHCO_3$ (41 mg, 0.493 mmol) in CH_2Cl_2 (23 mL) was added Dess-Martin periodinane (209 mg, 0.493 mmol) at 0 °C. The resulting solution was stirred at 0 °C for 20 minutes. The reaction mixture was quenched with saturated $Na_2S_2O_3$

solution, stirred until clarification, extracted with CH_2Cl_2 (3 × 25 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc, 8:1) to afford the enone **27** (229 mg, 98%) as a colorless oil. $[\alpha]_D^{18}$ +83.7 (*c* 0.52, $CHCl_3$); IR (neat) ν_{max} 3496, 2931, 2891, 2857, 1680, 1613, 1514, 1467, 1387, 1360, 1301, 1251, 1141, 1078, 1037, 967, 938, 903, 835, 779, 708, 667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 2H), 6.98 (dt, *J* = 6.0, 1.6 Hz, 1H), 6.91 – 6.82 (m, 2H), 4.57 (dd, *J* = 10.0, 2.4 Hz, 1H), 4.54 – 4.47 (m, 2H), 4.38 (dd, *J* = 6.0, 3.2 Hz, 1H), 4.24 (ddd, *J* = 14.4, 1.6, 0.8 Hz, 1H), 4.14 (dd, *J* = 14.4, 1.6 Hz, 1H), 3.81 (s, 3H), 3.74 (dd, *J* = 10.0, 3.2 Hz, 1H), 3.18 (d, *J* = 2.4 Hz, 1H), 0.93 (s, 9H), 0.89 (s, 9H), 0.15 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.1, 159.4, 143.1, 135.6, 130.0, 129.4, 114.0, 74.9, 74.3, 72.3, 68.2, 65.7, 55.4, 26.1, 25.9, 18.5, 18.3, –3.9, –4.2, –4.4, –4.4; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{27}H_{46}NaO_6Si_2$ 545.2731; Found 545.2733.

Compound 28: To a solution of **27** (95 mg, 0.183 mmol) in CH_2Cl_2 (3.7 mL) was added Et_3N (38.5 µL, 0.275 mmol) and DMAP (2.2 mg, 0.0183 mmol) at room temperature. Then Ac_2O (26 µL, 0.275 mmol) was slowly added dropwise. The reaction was allowed to stir at room temperature for 30 min, extracted with DCM (3 × 10 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 12:1) to give **28** (102 mg, quant.) as a colorless oil. $[\alpha]_D^{18}$ +86.8 (*c* 0.60, $CHCl_3$); IR (neat) ν_{max} 2932, 2892, 2858, 1754, 1693, 1613, 1514, 1467, 1376, 1301, 1251, 1137, 1088, 1036, 967, 839, 778, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.21 (m, 2H), 6.97 (dt, *J* = 6.0, 1.8 Hz, 1H), 6.91 – 6.84 (m, 2H), 5.71 (d, *J* = 10.0 Hz, 1H), 4.51 (d, *J* = 11.6 Hz, 1H), 4.48 (d, *J* = 11.6 Hz, 1H), 4.40 (dd, *J* = 6.0, 3.2 Hz, 1H), 4.22 (ddd, *J* = 14.8, 1.6, 0.8 Hz, 1H), 4.09 (dd, *J* = 14.8, 1.6 Hz, 1H), 4.02 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.80 (s, 3H), 2.17 (s, 3H), 0.90 (s, 9H), 0.89 (s,

9H), 0.13 (s, 3H), 0.10 (s, 3H), 0.09 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.2, 170.2, 159.4, 141.9, 136.7, 130.1, 129.4, 114.0, 75.5, 72.8, 71.9, 68.2, 65.6, 55.4, 25.9, 25.9, 21.0, 18.3, 18.2, –3.9, –4.0, –4.5, –4.7; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{29}H_{48}NaO_7Si_2$ 587.2836; Found 587.2833.

(+)-Gabosine Q (6): To a stirred solution of **28** (89 mg, 0.159 mmol) in CH_2Cl_2 (2.7 mL) was added TFA (0.9 mL) and H_2O (45 μL) at room temperature. The solution was stirred at room temperature for 30 h. The reaction was concentrated by rotary evaporation under reduced pressure. The residue followed by flash chromatography ($CHCl_3$/MeOH, 10:1) to yield (+)-**6** (26 mg, 77%) as a colorless crystalline solid. m.p. 133 – 135 ℃; $[\alpha]_D^{16}$ +138.4 (*c* 0.23, MeOH) {lit.[7] $[\alpha]_D^{21}$ +75.4 (*c* 0.42, MeOH)}; IR (neat) ν_{max} 3380, 2925, 1736, 1691, 1378, 1233, 1097, 1049, 953, 898 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 7.01 (dt, *J* = 6.0, 1.7 Hz, 1H), 5.59 (d, *J* = 10.8 Hz, 1H), 4.52 – 4.47 (m, 1H), 4.25 (d, *J* = 15.6 Hz, 1H), 4.19 (dd, *J* = 15.4, 1.4 Hz, 1H), 4.00 (dd, *J* = 10.8, 4.0 Hz, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 194.3, 172.2, 141.9, 140.5, 76.7, 71.1, 67.1, 59.3, 20.7; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_9H_{12}NaO_6$ 239.0532; Found 239.0527.

(+)-Gabosine E (7): To enone **27** (65 mg, 0.124 mmol) was added TFA (1.3 mL) and H_2O (65 μL). The solution was stirred at room temperature for 1h. Concentration of the solution followed by flash chromatography ($CHCl_3$/MeOH, 2:1) to yield (+)-**7** (18 mg, 81%) as a colorless oil. $[\alpha]_D^{17}$ +216.8 (*c* 0.27, MeOH) {lit.[2] $[\alpha]_D^{20}$ +148.0 (*c* 0.95, MeOH)}; IR (neat) ν_{max} 3362, 2923, 2870, 1684, 1388, 1185, 1137, 1092, 1052 cm^{-1}; ^{1}H NMR (400 MHz, MeOD) δ 6.93 (dt, *J* = 5.4, 1.8 Hz, 1H), 4.51 – 4.47 (m, 1H), 4.35 (d, *J* = 10,0 Hz, 1H), 4.30 – 4.24 (m, 1H), 4.21 (dd, *J* = 15.4,1.0 Hz, 1H), 3.77 (dd, *J* = 10.0, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, MeOD) δ 199.7, 141.9, 139.9, 75.1, 73.9, 67.1, 59.5; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_7H_{10}NaO_5$ 197.0426; Found 197.0426.

(-)-Gabosine I (11): To enone **20** (40 mg, 0.089 mmol) was added TFA (1 mL) and H_2O (50 μL). The solution was stirred at room temperature for 5 min. Concentration of the solution followed by flash chromatography ($CHCl_3$/MeOH, 6:1) to yield (–)-**11** (11 mg, 74%) as a colorless oil. $[\alpha]_D^{17}$ –140.0 (*c* 0.1, MeOH) {lit.[2] $[\alpha]_D^{20}$ –61.4 (*c* 1.0, MeOH)}; IR (neat) ν_{max} 3380, 2924, 2871, 1678, 1432, 1201, 1123, 1066, 1026 cm^{-1}; ^1H NMR (400 MHz, MeOD) δ 6.15 (q, *J* = 2.0 Hz, 1H), 4.54 – 4.47 (m, 1H), 4.39 – 4.30 (m, 2H), 4.02 (d, *J* = 10.8 Hz, 1H), 3.60 (dd, *J* = 10.8, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, MeOD) δ 199.5, 167.9, 121.3, 79.4, 78.0, 73.7, 62.0; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_7H_{10}NaO_5$ 197.0426; Found 197.0426.

(+)-Streptol (8): Compound **21a** (80 mg, 0.177 mmol) was dissolved in a mixture of TFA (1 mL) and H_2O (50 μL). The resulting solution was stirred at room temperature for 5 min. Concentration of the solution followed by purification through flash chromatography ($CHCl_3$/MeOH, 4:1) to yield (+)-**8** (24 mg, 77%) as a colorless oil. $[\alpha]_D^{17}$ +102.0 (*c* 0.23, MeOH) {lit.[26] $[\alpha]_D^{20}$ +95.6 (*c* 0.45, MeOH)}; IR (neat) ν_{max} 3354, 2922, 1642, 1405, 1261, 1098, 1059, 1014 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 5.84 – 5.80 (m, 1H), 4.25 – 4.12 (m, 3H), 3.99 (d, *J* = 7.2 Hz, 1H), 3.73 (dd, *J* = 10.0, 7.2 Hz, 1H), 3.47 (dd, *J* = 10.2, 4.2 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 144.1, 122.9, 74.1, 73.8, 72.6, 67.6, 62.9; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_7H_{12}NaO_5$ 199.0582; Found 199.0580.

Compound 29: To a stirred solution of **20** (155 mg, 0.345 mmol) in CH_2Cl_2 (26 mL) and phosphate buffer (pH = 7.2, 2.6 mL) was added DDQ (235 mg, 1.036 mmol) at 0 °C. The resulting mixture was stirred for 12 h at 0 °C. The separated organic layer was washed with saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$ (1:1), water and brine successively. The organic layer was concentrated by rotary evaporation under reduced pressure. The residue was purified by flash chromatography (petroleum

ether/EtOAc, 3:1) to yield **29** (100 mg, 88%) as a white solid. m.p. 73 – 75 ℃; $[\alpha]_D^{18}$ –42.6 (*c* 0.86, $CHCl_3$); IR (neat) ν_{max} 3447, 2933, 2857, 1684, 1618, 1468, 1380, 1229, 1147, 1114, 1047, 970, 918, 888, 842, 781 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.00 (dd, *J* = 4.0, 2.0 Hz, 1H), 4.53 (d, *J* = 17.6 Hz, 1H), 4.45 (d, *J* = 17.6 Hz, 1H), 4.35 (ddt, *J* = 8.8, 2.4, 1.2 Hz, 1H), 4.18 (d, *J* = 10.8 Hz, 1H), 3.80 (dd, *J* = 11.0, 8.6 Hz, 1H), 2.41 (s, 1H), 1.48 (s, 3H), 1.45 (s, 3H), 0.94 (s, 9H), 0.18 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 159.9, 122.5, 112.9, 82.5, 78.3, 75.9, 61.3, 26.9, 26.6, 25.9, 18.8, –4.5, –5.1; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{16}H_{28}NaO_5Si$ 351.1604; Found 351.1608.

Compound 30: To a stirred solution of **29** (120 mg, 0.365 mmol) in CH_2Cl_2 (8 mL) was added pyridine (44 μL, 0.548 mmol) and DMAP (4.5 mg, 0.0365 mmol) at 0 °C. Then Ac_2O (52 μL, 0.548 mmol) was slowly added dropwise at the same temperature. Then the reaction was stirred at room temperature for 30 min, extracted with CH_2Cl_2 (3 × 10 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 8:1) to give **30** (130 mg, 96%) as a white solid. m.p. 48 – 49 ℃; $[\alpha]_D^{18}$ –57.4 (*c* 0.34, $CHCl_3$); IR (neat) ν_{max} 2988, 2933, 2889, 2857, 1753, 1693, 1624, 1473, 1377, 1226, 1149, 1115, 1080, 1049, 969, 891, 843, 781, 675 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.91 (dd, *J* = 4.4, 2.0 Hz, 1H), 4.92 (t, *J* = 1.6 Hz, 2H), 4.37 – 4.32 (m, 1H), 4.18 (d, *J* = 11.2 Hz, 1H), 3.80 (dd, *J* = 11.2, 8.4 Hz, 1H), 2.13 (s, 3H), 1.48 (s, 3H), 1.45 (s, 3H), 0.93 (s, 9H), 0.18 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 170.2, 155.0, 123.1, 112.9, 82.4, 78.2, 75.5, 61.1, 26.9, 26.6, 25.9, 20.8, 18.8, –4.5, –5.1; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{18}H_{30}NaO_6Si$ 393.1709; Found 393.1710.

(-)-Gabosine G (10): To **30** (130 mg, 0.351 mmol) was added TFA (3 mL) and H_2O (0.15 mL). The solution was stirred at room temperature for 5 min. Concentration of the solution followed by flash

chromatography ($CHCl_3$/MeOH, 10:1) to yield (–)-**10** (55 mg, 72%) as a colorless oil. $[\alpha]_D^{17}$ –71.0 (*c* 0.40, MeOH) {lit.[27] $[\alpha]_D^{20}$ –41.8 (*c* 1.34, MeOH)}; IR (neat) ν_{max} 3380, 2925, 1742, 1685, 1426, 1373, 1230, 1122, 1053, 915, 886 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 6.00 (q, *J* = 2.0 Hz, 1H), 4.98(dt, *J* = 17.2, 1.6 Hz 1H), 4.90(dt, *J* = 17.2, 1.6 Hz 1H) (part of the peak was obscured by the solvent peak), 4.43 – 4.38 (m, 1H), 4.04 (d, *J* = 10.8 Hz, 1H), 3.61 (dd, *J* = 10.8, 8.4 Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 199.1, 171.9, 161.5, 122.5, 79.3, 78.0, 73.5, 63.7, 20.6; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_9H_{12}NaO_6$ 239.0532; Found 239.0534.

Compound 31: To a solution of **30** (140 mg, 0.378 mmol) in MeOH (3.8 mL) was added $CeCl_3 \cdot 7H_2O$ (168 mg, 0.453 mmol) at 0 °C. After stirring at 0 °C for 30 min, $NaBH_4$ (20 mg, 0.567 mmol) was added. The reaction was stirred at 0 °C for 10 min, quenched with saturated aqueous NH_4Cl, evaporated under reduced pressure and purified by flash column chromatography (petroleum ether/EtOAc, 8:1) on silica gel to give **31** (114 mg, 81%) as a colorless oil. $[\alpha]_D^{17}$ –41.1 (*c* 0.36, $CHCl_3$); IR (neat) ν_{max} 3473, 2987, 2932, 2892, 2857, 1746, 1466, 1376, 1230, 1175, 1107, 1073, 1001, 900, 841, 781, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.53 (tt, *J* = 2.8, 1.6 Hz, 1H), 4.73 – 4.62 (m, 2H), 4.34 – 4.26 (m, 1H), 4.22 – 4.16 (m, 1H), 3.95 (dd, *J* = 10.8, 6.4 Hz, 1H), 3.51 (dd, *J* = 10.8, 8.4 Hz, 1H), 2.10 (d, *J* = 6.6 Hz, 1H), 2.09 (s, 3H), 1.42 (s, 3H), 1.40 (s, 3H), 0.92 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 134.1, 125.3, 111.6, 80.2, 77.7, 77.6, 76.4, 62.3, 26.8, 26.6, 26.0, 21.0, 18.4, –4.2, –4.7; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{18}H_{32}NaO_6Si$ 395.1866; Found 395.1867.

(-)-Gabosine K (12): To a stirred solution of **31** (60 mg, 0.161 mmol) in CH_2Cl_2 (3.2 mL) was added TFA (220 μL) and H_2O (55 μL) at room temperature. The solution was stirred at room temperature for 11 h. The reaction was concentrated by rotary evaporation under reduced pressure. The residue followed by

flash chromatography ($CHCl_3$/MeOH, 8:1) to yield (–)-**12** (26 mg, 75%) as a colorless oil. $[\alpha]_D^{17}$ –61.9 (*c* 0.27, MeOH) {lit.[28] $[\alpha]_D^{20}$ –47.9 (*c* 0.52, MeOH)}; IR (neat) ν_{max} 3380, 2898, 1732, 1375, 1255, 1172, 1066, 1032, 968 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 5.60 (m, 1H), 4.73 (d, *J* = 13.2 Hz, 1H), 4.54 (d, *J* = 12.8 Hz, 1H), 4.12 – 4.04 (m, 2H), 3.46 – 3.33 (m, 2H) (part of the peak was obscured by the MeOH peak), 2.07 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 171.1, 134.8, 127.4, 76.1, 75.7, 72.1, 71.6, 63.4, 19.4; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_9H_{14}NaO_6$ 241.0688; Found 241.0690..

Compound 32: To a stirred solution of **14** (812 mg, 1.74 mmol) in THF (35 mL) was added TBAF (1 M in THF, 1.92 mL, 1.92 mmol) at 0 °C. The resulting mixture was stirred for 25 min at 0 °C before saturated aqueous NH_4Cl (5 mL) and EtOAc (35 mL) were added. The phases were separated and the aqueous phase was extracted with EtOAc (3 × 35 mL). After the organic layer was concentrated under reduced pressure, the residue was purified by flash chromatography (petroleum ether/EtOAc, 2:1) to yield diol **32** (570 mg, 93%) as a colorless oil. $[\alpha]_D^{18}$ –19.3 (*c* 0.30, $CHCl_3$); IR (neat) ν_{max} 3462, 2987, 2930, 1725, 1612, 1586, 1514, 1460, 1377, 1301, 1245, 1175, 1085, 962, 899, 847, 779, 735, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.19 (m, 2H), 6.93 – 6.84 (m, 2H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.49 (d, *J* = 11.6 Hz, 1H), 4.29 (d, *J* = 10.4 Hz, 1H), 4.02 (d, *J* = 9.2 Hz, 1H), 4.00 – 3.94 (m, 1H), 3.81 (s, 3H), 3.62 (s, 1H), 3.48 (d, *J* = 9.2 Hz, 1H), 3.42 (d, *J* = 9.2 Hz, 1H), 2.73 (d, *J* = 16.0 Hz, 1H), 2.67 (d, *J* = 16.0 Hz, 1H), 2.42 (s, 1H), 1.53 (s, 3H), 1.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2, 159.6, 129.6, 129.5, 114.0, 112.8, 77.9, 77.4, 77.4, 73.3, 72.7, 71.6, 55.4, 45.9, 27.3, 26.7; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{18}H_{24}NaO_7$ 375.1420; Found 375.1422.

Compound 33: To a stirred solution of diol **32** (523 mg, 1.48 mmol) in CH_2Cl_2 (30 mL) was added Et_3N (311 μL, 2.23 mmol) and DMAP (9 mg, 0.0742 mmol) at 0 °C. Then BzCl (205 μL, 1.78 mmol) was

slowly added dropwise. The reaction was stirred at 0 °C for 1 h, extracted with DCM (3 × 30 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 4:1) to give **33** (664 mg, 98%) as a colorless oil. $[\alpha]_D^{17}$ +24.2 (*c* 0.60, $CHCl_3$); IR (neat) ν_{max} 3477, 3065, 2988, 2932, 2863, 1741, 1609, 1585, 1513, 1455, 1378, 1275, 1176, 1074, 1033, 847, 780, 711, 672 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.08 (m, 2H), 7.60 – 7.54 (m, 1H), 7.46 – 7.42 (m, 2H), 7.28 – 7.22 (m, 2H) (part of the peak was obscured by the solvent peak), 6.94 – 6.83 (m, 2H), 5.65 (d, *J* = 11.6 Hz, 1H), 4.54 (d, *J* = 11.6 Hz, 1H), 4.50 (d, *J* = 11.6 Hz, 1H), 4.42 (dd, *J* = 11.6, 9.6 Hz, 1H), 4.17 (d, *J* = 9.2 Hz, 1H), 3.82 (s, 3H), 3.51 (d, *J* = 9.2 Hz, 1H), 3.47 (d, *J* = 9.2 Hz, 1H), 2.75 (d, *J* = 16.0 Hz, 1H), 2.70 (d, *J* = 16.4 Hz, 1H), 2.54 (s, 1H), 1.53 (s, 3H), 1.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0, 165.7, 159.6, 133.5, 130.2, 129.6, 129.5, 129.4, 128.4, 114.0, 112.9, 78.6, 78.5, 74.0, 73.3, 72.7, 71.1, 55.4, 47.1, 27.2, 26.8; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{25}H_{28}NaO_8$ 479.1682; Found 479.1679.

Compound 34: To a solution of **33** (532 mg, 1.17 mmol) in THF (23 mL) was added freshly prepared Burgess reagent (597 mg, 2.34 mmol) at room temperature. Then the reaction mixture was refluxed at 70 °C for 20 min, extracted with EtOAc (3 × 20mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 4:1) to give enone **34** (506 mg, 99%) as a colorless oil. $[\alpha]_D^{18}$ +6.2 (*c* 0.50, $CHCl_3$); IR (neat) ν_{max} 3066, 2988, 2929, 2856, 1731, 1689, 1613, 1514, 1452, 1378, 1344, 1271, 1248, 1176, 1148, 1100, 1074, 1032, 968, 927, 830, 776, 710 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.0Hz, 2H), 7.60 – 7.54 (m, 1H), 7.45 (t, *J* = 7.6Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 8.0 Hz, 2H), 6.25 (d, *J* = 1.2 Hz, 1H), 5.72 (d, *J* = 12.0 Hz, 1H), 4.62 – 4.49 (m, 3H), 4.38 (s, 2H), 4.16 (dd, *J* = 11.4, 8.6 Hz, 1H), 3.82 (s, 3H), 1.51 (s, 3H), 1.49 (s, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 191.9, 165.7, 159.6, 158.5, 133.5, 130.3, 129.5, 129.4, 129.4, 128.5, 122.8, 114.1, 113.6, 79.2, 77.0, 76.1, 73.1, 66.8, 55.4, 26.7, 26.7; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{25}H_{26}NaO_7$ 461.1576; Found 461.1575.

Compound 35: To a stirred solution of enone **34** (574 mg, 1.31 mmol) in CH_2Cl_2 (130 mL) and phosphate buffer (pH = 7.2, 13 mL) was added DDQ (892 mg, 3.93 mmol) at 0 °C. Then the resulting mixture was stirred for 9 h at room temperature. The separated organic layer was washed with saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$ (1:1), water and brine successively. The organic layer was concentrated by rotary evaporation under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 2:1) to yield **35** (371 mg, 89%) as a yellow-green crystalline solid. m.p. 139 – 141 ℃; $[\alpha]_D^{18}$ +14.8 (*c* 0.43, $CHCl_3$); IR (neat) ν_{max} 3459, 3067, 2989, 2933, 1731, 1688, 1617, 1452, 1381, 1323, 1272, 1230, 1177, 1147, 1098, 1064, 969, 919, 843, 767, 711, 646 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (dt, *J* = 8.0, 1.6 Hz, 2H), 7.61 – 7.56 (m, 1H), 7.48 – 7.42 (m, 2H), 6.16 (dd, *J* = 4.0, 2.0 Hz, 1H), 5.73 (d, *J* = 11.6 Hz, 1H), 4.65 – 4.58 (m, 2H), 4.54 (d, *J* = 18.0 Hz, 1H), 4.19 (dd, *J* = 11.8, 8.6 Hz, 1H), 2.22 (s, 1H), 1.53 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.0, 165.8, 160.4, 133.6, 130.3, 129.3, 128.5, 122.4, 113.8, 79.3, 77.1, 76.3, 61.2, 26.8, 26.7; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{17}H_{18}NaO_6$ 341.1001; Found 341.1004.

Compound 36: To a stirred solution of **35** (80 mg, 0.251 mmol) in CH_2Cl_2 (6 mL) was added DIPEA (66 μL, 0.377 mmol) and DMAP (3.1 mg, 0.0251 mmol) at 0 °C. Then BzCl (35 μL, 0.302 mmol) was slowly added dropwise at 0 °C. The reaction was stirred at room temperature for 30 min, quenched with saturated aqueous $NaHCO_3$, extracted with DCM (3 × 10 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 8:1) to give **36** (80 mg,

75%) as a colorless oil. $[\alpha]_D^{17}$ –24.6 (*c* 0.17, $CHCl_3$); IR (neat) ν_{max} 3066, 2988, 2928, 1729, 1692, 1623, 1602, 1585, 1492, 1451, 1378, 1315, 1270, 1226, 1176, 1149, 1103, 1027, 971, 931, 839, 803, 775, 710 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 – 8.06 (m, 4H), 7.69 – 7.55 (m, 2H), 7.54 – 7.38 (m, 4H), 6.17 (dd, *J* = 4.2, 2.2 Hz, 1H), 5.77 (d, *J* = 12.0 Hz, 1H), 5.33 – 5.27 (m, 1H), 5.27 – 5.20 (m, 1H), 4.69 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.25 (dd, *J* = 11.8, 8.6 Hz, 1H), 1.55 (s, 3H), 1.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.8, 165.7, 155.9, 133.8, 133.6, 130.3, 129.9, 129.3, 129.2, 128.8, 128.5, 122.9, 114.0, 79.2, 77.0, 76.0, 61.4, 26.8, 26.7; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{22}NaO_7$ 445.1263; Found 445.1260.

(-)-Uvamalol A (9): To a solution of **36** (37 mg, 0.0877 mmol) in MeOH (1.7 mL) was added $CeCl_3 \cdot 7H_2O$ (39 mg, 0.105 mmol) at 0 °C. After stirring at 0 °C for 30 min, $NaBH_4$ (5 mg, 0.132 mmol) was added at 0 °C. The reaction was stirred for 5 min, quenched with saturated aqueous NH_4Cl, evaporated under reduced pressure and purified by flash column chromatography (petroleum ether/EtOAc, 6:1) on silica gel to give the mixture of two diastereoisomers. The mixture (34 mg, 0.08 mmol) was dissolved in MeOH (1 mL), and PPTS was added (20 mg, 0.08 mmol) at room temperature. After stirring for 10 h, the reaction was evaporated under reduced pressure and purified by flash column chromatography (petroleum ether/EtOAc, 1:1) to give (–)-**9** (24 mg, 72% over two steps) as a white powder. m.p. 136 – 138 ℃; $[\alpha]_D^{17}$ –73.7 (*c* 0.30, MeOH) {lit.[9] $[\alpha]_D^{23}$ –78.0 (*c* 0.24, MeOH)}; IR (neat) ν_{max} 3413, 2922, 1713, 1602, 1449, 1274, 1177, 1114, 1069, 1022, 963, 858, 805, 710 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 8.16 – 8.03 (m, 4H), 7.65 – 7.58 (m, 2H), 7.53 – 7.45 (m, 4H), 5.81 (brs, 1H), 5.22 (dd, *J* = 10.8, 8.4 Hz, 1H), 5.04 (d, *J* = 13.6 Hz, 1H), 4.88 (d, *J* = 13.6Hz, 1H) (part of the peak was obscured by the solvent peak), 4.47 (d, *J* = 8.4 Hz, 1H), 4.36 (d, *J* = 8.0 Hz, 1H), 3.78 (dd, *J* = 10.8, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 168.00, 167.6, 136.8, 134.4, 134.1, 131.8, 131.4, 130.8, 130.6, 129.7, 129.4,

128.6, 78.7, 75.8, 73.6, 71.0, 65.1; HRMS (ESI - TOF) m/z $[M + Na]^+$ calcd for $C_{21}H_{20}NaO_7$ 407.1107; Found 407.1103.

Associated Content

Supporting Information

Copies of ^1H and ^{13}C NMR spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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References and Footnotes

(1) (a) Das, M.; Manna, K. *Curr. Bioact. Compd.* **2015**, *11*, 239–248. (b) Vogel, P. *Chimia* **2001**, *55*, 359–365. (c) Arjona, O.; Gómez, A. M.; López, J. C.; Plumet, J. *Chem. Rev.* **2007**, *107*, 1919−2036. (d) Marco-Contelles, J. *Eur. J. Org. Chem.* **2001**, *2001*, 1607−1618. (e) Mahmud, T. *Nat. Prod. Rep.* **2003**, *20*, 137−166. (f) Witte, M.; Kallemeijn, W. W.; Aten, J.; Li, K.-Y.; Strijland, A.; Donker-Koopman,

W. E.; Van Den Nieuwendijk, A. M. C. H.; Bleijlevens, B.; Kramer, G.; Florea, B. I.; Hooibrink, B.; Hollak, C. E. M.; Ottenhoff, R.; Boot, R. G.; Van Der Marel, G. A.; Overkleeft, H. S.; Aerts, J. M. F. G. *Nat. Chem. Biol.* **2010**, *6*, 907−913. (g) Kallemeijn, W. W.; Li, K.-Y.; Witte, M. D.; Marques, A. R. A.; Aten, J.; Scheij, S.; Jiang, J.; Willems, L. I.; Voorn-Brouwer, T. M.; Van Roomen, C. P. A. A.; Ottenhoff, R.; Boot, R. G.; Van Den Elst, H.; Walvoort, M. T. C.; Florea, B. I.; Codee, J. D. C.; Van Der Marel, G. A.; Aerts, J. M. F. G.; Overkleeft, H. S. *Angew. Chem. Int. Ed.* **2012**, *51*, 12529–12533.

(2) Bach, G.; Breiding-Mack, S.; Grabley, S.; Hammam, P.; Hütter, K.; Thiericke, R.; Uhr, H.; Wink, J.; Zeeck, A. *Liebigs Ann. Chem.* **1993**, *1993*, 241–250.

(3) (a) Huntley, C. F. M.; Hamilton, D. S.; Creighton, D. J.; Ganem, B. *Org. Lett* **2000**, *2*, 3143–3144. (b) Kamiya, D.; Uchihata, Y.; Ichikawa, E.; Kato, K.; Umezawa, K. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1111–1114.

(4) (a) Tang, Y. Q.; Maul, C.; Höfs, R.; Sattler, I.; Gabley, S.; Feng, X.-Z.; Zeeck, A.; Thiericke, R. *Eur. J. Org. Chem.* **2000**, *2000*, 149−153. (b) Maier, A.; Maul, C.; Zerlin, M.; Grabley, S.; Thiericke, R. *J. Antibiot.***1999**, *52*, 952−959.

(5) (a) Wang, C.-H.; Wu, H. T.; Cheng, H. M.; Yen, T.-J.; Lu, I.-H.; Chang, H. C.; Jao, S.-C.; Shing, T. K. M.; Li, W.-S. *J. Med. Chem.* **2011**, *54*, 8574−8581; (b) Shing, T. K. M.; Wu, H. T.; Kwok, H. F.; Lau, C. B. S. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 7562−7565.

(6) Tatsuka, K.; Tschuyia, T.; Mikami, M.; Umezawa, H.; Naganawa, H. *J. Antibiot.* **1974**, *27*, 579–586.

(7) Wei, J.; Liu, L.-L.; Dong, S.; Li, H.; Tang, D.; Zhang, Q.; Xue, Q.-H.; Gao, J.-M. *Bioorg. Med. Chem. Lett.* **2016**, *26*, 4903–4906.

(8) Isogai, A.; Sakuda, S.; Nakayama, J.; Watanabe, S.; Suzuki, A. *Agric. Biol. Chem.* **1987**, *51*,

2277−2279.

(9) Wang, S.; Zhang, P.-C.; Chen, R.-Y.; Dai, S.-J.; Yu, S.-S.; Yu, D.-Q. *J. Asian Nat. Prod. Res.* **2005**, *7*, 687−694.

(10) (a) Mac, D. H.; Chandrashekhar, S.; Gree, R. *Eur. J. Org. Chem.* **2012**, *2012*, 5881−5895, and references therein. (b) Bayón, P.; Figueredo, M. *Chem. Rev.* **2013**, *113*, 4680−4707, and references therein.

(11) For recent syntheses of gabosines, see: (a) Tibhe, G. D.; Macias, M. A.; Pandolfi, E.; Suescun, L.; Schapiro, V. *Synthesis* **2017,** *49*, 565−570. (b) Mondal, S.; Sureshan, K. M. *J. Org. Chem.* **2016**, *81*, 11635−11645. (c) Vulovic, B.; Kolarski, D.; Bihelovic, F.; Matovic, R.; Gruden, M. *Org. Lett.* **2016**, *18*, 3886−3889. (d) Fresneda, M. Á.; Alibés, R.; Bayón, P.; Figueredo, M. *Eur. J. Org. Chem.* **2016**, *2016*, 3568−3574. (e) Raju, G.; Rao, M. V.; Rao, B. V. *J. Carbohydr. Chem.* **2016**, *35*, 150−160. (f) Vidyasagar, A.; Sureshan, K. M. *Eur. J. Org. Chem.* **2014**, *2014*, 2349–2356. (g) Babu, D. C.; Rao, C. B.; Venkatesham, K.; Selvam, J. J. P.; Venkateswarlu, Y. *Carbohydr. Res.* **2014**, *388*, 130−137. (h) Fresneda, M. Á.; Alibés, R.; Font, J.; Bayón, P.; Figueredo, M. *Org. Biomol. Chem.* **2013**, *11*, 6562–6568. (i) Mondal, S.; Prathap, A.; Sureshan, K. M. *J. Org. Chem.* **2013**, *78*, 7690−7700.

(12) Toribio, G.; Marjanet, G.; Alibes, R.; de March, P.; Font, J.; Bayon, P.; Figuedero, M. *Eur. J. Org. Chem.* **2011**, *2011*, 1534–1543.

(13) Lubineau, A.; Billaut, I. *J. Org. Chem.* **1998**, *63*, 5668–5671.

(14) (a) Fernandes, R. A.; Chavan, V. P.; Mulay, S. V.; Manchoju, A. *J. Org. Chem.* **2012**, *77*, 10455−10460. (b) Long, D. D.; Smith, M. D.; Martín, A.; Wheatley, J. R.; Watkin, D. G.; Müller, M.; Fleet, G. W. J. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1982–1998.

(15) Hu, S.-G.; Hu, T.-S.; Wu, Y.-L. *Org. Biomol. Chem.* **2004**, *2*, 2305–2310.

(16) Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815–3818.

(17) (a) Shing, T. K. M.; Cheng, H. M. *Org. Biomol. Chem.* **2009**, *7*, 5098–5102. (b) Shing, T. K. M.; Cheng, H. M.; Wong, W. F.; Kwong, C. S. K.; Li, J.; Lau, C. B. S.; Leung, P. S.; Cheng, C. H. K. *Org. Lett.* **2008**, *10*, 3145–3148.

(18) Fukuda, Y.; Sakurai, M.; Okamoto, Y. *Tetrahedron Lett*. **2000**, *41*, 8505–8508.

(19) Snyder, S. A.; Wespe, D. A.; von Hof, J. M. *J. Am. Chem. Soc*. **2011**, *133*, 8850–8853.

(20) van Wyk, A. W. W.; Lobb, K. A.; Caira, M. R.; Hoppe, H. C.; Davies-Coleman, M. T. *J. Nat. Prod*. **2007**, *70*, 1253–1258.

(21) Cichowicz, N.; Kaplan, W.; Khomutnyk, Y.; Bhattarai, B.; Sun, Z.; Nagorny, P. *J. Am. Chem. Soc.* **2015**, *137*, 14341–14348.

(22) (a) Banerjee, S.; Santra, S. *Tetrahedron Lett.* **2009**, *50*, 2037–2040. (b) Christoffers, J.; Scharl, H. *Eur. J. Org. Chem.* **2002**, *2002*, 1505–1508.

(23) (a) Asamizu, S.; Xie, P.; Brumsted, C. J.; Flatt, P. M.; Mahmud, T. *J. Am. Chem. Soc.* **2012**, *134*, 12219–12229. (b) Floss, H. G.; Lee, S.; Tornus, I. U.S. Patent 6,150,568, November 21, 2000.

(24) Burgess, E. M.; Penton Jr., H. R.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26–31.

(25) Luche, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 2226−2227.

(26) Shing, T. K. M.; Chen, Y.; Ng, W.-L. *Tetrahedron* **2011**, *67*, 6001−6005.

(27) Shing, T. K. M.; Cheng, H. M. *J. Org. Chem.* **2007**, *72*, 6610−6613.

(28) Shing, T. K. M.; Cheng, H. M. *Synlett* **2010**, *1*, 142−144.