Organic & Biomolecular Chemistry

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/obc

Organic&Biomolecular Chemistry RSCPublishing

ARTICLE

Total syntheses of five uvacalols: Structural validation of uvacalol A, uvacalol B and uvacalol C and disproval of the structures of uvacalol E and uvacalol G

Cite this: DOI: 10.1039/xoxxoooooox

Received ooth January 2012,
Accepted ooth January 2012

DOI: 10.1039/xoxxoooooox

www.rsc.org/

Adiyala Vidyasagar and Kana M. Sureshan*

Uvacalols are novel carbasugars belonging to the family of C7-cyclitols, and are isolated from the roots of the medicinal plant, *Uvaria calamistrata*. In this study, we report the first syntheses of five uvacalols starting from a cheap and easily available chiral pool starting material, D-mannitol, in their optically pure form. D-Mannitol was converted to the alkene **2** through a series of regioselective and chemoselective transformations by following our previously reported strategies. Alkene **2** was converted to the enal **5** through a series of protective group manipulations. Enal **5** was converted to the diene **6** by the addition of vinylmagnesium bromide. Ring Closing Metathesis of the diene **6** using Grubbs' second generation catalyst installed the core cyclohexenyl unit. Through several iterative and selective manipulations of various hydroxyl groups, uvacalol A, uvacalol B, uvacalol C, uvacalol E and uvacalol G were synthesized. A comparison of the ^{1}H NMR and ^{13}C NMR data of these synthesized molecules with the reported data, revealed that the reported structures of uvacaols A-C are correct and those of uvacalols E and G are wrong.

Introduction

Carbohydrates play important roles in diverse biological processes; from signaling to energy storage.[1] There is considerable interest in synthesis of carbohydrate mimics not only to understand the structure activity relationship and decipher the mechanism of their biological actions but also to develop inhibitors of various enzymes involved in multitude of signaling pathways.[2] Carbasugars, wherein the endocyclic oxygen of the sugar is replaced by a methylene unit, are one family of carbohydrate-mimics that are stable to carbohydrate-metabolizing enzymes. Many carbasugars are natural products possessing wide range of biological activities such as antibacterial, antifungal, HIV inhibition, enzyme inhibition and anti-cancer properties etc.[3] Many of the natural carbasugars belongs to the C7-cyclitol family with six membered cyclitol core with a methyl or hydroxymethyl substituent. Cyclophellitol,[4] gabosines,[5] pericosines,[6] valienamine,[7] validamine[8] and streptol[9] are some of the bioactive natural products of the C7-cyclitol family (carbasugars). Uvacalols are a family of eleven substituted C7-cyclitols namely uvacalol A-K (Fig. 1) isolated from the ethanolic extract of the roots of *Uvaria calamistrata*.[10, 11]It is noteworthy that the ethanolic extract of this plant's roots showed considerable antitumor activity against some cancer cell lines.[12] Thus uvacalols are attractive natural products for synthesis and biological screening.

The structures of these uvacalols have been assigned based on NMR spectroscopy. Though the high resolution NMR techniques provide plentiful information regarding the structure of a molecule, several NMR-based structural assignments of natural products were proved to be wrong.[13] Particularly cyclohexane and cyclitol based natural products possesses multiple isoenergetic conformations in solutions and they often interconvert quickly leading to a time-averaged signal in NMR spectra. So the NMR-based structure assignments for this family of natural products are prone to be wrong.[14] Yet another complexity arises from the fact that the polyoxygenated cyclohexene natural products often occur in both enantiomeric series in same or different organisms.[15] For instance, the basic skeleton in uvacalols A-E is one enantiomer while the basic skeleton in uvacalols F-H is the opposite enantiomer. Thus, it is important to validate the structure and absolute configurations of these newly isolated natural products through chemical synthesis.

We have recently synthesized three of these molecules namely uvacalol I, J and K in racemic form and validated their

structures.[16] Pursuing our interest in cyclitols and cyclitol-based natural products, we were interested to synthesize these molecules in their enantiomerically pure form. D-mannitol is a cheap chiral pool starting material, which has been used for syntheses of many natural products.[17] We have recently reported the synthesis of (-)-gabosine J using D-mannitol as a chiral pool starting material.[17c] Herein, we report the first total syntheses of five more uvacalols namely uvacalol A, B, C, E and G from D-mannitol. Our syntheses revealed that the assigned structures of uvacalol A, B and C are correct, but those of uvacalol E and G are incorrect.

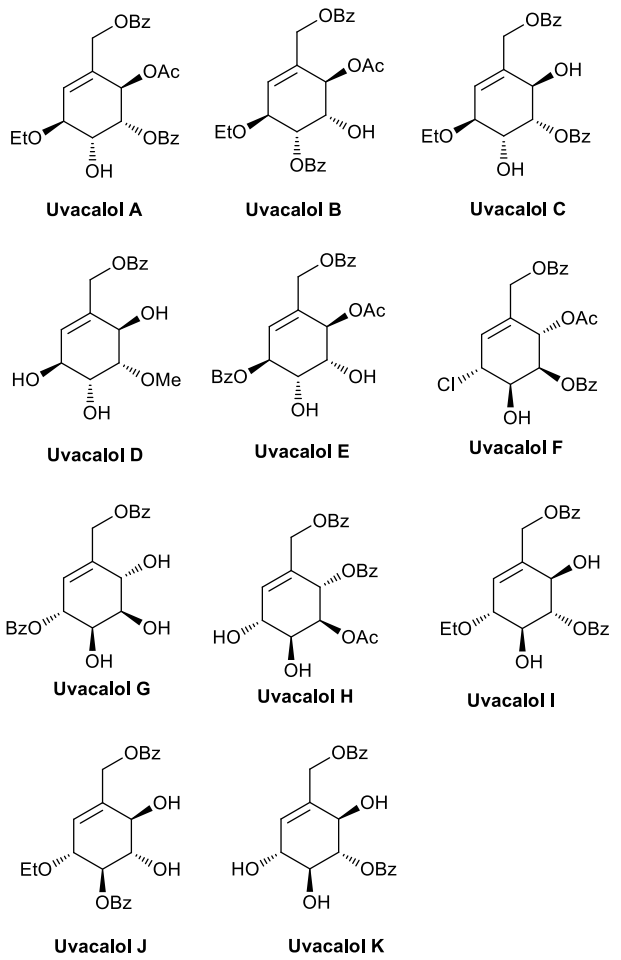
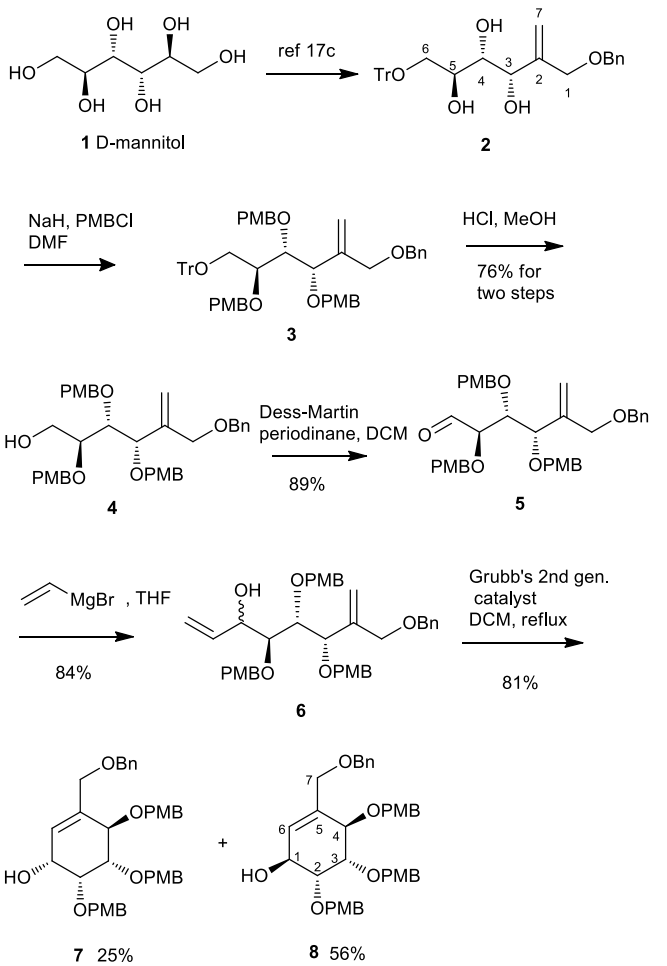


Fig. 1 Uvacalol family of natural products.

Results and Discussion

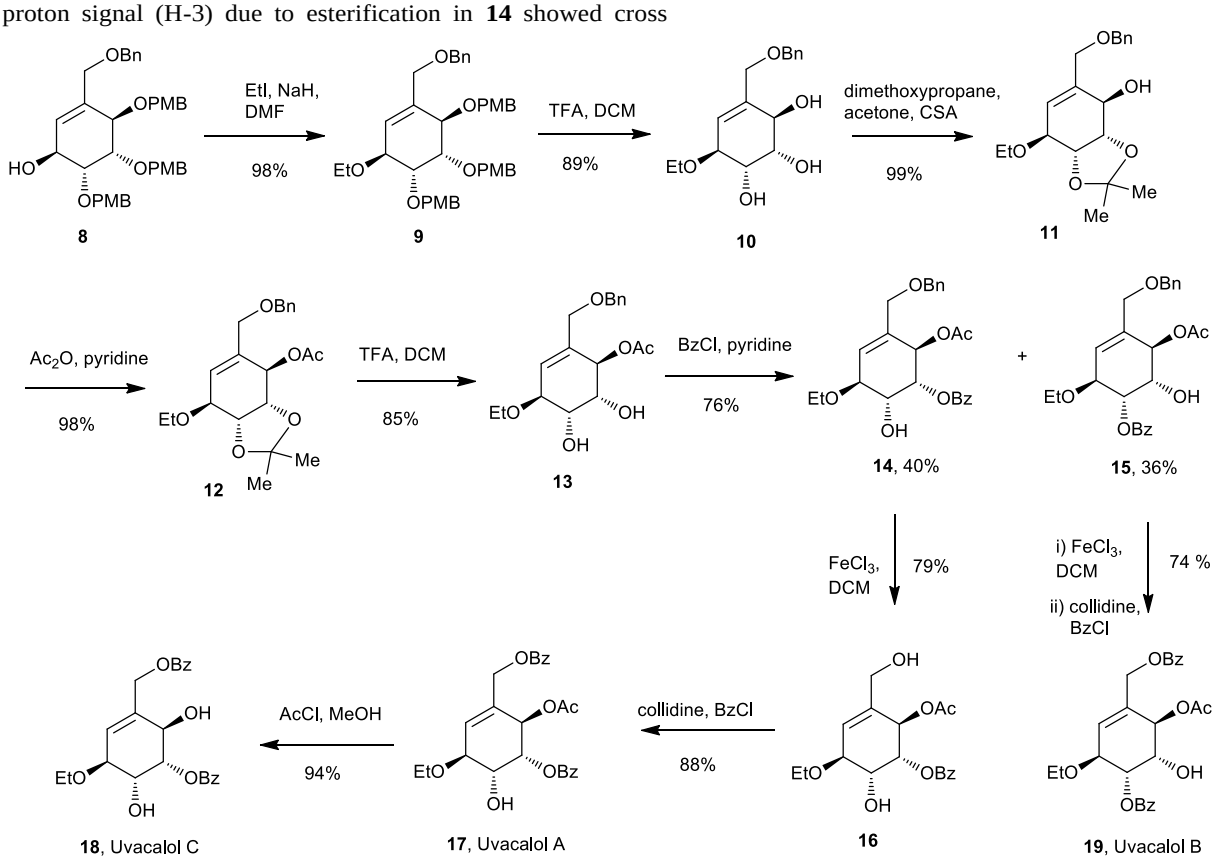
The triol **2** was synthesized in seven steps from D-mannitol by adopting the method we have reported recently.[17c] The triol **2** on exhaustive *para*-methoxybenzylation using *para*-methoxybenzyl chloride and NaH in DMF gave fully protected alkene **3**. Purification of **3** was marred by the cleavage of trityl group during chromatographic separation on silica gel column. Hence crude alkene **3** was used for the next step without purification. The cleavage of trityl group was achieved by using dil.HCl in methanol to furnish the primary alcohol **4** in good yield. The alcohol **4** on Dess-Martin periodinane oxidation[18] gave aldehyde **5** in 89% yield. The aldehyde **5** on treatment with vinyl magnesium bromide in dry THF gave diene **6** (70:30) as an inseparable mixture of two diastereomers. The mixture on ring closing metathesis reaction using Grubbs' 2nd generation catalyst[19] in DCM gave cyclohexenes **7** and **8** in the 3:7 ratio, which could be chromatographically separated at this stage. The formation of cyclic products was confirmed by the presence of alkenyl proton signals in their ^{1}HNMR spectra at 5.81 ppm and 5.71 ppm for **7** and **8** in respectively. The newly formed stereocenters in **7** and **8** were assigned by a comparison of $^3J_{H1H2}$ coupling constants. In compound **8,** the proton H-2 appeared as a doublet of doublet signal with coupling constants of 7.9 Hz and 2 Hz. The larger coupling constant (7.9 Hz) suggests the *anti*-relation of H-2 with the proton (H-1) at the newly formed center. On the other hand, in compound **7**, the H-1 proton showed a singlet signal, which suggests a *syn*-relation with the adjacent proton H-2.



Scheme 1 Synthesis of cyclic intermediate **8**.

The major compound **8** on ethylation using ethyl iodide and NaH in DMF gave the ethyl ether **9** quantitatively. The three PMB groups in alkene **9** were cleaved by using TFA in DCM to give

the triol **10**. The triol **10** on treatment with 2,2-dimethoxypropane in the presence of catalytic amount of camphorsulfonic acid gave regiospecifically the *cis* ketal **11** as the sole product in excellent yield. The formation of *cis*-ketal was confirmed by the coupling of –OH signal (3.22 ppm) with H-4 proton (4.05 ppm). Acetylation of compound **11** using acetic anhydride and pyridine gave the acetate **12**. The cleavage of isopropylidene group using trifluoroacetic acid in DCM gave the diol **13**. The benzoylation of the diol **13** using 1.2 eq. of benzoyl chloride, in presence of pyridine and catalytic amount of DMAP gave two chromatographically separable diesters **14** (40%) and **15** (36%) in ≈ 1:1 ratio. Despite having one equatorial and one axial hydroxyl group (*cis* diol) in compound **13**, both have shown similar reactivity towards esterification. The cyclohexene ring can undergo ring puckering to give either C-2 pseudoequatorial or C-3 pseudoequatorial conformers. These two conformers are likely to undergo rapid interconversion. This could be the reason for the formation of esters **14** and **15** in almost equal amounts (Fig. 2). The structures of these two positional isomers were confirmed by COSY spectra of **14** and **15**. The downfield shifted proton signal (H-3) due to esterification in **14** showed cross coupling with H-4 in COSY spectra, whereas in **15** the downfield shifted proton (H-2) showed a cross coupling with H-1. The compound **14** on treatment with $FeCl_3$ in dry DCM afforded the diol **16**. Prolonged reaction time or storage of the ester **16** at rt lead to the migration of acetate group to primary hydroxyl group. The compound **16** was directly used for next reaction without further purification. The benzoylation of compound **16** using BzCl, in presence of 2,4,6-collidine in DCM gave uvacalol A (**17**) as the sole product presumably due to the increased reactivity of primary and allylic hydroxyl group over the secondary hydroxyl. The formation of primary ester was confirmed by the downfield shift of methylene proton signals (H-7_A&H-7_B) to 4.83 ppm. The chemoselective methanolysis of the acetate group in compound **17** using acetyl chloride in methanol[20] gave uvacalol C (**18**) in very good yield. Uvacalol B (**19**) was synthesized by cleavage of benzyl group in **15** using $FeCl_3$, followed by regioselective benzoylation of primary hydroxyl group. The structures of these three natural products were confirmed by the 1D and 2D NMR spectra.



Scheme 2 Synthesis of uvacalol A, uvacalol B and uvacalol C.

To synthesize uvacalol E and *ent*-uvacalol G, we started from the major isomer **8**. The benzoylation of allylic alcohol **8** using benzoyl chloride in the presence of pyridine gave benzoate ester **20**. Acid mediated hydrolysis of *para*-methoxybenzyl groups in **20** using TFA in DCM afforded the triol **21** in good yield. Regioselective ketalization of the triol **21** using 2,2-dimethoxypropane, camphorsulfonic acid in acetone afforded the ketal **22** as the exclusive product as expected. Both kinetic and thermodynamic factors could contribute to this regiospecificity; the *cis*-diol is more nucleophilic due to the intramolecular hydrogen bonding (kinetic) and the *cis*-ketal is thermodynamically more stable (less strained) than *trans*-ketal

(more strained). Acetylation of the remaining hydroxyl group in **22** using acetic anhydride and pyridine gave the ester **23**. Deprotections of both isopropylidene and benzyl groups were achieved by the treatment with $FeCl_3$. It is noteworthy that the acetyl group migration was observed up on prolonged reaction time. The increased reactivity of primary alcohol (aliphatic) could be the reason for this transesterification. Regioselective benzoylation of the primary hydroxyl group using BzCl in presence of 2,4,6-collidine gave **24**. The structure of **24** was confirmed from the downfield shift of methylene proton signals, due to benzoylation of primary hydroxyl group, and also by COSY spectra. However a comparison of the NMR spectra of **24** with that of reported data of uvacalol E revealed that the assigned structure of uvacalol E is wrong.

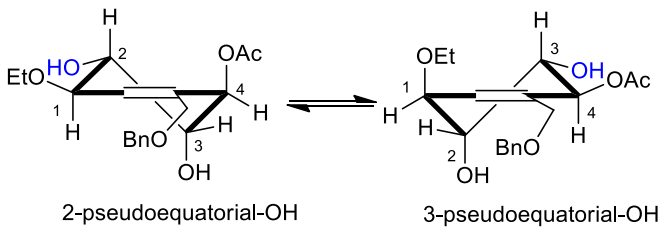


Fig. 2 Conformations of compound **13**.

DCM afforded the tetrol **25**. The tetrol **25** upon regioselective benzoylation using BzCl in presence of 2,4,6-collidine in DCM gave **26**. Alternatively, **26** can also be synthesized from **24** by the chemoselective alcoholysis of acetate ester by treating with acetyl chloride in methanol. The compound **26** was characterized using various spectral techniques. The structure was also confirmed by single crystal X-ray structure. Figure 3 shows the ORTEP diagram of triol **26**. From a comparison of the ^1H NMR spectra of triol **26** with that of reported data for uvacalol G, it has been found that the reported structure of uvacalol G is wrong.

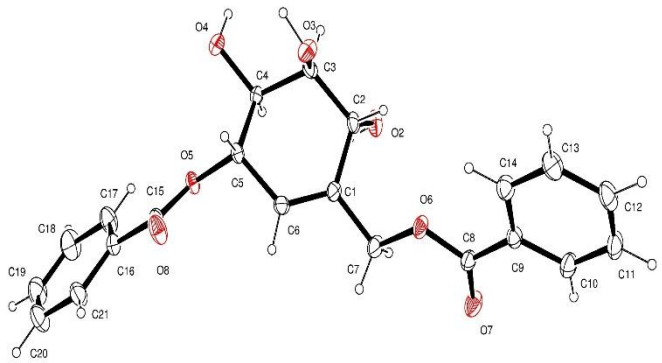
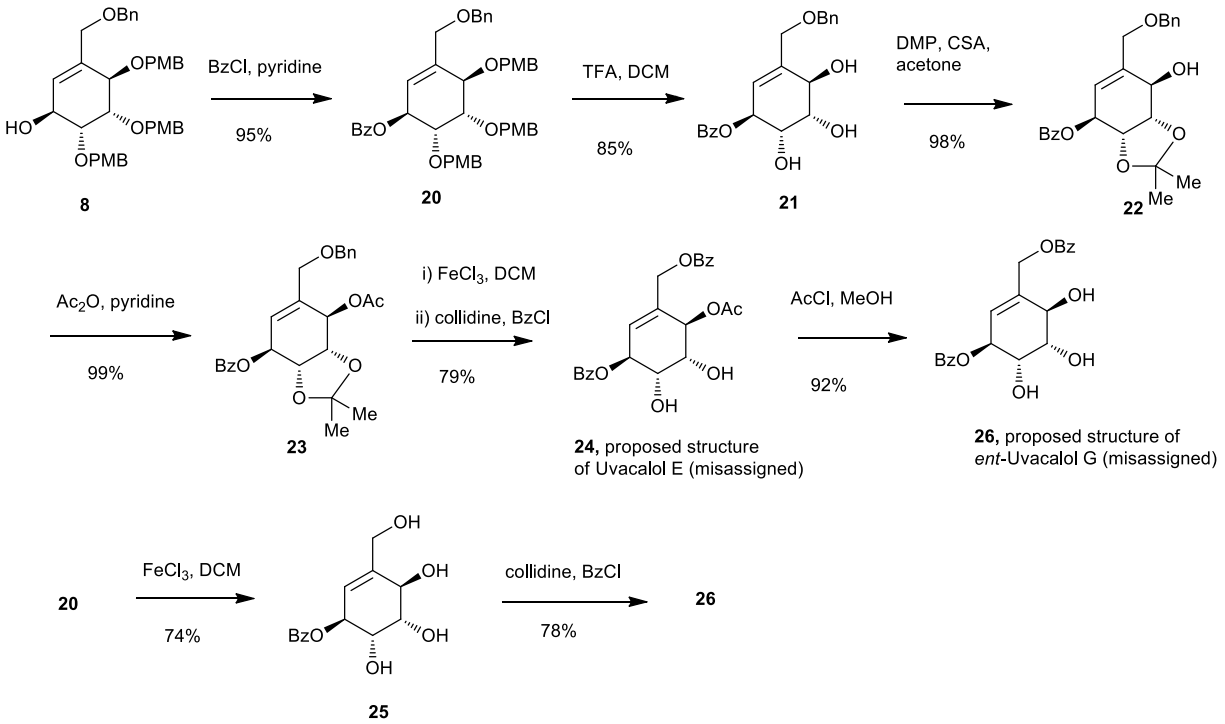


Fig. 3 ORTEP diagram of compound **26** (opposite enantiomer of the proposed structure of uvacalol G). CCDC 1040209

The synthesis of *ent*-uvacalol G started from fully protected derivative **20**. Reaction of benzoyl ester **20** with $FeCl_3$ in dry



Scheme 3. Synthesis of proposed structures of uvacalol E and *ent*-uvacalol G

Conclusion

In conclusion, for the first time, we have synthesized five structurally diverse uvacalols namely uvacalol A, B, C, E and G

from the chiral pool, D-mannitol. As all these cyclitols contain a cyclohexenyl core unit, we have strategically used ring closing metathesis as the key step. While this study validates the structural assignments of three uvacalols namely uvacalol A, uvacalol B and uvacalol C, it disproves the assigned structures of uvacalol E and uvacalol G. Our strategy is amenable to the synthesis of other uvacalols and other cyclitol derived natural products and derivatives for biological exploration.

Experimental section

General

Chemicals and solvents were purchased from commercial suppliers. Thin layer chromatography was carried out using pre-coated silica gel plates. Chromatograms were visualized under UV light and by dipping plates into either phosphomolybdic acid in MeOH or anisaldehyde in ethanol, followed by heating with a hot air gun. The ^{1}H NMR, COSY, DEPT, ^{13}C NMR and HMQC spectra were recorded in a 500 MHz NMR spectrometer. Proton chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.0 ppm) or with the solvent reference relative to TMS employed as the internal standard ($CDCl_3$, δ 7.26 ppm). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m)], coupling constants [Hz] and integration, peak identification). All NMR signals were assigned on the basis of ^{1}H NMR, ^{13}C NMR, COSY, DEPT and HMQC experiments. ^{13}C NMR spectra were recorded with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard. All NMR data were collected at 25 °C. Flash column chromatography was performed using silica gel (200-400 mesh).

(2S,3R,4S)-5-((benzyloxy)methyl)-2,3,4-tris((4-methoxybenzyl)oxy)hex-5-en-1-ol (**4**): To a solution of **2** (8.2 g, 16.11 mmol) in dry DMF at 0 °C, NaH (60% suspension in mineral oil, 2.56 g, 64.44 mmol) and p-methoxy benzyl chloride (10.06 g, 8.7 mL, 64.44 mmol) were added. The reaction mixture was stirred at the same temperature for 1h. When the reaction was complete, the DMF was evaporated under reduced pressure and the residue thus obtained was diluted with ethyl acetate. This solution was washed with water and the organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was dissolved in 1:1 (v/v) mixture of MeOH: $CHCl_3$ (80 mL) and conc. HCl (1 mL) was added at rt. The reaction mixture was stirred at rt for 3h. After the completion of the reaction, the reaction was quenched by the addition of triethylamine. The solvents were evaporated under reduced pressure and the crude material thus obtained was purified by column chromatography (ethyl acetate/petroleum ether, 1:5.6) to yield **4** (7.6 g, 76% for two steps) as a colorless oil. $[\alpha]_D^{25}$ = -10.9° (c 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26-7.20 (m, 5H, Ar-H), 7.14-7.10 (m, 4H, Ar-H), 7.03 (d, *J* = 8.5 Hz, 2H, Ar-H), 6.74-6.72 (m, 6H, Ar-H), 5.38 (s, 1H, H-7_A), 5.31 (s, 1H, H-7_B), 4.52 (q, *J* = 10.9, 13.4 Hz, 2H, -CH_2Ph), 4.48-4.41(m, 3H, -CH_2Ph), 4.22 (d, *J* = 11.0 Hz, 1H, -CHPh), 4.16 (d, *J* =11.4 Hz, 1H, -CHPh), 4.08 (d, *J* = 11.1 Hz, 1H, -CHPh), 4.05 (d, *J* = 4.7 Hz, 1H, H-3), 3.95 (q, *J* = 12.8 Hz, 23.2 Hz, 2H, H-1_A & H-1_B), 3.71 (m, 3H, H-6_A, H-6_B & H-4), 3.70 (s, 3H, -OCH_3), 3.69 (s, 3H, -OCH_3), 3.67 (s, 3H, -OCH_3), 3.51 (dd, *J* = 4.0, 9.5 Hz, 1H, H-5), 2.16 (t, *J* = 6.2 Hz, 1H, -OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.2, 158.19, 158.16, 141.8, 137.2, 129.4, 129.3, 129.2, 128.9, 128.8, 127.3, 126.5, 115.0, 112.8, 112.7, 112.6, 79.3, 79.0, 77.7, 73.8, 71.7, 70.8, 69.5, 69.3, 59.8, 54.23, 54.2; Elemental analysis calcd for $C_{38}H_{44}O_8$; C, 72.59; H, 7.05; found: C, 72.38; H, 7.21.

(2R,3R,4S)-5-((benzyloxy)methyl)-2,3,4-tris((4-methoxybenzyl)oxy)hex-5-enal (**5**): To a solution of **4** (3.2 g, 5.09 mmol) in dry DCM (80 mL) at rt, Dess-Martin periodinane (3.2 g, 7.64 mmol) was added and the mixture was stirred for 2h. After the completion of the reaction, it was quenched by the addition of saturated sodium thiosulphate solution. The mixture was then stirred for another 1h. The organic layer was washed successively with $NaHCO_3$, water and brine. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude material thus obtained was purified by column chromatography (ethyl acetate/petroleum ether, 1:10) to yield **5** (2.84 g, 89%) as a colorless syrup. $[\alpha]_D^{25}$ = -7.8° (c 0.218, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (s, 1H, -CHO), 7.35-7.16 (m, 11H, Ar-H), 6.83 (t, *J* = 81 Hz, 6H, Ar-H), 5.49 (s, 1H, H-7_A), 5.43 (s, 1H, H-7_B), 4.58 (q, *J* = 11.0, 24.1 Hz, 2H, -CH_2Ph), 4.54-4.51 (m, 3H, -CH_2Ph), 4.43 (d, *J* = 11.2 Hz, 1H, -CHPh), 4.28 (d, *J* = 4.9 Hz, 1H, -CHPh), 4.24 (dd, *J* = 5.1, 24.3 Hz, 1H, H-3), 4.01 (s, 2H, H-1_A & H-1_B), 3.98 (d, *J* = 4.0 Hz, 1H, H-5), 3.94 (t, *J* = 5.2 Hz, 1H, H-4), 3.81 (s, 3H, -OCH_3), 3.80 (s, 6H, -OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.7, 159.3, 159.2, 142.3, 138.2, 130.18, 130.14, 129.8, 129.7, 129.6, 129.5, 128.4, 127.6, 117.1, 113.8, 113.7, 113.6, 83.3, 81.2, 80.5, 74.1, 72.7, 72.1, 70.7, 70.3, 55.2; Elemental analysis calcd for $C_{38}H_{42}O_8$; C, 72.82; H, 6.75; found C, 72.72; H, 6.91.

(4S,5R,6S)-7-((benzyloxy)methyl)-4,5,6-tris((4-methoxybenzyl)oxy)octa-1,7-dien-3-ol (**6**): To a solution of **5** (2.8 g, 4.47 mmol) in dry THF at -78 °C, 1 M solution of vinylmagnesium bromide in THF (13.4 mL, 13.41 mmol) was added. When the reaction was complete, the reaction was quenched by the addition of saturated ammonium chloride solution. The THF was evaporated, diluted with ethyl acetate, washed with water and brine. The organic layer was dried over sodium sulphate and concentrated. The crude material thus obtained was purified by column chromatography (ethyl acetate/petroleum ether, 1:9) to yield **6** (2.45 g, 84%) as an yellowish syrup consisting of two diastereomers (7:3).

Ring closing metathesis of 6: To a solution of **6** (mixture of two isomers, 2.3 g, 2.97 mmol) in DCM (400 mL), Grubbs second generation catalyst (126 mg, 0.05 mmol) was added at rt and the mixture was refluxed for 8 h. When the starting material was completely disappeared, the solvent was evaporated under reduced pressure. The residue thus obtained was further purified by column chromatography (ethyl acetate/petroleum ether, 1:3) to yield **7** (0.450 g, 24%, R_f: 0.3) and **8** (1.05 g, 56%, R_f: 0.25).

(1R,4R,5S,6R)-3-((benzyloxy)methyl)-4,5,6-tris((4-methoxybenzyl)oxy)cyclohex-2-enol (**7**): $[\alpha]_D^{25}$ = -42.1° (c 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 -7.03 (m, 11H, Ar-

H), 6.79-6.74 (m, 6H, Ar-H), 5.81 (s, 1H, H-6), 4.60-4.57 (m, 3H, -CH_2Ph), 4.55-439 (m, 3H, -CH_2Ph), 4.33 (d, *J* = 10.7 Hz, 1H, -CHPh), 4.27 (d, *J* = 11.8 Hz, 1H, -CHPh), 4.12 (s, 1H, H-1), 4.09-4.07 (m, 2H, H-4 & H-7_A), 3.82-3.72 (m, 3H, H-2, H-3 & H-7_B), 3.72 (s, 3H, OCH_3), 3.72 (s, 3H, -OCH_3), 3.71 (s, 3H, -OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 159.2, 138.2, 134.9, 130.5, 130.2, 129.9, 129.6, 129.5, 129.4, 128.9, 128.3, 127.6, 127.5, 113.9, 113.83, 113.80, 74.8, 74.6, 73.3, 72.7, 71.6, 71.4, 70.3, 65.6, 55.2; Elemental analysis calcd for $C_{38}H_{42}O_8$; C, 72.82; H, 6.75; found: C, 72.55; H, 6.93.

(1S,4R,5S,6R)-3-((benzyloxy)methyl)-4,5,6-tris((4-methoxybenzyl)oxy)cyclohex-2-enol (8): $[\alpha]_D^{25}$ = +21.4° (c 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26-7.11(m, 9H, Ar-H), 7.03 (d, *J* = 8.5 Hz, 2H, Ar-H), 6.79-6.74 (m, 6H, Ar-H), 5.71 (s, 1H, H-6), 4.49-4.37 (m, 6H, -CH_2Ph & H-1), 4.31-4.24 (m, 3H, -CH_2Ph), 4.03 (d, *J* = 12.3 Hz, 1H, H-7_A), 3.89 (d, *J* = 2.9 Hz, 1H, H-4), 3.79-3.75 (m, 2H, H-3 & H-7_B), 3.72 (s, 3H, -OCH_3), 3.71 (s, 3H, -OCH_3), 3.71(s, 3H, -OCH_3), 3.57 (dd, *J* = 2.0, 7.9 Hz, 1H, H-2), 2.09 (s, 1H, -OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 159.3, 159.2, 138.3, 134.2, 130.6, 130.5, 130.4, 130.3, 129.6, 129.5, 129.4, 129.37, 129.32, 127.7, 127.5, 113.9, 113.8, 113.7, 80.6, 74.2, 73.5, 72.9, 72.0, 71.7, 71.6, 70.5, 68.1, 55.2; Elemental analysis calcd for $C_{38}H_{42}O_8$; C, 72.82; H, 6.75; found: C, 72.67; H, 6.99.

4,4',4''-((((1R,2S,3R,6S)-4-((benzyloxy)methyl)-6-ethoxycyclohex-4-ene-1,2,3-triyl)tris(oxy))tris(methylene))tris(methoxybenzene) (9): To a solution of **8** (1.0 g, 1.59 mmol) in dry DMF at 0 °C, NaH (60% suspension in mineral oil, 0.1 g, 2.39 mmol) and ethyl iodide (0.372 g, 2.39 mmol) were added. The resulting reaction mixture was stirred at the same temperature for 1h. When the reaction was complete, the reaction was quenched by the addition of ice. The DMF was evaporated under reduced pressure, the residue was diluted with ethyl acetate and washed with water. The organic layer was dried over Na_2SO_4, concentrated under reduced pressure and purified by column chromatography to yield **9** (1.02 g, 98%) as a viscous oily liquid. $[\alpha]_D^{25}$ = -2.19° (c 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24-7.18 (m, 7H, Ar-H), 7.14 (d, *J* = 8.6 Hz, 2H, Ar-H), 7.00 (d, *J* = 8.6 Hz, 2H Ar-H), 6.99-6.72 (m, 6H, Ar-H), 5.74 (t, *J* = 1.2 Hz, 1H, H-6), 4.55 (d, *J* = 9.2 Hz, 1H, -CH_2Ph), 4.53 (d, *J* = 9.3 Hz, 1H, -CH_2Ph), 4.47 (d, *J* = 7.7 Hz, 1H, -CH_2Ph), 4.45(d, *J* = 7.9 Hz, 1H, -CH_2Ph), 4.39 (d, *J* = 11.8 Hz, 1H, -CH_2Ph), 4.30 (d, *J* = 11.4 Hz, 1H, -CH_2Ph), 4.26 (d, *J* = 6.9 Hz, 1H, -CH_2Ph), 4.24 (d, *J* = 6.4 Hz, 1H, -CH_2Ph), 4.08 (d, *J* = 6.9 Hz , 1H, H-1), 4.04 (d, *J* = 12.4 Hz, 1H, H-7_A), 3.90 (d, *J* = 3.8 Hz, 1H, H-4), 3.78 (d, *J* = 12.4 Hz, 1H, H-7_B), 3.73-3.70 (m, 2H, H-3 & H-2), 3.73 (s, 3H, -OCH_3), 3.72 (s, 3H, -OCH_3), 3.71 (s, 3H, -OCH_3), 3.57-3.52 (m, 2H, -OCH_2), 1.11 (t, *J* = 6.9 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 159.1, 159.0, 138.4, 131.0, 130.7, 130.6, 129.5, 129.4, 129.3, 128.2, 127.7, 127.4, 113.6, 77.5, 75.7, 74.5, 72.9, 72.2, 72.1, 71.6, 70.6, 65.2, 55.3, 55.2, 15.7; Elemental analysis calcd for $C_{40}H_{46}O_8$; C, 73.37; H, 7.08; O, found: C, 73.09; H, 7.18.

(1S,2S,3R,6S)-4-((benzyloxy)methyl)-6-ethoxycyclohex-4-ene-1,2,3-triol (10): To a solution of **9** (1.3 g, 1.987 mmol) in DCM at rt, TFA (0.8 mL) was added. The reaction mixture was stirred at rt for 2h. When the reaction was complete, the solvents were evaporated under reduced pressure and the crude product thus obtained was purified by column chromatography to yield **10** (0.520 g, 89%) as an oily liquid. $[\alpha]_D^{25}$ = +27.7° (c 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-721 (m, 5H, Ar-H), 5.72 (d, *J* = 2.3 Hz, 1H, H-6), 4.46 (q, *J* = 11.8, 15.6 Hz, 2H, -CH_2Ph), 4.22(d, *J* = 4.9 Hz, 1H, H-4), 4.09 (d, *J* = 11.5 Hz, 1H, H-7_A), 4.02 (d, *J* = 11.5 Hz, 1H, H-7_B), 3.96 (dd, *J* = 2.4, 5.5 Hz, 1H, H-2), 3.92 (dd, *J* = 2.5, 5.0 Hz, 1H, H-3), 3.87 (bs, 1H, H-1), 3.63-3.51 (m, 2H, -OCH_2), 2.39 (bs, 3H, -OH), 1.15 (t, *J* = 6.9 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.5, 136.1, 128.5, 127.95, 127.91, 125.4, 76.4, 73.0, 72.7, 72.4, 70.6, 70.3, 65.1, 15.6; Elemental analysis calcd for $C_{16}H_{22}O_5$; C, 65.29; H, 7.53; found: C, 65.03; H, 7.71.

(3aS,4R,7S,7aR)-5-((benzyloxy)methyl)-7-ethoxy-2,2-dimethyl-3a,4,7,7a-tetrahydrobenzo[d][1,3]dioxol-4-ol (11): To a solution of **10** (0.60 g, 2.04 mmol) in dry acetone, catalytic amount of CSA (10 mg) and 2,2-dimethoxy propane (0.25 g, 2.44 mmol) were added. The resulting reaction mixture was stirred at rt for 1h. When the reaction was complete, the reaction mixture was quenched by the addition of triethylamine. The solvents were evaporated under reduced pressure, the crude product thus obtained was purified by column chromatography to yield **11** (0.675 g, 99%) as an oily liquid. $[\alpha]_D^{25}$ = +16.5° (c 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27-7.22 (m, 5H, Ar-H), 5.95 (d, *J* = 4.3 Hz, 1H, H-6), 4.50 (d, *J* = 11.7 Hz, 1H, -CHPh), 4.44 (d, *J* = 11.7 Hz, 1H, -CHPh), 4.36 (dd, *J* = 3.3, 7.5 Hz, 1H, H-2), 4.33 (dd, *J* = 1.9, 5.5 Hz, 1H, H-3), 4.12 (d, *J* = 13.2 Hz, 1H, H-7_A), 4.06 (d, *J* = 14 Hz, 1H, H-7_B), 4.05 (dd, *J* = 3.8, 8.8 Hz, 1H, H-4), 3.90 (t, *J* = 3.8 Hz, 1H, H-1) 3.57 (q, *J* = 7, 14 Hz, 2H, -OCH_2), 3.22 (d, *J* = 9.0 Hz, 1H, -OH), 1.31 (s, 3H, -CH_3), 1.27 (s, 3H, -CH_3), 1.14 (t, *J* = 7.0 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.1, 137.9, 128.4, 127.8, 127.7, 125.3, 108.8, 78.5, 76.6, 74.5, 72.2, 71.0, 68.5, 65.1, 26.5, 24.3, 15.4; Elemental analysis calcd for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84; found: C, 67.98; H, 8.01.

(3aS,4R,7S,7aR)-5-((benzyloxy)methyl)-7-ethoxy-2,2-dimethyl-3a,4,7,7a-tetrahydrobenzo[d][1,3]dioxol-4-yl acetate (12): To a solution of **11** (0.4 g, 1.19 mmol) in dry pyridine (10 mL) at 0 °C, Ac_2O (0.22 mL, 2.4 mmol) was added and the reaction mixture was stirred at the same temperature for 0.5 h. When the reaction was complete, solvents were evaporated under reduced pressure. The residue thus obtained was dissolved in ethyl acetate, washed with sodium bicarbonate solution, water and brine. The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The crude material thus obtained was purified by column chromatography to yield **12** (0.438 g, 98%) as an oily liquid. $[\alpha]_D^{25}$ = +15.3° (c 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.21 (m, 5H, Ar-H), 5.86 (s, 1H, H-6), 5.42 (dd, *J* = 2.2, 3.6 Hz, 1H, H-4), 4.42 (d, *J* = 11.8 Hz, 1H, -CHPh), 4.37 (d, *J* = 11.8 Hz, 1H, -CHPh), 4.17-4.12 (m, 2H, H-2 & H-3), 3.97 (d, *J* = 13.6 Hz, 1H, H-7_A), 3.92 (t, *J* = 1.8 Hz, 1H, H-1), 3.88-3.84 (m, 1H, H-7_B), 3.67-3.56 (m, 2H, -OCH_2), 2.01 (s, 3H, -$COCH_3$), 1.40 (s, 3H, -CH_3), 1.29 (s, 3H, -CH_3), 1.18 (t, *J* = 6.9 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 170.3, 137.9, 134.5, 128.3, 127.7, 127.6, 127.4, 109.5, 77.7, 76.8, 76.5, 72.3, 71.3, 69.2, 27.1, 25.0, 20.9, 15.4. Elemental analysis calcd for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50; found: C, 66.83; H, 7.06.

(1R,4S,5S,6R)-2-((benzyloxy)methyl)-4-ethoxy-5,6-dihydroxycyclohex-2-en-1-yl acetate (**13**): To a solution of **12** (0.3 g, 0.8 mmol) in DCM (20 mL) at rt, TFA (0.2 mL) was added and the mixture was stirred at rt for 1h. When the reaction was complete, the solvents were evaporated. The crude product thus obtained was purified by column chromatography to yield diol **13** (0.228 g, 85%) as a white sticky solid. $[\alpha]_D^{25}$ = +32.9˚ (c 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27- 7.20 (m, 5H, Ar-H), 5.96 (s, 1H, H-6), 5.35 (d, *J* = 4.2 Hz, 1H, H-4), 4.46 (d, *J* = 11.9 Hz, 1H, -CHPh), 4.36 (d, *J* = 11.9 Hz, 1H, -CHPh), 3.99-3.95 (m, 3H, H-1, H-3 & H-7_A), 3.86-3.82 (m, 2H, H-2 & H-7_B), 3.66-3.62 (m, 1H, -OCH_2), 3.58-3.53 (m, 1H, -OCH_2), 2.74 (bs, 1H, -OH), 2.49 (bs, 1H, -OH), 1.94 (s, 3H, -$COCH_3$), 1.17 (t, *J* = 7.0 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 137.9, 133.1, 128.4, 127.8, 127.7, 127.0, 75.9, 72.3, 71.3, 71.1, 70.8, 70.0, 65.2, 20.9, 15.6; Elemental analysis calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19; found: C, 64.19; H, 7.34.

Benzoylation of compound 13:

To a solution of **13** (0.168 g, 0.5 mmol) in dry DCM at 0 ˚C, N,N-diisopropylethylamine (0.060 g, 0.6 mmol) and benzoyl chloride (0.086 g, 0.6 mmol) and DMAP (0.002 g) were added. The resulting mixture was stirred at rt for 1h. When the reaction was complete, the solvents were evaporated under reduced pressure. The residue thus obtained was diluted with ethyl acetate and washed successively with dil.HCl, sodium bicarbonate, water and brine. The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The crude product thus obtained was purified by column chromatography to yield **14** (0.086 g, 39%) and **15** (0.080 g, 36%) as colorless gums.

(1R,2R,5S,6R)-2-acetoxy-3-((benzyloxy)methyl)-5-ethoxy-6-hydroxycyclohex-3-en-1-yl benzoate (**14**): $[\alpha]_D^{25}$ = -12.5˚ (c 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.4 Hz, 2H, Ar-H), 7.49 (t, *J* = 7.3 Hz, 1H, Ar-H), 7.35 (t, *J* = 7.6 Hz, 2H, Ar-H), 7.27-7.21 (m, 5H, Ar-H), 6.02 (s, 1H, H-6), 5.66 (d, *J* = 4.5 Hz, 1H, H-4), 4.42 (dd, *J* = 2.2, 4.5 Hz, 1H, H-3), 4.46 (d, *J* = 11.8 Hz, 1H, -CHPh), 4.37 (d, *J* = 11.8 Hz, 1H, -CHPh), 4.15 (dd, *J* = 2.1 Hz, 6 Hz, H-2), 4.01 (s, 1H, H-1), 3.97 (d, *J* = 12.9 Hz, 1H, H-7_A), 3.85 (d, *J* = 12.7 Hz, 1H, H-7_B), 3.68-3.59 (m, 2H, -OCH_2), 1.92 (s, 3H, -$COCH_3$), 1.20 (t, *J* = 5.8 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 165.9, 137.8, 133.6, 133.3, 129.8, 129.5, 128.5, 128.4, 127.8, 127.7, 127.2, 76.3, 73.3, 72.4, 69.8, 69.7, 67.9, 65.5, 20.8, 15.6; Elemental analysis calcd for $C_{25}H_{28}O_7$: C, 68.17; H, 6.41; found: C, 68.10; H, 6.55.

(1S,2S,5R,6S)-5-acetoxy-4-((benzyloxy)methyl)-2-ethoxy-6-hydroxycyclohex-3-en-1-yl benzoate (**15**): $[\alpha]_D^{25}$ = -5.8˚ (c 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.4 Hz, 1H, Ar-H), 7.50 (t, *J* = 7.4 Hz, 1H, Ar-H), 7.35 (t, *J* = 7.8 Hz, 2H, Ar-H), 7.29-7.22 (m, 5H, Ar-H), 5.94 (d, *J* = 2.3 Hz, 1H, H-6), 5.59 (d, *J* = 6.1 Hz, 1H, H-4), 5.38 (dd, *J* = 2.3, 4.8 Hz, 1H, H-2), 4.49 (d, *J* = 11.8 Hz, 1H, -CHPh), 4.37 (d, *J* = 11.8 Hz, 1H, -CHPh), 4.20 (bs, 1H, H-3), 4.14 (d, *J* = 4.0 Hz, 1H, H-1), 4.06 (d, *J* = 12.6 Hz, 1H, H-7_A), 3.87 (d, *J* = 12.6 Hz, 1H, H-7_B), 3.73-3.60 (m, 2H, -OCH_2), 2.02 (s, 3H, -$COCH_3$), 1.14 (t, *J* = 7.0 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 166.0, 137.9, 134.7, 133.3, 129.7, 128.5, 128.4, 127.7, 126.5, 73.5, 73.3, 72.3, 71.3, 69.8, 69.6, 65.9, 20.9, 15.6; Elemental analysis calcd for $C_{25}H_{28}O_7$: C, 68.17; H, 6.41; found: C, 68.03; H, 6.62.

(1R,2R,5S,6R)-2-acetoxy-5-ethoxy-6-hydroxy-3-(hydroxymethyl)cyclohex-3-en-1-yl benzoate (**16**): To a solution of **14** (0.070 g, 0.16 mmol) in dry DCM at rt, anhydrous $FeCl_3$ (0.029 g, 0.18 mmol) was added. The resulting mixture was stirred at rt for 30 min. When the reaction was complete, the reaction mixture was diluted with DCM and washed with water. The organic layer was dried over sodium sulphate and concentrated. The crude product thus obtained was purified by column chromatography to yield **16** (0.044 g, 79%) as a sticky gum. ^{1}H NMR (500 MHz, CD_3CN) δ 8.03 (d, *J* = 7.4 Hz, 2H, Ar-H), 7.66 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.53 (t, *J* = 7.2 Hz, 2H, Ar-H), 6.01 (s, 1H, H-6), 5.69 (d, *J* = 5.5 Hz, 1H), 5.34 (d, *J* = 3.8 Hz, 1H), 4.10 (s, 1H), 4.02-3.99 (m, 3H), 3.72-3.65(m, 2H, -OCH_2), 3.53 (d, *J* = 4.6 Hz, 1H), 2.02 (3H, -$COCH_3$), 1.21 (t, *J* = 6.8 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, CD_3CN) δ 170.8, 166.1, 137.7, 133.9, 130.6, 130.1, 129.1, 124.9, 117.9, 76.7, 74.1, 69.4, 68.4, 65.4, 61.9, 20.6, 15.6; Elemental analysis calcd for $C_{18}H_{22}O_7$ C, 61.71; H, 6.33; found C, 61.49; H, 6.51.

(1R,2R,5S,6R)-2-acetoxy-3-((benzoyloxy)methyl)-5-ethoxy-6-hydroxycyclohex-3-en-1-yl benzoate (**17**) (**uvacalol A**): To a solution of **16** (0.025 g, 0.071 mmol) in dry DCM (3 mL) at 0 ˚C, 2,4,6-collidine (0.5 mL) and benzoyl chloride (10 µL, 0.085 mmol) were added. The resulting mixture was warmed to rt. When the reaction was complete, the solvents were evaporated, diluted with ethyl acetate, washed successively with dilute HCl, saturated sodium bicarbonate, water and brine. The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The crude product thus obtained was purified by column chromatography to yield (uvacalol A) **17** (0.028 g, 88%). $[\alpha]_D^{18}$ = -2.27˚ (c 0.2, CH_3OH); (lit. value[10a] $[\alpha]_D^{18}$ = -53.9˚ (c 0.13, CH_3OH)); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (t, *J* = 7.0 Hz, 4H, Ar-H), 7.58-7.53 (m, 2H, Ar-H), 7.43-7.39 (m, 4H, Ar-H), 6.18 (s, 1H, H-6), 5.87 (d, *J* = 5.2 Hz, 1H, H-4), 5.52 (dd, *J* = 2.1, 5.2 Hz, 1H, H-3), 4.83 (s, 2H, H-7_A & H-7_B), 4.28 (dd, *J* = 2.0, 5.8 Hz, 1H, H-2), 4.09 (bs, 1H, H-1), 3.75-3.70 (m, 2H, -OCH_2), 2.03 (s, 3H, -$COCH_3$), 1.27 (t, *J* = 7.0 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 166.0, 165.9, 133.4, 133.1, 132.1, 130.1, 129.8, 129.6, 128.5, 128.47, 128.43, 76.1, 73.3, 69.5, 67.8, 65.8, 64.4, 20.7, 15.6; Elemental analysis calcd for $C_{25}H_{26}O_8$: C, 66.07; H, 5.77; found: C, 65.88; H, 5.91.

((3S,4R,5S,6R)-5-(benzoyloxy)-3-ethoxy-4,6-dihydroxycyclohex-1-en-1-yl)methyl benzoate (**18**) (**uvacalol C**): To a solution of **17** (0.020 g, 0.044 mmol) catalytic amount of AcCl (10 µL) was added and mixture was stirred at rt. When the reaction was complete, the reaction was quenched by the addition of $NaHCO_3$ solution. The mixture was extracted with ethyl acetate and the extract was washed with water. The crude product thus obtained was purified by column chromatography to yield (uvacalol C) **18** (0.0169 g, 94%); $[\alpha]_D^{25}$ = -6.6° (c 0.1,

CH_3OH); (lit. value[10a] $[\alpha]_D^{18}$ = +200˚ (c 1.4, CH_3OH)); ^1H NMR (500 MHz, $CDCl_3$) δ 8.03-8.01 (m, 4H, Ar-H), 7.59-7.55 (m, 2H, Ar-H), 7.46-7.40 (m, 4H, Ar-H), 6.08 (d, *J* = 2.4 Hz, 1H, H-6), 5.49 (dd, *J* = 2.4, 4.7 Hz, 1H, H-3), 5.09 (d, *J* = 13.0 Hz, 1H, H-7_A), 4.88 (d, *J* = 13.0 Hz, 1H, H-7_B), 4.52 (d, *J* = 3.7 Hz, 1H, H-4), 4.30 (dd, *J* = 1.8, 6.0 Hz, 1H, H-2), 4.13 (dd, *J* = 2.5, 6.2 Hz, 1H, H-1), 3.79-3.69 (m, 2H, -OCH_2), 1.28 (t, *J* = 6.7 Hz, 1H, -CH_3), ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 135.1, 133.4, 133.2, 129.8, 129.6, 128.4, 127.0, 76.5, 75.9, 69.0, 67.5, 65.4, 65.0, 15.6; Elemental analysis calcd for $C_{23}H_{24}O_7$: C, 66.98; H, 5.87; found: C, 66.75; H, 6.03.

(1S,2S,5R,6S)-5-acetoxy-4-((benzoyloxy)methyl)-2-ethoxy-6-hydroxycyclohex-3-en-1-yl benzoate (**19**) (**uvacalol B**): To a solution of **15** (0.064 g, 0.145 mmol) in dry DCM (5 mL), anhydrous $FeCl_3$ (0.026 g, 0.16 mmol) was added and the mixture was stirred at rt. When the reaction was complete, the reaction mixture was diluted with DCM and washed with water. The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The crude product was dissolved in dry DCM (2 mL) and to this solution, 2,4,6-collidine (0.5 mL) and BzCl (20 µL, 0.169 mmol) were added at 0 °C. The reaction mixture was allowed to warm to rt. When the reaction was complete, the solvents were evaporated under reduced pressure. The residue thus obtained was diluted with ethyl acetate, washed successively with dil. HCl, sat. $NaHCO_3$ and water. The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The crude product thus obtained was purified by column chromatography to yield (uvacalol B) **19** (0.048 g, 74%) as a sticky mass. $[\alpha]_D^{25}$ = -16.1° (c 0.2, CH_3OH); (lit. value[10a] $[\alpha]_D^{22}$ = -11˚ (c 0.13, CH_3OH)); ^1H NMR (500 MHz, $CDCl_3$) δ 7.99-7.91 (m, 4H, Ar-H), 7.53-7.48 (m, 2H, Ar-H), 7.40-7.31 (m, 4H, Ar-H), 6.04 (d, *J* = 3.0 Hz, 1H, H-6), 5.67 (d, *J* = 6.3 Hz, 1H, H-4), 5.40 (dd, *J* = 2.1, 4.2, Hz, 1H, H-2), 4.84 (d, *J* = 13.1 Hz, 1H, H-7_A), 4.77 (d, *J* = 13.0 Hz, 1H, H-7_B), 4.23 (dd, *J* = 2.2, 6.3 Hz, 1H, H-3), 4.19 (bs, 1H, H-1), 3.75-3.62 (m, 2H, -OCH_2), 2.06 (s, 3H, -$COCH_3$), 1.16 (t, *J* = 7.0 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 166.0, 165.9, 133.4, 133.2, 129.7, 129.6, 129.58, 128.52, 128.4, 128.0, 73,3, 73.2, 71.2, 69.5, 66.1, 64.1, 20.9, 15.5; Elemental analysis calcd for $C_{25}H_{26}O_8$: C, 66.07; H, 5.77; found: C, 65.88.; H, 5.81.

(1S,4R,5S,6R)-3-((benzyloxy)methyl)-4,5,6-tris((4-methoxybenzyl)oxy)cyclohex-2-en-1-yl benzoate (**20**): To a solution of **8** (0.6 g, 0.958 mmol) in dry pyridine (8 mL) at 0 °C, BzCl (0.202 g, 1.437 mmol) was added. The resulting mixture was stirred at same temperature for 1h. When the reaction was complete the solvents were evaporated under reduced pressure. The residue thus obtained was dissolved in ethyl acetate and washed successively with dil. HCl, sat. sodium bicarbonate solution, water and brine. The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The crude product thus obtained was purified by column chromatography to yield **20** (0.664 g, 95%) as an oily liquid. $[\alpha]_D^{25}$ = +29.4 (c 0.3, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.90-7.88 (m, 2H, Ar-H), 7.48-7.11 (m, 14H, Ar-H), 7.06-6.69 (m, 6H, Ar-H), 5.80 (s, 1H, H-1), 5.75 (s, 1H, H-6), 4.59 (d, *J* = 19.6 Hz, 1H, -CHPh), 4.55-4.46 (m, 3H, -CH_2Ph), 4.45-4.43 (m, 2H, -CH_2Ph), 4.34 (d, *J* = 11.0 Hz, 1H, -CHPh), 4.27 (d, *J* = 11.8 Hz, 1H, -CHPh), 4.07 (d, *J* = 12.6 Hz, 1H, H-7_A), 4.02 (d, *J* = 3.2 Hz, 1H, H-4), 3.91 (dd, *J* = 2.0, 7.0 Hz, 1H, H-2), 3.83 (dd, *J* = 2.2, 4.3 Hz, 1H, H-3), 3.79 (d, *J* = 12.6 Hz, 1H, H-7_B), 3.72 (s, 3H, -OCH_3), 3.70 (s, 3H, -OCH_3), 3.69 (s, 3H, -OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.03, 159.4, 159.2, 159.1, 138.2, 132.9, 130.5, 130.4, 130.3, 130.2, 129.7, 129.5, 128.3, 128.2, 127.7, 127.5, 113.8, 113.7, 75.9, 75.1, 74.6, 73.5, 72.2, 71.7, 71.1, 70.2, 55.3, 55.27, 55.23; Elemental analysis calcd for $C_{45}H_{46}O_9$: C, 73.95; H, 6.34; found: C, 73.88; H, 6.48.

(1S,4R,5S,6S)-3-((benzyloxy)methyl)-4,5,6-trihydroxycyclohex-2-en-1-yl benzoate (**21**): To a solution of **20** (0.630 g, 0.863 mmol) in DCM at rt, TFA (0.4 mL) was added. The resulting mixture was stirred at rt for 1h. When the reaction was complete, the solvents were evaporated under reduced pressure, the crude product thus obtained was purified by column chromatography to yield triol **21** (0.271 g, 85%) as an oily liquid. $[\alpha]_D^{25}$ = +61.5˚ (c 0.2, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 -8.08 (m, 2H, Ar-H), 7.61 (t, *J* = 7.4 Hz, 1H, Ar-H), 7.50-7.46 (m, 2H, Ar-H), 7.39-7.33 (m, 5H, Ar-H), 5.83 (d, *J* = 3.0 Hz, 1H, H-6), 5.65-5.64 (m, 1H, H-1), 4.59 (q, *J* = 11.7, 15.8 Hz, 2H, -CH_2Ph), 4.43 (d, *J* = 4.6 Hz, 1H, H-4), 4.27-4.23 (m, 2H, H-7_A & H-2), 4.20-4.18 (m, 1H, H-7_B), 4.11 (dd, *J* = 2.6, 4.7 Hz, 1H, H-3), 3.05 (bs, 2H, -OH), 2.66 (bs, 1H, -OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 138.1, 137.3, 133.4, 129.8, 129.5, 128.6, 128.4, 128.0, 127.9, 123.5, 73.3, 73.1, 73.0, 72.4, 70.4, 70.2 Elemental analysis calcd for $C_{21}H_{22}O_6$: C, 68.10; H, 5.99; found: C, 67.96; H, 6.11.

(3aR,4S,7R,7aS)-6-((benzyloxy)methyl)-7-hydroxy-2,2-dimethyl-3a,4,7,7a-tetrahydrobenzo[d][1,3]dioxol-4-yl benzoate (**22**): To a solution of **21** (0.240 g, 0.6486 mmol) in dry acetone (10 mL) at rt, catalytic amount of CSA (8 mg) and 2,2-dimethoxy propane (0.101 g, 0.973 mmol) were added. The resulting mixture was stirred at rt for 30 min. After the completion of the reaction, the reaction was quenched by the addition of triethylamine. The solvents were evaporated under reduced pressure and the crude product thus obtained was purified by column chromatography to yield **22** (0.260 g, 98%) as an oily liquid. $[\alpha]_D^{25}$ = +49.0 (c 0.4, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.00-7.98 (m, 2H, Ar-H), 7.50 (d, *J* = 7.4 Hz, 1H, Ar-H), 7.39-7.36 (m, 2H, Ar-H), 7.28-7.22 (m, 5H, Ar-H), 5.77 (d, *J* = 1.6 Hz, 1H, H-6), 5.46-5.44 (m, 1H, H-1), 4.50 (d, *J* = 11.7 Hz, 1H, -CHPh), 4.46-4.42(m, 2H, H-2 & -CHPh), 4.30-4.27(m, 2H, H-4 & H-3), 4.16 (d, *J* = 12.7 Hz, 1H, H-7_A), 4.08 (d, *J* = 12.5 Hz, 1H, H-7_B), 1.40 (s, 3H, -CH_3), 1.31 (s, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 139.7, 137.4, 133.3, 129.8, 129.7, 128.5, 128.4, 128.0, 127.9, 124.1, 109.6, 78.6, 75.7, 72.6, 72.1, 70.7, 70.4, 27.7, 24.7; Elemental analysis calcd for $C_{24}H_{26}O_6$; C, 70.23; H, 6.38; found: C, 70.19; H, 6.70.

(3aR,4S,7R,7aS)-7-acetoxy-6-((benzyloxy)methyl)-2,2-dimethyl-3a,4,7,7a-tetrahydrobenzo[d][1,3]dioxol-4-yl benzoate (**23**): To a solution of **22** (0.220 g, 0.536 mmol) in dry pyridine (5 mL) at 0 ˚C, Ac_2O (0.081 g, 0.80 mmol) was added. The mixture was stirred at same temperature for 1h. After completion of the reaction the solvents were evaporated and the residue thus obtained was diluted with ethyl acetate and washed

successively with sat. $NaHCO_3$ solution, water and brine. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product thus obtained was purified by column chromatography to yield **23** (0.229 g, 95%) as an oily liquid. $[\alpha]_D^{25}$ = +26.0˚ (c 0.3, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.00- 7.99 (m, 2H, Ar-H), 7.51-7.48 (m, 1H, Ar-H), 7.36 (t, *J* = 7.9 Hz, 2H, Ar-H), 7.27-7.18 (m, 5H, Ar-H), 6.06 (d, *J* = 3.7 Hz, 1H, H-6), 5.54-5.52 (m, 1H, H-1), 5.49 (d, *J* = 3.6 Hz, 1H, H-4), 4.47-4.44 (m, 2H, H-2 & -CHPh), 4.39-4.34 (m, 2H, H-3 & -CHPh), 4.02 (d, *J* = 13.4 Hz, 1H, H-7_A), 3.94 (m, *J* = 13.4 Hz, 1H, H-7_B), 1.98 (s, 3H, -$COCH_3$), 1.39 (s, 3H, -CH_3), 1,29 (s, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 165.6, 137.7, 137.2, 133.3, 129.8, 129.7, 128.48, 128.42, 127.8, 127.7, 125.5, 109.4, 75.9, 75.4, 72.2, 70.0, 69.9, 69.0, 26.8, 24.8, 21.1; Elemental analysis calcd for $C_{26}H_{28}O_7$: C, 69.01; H, 6.24; found: C, 68.83; H, 6.51.

(1S,4R,5R,6S)-4-acetoxy-3-((benzoyloxy)methyl)-5,6-dihydroxycyclohex-2-en-1-yl benzoate (**24**) (structure proposed for **uvacalol E**): To a solution of **23** (0.095 g, 0.210 mmol) in dry DCM (3 mL), anhydrous $FeCl_3$ (0.051 g, 0.315 mmol) was added. The mixture was stirred at rt for 30 min. when the reaction was complete, the reaction mixture was diluted with DCM and washed with water and brine. The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The crude product thus obtained was dissolved in dry in DCM. The solution was cooled to 0 ˚C and to this 2,4,6-collidine (0.5 mL) and BzCl (25 µL, 0.210 mmol) were added. The resulting mixture was stirred at same temperature for 1.5 h. After the completion of reaction the solvents were evaporated. The residue thus obtained was diluted with ethyl acetate and washed successively with dil. HCl, sat. $NaHCO_3$, water and brine. The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The crude product thus obtained was purified by column chromatography to yield **24** (0.070 g 79%) as a gummy solid. $[\alpha]_D^{25}$ = +45.0˚ (c 0.2, CH_3OH); ^1H NMR (500 MHz, $CDCl_3$) δ 8.01-7.97 (m, 4H, Ar-H), 7.54-7.48 (m, 2H, Ar-H), 7.41-7.36 (m, 4H, Ar-H), 6.05 (s, 1H, H-6), 5.64 (s, 1H, H-1), 5.54 (d, *J* = 3.5 Hz, 1H, H-4), 4.85 (d, *J* = 13.0 Hz, 1H, H-7_A), 4.77 (d, *J* = 13.4 Hz, 1H, H-7_B), 4.07 (s, 2H, H-2 & H-3), 2.01 (s, 3H, -$COCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 166.9, 166.0, 133.7, 133.5, 133.2, 129.9, 129.7, 129.6, 129.4, 128.5, 128.4, 126.6, 72.3, 71.2, 70.7, 70.6, 64.2, 20.8; Elemental analysis calcd for $C_{23}H_{22}O_8$: C, 64.78; H, 5.20; found: C, 64.66; H, 5.45.

(1S,4R,5S,6S)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-en-1-yl benzoate (**25**): To a solution of **20** (0.300 g, 0.395 mmol) in dry DCM at 0 ˚C, $FeCl_3$ (0.288 g, 1.78 mmol) was added. The mixture was stirred at same temperature for 2h. When the reaction was complete, the solvents were evaporated under reduced pressure. The residue thus obtained was purified by column chromatography to yield **25** (0.081 g, 74%); $[\alpha]_D^{25}$ = +126.0˚ (c 0.1, CH_3OH); m.p: 185-189 ˚C; ^1H NMR (500 MHz, CD_3OD) δ 7.95 (d, *J* = 7.5 Hz, 2H, Ar-H), 7.50 (t, *J* = 7.4 Hz, 1H, Ar-H), 7.37 (t, *J* = 7.7 Hz, 2H, Ar-H), 5.68 (s, 1H, H-6), 5.55 (d, *J* = 6.1 Hz, 1H, H-1), 4.11-4.06 (m, 3H, H-4, H-7_A& H-7_B), 4.03 (dd, *J* = 2.2, 8.6 Hz, 1H, H-2), 3.86 (dd, *J* = 2.3, 3.8 Hz, 1H, H-3); ^{13}C NMR (125 MHz, CD_3OD) δ 167.9, 143.1, 134.3, 131.6, 130.6, 129.5, 121.6, 75.2, 74.4, 70.8, 70.5, 63.4; Elemental analysis calcd for $C_{14}H_{16}O_6$: C, 59.99; H, 5.75; found: C, 60.05; H, 5.94.

((3S,4S,5S,6R)-3-(benzoyloxy)-4,5,6-trihydroxycyclohex-1-en-1-yl)methyl benzoate (**26**) (structure proposed for ***ent*-uvacalol G**):

Procedure 1: To a solution of **25** (0.040 g, 0.142 mmol) in a mixture of 2,4,6 –collidine and DCM (1:1) at 0 ˚C, BzCl (18 µL, 0.152 mmol) was added. The resulting mixture was allowed to warm to rt. When the reaction was complete, the solvents were evaporated under reduced pressure. The residue was diluted with ethyl acetate and washed successively with dil. HCl, sat. $NaHCO_3$, water and brine. The organic layer was dried over sodium sulphate and concentrated under reduced pressure. The crude product thus obtained was purified by column chromatography to yield **26** (0.042 g, 78%) as sticky a solid.

Procedure 2: To a solution of **24** (0.020 g, 0.047 mmol) in MeOH at rt, AcCl (10 µL) was added. The resulting mixture was stirred at rt for 3h. When the reaction was complete, the reaction mixture was quenched by the addition of $NaHCO_3$ solution and the mixture was diluted with DCM. The organic layer was washed with water and concentrated under reduced pressure. The crude product thus obtained was purified by column chromatography to yield **26** (0.016 g, 92%); $[\alpha]_D^{25}$ = +56.0˚ (c 0.3, CH_3OH); ^1H NMR (500 MHz, $CDCl_3$) δ 7.99-7.95 (m, 4H, Ar-H), 7.50 (t, *J* = 7.3 Hz, 2H, Ar-H), 7.38-7.34 (m, 4H, Ar-H), 5.87 (d, *J* = 2.6 Hz, 1H, H-6), 5.55 (s, 1H, H-1), 5.12 (d, *J* = 13.2 Hz, 1H, H-7_A), 4.75 (d, *J* = 13.2 Hz, 1H, H-7_B), 4.33 (d, *J* = 3.7 Hz, 1H, H-4), 4.15 (d, *J* = 2.0 Hz, 1H, H-2), 4.02 (s, 1H, H-3), 2.16 (bs, 3H, -OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 166.6, 138.0, 133.5, 133.4, 129.9, 129.8, 129.5, 129.4, 128.5, 128.4, 123.8, 73.0, 72.2, 70.5, 68.9, 64.9; Elemental analysis calcd for $C_{21}H_{20}O_7$: C, 65.62; H, 5.24; found: C, 65.49; H, 5.44.

Crystal data of 26: CCDC 1040209, $C_{12}H_{20}O_7$, M = 384.37, colorless hexagonal blocks, 0.25 x 0.15 x 0.15 mm^3, monoclinic, space group C_2, a = 27.206(5), b = 6.873 (5), c = 10.231(5) Å, V = 1911.7(17) $Å^3$, Z = 4, T = 296(2) K, $2\theta_{max}$ = 50.00°, Dcalc (g cm^{-3}) = 1.335, F(000) = 808.0, µ (mm-1) = 0.101, 7663 reflections collected, 2662 unique reflections (Rint = 0.02052), multi-scan absorption correction, T_{min} = 0.9850, T_{max} = 0.9753, number of parameters = 266, number of restraints = 4, GoF = 1.194, R_1 = 0.0326, wR_2 = 0.0939, R indices based on 2514 reflections with I >2s(I) (refinement on F2). Δρmax = 0.229, Δρmin = -0.214 (eÅ-3).

Acknowledgements

K.M.S. thanks the Department of Science and Technology, India, for financial support and Ramanujan Fellowship, Swarnajayanti Fellowship and CSIR for an EMR project grant.

Notes and references

School of Chemistry, Indian Institute of Science Education and Research, Thiruvananthapuram 695016, India. E-mail: kms@iisertvm.ac.in

Electronic Supplementary Information (ESI) available: Crystal data (CIF) of **26** (also available from Cambridge Crystallographic Data Center: CCDC 1040209), copies of ^{1}H NMR, ^{13}C NMR, DEPT, COSY and HMQC spectra of all the new compounds. See DOI: 10.1039/b000000x/

1) (a) T. K. Lindhorst, *Essentials of Carbohydrate Chemistry and Biochemistry*, Wiley-VCH, Weinheim, 2007; (b) B. Wang and G. -J. Boons, *Carbohydrate Recognition: Biological Problems, Methods and Applications*, Wiley, New Jersey, 2011; (c) B. Fraser-Reid, K. Tatsuta, J. Thiem, G. L. Cote, S. Flitsch, Y. Ito, H. Kondo, S.-i. Nishimura and B. Yu, *Glycoscience: Chemistry and Chemical Biology*, Springer, Heidelberg, 2008; (d) N. Gaidzik, U. Westerlind and H. Kunz, *Chem. Soc. Rev*., 2013, **42**, 4421; (e) C. Zong, A. Venot, O. Dhamale and G.-J. Boons, *Org. Lett.*, 2013, **15**, 342; (f) C. E. Martin, F. Broecker, M. A. Oberli, J. Komor, J. Mattner, C. Anish and P. H. Seeberger, *J. Am. Chem. Soc.*, 2013, **135**, 9713; (g) Z. Wang, Z. S. Chinoy, S. G. Ambre, W. Peng, R. Mcbride, R. P. de Vries, J. Glushka, J. C. Paulson and G.-J. Boons, *Science*, 2013, **341**, 379; (h) C. Anish, X. Guo, A. Wahlbrink and P. H. Seeberger, *Angew. Chem. Int. Ed.*, 2013, **52**, 9524; (i) P. Yasomanee and A. V. Demchenko, *Trends Glycosci. Glycotechnol*., 2013, **25**, 13; (j) D. C. Koester, E. Kriemen and D. B. Werz, *Angew. Chem. Int. Ed*., 2013, **52**, 2985; (k) Y. Geng, A. Kumar, H. M. Faidallah, H. A. Albar, I. A. Mhkalid and R. R. Schmidt, *Angew. Chem. Int. Ed.*, 2013, **52**, 10089; (l) N. Gaidzik, A. Kaiser, D. Kowalczyk, U. Westerlind, B. Gerlitzki, H. P. Sinn, E. Schmitt and H. Kunz, *Angew. Chem. Int. Ed*., 2011, **50**, 9977.

2) a) O. Arjona, A. M. Gomez, J. C. Lopez and J. Plumet, *Chem. Rev.*, 2007, **107**, 1919; b) R. Lahiri, A. A. Ansari and Y. D.Vankar, *Chem. Soc. Rev.*, 2013, **42**, 5102; (c) E. Leclerc, X. Pannecoucke, M. Etheve-Quelquejeu and M. Sollogoub, *Chem. Soc. Rev.*, 2013, **42**, 4270.

3) (a) T. Mahmud, *Nat. Prod. Rep.* 2003, **20**, 137; b) M. Witte, W. W. Kallemeijn, J. Aten, K.-Y. Li, A. Strijland, W. E. Donker-Koopman, A. M. C. H. Van Den Nieuwendijk, B. Bleijlevens, G. Kramer, B. I. Florea, B. Hooibrink, C. E. M. Hollak, R. Ottenhoff, R. G. Boot, G. A. Van Der Marel, H. S. Overkleeft, J. M. F. G. Aerts, *Nat. Chem. Biol.*, 2010, **6**, 907; (c) W. W. Kallemeijn, K.-Y. Li, M. D. Witte, A. R. A. Marques, J. Aten, S. Scheij, J. Jiang, L. I. Willems, T. M. Voorn-Brouwer, C. P. A. A. Van Roomen, R. Ottenhoff, R. G. Boot, H. Van Den Elst, M. T. C. Walvoort, B. I. Florea, J. D. C. Codee, G. A. Van Der Marel, J. M. F. G. Aerts and H. S. Overkleeft, *Angew. Chem. Int. Ed.*, 2012, **51**, 12529.

4) J. Marco-Contelles, *Eur. J. Org. Chem.*, 2001, 1607.

5) D. H. Mac, S. Chandrashekhar and R. Gree, *Eur. J. Org. Chem.*, 2012, 588.

6) Y. Usami and K. Mizuki, *J. Nat. Prod.*, 2011, **74**, 877.

7) (a) Y. Kameda, N. Asano, M. Yoshikawa and K. Matsui, *J. Antibiot.*, 1982, **35**, 1624; (b) Y. Kameda, N. Asano, M. Teranishi and K.Matsui, *J. Antibiot*., 1980, **33**, 1573.

8) (a) Y. Kameda and S. Horii, *J. Chem. Soc. Chem. Commun.*, 1972, 746; b) S. Horii, T. Iwasa, E. Mizuta and Y. Kameda, *J. Antibiotics*, 1971, **24**, 59.

9) A. Isogai, S. Sakuda, J. Nakayama, S. Watanabe and A. Suzuki, *Agric. Biol. Chem.*, 1987, **51**, 2277.

10) (a) G.-X. Zhou, R. -Y. Chen and D. -Q. Yu, *J. Asian Nat. Prod. Res.*, 1999, **1**, 227; (b) G.-X. Zhou, Y.-J. Zhang, R.-Y. Chen and D.-Q. Yu, *J. Asian Nat. Prod. Res.*, 2010, **12**, 696; (c) G.-X. Zhou, R. -Y. Chen and D. -Q. Yu, *Nat. Prod. Res.*, 2011, **25**, 161.

11) The names Uvacanols and uvacalols are synonymously used for these compounds. For the sake of consistency, we have used the terminology uvacalol throughout the manuscript.

12) (a) X. P. Pang and D. Q. Yu, *Chinese Chem. Lett.*, 1995, **6**, 305; (b) X. P. Pang and D. Q. Yu, *Phytochemistry*, 1995, **40**, 1709; (c) X. P. Pang, D. Q. Yu and K. H. Lee, *Chinese Chem. Lett.*, 1996, **7**, 241; (d) Y.-H. Liao, L.-Z. Xu, S.-L. Yang, J. Dai, Y.-S. Zhen, M. Zhu and N. J. Sun, *Phytochemistry*, 1997, **45**, 729.

13) (a) S. Yamaguchi, T. Hirokane, T. Yoshida, T. Tanaka, T. Hatano, H. Ito, G.-I. Nonaka and H. Yamada, *J. Org. Chem.*, 2013, **78**, 5410; (b) R. Wang, M. N. Paddon-Row and M. S. Sherburn, *Org. Lett.*, 2013, **15**, 5610; (c) K. R. Prasad and P. Gutala, *J. Org. Chem.*, 2013, **78**, 3313; (d) H. Fuwa, K. Sekine and M. Sasaki, *Org. Lett.*, 2013, **15**, 3970; (e) K. Kuramochi, K. Tsubaki, I. Kuriyama, Y. Mizushina, H. Yoshida, T. Takeuchi, S. Kamisuki, F. Sugawara and S. Kobayashi, *J. Nat. Prod.*, 2013, **76**, 1737; (f) P. D. Brown, A. C. Willis, M. S. Sherburn and A. L. Lawrence, *Angew. Chem. Int. Ed.*, 2013, **52**, 13273; (g) G. Carr, M. Poulsen, J. L. Klassen, Y. Hou, T. P. Wyche, T. S. Bugni, C. R. Currie and J. Clardy, *Org. Lett.*, 2012, **14**, 2822; (h) D. W. Lin, T. Masuda, M. B. Biskup, J. D. Nelson and P. S. Baran, *J. Org. Chem.*, 2011, **76**, 1013; (i) Z. Bian, C. C. Marvin and S. F. Martin, *J. Am. Chem. Soc.*, 2013, **135**, 10886; (j) H. Lei, J. Yan, J. Yu, Y. Liu, Z. Wang, Z. Xu and T. Ye, *Angew. Chem. Int. Ed.*, 2014, **53**, 1; (k) L. Song, K.-H. Lee, Z. Lin and R. Tong, *J. Org. Chem.*, 2014, **79**, 1493; (l) M. Jacolot, M. Jean, N. Tumma, A. Bondon, S. Chandrasekhar and P. Van De Weghe, *J. Org. Chem*., 2013, **78**, 7169; (m) A. Y. Hong and B. M. Stoltz, *Angew. Chem. Int. Ed.*, 2012, **51**, 9674; (n) J. Kim and M. Movassaghi, *J. Am. Chem. Soc*., 2011, **133**, 14940; (o) J. Kim and M. Movassaghi, *J. Am.Chem. Soc.*, 2010, **132**, 14376.

14) (a) M. Á. Fresneda, R. Alibés, J. Font, P. Bayón and M. Figueredo, *J. Org. Chem.*, 2012, **77**, 5030; (b) K. M. Sureshan, T. Miyasou, and Y. Watanabe, *Tetrahedron Lett.*, 2004, **45**, 3197; (c) T. K. M. Shing and H. M. Cheng, *Synlett*, 2010, 142; (d) Y. Usami and K. Mizuki, *J. Nat. Prod.*, 2011, **74**, 877.

15) (a) M. J. Palframan, G. Kociok-Köhn and S. E. Lewis, *Org. Lett*., 2011, **13**, 3150; b) S. Awale, J. Ueda, S. Athikomkulchai, S. Abdelhamed, S. Yokoyama, I. Saiki and R. Miyatake, *J. Nat. Prod*., 2012, **75**, 1177; c) M. J. Palframan, G. Kociok-Köhn and S. E. Lewis, *Chem. Eur. J.*, 2012, **18**, 4766.

16) S. Mondal and K. M. Sureshan, *Org. Biomol. Chem.*, 2014, **12**, 7279.

17) (a) C. Gravier-Pelletier, W. Maton, T. Dintinger, C. Tellierb and Y. L. Merrera, *Tetrahedron*, 2003, **59**, 8705; (b) Y. L. Merrer, C. Gravier-Pelletier, W. Maton, M. Numa and J.-C. Depezay, *Synlett*, 1999, 1322. (c) A. Vidyasagar and K. M. Sureshan, *Eur. J. Org. Chem.*, 2014, 2349. (d) Y. Le Merrer, C. Gravier-Pelletier, D. Micas-Languin, F. Mestre, A. DurBault and J. -C. Depezay, *J. Org. Chem*., 1989, **54**, 2409; (e) S. Ghosh and T. K. Pradhan, *J. Org. Chem*., 2010, **75**, 2107; (f) J. S. Ko, J. E. Keum and S. Y. Ko, *J. Org. Chem.*, 2010, **75**, 7006.

18) D. B. Dess and J. C. Martin, *J. Org. Chem.*, 1983, **48**, 4155.

19) M. Scholl, S. Ding, C. W. Lee and R. H. Grubbs, *Org. Lett.*, 1999, **1**, 953.

20) C. -E. Yeom, S. Y. Lee, Y. J. Kim and B. M. Kim, *Synlett*, 2005, 1527.

