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Total Syntheses and Structural Validation of Lincitol A, Lincitol B, Uvacalol I, Uvacalol J, and Uvacalol K

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Natural carbasugars are important class of biologically active compounds. Due to their conformational freedom and due to the subtle difference in spectral characteristics between isomers, often their NMR-based structural assignments are erroneous. It is thus important to validate their structural identity through chemical synthesis. We report the first total syntheses and structure-validation of five natural carbasugars namely lincitol A, lincitol B, uvacalol I, uvacalol J, and uvacalol K in their racemic form, from a *myo*-inositol-derived common intermediate. This intermediate was synthesized by the vinylogous ring opening of *myo*-inositol orthoester cage under mild acidic condition in six steps from *myo*-inositol. From this intermediate, we achieved the syntheses of (±)-lincitol A in six steps, (±)-lincitol B in seven steps, (±)-uvacalol I in five steps, (±)-uvacalol J in five steps, and (±)-uvacalol K in seven steps. The structure and relative stereochemistry of these natural products were confirmed by comparing the ^{1}H and ^{13}C NMR spectra of synthesised natural products with the reported data. These syntheses involved several unprecedented protecting group manipulations and unexpected reactivities.

Introduction

Carbasugars are sugar mimics having carbocyclic ring and are more stable than their parent sugar due to the absence of hemiacetal linkage. A large number of natural products such as gabosines,[1] pericosines,[2] cyclophellitol,[3] lincitols,[4] uvacalols,[5] uvamalols,[6] and various aminocyclitols[7] belong to the carbasugar family. Due to their carbohydrate-like structure, natural carbasugars possess interesting biological activities such as anticancer, antibacterial, antiviral, antioxidant, enzyme inhibitory activities.[8] Their attractive biological activities coupled with their scarce natural occurrence and bleak isolation protocols to supply sufficient quantities, encouraged chemists to synthesize these compounds. Several elegant total syntheses of many members of these natural products have been reported.[9] Many a times, the structure of a newly isolated natural product is assigned based on NMR data including coupling constants and n.O.e. Often, the reported structure of many natural products were found to be incorrect after tedious multi-step synthesis.[10] Especially this is a common problem in cyclitol derived natural products.[11,2] This is due to the possibility of multiple isoenergetic conformations in their solution further complicated by their fast interconversion leading to time averaged signals in NMR spectra which makes the NMR-based determination of the relative configuration error prone. Also, the subtle difference in the spectral characteristics between different isomers of cyclitols leads to wrong structural assignment. Thus, it is very important to validate their proposed structures (relative stereochemistry) of new natural products through an inexpensive racemic synthesis before attempting a tedious and costly asymmetric synthesis.

We herein report the first syntheses and structural validation of five carbasugar natural products namely lincitol A, lincitol B, uvacalol I, uvacalol J and uvacalol K in racemic form, from cheaply available *myo*-inositol, which has been used as the starting material for the syntheses of several natural products.[12]

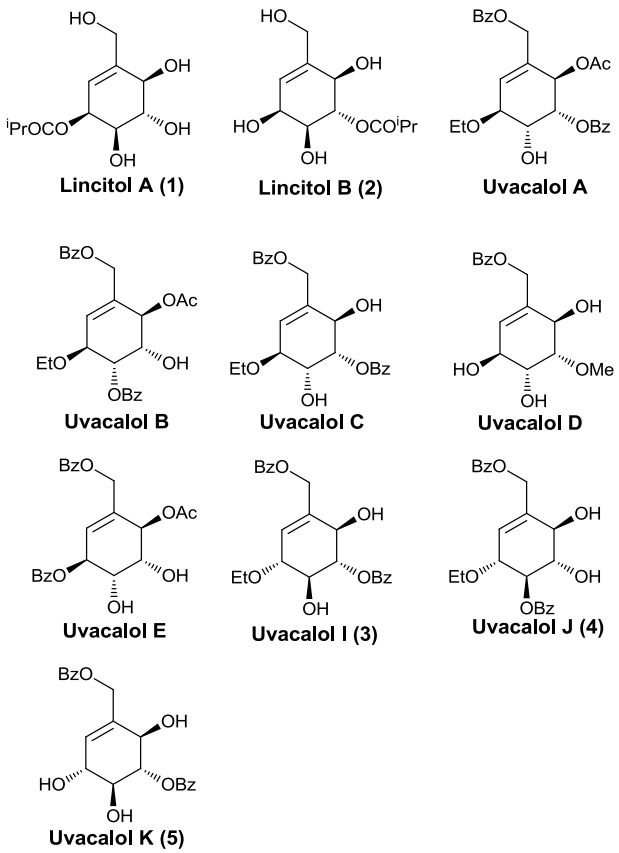
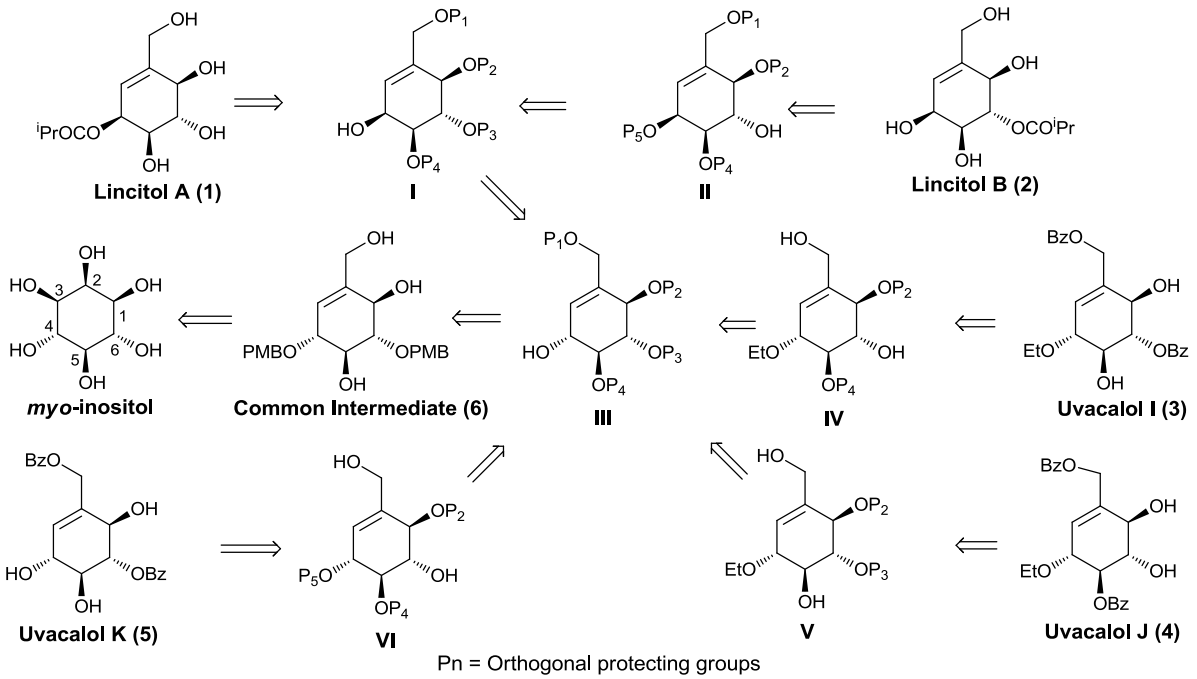


Fig. 1 Lincitols and uvacalols

Results and discussion

While (+)-lincitol A and (+)-lincitol B were isolated from the fungus *Streptomyces lincolnensis* in 2010,[4] (-)-uvacalol I-K were isolated from the roots of the plant *Uvaria calamistrata*.[5a] The



Scheme 1 Retrosynthetic analyses

biological activities of these natural products are yet to be explored. Retrosynthetic analyses (Scheme 1) of all these five natural products revealed that they can be synthesized from the common intermediate **6** (Scheme 2), which can be obtained from *myo*-inositol in ~40% yield in six steps as reported by our group recently.[13]This intermediate **6** which was synthesized from *myo*-inositol by the vinylogous cleavage of its orthoester,[13] has interesting structural features that can be exploited for the synthesis of many carbasugar-based natural products and their analogs. We have reported the synthesis of eight carbasugar natural products from this intermediate recently.

For the synthesis of lincitols A and B, the major steps are the inversion of the C-1 configuration and acylation of one of the five hydroxyl groups by the judicious choice of protecting groups. Deprotection of the PMB protecting groups of the triol **6** (Scheme 2) using 10% TFA in dichloromethane provided pentol **7** (1-*epi*-streptol) as reported.[13] It was planned to effect the C-1 epimerization through an oxidation-reduction sequence. Because of the presence of three allylic alcohols, it was necessary to protect other hydroxyl groups exposing the only the required C1-OH free. Treatment of pentol **7** with 2-methoxypropene in presence of camphorsulphonic acid (CSA) led to the formation of the known alcohol **8**[14] as an exclusive product (91%). The concurrence of ^{1}H NMR data with the reported values[14] confirmed the formation of 2,3:4,7-di-*O*-isopropylidene (**8**). Further evidence for the structure was obtained from its single crystal X-ray structure (Fig. 3). No traces of other isomeric ketals were observed. The formation of 4,7-*O*-isopropylidene is kinetically facile due to the more reactive nature of primary and allylic alcohols involved. Of the two theoretically possible trans-ketals (1,2-*O*-isopropylidene or 2,3-*O*-isopropylidene) that can be formed from the remaining three hydroxyl groups, 1,2-*O*-isopropylidene is less favored (though 1-OH is more reactive) due to the strain induced by the half-chair conformation cyclohexene skeleton. This is evident from the energy-minimized structure (MM2) of the 4,7-*O*-isopropylidene monoketal (Fig. 2), which showed a dihedral angle of 54° between 2- and 3-hydroxyl groups (which would lead to a less strained ketal) and 71° between 1- and 2-hydroxyl groups (which would lead to a more strained ketal). Also it is clear from a comparison of the calculated energies (MM2) of the two possible diacetonides of **7** (Fig. 2) that the 2,3:4,7-di-*O*-isopropylidene derivative **8** is more stable than the 1,2:4,7-di-*O*-isopropylidene

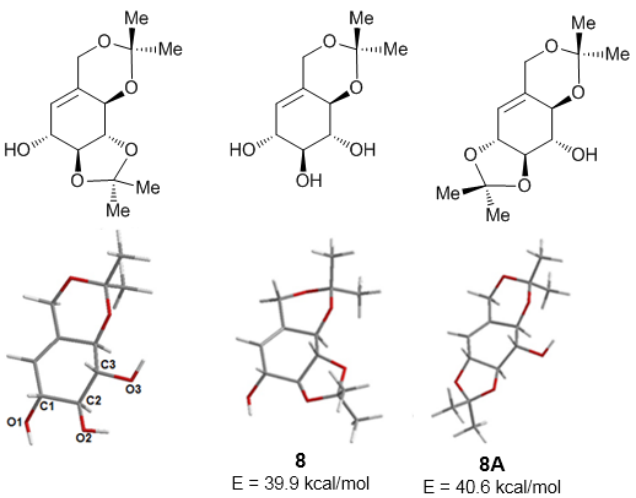
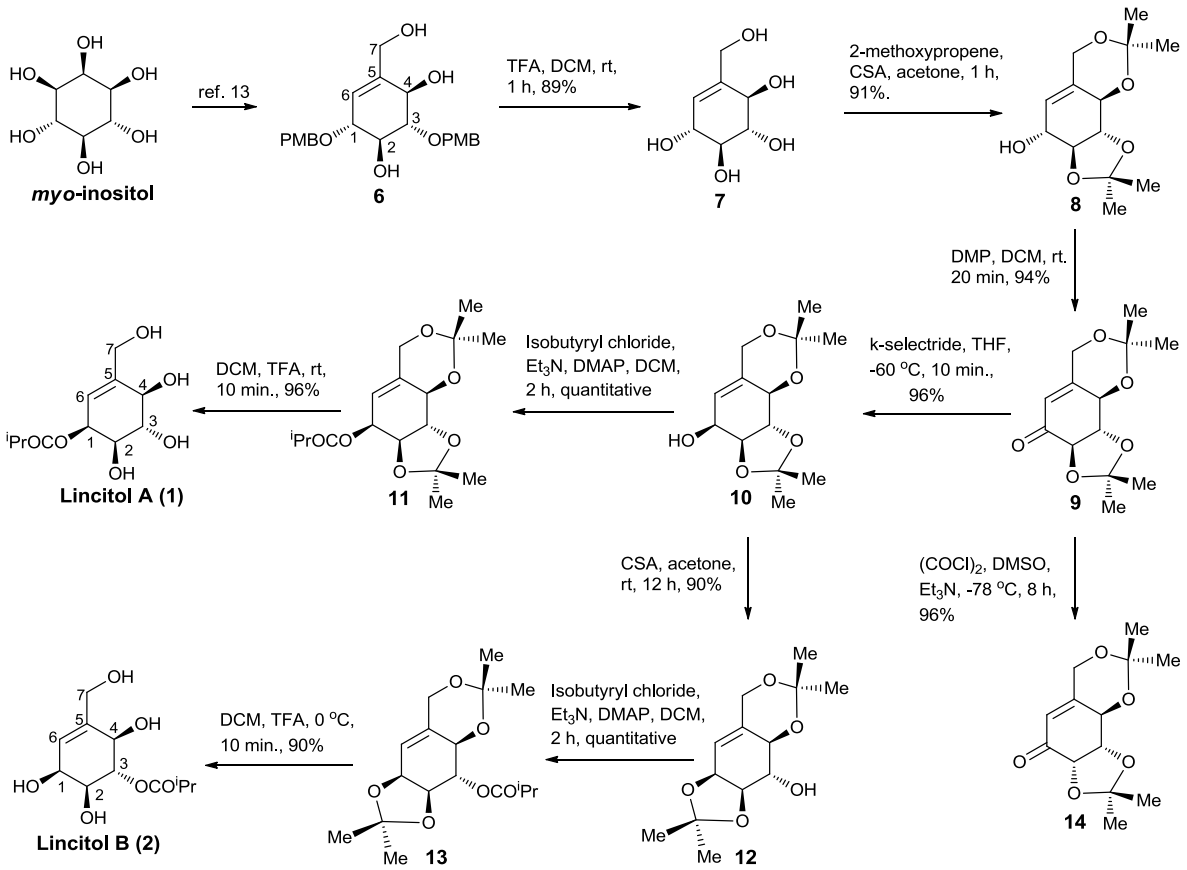


Fig. 2 Energy minimized structures of monoketal and two possible diketals of pentol **7**



Scheme 2 Total syntheses of licitol A and lincitol B

derivative **8A** by 0.7 kcal/mol. This may be the probable reason for the exclusive formation of alcohol **8**. Thus it is reasonable to say that an interplay of both kinetic and thermodynamic factors lead to the exclusive formation of **8**.

Oxidation of the alcohol **8** using Dess-Martin periodinane[15] provided the known ketone **9**.[16] It is worthy to note that Swern oxidation of **8** leads to epimerization of the trans-ketal to cis-ketal **14** and hence cannot be used for this transformation.[17] Reduction of enone **9** using K-selectride afforded alcohol **10** with desired stereochemistry in 90% yield over two steps. The bulky hydride donor ensured hydride delivery from opposite side of the protected O-2. Reaction of the alcohol **10** with isobutyryl chloride in presence of triethylamine and catalytic amount of DMAP gave the ester **11** in quantitative yield. Finally, deprotection of both the isopropylidene groups using trifluoroacetic acid (TFA) provided lincitol A (**1**) in 96% yield. Thus, the synthesis of lincitol A (**1**) could be achieved in six steps in 70.2% yield from the common intermediate **6**. The ^{1}H and ^{13}C NMR data were identical to the reported data,[4] validating the previous structural assignment.

For the synthesis of Lincitol B, we started from the alcohol **10**. It is necessary to protect the 1-OH and expose the 3-OH for the butyrylation. We envisioned that this protecting group bartering can be achieved by acid mediated transketalization of the strained trans-ketal in **10** to the thermodynamically more stable cis-ketal.[18] In order to test this idea, the alcohol **10** was treated with CSA in acetone at room temperature. To our satisfaction, alcohol **12** could be obtained in 90% yield (Scheme 2) after 12 h. Acylation of the alcohol **12** with isobutyryl chloride and triethylamine in presence of catalytic amount of DMAP yielded the ester **13** in quantitative yield. Finally, removal of both the isopropylidene groups using 10% TFA in dichloromethane provided lincitol B (**2**) in 90% yield. This constitute the first synthesis of lincitol B and was achieved in seven steps from the common intermediate **6** in 59.2% yield. The ^{1}H NMR and ^{13}C NMR data of lincitol B matches with the reported data, substantiating its proposed structure.

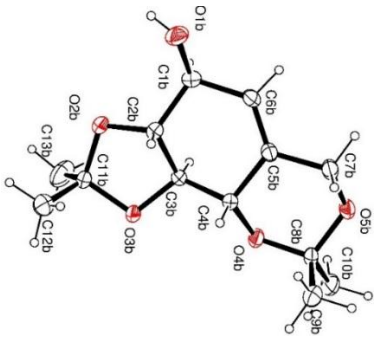
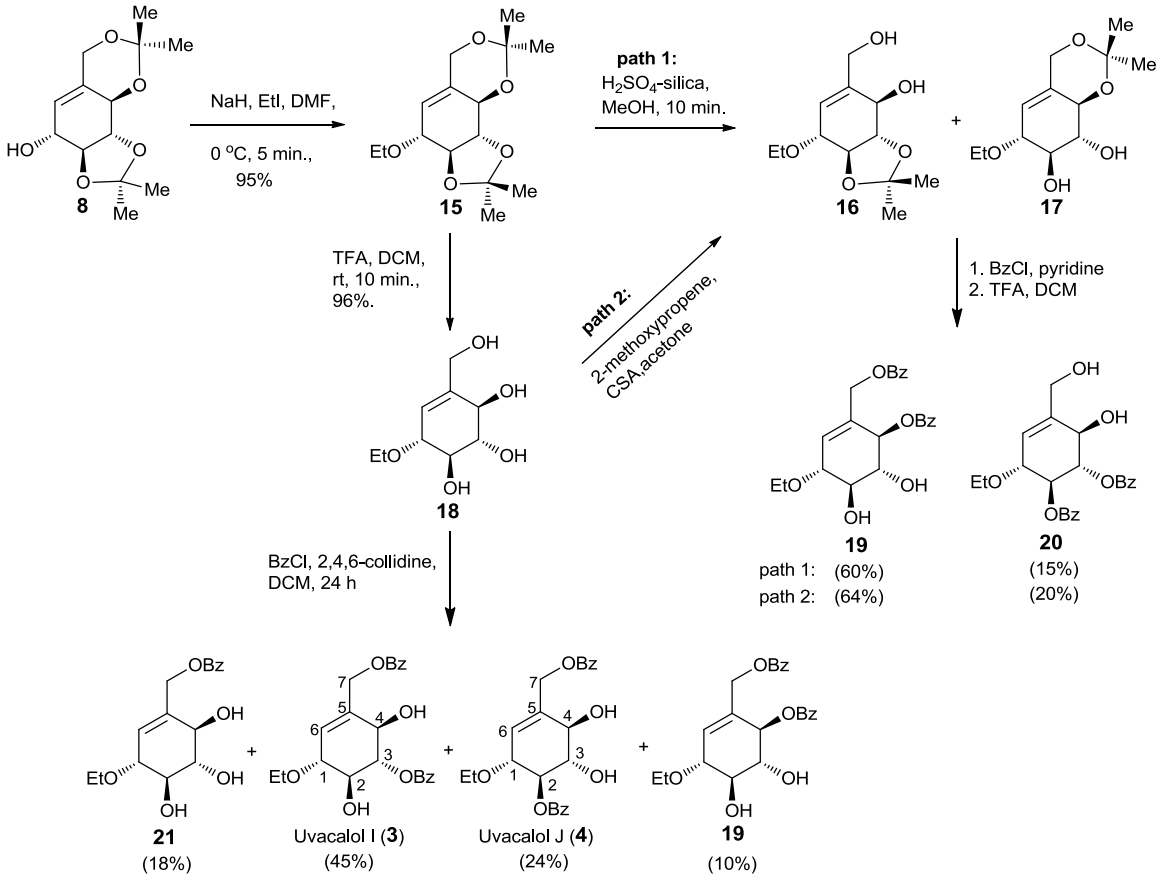


Fig. 3 ORTEP diagram of compound **8**

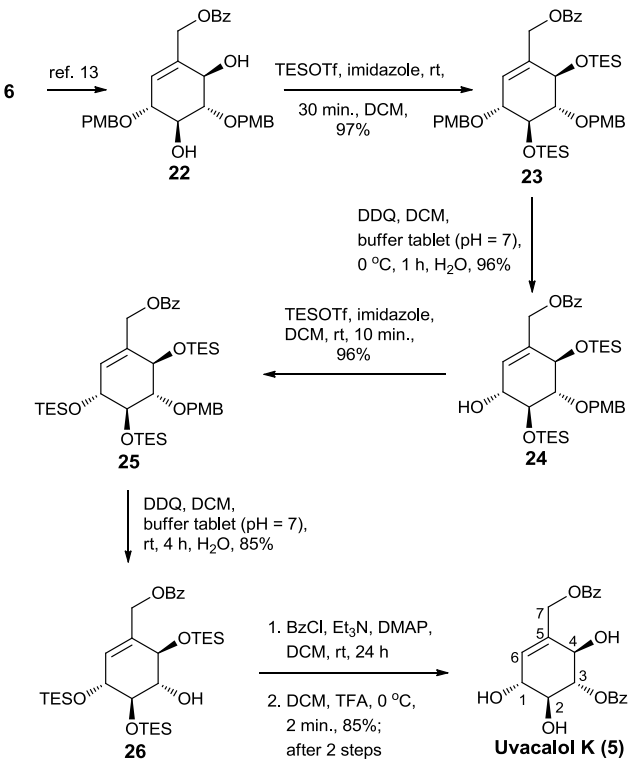


Scheme 3 Total syntheses of uvacalol I and uvacalol J

As both uvacalol I and uvacalol J have an ethoxy group at C1 position, it is easy to synthesize them from the alcohol **8**. Ethylation of alcohol **8** using ethyl iodide in presence of sodium hydride provided ethyl ether **15** in 95% yield (Scheme 3). It was envisaged that the benzoate group at 2-position (for uvacalol J) or3-position (for uvacalol I) could be introduced by the selective deprotection of less stable five-membered (1,3-dioxolane) *trans*-isopropylidene in presence of the six-membered (1,3-dioxane) isopropylidene under mildly acidic condition followed by the monobenzoylation of the resultant diol with benzoyl chloride in presence of pyridine at lower temperature. Thus diketal **15** was treated with H_2SO_4-silica[19] in methanol. To our surprise, a reversal of the expected selectivity was observed, forming a mixture of diol **16** and diol **17** in the ratio 4:1. Due to the similar R_f values of compound **16** and **17**, they were separated and characterized after benzoylation followed by isopropylidene deprotection as 4,7-dibenzoate **19** and 2,3-dibenzoate **20**. At this point, it was decided to make the diol **17** by the cleavage of both the isopropylidene groups to tetrol **18** followed by the selective mono-isopropylidenation of the kinetically more reactive 4,7-diol. Thus, diketal **15** on treatment with TFA afforded tetrol **18** in 96% yield. In order to make diol **17**, tetrol **18** was treated with one equivalent of 2-methoxypropene in presence of camphorsulfonic acid. However, in this case also, diol **16** was obtained as the major isomer (75%). Before attempting protection with different protecting groups, we tried direct benzoylation of tetrol **18** with 2.5 equivalents of benzoyl chloride in presence of a bulky base (2,4,6-collidine) at room temperature. To our delight, both uvacalol I (45%) and uvacalol J (24%) could be obtained in a single step along with mono-benzoate **21** (18%) and dibenzoate **19** (10%). Thus, we could achieve the synthesis of both uvacalol I and uvacalol J in five steps from the common intermediate **6**. The spectral data of both uvacalol I and uvacalol J are in agreement with the reported data.[5a]

Our next target, uvacalol K has the same relative stereochemistry as the intermediate **6** and is the 3,7-di-*O*-benzoyl derivative of 1-*epi*-streptol **7**. To achieve the total synthesis of uvacalol K, first triol **6** was treated with benzoyl chloride in presence of 2,4,6-collidine[20] to get primary monobenzoate **22**[13] regioselectively in 96% yield (Scheme 4). Introduction of the second benzoyl group at 3-OH requires protection of all other secondary hydroxyl groups. Silylation of diol **22** with TESOTf in presence of imidazole led to the formation of fully protected compound **23** in 97% yield. Then, it was envisaged that the benzoyl group at 3- position could be introduced by the deprotection of PMB groups with DDQ and followed by monobenzoylation of diol with benzoyl chloride or through a selective protection of the more reactive allylic 1-OH with a

protecting group (preferably TES protecting group) followed by benzoylation at 3-OH. With this aim, compound **23** was treated with DDQ at 0 °C. To our delight and surprise, alcohol **24** was obtained as the exclusive product (96%) through the selective deprotection of the allylic PMB group. The H-1 proton shows coupling with both OH proton and H-2 proton with *J* values 6.7 Hz and 6.9 Hz respectively which clearly indicates that OH group is connected at C1, *i.e.*, the allylic PMB ether is cleaved selectively. To the best of our knoweldge, such selectivity in PMB deprotection has not been reported. Utilizing the serendipity in our favor, the alcohol **24** was further silylated using TESOTf and imidazole to give tris-silylether **25** in 96% yield. Deprotection of the remaining PMB group by prolonged treatment with DDQ at room temperature provided the alcohol **26** in 85% yield. Benzoylation of the alcohol **26** using benzoyl chloride in presence of triethylamine afforded the cooresponding benzoate, whcih was difficult to purify to homogenity. This impure compound on TFA mediated deprotection of silyl protecting groups gave uvacalol K (**5**) in 85% yield. This constitutes the first total synthesis of uvacalol K and has been achieved in an overall yield of 62% in seven steps from the common intermediate **6**. The reported spectral data of uvacalol K is identical to the reported data[5a] and this confirms its structural identity.



Scheme 4 Total synthesis of uvacalol K

Conclusion

We have achieved the first syntheses of five new carbasugar natural products efficiently from an advanced common intermediate made from *myo*-inositol in six steps. Comparison of the spectral data with the reported data revealed that the reported structure of all these natural products are correct. While the existing methods for the chiral desymmetrization or enzymatic resolution[21] of *myo*-inositol[22] and its orthoester,[23] allow the syntheses of these natural products in any of their enantiomerically pure forms, from *myo*-insitol, the aim of this study is to substantiate the relative stereochemistry of these compounds. We hope these structural validation would be of interests to synthetic organic chemists as it give confidence to design even better synthetic strategies to make any given enantiomer of any of these compounds and analogs for study of their biological properties and structure-activity relationship studies.

Experimental section

General. Chromatograms were visualized under UV light and charring by heating after dipping the plate into ceric ammonium molybdate stain (10 mL con. H_2SO_4 in a solution of ceric sulphate (1 g) and ammonium molybdate (5 g) in 90 mL of distilled water). The ^{1}H NMR, ^{13}C NMR, COSY, DEPT and HMQC spectra were recorded on a 500 MHz NMR spectrometer. Proton chemical shifts were 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 of all new compounds 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. Melting points were determined using melting point apparatus and are uncorrected. Flash column chromatography was performed by using silica gel (200-400 mesh). All dry reactions were carried out with oven dried glassware under nitrogen atmosphere.

(±)-(1R,2S,3S,4R)-5-(hydroxymethyl)-2,3:4,7-di-*O*-isopropylidene-5-cyclohexene-1,2,3,4-tetrol (8). To a solution of pentol **7**[13] (1.0 g, 5.67 mmol) in acetone (20 mL), camphorsulfonic acid (100 mg) and 2-methoxypropene (1.63 mL, 17.01 mmol) were added at room temperature and the reaction mixture was stirred for 1 h at the same temperature. When the reaction was complete (checked by TLC), triethylamine was added to the reaction mixture to quench the camphorsulfonic acid and then concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:1; v/v) to get alcohol **8** (1.32 g, 91%) as a white solid. mp: 116-118 °C. ^{1}H NMR and ^{13}C NMR spectra were identical to the reported data.[14] ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.35 (s, 3H), 1.40 (s, 6H), 1.50 (s, 3H), 3.50 (dd, *J* = 9.8 Hz, 8.2 Hz, 1H), 3.63 (dd, *J* = 9.9 Hz, 8.1 Hz, 1H), 4.10 (d, *J* = 13.7 Hz, 1H), 4.43-4.46 (m, 2H), 4.58 (d, *J* = 8.0 Hz, 1H), 5.37 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.0, 27.0, 28.2, 62.8, 70.6, 70.8, 78.2, 80.7, 99.2, 112.1, 123.5, 138.2.

Crystal data of 8. CCDC 1009667. $C_{13}H_{20}O_5$, M = 256.29, colorless hexagonal blocks, monoclinic, space group P2(1)/n , a = 10.3575(2), b = 10.0578(3), c = 26.8362(7) Å, V = 2773.64(12)

Å^3, Z = 8, T = 296 K, $2\theta_{max}$ = 50.00°, Dcalc (g cm^{-3}) = 1.227, F(000) = 1104.0, μ (mm^{-1}) = 0.094, 4863 reflections collected, 3999 unique reflections (R_{int} = 0.049), multi-scan absorption correction, T_{min} = 0.983,T_{max} = 0.986, the final wR(F_2) was 0.1236 (all data).

(±)-(2R,3S,4R)-1-keto-5-(hydroxymethyl)-2,3:4,7-di-*O*-isopropylidene-5-cyclohexene-2,3,4-triol (9). To a solution of alcohol **8** (210 mg, 0.82 mmol) in dichloromethane (10 mL), Dess-Martin periodinane (415.65 mg, 0.98 mmol) was added at room temperature and the reaction mixture was stirred for 20 minutes at the same temperature. When the TLC showed completion of the reaction (1 h), the reaction mixture was diluted by adding dichloromethane (100 mL) and then the 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, 1:2; v/v) to get ketone **9** (195.85 mg, 94%) as a colorless liquid. ^{1}H NMR and ^{13}C NMR spectra were identical to the reported data.[16]

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.44 (s, 6H), 1,42 (s, 3H), 3.92 (dd, *J* = 11.0 Hz, 8.5 Hz, 1H), 4.09 (d, *J* = 10.7 Hz, 1H), 4.39 (d, *J* = 16.5 Hz, 1H), 4.50 (d, *J* = 16.4 Hz, 1H), 4.73 (dd, *J* = 8.4 Hz, 1.3 Hz, 1H), 5.75 (d, *J* = 1.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.2, 25.6, 26.6, 26.8, 61.7, 71.4, 79.3, 79.7, 100.6, 113.4, 121.5, 157.3, 191.5.

(±)-(1S,2S,3S,4R)-5-(hydroxymethyl)-2,3:4,7-di-*O*-isopropylidene-5-cyclohexene-1,2,3,4-tetrol (10). To a solution of ketone **9** (150 mg, 0.59 mmol) in THF (10 mL), K-selectride (0.71 mL, 1.0 M in THF, 0.71 mmol) was added at -60 °C and the reaction mixture was stirred for 10 minutes at the same temperature. After completion of the reaction (checked by TLC), excess K-selectride was quenched with acetone. Solvents were evaporated off under reduced pressure and the residue was dissolved in dichloromethane (100 mL), and was 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, 1:1; v/v) to get alcohol **10** (145 mg, 96%) as a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (s, 3H, -CH_3), 1.41 (s, 3H, -CH_3), 1.42 (s, 3H, -CH_3), 1.38 (s, 3H, -CH_3), 2.17 (br.s, 1H, OH-1), 3.45 (dd, *J* = 10.0 Hz, 3.7 Hz, 1H, H-2), 3.99 (dd, *J* = 9.7 Hz, 8.4 Hz, 1H, H-3), 4.18 (d, *J* = 14.4 Hz, 1H, H-7A), 4.38 (d, *J* = 14.4 Hz, 1H, H-7B), 4.44-4.47 (m, 2H, H-1 & H-4), 5.56 (d, *J* = 3.9 Hz, 1H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8, 26.7, 27.2, 27.4, 62.5 (C-7), 64.3 (H-1), 71.3 (C-3), 74.0 (C-4), 76.9 (C-2), 99.3, 111.7, 120.1 (C-6), 137.2. Elemental analysis calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.59; H, 7.91.

(±)-(1S,2S,3S,4R)-1-*O*-isobutyryl-5-(hydroxymethyl)-2,3:4,7-di-*O*-isopropylidene-5-cyclohexene-1-2,3,4-tetrol (11). To a solution of alcohol **10** (120 mg, 0.47 mmol) in dichloromethane (10 mL), triethylamine (1 mL), isobutyryl chloride (0.06 mL, 0.56 mmol), and catalytic amount DMAP (10 mg) were added at room temperature and the reaction mixture was stirred for 2 h at the same temperature. When the TLC showed disappearance of the starting material (2 h), dichloromethane (100 mL) was added to the reaction mixture and the organic layer was washed successively with aqueous $NaHCO_3$ 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, 1:3; v/v) to get ester **11** (152.8 mg, 100%) as a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (d, *J* = 7.0 Hz, 3H, -CH(C*H*$_3$)$_2$), 1.14 (d, *J* = 7.0 Hz, 3H, - CH(C*H*$_3$)$_2$), 1.37 (s, 6H, -CH_3), 1.38 (s, 3H, -CH_3), 1.40 (s, 3H, -CH_3), 2.49-2.54 (m, 1H, -C*H*(CH$_3$)$_2$), 3.55 (dd, *J* = 10.0 Hz, 3.7 Hz, 1H, H-2), 3.97 (dd, *J* = 9.9 Hz, 8.4 Hz, 1H, H-3), 4.17 (d, *J* = 14.4 Hz, 1H, H-7A), 4.41 (d, *J* = 14.4 Hz, 1H, H-7B), 4.46 (d, *J* = 8.2 Hz, 1H, H-4), 5.52 (d, *J* = 5.1 Hz, 1H, H-6), 5.55 (dd, *J* = 4.4 Hz, 4.1 Hz, 1H, H-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.8, 19.2, 20.4, 26.6, 27.1, 27.7, 34.1, 62.6 (C-7), 65.2 (C-1), 71.2 (C-4), 74.9 (C-3), 75.2 (C-2), 99.3, 111.9, 117.7 (C-6), 138.4, 176.3. Elemental analysis calcd for $C_{17}H_{26}O_6$: C, 62.56; H, 8.03. Found: C, 62.34; H, 8.31.

(±)-Lincitol A (1). To a solution of ester **11** (110 mg, 0.34 mmol) in DCM (10 mL), TFA (0.01 mL) was added at room temperature and the reaction mixture was stirred for 10 minutes at the same temperature. When the TLC showed disappearance of the starting material (10 min.), solid $NaHCO_3$ was added to the reaction mixture to quench TFA. The mixture was filtered and the filter (solid $NaHCO_3$) was washed with acetone (3×20 mL) and the combined filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography (EtOAc/acetone, 4:1; v/v) to get lincitol A (**1**, 79.7 mg, 96%) as a colorless oil. ^{1}H NMR and ^{13}C NMR were similar to the reported data.[4]

^{1}H NMR (500 MHz, CD_3OD) δ 1.17 (d, *J* = 7.0 Hz, 3H), 1.19 (d, *J* = 7.0 Hz, 3H), 2.57-2.62 (m, 1H), 3.66 (dd, *J* = 10.3 Hz, 4.1 Hz, 1H), 3.82 (dd, *J* = 10.3 Hz, 7.5 Hz, 1H), 4.03 (d, *J* = 7.4 Hz, 1H), 4.21 (s, 2H), 5.40 (dd, *J* = 4.8 Hz, 4.7 Hz, 1H), 5.82 (dd, *J* = 5.4 Hz, 1.4 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 19.3, 19.4, 35.3, 62.8, 70.5, 71.1, 74.0, 74.7, 118.8, 147.3, 178.5.

(±)-(1S,2S,3S,4R)-5-(Hydroxymethyl)-1,2:4,7-di-*O*-isopropylidene-5-cyclohexene-1,2,3,4-tetrol (12). To a solution of alcohol **10** (40 mg, 0.16 mmol) in acetone (5 mL), CSA (15 mg) was added at room temperature and the reaction mixture was stirred for 12 h at the same temperature. After the conversion of the major amount of starting material into product (checked by TLC, 12 h), the reaction mixture was quenched by adding triethylamine and then concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:1; v/v) to get alcohol **12** (36 mg, 90%) as a white solid.

mp: 141-143 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (s, 3H, -CH_3), 1.35 (s, 3H, -CH_3), 1.42 (s, 3H, -CH_3), 1.45 (s, 3H, -CH_3), 2.48 (d, *J* = 2.0 Hz, 1H, OH-3), 3.68 (ddd, *J* = 9.0 Hz, 4.5 Hz, 1.5 Hz, 1H, H-3), 4.05 (dd, *J* = 9.0 Hz, 7.0 Hz, 1H, H-2), 4.17 (d, *J* = 8.5 Hz, 1H, H-4), 4.21 (d, *J* = 15.3 Hz, 1H, H-7A), 4.30 (d, *J* = 14.7 Hz, 1H, H-7B), 4.56 (s, 1H, H-1), 5.51 (d, *J* = 1.7 Hz, 1H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 25.8, 26.7, 28.2, 61.6 (C-7), 70.4 (C-4), 72.2 (C-1), 73.1 (C-3), 77.2 (C-2), 99.7, 110.4, 115.6 (C-6), 137.6. Elemental analysis calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.61; H, 7.92.

(±)-(1S,2S,3S,4R)-3-*O*-Isobutyryl-5-(hydroxymethyl)-1,2:4,7-di-*O*-isopropylidene-5-cyclohexene-1,2,3,4-tetrol (13). To a solution of alcohol **12** (30 mg, 0.12 mmol) in dichloromethane (5

mL), triethylamine (1 mL), isobutyryl chloride (0.03 mL, 0.24 mmol), and catalytic amount DMAP (10 mg) were added at room temperature and the reaction mixture was stirred for 2 h at the same temperature. When the TLC showed disappearance of the starting material (2 h), dichloromethane (50 mL) was added to the reaction mixture and the organic layer was washed successively with aqueous $NaHCO_3$ 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, 1:3; v/v) to get ester **13** (38.2 mg, 100%) as a colorless liquid. Elemental analysis calcd for $C_{17}H_{26}O_6$: C, 62.56; H, 8.03. Found: C, 62.32; H, 8.25.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.11 (d, *J* = 6.0 Hz, 3H, -CH(CH_3)$_2$), 1.12 (d, *J* = 6.1 Hz, -3H, -CH(CH_3)$_2$), 1.27 (s, 3H, -CH_3), 1.30 (s, 3H, -CH_3), 1.33 (s, 3H, -CH_3), 1.46 (s, 3H, -CH_3), 2.51-2.57 (m, 1H, -C*H*(CH_3)$_2$), 4.10 (dd, *J* = 9.6 Hz, 6.0 Hz, 1H, H-2), 4.24 (d, *J* = 8.9 Hz, 1H, H-4), 4.25 (s, 2H, H-7A & 7B), 4.56 (t, *J* = 4.2 Hz, 1H, H-1), 5.13 (t, *J* = 9.3 Hz, 1H, H-3), 5.50 (dd, *J* = 3.5 Hz, 1.7 Hz, 1H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.7, 19.4, 21.9, 26.1, 26.3, 27.9, 34.1, 61.2 (C-7), 68.9 (C-4), 72.5 (C-3), 72.7 (C-1), 75.6 (C-2), 99.9, 110.8, 114.7 (C-6), 139.7, 176.3.

(±)-Lincitol B (2). To a solution of ester **13** (20 mg, 0.06 mmol) in DCM (5 mL), TFA (0.01 mL) was added at 0 ^{o}C and the reaction mixture was stirred for 10 minutes at the same temperature. When the TLC showed disappearance of the starting material (10 min.), the reaction mixture was concentrated under reduced pressure and then purified by flash column chromatography (EtOAc/acetone, 4:1; v/v) to get lincitol B (**2**, 13.6 mg, 90%) as a colorless oil. ^{1}H NMR and ^{13}C NMR were identical to the reported data.[4]

^{1}H NMR (500 MHz, CD_3OD) δ 1.23 (d, *J* = 7.0 Hz, 3H), 1.24 (d, *J* = 7.0 Hz, 3H), 2.64-2.70 (m, 1H), 3.62 (dd, *J* = 10.4 Hz, 4.2 Hz, 1H), 4.18-4.25 (m, 4H), 5.23 (dd, *J* = 10.4 Hz, 7.7 Hz, 1H), 5.88 (dd, *J* = 5.2 Hz, 1.4 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 19.4, 19.5, 35.5, 62.8, 67.9, 71.1, 71.6, 123.1, 144.0, 179.1.

(±)-(1R,2S,3S,4R)-1-*O*-Ethyl-5-(hydroxymethyl)-2,3:4,7-di-*O*-isopropylidene-5-cyclohexene-1,2,3,4-tetrol (15). To a solution of alcohol **8** (200 mg, 0.78 mmol) in DMF (10 mL), NaH (60% dispersion in mineral oil, 37.6 mg, 0.94 mmol) and ethyl iodide (0.075 mL, 0.94 mmol) were added at 0 ^{o}C and the reaction mixture was stirred for 5 minutes at the same temperature. After the completion of the reaction (checked by TLC, 5 min.), excess NaH was quenched with ice cold water. Then ethyl acetate (100 mL) was added to the reaction mixture and 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 (EtOAc/petroleum ether, 2:3; v/v) to get compound **15** (210.8 mg, 95%) as a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.65 (t, *J* = 7.0 Hz, 3H, -CH_2CH_3), 1.35 (s, 3H, -CH_3), 1.39 (s, 6H, -CH_3), 1.49 (s, 3H, -CH_3), 3.58-3.63 (m, 3H, H-2, H-3 & -C$H_A$$H_B$$CH_3$), 3.67-3.73 (m, 1H, -$CH_A$$H_B$$CH_3$), 4.07-4.10 (m, 2H, H-1 & H-7A), 4.43 (dd, *J* = 14.0 Hz, 1.3 Hz, 1H, H-7B), 4.55 (dd, *J* = 8.0 Hz, 1.0 Hz, 1H, H-4), 5.41 (s, 1H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5, 19.9, 27.0, 28.1, 62.8 (C-7), 65.4 (CH_2CH_3), 70.7 (C-4), 77.4 (C-1), 78.3 (C-3), 79.9 (C-2), 99.1, 111.8, 122.0 (C-6), 133.0. Elemental analysis calcd for $C_{15}H_{24}O_5$: C, 63.36; H, 8.51. Found: C, 63.02; H, 8.73.

(±)-(1S,2R,3R,4R)-1-*O*-ethyl-5-(hydroxymethyl)-5-cyclohexene-1,2,3,4-tetrol (18). To a solution of compound **15** (185 mg, 0.65 mmol) in DCM (10 mL), TFA (0.1 mL) was added at room temperature and the reaction mixture was stirred for 10 minutes at the same temperature. When the TLC showed disappearance of the starting material (10 min.), the solvents were evaporated off under reduced pressure and the crude product was purified by flash column chromatography (acetone/EtOAc, 1:9; v/v) to get tetrol **18** (127.6 mg, 96%) as a colorless liquid.

^{1}H NMR (500 MHz, CD_3OD) δ 1.11 (t, *J* = 7.0 Hz, 3H, -CH_2CH_3), 3.34-3.38 (m, 2H, H-2 & H-3), 3.56-3.64 (m, 2H, -CH_2CH_3), 3.76-3.78 (m, 1H, H-1), 3.99-4.04 (m, 3H, H-4 & H-7A & 7B), 5.58 (t, *J* = 1.7 Hz, 1H, H-6); ^{13}C NMR (125 MHz, CD_3OD) δ 15.9 (CH_2CH_3), 62.7 (C-7), 66.3 (CH_2CH_3), 73.4 (C-4), 75.8 (C-2), 77.8 (C-3), 81.2 (C-1), 122.9 (C-6), 141.3 (C-5). Elemental analysis calcd for $C_9H_{16}O_5$: C, 53.93; H, 7.90. Found: C, 53.72; H, 7.98.

Dibenzoate 19 and 20

Path 1: To a solution of **15** (90 mg, 0.32 mmol) in MeOH, H_2SO_4-silica (15 mg) was added at room temperature and the reaction mixture was stirred for 10 minutes at the same temperature. After the completion of the reaction (10 min.), Et_3N was added to the reaction mixture to neutralize the acid. Then the solid catalyst was filtered off and the solvents were evaporated off under reduced pressure and the residue was dissolved in dichloromethane and purified by flash column chromatography (ethyl acetate/petroleum ether, 1:2; v/v) to get an inseparable mixture of 2,3-isopropylidene **16** and 4,7-isopropylidene **17** (61.9 mg, 80%). This mixture was dissolved in pyridine (5 mL) and to this solution, benzoyl chloride (0.12 mL, 1.02 mmol) and DMAP (15 mg) were added at room temperature and the reaction mixture was stirred for 2 hours at the same temperature. Pyridine was evaporated off under reduced pressure and the dibenzoates were separated by column chromatography (ethyl acetate/petroleum ether, 1:4; v/v) to get 4,7 dibenzoate (85.9 mg, 60%, after two steps) and 2,3 dibenzoate (21.5 mg, 15%, after two steps). However these compounds were contaminated with some amounts of respective diols as a result of the cleavage of the isopropylidene ketal. Hence they were characterized as diol **19** and **20** after complete cleavage of isopropylidene group with 10 % TFA in DCM and followed by flash column chromatography (ethyl acetate/petroleum ether, 1:4; v/v).

Path 2: To a solution of tetrol **18** (65 mg, 0.32 mmol) in acetone (10 mL), camphorsulfonic acid (20 mg) and 2-methoxypropene (0.036 mL, 0.38 mmol) were added at room temperature and the reaction mixture was stirred for 1 h at the same temperature. When the reaction was complete (checked by TLC), triethylamine was added to the reaction mixture to quench the camphorsulfonic acid and then concentrated under reduced pressure. The crude product thus obtained was purified by flash column chromatography (EtOAc/petroleum ether, 1:2; v/v) to get an inseparable mixture of 2,3-isopropylidene **16** and 4,7-isopropylidene **17** (75.4 mg, 91%). These mixture of isomers were seperated and characterized as diol **19** and **20** by following the above procedure (path 1).

(±)-(1R,2R,3R,4R)-1-*O*-(Ethyl)-4-*O*-(benzoyl)-5-

(benzoyloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (19). After three steps, yield 60 % (78.3 mg, path 1); 64% (84.0 mg, path 2). Colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.19 (t, *J* = 6.9 Hz, 3H, CH_2CH_3), 3.67-3.71 (m, 2H, CH_2CH_3), 3.77 (dd, *J* = 9.6 Hz, 8.4 Hz, 1H, H-2), 3.87 (dd, *J* = 9.9 Hz, 7.8 Hz, 1H, H-3), 3.96 (d, *J* = 6.9 Hz, 1H, H-1), 4.78 (s, 2H, H-7A & 7B), 5.84 (d, *J* = 6.9 Hz, 1H, H-4), 5.98 (s, 1H, H-6), 7.30-7.35 (m, 4H, Ar-H), 7.45-7.51 (m, 2H, Ar-H), 7.87 (d, *J* = 7.4 Hz, 2H, Ar-H), 7.96 (d, *J* = 7.4 Hz, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6 (CH_2CH_3), 63.9 (C-7), 65.7 (CH_2CH_3), 74.5 (C-3), 74.8 (C-4), 75.0 (C-2), 78.4 (C-1), 128.4, 128.5, 129.4 (C-6), 129.6, 129.7, 129.9, 131.6, 133.1, 133.6, 166.0, 167.1. Elemental analysis calcd for $C_{23}H_{24}O_7$: C, 66.98; H, 5.87. Found: C, 66.67; H, 5.93.

(±)-(1S,2S,3R,4R)-1-*O*-(Ethyl)-2,3-di-*O*-(benzoyl)-5-(hydroxymethyl)-5-cyclohexene-1,2,3,4-tetrol (20). After three steps, yield 15 % (19.6 mg, path 1); 20% (26.25 mg, path 2). Colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (t, *J* = 6.0 Hz, 3H, CH_2CH_3), 3.48-3.62 (m, 2H, CH_2CH_3), 4.23 (m, 2H, H-7A & 7B), 4.31 (d, *J* = 6.8 Hz, 1H, H-1), 4.66 (d, *J* = 7.0 Hz, 1H, H-4), 5.34 (dd, *J* = 10.5 Hz, 7.8 Hz, 1H, H-3), 5.59 (dd, *J* = 10.2 Hz, 8.6 Hz, 1H, H-2), 5.77 (s, 1H, H-6), 7.23-7.88 (m, 10H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5 (CH_2CH_3), 63.0 (C-7), 64.5 (CH_2CH_3), 71.5 (C-4), 71.7 (C-2), 75.9 (C-1), 76.0 (C-3), 123.7 (C-6), 127.3, 127.4, 127.9, 128.6, 128.9, 132.1, 132.5, 137.6, 164.9, 166.6. Elemental analysis calcd for $C_{23}H_{24}O_7$: C, 66.98; H, 5.87. Found: C, 66.62; H, 5.91.

(±)-Uvacalol I (3) & (±)-Uvacalol J (4). To a solution of tetrol **18** (110 mg, 0.54 mmol) in dichloromethane (10 mL), collidine (1 mL) and benzoyl chloride (0.16 mL, 1.35 mmol) were added at 0 ^{o}C and the reaction mixture was stirred at the same temperature. After the disappearance of the starting material and the formation of new products (checked by the TLC, after 24 h), ethyl acetate (100 mL) was added to the reaction mixture and the organic layer was washed with dil. HCl, water and brine, separated, 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 monobenzoate **21** (R_f : 0.02, 29.9 mg, 18%, colorless liquid), uvacalol I (**3**, R_f : 0.3, 100 mg, 45%, white solid), uvacalol J (**4**, R_f : 0.21, 53.3 mg, 24%, white solid), and dibenzoate **19** (R_f : 0.15, 22.2 mg, 10%, white solid). ^{1}H NMR and ^{13}C NMR data of uvacalol I and uvacalol J were identical with the reported data.[5a]

(±)-Uvacalol I (3): mp: 137-139 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (t, *J* = 7.0 Hz, 3H), 3.58-3.65 (m, 2H), 3.87 (dd, *J* = 10.0 Hz, 8.0 Hz, 1H), 3.97 (d, *J* = 7.0 Hz, 1H), 4.43 (d, *J* = 7.0 Hz, 1H), 4.73 (d, *J* = 13.0 Hz, 1H), 5.01 (d, *J* = 13.0 Hz, 1H), 5.20 (d, *J* = 10 Hz, 7.5 Hz, 1H), 5.81 (s, 1H), 7.32-7.98 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6, 64.3, 65.8, 70.5, 72.7, 78.1, 79.1, 126.3, 128.4, 128.5, 129.6, 129.8, 130.0, 133.3, 133.4, 134.9, 166.6, 167.5.

(±)-Uvacalol J (4): mp: 127-129 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.06 (t, *J* = 7.0 Hz, 3H), 3.49-3.55 (m, 1H), 3.57-3.63 (m, 1H), 3.83 (dd, *J* = 10.1 Hz, 7.8 Hz, 1H), 4.22 (d, *J* = 7.3 Hz, 1H), 4.33 (d, *J* = 6.9 Hz, 1H), 4.74 (d, *J* = 13.0 Hz, 1H), 5.10 (d, *J* = 12.9 Hz, 1H), 5.32 (dd, *J* = 10.4 Hz, 7.8 Hz, 1H), 5.83 (s, 1H), 7.39-8.01 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6, 64.1, 65.5, 72.2, 74.7, 75.1, 126.4, 128.5, 129.7, 129.8, 129.9, 130.2, 133.36, 130.4, 135.4, 166.75, 166.8.

(±)-(1R,2R,3R,4S)-1-*O*-(Ethyl)-5-(benzoyloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (21). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.17 (t, *J* = 6.7 Hz, 3H, $-CH_2CH_3$), 3.58-3.67 (m, 4H, H-2, H-3, $-CH_2CH_3$), 3.87 (br.s, 1H, H-1), 4.19 (br.s, 1H, H-4), 4.64 (d, *J* = 12.6 Hz, 1H, H-7A), 5.08 (d, *J* = 12.7 Hz, 1H, H-7B), 5.78 (s, 1H, H-6), 7.36-7.39 (dd, *J* = 7.6 Hz, 7.4 Hz, 2H, Ar-H), 7.50 (d, *J* = 7.3 Hz, 1H, Ar-H), 7.96-8.02 (m, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5 (CH_2CH_3), 64.4 (C-7), 65.5 (CH_2CH_3), 71.7 (C-4), 73.9 (C-2 or C-3), 75.5 (C-2 or C-3), 79.2 (C-1), 126.6 (C-6), 128.5, 129.7, 129.8, 130.2, 133.3, 133.6, 135.0, 166.9. Elemental analysis calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.21; H, 6.73.

(±)-(1S,2R,3R,4S)-1,3-Di-*O*-(*p*-methoybenzyl)-2,4-di-*O*-triethylsilyl-5-(benzoyloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (23). To a solution of benzoate **22**[13] (800 mg, 1.54 mmol) in dichloromethane (20 mL), imidazole (314.5 mg, 4.62 mmol) and triethylsilyl trifluoromethanesulfonate (TESOTf) (1.04 mL, 4.62 mmol) were added at room temperature and the reaction mixture was stirred for 30 minutes at the same temperature. When the TLC showed disappearance of the starting material, dichloromethane (150 mL) was added to the reaction mixture and the organic layer was washed successively 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 compound **23** (1.12 g, 97%) as a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.46-0.54 (m, 12H, $-CH_2CH_3$), 0.77-0.84 (m, 18H, $-CH_2CH_3$), 3.36 (dd, *J* = 9.8 Hz, 7.5 Hz, 1H, H-3), 3.71 (s, 3H, $-OCH_3$), 3.74 (s, 3H, $-OCH_3$), 3.78 (dd, *J* = 9.8 Hz, 7.7 Hz, 1H, H-2), 3.91-3.94 (m, 1H, H-1), 4.34 (dd, *J* = 6.9 Hz, 0.7 Hz, 1H, H-4), 4.47 (q, *J* = 14.3 Hz, 2H, $-OCH_AH_B$-p-MeOPh), 4.51 (d, *J* = 11.7 Hz, 1H, $-OCH_A$-p-MeOPh), 4.74 (s, 2H, H-7A & 7B), 5.02 (d, *J* = 11.7 Hz, 1H, $-OCH_B$-p-MeOPh), 5.68 (s, 1H, H-6), 6.74-6.80 (m, 4H, Ar-H), 7.15-7.20 (m, 4H, Ar-H), 7.36-7.39 (m, 2H, Ar-H), 7.48-7.52 (m, 1H, Ar-H), 7.95-7.97 (m, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.0, 5.1, 6.9, 7.0, 55.2, 64.5 (C-7), 71.6, 72.8 (C-4), 74.3, 76.4 (C-2), 80.5 (C-1), 85.0 (C-3), 113.3, 113.7, 124.6 (C-6), 127.5, 128.4, 129.4, 129.6, 130.1, 130.4, 131.5, 133.0, 135.7, 158.4, 159.1, 166.1. Elemental analysis calcd for $C_{42}H_{60}O_8Si_2$: C, 67.34; H, 8.07. Found: C, 67.22; H, 8.24.

(±)-(1S,2R,3R,4S)-3-*O*-(*p*-Methoybenzyl)-2,4-di-*O*-triethylsilyl-5-(benzoyloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (24). To a solution of compound **23** (680 mg, 0.91 mmol) in dichloromethane (20 mL), water (5 mL), buffer tablet (pH = 7), and DDQ (308.72 mg, 1.36 mmol) were added at 0 ^{o}C and the reaction mixture was stirred for 1 h at the same temperature. When the TLC showed disappearance of the starting material, dichloromethane (200 mL) was added to the reaction mixture and the organic layer was washed successively 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 compound **24** (548.1 mg, 96%) as a colorless liquid.

^{1}H NMR (500 MHz, DMSO-d_6) δ 0.51-0.57 (m, 6H, $-CH_2CH_3$), 0.61-0.66 (m, 6H, $-CH_2CH_3$), 0.84-0.87 (m, 9H, $-CH_2CH_3$), 0.92-0.95 (m, 9H, $-CH_2CH_3$), 3.34 (m, 1H, H-3), 3.68 (dd, *J* = 10.0 Hz, 8.0 Hz, 1H, H-2), 4.05 (dd, *J* = 6.9 Hz, 6.7 Hz, 1H, H-1), 4.43 (d,

J =7.5 Hz, 1H, H-4), 4.55 (d, *J* = 11.5 Hz, 1H, -OC*H*$_A$-p-MeOPh), 4.79 (d, *J* = 13.0 Hz, 1H, H-7A), 4.84 (d, *J* = 13.0 Hz, 1H, H-7B), 5.13 (d, *J* = 11.5 Hz, 1H, -OC*H*$_B$-p-MeOPh), 5.20 (d, *J* = 6.5 Hz, 1H, OH-1), 5.74 (s, 1H, H-6), 6.95 (d, *J* = 9.0 Hz, 2H, Ar-H), 7.30 (d, *J* = 8.5 Hz, 2H, Ar-H), 6.94-8.06 (m, 5H, Ar-H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 4.5, 4.6, 6.76, 6.8, 55.0, 64.2 (C-7), 71.4 (C-1), 72.3 (C-4), 73.3, 78.2 (C-2), 84.2 (C-3), 113.3, 127.2, 128.8, 129.1, 129.5, 129.7 (C-6), 131.0, 133.0, 133.5, 158.1, 165.4. Elemental analysis calcd for $C_{34}H_{52}O_7Si_2$: C, 64.93; H, 8.33. Found: C, 64.79; H, 8.57.

(±)-(1S,2R,3R,4S)-3-*O*-(*p*-Methoybenzyl)-1,2,4-tris-*O*-triethylsilyl-5-(benzoyloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (25). To a solution of alcohol **24** (520 mg, 0.83 mmol) in dichloromethane (20 mL), imidazole (226.02 mg, 3.32 mmol) and triethylsilyl trifluoromethanesulfonate (0.28 mL, 1.25 mmol) were added at room temperaure and the reaction mixture was stirred for 10 minutes at the same temperature. When the TLC showed disappearance of the starting material, dichloromethane (100 mL) was added to the reaction mixture and the organic layer was washed successively 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, 1:19; v/v) to get compound **25** (589.8 mg, 96%) as a colorless liquid.

^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.48-0.59 (m, 18H, -CH_2CH$_3$), 0.79-0.89 (m, 27H, -CH$_2$CH_3), 3.30 (dd, *J* = 9.7 Hz, 7.6 Hz, 1H, H-3), 3.64 (dd, *J* = 9.7 Hz, 7.5 Hz, 1H, H-2), 3.74 (s, 3H, -OCH$_3$), 4.19-4.21 (m, 1H, H-1), 4.35 (d, *J* = 7.4 Hz, 1H, H-4), 4.52 (d, *J* = 11.7 Hz, 1H, -OC*H*$_A$-p-MeOPh), 4.76 (q, *J* = 15.5 Hz, 2H, H-7A & 7B), 4.97 (d, *J* = 11.7 Hz, 1H, -OC*H*$_B$-p-MeOPh), 5.61 (s, 1H, H-6), 6.78 (d, *J* = 8.7 Hz, 2H, Ar-H), 7.20 (d, *J* = 7.0 Hz, 2H, Ar-H), 7.37 (t, *J* = 7.5 Hz, 2H, Ar-H), 7.49 (t, *J* = 7.5 Hz, 1H, Ar-H), 8.00 (dd, *J* = 7.2 Hz, 1.2 Hz, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.1, 5.2, 6.9, 7.0, 7.1, 55.2, 64.3 (C-7), 73.0 (C-4), 74.0 (C-1), 74.4, 77.9 (C-2), 85.1 (C-3), 113.3, 127.4 (C-6), 127.6, 128.3, 129.6, 130.1, 131.4, 133.0, 134.6, 158.4, 166.1. Elemental analysis calcd for $C_{40}H_{66}O_7Si_3$: C, 64.64; H, 8.95. Found: C, 64.30; H, 9.01.

(±)-(1R,2R,3R,4S)-1,2,4-Tris-*O*-triethylsilyl-5-(benzoyloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (26). To a solution of compound **25** (510 mg, 0.69 mmol) in dichloromethane (20 mL), water (5 mL), buffer tablet (pH = 7), and DDQ (469.9 mg, 2.07 mmol) were added at room temperature and the reaction mixture was stirred for 4 h at the same temperature. When the TLC showed disappearance of the starting material, dichloromethane (150 mL) was added to the reaction mixture and the organic layer was washed successively 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 compound **26** (363.42 mg, 85%) as a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.57-0.65 (m, 18H, -CH_2CH$_3$), 0.85-0.94 (m, 27H, -CH$_2$CH_3), 2.34 (s, 1H, OH-3), 3.40-3.47 (m, 2H, H-2 & H-3), 4.13 (d, *J* = 6.6 Hz, 1H, H-1), 4.26 (d, *J* = 6.3 Hz, 1H, H-4), 4.76 (d, *J* = 13.6 Hz, 1H, H-7A), 4.82 (d, *J* = 13.7 Hz, 1H, H-7B), 5.58 (s, 1H, H-6), 7.37 (t, *J* = 7.0 Hz, 2H, Ar-H), 7.50 (t, *J* = 7.4 Hz, 1H, Ar-H), 8.00 (d, *J* = 7.8 Hz, 2H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.1, 5.3, 6.9, 6.95, 7.0, 64.2 (C-7), 73.0 (C-1), 73.1 (C-4), 76.8 (C-2 or C-3), 77.3 (C-2 or C-3), 127.2 (C-6), 128.3, 129.6, 130.1, 133.0, 134.5, 166.1. Elemental analysis calcd for $C_{32}H_{58}O_6Si_3$: C, 61.69; H, 9.38. Found: C, 61.41; H, 9.52.

(±)-Uvacalol K (**5**). To a solution of alcohol **26** (75 mg, 0.12 mmol) in DCM (5 mL), triethylamine (0.5 mL), DMAP (10 mg), and benzoyl chloride (0.027 mL, 0.24 mmol) were added at room temperature and the reaction mixture was stirred for 48 h at the same temperature. After the complete conversion of starting material into product (checked by TLC) solvents were evaporated off and the residue was dissolved in dichloromethane (100 mL) and washed successively with aqueous $NaHCO_3$, and brine. The organic layer was separated, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product thus obtained was chromatograped (EtOAc/petroleum ether, 1:19; v/v) to get a colorless liquid (78.8 mg), which was not pure and could not be characterized. This liquid was dissolved in dichloromethane (10 mL) and to this solution TFA (0.01 mL) was added at room temperature and the reaction mixture was stirred for 10 minutes at the same temperature. When the TLC showed disappearance of the starting material, the reaction mixture was concentrated under reduced pressure and purified by flash column chromatography (EtOAc/petroleum ether, 1:1; v/v) to get uvacalol K (**5**, 39.3 mg, 85% in two steps) as a white solid. ^{1}H NMR and ^{13}C NMR were similar to the reported data.[5a]

mp: 120-122 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$, D_2O exchange) δ 3.79 (dd, *J* = 10.5 Hz, 7.9 Hz, 1H), 4.35 (d, *J* = 7.9 Hz, 1H), 4.48 (d, *J* = 7.6 Hz, 1H), 4.75 (d, *J* = 13.1 Hz, 1H), 5.08 (d, *J* = 13.4 Hz, 1H), 5.18 (dd, *J* = 10.5 Hz, 7.5 Hz, 1H), 5.84 (s, 1H), 7.37-8.03 (m, 10H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 64.1, 70.8, 71.8, 74.5, 78.5, 127.9, 128.5, 128.6, 129.8, 130.0, 133.3, 133.7, 134.7, 166.7, 167.8.

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Notes and references

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