Tetrahedron 67 (2011) 4036–4047

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Stereoselective total syntheses of (+)-*exo*- and (−)-*exo*-brevicomins, (+)-*endo*- and (−)-*endo*-brevicomins, (+)- and (−)-cardiobutanolides, (+)-goniofufurone

Pinki Pal, Arun K. Shaw *

Division of Medicinal and Process Chemistry, Central Drug Research Institute (CDRI), CSIR, Lucknow 226 001, Uttar Pradesh, India

ARTICLE INFO

Article history:
Received 22 February 2011
Received in revised form 31 March 2011
Accepted 6 April 2011
Available online 12 April 2011

Keywords:
Brevicomin
Chiral building blocks
Cardiobutanolide
Goniofufurone
Vinylbutyrolactone

ABSTRACT

Stereoselective total syntheses of aggregation pheromones (+)-*exo*-brevicomin (**9a**), (−)-*exo*-brevicomin (**9b**), (+)-*endo*-brevicomin (**9c**), (−)-*endo*-brevicomin (**9d**) and styryllactones (+)-cardiobutanolide (**14a**), (−)-cardiobutanolide (**14b**), and (+)-goniofufurone (**19a**) were achieved in good yields from enantiomerically pure highly functionalized furanoid glycal building blocks (**1a**–**d**) involving similar synthetic strategies, thus making these furanoid glycals highly useful building blocks in diversity-oriented synthesis (DOS).

1. Introduction

The chiral building blocks (CBBs) derived from commercially available carbohydrates are most important chiral synthons for total synthesis of functionally and stereochemically simple and complex natural products. This approach of synthesis utilizing the stereochemistry of the starting material is customarily known as the 'chiron' approach synthesis[1a,b] and it becomes very cost effective if starting material is derived from inexpensive carbohydrate or amino acid. The stereoselective synthesis of small molecule natural products with multiple chiral centers starting from easily accessible starting material of choice is a challenging task to an organic chemist. However, their synthesis could be possible starting from inexpensive stereochemically pure building blocks or CBBs that should be either commercially available or synthesized in the laboratory. The preparation of attractive building blocks from carbohydrates and their use for the synthesis of various biologically active simple or complex natural products has received considerable attention from organic chemists. Therefore, the stereocontrolled synthesis of CBBs is an important objective in organic chemistry. Since last few years we are working toward the synthesis of enantiomerically pure sugar derived building blocks and their utilization to accomplish the total synthesis of target natural products[1d,f] and natural product like molecules.[1c,e,g,h,j] Recently, we disclosed an efficient protocol for the synthesis of stereochemically pure four different furanoid glycals **1a**–**d** (Fig. 1) synthesized from our earlier reported easily accessible enantiomerically pure 2,3,4-trisubstituted THF scaffolds.[1i] Now, to continue our ongoing programme and also to show the synthetic applications of these furanoid glycals or in other way their precursor THF scaffolds, we have identified few natural products with different biological activities, such as aggregation pheromones brevicomins (**9a**–**d**), styryllactones cardiobutanolides (**14a**,**b**) and (+)-goniofufurone (**19a**) (Fig. 2) whose syntheses can be possible from furanoid glycal building blocks (**1a**–**d**).

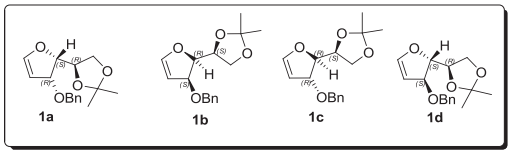


Fig. 1. Structures of furanoid glycals **1a**–**d**.

2. Results and discussion

2.1. Synthesis of brevicomins (9a–d)

The 6,8-dioxabicyclo[3.2.1]octane skeleton is a structural subunit in complex natural products like palytoxin[2a] and pinnatoxin A,[2b] and also in simpler insect pheromones, such as *exo*- and

* Corresponding author. E-mail address: akshaw55@yahoo.com (A.K. Shaw).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.04.014

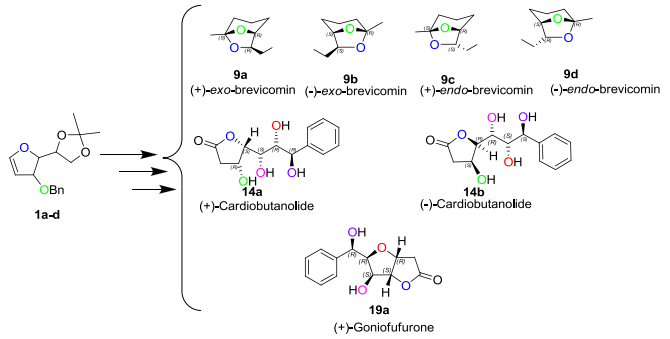
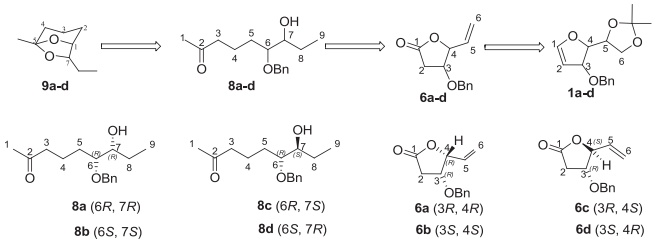


Fig. 2. Structures of brevicomins (**9a**–**d**), (+)-cardiobutanolide (**14a**), (−)-cardiobutanolide (**14b**), and (+)-goniofufurone (**19a**).

endo-brevicomins (**9a**–**d**, Fig. 2). Alkylated 6,8-dioxabicyclo[3.2.1] octanes are well-known aggregation pheromones isolated from several species of the bark beetles and play an important role in the system of chemical communication amongst them. These beetles infect pine trees causing great ecological and economic damage. Brevicomin and frontalin were some of the earliest alkylated 6,8-dioxabicyclo[3.2.1]octanes to be identified important head space volatiles obtained from different *Dendroctonus* species.[2c–e] The *exo*- and *endo*-isomers of brevicomin are component of the volatiles of several economically important bark beetles in the genera *Dendroctonus* and *Dryocoetes*.[2c–e,3,4] Amongst various alkyl derivatives, (+)-*exo*-brevicomin was identified as a key component of aggregation pheromone from the frass of the females of western pine beetle, *Dendroctonus brevicomis*, which is a principal pest in the timber regions on the western coast of North America.[2c–e,3] (+)-*endo*-Brevicomin is an aggregation pheromone of *Dryocoetes autographus*, a damaging pest of Norway spruce.[2d,4b] (+)-*endo*-Brevicomin also acts as an aggregation pheromone of southern pine beetles, *Dendroctonus frontalis*, to the female-produced pheromone frontalin, while (−)-*endo*-brevicomin acts as an antiaggregation pheromone for this insect.[4d,f]

Encouraged by biological activities of brevicomins, various synthetic approaches have been devised for their synthesis.[5,6] Herein, we report the synthesis of two pairs of enantiomer of brevicomins viz. (+)-*exo*-, (−)-*exo*-brevicomins and (+)-*endo*-, (−)-*endo*-brevicomins from similar type of furanoid glycals (**1a**–**d**), respectively.

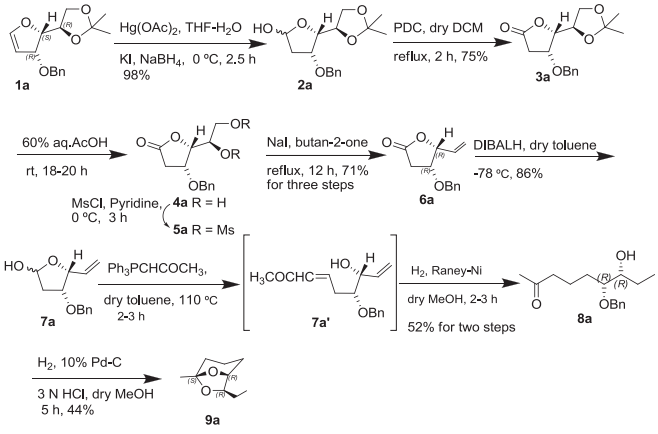
The general retrosynthetic prospective of brevicomins **9a**–**d** is delineated in Scheme 1. Here, we realized that the selection of the furanoid glycal building blocks could rely upon the two contiguous stereocenters of immediate precursors **8** of the target brevicomins. Thus, in the case of synthesis of (+)-*exo*-brevicomin **9a**, the C-6 and C-7 stereocenters of *threo*-alcohol **8a** could be derived from C-3 and C-4 of *threo*-furanoid glycal **1a**. Similarly, its optical antipode (−)-*exo*-brevicomin **9b** could be synthesized from *threo*-furanoid glycal **1b** via the intermediates *threo*-alcohol **8b** and *threo*-lactone **6b**. Further, based on the above argument the synthesis of



Scheme 1. General retrosynthetic strategy for brevicomins (**9a**–**d**) from enantiomerically pure similar furanoid glycals **1a**–**d**.

(+)-*endo*-brevicomin **9c** and its optical isomer **9d** could similarly be possible from enantiomerically pure *erythro*-furanoid glycals **1c** and **1d**, respectively.

Our synthetic strategy to synthesize (+)-*exo*-brevicomin from furanoid glycal **1a** (1,4-anhydro-2-deoxy-5,6-*O*-isopropylidene-3-*O*-benzyl-D-*arabino*-hex-1-enitol) is shown in Scheme 2. The glycal **1a** was converted into **2a** by oxymercuration–demercuration[7] sequence in 98% yield. The anomeric OH was oxidized with PDC in dry DCM at refluxing temperature for 2 h to obtain lactone **3a** as a white solid in 75% yield. Deprotection of the acetonide in **3a** was carried out smoothly with 60% aqueous AcOH at room temperature for 18–20 h to give diol **4a** as a white solid, which was without further purification, mesylated with MsCl in pyridine at 0 °C for 3 h to afford dimesyl derivative **5a**. The diester **5a** as such was immediately subjected to undergo reductive elimination[8] with NaI in butan-2-one at reflux temperature for 12 h to give vinylbutyrolactone derivative **6a** in 71% yield for three steps. Its reduction with DIBALH was carried out at −78 °C in dry toluene to obtain lactol **7a** in 86% yield. While Wittig olefination of lactol **7a** with $Ph_3PCHCOCH_3$ in dry acetonitrile to furnish an intermediate **7a′** by the literature method[5h] did not produce any result, performing the same reaction in dry toluene followed by Raney-Ni hydrogenation of the resulting product with two double bonds afforded column purified ketone **8a** in 52% yield in two steps. Finally, the simultaneous hydrogenolysis of OBn in **8a** in the presence of Pd/C in MeOH and intramolecular acetalization with a trace of 3 N HCl (Scheme 2) delivered the target (+)-*exo*-brevicomin **9a** in 44% yield.[5h,6i,k] The physical and spectroscopic data of our synthetic sample **9a** are identical to those of the reported natural and synthetic product.[2c]

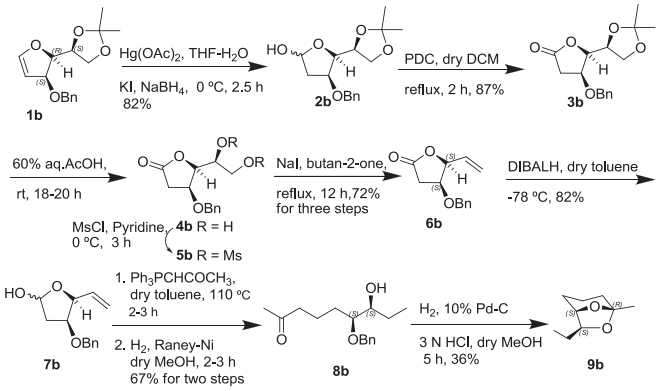


Scheme 2. Synthesis of (+)-*exo*-brevicomin **9a**.

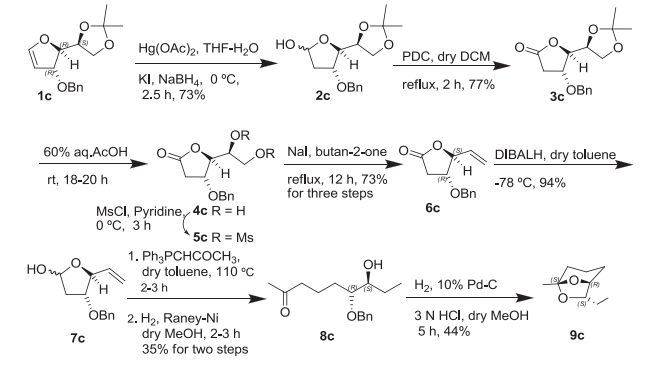
After having completed the total synthesis of (+)-*exo*-brevicomin **9a** from furanoid glycal **1a**, the similar reaction sequence was successfully followed for the synthesis of (−)-*exo*-brevicomin **9b** from **1b** (1,4-anhydro-2-deoxy-5,6-*O*-isopropylidene-3-*O*-benzyl-L-*arabino*-hex-1-enitol) (Scheme 3), (+)-*endo*-brevicomin **9c** from **1c** (1,4-anhydro-2-deoxy-5,6-*O*-isopropylidene-3-*O*-benzyl-L-*ribo*-hex-1-enitol) (Scheme 4) and (−)-*endo*-brevicomin **9d** from **1d** (1,4-anhydro-2-deoxy-5,6-*O*-isopropylidene-3-*O*-benzyl-D-*ribo*-hex-1-enitol) (Scheme 5).

2.2. Synthesis of cardiobutanolides (14a,b)

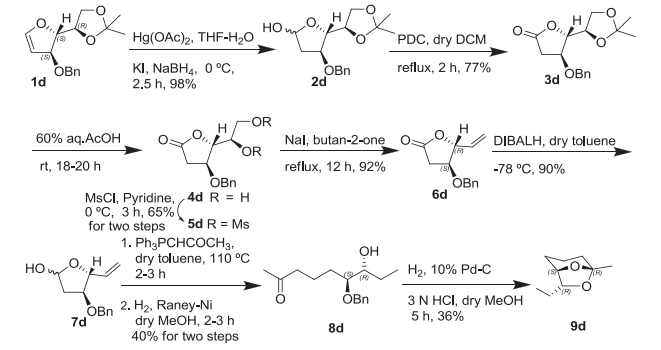
For a long time Asian trees of the genus *Goniothalamus* of the plant family Annonaceae have been the subject of extensive investigation most particularly due to its proven use in folk medicine as well as the diverse and potent polyketide constituents it offers.[9]



Scheme 3. Synthesis of (−)-*exo*-brevicomin **9b**.



Scheme 4. Synthesis of (+)-*endo*-brevicomin **9c**.



Scheme 5. Synthesis of (−)-*endo*-brevicomin **9d**.

The leaves and extracts of *Goniothalamus* are traditionally used for the treatments of edema and rheumatism,[9a] and also as a pain killer, mosquito repellent,[9b] and an abortifacient.[9c] The research group of McLaughlin have reported the isolation and characterization of a series of styryllactones from several species of the genus *Goniothalamus* (Annonaceae). These molecules were shown to possess various important biological activities like pesticidal, ratogenic, embryotoxic. The significant to marginal cytotoxic activity against human tumor cell lines were also found in these styryllactones (Fig. 3).[10–12] Hisham et al. have reported the isolation of (+)-cardiobutanolide **14a**, a pharmacologically active natural product from the stem bark of *Goniothalamus cardiopetalus*, along with other known styryllactones in 2003.[13] Its structural complexity owing to five contiguous chiral centers and potential pharmacological activity attracted the attention of synthetic organic chemists in recent years. After its first synthesis employing *anti* selective boronate aldol reaction of L-erythrulose derivative in

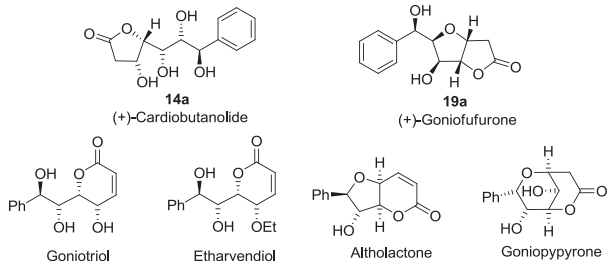
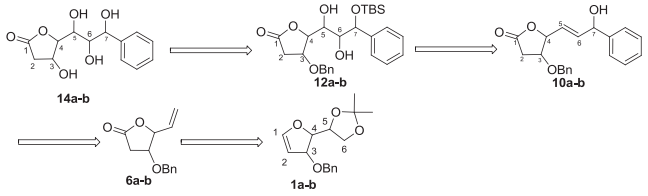


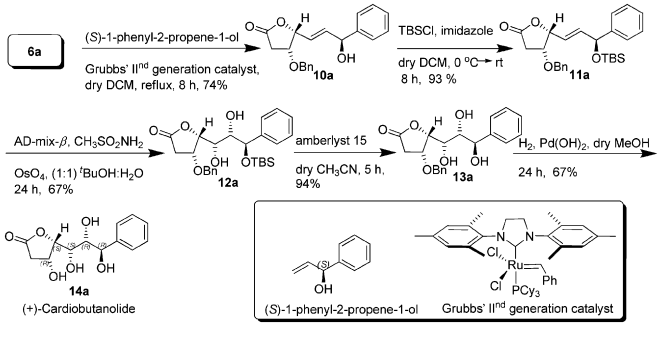
Fig. 3. Naturally occurring representative styryllactones.

9% overall yield reported by Murga et al.[14] six more total synthesis and one formal synthesis of this molecule have been reported.[15] Encouraged by the pharmacological activity and complex structure of (+)-cardiobutanolide **14a** endowed with five contiguous chiral centers each bearing oxygen functionality, we became also interested to take up the 'chiron' approach to synthesis of both the enantiomers of this molecule.

Based on the retrosynthetic plan as described in Scheme 6, we realized that while the stereocenters C-3 and C-4 of (+)-cardiobutanolide **14a** could be translated from furanoid glycal **1a**, the remaining three stereocenters have to be created. Thus, the synthesis of (+)-cardiobutanolide **14a** could be initiated from furanoid glycal **1a**. The key intermediate **6a** was prepared from the furanoid glycal **1a** as described in Scheme 2. The olefin cross metathesis reaction[15e] between **6a** and (*S*)-1-phenyl-2-propene-1-ol with Grubbs' second generation catalyst (2.8 mol %) in refluxing DCM furnished allylic alcohol **10a** in 74% yield. It was silylated with TBSCl in the presence of imidazole in dry DCM at 0 °C to afford silyl ether **11a** in 93% yield. Its asymmetric dihydroxylation with AD-mix-β in 1:1 ^{t}BuOH/H_2O afforded a separable mixture of diastereomers in 5% and 67% yield. Our desired compound identified as **12a** was obtained in 67% yield, which was utilized to complete the synthesis of the title compound. The silyl ether deprotection of **12a** with amberlyst 15 resin in dry acetonitrile produced **13a** in 94% yield. Finally, its *O*-benzyl deprotection by $Pd(OH)_2$ catalyzed hydrogenolysis in dry MeOH furnished the desired natural product (+)-cardiobutanolide **14a** in 67% yield (Scheme 7). The physical and spectroscopic data of our synthetic sample **14a** are identical to those of the reported natural and synthetic product.[14,15]

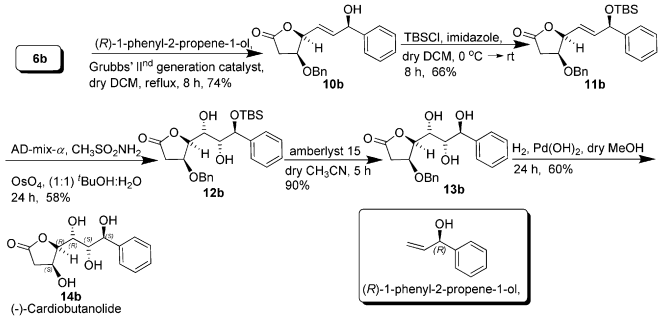


Scheme 6. General retrosynthetic strategy for cardiobutanolides (**14a**,**b**) from enantiomerically pure furanoid glycals **1a**,**b**.



Scheme 7. Synthesis of (+)-cardiobutanolide **14a**.

Similarly, the (−)-cardiobutanolide **14b** was synthesized from **1b**, an optical antipode of **1a** by adopting the reaction sequence similar to that employed for the synthesis of its enantiomer **14a**. The olefin cross metathesis reaction between compound **6b** derived from **1b** (Scheme 3) and (*R*)-1-phenyl-2-propene-1-ol with Grubbs' second generation catalyst (2.8 mol %) furnished allylic alcohol **10b** in 74% yield. Its silylated derivative **11b** on asymmetric dihydroxylation with AD-mix-α in 1:1 ^{t}BuOH/H_2O afforded a separable mixture of diastereomers. The desired isomer **12b** (enantiomer of **12a**) was obtained in 58% yield along with its other diastereomer in 8% yield. After having **12b** in hand, the remaining two synthetic steps similar to that employed for the synthesis of (+)-cardiobutanolide **14a** (vide supra) were followed to complete the synthesis of (−)-cardiobutanolide **14b** (Scheme 8). The spectral data of **14b** are in complete agreement with the reported natural product (+)-cardiobutanolide **14a**.[14,15]

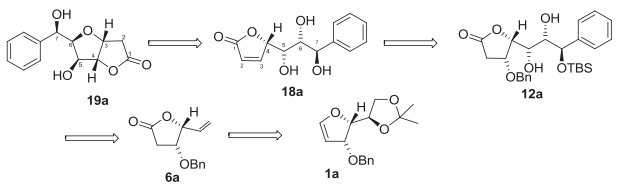


Scheme 8. Synthesis of (−)-Cardiobutanolide **14b**.

2.3. Synthesis of (+)-goniofufurone 19a

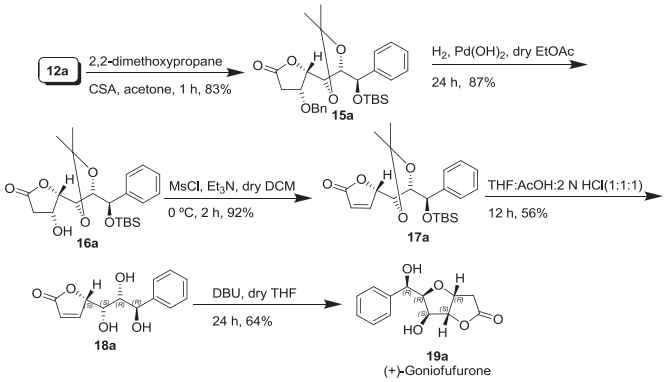
(+)-Goniofufurone (**19a**), a cytotoxic styryllactone that was isolated from the stem bark of *Goniothalamus giganteus* Hook. f., Thomas (Annonaceae), obtained from Thailand in 1990.[12c] The absolute configuration was significantly established independently by Shing and Jäger by synthesis of the unnatural *ent*-(−)-goniofufurone.[16] Owing to significant cytotoxic activity toward several human tumors cell lines and moderate toxicity to brine shrimp (BS), as well as the interesting heterocyclic skeletons, (+)-goniofufurone **19a** and its stereoisomers have been synthesized by many groups from different starting materials.[17] After successfully completing the total syntheses of isomeric four brevicomins and two cardiobutanolides from furanoid glycals, herein we wish to report the total synthesis of cytotoxic natural (+)-goniofufurone **19a**.

The retrosynthetic strategy of (+)-goniofufurone **19a** as shown below (Scheme 9) revealed that its synthesis could also be possible from furanoid glycal **1a** as we envisaged in the case of (+)-cardiobutanolide **14a**. Here, we visualized that the immediate precursor **18a** of the target natural product **19a** could easily be accessed from **12a**, which in turn could be obtained by the extension of furanoid glycal **1a** via the intermediates **2a**→**11a** as described in the synthesis of (+)-cardiobutanolide **14a** (Scheme 7).



Scheme 9. Retrosynthetic strategy for (+)-goniofufurone (**19a**) from enantiomerically pure furanoid glycal **1a**.

The acetonide protection of two free OH in **12a** afforded globally OH protected derivative **15a** in 83% yield. Its hydrogenolysis in the presence of $Pd(OH)_2$ in dry EtOAc gave *O*-benzyl deprotected derivative **16a** in 87% yield, which on mesylation with MsCl/Et_3N at 0 °C in dry DCM for 1 h followed by elimination[18]of MsOH under basic condition furnished the α,β-unsaturated lactone **17a** in 92% yield. Its treatment with THF/AcOH/2 N HCl (1:1:1) at room temperature delivered the triol **18a** in 56% yield.[17t] Finally, it was subjected to DBU catalyzed bicyclic ring formation by the participation of its 6-OH to furnish the title natural product (+)-goniofufurone **19a** as a white solid in 64% yield (Scheme 10). The physical and spectroscopic data of **19a** are identical to those of the reported natural and synthetic product.[12c,16,17]



Scheme 10. Synthesis of (+)-goniofufurone **19a**.

3. Conclusion

In conclusion, this paper reports the stereoselective total syntheses of four isomeric aggregation pheromones, (+)-*exo*-brevicomin **9a**, (−)-*exo*-brevicomin **9b**, (+)-*endo*-brevicomin **9c**, (−)-*endo*-brevicomin **9d**, two enantiomeric styryllactones (+)-cardiobutanolide **14a**, (−)-cardiobutanolide **14b**, and another styryllactone (+)-goniofufurone **19a** by utilizing our earlier reported stereochemically different furanoid glycal key building blocks (**1a**–**d**) derived from commercially available sugars.[1i] The selection of furanoid glycals (**1a**–**d**) in the present work was done on the basis of the stereochemistries of the chiral centers of the above mentioned target molecules. The importance of the work, described in this paper, lies in the fact that the strategies employed for the synthesis of all the title compounds can be followed to access some other unnatural diastereoisomers of cardiobutanolides, which are *hitherto* unreported and also natural and unnatural goniofufurones by using these furanoid glycals more efficiently compared to the synthetic routes previously reported in the literature. To the best of our knowledge the synthesis of unnatural (−)-cardiobutanolide **14b** has not yet been reported. Earlier, we have shown the importance of all the precursors (THF scaffolds) of these furanoid glycals by utilizing them as a source of chirality for the syntheses of natural products[1d,f] and different molecules of various biological properties as well.[1e,h,j] Therefore, it is worth mentioning that these enantiomerically pure furanoid glycals and their precursors, which can be prepared in multi gram scale have proven to be versatile building blocks for diversity-oriented synthesis (DOS) of variety of natural products and molecules of biological importance.

4. Experimental section

4.1. General

Organic solvents were dried by standard methods. All the products were characterized by ^{1}H, ^{13}C, two-dimensional

homonuclear COSY (correlation spectroscopy), heteronuclear single quantum coherence (HSQC), heteronuclear multiple bond correlation spectroscopy (HMBC), IR, DART–HRMS, and EI-HRMS (C, H, O). Analytical TLC was performed using 2.5×5 cm plates coated with a 0.25 mm thickness of silica gel (60F-254), visualization was accomplished with $CeSO_4$ or 10% H_2SO_4/MeOH and subsequent charring over hot plate. Column chromatography was performed using silica gel (60–120 mesh) and silica gel (230–400 mesh). NMR spectra were recorded on Bruker Avance 200 MHz spectrometer at 200 MHz (^{1}H) and 50 MHz (^{13}C), Bruker Avance 300 MHz spectrometer at 300 MHz (^{1}H) and 75 MHz (^{13}C), 400 MHz spectrometer at 400 MHz (^{1}H) and 100 MHz (^{13}C), and Bruker Avance 600 MHz spectrometer at 600 MHz (^{1}H). Experiments were recorded in $CDCl_3$ or $CDCl_3$+CCl_4 1:1 mixture, methanol-d_4 and acetone-d_6 at 25 °C. Chemical shifts are given on the δ scale and are referenced to the TMS at 0.00 ppm for proton and 0.00 ppm for carbon. For ^{13}C NMR reference $CDCl_3$ appeared at 77.00 ppm. For ^{13}C NMR in $CDCl_3$+CCl_4 mixture CCl_4 appeared at 96.2 ppm. For ^{1}H NMR spectra methanol-d_4 appeared at 3.35 ppm and for ^{13}C NMR spectra methanol-d_4 appeared at 49.00 ppm. For ^{1}H NMR spectra acetone-d_6 appeared at 2.83 ppm and for ^{13}C NMR spectra acetone-d_6 appeared at 206.4 ppm. For IR spectra were recorded on Perkin–Elmer 881 and FTIR-8210 PC Shimadzu Spectrophotometers. Mass spectra were recorded on a JEOL JMS-600H high resolution spectrometer using EI mode at 70 eV. DART–HRMS were recorded on a JEOL-AccuTOF, JMS-T100LC spectrometer. Optical rotations were determined on an Autopol III polarimeter using a 1 dm cell at 25–32 °C in chloroform and methanol as the solvents; concentrations mentioned are in g/100 mL. Systematic (IUPAC) names of all the compounds have been given based on THF derivative.

4.2. General procedure for the synthesis of compounds 2a–d

To the glycal **1a** (515 mg, 1.86 mmol) in THF/H_2O (1:1, 10 mL) $Hg(OAc)_2$ (654 mg, 2.05 mmol) was added at 25 °C. The reaction mixture was stirred at the same temperature for 30 min and afterward the solution was kept at 0 °C for 15 min. To this reaction mixture 1.7 mL aqueous solution of KI (4.38 g, 0.026 mol in 5 mL water) was added and the reaction mixture was stirred for another 15 min. To the resulting reaction mixture at 0 °C, 4.4 mL aqueous solution of $NaBH_4$ (80 mg, 2.11 mmol in 5 mL water) was added drop wise over 15 min and it was stirred for 1.5 h. The insoluble part was removed by filtration through a bed of Celite and washed with EtOAc (3×5 mL). The filtrate was separated and the organic layer was washed successively with saturated aqueous solutions of KI, $Na_2S_2O_7$ and brine. The organic layer was separated and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to a residue, which was purified by column chromatography (60–120 mesh silica gel) to obtain furanose **2a** (538 mg, 98%, α:β=1:1) as a pale yellow syrup. Analogous protocol was adopted for the synthesis of **2b–d**.

*4.2.1. (4R,5S)-4-(Benzyloxy)-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl) tetrahydrofuran-2-ol (**2a**).* Pale yellow syrup; yield: 98% (α:β=1:0.6) (538 mg). Eluent for column chromatography: EtOAc/hexane (4/21, v/v); R_f=0.39 (1/2 EtOAc/hexane); IR (neat): ν=761, 1072, 1216, 1617, 1711, 2360, 2931, 3022, 3443 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.40–1.42 (5.4H, m, J=3.6 Hz, Me, Me_D), 1.45–1.46 (5.2H, m, J=4.4 Hz, Me, Me_D), 1.99–2.12 (2H, m), 2.25–2.29 (2H, m), 3.75 (1H, d, J=11.8 Hz, –OH), 3.89 (1H, dd, J=3.5, 7.9 Hz), 3.97–4.28 (5.8H, m), 4.39–4.62 (2.8H, m), 4.69 (2H, s), 5.39 (1H, dd, J=4.7, 11.5 Hz), 5.67–5.73 (0.6H, m), 7.29–7.37 (8H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.3 (CH_{3D}), 25.4 (CH_3), 26.6 (CH_{3D}), 26.7 (CH_3), 39.4 (CH_2), 40.5 (CH_{2D}), 66.7 (CH_{2D}), 67.4 (CH_2), 71.5 (CH_{2D}), 72.2 (CH_2), 73.4 (CH_D), 73.9 (CH), 78.0 (CH), 78.5 (CH_D), 80.9 (CH_D), 84.0 (CH), 98.1 (CH_D), 99.1 (CH), 108.6 (qC_D), 108.9 (qC), 127.4, 127.5, 127.7, 127.9, 128.3, 128.4 (ArC, ArC_D), 137.4 (ArqC), 138.1 ($ArqC_D$); EI-HRMS: $[M]^{+\bullet}$, found 294.1457. $C_{16}H_{22}O_5$ requires 294.1467.

*4.2.2. (4S,5R)-4-(Benzyloxy)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl) tetrahydrofuran-2-ol (**2b**).* Pale yellow syrup; yield: 82% (α:β=1:1) (450 mg). Eluent for column chromatography: EtOAc/hexane (4/21, v/v); R_f=0.40 (1/2 EtOAc/hexane); IR (neat): ν=761, 1072, 1216, 1617, 1711, 2360, 2931, 3443 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37–1.39 (6H, m, J=4.8 Hz, Me, Me_D), 1.42 (6H, br s, Me, Me_D), 1.96–2.07 (2H, m), 2.21–2.31 (2H, m), 3.79–3.83 (1H, m), 3.87 (1H, dd, J=3.5, 7.8 Hz), 3.93–4.09 (3H, m), 4.14–4.26 (4H, m), 4.36–4.47 (2H, m), 4.49 (1H, d, J=11.9 Hz), 4.56 (1H, d, J=11.9 Hz), 4.61–4.69 (2H, m), 5.37 (1H, dd, J=5.0, 11.5 Hz), 5.64–5.66 (1H, m), 7.26–7.36 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.3 (CH_{3D}), 25.4 (CH_3), 26.6 (CH_{3D}), 26.7 (CH_3), 39.4 (CH_2), 40.5 (CH_{2D}), 66.7 (CH_{2D}), 67.4 (CH_2), 71.5 (CH_{2D}), 72.2 (CH_2), 73.4 (CH_D), 73.8 (CH), 77.9 (CH), 78.6 (CH_D), 80.9 (CH_D), 83.9 (CH), 98.1 (CH_D), 99.1 (CH), 108.6 (qC_D), 108.9 (qC), 127.4, 127.5, 127.7, 127.9, 128.3, 128.4 (ArC, ArC_D), 137.4 (ArqC), 138.1 ($ArqC_D$); EI-HRMS: $[M-CH_3]^{+\bullet}$, found 279.1221. $C_{15}H_{19}O_5$ requires 279.1232.

*4.2.3. (4R,5R)-4-(Benzyloxy)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl) tetrahydrofuran-2-ol (**2c**).* Pale yellow syrup; yield: 73% (α:β=1:1) (400 mg). Eluent for column chromatography: EtOAc/hexane (4/21, v/v); R_f=0.38 (1/2 EtOAc/hexane); IR (neat): ν=670, 761, 1216, 1636, 2361, 3022, 3427 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.33 (6H, s, Me, Me_D), 1.44 (6H, s, Me, Me_D), 2.01–2.29 (4H, m), 3.70–3.80 (3H, m), 3.86–3.94 (2H, m), 4.06–4.12 (3H, m), 4.17–4.31 (4H, m), 4.52–4.65 (4H, m), 5.42 (1.4H, dd, J=4.6, 10.9 Hz), 5.56–5.61 (0.5H, m) 7.28–7.38 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.9 (CH_{3D}), 25.0 (CH_3), 26.5 (CH_{3D}), 26.7 (CH_3), 38.8 (CH_2), 41.0 (CH_{2D}), 66.5 (CH_{2D}), 67.1 (CH_2), 71.3 (CH_2, CH_{2D}), 75.2 (CH), 76.2 (CH_D), 79.3 (CH_D), 79.6 (CH), 84.8 (CH), 84.9 (CH_D), 99.3 (CH_D), 99.4 (CH), 109.7 (qC), 109.8 (qC_D), 127.7, 127.8, 127.9, 128.4, 128.5 (ArC, ArC_D), 137.3 (ArqC), 137.8 ($ArqC_D$); EI-HRMS: $[M]^{+\bullet}$, found 294.1451. $C_{16}H_{22}O_5$ requires 294.1467.

*4.2.4. (4S,5S)-4-(Benzyloxy)-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl) tetrahydrofuran-2-ol (**2d**).* Pale yellow syrup; yield: 98% (α:β=1:1) (538 mg). Eluent for column chromatography: EtOAc/hexane (4/21, v/v); R_f=0.39 (1/2 EtOAc/hexane); IR (neat): ν=765, 1217, 1597, 2361, 2858, 2926, 3409 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+CCl_4): δ 1.31, 1.34 (6H, 2s, Me, Me_D), 1.42 (6H, s, Me, Me_D), 1.98–2.24 (4H, m), 3.62–3.74 (3H, m), 3.84–3.91 (2H, m), 3.98–4.27 (7H, m), 4.49–4.64 (4H, m), 5.37 (1.4H, dd, J=4.5, 10.7 Hz), 5.53–5.54 (0.6H, m), 7.23–7.36 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$+CCl_4): δ 25.2 (Me_D), 25.2 (Me), 26.7 (Me_D), 26.9 (Me), 38.9 (CH_2), 40.9 (CH_{2D}), 66.7 (CH_{2D}), 67.2 (CH_2), 71.3 (CH_2, CH_{2D}), 75.3 (CH), 76.3 (CH_D), 79.6 (CH_D), 79.7 (CH), 84.8 (CH), 85.0 (CH_D), 99.2 (CH_D), 99.3 (CH), 109.6 (qC), 109.7 (qC_D), 127.7, 127.8, 127.9, 128.0, 128.4, 128.5 (ArC, ArC_D), 137.4 (ArqC), 138.0 ($ArqC_D$); EI-HRMS: $[M]^{+\bullet}$, found 294.1465. $C_{16}H_{22}O_5$ requires 294.1467.

4.3. General procedure for the synthesis of compounds 3a–d

PDC (640 mg, 1.70 mmol) was added to a stirred solution of compound **2a** (500 mg, 1.70 mmol) in dry DCM (15 mL) containing 4 Å molecular sieves. The reaction mixture was refluxed for 2 h. After completion of the reaction (TLC control), it was filtered through Celite bed, which was rinsed with DCM (3×5 mL). After removal of the organic solvent, the crude product was purified by column chromatography (60–120 mesh silica gel) to obtain lactones **3a** in 75% yield (374 mg). Similar reaction protocol was adopted for the synthesis of **3b–d**.

*4.3.1. (4R,5S)-4-(Benzyloxy)-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl) dihydrofuran-2(3H)-one (**3a**).* White solid; yield: 75% (374 mg); mp 57–60 °C. Eluent for column chromatography: EtOAc/hexane (3/22,

v/v); $[\alpha]_D^{25}$ +40.9 (*c* 0.43, MeOH); R_f=0.55 (3/7 EtOAc/hexane); IR (KBr): ν=690, 773, 1041, 1272, 1382, 1778, 2364, 2929, 3406 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.39 (3H, s), 1.44 (3H, s), 2.66–2.67 (2H, m), 4.02 (1H, dd, *J*=5.3, 8.9 Hz), 4.15 (1H, dd, *J*=6.2, 8.9 Hz), 4.30–4.33 (1H, m), 4.39 (1H, dd, *J*=3.8, 7.2 Hz), 4.47–4.51 (1H, m), 4.56 (1H, d, *J*=11.9 Hz), 4.63 (1H, d, *J*=11.9 Hz), 7.27–7.38 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.3 (CH_3), 26.7 (CH_3), 36.1 (CH_2), 66.7 (CH_2), 71.8 (CH_2), 72.4 (CH), 74.4 (CH), 83.5 (CH), 109.4 (qC), 127.6, 128.0, 128.5 (ArC), 137.2 (ArqC), 174.6 (C=O); EI-HRMS: $[M]^{+\bullet}$, found 292.1312. $C_{16}H_{20}O_5$ requires 292.1311.

*4.3.2. (4S,5R)-4-(Benzyloxy)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl) dihydrofuran-2(3H)-one (**3b**).* White solid; yield: 87% (434 mg); mp 55–57 °C. Eluent for column chromatography: EtOAc/hexane (3/22, v/v); $[\alpha]_D^{25}$ −34.1 (*c* 0.57, MeOH); R_f=0.55 (3/7 EtOAc/hexane); IR (KBr): ν=762, 1045, 1216, 1521, 1639, 1781, 2360, 2400, 2929, 3406 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+CCl_4): δ 1.38 (3H, s), 1.43 (3H, s), 2.56–2.69 (2H, m), 4.01 (1H, dd, *J*=5.3, 8.9 Hz), 4.14 (1H, dd, *J*=6.2, 8.9 Hz), 4.26–4.34 (2H, m), 4.45–4.52 (1H, m), 4.56 (1H, d, *J*=11.9 Hz), 4.63 (1H, d, *J*=11.9 Hz), 7.28–7.36 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$+CCl_4): δ 25.5 (CH_3), 26.9 (CH_3), 36.1 (CH_2), 66.8 (CH_2), 71.8 (CH_2), 72.3 (CH), 74.3 (CH), 83.4 (CH), 109.4 (qC), 127.7, 128.1, 128.5 (ArC), 137.2 (ArqC), 173.9 (C=O); EI-HRMS: $[M]^{+\bullet}$, found 292.1320. $C_{16}H_{20}O_5$ requires 292.1311.

*4.3.3. (4R,5R)-4-(Benzyloxy)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl) dihydrofuran-2(3H)-one (**3c**).* White solid; yield: 77% (384 mg); mp 84–86 °C. Eluent for column chromatography: EtOAc/hexane (3/22, v/v); $[\alpha]_D^{32}$ −3.35 (*c* 0.30, MeOH); R_f=0.52 (3/7 EtOAc/hexane); IR (KBr): ν=699, 764, 1071, 1158, 1258, 1377, 1782, 2340, 2368, 2928, 3040 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.34 (3H, s), 1.44 (3H, s), 2.61 (1H, dd, *J*=2.0, 18.3 Hz), 2.81 (1H, dd, *J*=6.9, 18.3 Hz), 3.83–3.92 (1H, m), 4.06–4.15 (2H, m), 4.29–4.32 (1H, m), 4.44 (1H, dd, *J*=1.4, 6.2 Hz), 4.55 (2H, br s), 7.28–7.39 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.6 (CH_3), 26.4 (CH_3), 34.9 (CH_2), 66.1 (CH_2), 71.1 (CH_2), 74.4 (CH), 74.7 (CH), 85.1 (CH), 110.3 (qC), 127.7, 128.1, 128.5 (ArC), 136.9 (ArqC), 174.9 (C=O); EI-HRMS: $[M-CH_3]^{+\bullet}$, found 277.1063. $C_{15}H_{17}O_5$ requires 277.1076.

*4.3.4. (4S,5S)-4-(Benzyloxy)-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl) dihydrofuran-2(3H)-one (**3d**).* White solid; yield: 77% (384 mg); mp 85–87 °C. Eluent for column chromatography: EtOAc/hexane (3/22, v/v); $[\alpha]_D^{32}$ +1.95 (*c* 0.13, $CHCl_3$); R_f=0.55 (3/7 EtOAc/hexane); IR (KBr): ν=761, 1216, 1597, 1784, 2360, 2926, 3020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+CCl_4): δ 1.32 (3H, s), 1.42 (3H, s), 2.56 (1H, dd, *J*=2.1, 18.2 Hz), 2.75 (1H, dd, *J*=6.9, 18.2 Hz), 3.84 (1H, dd, *J*=4.4, 8.2 Hz), 3.99–4.12 (2H, m), 4.25–4.28 (1H, m), 4.38 (1H, dd, *J*=1.1, 6.3 Hz), 4.53 (2H, br s), 7.25–7.33 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$+CCl_4): δ 24.8 (CH_3), 26.6 (CH_3), 34.9 (CH_2), 66.4 (CH_2), 71.1 (CH_2), 74.6 (CH), 74.8 (CH), 85.0 (CH), 110.3 (qC), 127.8, 128.1, 128.6 (ArC), 137.1 (ArqC), 174.1 (C=O); EI-HRMS: $[M]^{+\bullet}$, found 292.1287. $C_{16}H_{20}O_5$ requires 292.1311.

4.4. General procedure for the synthesis of compounds 6a–d

Compound **3a** (374 mg, 1.28 mmol) was dissolved in 60% aqueous AcOH solution (10 mL) and it was stirred at room temperature for 18–20 h. After completion of the reaction (TLC control), the reaction mixture was concentrated in vacuum. Toluene was added to it and co-evaporated under reduced pressure to obtain diol **4a** as a white solid (295 mg), which was used for mesylation without further purification.

To a stirred solution of compound **4a** (295 mg, 1.17 mmol) in pyridine at 0 °C, methanesulfonyl chloride (MsCl) (0.27 mL, 3.51 mmol) was added drop wise over 15 min and stirring was continued at 0 °C for 3 h. The reaction mixture was diluted with water to separate the organic layer. The aqueous layer was washed with DCM (2×5 mL) and the combined organic layer was dried over anhydrous Na_2SO_4 and concentrated to obtain the crude product, which was used as such for next step without further purification.

To the mesylated crude compound **5a** in butan-2-one (15 mL), NaI (418 mg, 2.78 mmol) was added and the reaction mixture was stirred for 12 h under refluxing condition. Solvent was removed under vacuum after completion of the reaction. Saturated aqueous $Na_2S_2O_7$ solution (10 mL) was added to the residue and the mixture was extracted with diethyl ether (3×5 mL). The combined organic extract was dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by column chromatography (60–120 mesh silica gel) to obtain a white solid **6a** (214 mg, 77% for three steps). The synthesis of **6b–d** was completed by adopting the similar reaction sequences.

*4.4.1. (4R,5R)-4-(Benzyloxy)-5-((R)-1,2-dihydroxyethyl)dihydrofuran-2(3H)-one (**4a**).* White solid. R_f=0.21 (1/1 EtOAc/hexane); IR (KBr): ν=690, 771, 1168, 1209, 1339, 1781, 2365, 3434 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 2.62–2.68 (1H, m), 2.81 (1H, dd, *J*=4.5, 17.7 Hz), 3.65 (1H, dd, *J*=5.1, 11.7 Hz), 3.79 (1H, dd, *J*=2.6, 11.7 Hz), 4.03–4.09 (1H, m), 4.41–4.45 (2H, m), 4.57–4.66 (2H, m), 7.24–7.38 (5H, m); ^{13}C NMR (75 MHz, CD_3OD): δ 37.1 (CH_2), 64.8 (CH_2), 69.5 (CH), 72.7 (CH_2), 76.4 (CH), 83.8 (CH), 128.8, 128.9, 129.4 (ArC), 139.3 (ArqC), 177.8 (C=O); EI-HRMS: $[M]^{+\bullet}$, found 252.0996. $C_{13}H_{16}O_5$ requires 252.0998.

*4.4.2. (4R,5R)-4-(Benzyloxy)-5-vinyldihydrofuran-2(3H)-one (**6a**).* White solid; yield: 77% for three steps (214 mg); mp 52–54 °C. Eluent for column chromatography: EtOAc/hexane (3/22, v/v); $[\alpha]_D^{25}$ −2.17 (*c* 0.50, MeOH); R_f=0.40 (3/7 EtOAc/hexane); IR (KBr): ν=698, 738, 1023, 1157, 1208, 1773, 2366, 2857, 2943 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.60 (2H, d, *J*=4.4 Hz), 4.21 (1H, dd, *J*=4.5, 8.9 Hz), 4.42 (1H, d, *J*=12.0 Hz), 4.49 (1H, d, *J*=12.0 Hz), 4.80–4.84 (1H, m), 5.37 (2H, dd, *J*=17.3, 21.1 Hz), 5.95–6.07 (1H, m), 7.18–7.30 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.6 (CH_2), 71.7 (CH_2), 75.9 (CH), 83.9 (CH), 120.0 (CH_2), 127.5, 127.9, 128.5 (ArC), 131.2 (CH), 137.0 (ArqC), 174.6 (C=O); DART–HRMS: $[M+H]^{+\bullet}$, found 219.1037. $C_{13}H_{15}O_3$ requires 219.1021.

*4.4.3. (4S,5S)-4-(Benzyloxy)-5-((S)-1,2-dihydroxyethyl)dihydro-furan-2(3H)-one (**4b**).* White solid. R_f=0.20 (1/1 EtOAc/hexane); IR (neat): ν=766, 1044, 1216, 1522, 1648, 1779, 2361, 3021, 3423 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 2.58–2.64 (1H, m), 2.78 (1H, dd, *J*=4.6, 17.7 Hz), 3.61 (1H, dd, *J*=5.1, 11.7 Hz), 3.75 (1H, dd, *J*=2.6, 11.7 Hz), 3.99–4.08 (1H, m), 4.34–4.41 (2H, m), 4.52–4.67 (2H, m), 7.23–7.35 (5H, m); ^{13}C NMR (75 MHz, CD_3OD): δ 37.1 (CH_2), 64.8 (CH_2), 69.5 (CH), 72.7 (CH_2), 76.4 (CH), 83.7 (CH), 128.8, 128.9, 129.2, 129.4 (ArC), 139.3 (ArqC), 177.8 (C=O); EI-HRMS: $[M]^{+\bullet}$, found 252.0988. $C_{13}H_{16}O_5$ requires 252.0998.

*4.4.4. (4S,5S)-4-(Benzyloxy)-5-vinyldihydrofuran-2(3H)-one (**6b**).* Pale yellow solid; yield: 72% for three steps (200 mg); mp 54–56 °C. Eluent for column chromatography: EtOAc/hexane (3/22, v/v); $[\alpha]_D^{25}$ +1.0 (*c* 0.30, MeOH); R_f=0.40 (3/7 EtOAc/hexane); IR (KBr): ν=763, 1216, 1522, 1645, 1777, 2359, 3021, 3430 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.62 (2H, d, *J*=4.5 Hz), 4.22 (1H, dd, *J*=4.6, 9.2 Hz), 4.44 (1H, d, *J*=12.0 Hz), 4.51 (1H, d, *J*=12.0 Hz), 4.82–4.86 (1H, m), 5.34–5.44 (2H, m), 5.97–6.08 (1H, m), 7.19–7.32 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.6 (CH_2), 71.7 (CH_2), 75.9 (CH), 83.9 (CH), 120.1 (CH_2), 127.5, 128.0, 128.5 (ArC), 131.2 (CH), 137.0 (ArqC), 174.6 (C=O); DART–HRMS: $[M+NH_4]^{+\bullet}$, found 236.1319. $C_{13}H_{18}NO_3$ requires 236.1287.

*4.4.5. (4R,5S)-4-(Benzyloxy)-5-((S)-1,2-dihydroxyethyl)dihydrofuran-2(3H)-one (**4c**).* White solid. R_f=0.21 (1/1 EtOAc/hexane); IR (KBr): ν=675, 770, 1218, 1778, 2361, 3432 cm^{-1}; ^1H NMR

(300 MHz, CD_3OD): δ 2.54–2.60 (1H, m), 2.95 (1H, dd, J=6.8, 18.2 Hz), 3.64 (2H, d, J=5.8 Hz), 3.82 (1H, dd, J=5.6, 10.3 Hz), 4.46 (1H, d, J=6.8 Hz), 4.62 (2H, br s), 4.69 (1H, d, J=3.9 Hz), 7.33–7.40 (5H, m); ^{13}C NMR (75 MHz, CD_3OD): δ 36.7 (CH_2), 63.6 (CH_2), 71.8 (CH_2), 72.5 (CH), 75.7 (CH), 87.6 (CH), 128.9, 129.0, 129.5 (ArC), 139.1 (ArqC), 178.5 (C=O); EI-HRMS: $[M+H]^+$•, found 253.1078. $C_{13}H_{17}O_5$ requires 253.1076.

*4.4.6. (4R,5S)-4-(Benzyloxy)-5-vinyldihydrofuran-2(3H)-one (**6c**).* Pale yellow syrup; yield: 73% for three steps (203 mg). Eluent for column chromatography: EtOAc/hexane (3/22, v/v); $[\alpha]_D^{25}$ −82.9 (c 0.50, MeOH); R_f=0.30 (1/4 EtOAc/hexane); IR (neat): ν=670, 762, 1216, 1636, 1782, 2364, 3023 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.58 (1H, dd, J=3.3, 17.9 Hz), 2.74 (1H, dd, J=6.4, 17.9 Hz), 4.04–4.09 (1H, m), 4.57 (2H, br s), 4.97–4.98 (1H, m), 5.29 (1H, d, J=10.6 Hz), 5.41 (1H, d, J=17.2 Hz), 5.77–5.88 (1H, m), 7.31–7.40 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.3 (CH_2), 71.5 (CH_2), 78.2 (CH), 84.5 (CH), 117.9 (CH_2), 127.7, 128.1, 128.6 (ArC), 133.2 (CH), 136.9 (ArqC), 174.6 (C=O); DART–HRMS: $[M+H]^+$•, found 219.1040. $C_{13}H_{15}O_3$ requires 219.1021.

*4.4.7. (4S,5R)-4-(Benzyloxy)-5-((R)-1,2-dihydroxyethyl)-dihydrofuran-2(3H)-one (**4d**).* White solid; R_f=0.21 (1/1 EtOAc/hexane); IR (KBr): ν=762, 1216, 1348, 1597, 1783, 2361, 3021, 3409 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD): δ 2.51–2.57 (1H, m), 2.92 (1H, dd, J=6.8, 18.2 Hz), 3.60 (2H, d, J=5.8 Hz), 3.78 (1H, dd, J=5.8, 10.1 Hz), 4.43 (1H, d, J=6.7 Hz), 4.59–4.67 (3H, m), 7.29–7.37 (5H, m); ^{13}C NMR (75 MHz, CD_3OD): δ 36.7 (CH_2), 63.6 (CH_2), 71.8 (CH_2), 72.5 (CH), 75.7 (CH), 87.6 (CH), 128.9, 129.0, 129.5 (ArC), 139.1 (ArqC), 178.5 (C=O); EI-HRMS: $[M]^+$•, found 252.1002. $C_{13}H_{16}O_5$ requires 252.0998.

*4.4.8. (R)-1-((2S,3S)-3-(Benzyloxy)-5-oxotetrahydrofuran-2-yl)ethane-1,2-diyl dimethanesulfonate (**5d**).* Purification of a small amount of crude product by column chromatography for data afforded pure mesylated-ester **5d** (350 mg, 65% yield, for two steps) as a white solid; mp 120–122 °C. Eluent for column chromatography: MeOH/$CHCl_3$ (1/49, v/v); $[\alpha]_D^{25}$ +11.5 (c 0.26, $CHCl_3$); R_f=0.45 (1/1 EtOAc/hexane); IR (KBr): ν=761, 1216, 1361, 1793, 2360, 3020 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+CCl_4): δ 2.63 (1H, dd, J=3.4, 18.4 Hz), 2.82 (1H, dd, J=7.0, 18.2 Hz), 3.06 (3H, s), 3.09 (3H, s), 4.35 (1H, dd, J=5.6, 11.7 Hz), 4.42–4.52 (2H, m), 4.57–4.62 (3H, m), 4.82–4.87 (1H, m), 7.31–7.39 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.8 (CH_2), 37.7 (CH_3), 38.8 (CH_3), 66.5 (CH_2), 71.9 (CH_2), 74.1 (CH), 76.0 (CH), 81.2 (CH), 128.0, 128.4, 128.7 (ArC), 136.4 (ArqC), 173.4 (C=O); EI-HRMS: $[M]^+$•, found 408.0544. $C_{15}H_{20}O_9S_2$ requires 408.0549.

*4.4.9. (4S,5R)-4-(Benzyloxy)-5-vinyldihydrofuran-2(3H)-one (**6d**).* Pale yellow syrup; yield: 92% (160 mg) (starting dimesyl derivative was 325 mg). Eluent for column chromatography: EtOAc/hexane (3/22, v/v); $[\alpha]_D^{25}$ +14.4 (c 0.17, MeOH); R_f=0.32 (1/4 EtOAc/hexane); IR (neat): ν=760, 1216, 1354, 1782, 2361, 3020 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.58 (1H, dd, J=3.3, 17.8 Hz), 2.73 (1H, dd, J=6.4, 17.9 Hz), 4.04–4.08 (1H, m), 4.57 (2H, br s), 4.96–4.97 (1H, m), 5.29 (1H, d, J=10.6 Hz), 5.41 (1H, d, J=17.1 Hz), 5.77–5.88 (1H, m), 7.30–7.36 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.3 (CH_2), 71.5 (CH_2), 78.2 (CH), 84.5 (CH), 118.0 (CH_2), 127.7, 128.2, 128.6 (ArC), 133.2 (CH), 136.8 (ArqC), 174.7 (C=O); EI-HRMS: $[M]^+$•, found 218.0930. $C_{13}H_{14}O_3$ requires 218.0943.

4.5. General procedure for the synthesis of compounds 7a–d

Diisobutylaluminum hydride (1.0 M) in toluene (1.37 mL, 1.37 mmol) was added drop wise to a stirred solution of lactone **6a** (200 mg, 0.92 mmol) in dry toluene (2 mL) at −78 °C. The reaction mixture was stirred for 2 h at −78 °C under an atmosphere of nitrogen. The reaction was quenched with water (20 mL) and allowed to warm to bring it at room temperature. Saturated aqueous sodium/potassium tartrate solution (2 mL) was added and the resulting mixture was stirred for 1 h after which the product was extracted with EtOAc (3×5 mL). The combined organic extract was dried over Na_2SO_4, concentrated in vacuo. The residue obtained was purified by flash column chromatography (230–400 mesh) to afford the protected lactol **7a** (173 mg, 86%). Similar reaction protocol was adopted for the synthesis of **7b**–**d**.

*4.5.1. (4R,5R)-4-(Benzyloxy)-5-vinyltetrahydrofuran-2-ol (**7a**).* Brown syrup; yield: 86% (α:β=1:0.3) (173 mg). Eluent for column chromatography: EtOAc/hexane (7/43, v/v); R_f=0.39 (3/7 EtOAc/hexane); IR (neat): ν=696, 770, 1107, 1219, 1636, 2362, 3421 cm^{-1}; ^{1}H NMR (300 MHz, $(CD_3)_2C$=O): δ 1.91–2.00 (2H, m, 1H+solvent), 2.03–2.05 (0.2H, m), 2.09–2.21 (1.3H, m), 4.05–4.09 (0.3H, m), 4.13–4.18 (1H, m), 4.27–4.31 (0.3H, m), 4.36–4.54 (3.5H, m), 5.07–5.30 (3.8H, m), 5.48–5.50 (1H, m), 5.88–6.10 (1.3H, m), 7.14–7.26 (6.4H, m); ^{13}C NMR (75 MHz, $(CD_3)_2C$=O): δ 40.1 (CH_{2D}), 41.3 (CH_2), 71.8 (CH_2), 72.0 (CH_{2D}), 80.5 (CH_D), 81.3 (CH), 81.9 (CH), 83.8 (CH_D), 98.0 (CH), 98.9 (CH_D), 117.0 (CH_2, CH_{2D}), 128.1, 128.2, 128.25, 128.29, 128.9, 129.1 (ArC, ArC_D), 136.2 (CH), 137.2 (CH_D), 139.4 ($ArqC_D$), 139.7 (ArqC); DART–HRMS: $[M-OH]^+$•, found 203.1058. $C_{13}H_{15}O_2$ requires 203.1072.

*4.5.2. (4S,5S)-4-(Benzyloxy)-5-vinyltetrahydrofuran-2-ol (**7b**).* Pale yellow syrup; yield: 82% (α:β=1:0.3) (165 mg). Eluent for column chromatography: EtOAc/hexane (7/43, v/v); R_f=0.37 (3/7 EtOAc/hexane); IR (neat): ν=763, 1216, 1636, 2361, 2931, 3021, 3429 cm^{-1}; ^{1}H NMR (300 MHz, $(CD_3)_2C$=O): δ 1.91–2.00 (1.7H, m, 1H+solvent), 2.03–2.05 (0.2H, m), 2.09–2.21 (1.3H, m), 4.05–4.09 (0.3H, m), 4.13–4.18 (1H, m), 4.27–4.31(0.3H, m), 4.36–4.53 (3.6H, m), 5.06–5.11 (2H, m), 5.19–5.30 (1.6H, m), 5.49–5.53 (1H, m), 5.89–6.11 (1.2H, m), 7.13–7.28 (6.3H, m); ^{13}C NMR (75 MHz, $(CD_3)_2C$=O): δ 40.2 (CH_{2D}), 41.3 (CH_2), 71.8 (CH_2), 72.1 (CH_{2D}), 80.6 (CH_D), 81.4 (CH), 81.9 (CH), 83.8 (CH_D), 98.0 (CH), 98.9 (CH_D), 117.0 (CH_2, CH_{2D}), 128.0, 128.1, 128.2, 128.3, 128.9, 129.0 (ArC, ArC_D), 136.2 (CH), 137.3 (CH_D), 139.4 ($ArqC_D$), 139.8 (ArqC); DART–HRMS: $[M-OH]^+$•, found 203.1068. $C_{13}H_{15}O_2$ requires 203.1072.

*4.5.3. (4R,5S)-4-(Benzyloxy)-5-vinyltetrahydrofuran-2-ol (**7c**).* Colorless oil; yield: 94% (α:β=1:1) (189 mg). Eluent for column chromatography: EtOAc/hexane (7/43, v/v); R_f=0.40 (2/3 EtOAc/hexane); IR (neat): ν=670, 763, 1216, 1631, 2364, 2927, 3021, 3432 cm^{-1}; ^{1}H NMR (300 MHz, $(CD_3)_2C$=O): δ 1.81–1.88 (1H, m), 1.95–2.00 (4H, m, $1H_D$+solvent), 2.18–2.27 (1H, m), 3.77–3.82 (1H, m), 3.95–4.00 (1H, m), 4.25–4.28 (1H, m), 4.48 (5H, d, J=8.7 Hz), 4.79–4.87 (1H, m, −OH), 4.97–5.03 (2H, m), 5.17–5.29 (2H, m), 5.33–5.39 (2H, m), 5.46 (1H, dd, J=3.9, 8.1 Hz), 5.71–5.94 (2H, m), 7.17–7.29 (10H, m); ^{13}C NMR (75 MHz, $(CD_3)_2C$=O): δ 39.9 (CH_2), 40.4 (CH_{2D}), 71.9 (CH_2), 72.1 (CH_{2D}), 83.4 (CH), 83.6 (CH_D), 83.8 (CH), 85.2 (CH_D), 98.8 (CH), 99.4 (CH_D), 115.8 (CH_2), 115.9 (CH_{2D}), 128.2, 128.3, 128.4, 128.5, 129.06, 129.09 (ArC, ArC_D), 138.3 (CH), 139.4 (ArqC), 139.6 ($ArqC_D$), 140.3 (CH_D); DART–HRMS: $[M-OH]^+$•, found 203.1085. $C_{13}H_{15}O_2$ requires 203.1072.

*4.5.4. (4S,5R)-4-(Benzyloxy)-5-vinyltetrahydrofuran-2-ol (**7d**).* Colorless oil; 90% (181 mg) (α:β=1:1). Eluent for column chromatography: EtOAc/hexane (7/43, v/v); R_f=0.40 (2/3 EtOAc/hexane); IR (neat): ν=762, 1216, 1637, 1711, 2361, 3021, 3442 cm^{-1}; ^{1}H NMR (300 MHz, $(CD_3)_2C$=O): δ 1.82–1.88 (1H, m), 1.94–2.00 (3H, m, $1H_D$+solvent), 2.17–2.26 (1H, m), 3.77–3.82 (1H, m), 3.95–4.00 (1H, m), 4.25–4.28 (1H, m), 4.48 (5H, d, J=8.6 Hz), 4.69 (1H, d, J=6.8 Hz, −OH), 4.97–5.03 (2H, m), 5.17–5.29 (3H, m), 5.35–5.39 (1H, m), 5.46 (1H, dd, J=4.2, 8.5 Hz), 5.71–5.92 (2H, m), 7.16–7.29 (10H, m); ^{13}C NMR (75 MHz, $(CD_3)_2C$=O): δ 40.0 (CH_2),

40.5 (CH_{2D}), 71.9 (CH_2), 72.1 (CH_{2D}), 83.5 (CH), 83.6 (CH_D), 83.8 (CH), 85.2 (CH_D), 98.9 (CH), 99.4 (CH_D), 115.8 (CH_2), 115.9 (CH_{2D}), 128.2, 128.3, 128.4, 128.5, 129.06, 129.1 (ArC, ArC_D), 138.3 (CH), 139.5 (ArqC), 139.6 ($ArqC_D$), 140.3 (CH_D); DART−HRMS: $[M]^{+\bullet}$, found 220.1087. $C_{13}H_{16}O_3$ requires 220.1099.

4.6. General procedure for the synthesis of compounds 8a–d

To the lactol **7a** (146 mg, 0.66 mmol) in dry toluene (20 mL), 1-(triphenylphosphoranylidene)-2-propanone ($Ph_3PCHCOCH_3$) (317 mg, 0.99 mmol) was added and the solution was heated to reflux till the completion of reaction (TLC viewed by UV light), which took 2 h. The reaction mixture was cooled to room temperature and solvent was removed under vacuum. The resulting residue was used as such for next step without further purification.

The above residue in 50 mL round bottomed flask was immediately dissolved in absolute ethanol. Raney-Ni as a catalyst was added to this solution. A vacuum was created in the round bottomed flask containing the above reaction mixture with the help of pump and the mixture was stirred under H_2 in a balloon at 1 atm. After the completion of the reaction (TLC, 2 h) catalyst was removed by filtration, washed with methanol twice and the combined filtrate was concentrated and purified by silica gel (230–400 mesh) column chromatography to afford **8a** as a pale yellow syrup (91 mg, 52% for two steps). The synthesis of **8b**–**d** was achieved by adopting the similar reaction protocol.

*4.6.1. (6R,7R)-6-(Benzyloxy)-7-hydroxynonan-2-one (**8a**).* Pale yellow syrup; yield: 52% for two steps (91 mg). Eluent for column chromatography: EtOAc/hexane (1/9, v/v); $[\alpha]_D^{25}$ −8.54 (*c* 1.02, $CHCl_3$) [lit. $[\alpha]_D^{27}$ −12.8 (*c* 1.3, $CHCl_3$)][6i,k]; R_f=0.60 (3/7 EtOAc/hexane); IR (neat): ν=767, 1088, 1218, 1639, 1706, 2363, 2925, 3422 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.00 (3H, t, *J*=7.4 Hz), 1.56–1.74 (6H, m), 2.16 (3H, s), 2.47 (2H, t, *J*=6.7 Hz), 3.31–3.36 (1H, m), 3.50–3.51 (1H, m), 4.54 (1H, d, *J*=11.4 Hz), 4.68 (1H, d, *J*=11.3 Hz), 7.30–7.44 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.2 (CH_3), 19.3 (CH_2), 26.3 (CH_2), 29.7 (CH_2), 29.9 (CH_3), 43.6 (CH_2), 72.5 (CH_2), 73.9 (CH), 81.6 (CH), 127.8, 127.9, 128.5 (ArC), 138.3 (ArqC), 208.7 (C=O); DART−HRMS: $[M-OH]^{+\bullet}$, found 247.1699. $C_{16}H_{23}O_2$ requires 247.1698.

*4.6.2. (6S,7S)-6-(Benzyloxy)-7-hydroxynonan-2-one (**8b**).* Pale yellow syrup; yield: 67% for two steps (117 mg). Eluent for column chromatography: EtOAc/hexane (1/9, v/v); $[\alpha]_D^{25}$ +10.48 (*c* 0.85, $CHCl_3$) [lit. $[\alpha]_D^{20}$ +13.0 (*c* 1.7, $CHCl_3$)][5q]; R_f=0.60 (3/7 EtOAc/hexane); IR (neat): ν=761, 1072, 1216, 1617, 1711, 2360, 2931, 3443 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.97 (3H, t, *J*=7.4 Hz), 1.49–1.69 (6H, m), 2.12 (3H, s), 2.44 (2H, t, *J*=6.8 Hz), 3.28–3.33 (1H, m), 3.45–3.51 (1H, m), 4.51 (1H, d, *J*=11.3 Hz), 4.65 (1H, d, *J*=11.3 Hz), 7.31–7.35 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.2 (CH_3), 19.3 (CH_2), 26.4 (CH_2), 29.7 (CH_2), 29.9 (CH_3), 43.6 (CH_2), 72.5 (CH_2), 73.9 (CH), 81.7 (CH), 127.8, 127.9, 128.5 (ArC), 138.3 (ArqC), 208.7 (C=O); EI-HRMS: $[M]^{+\bullet}$, found 264.1723. $C_{16}H_{24}O_3$ requires 264.1726.

*4.6.3. (6R,7S)-6-(Benzyloxy)-7-hydroxynonan-2-one (**8c**).* Yellow syrup; yield: 35% for two steps (61 mg). Eluent for column chromatography: EtOAc/hexane (1/9, v/v); $[\alpha]_D^{25}$ +9.81 (*c* 0.46, $CHCl_3$); R_f=0.28 (2/3 EtOAc/hexane); IR (neat): ν=670, 761, 1631, 2362, 3021, 3425 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 0.98 (3H, t, *J*=7.4 Hz), 1.49–1.68 (6H, m), 2.11 (3H, s), 2.39–2.43 (2H, m), 3.33–3.38 (1H, m), 3.72–3.77 (1H, m), 4.53 (1H, d, *J*=11.4 Hz), 4.61 (1H, d, *J*=11.5 Hz), 7.29–7.35 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.6 (CH_3), 19.9 (CH_2), 25.1 (CH_2), 27.9 (CH_2), 29.9 (CH_3), 43.6 (CH_2), 71.8 (CH_2), 72.9 (CH), 81.6 (CH), 127.8, 127.9, 128.5 (ArC), 138.3 (ArqC), 209.0 (C=O); DART−HRMS: $[M-OH]^{+\bullet}$, found 247.1701. $C_{16}H_{23}O_2$ requires 247.1698.

*4.6.4. (6S,7R)-6-(Benzyloxy)-7-hydroxynonan-2-one (**8d**).* Pale yellow syrup; yield: 40% for two steps (70 mg). Eluent for column chromatography: EtOAc/hexane (1/9, v/v); $[\alpha]_D^{25}$ −9.81 (*c* 0.33, $CHCl_3$); R_f=0.40 (3/7 EtOAc/hexane); IR (neat): ν=763, 1216, 1636, 2363, 3021, 3429 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.98 (3H, t, *J*=7.4 Hz), 1.45–1.61 (6H, m), 2.11 (3H, s), 2.39–2.43 (2H, m), 3.33–3.37 (1H, m), 3.69–3.75 (1H, m), 4.53 (1H, d, *J*=11.4 Hz), 4.61 (1H, d, *J*=11.4 Hz), 7.29–7.35 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.5 (CH_3), 19.9 (CH_2), 25.1 (CH_2), 27.9 (CH_2), 29.9 (CH_3), 43.6 (CH_2), 71.8 (CH_2), 72.9 (CH), 81.7 (CH), 127.8, 127.9, 128.5 (ArC), 138.3 (ArqC), 208.9 (C=O); DART−HRMS: $[M+H]^{+\bullet}$, found 265.1775. $C_{16}H_{25}O_3$ requires 265.1804.

4.7. General procedure for the synthesis of compounds 9a–d

To a round bottomed flask containing the compound **8a** (19 mg, 0.072 mmol) in methanol (5 mL) were added catalytic amount of 10% Pd/C (5 mg) and 0.02 mL of 3 N HCl at room temperature. A vacuum was created in this flask containing the above reaction mixture with the help of pump and was stirred under H_2 in a balloon at 1 atms. After the completion of the reaction (TLC, 24 h) catalyst was removed by filtration, washed with methanol twice and the combined filtrate was concentrated on a rotary evaporator at 20 °C to afford (+)-*exo*-brevicomin **9a** (5 mg, 44%). It was immediately submitted for recording the data due to its volatile nature. Analogous reaction protocol was adopted for the synthesis of **9b**–**d**.

*4.7.1. (+)-exo-Brevicomin (**9a**).* Yield: 44% (5 mg). $[\alpha]_D^{29}$ +16.0 (*c* 0.17, $CHCl_3$) [lit. $[\alpha]_D^{27}$ +59.0 (*c* 2.5, $CHCl_3$)][5i]; IR (neat): ν=770, 1091, 1218, 1461, 2857, 2922 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.90–0.98 (3H, m), 1.26 (3H, s), 1.41–1.78 (6H, m), 2.17–2.29 (2H, m), 3.93–4.02 (2H, m); DART−HRMS: $[M+H]^{+\bullet}$, found 157.1224. $C_9H_{17}O_2$ requires 157.1229.

*4.7.2. (−)-exo-Brevicomin (**9b**).* Yield: 36% (4 mg). $[\alpha]_D^{29}$ −31.9 (*c* 0.40, Et_2O)[lit. $[\alpha]_D^{29}$ −60.0 (*c* 2.57, Et_2O)][5l]; IR (neat): ν=770, 1090, 1218, 1461, 2857, 2922 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.90–0.98 (3H, m), 1.26 (3H, s), 1.41–1.78 (6H, m), 2.17–2.29 (2H, m), 3.93–4.02 (2H, m); DART−HRMS: $[M+H]^{+\bullet}$, found 157.1243. $C_9H_{17}O_2$ requires 157.1229.

*4.7.3. (+)-endo-Brevicomin (**9c**).* Yield: 44% (5 mg). $[\alpha]_D^{30}$ +20.4 (*c* 0.23, $CHCl_3$) [lit. $[\alpha]_D^{25}$ +64.2 (*c* 2.3, Et_2O), $[\alpha]_D^{22}$ +39.5 (*c* 1.00, Et_2O)][4e,f]; IR (neat): ν=768, 1045, 1114, 1218, 1464, 2854, 2923 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.90–0.98 (3H, m), 1.46 (3H, s), 1.82–2.02 (6H, m), 2.13–2.34 (2H, m), 3.76–3.85 (1H, m), 4.15–4.21 (1H, m); DART−HRMS: $[M+H]^{+\bullet}$, found 157.1233. $C_9H_{17}O_2$ requires 157.1229.

*4.7.4. (−)-endo-Brevicomin (**9d**).* Yield: 36% (4 mg). $[\alpha]_D^{30}$ −42.1 (*c* 0.28, $CHCl_3$) [lit. $[\alpha]_D^{25}$ −78.9 (*c* 0.99, Et_2O)][5p]; IR (neat): ν=768, 1045, 1114, 1218, 1464, 2854, 2923 cm^{-1}; 1H NMR (300 MHz, $CDCl_3$): δ 0.90–0.98 (3H, m), 1.46 (3H, s), 1.82–2.02 (6H, m), 2.13–2.34 (2H, m), 3.76–3.85 (1H, m), 4.15–4.21 (1H, m); DART−HRMS: $[M+H]^{+\bullet}$, found 157.1222. $C_9H_{17}O_2$ requires 157.1229.

4.8. General procedure for the synthesis of compound 10a,b

To a 50 mL two necked oven dried round bottomed flask fitted with a reflux condenser and septum was added Grubbs' second generation catalyst (50 mg, 0.058 mmol) under argon atmosphere. Dry degassed DCM (3 mL) was then added to the above solution through a syringe and it was kept for stirring. Compound **6a** (500 mg, 2.29 mmol) and (*S*)-1-phenyl-2-propene-1-ol (282 mg, 2.10 mmol) in DCM (2 mL each) were added simultaneously

through a syringe to the stirring solution. The septum was replaced with a glass stopper while the stirring was continued. The solution was refluxed for 8 h. The temperature of the mixture was cooled slowly to room temperature. The organic solvent was evaporated under reduced pressure to give a brown residue, which was purified by column chromatography (230–400 mesh) to give **10a** as a white solid (557 mg, 74%). Similar reaction protocol was adopted for the synthesis of **10b**. In this case metathesis was performed between compound **6b** and (*R*)-1-phenyl-2-propene-1-ol in dry DCM.

*4.8.1. (4R,5R)-4-(Benzyloxy)-5-((S,E)-3-hydroxy-3-phenylprop-1-enyl)dihydrofuran-2(3H)-one (**10a**).* White solid; yield: 74% (557 mg); mp 95–98 °C. Eluent for column chromatography: EtOAc/hexane (4/21, v/v); $[\alpha]_D^{31}$ +1.00 (*c* 0.32, MeOH); R_f=0.27 (2/3 EtOAc/hexane); IR (KBr): ν=771, 1217, 1461, 1543, 1651, 1750, 2359, 2924, 3021, 3441 cm^{-1}; ^1H NMR(300 MHz, $CDCl_3$): δ 2.68 (2H, d, *J*=4.3 Hz), 4.27 (1H, dd, *J*=4.5, 8.9 Hz), 4.48 (1H, d, *J*=12.0 Hz), 4.57 (1H, dd, *J*=12.0 Hz), 4.92–4.95 (1H, m), 5.29–5.30 (1H, m), 6.01–6.14 (2H, m), 7.26–7.38 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.7 (CH_2), 71.7 (CH_2), 73.9 (CH), 75.9 (CH), 83.4 (CH), 123.3 (CH), 126.3, 127.6, 127.9, 128.0, 128.5, 128.6 (ArC), 137.0 (ArqC), 137.9 (CH), 141.9 (ArqC), 174.6 (C=O); DART–HRMS: $[M-OH]^+$•, found 307.1333. $C_{20}H_{19}O_3$ requires 307.1334.

*4.8.2. (4S,5S)-4-(Benzyloxy)-5-((R,E)-3-hydroxy-3-phenylprop-1-enyl)dihydrofuran-2(3H)-one (**10b**).* White solid; yield: 74% (557 mg); mp 98–100 °C. Eluent for column chromatography: EtOAc/hexane (4/21, v/v); $[\alpha]_D^{31}$ −2.8 (*c* 0.27, MeOH); R_f=0.27 (2/3 EtOAc/hexane); IR (KBr): ν=765, 1215, 1456, 1543, 1777, 2363, 2856, 2924, 3021, 3449 cm^{-1}; ^1H NMR(300 MHz, $CDCl_3$): δ 2.71 (2H, d, *J*=4.3 Hz), 4.29 (1H, dd, *J*=4.5, 8.9 Hz), 4.51 (1H, d, *J*=11.9 Hz), 4.59 (1H, d, *J*=12.0 Hz), 4.96 (1H, t, *J*=4.7 Hz), 5.33 (1H, br s), 6.04–6.16 (2H, m), 7.28–7.38 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.7 (CH_2), 71.8 (CH_2), 73.9 (CH), 75.9 (CH), 83.3 (CH), 123.4 (CH), 126.3, 127.6, 127.9, 128.0, 128.6, 128.7 (ArC), 137.1 (ArqC), 137.9 (CH), 142.0 (ArqC), 174.5 (C=O); DART–HRMS: $[M-OH]^+$•, found 307.1328. $C_{20}H_{19}O_3$ requires 307.1334.

4.9. General procedure for the synthesis of compound 11a,b

To the stirring solution of compound **10a** (540 mg, 1.67 mmol) in dry DCM (10 mL) at 0 °C imidazole (239 mg, 3.31 mmol) and TBSCl (275 mg, 1.82 mmol) were added. The temperature of the reaction mixture was raised to room temperature. After 8 h, a saturated aqueous solution of NH_4Cl (15 mL) was added and the resulting solution was extracted with DCM (3×10 mL). The combined organic phases were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography (230–400 mesh) to furnish **11a** (676 mg, 93%) as a white solid. Similar reaction protocol was adopted for the synthesis of **11b**.

*4.9.1. (4R,5R)-4-(Benzyloxy)-5-((S,E)-3-(tert-butyldimethyl-silyloxy)-3-phenylprop-1-enyl)dihydrofuran-2(3H)-one (**11a**).* White solid; yield: 93% (676 mg); mp 90–92 °C. Eluent for column chromatography: EtOAc/hexane (3/22, v/v); $[\alpha]_D^{30}$ −37.1 (*c* 0.80, $CHCl_3$); R_f=0.60 (2/3 EtOAc/hexane); IR (KBr): ν=771, 1216, 1578, 1781, 2360, 2860, 2933, 3027 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ −0.10 (3H, s), 0.00 (3H, s), 0.84 (9H, s), 2.59 (2H, d, *J*=4.2 Hz), 4.15 (1H, dd, *J*=4.4, 8.4 Hz), 4.40–4.49 (2H, m), 4.82 (1H, dd, *J*=4.7, 6.9 Hz), 5.20 (1H, d, *J*=4.2 Hz), 5.88–6.06 (2H, m), 7.15–7.29 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ −4.9 (CH_3), −4.8 (CH_3), 25.8 ($3CH_3$), 35.8 (CH_2), 71.7 (CH_2), 74.4 (CH), 76.1 (CH), 83.7 (CH), 121.4 (CH), 125.9, 127.2, 127.5, 127.9, 128.3, 128.4 (ArC), 137.1 (ArqC), 139.5 (CH), 142.9 (ArqC), 174.7 (C=O); DART–HRMS: $[M+H]^+$•, found 439.2299. $C_{26}H_{35}O_4Si$ requires 439.2305.

*4.9.2. (4S,5S)-4-(Benzyloxy)-5-((R,E)-3-(tert-butyldimethyl-silyloxy)-3-phenylprop-1-enyl)dihydrofuran-2(3H)-one (**11b**).* White solid; yield: 66% (480 mg); mp 85–88 °C. Eluent for column chromatography: EtOAc/hexane (3/22, v/v); $[\alpha]_D^{31}$ +33.1 (*c* 0.33, $CHCl_3$); R_f=0.60 (2/3 EtOAc/hexane); IR (KBr): ν=769, 1215, 1651, 1780, 2358, 2857, 2926, 3025 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ −0.09 (3H, s), 0.00 (3H, s), 0.85 (9H, s), 2.61 (2H, d, *J*=4.5 Hz), 4.17 (1H, dd, *J*=4.5, 8.5 Hz), 4.42–4.50 (2H, m), 4.84 (1H, dd, *J*=4.6, 6.9 Hz), 5.21 (1H, d, *J*=4.3 Hz), 5.89–6.06 (2H, m), 7.17–7.28 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ −4.9 (CH_3), −4.8 (CH_3), 25.8 ($3CH_3$), 35.8 (CH_2), 71.7 (CH_2), 74.4 (CH), 76.1 (CH), 83.7 (CH), 121.4 (CH), 125.9, 127.3, 127.5, 127.9, 128.3, 128.5 (ArC), 137.1 (ArqC), 139.6 (CH), 143.0 (ArqC), 174.7 (C=O); DART–HRMS: $[M+H]^+$•, found 439.2309. $C_{26}H_{35}O_4Si$ requires 439.2305.

4.10. General procedure for the synthesis of compound 12a,b

To a stirred solution of ^{t}BuOH (5 mL) and water (5 mL) were added AD-mix-β (4.0 g) and methanesulfonamide ($CH_3SO_2NH_2$) (0.100 g, 1.05 mmol) at room temperature. The mixture was vigorously stirred at room temperature until both phases were clear and then cooled to 0 °C. A solution of compound **11a** (500 mg, 1.14 mmol) in ^{t}BuOH (5 mL) and catalytic amount of OsO_4 were added simultaneously at 0 °C to the above reaction mixture. It was stirred at the same temperature for 24 h. The reaction was quenched at 0 °C by the addition of sodium sulfite (1.2 g), warmed to room temperature, and further stirred for 30 min. The resulting mixture was extracted with EtOAc (3×10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Purification of the crude product by silica gel (230–400 mesh) column chromatography afforded **12a** (362 mg, 67%) as a white solid. Similar reaction procedure was adopted for the synthesis of **12b** from **11b** by using AD-mix-α.

*4.10.1. (4R,5R)-4-(Benzyloxy)-5-((1S,2S,3R)-3-(tert-butyldimethyl-silyloxy)-1,2-dihydroxy-3-phenylpropyl)dihydrofuran-2(3H)-one (**12a**).* White solid; yield: 67% (362 mg); mp 102–105 °C. Eluent for column chromatography: EtOAc/hexane (1/4, v/v); $[\alpha]_D^{31}$ −46.5 (*c* 0.73, MeOH); R_f=0.38 (1/2 EtOAc/hexane); IR (KBr): ν=767, 1216, 1590, 1777, 2359, 2857, 2928, 3021, 3462 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ −0.10 (3H, s), 0.09 (3H, s), 0.89 (9H, s), 2.34 (1H, d, *J*=7.6 Hz, −OH), 2.62 (1H, dd, *J*=5.6, 17.5 Hz), 2.74–2.81 (1H, m), 3.66 (1H, t, *J*=6.6 Hz), 4.29–4.33 (2H, m), 4.49–4.60 (3H, m), 4.85 (1H, d, *J*=6.4 Hz), 7.21–7.34 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ −5.3 (CH_3), −4.7 (CH_3), 25.7 ($3CH_3$), 35.2 (CH_2), 67.9 (CH), 71.1 (CH_2), 73.9 (CH), 74.1 (CH), 76.7 (CH), 84.5 (CH), 126.7, 127.8, 127.9, 128.1, 128.4, 128.6 (ArC), 136.4 (ArqC), 141.1 (ArqC), 174.5 (C=O); DART–HRMS: $[M+H]^+$•, found 473.2349. $C_{26}H_{37}O_6Si$ requires 473.2359.

*4.10.2. (4S,5S)-4-(Benzyloxy)-5-((1R,2R,3S)-3-(tert-butyldimethyl-silyloxy)-1,2-dihydroxy-3-phenylpropyl)dihydrofuran-2(3H)-one (**12b**).* White solid; yield: 58% (313 mg); mp 100–102 °C. Eluent for column chromatography: EtOAc/hexane (1/4, v/v); $[\alpha]_D^{31}$ +47.2 (*c* 0.23, MeOH); R_f=0.38 (1/2 EtOAc/hexane); IR (KBr): ν=772, 1217, 1645, 1750, 2360, 2859, 2927, 3423 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ −0.14 (3H, s), 0.09 (3H, s), 0.89 (9H, s), 2.62 (1H, dd, *J*=5.6, 17.5 Hz), 2.75–2.81 (1H, m), 3.65 (1H, br s), 4.29–4.32 (2H, m), 4.49–4.59 (3H, m), 4.86 (1H, d, *J*=6.3 Hz), 7.21–7.34 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ −5.2 (CH_3), −4.7 (CH_3), 25.7 ($3CH_3$), 35.2 (CH_2), 67.9 (CH), 71.2 (CH_2), 74.0 (CH), 74.2 (CH), 76.7 (CH), 84.5 (CH), 126.8, 127.9, 128.0, 128.2, 128.4, 128.6 (ArC), 136.5 (ArqC), 141.1 (ArqC), 174.3 (C=O); DART–HRMS: $[M+H]^+$•, found 473.2353. $C_{26}H_{37}O_6Si$ requires 473.2359.

4.11. General procedure for the synthesis of compound 13a,b

To a stirred solution of compound **12a** (122 mg, 0.26 mmol) in dry acetonitrile Amberlyst 15 resin (150 mg) was added at 0 °C. The mixture was vigorously stirred at room temperature for 5 h to complete the reaction. After that, the reaction mixture was filtered through a Celite pad and then concentrated in vacuo to give a white solid **13a** (87 mg, 94%). The product did not require any purification. Similar reaction protocol was adopted for the synthesis of **13b**.

*4.11.1. (4R,5R)-4-(Benzyloxy)-5-((1S,2R,3R)-1,2,3-trihydroxy-3-phenylpropyl)dihydrofuran-2(3H)-one (**13a**).* White solid; yield: 94% (87 mg); mp 160–162 °C. Eluent for column chromatography: EtOAc/hexane (2/3, v/v); $[\alpha]_D^{27}$ −33.5 (*c* 0.43, MeOH); R_f=0.24 (4/1 EtOAc/hexane); IR (KBr): ν=765, 1216, 1602, 1765, 2364, 2858, 2925, 3022, 3426 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 2.77–2.78 (2H, m), 3.71–3.74 (1H, m), 4.32–4.67 (5H, m), 4.74 (1H, d, *J*=7.9 Hz), 7.19–7.42 (10H, m); ^{13}C NMR (75 MHz, CD_3OD): δ 36.7 (CH_2), 69.9 (CH), 71.9 (CH_2), 74.4 (CH), 75.5 (CH), 76.0 (CH), 87.5 (CH), 128.3, 128.4, 128.9, 129.1, 129.3, 129.5 (ArC), 138.7 (ArqC), 144.2 (ArqC), 177.9 (C=O); DART–HRMS: $[M-OH]^+$•, found 341.1408. $C_{20}H_{21}O_5$ requires 341.1389.

*4.11.2. (4S,5S)-4-(Benzyloxy)-5-((1R,2S,3S)-1,2,3-trihydroxy-3-phenylpropyl)dihydrofuran-2(3H)-one (**13b**).* White solid; yield: 90% (84 mg); mp 160–164 °C. Eluent for column chromatography: EtOAc/hexane (2/3, v/v); $[\alpha]_D^{31}$ +33.3 (*c* 0.27, MeOH); R_f=0.24 (4/1 EtOAc/hexane); IR (KBr): ν=763, 1216, 1632, 1766, 2371, 2857, 2927, 3022, 3418 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 2.86–2.87 (2H, m), 3.83 (1H, d, *J*=6.7 Hz), 4.44–4.78 (6H, m), 7.31–7.47 (10H, m); ^{13}C NMR (75 MHz, CD_3OD): δ 36.8 (CH_2), 70.1 (CH), 72.0 (CH_2), 74.5 (CH), 75.6 (CH), 76.1 (CH), 87.5 (CH), 128.4, 128.5, 129.0, 129.2, 129.4, 129.6 (ArC), 138.8 (ArqC), 144.3 (ArqC), 178.1 (C=O); DART–HRMS: $[M-H]^+$•, found 357.1321. $C_{20}H_{21}O_6$ requires 357.1338.

4.12. General procedure for the synthesis of compound 14a,b

A catalytic amount of $Pd(OH)_2$ (5 mg) was added to a solution of **13a** (20 mg, 0.056 mmol) in methanol (5 mL). A vacuum was created in a round bottomed flask containing the above reaction mixture with the help of pump and the mixture was stirred under H_2 in a balloon at 1 atms. After the completion of the reaction (TLC, 24 h) catalyst was removed by filtration, washed with methanol twice and the combined filtrate was concentrated and purified by silica gel (230–400 mesh) column chromatography to afford (+)-cardiobutanolide **14a** (10 mg, 67%) as a white solid. Analogous procedure was adopted for the synthesis of (−)-cardiobutanolide **14b** from **13b**.

*4.12.1. (+)-Cardiobutanolide (**14a**).* White solid; yield: 67% (10 mg); mp 192–194 °C; Eluent for column chromatography: EtOAc/hexane (9/11, v/v); $[\alpha]_D^{29}$ +6.1 (*c* 0.4, MeOH) [lit. mp 189–190 °C; lit. $[\alpha]_D^{24}$ +6.4 (*c* 0.28, MeOH)][13]; R_f=0.37 (EtOAc); IR (KBr): ν=769, 1218, 1590, 1772, 2340, 2858, 2927, 3371 cm^{-1}; ^1H NMR (600 MHz, $(CD_3)_2C=O$): δ 2.38 (1H, d, *J*=17.4 Hz), 2.86–2.89 (1H+solvent, m), 3.93 (1H, dd, *J*=1.2, 7.8 Hz), 4.40 (1H, dd, *J*=1.2, 7.2 Hz), 4.57 (1H, dd, *J*=3.6, 7.8 Hz), 4.62–4.64 (1H, m), 4.80 (1H, d, *J*=7.8 Hz), 7.21–7.24 (1H, m), 7.31 (2H, t, *J*=7.8 Hz), 7.45 (2H, d, *J*=7.8 Hz); ^{13}C NMR (100 MHz, $(CD_3)_2C=O$): δ 40.4 (CH_2), 68.7 (CH), 70.4 (CH), 74.2 (CH), 75.6 (CH), 86.6 (CH), 127.9, 128.0, 128.6 (ArC), 144.3 (ArqC), 176.1 (C=O); DART–HRMS: $[M]^+$•, found 268.0947. $C_{13}H_{16}O_6$ requires 268.0946.

*4.12.2. (−)-Cardiobutanolide (**14b**).* White solid; yield: 60% (9 mg); mp 194–195 °C. Eluent for column chromatography: EtOAc/hexane (9/11, v/v); $[\alpha]_D^{28}$ −2.72 (*c* 0.2, MeOH) [for (+)-cardiobutanolide lit. mp 189–190 °C; lit. $[\alpha]_D^{24}$ +6.4 (*c* 0.28, MeOH)][13]; R_f=0.37 (EtOAc); IR (KBr): ν=762, 1186, 1369, 1703, 2339, 2369, 2932, 2976, 3452 cm^{-1}; ^1H NMR (400 MHz, $(CD_3)_2C=O$): δ 2.38 (1H, d, *J*=17.1 Hz), 2.79–2.82 (1H+solvent, m), 3.79 (1H, d, *J*=8.4 Hz, −OH), 3.93 (1H, t, *J*=7.0 Hz), 4.31 (1H, d, *J*=5.2 Hz, −OH), 4.38–4.39 (1H, m), 4.57 (1H, dd, *J*=2.8, 7.5 Hz), 4.63–4.67 (2H, m), 4.79–4.84 (1H, m), 7.21–7.25 (1H, m), 7.29–7.32 (2H, m), 7.45 (2H, d, *J*=7.3 Hz); ^{13}C NMR (100 MHz, $(CD_3)_2C=O$): δ 40.4 (CH_2), 68.7 (CH), 70.3 (CH), 74.2 (CH), 75.6 (CH), 86.7 (CH), 127.9, 128.0, 128.6 (ArC), 144.3 (ArqC), 176.2 (C=O); DART–HRMS: $[M-H]^+$•, found 267.0893. $C_{13}H_{15}O_6$ requires 267.0869.

4.13. Synthesis of (4*R*,5*S*)-4-(benzyloxy)-5-((4*S*,5*S*)-5-((*R*)-(*tert*-butyldimethylsilyloxy)(phenyl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)dihydrofuran-2(3*H*)-one (15a)

To a stirred solution of **12a** (200 mg, 0.42 mmol) in acetone (3 mL) was added 2,2-dimethoxypropane (DMP) (0.08 mL, 0.63 mmol) followed by camphorsulfonic acid (CSA) (10 mg, 0.043 mmol). The reaction mixture was stirred till the consumption of starting material (2 h). Afterward, the reaction mixture was concentrated under reduced pressure to colorless oil, which was dissolved in EtOAc (5 mL) and extracted with the same solvent (3×10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Purification of the crude product by silica gel column chromatography (230–400 mesh) afforded pure **15a** (180 mg, 83%) as a yellow gum. Eluent for column chromatography: EtOAc/hexane (1/24, v/v); $[\alpha]_D^{27}$ −10.73 (*c* 0.60, MeOH); R_f=0.58 (1/4 EtOAc/hexane); IR (neat): ν=770, 1219, 1369, 1589, 1661, 1791, 2338, 2370, 2930 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ −0.08 (3H, s), 0.13 (3H, s), 0.93 (9H, s), 1.28 (3H, s), 1.35 (3H, s), 2.50 (1H, dd, *J*=8.6, 16.8 Hz), 2.80 (1H, dd, *J*=10.0, 16.9 Hz), 3.77 (1H, d, *J*=7.7 Hz), 4.22–4.32 (2H, m), 4.57–4.59 (3H, m), 4.99 (1H, d, *J*=4.5 Hz), 7.28–7.40 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ −4.8 (CH_3), −4.7 (CH_3), 25.9 ($3CH_3$), 26.2 (CH_3), 27.7 (CH_3), 34.1 (CH_2), 72.3 (CH_2), 73.9 (CH), 74.1 (CH), 74.3 (CH), 78.0 (CH), 80.6 (CH), 110.2 (qC), 126.2, 127.5, 127.8, 128.0, 128.4, 128.6 (ArC), 137.2 (ArqC), 141.0 (ArqC), 174.4 (C=O); DART–HRMS: $[M+H]^+$•, found 513.2673. $C_{29}H_{41}O_6Si$ requires 513.2672.

4.14. Synthesis of (4*R*,5*S*)-5-((4*S*,5*S*)-5-((*R*)-(*tert*-butyldimethyl-silyloxy)(phenyl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-hydroxydihydrofuran-2(3*H*)-one (16a)

To a solution of **15a** (136 mg, 0.26 mmol) in dry EtOAc (5 mL) taken in a round bottomed flask was added a catalytic amount of $Pd(OH)_2$ (10 mg). A vacuum was created in this flask containing the above reaction mixture with the help of pump and was stirred under H_2 in a balloon at 1 atms. After the completion of the reaction (TLC, 24 h) catalyst was removed by filtration, washed with EtOAc twice and the combined filtrate was concentrated to afford a colorless oil, which on column chromatographic (230–400 mesh silica gel) purification gave the pure compound **16a** (97 mg, 87%) as a yellow gum. Eluent for column chromatography: EtOAc/hexane (7/43, v/v); $[\alpha]_D^{28}$ +4.58 (*c* 0.50, MeOH); R_f=0.21 (1/4 EtOAc/hexane); IR (neat): ν=770, 1219, 1374, 1462, 1727, 1784, 2340, 2369, 2856, 2926, 3486 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ −0.06 (3H, s), 0.11 (3H, s), 0.93 (9H, s), 1.39 (3H, s), 1.49 (3H, s), 2.54 (1H, dd, *J*=5.5, 17.8 Hz), 2.69 (1H, dd, *J*=7.6, 17.8 Hz), 3.68 (1H, d, *J*=6.3 Hz), 4.36 (1H, dd, *J*=4.4, 7.9 Hz), 4.48–4.55 (2H, m), 4.93–5.03 (1H, m), 7.28–7.37 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ −4.8 (CH_3), −4.7 (CH_3), 25.9 ($3CH_3$), 26.3 (CH_3), 27.5 (CH_3), 38.5 (CH_2), 69.1 (CH), 73.7 (CH), 75.3 (CH), 80.1 (CH), 80.7 (CH), 110.5 (qC), 126.1, 127.9, 128.4 (ArC), 140.4 (ArqC), 174.6 (C=O); DART–HRMS: $[M+H]^+$•, found 423.2208. $C_{22}H_{35}O_6Si$ requires 423.2203.

4.15. Synthesis of (*S*)-5-((4*R*,5*S*)-5-((*R*)-(*tert*-butyldimethylsilyloxy)(phenyl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-furan-2(5*H*)-one (17a)

To a stirred solution of **16a** (102 mg, 0.24 mmol) dissolved in dry DCM (10 mL) was added Et_3N (0.08 mL, 0.60 mmol) drop wise at 0 °C and left the reaction mixture for stirring for 10 min. The methanesulfonyl chloride (MsCl) (0.02 mL, 0.29 mmol) was added drop wise to this reaction mixture at the same temperature and stirring was further continued for 3 h at the same temperature for the completion of the reaction. The reaction mixture was diluted with water, organic layer was separated and the aqueous layer was extracted with DCM (3×10 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated to obtain the crude product which on column chromatographic purification (230–400 mesh silica gel) gave pure **17a** (90 mg, 92%) as a pale yellow oil. Eluent for column chromatography: EtOAc/hexane (1/49, v/v); $[\alpha]_D^{32}$ −14.89 (*c* 0.63, MeOH); R_f=0.68 (1/4 EtOAc/hexane); IR (neat): ν=770, 1155, 1254, 1460, 1767, 2362, 2858, 2925 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ −0.17 (3H, s), 0.00 (3H, s), 0.82 (9H, s), 1.21 (3H, s), 1.31 (3H, s), 4.05–4.06 (1H, m), 4.18–4.20 (1H, m), 4.32 (1H, dd, *J*=4.2, 7.7 Hz), 4.90 (1H, d, *J*=4.2 Hz), 5.95 (1H, dd, *J*=1.9, 5.6 Hz), 7.16–7.27 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ −4.8 (CH_3), −4.7 (CH_3), 25.9 ($3CH_3$), 26.1 (CH_3), 27.3 (CH_3), 73.7 (CH), 74.9 (CH), 81.1 (CH), 81.8 (CH), 110.3 (qC), 122.1 (=CH), 126.0, 127.9, 128.5 (ArC), 140.5 (ArqC), 153.2 (=CH), 172.9 (C=O); DART–HRMS: $[M+H]^+$•, found 405. 2092. $C_{22}H_{33}O_5Si$ requires 405.2097.

4.16. Synthesis of (*S*)-5-((1*S*,2*R*,3*R*)-1,2,3-trihydroxy-3-phenylpropyl)furan-2(5*H*)-one (18a)

To a stirred solution of **17a** (79 mg, 0.19 mmol) in 2.5 mL of THF were added 2.5 mL AcOH and 2.5 mL 2 N HCl at room temperature. The stirring of the reaction mixture was continued for 24 h at the same temperature. After the reaction was completed (TLC), the volatiles were removed under reduced pressure and the residue obtained was purified by silica gel (230–400 mesh) column chromatography to give **18a** (27 mg, 56%) as a white solid. Eluent for column chromatography: EtOAc/hexane (3/7, v/v); mp 106–108 °C; $[\alpha]_D^{32}$ −69.8 (*c* 0.3, MeOH) [lit. mp 109–111 °C; $[\alpha]_D^{24}$ −68 (*c* 0.6, EtOAc)][17d]; R_f=0.52 (4/1 EtOAc/hexane); IR (KBr): ν=769, 1047, 1218, 1461, 1656, 1744, 2366, 2856, 2925, 3404 cm^{-1}; ^1H NMR (200 MHz, CD_3OD): δ 3.64 (1H, dd, *J*=2.0, 8.2 Hz), 4.07 (1H, dd, *J*=2.0, 6.0 Hz), 4.72 (1H, d, *J*=8.2 Hz), 5.24–5.29 (1H, m), 6.16 (1H, dd, *J*=2.1, 5.8 Hz), 7.21–7.45 (5H, m), 7.76 (1H, dd, *J*=1.5, 5.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 72.8 (CH), 74.9 (CH), 75.1 (CH), 87.5 (CH), 122.2 (=CH), 128.4, 128.5, 129.1 (ArC), 144.0 (ArqC), 156.9 (=CH), 175.6 (C=O); DART–HRMS: $[M+H]^+$•, found 251.0908. $C_{13}H_{15}O_5$ requires 251.0919.

4.17. Synthesis of compound (+)-goniofufurone (19a)

A solution of unsaturated lactone **18a** (0.017 g, 0.068 mmol) in dry THF (10 mL) containing DBU (6 μL) was stirred at room temperature for 24 h. The solution was then filtered through a short pad of silica gel topped with Celite. Removal of the solvent from the filtrate in vacuo gave a residue, which was crystallized from EtOAc/hexane (1/20, v/v) to give a white solids **19a** (11 mg, 65%); mp 150–152 °C. Crystallized from EtOAc/hexane. $[\alpha]_D^{31}$ +5.1 (*c* 0.23, MeOH) [lit. mp 152–154 °C; lit. $[\alpha]_D^{22}$ +9.0 (*c* 0.5, EtOH)][12c]; R_f=0.57 (EtOAc); IR (KBr): ν=771, 1045, 1219, 1463, 1652, 1774, 2364, 2852, 2918, 3443 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.64–2.80 (2H, m), 2.99 (1H, br s, −OH), 4.11 (1H, dd, *J*=2.8, 4.8 Hz), 4.21 (1H, br s, −OH), 4.42 (1H, br s), 4.87 (1H, d, *J*=4.1 Hz), 5.12 (1H, t, *J*=4.3 Hz), 5.19 (1H, d, *J*=4.6 Hz), 7.34–7.44 (5H, m); ^{13}C NMR (50 MHz, $CDCl_3$): δ 36.1 (CH_2), 73.5 (CH), 74.5 (CH), 77.3 (CH), 82.9 (CH), 87.4 (CH), 125.9, 128.5, 128.8 (ArC), 138.9 (ArqC), 175.3 (C=O); DART–HRMS: $[M+H]^+$•, found 251.0918. $C_{13}H_{15}O_5$ requires 251.0919.

Acknowledgements

We are thankful to Sophisticated Analytical Instrument Facility, CDRI for providing spectral data, "DST (project SR/SI/OC-17/2010) for financial support and Mr. A.K. Pandey for technical assistance. P.P. thanks CSIR New Delhi for awarding Senior Research Fellowship. CDRI Communication no. 8048.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2011.04.014. These data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

1. (a) Hanessian, S. *Total Synthesis of Natural Products: The 'Chiron' Approach*; Pergamon: Oxford, 1983; (b) Ducatti, D. R. B.; Massi, A.; Noseda, M. D.; Durate, M. E. R.; Dondoni, A. *Org. Biomol. Chem.* **2009**, *7*, 576–588; (c) Saquib, M.; Gupta, M. K.; Sagar, R.; Prabhakar, Y. S.; Shaw, A. K.; Kumar, R.; Maulik, P. R.; Gaikwad, A. N.; Sinha, S.; Srivastava, A. K.; Chaturvedi, V.; Srivastava, R.; Srivastava, B. S. *J. Med. Chem.* **2007**, *50*, 2942–2950; (d) Reddy, L. V. R.; Reddy, P. V.; Shaw, A. K. *Tetrahedron: Asymmetry* **2007**, *18*, 542–546; (e) Reddy, P. V.; Reddy, L. V. R.; Kumar, B.; Kumar, R.; Maulik, P. R.; Shaw, A. K. *Tetrahedron* **2008**, *64*, 2153–2159; (f) Reddy, L. V. R.; Swamy, G. N.; Shaw, A. K. *Tetrahedron: Asymmetry* **2008**, *19*, 1372–1375; (g) Saquib, M.; Hussain, I.; Kumar, B.; Shaw, A. K. *Chem.—Eur. J.* **2009**, *15*, 6041–6049; (h) Reddy, L. V. R.; Reddy, P. V.; Mishra, N. N.; Shukla, P. K.; Yadav, G.; Srivastava, R.; Shaw, A. K. *Carbohydr. Res.* **2010**, *345*, 1515–1521; (i) Pal, P.; Kumar, B.; Shaw, A. K. *Eur. J. Org. Chem.* **2009**, 2179–2184; (j) Reddy, P. V.; Bajpai, B.; Kumar, B.; Shaw, A. K. *Eur. J. Org. Chem.* **2011,** 1575–1586.
2. (a) Moore, R. E. *Prog. Chem. Org. Nat. Prod.* **1985**, *48*, 81–202; (b) Chou, T.; Kamo, O.; Uemura, D. *Tetrahedron Lett.* **1996**, *37*, 4023–4026; (c) Silverstein, R. M. *J. Chem. Educ.* **1968**, *45*, 794–797; (d) Silverstein, R. M.; Brownlee, R. G.; Bellas, T. E.; Wood, D. L.; Browne, L. E. *Science* **1968**, *159*, 889–891; (e) Wood, D. L.; Browne, L. E.; Ewing, B.; Lindahl, K.; Bedard, W. D.; Tilden, P. E.; Mori, K.; Pitman, G. B.; Hughes, P. R. *Science* **1976**, *192*, 896–898.
3. Joshi, N. N.; Mamdapur, V. R.; Chadha, M. S. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2963–2966 and references cited therein.
4. *endo*-Brevicomin. (a) Minor component of volatiles of mountain pine beetle, Dendroctonus ponderosae, and western balsam bark beetle, Dryocoetes confusus Schurig, V.; Weber, R.; Nicholson, G. J.; Oehlschlager, A. C.; Pierce, H., Jr.; Pierce, A. M.; Borden, J. H.; Ryker, L. C. *Naturwissenschaften* **1983**, *70*, 92–93; (b) Aggregation pheromone of Dryocoetes autographus Mori, K.; Seu, Y.-B. *Tetrahedron* **1985**, *41*, 3429–3431; (c) (±)-Antiaggregation pheromone for southern pine beetle, Dendroctonus frontalis Vité, J. P.; Renwick, J. A. A. *Naturwissenschaften* **1971**, *7*, 578–582; (d) (−)-Antiaggregation pheromone and (+) aggregation pheromone for D. frontalis Vité, J. P.; Billings, R. F.; Ware, C. W.; Mori, K. *Naturwissenschaften* **1985**, *72*, 99–100; (e) Oehlschlager, A. C.; Johnston, B. D. *J. Org. Chem.* **1987**, *52*, 940–943; (f) Burke, S. D.; Müller, N.; Beaudry, C. M. *Org. Lett.* **1999**, *1*, 1827–1829 and references cited therein.
5. Some synthesis of brevicomins: (a) Perez, A. L.; Gries, R.; Gries, G.; Oehlschlager, A. L. *Bioorg. Med. Chem.* **1966**, *4*, 445–450; (b) Wasserman, H. H.; Barber, E. H. *J. Am. Chem. Soc.* **1969**, *36*, 3674–3675; (c) Bellas, T. E.; Brownlee, R. G.; Silverstein, R. M. *Tetrahedron* **1969**, *25*, 5149–5153; (d) Mori, K. *Tetrahedron* **1974**, *30*, 4223–4227; (e) Kocienski, P. J.; Ostrow, R. W. *J. Org. Chem.* **1976**, *41*, 398–400; (f) Cahiez, G.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1980**, *21*, 1433–1436; (g) Bernardi, R.; Fuganti, C.; Grasselli, P. *Tetrahedron Lett.* **1981**, *22*, 4021–4024; (h) Sherk, A. E.; Fraser-Reid, B. *J. Org. Chem.* **1982**, *47*, 932–935; (i) Johnston, B. D.; Oehlschlager, A. C. *J. Org. Chem.* **1982**, *47*, 5384–5386; (j) Ferrier, R. J.; Prasit, P. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1645–1647; (k) Asami, M.; Mukaiyama, T. *Chem. Lett.* **1983**, 93–96; (l) Wuts, P. G. M.; Bigelow, S. S. *J. Chem. Soc., Chem. Commun.* **1984**, 736–737; (m) Bhupathy, M.; Cohen, T. *Tetrahedron Lett.* **1985**, *26*, 2619–2622; (n) Küfner, U.; Schmidt, R. R. *Synth. Commun.* **1985**, 1060–1062; (o) Ferrier, R. J.; Schmidt, P.; Tyler, P. C. *J. Chem. Soc., Perkin Trans. 1* **1985**, 301–303; (p) Yusufoğlu, A.; Antons, S.; Scharf, H.-D. *J. Org. Chem.* **1986**, *51*, 3485–3487; (q) Mulzer, J.; Angermann, A.; Münch, W. *Liebigs Ann. Chem.* **1986**, 825–838; (r) Mori, K.; Seu, Y.-B. *Liebigs Ann. Chem.* **1986**, 205–209; (s) Tamao, K.; Nakajo, E.; Ito, Y. *J. Org. Chem.* **1987**, *52*, 4412–4414; (t) Kotsuki, H.; Kadota, I.; Ochi, M. *Tetrahedron Lett.* **1989**, *30*, 3999–4000; (u) Padwa, A.; Chinn, R. L.; Zhi, L. *Tetrahedron Lett.* **1989**, *30*, 1491–1494; (v) Kotsuki, H.; Kadota, I.; Ochi, M. *J. Org. Chem.* **1990**, *55*, 4417–4422; (w) Matsumoto, K.; Suzuki, N.; Ohta, H. *Tetrahedron Lett.* **1990**, *31*, 7163–7166; (x) Myles, D. C.; Andrulis, P. J., III; Whitesides, G. M. *Tetrahedron Lett.* **1991**, *32*, 4835–4838; (y) Kim, M.-J.; Choi, G.-B.; Kim, J.-Y.; Kim, H.-J. *Tetrahedron Lett.* **1995**, *36*, 6253–6256; (z) Takahata, H.;

Kusunoki, M.; Takeda, Y.; Momose, T. *Tetrahedron: Asymmetry* **1996**, *7*, 2093–2098.
6. (a) Vettel, S.; Lutz, C.; Diefenbach, A.; Haderlein, G.; Hammerschmidt, S.; Kühling, K.; Mofid, M.-R.; Zimmermann, T.; Knochel, P. *Tetrahedron: Asymmetry* **1997**, *8*, 779–800; (b) Hu, S.; Jayaraman, S.; Oehlschlager, A. C. *J. Org. Chem.* **1999**, *64*, 2524–2526; (c) Gallos, J. K.; Kyradjoglou, L. C.; Koftis, T. V. *Heterocycles* **2001**, *55*, 781–784; (d) de Sousa, A. L.; Resck, I. S. *J. Braz. Chem. Soc.* **2002**, *13*, 233–237; (e) Mayer, S. F.; Mang, H.; Steinreiber, A.; Saf, R.; Faber, K. *Can. J. Chem.* **2002**, *80*, 362–369; (f) Raghavan, S.; Joseph, S. C. *Tetrahedron Lett.* **2003**, *44*, 8237–8239; (g) Kumar, D. N.; Rao, B. V. *Tetrahedron Lett.* **2004**, *45*, 2227–2229; (h) Tyvorskii, V. I.; Astashko, D. A.; Kulinkovich, O. G. *Tetrahedron* **2004**, *60*, 1473–1479; (i) Prasad, K. R.; Anbarasan, P. *Tetrahedron: Asymmetry* **2005**, *16*, 3951–3953; (j) Kim, S.-G.; Park, T.-H.; Kim, B. J. *Tetrahedron Lett.* **2006**, *47*, 6369–6372; (k) Prasad, K. R.; Anbarasan, P. *Tetrahedron: Asymmetry* **2007**, *18*, 1419–1427; (l) Singh, S.; Guiry, P. J. *J. Org. Chem.* **2009**, *74*, 5758–5761.
7. Oishi, T.; Ando, K.; Chida, N. *Chem. Commun.* **2001**, 1932–1933 and references cited therein.
8. Mereyala, H. B.; Gadikota, R. R.; Krishnan, R. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3567–3571 and references cited therein.
9. (a) Wu, Y.-C.; Duh, C.-Y.; Chang, F.-R.; Chang, G.-Y.; Wang, S.-K.; Chang, J.-J.; McPhail, D. R.; McPhail, A. T.; Lee, K.-H. *J. Nat. Prod.* **1991**, *54*, 1077–1081; (b) Talapatra, S. K.; Basu, D.; Deb, T.; Goswami, S.; Talapatra, B. *Indian J. Chem., Sect. B* **1985**, *24*, 29–34; (c) Sam, T. W.; Sew-Yeu, C.; Matsjeh, S.; Gan, E. K.; Razak, D.; Mohamed, A. L. *Tetrahedron Lett.* **1987**, *28*, 2541–2544; (d) Cavé, A.; Figadère, B.; Laurens, A.; Cortés, D. *Prog. Chem. Org. Nat. Prod.* **1997**, *70*, 81–288; (e) Zafra-Polo, M. C.; Figadère, B.; Gallardo, T.; Tormo, J. R.; Cortés, D. *Phytochemistry* **1998**, *48*, 1087–1117; (f) Alali, F. Q.; Liu, X.-X.; Mclaughlin, J. L. *J. Nat. Prod.* **1999**, *62*, 504–540.
10. On the cytotoxic activity and other bioactivity of styryllactones, see: (a) Blázquez, M. A.; Bermejo, A.; Zafra-Polo, M. C.; Cortes, D. *Phytochem. Anal.* **1999**, *10*, 161–170; (b) Mereyala, H. B.; Joe, M. *Curr. Med. Chem.: Anti-Cancer Agents* **2001**, *1*, 293–300.
11. For a review on the synthesis of styryllactones, see: Mondon, M.; Gesson, J.-P. *Curr. Org. Synth.* **2006**, *3*, 41–75.
12. Isolation of styryllactones: (a) El-Zayat, A. A. E.; Ferrigni, N. R.; McCloud, T. G.; McKenzie, A. T.; Byrn, S. R.; Cassady, J. M.; Chang, C.-J.; McLaughlin, J. L. *Tetrahedron Lett.* **1985**, *26*, 955–956; (b) Alkofahi, A.; Ma, W.-W.; McKenzie, A. T.; Byrn, S. R.; McLaughlin, J. L. *J. Nat. Prod.* **1989**, *52*, 1371–1373; (c) Fang, X.-P.; Anderson, J. E.; Chang, C.-J.; Fanwick, P. E.; McLaughlin, J. L. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1655–1661 and references cited therein; (d) Fang, X.-P.; Anderson, J. E.; Chang, C.-J.; McLaughlin, J. L.; Fanwick, P. E. *J. Nat. Prod.* **1991**, *54*, 1034–1043 and references cited therein; (e) Fang, X.-P.; Anderson, J. E.; Chang, C.-J.; McLaughlin, J. L. *Tetrahedron* **1991**, *47*, 9751–9758.
13. Hisham, A.; Toubi, M.; Shuaily, W.; Bai, M. D. A.; Fujimoto, Y. *Phytochemistry* **2003**, *62*, 597–600.
14. Ruiz, P.; Murga, J.; Carda, M.; Marco, J. A. *J. Org. Chem.* **2005**, *70*, 713–716.
15. (a) Matsuura, D.; Takabe, K.; Yoda, H. *Tetrahedron Lett.* **2006**, *47*, 1371–1374; (b) Krishna, P. R.; Reddy, P. V. N. *Tetrahedron Lett.* **2006**, *47*, 4627–4630; (c) Garg, A.; Singh, R. P.; Singh, V. K. *Tetrahedron* **2006**, *62*, 11240–11244; (d) Prasad, K. R.; Gholap, S. L. *J. Org. Chem.* **2008**, *73*, 2916–2919; (e) Krishna, P. R.; Kumar, E. S. *Tetrahedron Lett.* **2009**, *50*, 6676–6679; (f) Yadav, J. S.; Madhavarao, B.; Rao, K. S. *Synlett* **2009**, 3179–3181; (g) Chandrasekhar, S.; Kiranmai, N. *Tetrahedron Lett.* **2010**, *51*, 4058–4060.
16. (a) Shing, T. K. M.; Tsui, H.-C. *J. Chem. Soc., Chem. Commun.* **1992**, 432; (b) Shing, T. K. M.; Tsui, H.-C.; Zhou, Z.-H. *J. Chem. Soc., Chem. Commun.* **1992**, 810–811; (c) Shing, T. K. M.; Tsui, H.-C.; Zhou, Z.-H. *Tetrahedron* **1992**, *48*, 8659–8666 and references cited therein; (d) Gracza, T.; Jäger, V. *Synlett* **1992**, 191–193; (e) Gracza, T.; Jäger, V. *Synthesis* **1994**, 1359–1368; (f) Bermejo, A.; Blazquez, M. A.; Rao, K. S.; Cortes, D. *Phytochemistry* **1998**, *47*, 1375–1380.
17. (a) Prakash, K. R. C.; Rao, S. P. *Tetrahedron* **1993**, *49*, 1505–1510; (b) Ye, J.; Bhatt, R. K.; Falck, J. R. *Tetrahedron Lett.* **1993**, *34*, 8007–8010; (c) Yang, Z.-C.; Zhou, W.-S. *Tetrahedron* **1995**, *51*, 1429–1436; (d) Shing, T. K. M.; Tsui, H.-C.; Zhou, Z.-H. *J. Org. Chem.* **1995**, *60*, 3121–3130; (e) Mukai, C.; Hirai, S.; Kim, I. J.; Kido, M.; Hanaoka, M. *Tetrahedron* **1996**, *52*, 6547–6560; (f) Surivet, J.-P.; Vatèle, J.-M. *Tetrahedron Lett.* **1996**, *37*, 4373–4376; (g) Surivet, J.-P.; Vatèle, J.-M. *Tetrahedron Lett.* **1997**, *38*, 819–820; (h) Cagnolini, C.; Ferri, M.; Jones, P. R.; Murphy, P. J. *Tetrahedron* **1997**, *53*, 4815–4820; (i) Yi, X.-H.; Meng, Y.; Hua, X.-G.; Li, C.-J. *J. Org. Chem.* **1998**, *63*, 7472–7480; (j) Mereyala, H. B.; Gadikota, R. R.; Joe, M.; Arora, S. K.; Dastidar, S. G.; Agarwal, S. *Bioorg. Med. Chem.* **1999**, *7*, 2095–2103; (k) Chen, W.-P.; Roberts, S. M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 103–105; (l) Tsubuki, M.; Kanai, K.; Nagase, H.; Honda, T. *Tetrahedron* **1999**, *55*, 2493–2514; (m) Bruns, R.; Wernicke, A.; Köll, P. *Tetrahedron* **1999**, *55*, 9793–9800; (n) Surivet, J.-P.; Vatèle, J.-M. *Tetrahedron* **1999**, *55*, 13011–13028; (o) Su, Y.-L.; Yang, C.-S.; Teng, S.-J.; Zhao, G.; Ding, Y. *Tetrahedron* **2001**, *57*, 2147–2153; (p) Prasad, K. R.; Gholap, S. L. *Synlett* **2005**, 2260–2262; (q) Yadav, V. K.; Agrawal, D. *Chem. Commun.* **2007**, 5232–5234; (r) Popsavin, V.; Benedekovic, G.; Sreco, B.; Popsavin, M.; Francuz, J.; Kojic, V.; Bogdanovic, G. *Org. Lett.* **2007**, *9*, 4235–4238; (s) Prasad, K. R.; Dhaware, M. G. *Synthesis* **2007**, 3697–3705; (t) Prasad, K. R.; Gholap, S. L. *J. Org. Chem.* **2008**, *73*, 2–11; (u) Popsavin, V.; Benedekovic, G.; Sreco, B.; Popsavin, M.; Francuz, J.; Kojic, V.; Bogdanovic, G. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 5178–5181; (v) Hernández-García, L.; Quintero, L.; Höpfl, H.; Sosa, M.; Sartillo-Piscil, F. *Tetrahedron* **2009**, *65*, 139–144; (w) Popsavin, V.; Sreco, B.; Benedekovic, G.; Francuz, J.; Popsavin, M.; Kojic, V.; Bogdanovic, G. *Eur. J. Med. Chem.* **2010**, *45*, 2876–2883; (x) Sharma, G. V. M.; Mallesham, S. *Tetrahedron: Asymmetry* **2010**, *21*, 2646–2658.
18. Mosimann, M.; Küpfer, P. A.; Leumann, C. J. *Org. Lett.* **2005**, *7*, 5211–5214.