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Carbasugar Synthesis via Vinylogous Ketal: Total Syntheses of (+)-MK7607, (−)-MK7607, (−)-Gabosine A, (−)-Epoxydine B, (−)-Epoxydine C, *epi*-(+)-Gabosine E and *epi*-(+)-MK7607

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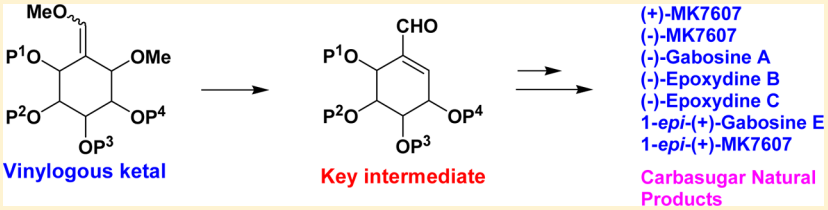
Supporting Information



ABSTRACT: Carbasugars, the carbocyclic analogues of sugars, constitute an important class of natural products with more than 140 members known and have attracted much attention due to their diverse biological activities like anticancer, antibacterial, herbicidal, and various enzyme inhibitory activities. As many carbohydrates are involved in various cellular signaling pathways, there is great interest in synthesis and biological exploration of carbasugars. Herein, we have developed a methodology to install an α,β-unsaturated aldehyde functionality on different inositols and derivatives by vinylogous elimination of the O-protecting group under mildly acidic condition. We have illustrated the versatility and utility of our methodology by the total syntheses of seven carbasugars viz. (−)-MK7607, (−)-gabosine A, (−)-epoxydine B, (−)-epoxydine C, (+)-MK7607, 1-*epi*-(+)-MK7607 and 1-*epi*-(+)-gabosine E.

INTRODUCTION

Carbasugars, a subclass of cyclitols, are structural mimics of glycopyranosides wherein the ring oxygen is replaced by a methylene (or methyne) group. More than 140 natural carbasugars are known and they are known to possess a diverse range of biological activities.[1] A major fraction of carbasugars are C_7-cyclitols with polyhydroxylated cyclohexene having a one-carbon side chain in the form of methyl, hydroxymethyl, carboxyl or formyl group (Chart 1).

By using this basic structural motif, nature has made a combinatorial library of diverse natural products by exploiting the variables such as stereochemistry, double bond, oxidation states, position and number of substituents.[2] Due to their structural diversity and promising biological activities, there is great interest in the synthesis of carbasugars and their analogues.[3] The crucial step in all these syntheses is the construction of cyclohexenyl ring.[4] Synthesis from inositol derivatives would be ideal as it not only eliminates the tedious cyclization step but also offers several preinstalled stereogenic centers. In this context, recently, we have developed a methodology for the synthesis of C_7-cyclitols from *myo*-inositol by incorporating an α,β-unsaturated aldehyde moiety through a vinylogous ring opening of its orthoester cage under mildly acidic condition. By applying this methodology, we have synthesized several natural carbasugars in their racemic form.[5] However, this methodology is limited to syntheses starting from inositols which can form stable orthoesters. Herein, we report a general method for the synthesis of carbasugar natural products and demonstrate the utility of this method by synthesizing five carbasugar natural products and two unnatural carbasugars, viz. (+)-MK7607, (−)-MK7607, (−)-Gabosine A, (−)-Epoxydine B, (−)-Epoxydine C, 1-*epi*-(+)-MK7607 and 1-*epi*-(+)-Gabosine E.

Several chiral *O*-methyl-inositols occur in nature; L-quebrachitol (2-*O*-methyl-L-*chiro*-inositol) and D-pinitol (3-*O*-methyl-D-*chiro*-inositol) are abundant and cheaply available. Though they have been used as chiral pool for the synthesis of many natural products,[6] they have not been used for the synthesis of carbasugars. We envisaged to use these cyclitols as chiral pools for the synthesis of carbasugars. One of the limitations for their use as starting material is the laborious and low-yielding demethylation. To use them for carbasugar synthesis, in addition to the introduction of the double bond and the side chain, an effective demethylation strategy is also essential. We envisioned to do all these three structural modifications by a single reaction; via the introduction of a methoxymethylidene group at the vicinal carbon with respect to the methoxy group and cleavage of the vinylogous ketal thus formed under mildly acidic condition (Figure 1). Homologation of pyranosides by vinylogous elimination of alkoxy group has been reported.[7]

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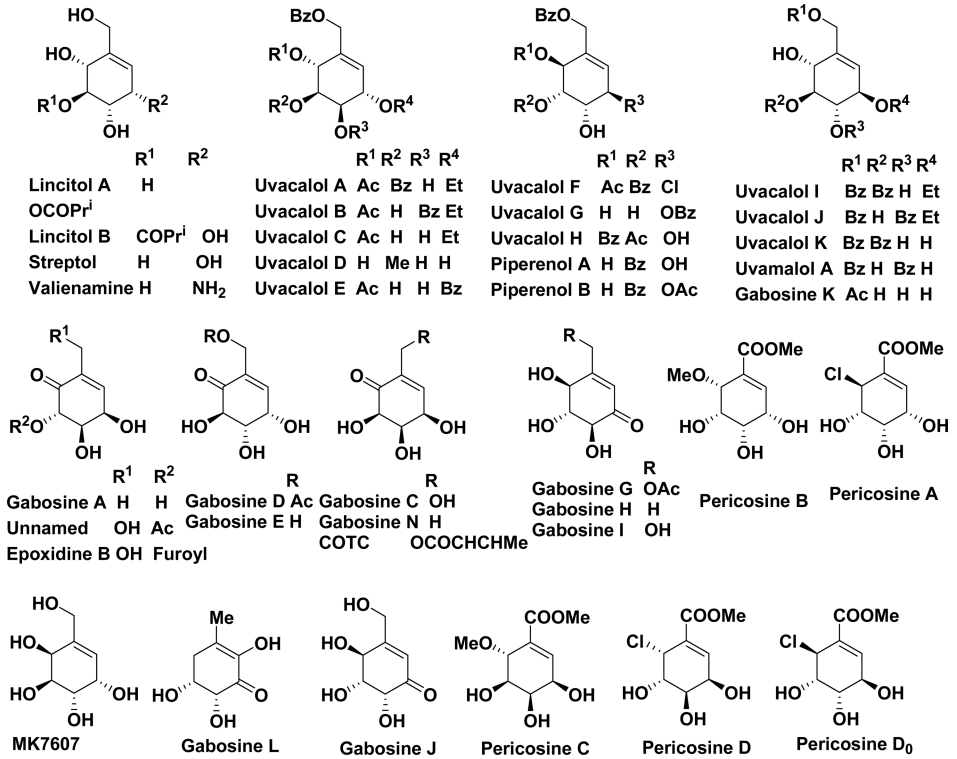
Chart 1. Representative C_7-Carbasugar Natural Products with Cyclohexenyl Core



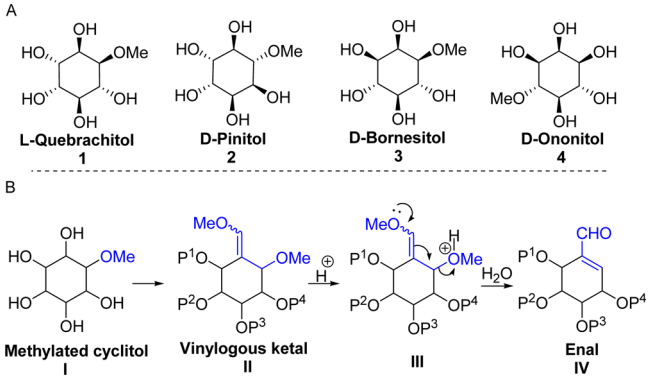
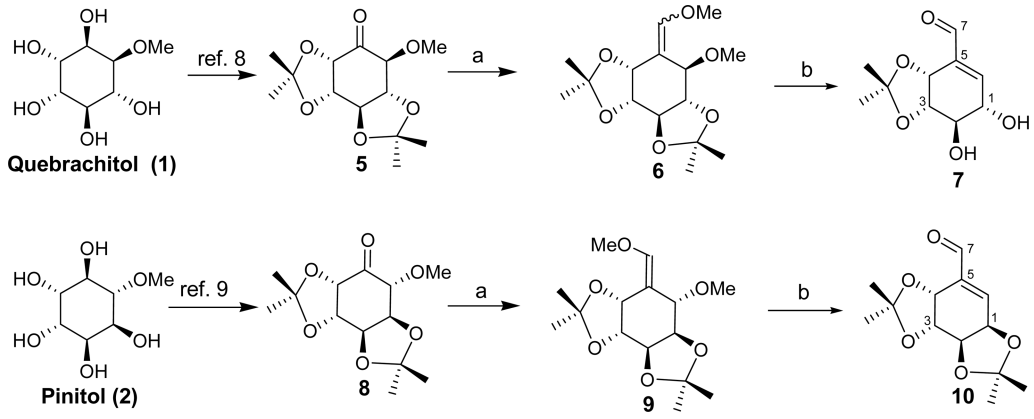


Figure 1. (A) Chiral methyl inositol. (B) Proposed generation of C_7-cyclitol skeleton via vinylogous ketal cleavage.

RESULTS AND DISCUSSION

To test our hypothesis, L-quebrachitol (**1**) was converted to the ketone **5**,[8] which on Wittig reaction with methoxymethyl-triphenylphosphonium chloride and ^{n}BuLi produced the enol-ether **6**. Similarly, D-pinitol (**2**) was converted to the enol-ether **9** through a sequence of ketalization, oxidation[9] and Wittig reactions. While the enol ether **6** was obtained as an inseparable mixture of *E*/*Z* isomers, the enol ether **9** was obtained as a single isomer. However, we have not assigned the geometry of the double bond as it is inconsequential for further reactions. The enol-ether **6** on treatment with CSA in wet acetone at rt produced the diol aldehyde **7** in 94% yield. On the other hand, the pinitol derived enol-ether **9** under similar condition gave the aldehyde **10** as the exclusive product. It is interesting to note that compound **6** having three different kinds of ketals; a

Scheme 1. Demethylative Construction of Cyclohexenal Intermediate by Vinylogous Ketal Cleavage[a]



[a]Reagents and conditions: (a) Ph_3PCH_2OMeCl, ^{n}BuLi, THF, 8 h, (**6**: 55%; **9**: 62%); (b) CSA, acetone, rt, (**7**: 1 h, 94%; **10**: 30 min, 94%).

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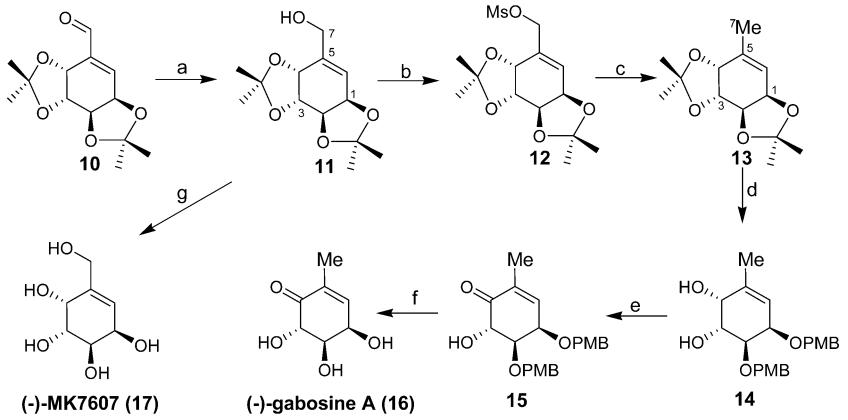
Scheme 2. Total Syntheses of (−)-Gabosine A (16) and (−)-MK7607 (17)[a]



[a]Reagents and conditions: (a) $NaBH_4$, MeOH, rt, 30 min, 90%; (b) MsCl, Et_3N, 0 °C, 20 min, 97%; (c) $LiAlH_4$, THF, 0 °C to rt, 1 h, 91%; (d) i. CSA, MeOH, 2 h; ii. PMBCl, NaH, DMF, 0 °C, 30 min.; iii. CSA, MeOH, rt, 2 h, (60% in 3 steps); (e) PDC, DCM, rt, 30 min, 85%; (f) TFA, DCM, rt, 20 min, 81%; (g) TFA, DCM, rt, 10 min, 100%.

cis-ketal, a *trans*-ketal and a vinylogous ketal, underwent hydrolysis cleaving the latter two, but the enol-ether **9** having two *cis*-ketals and a vinylogous ketal, underwent hydrolysis cleaving the latter alone. It is clear that the *cis*-ketals are stable irrespective of their position, under the conditions for cleavage of vinylogous ketal (Scheme 1). The relatively higher stability of *cis*-ketals over *trans*-ketals under mildly acidic condition is documented in the literature.[10] In both **6** and **9**, the methoxymethylidene motif is flanked by a methoxy group and a *cis*-ketal group. It was delighting to note the regiospecific vinylogous ketal cleavage leading to the cleavage of the methyl ether alone leaving the *cis*-ketal unaffected. The advanced intermediates **7** and **10** can be used for the synthesis of several carbasugar natural products.

(−)-Gabosine A, isolated from the *Streptomyces* strain,[11] shows DNA binding activity and it has been a target for total synthesis.[12] In order to illustrate the utility of our methodology, we have planned to synthesize (−)-gabosine A (Scheme 2). Thus, the aldehyde **10** was reduced to the primary alcohol **11** in 90% yield. The alcohol **11** was mesylated and the mesylate **12** (97%) was treated with $LiAlH_4$ in THF at 0 °C to get the diacetonide **13** in 91% yield. The diketal **13** was treated with CSA in methanol to get an inseparable mixture of diols. These diols were alkylated with PMBCl and the resulting di-PMB derivatives were also inseparable. Deprotection of the remaining isopropylidene group with CSA in methanol afforded two diols and the major isomer **14** was isolated in 60% yield over three steps. Then it was envisaged that gabosine A could be obtained from diol **14** by chemoselective oxidation of the allylic hydroxyl group followed by the deprotection of protecting groups. Chemoselective allylic oxidation of diol **14** with PDC in DCM gave the ketone **15** (85%) as expected. The structure of the ketone **15** was confirmed by the 2D NMR techniques. The coupling of H-2 with H-1 and H-3 with coupling constants 3.5 and 10.6 Hz respectively suggested that H-2 is flanked by H-1 and H-3, suggesting that the allylic hydroxyl group (4-OH) was oxidized selectively. Finally, deprotection of PMB groups gave (−)-gabosine A (**16**) in 81% yield (overall yield from pinitol: 20%).

(+)-MK7607, is an α-galactose mimic and was isolated from the cultures of *Curvularia eragrostidis D2452*. Due to its potent herbicidal activity,[13] there is considerable interest in total synthesis of both natural[2c,3e] and unnatural[14] enantiomers. We have decided to synthesize (−)-MK7607 from alcohol **11** by cleavage of the ketal protecting groups. Thus, the treatment of **11** with TFA gave (−)-MK7607 (**17**) in quantitative yield (Scheme 2). To the best of our knowledge, this six-step synthesis from D-pinitol (overall yield of 40%) is the shortest synthesis of (−)-MK7607.

Epoxydine B (**20**) and epoxydine C (**22**) are two structurally related natural carbasugars known to possess antibacterial, antifungal and antialgal activities.[15] Though the compound **22** was not given any name in the literature, as it was isolated from the same source as epoxydine B and its structure is similar to epoxydine B, for the sake of convenience, we tentatively named it as epoxydine C. To the best of our knowledge, no synthesis of any of these natural products has been reported so far. Hence, we have planned to synthesize and validate the structures of these two carbasugars by using our methodology. Partial cleavage of the ketal groups in the alcohol **11** by the treatment with CSA in methanol, gave an inseparable mixture of two triols, which on alkylation with excess PMBCl followed by the acid catalyzed cleavage of the remaining ketal group gave the diol **18** (46%) as the major product (Scheme 3). Furoylation of the diol **18** gave an inseparable mixture of two monoesters in 1:1 ratio (92%). Interestingly, both hydroxyl groups of the *cis*-diol **18** (one pseudoequatorial and one pseudoaxial hydroxyl groups) have shown similar reactivity toward esterification. This could be due to the ring puckering of cyclohexene ring to form either C-3 endo (A) or C-2 endo (B) conformers, which can interconvert rapidly at the room temperature. While in the C-2 endo conformer 3-OH is pseudoaxial and 4-OH is pseudoequatorial, in the C-3 endo conformer, 3-OH is pseudoequatorial and 4-OH is pseudoaxial. The plausible interconversion of these conformers could make both the hydroxyl groups almost equivalent (both attain pseudoaxial and pseudoequatorial orientation) in reactivity. This is a probable reason for the formation of both the esters in equal amounts (Chart. 2).

As one of the esters is having an allylic alcohol, we envisioned that this compound can be selectively oxidized in preference of the nonallylic alcohol. Thus, the mixture of esters was treated with PDC in DCM and to our satisfaction, the ester containing allylic hydroxyl group underwent selective oxidation to give the ketone **19** in 38% yield over two steps. COSY NMR spectrum of the ketone **19** revealed that H-2 couples with H-1 and H-3

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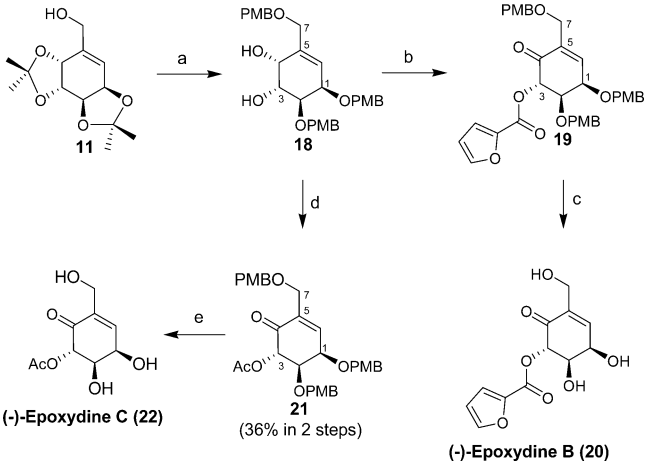
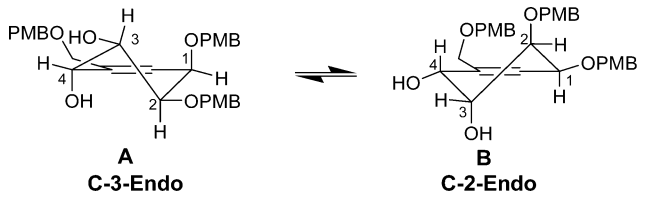
Scheme 3. Total Synthesis of (−)-Epoxydine B (20) and (−)-Epoxydine C (22)[a]



[a]Reagents and conditions: (a) i. CSA, MeOH, 3 h; ii. PMBCl, NaH, DMF, 0 °C, 30 min.; iii. CSA, MeOH, rt, 4 h, (46% in 3 steps); (b) i. furoyl chloride, pyr, 0 °C to rt, 2 h; ii. PDC, DCM, rt, 30 min, 38% in 2 steps; (c) TFA, DCM, rt, 20 min, 81%; (d) AcCl, pyr, 0 °C to rt, 2 h; ii. PDC, DCM, rt, 25 min, 36% from 2 steps; (e) TFA, DCM, rt, 20 min, 87%.

Chart 2. Plausible Conformations of Diol 18

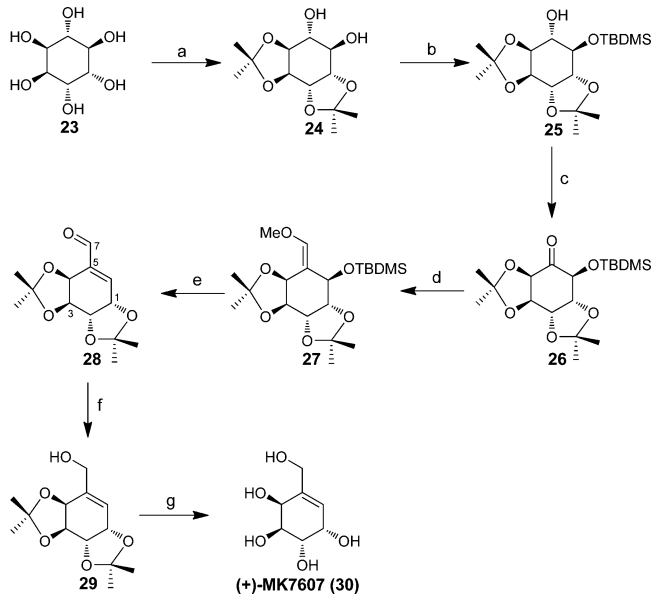


with coupling constants 3.4 Hz ($^3J_{H1H2}$) and 10.6 Hz ($^3J_{H2H3}$), which is possible only if the allylic alcohol is oxidized. Final deprotection of the hydroxyl groups by treatment of the ketone **19** with 10% TFA in DCM gave (−)-epoxydine B (**20**) in 81% yield (Scheme 3). ^{1}H and ^{13}C NMR spectra were found to match with the reported data.[15b]

Similarly, for the total synthesis of the epoxydine C, the diol **18** was treated with one equivalent of acetyl chloride in pyridine to introduce one acetyl group at 3-position. But, in this case also, an inseparable mixture of two monoacetates (3-ester and 4-ester) was obtained in 1:1 ratio. These monoesters on treatment with PDC in DCM underwent selective oxidation of only the compound having the allylic alcohol giving the ketone **21**. Structure of the ketone **21** was confirmed by COSY NMR spectroscopy. Coupling of H-2 with H-1 and H-3 with coupling constants 3.5 Hz (J_{H1H2}) and 10.6 Hz (J_{H2H3}) respectively proved that H-2 is flanked by H-1 and H-3 and this is possible only if the allylic position is oxidized. The ketone could be separated (36% over two steps) from the unreacted monoester by column chromatography. The ketone **21** on treatment with TFA in DCM underwent smooth PMB cleavage to give epoxydine C (**22**) in 87% yield (Scheme 3). The H-3 signal appeared as a doublet with J_{H2H3} coupling constant of 10.5 Hz suggestingthat no epimerization has happened at C-3 during the hydrolysis. The NMR data were found to match with the reported data.[15a]

We wondered whether this methodology is applicable in polyols having other *O*-protecting groups than methyl ether. In order to test this, we have decided to use TBDMS ether instead of methyl ether (Scheme 4). Thus, L-*chiro* inositol-derived diol

Scheme 4. Total Synthesis of (+)-MK7607 (30)[a]



[a]Reagents and conditions: (a) 2-methoxypropene, DMF, 60 °C, 1 h, 89%; (b) TBDMSCl, imidazole, DCM, rt, 4 h, 91%; (c) DMP, DCM, rt, 1 h, 94%; (d) Ph_3PCH_2OMeCl, ^{n}BuLi, THF, −40 °C to rt, 8 h, 56%; (e) CSA, acetone, rt, 1 h, 92%; (f) $NaBH_4$, MeOH, rt, 30 min, 91%; (g) TFA, DCM, rt, 20 min, 100%.

24[16] was monosilylated and the resultant alcohol **25** (91% yield) was oxidized to the ketone **26**, in 94% yield. Wittig reaction of the ketone **26** gave the enol-ether **27** (56%) as a single isomer. However, the stereochemistry of the double bond was not assigned as it is irrelevant for further reactions. The enol-ether **27** on treatment with the catalytic amount of CSA gave the aldehyde **28** in 92% yield. It is worthy to note that change of methyl ether to silyl ether neither affected the course of the reaction nor the regiospecificity suggesting that our methodology can be extended to systems not having a methoxy unit also. As observed earlier, the *cis*-ketal was found to be more stable than TBDMS ether. Reduction of the aldehyde **28** gave the alcohol **29** (91%), which on global deprotection with TFA yielded (+)-MK7607 (**30**) in quantitative yield. Thus, we could achieve the total synthesis of (+)-MK7607 in seven steps from L-*chiro*-inositol in 31% overall yield. To the best of our knowledge, this is the shortest synthesis of (+)-MK7607, so far.

1-*epi*-(+)-MK7607 (**37**) is a synthetic carbasugar having the high affinity for galactose-binding lectin and thus has the potential to be a competitive inhibitor for this lectin.[2c] Another carbasugar having antimicrobial activity and spermicidal activity, isolated from *Aspergillus varians* (KMM4630) was given the structure **41** (1-*epi*-gabosine E).[17] We have planned to synthesize these carbasugars from *myo*-inositol derived diol (+)-**31** (Scheme 5).[18] Diol **31** was converted to the ketone **33**. Wittig reaction provided *E* and *Z* isomers of the enol-ether **34** (73%), which on treatment with CSA in wet acetone yielded the enal **35** exclusively (92%). In the enol-ether **34**, the *trans*-ketal is also part of the vinylogous ketal. It is interesting to note that, in this case, the *trans*-ketal prefers to be cleaved vinylogously. Reduction of the enal **35** gave the diol, which

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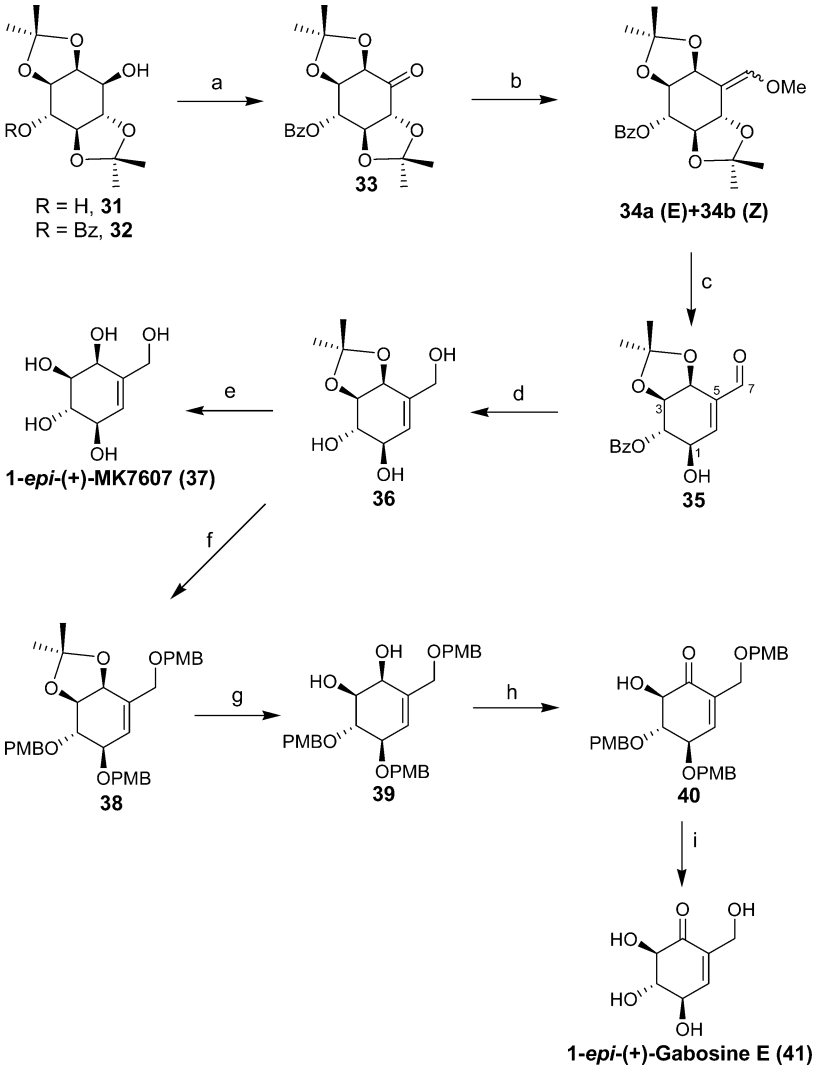
Scheme 5. Total Synthesis of 1-*epi*-(+)-MK7607 (37) and 1-*epi*-(+)-Gabosine E (41)[a]



[a]Reagents and conditions: (a) DMP, DCM, 1 h, 94%; (b) Ph_3PCH_2OMeCl, ^tBuOK, THF, −0 °C to rt, 8 h, 73% (*E*:*Z*, 1:1); (c) CSA, acetone, rt, 30 min, 92%; (d) i. $NaBH_4$, MeOH, rt, 30 min.; ii. NaOH, MeOH, rt, 10 min, 85% from 2 steps; (e) HCl, MeOH, 10 min, 100%; (f) PMBCl, NaH, DMF, 0 °C to rt, 20 min, 92%; (g) CSA, MeOH, 1 h, 89%; (h) DMP, DCM, rt, 15 min, 89%; (i) TFA, DCM, rt, 20 min, 85%.

on alcoholysis provided the triol **36** (85% in two steps). Hydrolytic removal of the ketal motif provided 1-*epi*-(+)-MK7607 (**37**) in quantitative yield.

For the synthesis of 1-*epi*-gabosine E, the triol **36** was converted to the diol **39** in an overall yield of 82% over two steps through alkylation using PMBCl followed by the cleavage of the *cis*-ketal. Chemoselective oxidation of the allylic alcohol in **39** gave the enone **40** (89%), which on treatment with TFA provided **41** in 85% yield. The H-3 signal appeared as a doublet with J_{H2H3} coupling constant of 10.9 Hz suggestingthat no epimerization has happened at C-3 during the hydrolysis. The NMR data of **41** are in agreement with its structure. Though this is the first synthesis of 1-*epi*-gabosine E, the NMR data (chemical shifts, coupling constants and the pattern) of this compound did not match with the reported data[17] of the natural carbasugar. For instance, reported chemical shifts of H-1, H-2, H-3, H-6 and H-7 signals of the natural carbasugar were 4.43, 3.68, 4.57, 6.86, and 4.13 ppm respectively, but those of **41** were found to be 4.67, 3.65, 4.10, 6.93, and 4.24 ppm, respectively. Similarly, the ^{13}C NMR data were also different from the reported data. This suggests that the structural assignment of the carbasugar isolated from *Asperigillus varians* was wrong.

■ CONCLUSIONS

In conclusion, we have developed a new methodology to install *α*,*β*-unsaturated aldehyde group in different protected cyclitols by vinylogous ketal cleavage under mildly acidic condition. We could demonstrate the utility of this methodology by total syntheses of seven structurally different carbasugars viz. (+)-MK7607, (−)-MK7607, (−)-Gabosine A, (−)-epoxidine B, (−)-epoxydine C, 1-*epi*-(+)-MK7607 and 1-*epi*-(+)-Gabosine E by simple protecting groups manipulations. It could also be possible to achieve several carbasugars with different stereochemistry by inserting the enol-ether group at different position of cyclitols. Also, this vinylogous ketal cleavage to introduce *α*,*β*-unsaturated aldehyde can be applied to other polyols. This methodology would allow the conversion of cheap and abundant natural polyols with preinstalled stereogenic centers such as sugars and cyclitols to advanced value added feedstocks for various total syntheses.

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EXPERIMENTAL SECTION

General Procedure. TLC analyses were performed using silica gel TLC plates. UV active compounds were spotted on silica gel TLC plates and were visualized under UV light and also, by spraying ceric ammonium molybdate stain followed by heating with a hot air gun. The ^{1}H NMR, ^{13}C NMR, DEPT, COSY and HMQC spectra were recorded using a 500 MHz NMR spectrometer at 25 °C. Proton chemical shifts were reported in ppm (δ) relative to tetramethylsilane (TMS, δ 0.0 ppm) as the internal standard or with the solvent reference relative to TMS ($CDCl_3$, δ 7.26 ppm; D_2O, δ 4.79 ppm). Data were reported as follows: chemical shift [multiplicity (s for singlet, d for doublet, t for triplet, q for quartet, and m for multiplet), coupling constants in Hz, peak integration and peak identification]. All unknown compounds were characterized by ^{1}H NMR, ^{13}C NMR, DEPT, COSY and HMQC experiments. ^{13}C spectra were recorded with complete proton decoupling. Carbon chemical shifts were recorded in ppm (δ) relative to TMS as the internal standard. Melting points were determined using a melting point apparatus and are uncorrected. Flash column chromatography was performed using silica gel (200−400 mesh). All moisture sensitive reactions were carried out under inert atmosphere (argon or nitrogen) using oven-dried glassware.

*(1S,2R,3R,4R)-5-Formyl-3,4-O-isopropylidene-cyclohex-5-ene-1,2,3,4-tetrol (**7**).* To a suspension of (methoxymethyl)-triphenylphosphonium chloride (207.73 mg, 0.61 mmol) in THF (10 mL), ^{n}BuLi (0.5 mL, 0.81 mmol, 1.6 M solution in hexane) was added slowly at −40 °C under N_2 atmosphere. To the resultant orange suspension, a solution of ketone **5** (110 mg, 0.40 mmol) in dry THF (5 mL) was added slowly at the same temperature. The mixture was allowed to warm to room temperature slowly and then further stirred for 8 h. After the completion of the reaction, THF was evaporated under reduced pressure and the residue was dissolved in dichloromethane (DCM) (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 (EtOAc/petroleum ether, 1:5; v/v, TLC: R_f = 0.45) to get the enol ether **6** (66.0 mg, 54.4%) as an inseparable mixture of *E*/*Z*-isomers with some impurities as a colorless oil. This mixture of *E*/*Z*-isomers was used for the next step without further purification. Thus, the enol ether **6** was dissolved in wet acetone (15 mL) and CSA (50.0 mg) was added to it at room temperature. The reaction mixture was stirred for 1 h at the same temperature. After the completion of the reaction (1 h), the solvent was evaporated under reduced pressure and the crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:1; v/v) to get the aldehyde **7** (52.5 mg, 94%) as a colorless liquid. ^{1}H NMR (500 MHz in $CDCl_3$) δ 1.39 (s, 3H, $-CH_3$), 1.44 (s, 3H, $-CH_3$), 3.69 (t, J = 8.7 Hz, 1H, H-2), 4.08 (dd, J = 8.7 Hz, 6.2 Hz, 1H, H-3), 4.29 (d, J = 8.5 Hz, 1H, H-1), 4.88 (d, J = 6.1 Hz, 1H, H-4), 6.79 (d, J = 2.0 Hz, 1H, H-6), 9.55 (s, 1H, −CHO); ^{13}C NMR (125 MHz in $CDCl_3$) δ 26.2, 28.3, 69.2 (C-4), 70.3 (C-1), 74.2 (C-2), 77.5 (C-3), 111.6, 150.9 (C-6), 191.3. $[\alpha]_D^{25}$ + 7.6 (c 0.14, acetone). Elemental analysis calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59. Found: C, 55.81; H, 6.72.

*(1R,2R,3R,4R,6S)-6-O-Methyl-5-methoxymethylene-1,2:3,4-di-O-isopropylidene-cyclohexane-1,2,3,5,6-pentol (**9**).* To a suspension of (methoxymethyl)triphenylphosphonium chloride (1.48 g, 4.31 mmol) in dry THF (30 mL), ^{n}BuLi (2.69 mL, 4.31 mmol, 1.6 M solution in hexane) was added slowly added at −40 °C under N_2 atmosphere. To the resultant orange suspension, a solution of the ketone **8** (469.72 mg, 1.73 mmol) in dry THF (20 mL) was added slowly at the same temperature. The mixture was allowed to warm to room temperature slowly and then further stirred for 8 h. After The completion of the reaction, THF was evaporated under reduced pressure. The residue was dissolved in DCM (150 mL) 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 (EtOAc/petroleum ether, 1:5; v/v) yielded the enol ether **9** (321.2 mg, 62%) as a colorless oil. ^{1}H NMR (500 MHz in $CDCl_3$) δ 1.24 (s, 3H, $-CH_3$), 1.27 (s, 3H, $-CH_3$), 1.28 (s, 3H, $-CH_3$), 1.37 (s, 3H, $-CH_3$), 3.16 (s, 3H, $-OCH_3$), 3.34 (s, 1H, H-5), 4.36 (d, J = 7.0 Hz, 1H, H-3), 4.45 (d, J = 8.0 Hz, 1H, H-1), 4.55 (d, J = 6.5 Hz, 1H, H-2), 5.09 (d, J = 7.5 Hz, 1H, H-6), 6.16 (s, 1H, H-7); ^{13}C NMR (125 MHz in $CDCl_3$) δ 24.0, 25.8, 26.4, 55.3, 60.5, 67.1 (C-3), 72.8 (C-1), 73.1 (C-2), 75.7 (C-6), 79.4 (C-5), 106.3, 107.4, 108.4, 152.2 (C-7). $[\alpha]_D^{25}$ + 70.6 (c 0.16, acetone). Elemental analysis calcd for $C_{15}H_{24}O_6$: C, 59.98; H, 8.05. Found: C, 59.71; H, 8.33.

*(1R,2R,3R,4R)-5-Formyl-1,2:3,4-di-O-isopropylidene-cyclohex-5-ene-1,2,3,4-tetrol (**10**).* To a solution of the enol ether **9** (220 mg, 0.73 mmol) in acetone (15 mL), CSA (20 mg) was added at room temperature and the reaction mixture was stirred for 30 min at the same temperature. After the completion of the reaction, CSA was quenched with triethylamine and the reaction mixture was concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:5, v/v) to get the enal **10** (159.3 mg, 94%) as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 6H, $-CH_3$), 1.40 (s, 6H, $-CH_3$), 4.64 (d, J = 3.5 Hz, 1H, H-2), 4.70 (dd, J = 5.6 Hz, 2.5 Hz, 1H, H-3), 4.79 (d, J = 2.5 Hz, 1H, H-1), 4.95 (d, J = 5.8 Hz, 1H, H-4), 6.60 (s, 1H, H-6), 9.60 (s, 1H, −CHO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.5, 26.2, 27.4, 27.9, 67.0 (C-4), 70.5 (C-1), 72.0 (C-3), 74.0 (C-2), 109.5, 109.9, 137.2, 145.5 (C-6). $[\alpha]_D^{25}$ −19.0 (c 0.1, acetone). Elemental analysis calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.14. Found: C, 61.28; H, 7.31.

*(1R,2R,3R,4R)-5-Hydroxymethyl-1,2:3,4-di-O-isopropylidene-cyclohex-5-ene-1,2,3,4-tetrol (**11**).* To a solution of the aldehyde **10** (112 mg, 0.44 mmol) in methanol (10 mL), $NaBH_4$ (16.65 mg, 0.44 mmol) was added at room temperature and the reaction mixture was stirred for 30 min at the same temperature. After the completion of the reaction (checked by the TLC), methanol was evaporated off under reduced pressure and the crude product was dissolved in ethyl acetate (100 mL) and washed with water and brine. The organic layer was separated, concentrated under reduced pressure and purified by flash column chromatography (EtOAc/petroleum ether, 1:4, v/v) to get the alcohol **11** (101.6 mg, 90%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28 (s, 3H, $-CH_3$), 1.29 (s, 3H, $-CH_3$), 1.31 (s, 3H, $-CH_3$), 1.32 (s, 3H, $-CH_3$), 4.14−4.21 (m, 2H, H-7A and 7B), 4.49−4.56 (m, 4H, H-1, H-2, H-3, H-4), 5.63 (s, 1H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.2, 26.4, 27.7, 28.0, 64.4 (C-7), 70.8, 71.4, 73.3, 73.4, 109.2, 109.4, 122.8 (C-6), 136.1. $[\alpha]_D^{25}$ + 7.1 (c 0.17, acetone). Elemental analysis calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.78; H, 7.98.

*(1R,2R,3R,4R)-5-(Mesyl(oxy)methyl)-1,2:3,4-di-O-isopropylidene-cyclohex-5-ene-1,2,3,4-tetrol (**12**).* To a solution of the alcohol **11** (91 mg, 0.36 mmol) in triethylamine (10 mL), mesyl chloride (0.4 mL, 0.54 mmol) was added at 0 °C and the reaction mixture was stirred for 20 min at the same temperature. When TLC showed completion of the reaction (after 20 min.), the reaction mixture was concentrated under reduced pressure. The crude product was dissolved in DCM (100 mL) and washed with water and brine. The organic layer was separated and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:5; v/v) to get the mesylate **12** (115.2 mg, 97%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26 (s, 3H, $-OCH_3$), 1.28 (s, 3H, $-OCH_3$), 1.31 (s, 3H, $-OCH_3$), 1.32 (s, 3H, $-OCH_3$), 2.98 (s, 3H, $-SCH_3$), 4.52−4.53 (brd, J = 5.3 Hz, 3H), 4.58 (dd, J = 5.0 Hz, 1.4 Hz, 1H), 4.65 (d (AB), J = 12.0 Hz, 1H), 4.81 (d (AB), J = 11.9 Hz, 1H), 5.76 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.3, 26.4, 27.7, 27.9, 37.7, 69.5, 69.7, 70.4, 72.9, 73.2, 109.6, 109.7, 127.2, 130.7. $[\alpha]_D^{25}$ + 37.7 (c 0.94, acetone). Elemental analysis calcd for $C_{14}H_{22}O_7S$: C, 50.29; H, 6.63; S 9.59. Found: C, 50.04; H, 6.82; S 9.38.

*(1R,2R,3R,4R)-5-Methyl-1,2:3,4-di-O-isopropylidene-cyclohex-5-ene-1,2,3,4-tetrol (**13**).* To a solution of mesylate **12** (109 mg, 0.33 mmol) in THF (10 mL), $LiAlH_4$ (12.5 mg, 0.33 mmol) was added at 0 °C and the reaction mixture was stirred for 1 h at room temperature. After the completion of the reaction (1 h), the reaction mixture was passed through a Celite bed, washed with acetone (two times), and collected. The combined organic layer was concentrated under reduced pressure and the crude product thus obtained was purified

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by flash column chromatography (EtOAc/petroleum ether, 1:9; v/v) to get the diketal **13** (71.3 mg, 91%) as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27 (s, 3H, $-OCH_3$), 1.29 (s, 3H, $-OCH_3$), 1.30 (s, 3H, $-OCH_3$), 1.31 (s, 3H, $-OCH_3$), 1.75 (s, 3H, $-CH_3$), 4.30 (d, J = 5.0 Hz, 1H, H-4), 4.43−4.47 (m, 3H, H-1, H-2, H-3), 5.37 (d, J = 1.1 Hz, 1H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.6, 26.4, 26.5, 27.6, 27.9, 29.7, 71.2, 73.3, 73.68, 73.72 (C-4), 108.9, 109.1, 122.3 (C-6), 134.1. $[\alpha]_D^{25}$ −105.5 (c 0.2, acetone). Elemental analysis calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.76; H, 8.57.

*(1R,2S,3R,4R)-1,2-Bis((4-methoxybenzyl)oxy)-5-methyl-cyclohex-5-ene-1,2,3,4-diol (**14**).* To a solution of the diketal **13** (65 mg, 0.27 mmol) in methanol (20 mL), CSA (10 mg) was added at the room temperature and the reaction mixture was stirred for 2 h at the same temperature. After the completion of the reaction, the solvent was evaporated under reduced pressure and the crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:1, v/v) to get an inseparable mixture of 1,2-diol and 3,4-diol (46.1 mg, 85%, brsm) as a colorless oil. This mixture of diols (46.1 mg) was treated with NaH (27.6 mg, 0.69 mmol, 60% dispersed in mineral oil) and PMBCl (0.093 mL, 0.69 mmol) at 0 °C for 30 min to get an inseparable mixture of diPMB ethers (96.4 mg, 95%). Then this mixture of compounds was treated with CSA (50 mg) in MeOH (10 mL) for 2 h to get the diol **14** (71.8 mg, 60% after 3 steps) as the major isomer after purification by column chromatography (EtOAc/petroleum ether, 1:1.5, v/v). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.79 (s, 3H, $-CH_3$), 2.67 (s, 1H, OH-3 or OH-4), 2.69 (s, 1H, OH-3 or OH-4), 3.66 (dd, J = 9.6 Hz, 3.8 Hz, 1H, H-2), 3.74 (s, 6H, $-OCH_3$), 3.99 (t, J = 4.4 Hz, 1H, H-1), 4.09−4.36 (m, 2H, H-3 and H-4), 4.34 (d, J = 11.4 Hz, 1H, $-CH_aPhOMe$), 4.51 (d, J = 11.4 Hz, 1H, $-CH_aPhOMe$), 4.54 (d, J = 13.2 Hz, 1H, $-CH_bPhOMe$), 4.57 (d, J = 11.4 Hz, 1H, $-CH_bPhOMe$), 5.59 (s, 1H, H-6), 6.80−7.22 (m, 8H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 55.3, 67.9, 69.7, 70.1, 71.5, 71.6, 76.1, 113.8, 114.0, 123.0, 129.5, 129.6, 130.0, 130.6, 138.3, 159.3, 159.5. $[\alpha]_D^{25}$ −91.5 (c 0.20, acetone). Elemental analysis calcd for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 68.71; H, 7.21.

*(1R,2S,3S)-1,2-Bis((4-methoxybenzyl)oxy)-5-methyl-cyclohex-5-ene-4-one-1,2,3-triol (**15**).* To a solution of the diol **14** (30 mg, 0.075 mmol) in DCM (10 mL), PDC (56.4 mg, 0.15 mmol) was added at room temperature and the reaction mixture was stirred for 30 min at the same temperature. After the completion of the reaction (checked by TLC), the reaction mixture was concentrated under reduced pressure and the crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:3, v/v) to get the enone **15** (25.4 mg, 85%) as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.74 (s, 3H, $-CH_3$), 3.36 (d, J = 1.8 Hz, 1H, OH-4), 3.53 (dd, J = 10.5 Hz, 3.6 Hz, 1H, H-2), 3.74 (s, 6H, $-OCH_3$), 4.09 (dd, J = 5.7 Hz, 3.5 Hz, 1H, H-1), 4.56 (d (AB), J = 11.5 Hz, 1H, $-CH_aPhOMe$), 4.62 (d (AB), J = 11.8 Hz, 1H, $-CH_aPhOMe$), 4.70 (dd, J = 10.5 Hz, 1.8 Hz, 1H, H-3), 4.77 (d (AB), J = 11.4 Hz, 1H, $-CH_bPhOMe$), 4.78 (d (AB), J = 11.8 Hz, 1H, $-CH_bPhOMe$), 6.52 (dd, J = 6.1 Hz, 1.4 Hz, 1H, H-6), 6.81 (d, J = 8.6 Hz, 4H, Ar−H), 7.21−7.25 (m, 4H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.4, 55.29, 55.3, 71.1 (C-1), 72.7, 73.1, 74.4 (C-3), 79.7 (C-2), 113.85, 113.9, 129.5, 129.7, 130.4, 136.1, 140.6 (C-6), 159.3, 159.5, 199.1. $[\alpha]_D^{25}$ −55.8 (c 0.24, acetone). Elemental analysis calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 69.11; H, 6.82.

*(−)-Gabosine A (**16**).* To a solution of ketone **15** in DCM (10 mL), TFA (0.05 mL) was added at room temperature and the reaction mixture was stirred for 20 min at the same temperature. After the completion of the reaction (checked by TLC), the reaction mixture was concentrated under the reduced pressure and the crude product thus obtained was purified by flash column chromatography (EtOAc) to get (−)-gabosine A (**16**) (8.2 mg, 81%). ^{1}H NMR (500 MHz, CD_3OD) δ 1.72 (s, 3H, $-CH_3$), 3.63 (dd, J = 10.0 Hz, 4.0 Hz,1H), 4.23 (d, J = 10.0 Hz, 1H), 4.29 (t, J = 5.0 Hz, 1H), 6.65 (dd, J = 4.0 Hz, 1.0 Hz, 1H); ^{1}H NMR (125 MHz, CD_3OD) δ 14.1, 66.0, 72.5, 73.7, 135.5, 141.6. ^{1}H and ^{13}C are similar to the reported data.[12b]

*(−)-MK7607 (**17**).* To a solution of the alcohol **11** (40 mg, 0.156 mmol) in DCM (10 mL), TFA (0.01 mL) was added at room temperature and the reaction mixture was stirred for 10 min at the same temperature. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography (EtOAc/acetone, 1:4) to get (−)-MK7607 **17** (27.49 mg, 100%) as a colorless liquid. ^{1}H NMR (500 MHz, D_2O) δ 3.81−3.87 (m, 2H), 4.11 (s, 2H), 4.21 (d, J = 3.5 Hz, 1H), 4.28 (apr t, 1H), 5.82 (d, J = 4.5 Hz, 1H); ^{13}C NMR (125 MHz, D_2O) δ 62.1, 66.1, 66.7, 68.4, 68.7, 124.1, 140.3. ^{1}H and ^{13}C values are similar to the reported data.[2c]

*(1R,2S,3R,4R)-1,2-Bis((4-methoxybenzyl)oxy)-5-(((4-methoxybenzyl)oxy)methyl)cyclohex-5-ene-1,2,3,4-tetrol (**18**).* To a solution of the alcohol **11** (240 mg, 0.93 mmol) in methanol (20 mL), CSA (15 mg) was added at room temperature and the reaction mixture was stirred for 3 h at the same temperature. After completion of the reaction, the solvent was evaporated off under reduced pressure and the residue was purified by flash column chromatography (EtOAc) to get an inseparable mixture of triols (155.7 mg, 78%, brsm, overall yield) as a colorless oil. The mixture of triols (157.7 mg) was dissolved in DMF (20 mL), NaH (102.4 mg, 2.56 mmol) and PMBCl (0.35 mL, 2.56 mmol) were added to it at 0 °C and the reaction mixture was stirred for 30 min at room temperature. After the completion of the reaction, excess NaH was quenched with ice-cold water and the reaction mixture was concentrated under reduced pressure. The residue was dissolved in DCM (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 (EtOAc/petroleum ether, 1:4, v/v) to get an inseparable mixture of triPMB ethers (383.2 mg, 91%). The remaining acetonide group of the triPMB ethers (383.2 mg) was deprotected by the treatment with CSA (100 mg) in methanol (20 mL) at room temperature for 4 h. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography (EtOAc/petroleum ether,1:1, v/v) to get the diol **18** (276.0 mg, 46% after three steps) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.73 (d, J = 1.8 Hz, 1H, OH-3), 3.09 (d, J = 1.1 Hz, 1H, OH-4), 3.73 (s, 9H, $-OCH_3$), 3.79 (dd, J = 9.1 Hz, 3.9 Hz, 1H, H-2), 4.00 (s, 2H, H-7A and 7B), 4.09−4.10 (m, 2H, H-1 and H-3), 4.31 (d, J = 4.0 Hz, 1H, H-4), 4.38 (s, 2H, $-CH_2PhOMe$), 4.41 (d (AB), J = 11.5 Hz, 1H, $-CH_aPhOMe$), 4.48 (d (AB), J = 11.6 Hz, 1H, $-CH_aPhOMe$), 4.52 (d (AB), J = 11.6 Hz, 1H, $-CH_bPhOMe$), 4.57 (d (AB), J = 11.5 Hz, 1H, $-CH_bPhOMe$), 5.82 (d, J = 4.9 Hz, 1H, H-6), 6.78−6.81 (m, 6H, Ar−H), 7.17−7.19 (m, 6H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 67.6 (C-4), 68.1 (C-3), 70.4 (C-1), 71.4, 71.9, 72.0, 72.4 (C-7), 75.9 (C-2), 113.8, 113.88, 113.9, 125.2 (C-6), 129.5, 129.6, 129.8, 130.2, 130.6, 137.1, 159.3, 159.35, 159.38. $[\alpha]_D^{25}$ −87.5 (c 0.12, acetone). Elemental analysis calcd for $C_{31}H_{36}O_8$: C, 69.39; H, 6.76. Found: C, 69.21; H, 6.95.

*(1R,2R,3S)-1,2-Bis((4-methoxybenzyl)oxy)-5-(((4-methoxybenzyl)-oxy)methyl)-4-oxocyclohex-5-en-3-yl furan-2-carboxylate (**19**).* To a solution of the diol **18** (100 mg, 0.19 mmol) in pyridine (15 mL), furoyl chloride (0.037 mL, 0.38 mmol) was added at 0 °C and the reaction mixture was stirred for 2 h at room temperature. When TLC showed completion of the reaction (after 2 h), the reaction mixture was concentrated under reduced pressure. The crude product thus obtained was dissolved in DCM (100 mL) and washed with water and brine. The organic layer was separated and dried over anhydrous Na_2SO_4 andconcentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:1; v/v) to get an inseparable mixture (1:1) of alcohols (104.6 mg, 89%) as a colorless oil. This mixture of alcohols (104.6 mg) was taken in DCM (10 mL) under nitrogen atmosphere and treated with PDC (124.8 mg, 0.33 mmol) at room temperature for 30 min. When the reaction was approximately 40% advanced as judged by the disappearance of the starting materials (checked by TLC), the reaction mixture was concentrated under reduced pressure and the crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:2, v/v) to get the enone **19** (44.5 mg, 38% after two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.72 (s, 3H, $-OCH_3$), 3.74 (s, 6H, $-OCH_3$), 3.96 (dd, J =

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10.6 Hz, 3.4 Hz, 1H, H-2), 4.03 (d (AB), J = 14.8 Hz, 1H, H-7A), 4.14 (d (AB), J = 14.9 Hz, 1H, H-7B), 4.21 (dd, J = 5.7 Hz, 3.6 Hz, 1H, H-1), 4.38 (d (AB), J = 11.4 Hz, 1H, −CH_aPhOMe), 4.41 (d (AB), J = 11.5 Hz, 1H, −CH_bPhOMe), 4.53−4.60 (m, 3H, −CHPhOMe), 4.73 (d (AB), J = 11.6 Hz, 1H, −CH_aPhOMe), 5.97 (d, J = 10.6 Hz, 1H, H-3), 6.47 (dd, J = 3.5 Hz, 1.7 Hz, 1H, Ar−H), 6.74 (d, J = 8.6 Hz, 2H, Ar−H), 6.80−6.82 (m, 4H, Ar−H), 6.86 (d, J = 6.1 Hz, 1H, H-6), 7.13−7.23 (m, 7H, Ar−H), 7.55 (t, J = 0.7, 1H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.27, 55.31, 65.7, 70.3 (C-1), 72.5, 72.8, 72.9 (C-3), 75.2 (C-2), 112.0, 113.8, 113.86, 113.91, 118.8, 129.4, 129.6, 129.7, 129.8, 130.1, 137.9, 139.5 (C-6), 144.2, 146.7, 157.7, 159.4, 159.5. $[\alpha]_D^{25}$ −101.5 (c 0.1, acetone). Elemental analysis calcd for $C_{36}H_{36}O_{10}$: C, 68.78; H, 5.77. Found: C, 68.59; H, 5.84.

*(−)-Epoxydine B (**20**).* To a solution of the ketone **19** (20 mg, 0.031 mmol) in DCM (10 mL), TFA (0.1 mL) was added at room temperature and the reaction mixture was stirred for 20 min at the same temperature. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and the crude product was purified by flash column chromatography (EtOAc) to get epoxydine B (**20**) (10 mg, 81%) as a colorless liquid. ^{1}H NMR (500 MHz, CD_3OD) δ 4.16 (dd, J = 10.8 Hz, 4.0 Hz, 1H), 4.26 (dd (AB), J = 15.5 Hz, 1.3 Hz, 1H), 4.29 (d (AB), J = 15.5 Hz, 1H)4.56 (t, J = 4.9 Hz, 1H), 5.80 (d, J = 10.8 Hz, 1H), 6.66 (dd, J = 3.5 Hz, 1.7 Hz, 1H), 7.07 (dt, J = 6.0 Hz, 1.6 Hz, 1H), 7.35 (dd, J = 2.9 Hz, 0.6 Hz, 1H), 7.80 (d, J = 0.9 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 57.96, 65.8, 69.7, 75.7, 111.7, 118.5, 139.1, 140.7, 144.1, 147.1, 192.5. $[\alpha]_D^{25}$ −120.5 (c 0.1, acetone). Elemental analysis calcd for $C_{12}H_{12}O_7$: C, 53.74; H, 4.51. Found: C, 53.51; H, 4.73. ^{1}H and ^{13}C NMR are similar to the reported data.[15b] The specific rotation of epoxydine B was reported in chloroform (−72.7, c 0.11), but in our hand the solubility of **20** in chloroform was very low and hence we have measured its specific rotation in acetone (−120.5, c 0.1). The large difference could be due to the change of solvent. However, we could measure the specific rotation in chloroform at very low concentration of c = 0.04 and the value was −60.4 which was close to the reported value.

*(1R,2R,3S)-1,2-Bis((4-methoxybenzyl)oxy)-5-(((4-methoxybenzyl)-oxy)methyl)-4-oxocyclohex-5-en-3-yl acetate (**21**).* To a solution of the diol **18** (110 mg, 0.20 mmol) in pyridine (10 mL), acetyl chloride (0.029 mL, 0.4 mmol) was added at 0 °C and the reaction mixture was stirred for 2 h at room temperature. When the TLC showed completion of the reaction (after 2 h), the reaction mixture was concentrated under reduced pressure. The residue was dissolved in DCM (100 mL) and washed with water and brine. The organic layer was separated and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:1; v/v) to get an inseparable mixture (1:1) of two esters (104.4 mg, 88%) as a colorless oil. Then, the mixture of esters (104.4 mg) was taken in DCM (10 mL) under the nitrogen atmosphere and treated with PDC (135.4 mg, 0.36 mmol) at room temperature for 25 min. When the reaction was approximately 40% advanced as judged by the disappearance of the starting materials (checked by TLC), the reaction mixture was concentrated under reduced pressure and the crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:2, v/v) to get the enone **21** (42.1 mg, colorless oil, 36% after two steps) selectively. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.10 (s, 3H, −CH_3), 3.74 (s, 9H, −OCH_3), 3.83 (dd, J = 10.6 Hz, 3.5 Hz, 1H, H-2), 4.00 (dd (AB), J = 14.9 Hz, 1.7 Hz, 1H, H-7A), 4.12 (d (AB), J = 14.9 Hz, 1H, H-7B), 4.16 (dd, J = 5.6 Hz, 3.7 Hz, 1H, H-1), 4.37 (d (AB), J = 11.5 Hz, 1H, −CH_aPhOMe), 4.40 (d (AB), J = 11.5 Hz, 1H, −CH_bPhOMe), 4.51 (d (AB), J = 11.9 Hz, 1H, −CH_aPhOMe), 4.54 (d (AB), J = 9.1 Hz, 1H, −CH_aPhOMe), 4.57 (d (AB), J = 9.4 Hz, 1H, −CH_bPhOMe), 4.70 (d (AB), J = 13.4 Hz, 1H, −CH_bPhOMe), 5.76 (d, J = 10.6 Hz, 1H, H-3), 6.79−6.82 (m, 7H, Ar−H and H-6), 7.15−7.17 (m, 6H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8, 55.3, 65.7, 70.3 (C-1), 72.5, 72.7, 72.9 (C-3), 74.8 (C-2), 113.86, 113.89, 129.4, 129.5, 129.7, 129.8, 129.9, 130.1, 137.8, 139.4, 159.4, 159.5, 170.0, 192.3. $[\alpha]_D^{25}$ −80.5 (c 0.1, acetone). Elemental analysis calcd for $C_{33}H_{36}O_9$: C, 68.74; H, 6.29. Found: C, 68.58; H, 6.71.

*(−)-Epoxydine C (**22**).* To a solution of the ketone **21** (25 mg, 0.043 mmol) in DCM (10 mL), TFA (0.1 mL) was added at room temperature and the reaction mixture was stirred for 20 min at the same temperature. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and the crude product thus obtained was purified by flash column chromatography (EtOAc) to get epoxydine C **22** (12.7 mg, 87%) as a colorless liquid. ^{1}H NMR (500 MHz, CD_3COCD_3) δ 2.1 (s, 3H, CH_3), 4.05 (dd, J = 11.0 Hz, 4.0 Hz, 1H, H-2), 4.19−4.25 (m, 2H, H-7A and 7B), 4.58 (dd, J = 5.0 Hz, 4.5 Hz, 1H, H-1), 5.57 (d, J = 10.5 Hz, 1H, H-3), 7.04 (d, J = 5.5 Hz, 1H, H-6); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 19.8, 58.2, 65.7, 69.9, 75.4, 139.4, 140.2, 169.7. Elemental analysis calcd for $C_9H_{12}O_6$: C, 50.00; H, 5.59. Found: C, 49.61; H, 5.95. ^{1}H NMR data were similar to the reported data.[15a]

The reported NMR data for epoxydine C in acetone-d_6: 2.10 (s, 3H, −$OCOCH_3$), 4.01 (dd, J = 10.8 Hz, 5.4 Hz, 1H, H-2), 4.21 (2H, H-7A and H-7B), 4.54 (t, J = 5.4 Hz, 1H, H-1), 5.54 (d, J = 10.8 Hz, 1H, H-3), 7.01 (dt, J = 5.4 Hz, 2.0 Hz, 1H, H-6).

*(1R,2R,3S,4S,5S,6R)-1,2:3,4-Di-O-isopropylidene-6-O-((tert(butyl)-di(methyl)silyl))-cyclohexane-1,2,3,4,5,6-hexol (**25**).*[19] To a solution of the diol **24** (400 mg, 1.54 mmol) in dry DCM (20 mL), TBDMSCl (278.83 mg, 1.85 mmol) and imidazole (314.52 mmol, 4.62 mmol) were added at the room temperature and the reaction mixture was stirred for 4 h at the same temperature. After the completion of the reaction (4 h), DCM (100 mL) was added to the reaction mixture and 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 (EtOAc/petroleum ether, 1:9, v/v) to get the alcohol **25** (523.79 mg, 91%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.15 (s, 3H, −CH_3), 0.18 (s, 3H, −CH_3), 0.93 (s, 9H, −$C(CH_3)_3$), 1.33 (s, 3H, −CH_3), 1.36 (s, 3H, −CH_3), 1.50 (s, 3H, −CH_3), 1.52 (s, 3H, −CH_3), 2.63 (s, 1H, OH), 3.52−3.58 (m, 2H), 4.09−4.11 (m, 1H), 4.19−4.26 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.0, −4.3, 18.1, 25.00, 25.03, 25.9, 27.6, 27.7, 72.4, 74.2, 76.8, 77.1, 78.2, 79.5, 109.5, 110.0. $[\alpha]_D^{25}$ + 22.0 (c 0.1, acetone). Elemental analysis calcd for $C_{18}H_{34}O_6Si$: C, 57.72; H, 9.15. Found: C, 57.51; H, 9.37.

*(1S,2S,3R,4R,6R)-3-O-tert(Butyl)-di(((methyl)silyl)-4-(methoxy-methylene))-1,2:5,6-di-O-isopropylidene-cyclohexane-1,2,3,4,6-pentol (**27**).* To a solution of the alcohol **25** (510 mg, 1.36 mmol) in dry DCM (10 mL), Dess-Martin periodinane (691.35 mg, 1.63 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 (after 1 h), the reaction mixture was diluted by adding DCM (100 mL) and then the organic layer was washed successively with aq. $Na_2S_2O_3$, 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 (EtOAc/petroleum ether, 1:2; v/v) to get the ketone **26** (476.8 mg, 94%) as a colorless liquid. The ketone **26** exists in equilibrium with its *gem*-diol. So, the ketone was used for the next step after coevaporation with toluene (3 times). This ketone (374.5 mg, 1.0 mmol) in dry THF (20 mL) was added to the orange suspension, formed by the addition of ^{n}BuLi (1.88 mL, 3.0 mmol, 1.6 M solution in hexane) to a suspension of methoxymethyltriphenylphosphonium chloride (1.03 g, 3.0 mmol) in dry THF (20 mL), at −40 °C under N_2 atmosphere. The mixture was allowed to warm to room temperature and then further stirred for 8 h. THF was evaporated under reduced pressure. The residue was dissolved in DCM (100 mL) 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 (EtOAc/petroleum ether, 1:9; v/v) gave the enol ether **27** (261.8 mg, 56%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.02 (s, 3H, −CH_3), 0.00 (s, 3H, −CH_3), 0.79 (s, 9H, −CH_3), 1.21 (s, 3H, −CH_3), 1.26 (s, 6H, −CH_3), 1.38 (s, 3H, −CH_3), 3.57 (s, 3H, −OCH_3), 3.91 (d, J = 3.1 Hz, 1H, H-6), 4.11 (dd, J = 7.0 Hz, 3.1 Hz, 1H, H-1), 4.25 (dd, J = 7.2 Hz, 3.1 Hz, 1H, H-3), 4.35 (dd, J = 7.0 Hz, 3.5 Hz, 1H, H-2), 5.01 (d, J = 7.3 Hz, 1H, H-4), 6.12 (s, 1H, H-7); ^{13}C NMR (125 MHz, $CDCl_3$) δ18.0, 25.5, 25.6, 26.2, 27.4, 27.9, 50.9, 67.0, 70.5, 72.0, 74.0, 109.5, 109.9,

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137.2, 145.5, 192.7. $[\alpha]_D^{25}$ −67.1 (*c* 0.24, acetone). Elemental analysis calcd for $C_{20}H_{36}O_6Si$: C, 59.97; H, 9.06. Found: C, 59.77; H, 9.17.

*(1S,2S,3S,4S)-5-Formyl-1,2:3,4-di-O-isopropylidene-cyclohex-5-ene-1,2,3,4-tetrol (**28**).* To a solution of the enol ether **27** (110 mg, 0.27 mmol) in acetone (15 mL), CSA (10 mg) was added at room temperature and the reaction mixture was stirred for 1 h at the same temperature. After the completion of the reaction, the CSA was quenched with triethylamine and the reaction mixture was concentrated under reduced pressure. The crude product was purified by flash column chromatography (EtOAc/petroleum ether, 1:5, v/v) to get the aldehyde **28** (64.24 mg, 92%) as a colorless liquid. ^{1}H NMR is similar to the compound **10** which is its enantiomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.33 (s, 3H), 1.42 (s, 3H), 1.43 (s, 3H), 4.65−4.67 (m, 1H), 4.71−4.72 (m, 1H), 4.81−4.82 (m, 1H), 4.97 (d, *J* = 5.5 Hz, 1H), 6.62−624 (m, 1H), 9.62 (s, 1H).

^{1}H NMR (500 MHz, DMSO-d_6) δ 1.15 (s, 3H, $-CH_3$); 1.16 (s, 3H, $-CH_3$), 1.24 (s, 3H, $-CH_3$), 1.25 (s, 3H, $-CH_3$), 4.48−4.49 (m, 1H), 4.55−4.56 (m, 1H), 4.73−4.76 (m, 2H), 6.74 (s, 1H), 9.51 (s, 1H); ^{13}C NMR (500 MHz, DMSO-d_6) δ 25.8, 26.5, 27.6, 28.2, 66.5, 70.5, 72.0, 72.1, 74.3, 108.8, 109.3, 136.9, 147.1, 194.1. $[\alpha]_D^{25}$ + 23.1 (*c* 0.12, acetone). Elemental analysis calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.14. Found: C, 61.31; H, 7.41.

*(1S,2S,3S,4S)-5-Hydroxymethyl-1,2:3,4-di-O-isopropylidene-cyclohex-5-ene1,2,3,4-tetrol (**29**).* To a solution of the aldehyde **28** (45.5 mg, 0.18 mmol) in methanol (10 mL), $NaBH_4$ (6.8 mg, 0.18 mmol) was added at room temperature and the reaction mixture was stirred for 30 min at the same temperature. After completion of the reaction, the solvent was evaporated under reduced pressure and the crude product thus obtained was dissolved in ethyl acetate (100 mL) and washed successively with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure and purified by flash column chromatography (EtOAc/petroleum ether, 1:4, v/v) to get the alcohol **29** (41.7 mg, 91%) as a colorless oil. ^{1}H NMR is similar to the compound **11**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28 (s, 3H), 1.30 (s, 3H), 1.31 (s, 3H), 1.32 (s, 3H), 4.17−4.22 (m, 2H), 4.48−4.57 (m, 4H), 5.64 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.2, 26.4, 27.7, 28.0, 64.5, 70.7, 71.5, 73.2, 73.4, 109.2, 109.4, 122.9, 136.0. $[\alpha]_D^{25}$ −10.2 (*c* 0.18, acetone). Elemental analysis calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.68; H, 7.91.

*(+)-MK7607 (**30**).* To a solution of the alcohol **29** (31 mg, 0.12 mmol) in DCM (10 mL), TFA (0.05 mL) was added at room temperature and the reaction mixture was stirred for 20 min at the same temperature. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and the crude product thus obtained was purified by flash column chromatography (acetone) to get (+)-MK7607 (**30**) (21.2 mg, 100%) as a colorless liquid. ^{1}H NMR (500 MHz, D_2O) δ 3.79−3.85 (m, 2H), 4.10 (s, 2H), 4.20 (d, *J* = 3.5 Hz, 1H), 4.28 (apr t, *J* = 4.5 Hz, 1H), 5.82 (d, *J* = 4.5 Hz, 1H); ^{13}C NMR (125 MHz, D_2O) δ 62.0, 66.0, 66.6, 68.3, 68.6, 124.1, 140.2. ^{1}H and ^{13}C values are similar to the reported data.[2c]

*Synthesis of Enol Ether **34a** and **34b**.* To a suspension of (methoxymethyl)triphenylphosphonium chloride (4.07 g, 11.87 mmol) in dry THF (20 mL), ^{t}BuOK (1.33 g, 11.87 mmol) was added at 0 °C under N_2 atmosphere. To the resultant orange suspension, a solution of the ketone **33** (1.72 g, 4.75 mmol) in dry THF (20 mL) was added slowly at 0 °C. The mixture was allowed to warm to room temperature and then further stirred for 8 h. The THF was evaporated under reduced pressure. The residue was dissolved in DCM (150 mL) 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 (EtOAc/petroleum ether, 1:2; v/v) gave the enol ether **34a** (680 mg) and **34b** (670 mg) (1.35 g, overall yield =73%) as white solids.

*(1R,2R,3S,4S,6S,E)-5-Methoxymethylene-2-O-benzoyl-1,6:3,4-di-O-isopropylidene-cyclohexane-1,2,3,4,6-pentol (**34a**).* mp 156−158 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (s, 3H, $-CH_3$), 1.41 (s, 3H, $-CH_3$), 1.44 (s, 3H, $-CH_3$), 1.53 (s, 3H, $-CH_3$), 3.54 (dd, *J* = 11.0 Hz, 9.5 Hz, 1H, H-4), 3.67 (s, 1H, $-OCH_3$), 4.16 (dd, *J* = 7.0 Hz, 5.0 Hz, 1H, H-3), 4.44−4.46 (m, 2H, H-4 and H-6), 5.48 (dd, *J* = 11.0 Hz, 7.5 Hz, 1H, H-2), 7.36 (t, *J* = 7.5 Hz, 2H, Ar−H), 7.48 (t, *J* = 7.5 Hz, 1H, Ar−H), 8.01 (dd, *J* = 7.0 Hz, 1.0 Hz, 2H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.2, 26.92, 26.94, 27.8, 61.5, 75.5 (C-6), 75.7 (C-2 or C-4), 78.6 (C-2 or C-4), 79.32 (C-5), 79.34 (C-1), 104.6, 109.8, 112.6, 128.2, 129.99, 130.0, 133.0, 148.6. $[\alpha]_D^{25}$ −1.5 (*c* 0.36, acetone). Elemental analysis calcd for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C, 64.41; H, 6.84.

*(1R,2S,3S,4S,6S,Z)-5-(Methoxymethylene)-2-O-(benzoyl)-1,2:4,5-di-O-(isopropylidene)-cyclohexane-1,2,3,4,6-pentol (**34b**).* mp 194−196 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34 (s, 3H, $-CH_3$), 1.37 (s, 3H, $-CH_3$), 1.42 (s, 3H, $-CH_3$), 1.52 (s, 3H, $-CH_3$), 3.42 (dd, *J* = 10.8 Hz, 9.5 Hz, 1H, H-1), 3.65 (s, 3H, $-OCH_3$), 4.18 (dd, *J* = 6.7 Hz, 5.7 Hz, 1H, H-3), 4.31(dd, *J* = 9.4 Hz, 2.0 Hz, 1H, H-6), 5.19 (d, *J* = 5.5 Hz, 1H, H-4), 5.46 (dd, *J* = 10.9 Hz, 6.9 Hz, 1H, H-2), 6.28 (d, *J* = 2.0 Hz, 1H, H-7), 7.36 (dd, *J* = 7.9 Hz, 7.7 Hz, 2H, Ar−H), 7.47 (t, *J* = 7.4 Hz, 1H, Ar−H), 8.01 (dd, *J* = 7.1 Hz, 1.3 Hz, 2H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.0, 26.9, 27.1, 27.8, 60.5, 71.4 (C-2), 74.5 (C-4), 75.6 (C-6), 79.6 (C-1), 80.4 (C-5), 105.5, 110.1, 112.8, 128.2, 130.0, 133.0, 145.9 (C-7), 165.6. $[\alpha]_D^{25}$ + 3.0 (*c* 0.1, acetone). Elemental analysis calcd for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C, 64.34; H, 6.82.

*(1R,2S,3S,4S)-5-Formyl-2-O-benzoyl-3,4-O-isopropylidene-cyclohex-5-ene-1,2,3,4-tetrol (**35**).* To a solution of the enol ethers (**34a and 34b**) (615 mg, 1.58 mmol) in acetone (20 mL), CSA (50 mg) was added at room temperature and the reaction mixture was stirred for 30 min at the same temperature. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure. The crude product, thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:2, v/v) to get the aldehyde **35** (461.3 mg, 92%) as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (s, 3H, $-CH_3$), 1.43 (s, 3H, $-CH_3$), 4.42 (dd, *J* = 7.9 Hz, 5.8 Hz, 1H, H-3), 4.45 (dd, *J* = 7.3 Hz, 2.4 Hz, 1H, H-1), 4.95 (d, *J* = 5.7 Hz, 1H, H-4), 5.36 (t, *J* = 7.6 Hz, 1H, H-2), 6.84 (d, *J* = 2.8 Hz, 1H, H-6), 7.38 (dd, *J* = 9.5 Hz, 8.0 Hz, 2H, Ar−H), 7.52 (t, *J* = 7.5 Hz, 1H, Ar−H), 7.97 (dd, *J* = 7.2 Hz, 1.3 Hz, 2H, Ar−H), 9.58 (s, 1H, −CHO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.3, 28.0, 68.7 (C-1), 69.0 (C-4), 74.4 (C-3), 74.8 (C-2), 111.9, 128.5, 129.2, 130.0, 133.7, 136.7, 149.8 (C-6), 166.8, 191.6. $[\alpha]_D^{25}$ + 3.25 (*c* 0.4, acetone). Elemental analysis calcd for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 64.09; H, 5.81.

*(1R,2S,3S,4S)-5-Methoxymethyl-3,4-O-isopropylidene-cyclohex-5-ene-1,2,3,4-tetrol (**36**).* To a solution of the enal **35** (450 mg, 1.41 mmol) in methanol (10 mL), $NaBH_4$ (53.34 mg, 1.41 mmol) was added at room temperature and the reaction mixture was stirred for 30 min at the same temperature. After the completion of the reaction, NaOH (84.6 mg, 2.12 mmol) was added to the reaction mixture and the reaction mixture was further stirred for 10 min at the same temperature. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and the crude product was purified by flash column chromatography (EtOAc/petroleum ether, 4:1, v/v) to get the triol **36** (260 mg, 85%) as a colorless oil. ^{1}H NMR (500 MHz, CD_3OD) δ 1.27 (s, 3H, $-CH_3$), 1.37 (s, 3H, $-CH_3$), 3.31 (t, *J* = 9.0 Hz, 1H, H-2), 3.87 (d, *J* = 9 Hz, 1H, H-1), 3.95 (dd, *J* = 9.0 Hz, 7.0 Hz, 1H, H-3), 4.02 (s, 2H, H-7A and 7B), 4.55 (d, *J* = 6.5 Hz, 1H, H-4), 5.66 (d, *J* = 1.0 Hz, 1H, H-6); ^{13}C NMR (125 MHz, CD_3OD) δ 24.8, 27.2, 62.0 (C-7), 70.2 (C-1), 72.4 (C-4), 74.8 (C-2), 78.0 (C-3), 109.9, 128.1 (C-6), 134.9. $[\alpha]_D^{25}$ −19.4 (*c* 0.16, MeOH). Elemental analysis calcd for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found: C, 55.34; H, 7.51.

*1-epi-(+)-MK7607 (**37**).* To a solution of the triol **36** (30 mg, 0.14 mmol) in methanol (10 mL), HCl (0.01 mL, 12 M) was added at room temperature and the reaction mixture was stirred for 10 min at the same temperature. After completion of the reaction (checked by the TLC), the reaction mixture was concentrated under reduced pressure to get (−)-1-*epi*-MK7607 (**37**) (24.44 mg, 100%) as a colorless oil. ^{1}H NMR (500 MHz, D_2O) δ 3.47 (dd, *J* = 10.8 Hz, 4.1 Hz, 1H), 3.57 (dd, *J* = 10.8 Hz, 7.8 Hz, 1H), 4.01−4.03 (m, 1H), 4.05−4.11 (m, 2H), 4.15 (d, *J* = 4.0 Hz, 1H), 5.63 (d, *J* = 0.9 Hz, 1H); ^{13}C NMR (125 MHz, D_2O) δ 61.9, 66.6, 70.8, 71.8, 72.4, 127.0, 137.6.

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$[\alpha]_D^{25}$ −16.7 (*c* 0.08, H_2O). ^1H and ^{13}C values are similar to the reported data.[2c]

*(1R,2S,3S,4S)-3,4-O-Isopropylidene-5-(4-methoxybenzyl(oxy)-methyl)-1,2-di-O-((4-methoxybenzyl)-cyclohex-5-ene-1,2,3,4-tetrol (**38**).* To a solution of **36** (320 mg, 1.48 mmol) in DMF (10 mL), NaH (236.78 mg, 5.92 mmol, 60% dispersed in mineral oil) and followed by PMBCl (0.80 mL, 5.92 mmol) were added at 0 °C and the reaction mixture was stirred for 20 min at room temperature. After the completion of the reaction (20 min.), excess NaH was quenched with ice-cold water and DMF was evaporated off under reduced pressure. The residue was dissolved in ethyl acetate (100 mL) and washed successively 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 (EtOAc/petroleum ether, 1:5, v/v) to get the compound **38** (785.15 mg, 92%) as a colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 1.31 (s, 3H, $-CH_3$), 1.37 (s, 3H, $-CH_3$), 3.52 (t, *J* = 8.7 Hz, 1H, H-2), 3.73 (s, 9H, $-OCH_3$), 3.91 (d, *J* = 6.4 Hz, 1H, H-1), 3.93 (s, 1H, H-7A), 4.02 (d (AB), *J* = 12.5 Hz, 1H, H-7B), 4.12 (dd, *J* = 8.9 Hz, 6.5 Hz, 1H, H-3), 4.38 (d (AB), *J* = 11.5 Hz, 1H, $-CH_aPhOMe$), 4.42 (d (AB), *J* = 11.5 Hz, 1H, $-CH_bPhOMe$), 4.52 (d, *J* = 5.9 Hz, 1H, H-4), 4.54 (d (AB), *J* = 10.6 Hz, 1H, $-CH_aPhOMe$), 4.57 (d (AB), *J* = 11.3 Hz, 1H, $-CH_bPhOMe$), 4.68 (d (AB), *J* = 11.0 Hz, 1H, $-CH_aPhOMe$), 4.79 (d (AB), *J* = 11.1 Hz, 1H, $-CH_bPhOMe$), 5.79 (s, 1H, H-6), 6.77−7.26 (m, 12H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.1, 28.2, 55.3, 70.2 (C-7), 72.2, 72.7, 74.0 (C-4), 77.6 (C-1), 78.2 (C-3), 80.9 (C-2), 110.1, 113.7, 113.79, 113.8, 128.5 (C-6), 129.4, 129.7, 130.2, 130.5, 131.0, 132.5, 159.1, 159.2, 159.3. $[\alpha]_D^{25}$ + 2.7 (c, 0.3, $CHCl_3$). Elemental analysis calcd for $C_{34}H_{40}O_8$: C, 70.81; H, 6.99. Found: C, 70.65; H, 7.05.

*(1R,2R,3S,4S)-1,2-Bis((4-methoxybenzyl)oxy)-5-(((4-methoxybenzyl)oxy)methyl)cyclohex-5-ene-1,2,3,4-tetrol (**39**).* To a solution of the compound **38** (520 mg, 0.90 mmol) in MeOH (20 mL), CSA (100 mg) was added at room temperature and the reaction mixture was stirred for 1 h at the same temperature. After the completion of the reaction, the acid was quenched with triethylamine and concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:3, v/v) to get the diol **39** (497.35 mg, 89%) as a colorless liquid. ^1H NMR (500 MHz, $CDCl_3$) δ 2.70 (brs, 1H, OH-4), 2.81 (brs, 1H, OH-3), 3.55 (d, *J* = 7.0 Hz, 1H, H-3), 3.72 (s, 9H, $-OCH_3$), 3.80 (dd, *J* = 9.6 Hz, 7.1 Hz, 1H, H-2), 3.94−3.99 (m, 2H, H-1 and H-7A), 4.03 (d (AB), *J* = 12.2 Hz, 1H, H-7B), 4.23 (s, 1H, H-4), 4.40 (s, 2H, CH_2Ph), 4.50 (d (AB), *J* = 11.3 Hz, 1H, $-CH_aPhOMe$), 4.55 (d (AB), *J* = 11.4 Hz, 1H, $-CH_bPhOMe$), 4.58 (d (AB), *J* = 11.1 Hz, 1H, $-CH_aPhOMe$), 4.78 (d (AB), *J* = 11.1 Hz, 1H, $-CH_bPhOMe$), 5.75 (s, 1H, H-6), 6.79−6.81 (m, 6H, Ar−H), 7.17−7.20 (m, 6H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 67.2 (C-4), 70.7 (C-3), 71.1 (C-7), 71.13, 72.5, 74.1, 78.4 (C-2), 78.6 (C-1), 113.9, 114.0, 126.0 (C-6), 129.5, 129.7, 130.0, 130.2, 130.6, 136.3, 159.3, 159.4. $[\alpha]_D^{25}$ + 2.3 (*c* 0.14, acetone). Elemental analysis calcd for $C_{31}H_{36}O_8$: C, 69.39; H, 6.76. Found: C, 69.21; H, 6.85.

*(1R,2R,3R)-3-Hydroxy-1,2-bis((4-methoxybenzyl)oxy)-5-(((4-methoxybenzyl)oxy)methyl)cyclohex-5-ene-4-one (**40**).* To a solution of the diol **39** (223 mg, 0.42 mmol) in dichloromethane (15 mL), Dess-Martin periodinane (267.2 mg, 0.63 mmol) was added at the room temperature and the reaction mixture was stirred for 15 min at the same temperature. When the TLC showed completion of the reaction (after 15 min.), the reaction mixture was diluted by adding DCM (100 mL) and then the reaction mixture was washed successively with aq. $Na_2S_2O_3$, 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 (EtOAc/petroleum ether, 1:5; v/v) to get the ketone **40** (197.72 mg, 89%) as a colorless oil. This ketone exists in equilibrium with its diol form. ^1H NMR (500 MHz, $CDCl_3$) δ 3.52 (d, *J* = 2.2 Hz, 1H, OH-3), 3.68 (dd, *J* = 10.7 Hz, 8.3 Hz, 1H, H-2), 3.74 (s, 9H, $-OCH_3$), 4.05−4.14 (m, 3H, H-3, 7A and 7B), 4.25−4.28 (m, 1H, H-1), 4.42 (s, 2H, $-CH_aH_bPhOMe$), 4.62 (d (AB), *J* = 11.2 Hz, 1H, $-CH_aPhOMe$), 4.67 (d (AB), *J* = 11.2 Hz, 1H, $-CH_bPhOMe$), 4.71 (d (AB), *J* = 10.8 Hz, 1H, $-CH_aPhOMe$), 4.85 (d (AB), *J* = 10.9 Hz, 1H, $-CH_bPhOMe$), 6.78−7.27 (m, 14H, H-6, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 65.5 (C-7), 73.0, 73.2, 74.7, 77.6 (C-1 and C-3), 85.7 (C-2), 113.8, 113.89, 113.92, 129.3, 129.5, 129.6, 129.71, 129.74, 129.9, 130.3. 130.4, 134.2, 145.5, 159.3, 159.4, 159.5, 197.3. Elemental analysis calcd for $C_{31}H_{34}O_8$: C, 69.65; H, 6.41. Found: C, 69.41; H, 6.65.

*1-epi-Gabosine E (**41**).* To a solution of the ketone **40** (40 mg, 0.17 mmol) in DCM (10 mL), TFA (0.05 mL) was added at room temperature and the reaction mixture was stirred for 20 min at the same temperature. The reaction mixture was concentrated under reduced pressure and the crude product thus obtained was purified by flash column chromatography (EtOAc/acetone, 4:1, v/v) to get 1-*epi*-gabosine E (**41**) (11 mg, 85%) as a colorless liquid. ^1H NMR (500 MHz, CD_3COCD_3) δ 3.65 (dd, *J* = 10.8 Hz, 8.2 Hz, 1H, H-2), 4.1 (d, *J* = 10.9 Hz, 1H, H-3), 4.21 (d (AB), 1H, *J* = 15.2 Hz, H-7A), 4.28 (d (AB), 1H, *J* = 15.1 Hz, H-7B), 4.56−4.78 (m, 1H, H-1), 6.93 (d, *J* = 1.5 Hz, 1H, H-6); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 58.0 (C-7), 71.3 (C-1), 76.9 (C-3), 79.0 (C-2), 136.7 (C-5), 146.2 (C-6), 198.3 (C-4). $[\alpha]_D^{25}$ + 41.8 (*c* 0.14, acetone). Elemental analysis calcd for $C_7H_{10}O_5$: C, 48.28; H, 5.79. Found: C, 48.12; H, 5.92. ^1H and ^{13}C NMR did not match with the reported data.[17] The reported NMR data of natural carbasugar (in acetone-d_6): ^1H NMR (300 MHz, CD_3COCD_3) δ 3.68 (dd, *J* = 11.4, 8.3, 1H, H-2), 4.13 (m, 2H, H-7), 4.43 (dq, *J* = 8.3, 2.2, 1H, H-1), 4.57 (d, *J* = 11.4, 1H, H-3), 6.86 (q, *J* = 1.7, 1H, H-6); ^{13}C NMR (75.4 MHz, CD_3COCD_3) δ 58.4 (C-7), 67.2 (C-3), 71.7 (C-1), 78.0 (C-2), 137.3 (C-5), 147.1 (C-6), 192.1 (C-4).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01876.

ORTEP diagram and crystal data of **34a** and spectroscopic data for all new compounds (PDF)

Crystal data (CIF)

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Notes

The authors declare no competing financial interest.

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