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Vinylogy in Orthoester Hydrolysis: Total Syntheses of Cyclophellitol, Valienamine, Gabosine K, Valienone, Gabosine G, 1-*epi*-Streptol, Streptol, and Uvamalol A

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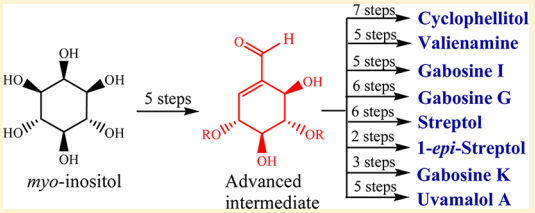
Supporting Information

ABSTRACT: C7-cyclitols represent an important category of natural products possessing a broad spectrum of biological activities. As each member of these compounds is structurally unique, the usual practice is to synthesize them individually from appropriate polyhydroxylated chiral pools. We have observed an unusual vinylogy in acid mediated hydrolysis of enol ethers of *myo*-inositol 1,3,5-orthoesters giving a synthetically versatile polyhydroxylated cyclohexenal intermediate. We have exploited this unprecedented reaction for developing a general strategy for the rapid and efficient syntheses of several structurally diverse natural products of C7-cyclitol family. We have made an appropriately protected advanced intermediate 25 in five steps from the cheap and commercially available *myo*-inositol, and this common intermediate has been used to synthesize eight natural products in racemic form. We could synthesize (±)-cyclophellitol in seven steps, (±)-valienamine in five steps, (±)-gabosine I in five steps, (±)-gabosine G in six steps, (±)-gabosine K in three steps, (±)-streptol in six steps, (±)-1-*epi*-streptol in two steps, and (±)-uvamalol A in five steps from this intermediate.



INTRODUCTION

C7-cyclitols, polyhydroxycyclohexane with an exocyclic methyl or hydroxymethyl substituent, represent an important category of natural products possessing a broad spectrum of biological activities such as anticancer, antibacterial, antifungal, HIV inhibitory, enzyme inhibitory activities, etc.[1−5] Gabosines,[2] pericosines,[3] cyclophellitol,[4] C7-aminocyclitols[5] such as valienamine, valiolamine and validamine are some of the members of this family of cyclitols (Figure 1). For instance, cyclophellitol, isolated from the mushroom *Phellinus sp.*,[6] is a potent β-glucosidase inhibitor, and it also possesses HIV inhibitory activity.[7] Valienamine, a strong α-glucosidase inhibitor,[8] is a metabolite in the microbial[9] degradation of validoxylamine A. Gabosine I (valienone), gabosine G and gabosine K are the prominent members of gabosine family. They were isolated from *Streptomyces* strain and shown to possess antibiotic, anticancer and DNA binding properties.[10] Streptol (valienol) was also isolated from *Streptomyces sp.*, and it has plant growth inhibitory activity.[11] 1-*epi*-Streptol (1-*epi*-valienol) is an intermediate involved in the biosynthesis of acarbose, an α-glucosidase inhibitor, in *Actinoplanes* and *Streptomyces*.[12] Many of these natural cyclitols have been the targets of several total syntheses due to their attractive biological properties.[2,13] Because of their structural diversity, it has been a usual practice to synthesize them individually from different polyhydroxylated chiral pools such as D-glucose, D-xylose, quebrachitol, etc., and these strategies often necessitate multiple protecting group manipulations.[14] We herein report an unusual conjugative ring-opening of the orthoester cage in *myo*-inositol 1,3,5-orthoesters giving a synthetically versatile polyhydroxylated cyclohexenal intermediate and the exploitation of this unprecedented reaction in developing a general strategy for the rapid and efficient syntheses of eight structurally diverse natural products of C7-cyclitol family, namely, (±)-cyclophellitol, (±)-valienamine, (±)-gabosine K, (±)-gabosine G, (±)-valienone, (±)-1-*epi*-streptol, (±)-streptol and (±)-uvamalol A.

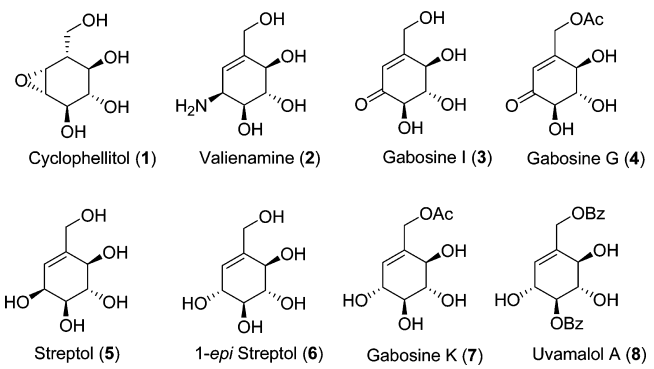


Figure 1. Representative C-7 cyclitol natural products.

RESULTS AND DISCUSSION

Because of the importance of carbohydrates in various biological processes, sugar mimics received much attention as

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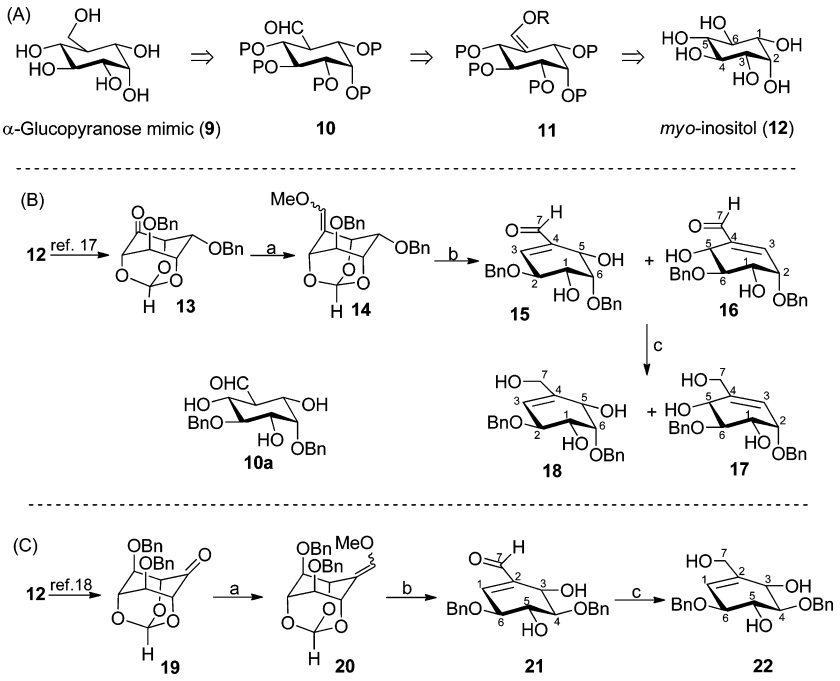
Scheme 1. Unusual Vinylogy in the Hydrolysis of Differently Protected *myo*-Inositol Orthoesters[a]



[a]Reagents and conditions: (a) PPh_3CH_2OMeCl, ^tBuOK, THF, 0 °C to reflux, 2 h, (14; 92%, 20; 90%). (b) 0.1 M aq. HCl, THF, rt, 1 h. (c) $NaBH_4$, $CeCl_3$, MeOH, 0 °C, 1 h (17 + 18; 90% 2 steps, 22; 91%, 2 steps).

potential inhibitors for the glycan processing enzymes.[15] Inositols, cyclohexane hexols, are carbocyclic mimics of hexopyranoses lacking the exocyclic hydroxymethyl group. As part of our program to synthesize inhibitors of various glycosidases, we planned to synthesize various carbasugars from inositols by converting a hydroxyl group to an exocyclic hydroxymethyl group via the one carbon homologation of the corresponding protected inosose to the exocyclic aldehyde by adopting the method of Barton et al. (Scheme 1A).[16] In order to test this hypothesis, readily available unsymmetrical inosose **13**[17] was converted to the Wittig product **14** as an inseparable mixture of *E*/*Z* (1:1) isomers in 92% yield. Acidic hydrolysis of **14** surprisingly gave an inseparable mixture of α,β-unsaturated aldehydes **15** and **16** (Scheme 1B) instead of the expected aldehyde **10a**. This mixture of aldehydes on reduction gave alcohols **17** and **18**, which could be separated by chromatography. The stereochemistry of alcohols **17** and **18** were assigned after acetylation. In order to check the generality of this unusual reaction, the methoxy-Wittig product **20** obtained from the known symmetrical inosose **19**[18] was treated with dilute acid. Interestingly, in this case also, the corresponding enal **21** (Scheme 1C) was formed along with its formate ester as an inseparable mixture, which on reduction gave the triol **22** as the only product (91%) suggesting that the observed vinylogous ring-opening reaction is general (see Supporting Information for mechanistic details). This intriguing reaction is very attractive as many natural C7-cyclitols and analogues can be made from the α,β-unsaturated aldehydes produced in these reactions (e.g., **15**, **16**, **21**) by choosing appropriate protecting groups. In order to illustrate the synthetic utility of this interesting transformation, we have undertaken the syntheses of cyclophellitol (**1**), valienamine (**2**), gabosine I (**3**), gabosine G (**4**), streptol (**5**), 1-*epi*-streptol (**6**), gabosine K (**7**) and uvamalol A (**8**). All these eight C7-cyclitols contain three common contiguous stereogenic centers at C-2, C-3 and C-4 positions, which is present in the enal **21** too. Hence, minimal synthetic manipulations of stereogenic centers are sufficient to synthesize these target compounds from such α,β-unsaturated aldehydes. The retrosynthetic analyses (see the Supporting Information) reveal that all of these natural products can be synthesized from the enal **25**, which can be prepared from the *myo*-inositol derived ketone **23**.[19]

The ketone **23** was prepared, in 42% yield, from commercially available *myo*-inositol as reported.[19] The ketone **23** on Wittig reaction with methoxymethyltriphenylphosphonium chloride gave the enol ether **24** in 95% yield. The enol ether **24** on acidic hydrolysis with a few drops of aqueous HCl (0.1 M) in THF gave the advanced intermediate, enal **25**, in quantitative yield. The structure of the compound **25** was established by both NMR experiments and X-ray crystallographic analysis (see the Supporting Information, Figure S1). This advanced intermediate can be made in multigram quantities from cheaply available *myo*-inositol in overall yields up to 40%.

Luche reduction[20] of the α,β-unsaturated aldehyde **25** resulted in the formation of the triol **26** in 92% yield (Scheme 2). Benzylation of triol **26** with excess of benzyl bromide gave the tribenzyl ether **27** in 91% yield. Hydroboration[21] of the alkene **27** with $BH_3{\cdot}Me_2S$ followed by oxidation with H_2O_2/NaOH gave the alcohol **28**, as the exclusive diastereomer (81%). While the anti-Markovnikov's addition of the borane dictated the regiochemistry, the steric hindrance by the bulky PMB group dictated the stereochemistry. The relative stereochemistry of **28** was assigned after acetylation using NMR spectroscopy. As anticipated, the hydroboration of **28** has taken place from the face opposite to the bulky PMB group at C-1. The compound **28** was reacted with mesyl chloride to give the mesylate **29** in quantitative yield. TFA mediated removal of PMB ether protecting groups gave the diol **30** (88%), wherein hydroxyl group at C-1 and mesyloxy group are disposed in *anti*

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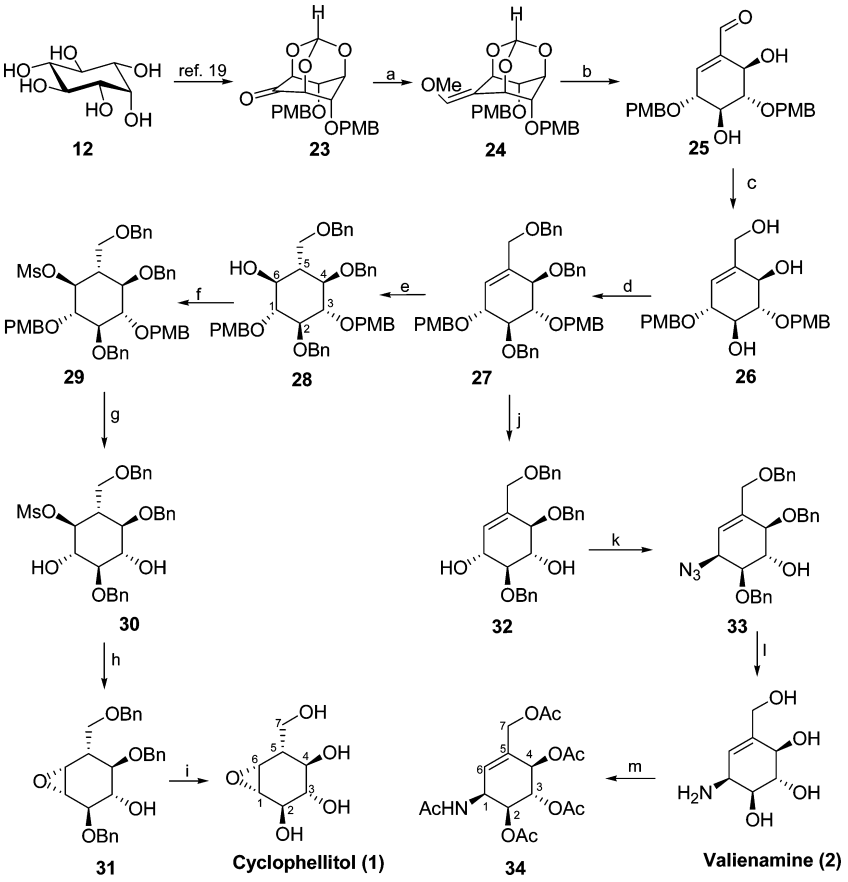
Scheme 2. Total Syntheses of (±)-Cyclophellitol and (±)-Valienamine[a]



[a]Reagents and conditions: (a) PPh_3CH_2OMeCl, ^tBuOK, THF, 0 °C to reflux, 2 h, 95%. (b) 0.1 N aq. HCl, THF, rt, 8 h, quantitative. (c) $NaBH_4$, $CeCl_3{\cdot}7H_2O$, MeOH, 0 °C, 1 h, 92%. (d) NaH, BnBr, DMF, 0 °C, 20 min, 91%. (e) $BH_3{\cdot}SMe_2$, H_2O_2, NaOH, 10 h, (81%). (f) Pyridine, MsCl, 0 °C, 1 h, quantitative. (g) TFA, DCM, rt, 1 h, 88%. (h) NaH, DMF, 0 °C, 20 min, 91%. (i) Pd/C, H_2 (1 atm), EtOAc, 0 °C, overnight, quantitative. (j) TFA (10% in DCM), rt, 1 h, 91%. (k) DPPA, DBU, 0 °C, NaN_3, Toluene, 83%. (l) BCl_3 (1 M solution in toluene), −60 °C to rt, 4 h, 80%. (m) Ac_2O, Pyridine, DMAP, rt, overnight, 90%.

orientation. Diol **30** on treatment with NaH produced the epoxide **31** in 91% yield. Finally, the global deprotection, by hydrogenolysis, provided (±)-cyclophellitol (**1**) in quantitative yield. Thus, we could synthesize cyclophellitol in an overall yield of 54% in seven steps from the common intermediate **25**.

Having successfully exploited the vinylogous opening of the orthoester in synthesizing cyclophellitol, we set out to generalize this methodology for the synthesis of other C-7 cyclitol natural products. Thus, we carried out the synthesis of (±)-valienamine as follows. Alkene **27**, obtained from **25**, on acidic hydrolysis gave the diol **32** in 91% yield (Scheme 2). Diol **32** on Mitsunobu reaction using diphenylphosphorylazide (DPPA) and 1,8-diaza-bicyclo-undec-7-ene (DBU) gave the azide **33** regioselectively in 83% yield.[22] The structural assignment was done with the help of various 2D NMR techniques. The small value of $^3J_{H1H2}$ coupling constant (4.15 Hz) is supportive of *syn* relationship of H1 (H on azide connected carbon) and H2 in a cyclohexane skeleton. This high selectivity in the nucleophilic substitution reaction arises from the increased reactivity of allylic hydroxyl group and its less steric hindrance compared to the other hydroxyl group. As BCl_3 is known to deprotect the benzyl ether[23] and reduce the azide to amine,[24] azide **33** was treated with BCl_3, for one-pot benzyl deprotection and azide reduction. This provided (±)-valienamine (**2**) in 80% yield, which was characterized as its pentaacetyl derivative **34**, whose ^1H NMR spectrum was identical to the reported[13i] spectrum. We, therefore, could achieve the total synthesis of (±)-valienamine in an overall yield of 50.6% in five steps from the enal **25**.

Next, we turned our attention to the synthesis of (±)-gabosine G and (±)-gabosine I. Diol **32** on selective oxidation of the allylic alcohol functionality using Dess−Martin periodinane[25] gave the enone **35** (Scheme 3). Absence of any $^3J_{HH}$ coupling for the olefinic proton indicates the chemoselective oxidation of allylic alcohol. The removal of benzyl ether protecting groups using BCl_3 gave (±)-gabosine I (**3**) in 75% yield. It is noteworthy that **3** could be synthesized in just five steps from enal **25** in an overall yield of 53.7%, making it an attractive synthesis over many previous syntheses. (±)-Gabosine G (**4**) was obtained by selective acetylation of the primary hydroxyl group in (±)-valienone **3** using acetyl chloride and 2,4,6-collidine[26] in 70% yield (37.4% from the enal **25** in six steps; Scheme 3). We have chosen (±)-streptol as our next synthetic target because of its interesting biological property as plant growth inhibitor. As streptol (**5**) and the diol **32** have a single stereochemical difference (at C1), it is reasonable to invert the stereochemistry at C1 by an oxidation reduction sequence to streptol. Thus, the enone **35** obtained from **32** was subjected to reduction. Surprisingly, reduction of enone **35** using $NaBH_4$ gave back the diol **32** as the exclusive product.

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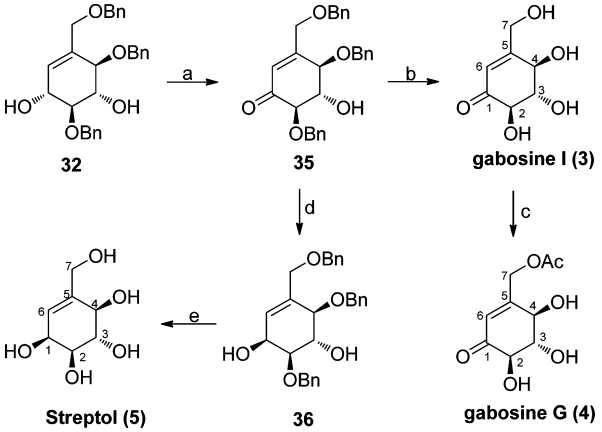
Scheme 3. Total Syntheses of (±)-Gabosine I, (±)-Gabosine G and (±)-Streptol[a]



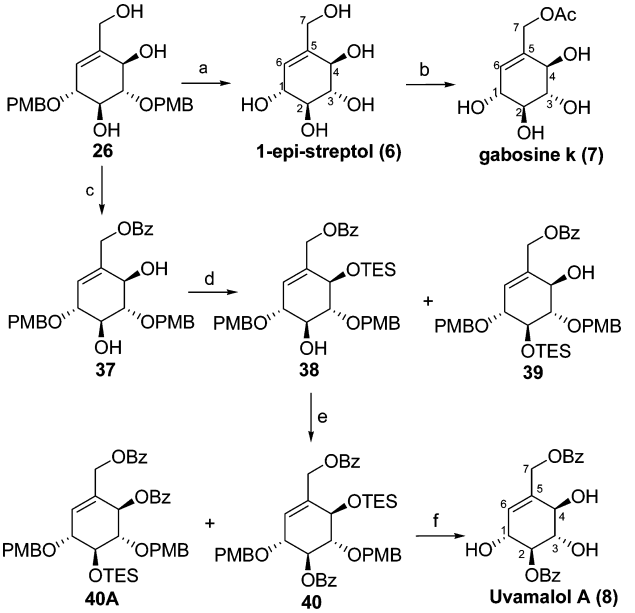
[a]Reagents and conditions: (a) DMP, CH_2Cl_2, rt, 1 h, 94%. (b) BCl_3 (1.0 M in toluene), −40 °C, 2 h, 75%. (c) 2,4,6-collidine, AcCl, −60 °C to rt, 1 h, 70%. (d) K-Selectride, −78 °C, THF, 1 h, 90%. (e) BCl_3 (1.0 M in toluene), DCM, −78 °C, 4 h, 70%.

However, to our satisfaction, reduction with K-selectride gave the reqired diol **36** stereospecifically. The bulky reducing agent ensured the hydride delivery from the side opposite to the benzyloxy group at C2. Though the less bulky $NaBH_4$ has the opportunity to attack from either sides, the stability of the product (product **32** with all equatorial substituents is more stable than the product **36** with an axial subtituent) might be controlling the stereochemistry. Finally, benzyl ether protecting groups were removed using BCl_3 (Scheme 3) to get (±)-streptol (**5**). Thus the synthesis of (±)-streptol could be completed in six steps from the common intermediate **25** in an overall 45% yield.

1-*epi*-Streptol and its monoacetate gabosine K are two other C7-cyclitols of our choice for the illustration of the utility of our methodology. The stereochemical similarity of these molecules with the intermediate **25** allow their synthesis in very few steps. The triol **26**, which could be prepared from the enal **25** in 92% yield, on treatment with 10% triflic acid in DCM gave (±)-1-*epi*-streptol (**6**) in 89% yield (Scheme 4). The primary hydroxyl group in pentol **6** was selectively acetylated using acetyl chloride and 2,4,6-collidine to afford (±)-gabosine K (**7**) in 62% yield (Scheme 4). Thus 1-*epi*-streptol and gabosine K could be synthesized from the common intermediate **25** in overall yields of 82 and 50.8%, respectively, in two and three steps.

We next turned our attention to the synthesis of uvamalol A, which was isolated from the roots of *Uvaria macrophylla*[27] and for which no synthesis or biological activity has been reported to date. Triol **26** on selective benzoylation of primary alcohol with benzoyl chloride in presence of 2,4,6-collidine gave the benzoate **37** (Scheme 4) in 95% yield. Reaction of the benzoate **37** with TESOTf in presence of imidazole gave an inseparable mixture of regioisomers **38** and **39** in 1.2:1 ratio (by ^{1}H NMR). These isomers were purified by column chromatography after bezoylation with benzoyl chloride in pyridine. The desired compound **40** was obtained in 36% yield (two steps). Deprotection of both PMB groups and TES group using 10% TFA in DCM led to the formation of (±)-uvamalol A (**8**) in 86% yield. Thus we could achieve the synthesis of Uvamalol A in five steps from the common intermediate **25** in 27% overall

Scheme 4. Total Syntheses of (±)-1-*epi*-Streptol, (±)-Gabosine K, and (±)-Uvamalol A[a]



[a]Reagents and conditions: (a) TFA (10% in DCM), rt, 1 h, 89%. (b) 2,4,6-collidine, AcCl, −60 °C, 1 h, 62%. (c) 2,4,6-collidine, BzCl, −0 °C to rt, 1 h, 95%. (d) TESOTf, DCM, imidazole, 0 °C, 2 h, 38:39 = 1.2:1, 68% overall. (e) pyridine, DMAP, BzCl, rt, 1 h, 36% (two steps). (f) TFA, DCM, rt, 1 h, 86%.

yield. To the best of our knowledge, this is the first synthesis of uvamalol A. The agreement between ^{1}H NMR and ^{13}C NMR spectra of **8** with the reported data substantiates the previously assigned structure of uvamalol.

Because of the dense functionality, *myo*-inositol has been exploited as the starting material for the syntheses of several natural products such as polyoxin J,[28] tetrodotoxin,[29] nojirimycin,[30] brahol, pinpollitol,[31] etc. The novel vinylogous orthoester hydrolysis reported here affords synthetically versatile enal, which has tremendous potential to be exploited for the synthesis of many complex natural products. The well-known protection−deprotection strategy in the chemistry of *myo*-inositol[32] can be judiciously exploited further to make orthogonally protected intermediates for complex natural product synthesis. The eight natural products we have synthesized are only a small sample of the variety of natural products that can be made using our methodology.

■ CONCLUSION

We have encountered an interesting ring-opening of the orthoester cage in *myo*-inositol orthoesters. The synthetic utility of this transformation has been illustrated by the concise syntheses of eight structurally diverse natural products. We have prepared a common α,β-unsaturated aldehyde intermediate in multigram quantities in five steps from *myo*-inositol for the synthesis of these compounds. This advanced intermediate served as the synthon for the rapid and efficient syntheses of (±)-cyclophellitol in seven steps, (±)-valienamine in five steps, (±)-1-*epi*-streptol in two steps, (±)-gabosine K in three steps, (±)-gabosine I in five steps, (±)-gabosine G in six steps, (±)-streptol in six steps and (±)-uvamalol A in five steps in very good yields in their racemic form. Many known elegant methods for chiral desymmetrization of *myo*-inositol[33] and its

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orthoesters[32b,34] and enzymatic resolution[35] might allow the synthesis of these C7-cyclitols and analogues in enantiomerically pure form. We hope this report will attract chemists to exploit this strategy in future synthetic design and this methodology might take a prominent place in chemical lexicon.

EXPERIMENTAL SECTION

General Methods. Chromatograms were visualized under UV light and by dipping plates into ceric ammonium molybdate stain followed by heating. The stain was prepared by slowly adding 10 mL of con. H_2SO_4 into the solution of ceric sulfate (1 g) and ammonium molybdate (5 g) in 90 mL of distilled water. The ^{1}H NMR, ^{13}C NMR, COSY and HMQC spectra were recorded on a 500 MHz NMR spectrometer. Proton chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.0 ppm) or with the solvent reference relative to TMS employed as the internal standard ($CDCl_3$, δ 7.26 ppm; D_2O, δ 4.79 ppm). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m)], coupling constants [Hz], integration and peak identification). All NMR signals were assigned on the basis of ^{1}H NMR, ^{13}C NMR, DEPT, COSY and HMQC experiments. ^{13}C spectra were recorded with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard. All NMR data were collected at 25 °C. Mass spectrometry were recorded by Q-TOF using electrospray ionization (ESI) mode. Melting points were determined using melting point apparatus and are uncorrected. Flash column chromatography was performed using silica gel (200−400 mesh). All reactions were carried out under argon or nitrogen atmosphere employing oven-dried glassware.

(±)-(1*R*,2*S*,5*S*,6*S*)-2,6-Bis(benzyloxy)-4-(hydroxymethyl)-cyclohex-3-ene-1,5-diol (17) and (±)-(1*S*,2*S*,5*R*,6*S*)-2,6-Bis-(benzyloxy)-4-(hydroxymethyl)cyclohex-3-ene-1,5-diol (18). To a suspension of methoxymethyltriphenylphosphonium chloride (6.3 g, 18.38 mmol) in dry THF (50 mL), a solution of potassium *tert*-butoxide (2.07 g, 18.45 mmol) in dry THF (20 mL) was added slowly at 0 °C under N_2 atmosphere. To the resultant orange suspension, a solution of ketone **13** (1.70 g, 4.6 mmol) in dry THF (15 mL) was added dropwise at 0 °C. As the reaction was very sluggish at this temperature, the mixture was allowed to warm to room temperature and then refluxed for 2 h. THF was then evaporated off under reduced pressure, and the orange residue thus obtained was dissolved in ethyl acetate and washed successively with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (ethyl acetate/petroleum ether, 1:4; v/v) gave an inseparable *E*/*Z* mixture of enol ether **14** (1.68 g, 92%) as a colorless gum. To the solution of **14** (520 mg, 1.3 mmol) in THF (10 mL), 0.1 N aqueous HCl (2 mL) was added, and the mixture was stirred for 3 h at room temperature. THF was evaporated off under reduced pressure. The residue was dissolved in ethyl acetate (EtOAc) and washed successively with aqueous $NaHCO_3$ solution, water and then with brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:2; v/v) to give an inseparable mixture of aldehydes **15** and **16** (440 mg) as a colorless gum. This gummy residue was dissolved in methanol (20 mL), and $CeCl_3{\cdot}7H_2O$ (488 mg, 1.3 mmol) was added slowly. Then $NaBH_4$ (50 mg, 1.3 mmol) was added slowly to it at 0 °C and stirred for 1 h at the same temperature. Excess $NaBH_4$ was quenched by the addition of acetone. Methanol was evaporated off in vacuo, and the resultant residue was dissolved in ethyl acetate, washed with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by column chromatography (ethyl acetate/petroleum ether, 3:2; v/v) to get a mixture of diastereomers **17** and **18** (420 mg, 90%) in 1:1 ratio as a colorless liquid. 100 mg of this diastereomeric mixture was further purified by Recycling HPLC using chiral OA-JAIGEL-4100 column and HPLC grade $CHCl_3$ as the mobile phase to get pure **17** (46 mg) and **18** (44 mg).

17: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.80 (br s, 1H, OH), 3.85 (dd, *J* = 6.2 Hz, 4.3 Hz, 1H, H-6), 3.98 (dd, *J* = 10.4 Hz, 6.2 Hz, 1H, H-1), 4.05 (d, *J* = 3.9 Hz, 1H, H-5), 4.12−4.20 (m, *J* = 3.9 Hz, 3H, H-2, H-7A and 7A′), 4.55−4.67 (m, 4H, -OC$H_A$$H_B$Ph), 5.68 (s, 1H, H-3), 7.23−7.30 (m, 10H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 64.7 (C-7), 68.6 (C-1), 69.1 (C-5), 71.6 (-OCH_2Ph), 73.3 (-OCH_2Ph), 73.5 (C-2), 79.3 (C-6), 121.3 (C-3), 127.8, 127.9, 127.9, 128.0, 128.5, 128.6, 137.7, 138.1, 140.3. Elemental analysis calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79. Found: C, 70.91; H, 6.64.

18: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.12 (br s, 3H, OH), 3.88 (dd, *J* = 4.0 Hz, 2.0 Hz, 1H, H-6), 3.97 (dd, *J* = 4.8 Hz, 1.6 Hz, 1H, H-1), 4.16−4.12 (m, 3H, H-2, H-7A and 7A′), 4.28 (d, *J* = 3.8 Hz, 1H, H-5), 4.52 (d, *J* = 11.6 Hz, 1H, -OCH_APh), 4.59 (d, *J* = 11.6 Hz, 1H, -OCH_BPh), 4.64 (d, *J* = 11.5 Hz, 1H, -OCH_APh), 4.78 (d, *J* = 11.5 Hz, 1H, -OCH_BPh), 5.78 (d, *J* = 2.2 Hz, 1H, H-3), 7.23−7.25 (m, 10H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 64.6 (C-7), 67.3 (C-5), 71.6 (C-1), 71.7 (-OCH_2Ph), 72.8 (-OCH_2Ph), 76.2 (C-6), 76.9 (C-2), 122.5 (C-3), 127.8, 127.9, 128.0, 128.1, 128.5, 128.6, 137.8, 138.0, 140.1. Elemental analysis calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79. Found: C, 71.08; H, 6.88.

(±)-(1*S*,3*R*,4*S*,5*S*,6*R*,2*E*/*Z*)-2-Methoxymethyl-4,6-di-*O*-(benzyl)-*myo*-inositol 1,3,5-orthoformate (20). To a suspension of methoxymethyltriphenylphosphonium chloride (1.11 g, 3.2 mmol) in dry THF (5 mL), a solution of potassium *tert*-butoxide (365 mg, 3.2 mmol) in dry THF (5 mL) was added slowly at 0 °C under N_2 atmosphere. To this mixture, a solution of ketone **19** (240 mg, 0.65 mmol) in dry THF (10 mL) was added dropwise at 0 °C. The mixture was warmed to room temperature and then refluxed for 2 h. THF was evaporated off in vacuo. The orange residue thus obtained was dissolved in ethyl acetate and washed with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (ethyl acetate/petroleum ether, 1:6; v/v) gave the enol ether **20** (232 mg, 90%) as a gummy liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.58 (s, 3H, -OCH_3), 4.13 (t, *J* = 2.7 Hz, 1H, H-6), 4.19−4.20 (m, 2H, H-1, H-4), 4.34 (s, 1H, H-5), 4.49 (d, *J* = 3.3 Hz, 1H, -OCH_APh), 4.52 (d, *J* = 3.1 Hz, 1H, -OCH_BPh), 4.60 (d, *J* = 12.1 Hz, 1H, -OCH_APh), 4.64 (d, *J* = 11.9 Hz, 1H, -OCH_BPh), 5.02 (d, *J* = 1.5 Hz, 1H, H-3), 5.52 (s, 1H, H-7), 6.17 (s, 1H, H-8), 7.21−7.19 (m, 10H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 59.2, 65.6 (C-3), 68.6 (C-5), 70.1, 70.2, 70.7, 72.0 (C-1 and C-4), 72.3 (C-6), 76.2, 103.6, 105.3, 126.6, 126.7, 126.76, 126.8, 126.9, 127.0, 127.2, 127.3, 127.36, 127.4, 127.6, 136.9, 137.0, 144.7. Elemental analysis calcd for $C_{23}H_{24}O_6$: C, 69.68; H, 6.10. Found: C, 69.96; H, 6.38.

(±)-(3*S*,4*R*,5*R*,6*S*)-4,6-Bis(benzyloxy)-2-(hydroxymethyl)-cyclohex-1-ene-3,5-diol (22). To a solution of **20** (155 mg, 0.39 mmol) in THF (10 mL), 0.1 N aqueous HCl (2 mL) was added, and the mixture was stirred for 2 h at room temperature. THF was evaporated off under reduced pressure. The residue was dissolved in ethyl acetate and washed successively with saturated $NaHCO_3$ solution, water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude mass was purified by flash column chromatography (ethyl acetate/petroleum ether, 3:7; v/v) to give the aldehyde **21** (142 mg) along with its formate ester as a colorless oil. This residue was dissolved in methanol (10 mL), and to this solution, $CeCl_3{\cdot}7H_2O$ (156 mg, 0.41 mmol) was slowly added. Then $NaBH_4$ (19 mg, 0.50 mmol) was added slowly to it at 0 °C and stirred for 1 h at the same temperature. Excess $NaBH_4$ was quenched with acetone. Methanol was evaporated off in vacuo, and the residue was dissolved in ethyl acetate, washed with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (ethyl acetate/petroleum ether, 3:2; v/v) to give compound **22** (127 mg, 91%) as a white solid: mp 79−81 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.5 (br s, 3H, OH), 3.41 (dd, *J* = 10.1 Hz, 7.9 Hz, 1H, H-4), 3.73 (dd, *J* = 10.2 Hz, 7.9 Hz, 1H, H-5), 4.02 (d, *J* = 7.6 Hz, 1H, H-6), 4.06 (s, 2H, H-7A and 7A′), 4.32 (d, *J* = 7.6 Hz, 1H, H-3), 4.64 (d, *J* =

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11.6 Hz, 1H, -OCH_APh), 4.67 (d, J = 11.8 Hz, 1H, -OCH_BPh), 4.78 (d, J = 11.6 Hz, 1H, -OCH_APh), 4.82 (d, J = 11.5 Hz, 1H, -OCH_BPh), 5.56 (s, 1H, H-1), 7.3−7.22 (m, 10H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 64.1 (C-7), 72.3, 73.2 (C-3), 74.9 (C-5), 75.0, 76.7, 77.0, 77.2, 79.3 (C-6), 84.1 (C-4), 124.1 (C-1), 127.8, 127.9, 128.0, 128.1, 128.5, 128.7, 138.2, 138.4, 138.5. Elemental analysis calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79. Found: C, 70.90; H, 6.71.

(±)-(1*R*,3*S*,4*R*,5*S*,6*S*,2*E*/*Z*)-2-Methoxymethyl-4,6-di-*O*-(4-methoxybenzyl)-*myo*-inositol 1,3,5-orthoformate (24). To a suspension of methoxymethyltriphenylphosphonium chloride (14.86 g, 43.35 mmol) in dry THF (50 mL) was added a solution of potassium *tert*-butoxide (4.86 g, 43.35 mmol) in dry THF (20 mL) slowly at 0 °C under N_2 atmosphere. To the resultant orange suspension, a solution of ketone **23** (6.12 g, 14.2 mmol) in dry THF (20 mL) was added slowly at 0 °C. The mixture was warmed to room temperature and then refluxed for 2 h. The THF was evaporated in vacuo. The orange residue was dissolved in ethyl acetate and washed with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (ethyl acetate/petroleum ether, 1:4; v/v) gave the enol ether **24** (6.19 g, 95%) as a white crystalline solid: mp 80−82 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.61 (s, 3H, -OCH_3), 3.74 (s, 3H, -OCH_3), 3.75 (s, 3H, -OCH_3), 4.07 (d, J = 3.2 Hz, 1H, H-4), 4.14 (dd, J = 3.2 Hz, 2.3 Hz, 1H, H-6), 4.37 (dd, J = 3.2 Hz, 1.7 Hz, 1H, H-3), 4.48 (d, J = 12.5 Hz, 2H, OCH_AH_B-*p*-MeOPh), 4.51 (d, J = 14.3 Hz, 2H, OCH_AH_B-*p*-MeOPh), 4.54 (dd, J = 3.3 Hz, 1.7 Hz, 1H, H-5), 4.89 (dd, J = 3.1 Hz, 1.6 Hz, 1H, H-1), 5.66 (s, 1H, H-7), 6.38 (s, 1H, H-8), 6.82 (d, J = 8.7 Hz, 2H, Ar−H), 6.86 (d, J = 8.7 Hz, 2H, Ar−H), 7.19 (d, J = 8.7 Hz, 2H, Ar−H), 7.22 (d, J = 8.7 Hz, 2H, Ar−H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 54.9, 54.9, 59.7, 66.0 (C-1), 68.5 (C-5), 69.4, 69.6, 70.5 (C-3), 72.8 (C-4 and C-6), 103.8 (C-2), 106.4, 113.4, 113.5, 129.2, 129.3, 130.1, 130.2, 145.4, 158.6, 158.6. Elemental analysis calcd for $C_{25}H_{28}O_8$: C, 65.78; H, 6.18. Found: C, 65.79; H, 6.12.

(±)-(1*R*,2*S*,3*S*,4*R*)-2,4-Dihydroxy-1,3-bis((4-methoxybenzyl)-oxy)cyclohex-5-ene-carb-5-aldehyde (25). To a solution of **24** (2.4 g, 5.26 mmol) in THF (20 mL) was added 0.1 N aqueous HCl (5 mL) at room temperature, and the mixture was stirred for 8 h at the same temperature. THF was evaporated off in vacuo. The residue was dissolved in ethyl acetate and washed with aqueous $NaHCO_3$ solution, water and then with brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude material thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:3; v/v) to give the compound **25** (2.17 g, 100%) as a white solid: mp 126−128 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.58 (dd, J = 10.3 Hz, 7.4 Hz, 1H, H-3), 3.77 (dd, J = 10.3 Hz, 8.3 Hz, 1H, H-2), 3.84 (s, 6H, -OCH_3), 4.30 (td, J = 8.2 Hz, 2.2 Hz, 1H, H-1), 4.72−4.88 (m, 3H, H-4, -OCH_AH_B-*p*-MeOPh), 4.87 (d, J = 11.3 Hz, 1H, -OCH_A-*p*-MeOPh), 5.04 (d, J = 11 Hz, 1H, -OCH_B-*p*-MeOPh), 6.57 (s, 1H, H-6), 6.92 (d, J = 2.1 Hz, 2H, Ar−H), 6.93 (d, J = 2.1 Hz, 2H, Ar−H), 7.34 (d, J = 3.1 Hz, 2H, Ar−H), 7.36 (d, J = 3.4 Hz, 2H, Ar−H), 9.47 (s, 1H, H-7); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3 (-OCH_3), 71.2 (C-4), 73.1, 73.5 (C-2), 74.6, 77.5 (C-1), 81.9 (C-3), 113.9, 114.0, 129.7, 129.8, 129.9, 130.2, 139.5, 148.2 (C-6), 157.4, 159.5, 194.4 (C-7); IR (neat) 3404, 1743, 1685, 1612 cm^{-1}. Elemental analysis calcd for $C_{23}H_{26}O_7$: C, 66.65; H, 6.32. Found: C, 66.71; H, 6.52.

(±)-(1*R*,2*S*,3*S*,4*R*)-4-(Hydroxymethyl)-1,3-bis((4-methoxybenzyl)oxy)cyclohex-5-ene-2,4-diol (26). To a solution of **25** (1 g, 2.41 mmol) in MeOH (15 mL) was slowly added $CeCl_3·7H_2O$ (1.7 g, 4.56 mmol) and then $NaBH_4$ (132 mg, 3.48 mmol) at 0 °C, and the mixture was stirred for 1 h at the same temperature. Excess $NaBH_4$ was quenched by the addition of acetone. Methanol was evaporated off in vacuo, and the residue was dissolved in ethyl acetate, washed with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:1; v/v) to give compound **26** (0.92 g, 92%) as a white solid: mp 83−85 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.32 (br s, 1H, OH-7), 2.65 (s, 1H, OH-2), 2.70 (br s, 1H, OH-4), 3.39 (dd, J = 10 Hz, 8.2 Hz, 1H, H-3), 3.67−3.72 (m, 7H, H-2, -OCH_3), 3.99 (d, J = 7.5 Hz, 1H, H-1), 4.08 (s, 2H, H-7A and 7A′), 4.29 (d, J = 6.9 Hz, 1H, H-4), 4.57 (s, 2H, -OCH_AH_B-*p*-MeOPh), 4.68 (d, J = 11.5 Hz, 1H, -OCH_A-*p*-MeOPh), 4.76 (d, J = 11 Hz, 1H, -OCH_B-*p*-MeOPh), 5.55 (s, 1H, H-6), 6.80 (d, J = 8.7 Hz, 2H, Ar−H), 6.82 (d, J = 8.25 Hz, 2H, Ar−H), 7.19 (d, J = 8.7 Hz, 2H, Ar−H), 7.23 (d, J = 8.9 Hz, 2H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 64.2 (C-7), 71.9, 73.3 (C-4), 74.7, 74.9 (C-2), 78.9 (C-1), 83.7 (C-3), 113.9, 114.1, 124.2 (C-6), 129.5, 129.7, 130.2, 130.5, 138.3 (C-5), 159.3, 159.5. Elemental analysis calcd for $C_{23}H_{28}O_7$: C, 66.33; H, 6.78. Found: C, 66.29; H, 6.80.

(±)-(1*R*,2*S*,3*S*,4*R*)-4-(Benzyloxymethyl)-2,4-bis(benzyloxy)-1,3-bis((4-methoxybenzyl)oxy)cyclohex-5-ene (27). To a solution of **26** (500 mg, 1.2 mmol) in DMF (10 mL), NaH (60% dispersion in mineral oil, 192 mg, 4.8 mmol) was added slowly at 0 °C over a period of 5 min. To this solution, BnBr (0.58 mL, 4.8 mmol) was added dropwise at 0 °C, and the reaction mixture was further stirred for 20 min at the same temperature, by which time TLC showed completion of the reaction. Excess NaH was quenched by adding ice cold water, and the solvents were evaporated off in vacuo. The residue was taken in dichloromethane (150 mL), washed with water and brine. Organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:5; v/v) to get **27** (754 mg, 91%) as a white solid: mp 54−56 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66 (dd, J = 10.4 Hz, 7.7 Hz, 1H, H-3), 3.71−3.74 (m, 7H, H-2, -OCH_3), 3.84 (d, J = 12.1 Hz, 1H, H-7A), 4.11−4.13 (m, 2H, H-4, H-7A′), 4.20 (d, J = 7.5 Hz, 1H, H-1), 4.27 (d, J = 11.8 Hz, 1H, -OCH_APh), 4.44 (d, J = 11.8 Hz, 1H, -OCH_BPh), 4.56 (s, 2H, -OCH_AH_BPh), 4.60−4.66 (m, 2H, -OCH_AH_BPh), 4.75 (d, J = 9.9 Hz, 1H, -OCH_APh), 4.81−4.83 (m, 3H, -OCH_AH_BPh), 5.68 (s, 1H, H-5), 6.74 (d, J = 8.6 Hz, 2H, Ar−H), 6.77 (d, J = 8.6 Hz, 2H, Ar−H), 7.13−7.29 (m, 19H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.5 (-OCH_3), 69.9 (C-7), 72.1, 72.2, 74.8, 75.2, 75.4, 79.5 (C-4), 80.1 (C-1), 83.8 (C-2), 84.2 (C-3), 113.8, 113.8, 125.2 (C-5), 127.5, 127.6, 127.7, 127.8, 127.9, 128.3, 129.4, 129.5, 129.6, 130.4, 130.8, 136.3, 138.1, 138.5, 138.8, 159.2. Elemental analysis calcd for $C_{44}H_{46}O_7$: C, 76.94; H, 6.75. Found: C, 77.24; H, 7.02.

(±)-(1*R*,2*S*,3*S*,4*R*,5*S*,6*S*)-2,4-Bis(benzyloxy)-5-((benzyloxy)-methyl)-1,3-bis((4-methoxybenzyl)oxy)cyclohexan-6-ol (28). To a solution of $BH_3·SMe_2$ (1.0 M in THF, 1.23 mL, 1.23 mmol) in anhydrous THF (5 mL) at 0 °C, a solution of **27** (850 mg, 1.23 mmol) in THF (10 mL) dropwise was added. The reaction mixture was stirred for 8 h at room temperature and then cooled to 10 °C. To this solution, 30% H_2O_2 (0.4 mL) and 3 M NaOH (1.2 mL) were added slowly, and the mixture was further stirred for 8 h at ambient temperature. THF was evaporated off under reduced pressure, and the aqueous layer was extracted with ethyl acetate (200 mL). The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue thus obtained on flash column chromatography (ethyl acetate/petroleum ether, 1:3; v/v) yielded **28** (706.5 mg, 81%) as pure white solid: mp 82−84 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.52 (dd, J = 9.4 Hz, 9.2 Hz, 1H, H-5), 3.31−3.34 (m, 2H, H-1, H-4), 3.50−3.52 (m, 3H, H-2, H-3, H-6), 3.67 (d, J = 7.6 Hz, 1H, H-7A), 3.72 (s, 3H, -OCH_3), 3.73 (s, 3H, -OCH_3), 3.78 (d, J = 8.1 Hz, 1H, H-7A′), 4.42−4.54 (m, 3H, -OCH_AH_BPh), 4.63−4.83 (m, 7H, -OCH_AH_BPh), 5.17 (d, J = 6.3 Hz, 1H, OH-6), 6.82 (d, J = 4.7 Hz, 2H, Ar−H), 6.84 (d, J = 4.5 Hz, 2H, Ar−H), 7.17 (d, J = 8.4 Hz, 2H, Ar−H), 7.20 (d, J = 10 Hz, 2H, Ar−H), 7.26−7.38 (m, 15H, Ar−H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 51.3 (C-5), 60.2 (-OCH_3), 69.7 (C-7), 73.6, 77.5, 79.2, 79.4, 79.8, 82.4, 87.5, 90.2, 90.6, 118.5, 118.7, 132.5, 132.8, 133.4, 134.2, 134.4, 136.0, 136.4, 143.9, 144.1, 163.7, 163.8. Elemental analysis calcd for $C_{44}H_{48}O_8$: C, 74.98; H, 6.86. Found: C, 74.93; H, 6.90.

(±)-(1*S*,2*R*,3*S*,4*R*,5*R*,6*S*)-2,4-Bis(benzyloxy)-5-((benzyloxy)-methyl)-1,3-bis((4-methoxybenzyl)oxy)-cyclohex-6-yl methanesulfonate (29). To a solution of **28** (620 mg, 0.88 mmol) in pyridine (10 mL), MsCl (0.136 mL, 1.76 mmol) was added at 0 °C, and the mixture was stirred for 1 h at the same temperature. Pyridine

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was evaporated off under reduced pressure, and the residue was dissolved in ethyl acetate, washed with diluted HCl, water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Crude product thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:3; v/v) to get **29** (688 mg, 100%) as a white solid: mp 80−82 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.84 (dd, J = 11 Hz, 10.9 Hz, 1H, H-5), 2.81 (s, 3H, -CH_3), 3.55−3.61 (m, 3H, H-1, H-2, H-3), 3.65 (d, J = 9.3 Hz, 1H, H-7A), 3.71 (dd, J = 11 Hz, 9.5 Hz, 1H, H-4), 3.77 (s, 3H, -OCH_3), 3.78 (s, 3H, -OCH_3), 3.85 (dd, J = 9.3 Hz, 2.0 Hz, 1H, H-7A′), 4.35 (d, J = 13.1 Hz, 1H, -OCH_A-*p*-MeOPh), 4.53 (d, J = 10.6 Hz, 1H, C*H*Ph), 4.58 (d, J = 11.3 Hz, 1H, -OCH_B-*p*-MeOPh), 4.65 (d, J = 10.7 Hz, 1H, C*H*Ph), 4.79−4.87 (m, 5H, H-6, CH_2Ph), 4.92 (d, J = 10.7 Hz, 1H, C*H*Ph), 4.97 (d, J = 10.7 Hz, 1H, C*H*Ph), 6.80 (d, J = 15.2 Hz, 2H, Ar−H), 6.83 (d, J = 8.6 Hz, 2H, Ar−H), 7.16−7.35 (m, 19H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 38.7, 45.3 (C-5), 55.2, 63.8, 73.0, 74.9, 75.4, 75.6, 75.8, 76.4, 76.7, 77.0, 77.2, 77.5, 79.5, 82.4, 82.6, 85.3, 113.8, 113.82, 127.6, 127.7, 127.8, 127.9, 128.1, 128.3, 128.4, 128.9, 129.3, 130.0, 130.5, 138.1, 138.2, 138.3, 159.1, 159.2. Elemental analysis calcd for $C_{45}H_{50}O_{10}S$: C, 69.03; H, 6.44; S, 4.10. Found: C, 69.32; H, 6.41; S, 3.84.

(±)-(1*S*,2*R*,3*S*,4*R*,5*R*,6*S*)-2,4-Bis(benzyloxy)-5-((benzyloxy)-methyl)-1,3-dihydroxycyclohex-6-yl methanesulfonate (30). To a solution of **29** (660 mg, 0.84 mmol) in dichloromethane (10 mL), TFA (1 mL) was added at room temperature, and then the reaction mixture was stirred for 1 h at the same temperature. Dichloromethane was evaporated off in vacuo, and the residue was dissolved in ethyl acetate and washed successively with aqueous sodium bicarbonate solution, water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:2; v/v) to get **30** (400 mg, 88%) as a colorless liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.73 (dd, J = 10.7 Hz, 10.6 Hz, 1H, H-5), 2.37 (s, 1H, OH), 2.7 (s, 1H, OH), 3.01 (s, 3H, -CH_3), 3.17 (dd, J = 9.2 Hz, 9.2 Hz, 1H, H-2), 3.4−3.61 (m, 4H, H-1, H-3, H-4, H-7A), 3.75 (d, J = 9.4 Hz, 1H, H-7A′), 4.33 (d, J = 11.3 Hz, 1H, -OCH_APh), 4.54 (d, J = 11.3 Hz, 2H, -OCH_BPh), 4.64−4.77 (m, 3H, -OCH_AH_BPh, H-6), 4.86 (d, J = 11.3 Hz, 1H, -OCH_APh), 7.16−7.32 (m, 15H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 37.8, 43.7 (C-5), 62.7 (C-7), 72.4, 73.5, 74.2, 74.3, 75.7, 75.8, 79.0 (C-6), 80.4 (C-2), 126.7, 126.9, 127.0, 127.1, 127.3, 127.4, 127.6, 127.7, 136.9, 137.1. Elemental analysis calcd for $C_{29}H_{34}O_8S$: C, 64.19 H, 6.32 S, 5.91. Found: C, 64.50; H, 6.12; S, 5.67.

(±)-(1*R*,2*R*,3*S*,4*R*,5*R*,6*R*)-2,4-Bis(benzyloxy)-5-((benzyloxy)-methyl)-7-oxabicyclo[4.1.0]heptan-3-ol (31). To a solution of **30** (360 mg, 0.66 mmol) in DMF (10 mL), NaH (60% dispersion in mineral oil, 39.6 mg, 0.99 mmol) was added at 0 °C, and the mixture was stirred for 20 min at the same temperature. Excess NaH was quenched by adding ice cold water. Ethyl acetate (150 mL) was added to it, and the mixture was washed with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:5; v/v) to get **31** (270 mg, 91%) as a white solid: mp 64−66 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.19−2.22 (m, 1H), 3.11−3.16 (m, 2H), 3.39 (d, J = 2.9 Hz, 1H), 3.55−3.64 (m, 3H), 3.70 (dd, J = 8.9 Hz, 3.6 Hz, 1H), 4.42 (d, J = 11.1 Hz, 1H), 4.48 (s, 2H), 4.70 (d, J = 11.6 Hz, 1H), 4.70 (d, J = 11.6 Hz, 1H), 4.75 (d, J = 11.6 Hz, 1H), 7.17−7.34 (m, 15H, Ar−H). NMR data are similar to the reported values.[36] Elemental analysis calcd for $C_{28}H_{30}O_5$: C, 75.31; H, 6.77. Found: C, 75.55; H, 6.78.

Cyclophellitol (1). To a solution of **31** (25 mg, 0.05 mmol) in ethyl acetate (5 mL), 10% Pd/C (15 mg) was added, and the resulting suspension was stirred under hydrogen atmosphere (1 atm, hydrogen balloon) for overnight at 0 °C. The reaction mixture was then filtered through a sterile syringe filter (0.20 μm), the residue was washed with MeOH. The combined filtrate was concentrated in vacuo at low temperature, and the product, **1** was isolated as a white solid (9.8 mg, 100%) without further purification. ^{1}H NMR data are similar to the reported values:[13c] mp 150−151 °C; ^{1}H NMR (500 MHz, D_2O) 2.01−2.05 (m, 1H), 3.14−3.18 (m, 2H), 3.28 (dd, J = 10.5 Hz, 9 Hz, 1H), 3.47 (d, J = 2.0 Hz, 1H), 3.69−3.91 (m, 2H), 3.93 (dd, J = 11.5 Hz, 4 Hz, 1H).

(±)-(1*R*,2*S*,3*S*,4*R*)-2,4-Bis(benzyloxy)-5-((benzyloxy)methyl)-cyclohex-5-ene-1,3-diol (32). To a 10% solution of TFA in DCM (10 mL), tribenzyl ether **27** (470 mg, 0.68 mmol) was added at room temperature, and the reaction mixture was stirred for 1 h at the same temperature. Excess TFA was quenched by adding aqueous $NaHCO_3$, and the solution was extracted with ethyl acetate (150 mL). The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:2; v/v) to get diol **32** (280 mg, 91%) as a colorless oil: ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.26 (dd, J = 10.5 Hz, 8 Hz, 1H, H-2), 3.66−3.72 (m, 1H, H-3), 3.88 (d, J = 12 Hz, 1H, H-7A), 4.04−4.10 (m, 3H, H-1, H-4, H-7A′), 4.42 (d, J = 12 Hz, 1H, -OCH_APh), 4.47 (d, J = 11.5 Hz, 1H, -OCH_BPh), 4.60 (d, J = 11 Hz, 1H, -OCH_APh), 4.79−4.85 (m, 3H, -OCH_AH_BPh), 5.2 (d, J = 5.5 Hz, 1H, OH-1), 5.29 (d, J = 5.5 Hz, 1H, OH-3), 5.59 (s, 1H, H-6), 7.25−7.47 (m, 15H, Ar−H); ^{13}C NMR (500 MHz, DMSO-d_6) δ 69.7 (C-7), 70.9 (C-1), 71.8, 73.5, 74.0, 75.6 (C-3), 80.9 (C-4), 84.9 (C-2), 127.5, 127.7, 127.9, 127.9, 128.0, 128.1, 128.3, 128.5, 128.7, 129.5, 134.6 (C-6), 138.8, 139.5, 139.9. Elemental analysis calcd for $C_{28}H_{30}O_5$: C, 75.31; H, 6.77. Found: C, 75.14; H, 6.80.

(±)-(1*S*,2*S*,3*S*,4*R*)-1-Azido-2,4-bis(benzyloxy)-5-((benzyloxy)-methyl)cyclohex-5-en-3-ol (33). To a solution of diol **32** (35 mg, 0.07 mmol) in toluene (3 mL), diphenylphosphorylazide (0.05 mL, 0.23 mmol) and 1,8-diazabicycloundec-7-ene (0.03 mL, 0.23 mmol) were added at 0 °C.[22] The reaction mixture was stirred for 4 h at the same temperature. Then, NaN_3 was added to the reaction mixture at 0 °C, and it was further stirred for 4 h at room temperature. The reaction was quenched by adding 2 N HCl (1 mL) and diluted with ethyl acetate (50 mL). The organic layer was washed with water and brine, separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:4; v/v) to get **33** (30.6 mg, 83%) as a colorless liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.43 (dd, J = 10.3 Hz, 4.1 Hz, 1H, H-2), 3.93 (d, J = 12.9 Hz, 1H, H-7A), 3.99 (d, J = 7.8 Hz, 1H, H-4), 4.08 (d, J = 13 Hz, 1H, H-7A'), 4.10 (dd, J = 10.3 Hz, 7.8 Hz, 1H, H-3), 4.12 (dd, J = 4.7 Hz, 4.2 Hz, 1H, H-1), 4.38−4.44 (m, 2H, -OCH_AH_BPh), 4.54 (d, J = 11.5 Hz, 1H, -OCH_APh), 4.62 (d, J = 11.4 Hz, 1H, -OCH_APh), 4.7 (d, J = 11.5 Hz, 1H, -OCH_BPh), 4.83 (d, J = 11.3 Hz, 1H, -OCH_BPh), 5.78 (dd, J = 4.7 Hz, 1.1 Hz, 1H, H-6), 7.18−7.31 (m, 15H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.2 (C-1), 69.8 (C-7), 72.3 (C-3), 73.0, 73.6, 78.7 (C-2), 79.4 (C-4), 119.7 (C-6), 127.6, 127.7, 127.9, 128.1, 128.2, 128.3, 128.4, 128.45, 128.5, 128.6, 128.7, 137.2, 137.9, 138.5, 141.7; IR (neat) 3012, 2106, 1496, 1454 cm^{-1}. Elemental analysis calcd for $C_{28}H_{29}N_3O_4$: C, 71.32; H, 6.20 N, 8.91. Found: C, 71.07; H, 6.37; N, 8.79.

Valienamine (2). To a solution of azide **33** (20 mg, 0.05 mmol) in DCM (5 mL), a 1 M solution of BCl_3 in toluene (0.2 mL, 0.2 mmol) was added at −60 °C, and the reaction mixture was allowed to warm to room temperature slowly over a period of 4 h. Excess BCl_3 was quenched by adding aqueous NH_3 solution. The reaction mixture was evaporated to dryness completely under reduced pressure. The residue thus obtained was chromatographed to get valienamine (**2**) as a syrupy material (5.9 mg, 80%). Because of its hygroscopic nature and broadened signals in ^{1}H NMR, it was characterized as its pentaacetate **34**. The above syrupy **2** was dissolved in pyridine (5 mL), and to this solution acetic anhydride (1 mL) and DMAP (2 mg) were added, and the reaction mixture was stirred for overnight at room temperature. Pyridine was evaporated off under reduced pressure, and the residue was dissolved in ethyl acetate and washed with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated. Flash column chromatography (acetone/petroleum ether, 1:6; v/v) gave pentaacetate **34** (11.6 mg, 90%) as a white solid, whose ^{1}H NMR data was identical with the reported data:[13i] mp 92−94 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.95−2.00 (m, 15H), 4.33

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(d, J = 13.3 Hz, 1H), 4.57 (d, J = 13.3 Hz, 1H), 4.96−5.03 (m, 2H), 5.29 (d, J = 6.2 Hz, 1H), 5.39 (dd, J = 9.9 Hz, 6.4 Hz, 1H), 5.57 (d, J = 8.9 Hz, 1H), 5.82 (d, J = 4.9 Hz, 1H).

(±)-(2*R*,3*S*,4*R*)-2,4-Bis(benzyloxy)-5-((benzyloxy)methyl)-3-hydroxycyclohex-5-en-1-one (35). To a solution of diol **32** (165 mg, 0.37 mmol) in DCM (5 mL), Dess−Martin periodinane (227.8 mg, 0.55 mmol) was added at room temperature, and the reaction mixture was stirred for 1 h at the same temperature. When the TLC showed, completion of the reaction (1 h), the reaction mixture was diluted by adding chloroform (50 mL), and then the mixture was washed successively with aqueous $Na_2S_2O_3$, water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:4; v/v) to get ketone **35** (155 mg, 94%) as a light brown liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (d, J = 10.7 Hz, 1H, H-2), 4.08−4.14 (m, 2H, H-3, H-7A), 4.28−4.32 (m, 2H, H-4, H-7A′), 4.52 (d, J = 12.1 Hz, 1H, -OCH_APh), 4.54 (d, J = 13.7 Hz, 1H, -OCH_BPh), 4.65 (d, J = 11.2 Hz, 1H, -OCH_APh), 4.74 (d, J = 11.3 Hz, 1H, -OCH_APh), 4.98 (d, J = 11.3 Hz, 1H, -OCH_BPh), 5.15 (d, J = 11.2 Hz, 1H, -OCH_BPh), 6.22 (d, J = 1.8 Hz, 1H, H-6), 7.25−7.43 (m, 15H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 68.9 (C-7), 73.2, 73.9, 75.0, 76.9 (C-3), 78.9 (C-4), 82.6 (C-2), 123.7 (C-6), 127.7, 127.9, 128.0, 128.1, 128.2, 128.4, 128.5, 128.51, 128.6, 137.4, 137.5, 137.8, 158, 196 (C-1); IR (neat) 3587, 3010, 2866, 1718, 1496, 1454 cm^{-1}. Elemental analysis calcd for $C_{28}H_{28}O_5$: C, 75.65; H, 6.35. Found: C, 75.58; H, 6.25.

Gabosine I (3). To a solution of ketone **35** (60 mg, 0.13 mmol) in DCM (5 mL), a 1.0 M solution of BCl_3 in toluene (0.67 mL, 0.67 mmol) was added at −40 °C and stirred for 2 h at the same temperature. Excess BCl_3 was quenched by adding aqueous NH_3 solution. When the TLC showed completion of the reaction (2 h), the solvents were evaporated, and the crude residue was purified by flash column chromatography ($CHCl_3$/MeOH, 8:1; v/v) to get valienone (**3**) (17.6 mg, 75%) as a pale brown oil, whose ^{1}H NMR data were identical to the reported data:[13o] ^{1}H NMR (500 MHz, CD_3OD) δ 3.51 (dd, J = 10.8 Hz, 8.3 Hz, 1H), 3.94 (d, J = 10.8 Hz, 1H), 4.22−4.43 (m, 2H), 4.41 (d, J = 18.3 Hz, 1H), 6.07 (d, J = 2 Hz, 1H).

Gabosine G (4). To a solution of **3** (65 mg, 0.37 mmol) in 2,4,6-collidine (2 mL), AcCl (0.02 mL, 0.4 mmol) was added at −60 °C, and the reaction mixture was stirred for 1 h at the same temperature. When the reaction was complete (judged by TLC), collidine was evaporated off under reduced pressure. The crude residue thus obtained was purified by flash column chromatography (ethyl acetate) to get gabosine G (**4**) (56.4 mg, 70%) as a colorless oil:[13o] ^{1}H NMR (500 MHz, CD_3OD) δ 2.04 (s, 3H), 3.53 (dd, J = 10.7 Hz, 8.4 Hz, 1H), 3.95 (d, J = 10.9 Hz, 1H), 4.31−4.33 (m, 1H), 4.84−4.87 (m, 2H), 5.92 (d, J = 1.9 Hz, 1H).

(±)-(1*S*,2*S*,3*S*,4*R*)-2,4-Bis(benzyloxy)-5-((benzyloxy)methyl)-cyclohex-5-ene-1,3-diol (36). To a solution of **35** (100 mg, 0.22 mmol) in THF (5 mL), K-selectride (0.3 mL, 1.0 M in THF, 0.3 mmol) was added at −78 °C, and the reaction mixture was stirred for 1 h at the same temperature. THF was evaporated off under reduced pressure, and the residue was dissolved in ethyl acetate (100 mL), washed twice with brine solution. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:4; v/v) to get diol **36** (90 mg, 90%) as a colorless liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.32 (dd, J = 10.3 Hz, 3.9 Hz, 1H, H-2), 3.9 (d, J = 12.5 Hz, 1H, H-7A), 4.01 (d, J = 7.4 Hz, 1H, H-4), 4.09−4.15 (m, 2H, H-3, H-7A′), 4.23 (dd, J = 5.0 Hz, 4.5 Hz, 1H, H-1), 4.39 (d, J = 11.8 Hz, 1H, -OCH_APh), 4.43 (d, J = 11.8 Hz, 1H, -OCH_BPh), 4.59−4.68 (m, 3H, -OCH_ACH_BPh), 4.81 (d, J = 11.4 Hz, 1H, -OCH_APh), 5.89 (dd, J = 4.5 Hz, 1.0 Hz, 1H, H-6), 7.18−7.3 (m, 15H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 62.4 (C-1), 69.1, 70.6 (C-3), 71.2, 71.8, 72.6, 78.2 (C-2), 78.6 (C-4), 122.7 (C-6), 126.5, 126.6, 126.7, 127.0, 127.2, 127.3, 127.4, 127.7, 136.5, 137, 137.6, 139.3. Elemental analysis calcd for $C_{28}H_{30}O_5$: C, 75.31; H, 6.77. Found: C, 75.09; H, 6.92.

Streptol (5). To a solution of diol **36** (90 mg, 0.20 mmol) in DCM (10 mL), a 1.0 M solution of BCl_3 in toluene (1 mL, 1.0 mmol) was added at −78 °C, and the reaction mixture was stirred for 4 h at the same temperature. Excess BCl_3 was quenched by adding aqueous NH_3. The solvents were evaporated under reduced pressure to get a white solid. This residue was purified by flash column chromatography ($CHCl_3$/MeOH, 4:1; v/v) to obtain pure streptol **5** (25 mg, 70%) as a colorless oil, whose ^{1}H NMR data were similar to the reported data:[13n] ^{1}H NMR (500 MHz, CD_3OD) δ 3.22−3.24 (m, 1H), 3.65 (dd, J = 10.0 Hz, 7.3 Hz, 1H), 3.90 (d, J = 7.6 Hz, 1H), 4.09−4.13 (m, 3H), 5.73−5.74 (m, 1H).

1-*epi*-Streptol (6). To a 10% solution of TFA in DCM (10 mL), triol **26** (40 mg, 0.09 mmol) was added at room temperature, and the reaction mixture was stirred for 1 h at the same temperature. DCM was evaporated off to dryness to get a white residue. This residue was further purified by washing with DCM (10 mL × 3) to get pure 1-*epi*-streptol **6** (15 mg, 89%) as a white solid: mp 134−136 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.10 (dd, J = 9.3 Hz, 8.3 Hz, 1H, H-2), 3.19 (dd, J = 9.6 Hz, 7.8 Hz, 1H, H-3), 3.86−3.97 (m, 4H, H-1, H-4, H-7A, H-7A′), 4.57 (dd, J = 5.2 Hz, 4.8 Hz, 1H, OH), 4.58−4.83 (m, 4H, OH), 5.39 (s, 1H, H-6); ^{13}C NMR (125 MHz, DMSO-d_6) δ 60.6 (C-7), 71.2 (C-1), 72.2 (C-4), 75.9 (C-2), 76.1 (C-3), 123.7 (C-6), 139.2 (C-5). Elemental analysis calcd for $C_7H_{12}O_5$: C, 47.72; H, 6.87. Found: C, 47.82; H, 6.92.

Gabosine K (7). To a solution of **6** (65 mg, 0.36 mmol) in 2,4,6-collidine (2 mL), AcCl (0.02 mL, 0.4 mmol) was added at −60 °C, and the reaction mixture was stirred for 1 h at the same temperature. When the reaction was complete (judged by TLC), collidine was evaporated off under reduced pressure. The crude residue thus obtained was purified by flash column chromatography (ethyl acetate/MeOH, 10:1; v/v) to get gabosine K (**7**) (50 mg, 62%) as a colorless oil: ^{1}H NMR (500 MHz, CD_3OD) δ 1.96 (s, 3H), 3.24−3.27 (m, 1H), 3.31−3.35 (m, 1H), 3.96−3.99 (m, 2H), 4.43 (d, J = 13 Hz, 1H), 4.63 (d, J = 13 Hz, 1H), 5.50 (s, 1H). ^{1}H NMR data are identical to the reported values.[13n]

(±)-((1*R*,2*S*,3*S*,4*R*)-2,4-Dihydroxy-1,3-bis((4-methoxybenzyl)-oxy)cyclohex-5-en-5-yl)methyl benzoate (37). To a solution of **26** (432 mg, 1.03 mmol) in DCM (10 mL), 2,4,6-collidine (1 mL) and benzoyl chloride (0.18 mL, 1.54 mmol) were added at 0 °C, and the reaction mixture was stirred for 1 h at the same temperature. When the reaction was complete (by TLC), ethyl acetate (100 mL) was added to the reaction mixture, and the organic layer was washed successively with diluted HCl, water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:1; v/v) to get pure **37** (513 mg, 95%) as a white solid: mp 88−90 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.44 (dd, J = 10.3 Hz, 7.8 Hz, 1H, H-3), 3.72−3.73 (m, 7H, H-2, -OCH_3), 4.02 (d, J = 7.8 Hz, 1H, H-1), 4.26 (d, J = 7.6 Hz, 1H, H-4), 4.57−4.60 (m, 2H, -OCH_A-*p*-MeOPh, H-7A), 4.64 (d, J = 11.3 Hz, 1H, -OCH_B-*p*-MeOPh), 4.74 (d, J = 11.2 Hz,1H, -OCH_B-*p*-MeOPh), 4.80 (d, J = 11.2 Hz, 1H, -OCH_A-*p*-MeOPh), 5.07 (d, J = 12.8 Hz, 1H, H-7A′), 5.72 (s, 1H, H-6), 6.80 (d, J = 8.6 Hz, 2H, Ar−H), 6.82 (d, J = 8.6 Hz, 2H, Ar−H), 7.22 (d, J = 8.6 Hz, 2H, Ar−H), 7.24 (d, J = 8.6 Hz, 2H, Ar−H), 7.37 (t, J = 7.8 Hz, 2H, Ar−H), 7.49−7.52 (m, 1H, Ar−H), 7.96 (dd, J = 7.3 Hz, 0.7 Hz, 2H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3 (-OCH_3), 64.4 (C-7), 71.8 (C-4), 72.1 (-OCH_2-*p*-MeOPh), 74.6 (C-2), 74.8 (-OCH_2-*p*-MeOPh), 78.6 (C-1), 83.4 (C-3), 113.9, 114.1, 127.1 (C-6), 128.4, 129.5, 129.6, 129.7, 129.8, 130.1, 130.2, 130.4, 133.3, 135.1, 159.3, 159.4, 166.9. Elemental analysis calcd for $C_{30}H_{32}O_8$: C, 69.22; H, 6.20. Found: C, 69.22; H, 6.21.

((1*R*,2*S*,3*R*,4*R*)-2-(Benzoyloxy)-1,3-bis((4-methoxybenzyl)-oxy)-4-((triethylsilyl)oxy)cyclohex-5-en-5-yl)methyl benzoate (40). To a solution of benzoate **37** (150 mg, 0.28 mmol) in DCM, imidazole (114.4 mg, 1.68 mmol) and TESOTf (0.09 mL, 0.42 mmol) were added at 0 °C, and the reaction mixture was stirred for 1 h at the same temperature. When the TLC showed disappearance of the starting material, ethyl acetate (50 mL) was added to the reaction mixture, and the organic layer was washed successively with water and

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brine, separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (ethyl acetate/petroleum ether, 1:5; v/v) to get an inseparable mixture of regioisomers **38** and **39** (1.2:1, 124 mg, overall yield = 68%) as a colorless liquid.

To a solution of the above mixture of **38** and **39** (85 mg, 0.13 mmol) in pyridine (5 mL), BzCl (0.02 mL, 0.22 mmol) and DMAP (5 mg) were added at room temperature. The reaction mixture was stirred for 4 h at rt. When the reaction was complete (monitored by TLC), pyridine was evaporated under reduced pressure. The residue was dissolved in ethyl acetate (100 mL) and washed with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:9; v/v) to get the required isomer **40** (52.3 mg, 36% after two steps) as a colorless oil and also isomer **40A** (43.6 mg, 30% after two steps).

Inseparable Mixture of 38 and 39. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.55−0.60 (m, 12H), 0.85−0.89 (m, 18H), 3.42−3.48 (m, 2H), 3.71−3.73 (m, 12H), 3.78 (dd, J = 9.4 Hz, 7.1 Hz, 1H), 3.82−3.88 (m, 2H), 4.00−4.01 (m, 1H), 4.11−4.13 (m, 1H), 4.37 (d, J = 6.4 Hz, 1H), 4.47−4.55 (m, 5H), 4.64−4.78 (m, 6H), 4.92 (d, J = 13.4 Hz, 1H), 5.70 (s, 1H), 5.75 (s, 1H), 6.77−6.82 (m, 8H), 7.18−7.24 (m, 10H), 7.37 (dd, J = 14.4 Hz, 7.65 Hz, 4H), 7.47−7.50 (m, 2H), 7.94−7.97 (m, 4H).

40: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.63 (q, J = 8 Hz, 6H, -CH_2CH_3), 0.92 (t, J = 8.0 Hz, 9H, -CH_2CH_3), 3.73−3.76 (m, 7H, -OCH_3, H-3), 4.35 (d, J = 8.5 Hz, 1H, H-1), 4.49 (d, J = 11.6 Hz, 1H, -OCH_A-*p*-MeOPh), 4.59−4.62 (m, 3H, -OCH_AH_B-*p*-MeOPh, H-4), 4.68 (d, J = 10.7 Hz, 1H, -OCH_A-*p*-MeOPh), 4.88 (d, J = 13.4 Hz, 1H, H-7A), 4.92 (d, J = 13.3 Hz, 1H, H-7A′), 5.64 (dd, J = 9.7 Hz, 7.7 Hz, 1H, H-2), 5.92 (s, 1H, H-6), 6.68 (d, J = 8.6 Hz, 2H, Ar−H), 6.72 (d, J = 8.6 Hz, 2H, Ar−H), 7.04 (d, J = 8.6 Hz, 2H, Ar−H), 7.14 (d, J = 8.6 Hz, 2H, Ar−H), 7.44 (t, J = 7.8 Hz, 2H, Ar−H), 7.49 (t, J = 7.7 Hz, 2H, Ar−H), 7.56−7.61 (m, 2H, Ar−H), 8.0 (dd, J = 7.1 Hz, 1.25 Hz, 2H, Ar−H), 8.09 (dd, J = 7.1 Hz, 1.25 Hz, 2H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.0 (-CH_2CH_3), 6.9 (-CH_2CH_3), 55.1 (-OCH_3), 55.2 (-OCH_3), 64.4 (C-7), 70.6, 72.4 (C-4), 74.3, 74.5 (C-5), 77.2 (C-2), 82.2 (C-4), 113.4, 113.7, 125.0 (C-6), 128.2, 128.4, 128.9, 129.5, 129.6, 129.7, 129.9, 129.9, 130.1, 130.14, 132.9, 133.1, 136.4, 158.8, 159.1, 165.6, 166.1. Elemental analysis calcd for $C_{43}H_{50}O_9Si$: C, 69.89; H, 6.82. Found: C, 69.62; H, 7.00.

40A: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.69 (q, J = 8.0 Hz, 6H, -CH_2CH_3), 0.98 (t, J = 8.0 Hz, 9H, -CH_2CH_3), 3.67 (s, 3H), 3.77 (dd, J = 10.0 Hz, 8.0 Hz, 1H, H-3), 3.82 (s, 3H), 3.99 (dd, J = 9.5 Hz, 7.5 Hz, 1H, H-2), 4.09 (d, J = 8.0 Hz, 1H, H-1), 4.57−4.67 (m, 3H), 4.75−4.78 (m, 3H), 5.93 (s, 1H, H-6), 6.03 (d, J = 7.1 Hz, 1H, H-4), 6.59 (d, J = 8.6 Hz, 2H, Ar−H), 6.89 (d, J = 8.6 Hz, 2H, Ar−H), 7.09 (d, J = 8.6 Hz, 2H, Ar−H), 7.31 (d, J = 8.6 Hz, 1H, Ar−H), 7.38 (dd, J = 16.9 Hz, 8.1 Hz, 4H, Ar−H), 7.49−7.56 (m, 3H, Ar−H), 7.86−7.88 (m, 2H, Ar−H), 7.93 (m, 2H, Ar−H).

Uvamalol A (8). To a solution of **40** (10 mg, 0.013 mmol) in DCM (5 mL), TFA (0.25 mL) was added at rt, and the reaction was stirred for 30 min at the same temperature. When the reaction was complete (by TLC), TFA was quenched by adding aqueous $NaHCO_3$ solution, and then ethyl acetate (20 mL) was added to the reaction mixture. The organic layer was washed successively with water and brine, and then separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:1, v/v) to obtain uvamalol A (**8**) (4.5 mg, 86%) as a white solid. ^{1}H NMR and ^{13}C NMR spectrum of **8** was identical to the reported data:[27] mp 146−148 °C; ^{1}H NMR (500 MHz, CD_3OD) δ 3.80 (dd, J = 10.8 Hz, 7.9 Hz, 1H), 4.38 (d, J = 7.8 Hz, 1H), 4.49 (d, J = 8.3 Hz, 1H), 4.88−4.92 (m, 1H), 5.06 (d, J = 13.4 Hz, 1H), 5.23 (dd, J = 10.8 Hz, 8.3 Hz, 1H), 5.83 (s, 1H), 7.49−7.54 (m, 4H), 7.61−7.67 (m, 2H), 8.09−8.12 (m, 4H); ^{13}C NMR (125 MHz, CD_3OD) δ 65.1, 71.0, 73.6, 75.8, 78.8, 78.84, 128.6, 129.4, 129.7, 130.6, 130.8, 131.4, 131.9, 134.1, 134.4, 136.8, 167.8, 168.0.

Structural Assignment of 17 by Acetylation. To a solution of **17** (5 mg, 0.014 mmol) and triethylamine (1 mL) in DCM (5 mL), acetic anhydride (0.01 mL) was added, and the reaction mixture was stirred for overnight at room temperature. The solvent was evaporated under reduced pressure, the residue was dissolved in ethyl acetate and washed successively with water, aqueous $NaHCO_3$ solution and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated. Flash column chromatography (ethyl acetate/petroleum ether, 1:9, v/v) gave triacetate **46** (structure was confirmed by COSY and comparing the coupling constants of various protons) as a colorless gum (6 mg, 88%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.91 (s, 3H, -$OCOCH_3$), 1.97 (s, 3H, -$OCOCH_3$), 1.98 (s, 3H, -$OCOCH_3$), 4.00 (dd, J = 7.9 Hz, 5.1 Hz, 1H, H-6), 4.25 (t, J = 3.7 Hz, 1H, H-2), 4.32 (d, J = 13.2 Hz, 1H, H-7A), 4.50 (d, J = 11.9 Hz, 1H, -OCH_APh), 4.57−4.63 (m, 4H, H-7A′, -OCH_AH_BPh), 5.09 (dd, J = 7.9 Hz, 3.8 Hz, 1H, H-1), 5.45 (d, J = 4.8 Hz, 1H, H-5), 5.88 (d, J = 3.3 Hz, 1H, H-3), 7.27−7.20 (m, 10H, Ar−H).

Stereochemical Assignment of 18 by Acetylation. To a solution of **18** (5 mg, 0.014 mmol) and triethylamine (1 mL) in DCM (5 mL), acetic anhydride (0.01 mL) was added, and the reaction mixture was stirred at room temperature for 12 h. The solvent was evaporated off under reduced pressure, the residue was dissolved in ethyl acetate and washed successively with water, aqueous $NaHCO_3$ solution and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (ethyl acetate/petroleum ether, 1:9; v/v) gave triacetate **47** (structure was confirmed by COSY and comparing the coupling constants of various protons) as colorless oil (5 mg, 75%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.92 (s, 3H, -$OCOCH_3$), 1.97 (s, 3H, -$OCOCH_3$), 1.98 (s, 3H, -$OCOCH_3$), 4.11 (dd, J = 3.7 Hz, 2.0 Hz, 1H, H-6), 4.36−4.38 (m, 2H, H-2, H-7A), 4.51−4.63 (m, 5H, -OCH_AH_BPh, H-7A′), 5.08 (dd, J = 7.2 Hz, 2.0 Hz, 1H, H-1), 5.61 (s, 1H, H-5), 5.88 (s, 1H, H-3), 7.23−7.27 (m, 10H, Ar−H).

Stereochemical Assignment of 28 by Acetylation. In order to assign the stereochemistry of alcohol **28**, we made its acetyl derivative **48**. For this, a solution of **28** (10 mg, 0.01 mmol) and acetic anhydride (0.05 mL) in pyridine (5 mL) was stirred at room temperature for 3 h. The solvents were evaporated, the residue was dissolved in ethyl acetate and washed successively with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude material thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:3; v/v) to obtain the pure acetate **48** (10 mg, 94%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.64−1.69 (m, 1H, H-5), 1.82 (s, 3H, $OCOCH_3$), 3.22 (d, J = 7.7 Hz, 1H, H-7A), 3.42−3.44 (m, 1H, H-1), 3.48−3.50 (m, 2H, H-2, H-3), 3.60−3.61 (m, 2H, H-4, H-7A′), 3.71 (s, 3H, -OCH_3), 3.71 (s, 3H, -OCH_3), 4.29−4.30 (m, 2H, -OCH_AH_BPh), 4.49 (dd, J = 10.1 Hz, 9.6 Hz, 2H, -OCH_AH_BPh), 4.67−4.82 (m, 6H, -OCH_AH_BPh), 5.17 (dd, J = 10.9 Hz, 9.8 Hz, 1H, H-6), 6.73 (d, J = 8.7 Hz, 2H, Ar−H), 6.76 (d, J = 8.7 Hz, 2H, Ar−H), 7.08−7.18 (m, 19H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.9, 44.5 (C-5), 55.2, 64.4, 70.3 (C-6), 73.3, 75.0, 75.4, 75.5, 75.8, 77.0 (C-4), 82.9, 83.2, 85.55, 113.7, 113.8, 127.5, 127.6, 127.6, 127.8, 127.9, 127.9, 128.2, 128.4, 128.4, 129.2, 129.3, 130.7, 130.8, 138.1, 138.5, 159.1, 169.7.

In ^{1}H NMR spectrum of the acetate **48**, the most deshielded methyne proton (because of acetylation of the OH connected to the same carbon) at δ 5.17 (H-6; as per cyclophellitol numbering) showed a dd signal with $^3J_{HH}$ coupling constants 10.9 and 9.8 Hz, typical of a proton having two diaxially oriented protons on its either sides.

42. To a solution of **41** (500 mg, 2.0 mmol) in dry DMF, 60% NaH (170 mg, 4.2 mmol) was added at 0 °C in small portions. To this suspension, benzyl bromide (0.52 mL, 4.2 mmol) was added and stirred for an hour at 0 °C. Excess NaH was quenched with ice cold water. DMF was evaporated off in vacuo, and the residue was dissolved in EtOAc, washed with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (EtOAc/petroleum ether, 2:3; v/v) to give

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compound **42** (452 mg, 51%) as a white solid: mp 56−58 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.74 (t, J = 7 Hz, 3H, -$CH_2CH_2CH_2CH_3$), 1.14−1.17 (m, 2H, -$CH_2CH_2CH_2CH_3$), 1.22−1.25 (m, 2H, -$CH_2CH_2CH_2CH_3$), 1.45 (t, J = 7.4 Hz, 2H, -$CH_2CH_2CH_2CH_3$), 3.87 (s, 1H, H-5), 4.03 (s, 2H, H-4, H-6), 4.09 (s, 2H, H-1, H-3), 4.46 (s, 1H, H-2), 4.49 (d, J = 11.7 Hz, 2H, -OCH_AH_BPh), 4.56 (d, J = 11.7 Hz, 2H, -OCH_AH_BPh), 5.11 (s, 1H, OH), 7.19 (s, 10H, Ar−H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 14.3 (−$CH_3CH_2CH_2CH_2$), 22.4 (-$CH_3CH_2CH_2CH_2$), 25.0 (-$CH_3CH_2CH_2CH_2$), 37.1 (-$CH_3CH_2CH_2CH_2$), 59.0 (C-5), 67.4 (C-2), 71.0 (-OCH_2Ph), 73.3 (C-4, C-6), 74.3 (C-1, C-3), 109.5, 127.9, 123.0, 128.6, 138.6 (C-7). Elemental analysis calcd for $C_{25}H_{30}O_6$: C, 70.40; H, 7.09. Found: C, 70.44; H, 7.01.

(±)-(1*R*,3*S*,4*R*,5*S*,6*S*,2*E*/*Z*)-2-Methoxymethyl-4,6-di-*O*-(benzyl)-*myo*-inositol 1,3,5-orthopentanoate (44). To a solution of oxalyl chloride (0.07 mL, 0.84 mmol) in dichloromethane (5 mL), a solution of DMSO (0.06 mL, 0.84 mmol) in dichloromethane (5 mL) was added carefully at −78 °C, and the mixture was stirred for 5 min at the same temperature. Solution of compound **42** (140 mg, 0.32 mmol) in dichloromethane (5 mL) was added to the reaction mixture slowly at the same temperature, and the reaction mixture was stirred for 10 min before adding triethyl amine (0.22 mL). When the TLC showed completion of the reaction (10 min), the reaction mixture was diluted by adding chloroform (20 mL), and then the mixture was washed successively with aqueous $NaHCO_3$, water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (ethyl acetate/petroleum ether, 1:4; v/v) to get ketone **43** (139 mg, 100%) along with the inseparable gem-diol as a white gummy material. This gummy material was dissolved in dry THF (5 mL) and was added dropwise to the orange suspension obtained by slowly adding a solution of potassium *tert*-butoxide (183 mg, 1.63 mmol) in dry THF (2 mL) to a solution of methoxymethyltriphenylphosphonium chloride (561 mg, 1.63 mmol) in dry THF (5 mL) at 0 °C under N_2 atmosphere. The mixture was allowed to warm to room temperature and then refluxed for 2 h. THF was evaporated in vacuo. The orange residue was taken in ethyl acetate and washed with water and brine. Organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (ethyl acetate/petroleum ether, 1:4; v/v) gave enol ether **44** (140 mg, 94%) as a resin-like mass.

44: ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.73 (t, J = 7.3 Hz, 3H, -$CH_2CH_2CH_2CH_3$), 1.11−1.15 (m, 2H, -$CH_2CH_2CH_2CH_3$), 1.19−1.24 (m, 2H, -$CH_2CH_2CH_2CH_3$), 1.42−1.45 (m, 2H, -$CH_2CH_2CH_2CH_3$), 3.24 (s, 3H, -OCH_3), 3.97 (d, J = 3.4 Hz, 1H, H-6), 4.03 (d, J = 3.4 Hz, 1H, H-4), 4.32 (t, J = 3.3 Hz, 1.6 Hz, 1H, H-1), 4.45 (t, J = 3.1 Hz, 1.3 Hz, 1H, H-5), 4.48−4.51 (m, 5H, -OCH_AH_BPh), 4.84 (d, J = 1.6 Hz, 1H, H-3), 6.27 (s, 1H, H-7), 7.21−7.15 (m, 10H, Ar−H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 14.3 (−$CH_3CH_2CH_2CH_2$), 22.4 (-$CH_3CH_2CH_2CH_2$), 25.2 (-$CH_3CH_2CH_2CH_2$), 37.2 (-$CH_3CH_2CH_2CH_2$), 60.2 (-OCH_3), 66.8 (C-3), 69.0 (C-5), 70.2 (-OCH_2Ph), 70.5(-OCH_2Ph), 71.3 (C-1), 73.6 (C-6), 73.7 (C-4), 106.5, 110.9, 127.8, 127.96, 128.04, 128.5, 138.8, 138.9, 145.8 (C-7). HRMS (ESI) calcd for $C_{27}H_{33}O_6$ 453.2277, found 453.2269 (MH^+).

45. To a solution of **44** (130 mg, 0.22 mmol) in THF (10 mL), 0.1 N aqueous HCl (2 mL) was added and stirred for 3 h at room temperature. THF was evaporated off in vacuo. Residue was dissolved in EtOAc and washed with $NaHCO_3$ solution, water and then with brine. Organic layer was separated, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Mixture was purified by flash column chromatography (EtOAc/petroleum ether, 1:3; v/v) to give the compound **45** (125 mg, 100%) as a colorless sticky mass: ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.69−0.72 (m, 3H, -$CH_2CH_2CH_2CH_3$), 1.12−1.16 (m, 2H, -$CH_2CH_2CH_2CH_3$), 1.34−1.36 (m, 2H, -$CH_2CH_2CH_2CH_3$), 2.11−2.14 (m, 2H, -$CH_2CH_2CH_2CH_3$), 3.57 (dd, J = 9.5 Hz, 6.9 Hz, 1H, H-4), 4.40 (d, J = 8.4 Hz, 1H, H-6), 4.46 (d, J = 11.9 Hz, 1H, -OCH_APh), 4.51 (s, 1H, H-3), 4.52 (d, J = 11.8 Hz, 1H, -OCH_BPh), 4.63 (d, J = 11.8 Hz, 1H, -OCH_APh), 4.73 (d, J = 11.7, 1H, -OCH_BPh), 4.97 (t, J = 9.2 Hz, 1H, H-5), 5.56 (d, J = 6.6 Hz, 1H, OH-3), 6.81 (s, 1H, H-1), 7.18−7.26 (m, 10H, Ar−H), 9.48 (s, 1H, -CHO); ^{13}C NMR (125 MHz, DMSO-d_6) δ 14.0 (-CH_2CH_3), 22.0 (−CH_2CH_3), 26.9 (-$COCH_2CH_2$), 33.8 (-$COCH_2$), 69.2 (C-3), 71.2 (−CH_2Ph), 73.3 (C-5), 73.9 (−CH_2Ph), 76.5 (C-6), 82.4 (C-4), 127.7, 127.8, 128.1, 128.5, 128.7, 138.4, 139.1, 141.0, 143.7 (C-1), 172.5, 193.2 (C-7). HRMS (ESI) calcd for $C_{26}H_{31}O_6$ 439.2121, found 439.2118 (MH^+).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Retrosynthetic analysis, the mechanistic illustration, crystal data (CIF) of **25** and spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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