Tetrahedron 64 (2008) 10207–10213

Contents lists available at ScienceDirect

Tetrahedron

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

Stereoselective total synthesis of (+)-(6*R*,2′*S*)-cryptocaryalactone and (−)-(6*S*,2′*S*)-*epi* cryptocaryalactone

Gowravaram Sabitha *, V. Bhaskar, S. Siva Sankara Reddy, J.S. Yadav

Organic Division I, Indian Institute of Chemical Technology, Hyderabad 500 007, India

ARTICLE INFO

Article history:
Received 12 June 2008
Received in revised form 12 August 2008
Accepted 13 August 2008
Available online 15 August 2008

Keywords:
α,β-Unsaturated δ-lactone
Base catalyzed conjugate addition
Z-Wittig olefination
Stereoselective reduction
cis Wittig olefination
1,3-Polyol

ABSTRACT

The total synthesis of (+)-(6*R*,2′*S*)-cryptocaryalactone and (−)-(6*S*,2′*S*)-*epi* cryptocaryalactone is reported based on stereoselective reduction of δ-hydroxy β-keto ester to install 1,3-polyol system, cis Wittig olefination, and lactonization as the key steps. The synthesis of (−)-(6*S*,2′*S*)-*epi* cryptocaryalactone is also reported using *syn*-benzylidene acetal formation and a preferential *Z*-Wittig olefination reaction and lactonization as the key steps.

1. Introduction

Substituted α,β-unsaturated δ-lactones (e.g., styryllactones) are an important class of natural products with a wide range of biological activity.[1] Over the past two decades an increasing number of α-pyrones have been isolated from a variety of sources. Recently identified lactone natural products include Tarchonanthus lactone **1**,[2] Strictifolione **2**,[3] Cryptocarya diacetate **3**,[4] and Cryptocarya triacetate **4**.[4] (+)-(6*R*,2′*R*)-Cryptocaryalactone **5**,[5] (+)-(6*R*,2′*S*)-cryptocaryalactone **7**,[6] and its enantiomer (−)-(6*S*,2′*R*)-cryptocaryalactone **8**[7] (1,3-polyol-derived α,β-unsaturated δ-lactones) are such examples isolated from *Cryptocarya wyliei*, *Cryptocarya bourdilloni*, and *Cryptocarya moschata*, respectively (Fig. 1). Meyer synthesized (−)-(6*S*,2′*S*)-*epi* cryptocaryalactone **6**,[8] enantiomeric pair of (+)-(6*R*,2′*R*)-cryptocaryalactone **5**. *Cryptocarya* species have been used as traditional medicines in South Africa for their anti-inflammatory and other activities.[9,10] Some of the pyrones and styrylpyrones showed larvicidal and antifertility activities, in addition to inhibition of breast cancer cell lines growth.[11–14]

Therefore, the synthesis of various cryptolactones is of much importance. Till date, two reports on the synthesis of (+)-(6*R*,2′*S*)-cryptocaryalactone **7**[15,8] and a single report on the synthesis of (−)-(6*S*,2′*S*)-*epi* cryptocaryalactone **6**[8] have appeared. As part of our studies directed toward the synthesis of biologically active lactones,[16] we herein report the synthesis of (+)-(6*R*,2′*S*)-cryptocaryalactone **7** and (−)-(6*S*,2′*S*)-*epi* cryptocaryalactone **6**.

2. Results and discussion

The synthesis of these molecules started from δ-hydroxy β-keto ester **11** (Schemes 1 and 2) prepared from iodobenzene **9** and chiral acetylenic alcohol **10** using Cosford protocol as reported by us.[16d] *anti*-Selective reduction of **11** with $Me_4NBH(OAc)_3$[17] in acetonitrile/acetic acid (1:1) at 0 °C resulted in exclusive formation of the *anti*-3,5-dihydroxy ester **12** in 79% yield (*syn*/*anti* 1:9). The mixture was separated by flash column chromatography, and the *anti*-dihydroxy ester **12** was characterized as acetonide **13** (91%), prepared under conventional reaction conditions using 2,2′-dimethoxy propane in CH_2Cl_2 catalyzed by pyridinium *para*-toluenesulfonate. The stereochemical assignment of the newly created center was made based on Rychnovsky's analogy[18] wherein the ^{13}C NMR spectra of **13** exhibited acetonide methyl carbon peaks at δ 24.6 and 25.2 and quaternary carbon at δ 100.7, which were characteristic of the acetonide of an *anti*-1,3-diol moiety (Scheme 1).

The ester group in **13** was reduced by LAH in THF at 0 °C, the subsequent oxidation of which by *ortho*-iodoxybenzoic acid (IBX) in DCM/DMSO at 0 °C furnished the corresponding aldehyde in good yield, which was then chain-elongated on reaction with a Still–Gennari reagent[19] [$(F_3CCH_2O)_2POCH_2COOMe$, NaH, THF, −78 °C, 67% over three steps] to provide the corresponding α,β-unsaturated ester **14** predominantly as the (*Z*)-isomer, along with

* Corresponding author. Tel./fax: +91 40 27160512.
E-mail address: gowravaramsr@yahoo.com (G. Sabitha).

0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.08.032

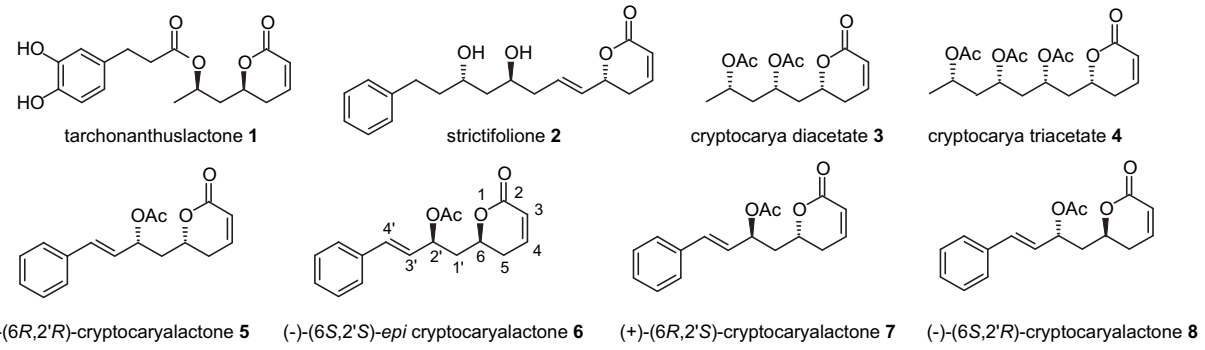
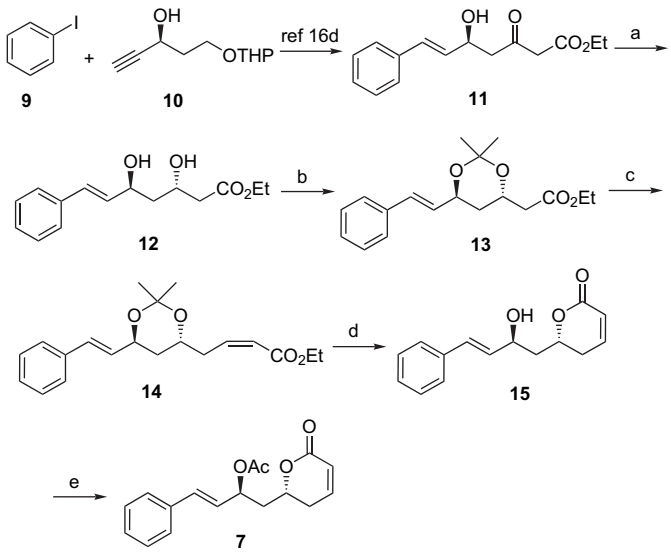
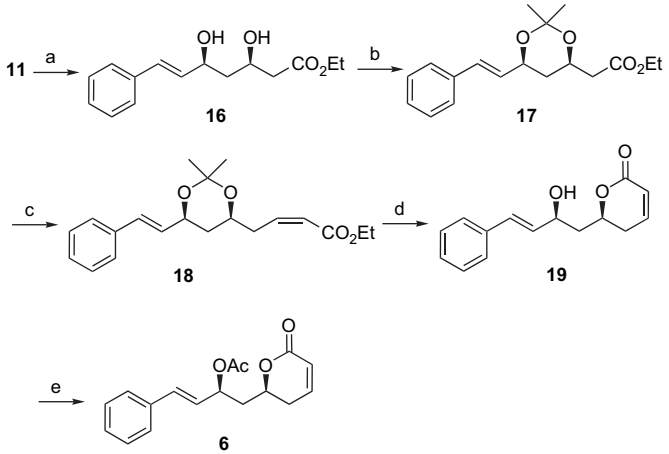


Figure 1.



Scheme 1. Reagents and conditions: (a) $Me_4NBH(OAc)_3$, acetonitrile/acetic acid (1:1), 0 °C, 3 h, 79%; (b) 2,2′-dimethoxy propane, CH_2Cl_2, PPTS, 2 h, rt, 91%; (c) (i) $LiAlH_4$, THF, 30 min, 0 °C to rt, 30 min; (ii) IBX, DCM/DMSO, 0 °C to rt, 4 h; (iii) $(F_3CCH_2O)_2POCH_2CO_2Me$, NaH, dry THF, −78 °C, 60 min, 67% (over three steps); (d) PPTS, methanol, rt, 4 h; (e) Ac_2O/pyridine, CH_2Cl_2, rt, 2 h, 56%.

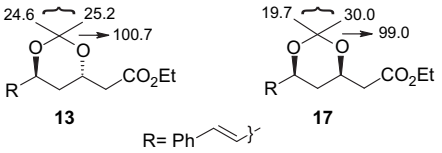


Scheme 2. Reagents and conditions: (a) catecholborane, dry THF, −10 °C, 4 h, 92%; (b) 2,2′-dimethoxy propane, CH_2Cl_2, PPTS, 2 h, rt, 89%; (c) (i) DIBAL–H, DCM, −78 °C, 60 min; (ii) $(F_3CCH_2O)_2POCH_2CO_2Me$, NaH, dry THF, −78 °C, 30 min, 66% (over two steps); (d) PPTS, methanol, rt, 4 h, 63%; (e) Ac_2O/pyridine, CH_2Cl_2, 0 °C to rt, 1 h, 57%.

the traces of trans isomer that could be separated by flash column chromatography. Compound **14** was characterized by ^1H and ^{13}C NMR spectroscopy. In the ^1H NMR spectrum, the olefinic protons resonated at δ 5.84 as a doublet of triplet (J=11.7, 1.5 Hz) and at δ 6.35 as doublet of doublet (J=11.7, 4.7 Hz) confirming the (*Z*)-geometry of the double bond. Finally, acid catalyzed deprotection of the acetonide group, concomitant cyclization using pyridinium *para*-toluenesulfonate in methanol at room temperature for 4 h, and acetylation (Ac_2O/pyridine/CH_2Cl_2/rt) afforded the target compound **7** (56% over two steps), $[\alpha]_D^{25}$ +17.8 (*c* 0.25, $CHCl_3$); lit.[6] $[\alpha]_D^{25}$ +15.55 (*c* 2.52, $CHCl_3$). The spectral data of synthetic **7** were in accordance with those of the natural product.[6]

Similarly, the other stereoisomer **6**, $[\alpha]_D^{25}$ −75.4 (*c* 0.7, $CHCl_3$), lit.[8] $[\alpha]_D^{25}$ −75.1 (*c* 0.68, $CHCl_3$) (Scheme 2), was also obtained from **11** by stereoselective *syn* reduction using catecholborane[18b,20] and then by following a similar sequence of reactions as detailed in Scheme 1. The stereochemical assignment of the newly created center was made based on Rychnovsky's analogy[18] wherein the ^{13}C NMR spectra of **17** exhibited acetonide methyl carbon peaks at δ 19.7 and 30.0 and quaternary carbon at δ 99.0, which were characteristic of the acetonide of *syn*-1,3-diol moiety. The target molecule **6** was isolated as a white solid, mp 127–129 °C (reported as liquid in lit. 8).

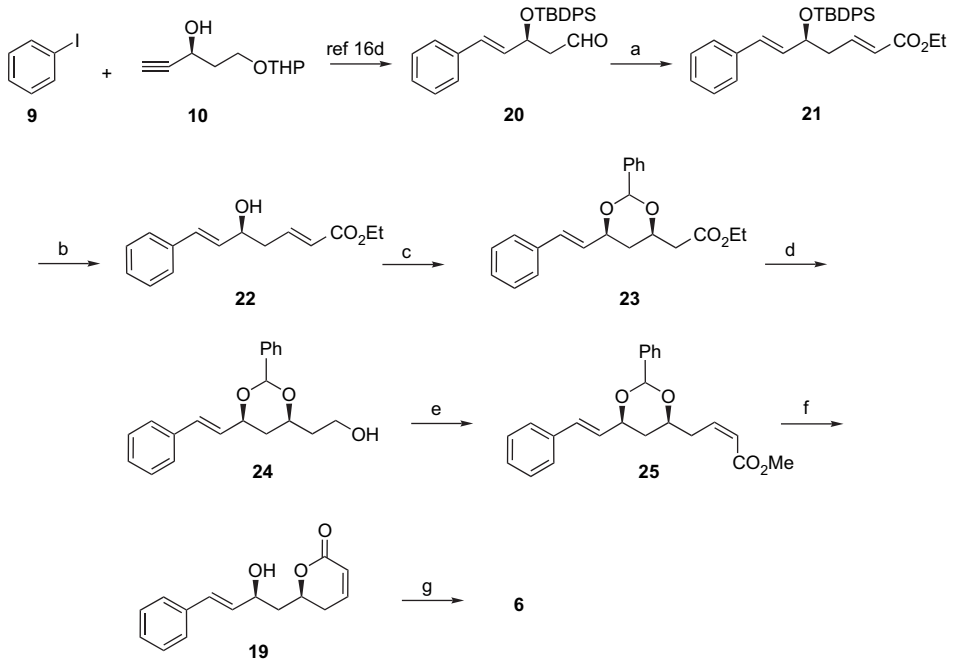
Diagnostic ^{13}C NMR shifts of the acetonides **13** and **17** derived from the diols **12** and **16** are shown in Scheme 3.



Scheme 3.

We also report an alternate and convenient synthesis of (−)-(6*S*,2′*S*)-*epi* cryptocaryalactone **6** based on benzylidene acetal and *Z*-Wittig olefination reactions as key steps (Scheme 4). The synthesis of **6** began from the known aldehyde **20**[16d] prepared from iodobenzene **9** and an acetylenic alcohol **10**. The aldehyde **20** was subjected to a Wittig reaction with the stable ylide, ethoxycarbonylmethylene triphenylphosphorane to furnish the α,β-unsaturated ester **21** in 91% yield. Next, the TBDPS group was removed using TBAF in THF to afford **22** in 82% yield. Benzylidene acetal (protected *syn*-1,3-diol) **23** was prepared in 60% yield by base catalyzed intramolecular conjugate addition using benzaldehyde and potassium *tert*-butoxide in dry THF at 0 °C for 2 h and pH 7 buffer phosphate solution.[21]

Next, the ester group in **23** was reduced with LAH in THF to furnish the alcohol **24** in 85% yield. The primary alcohol **24** was subjected to oxidation in the presence of *o*-iodoxybenzoic acid (IBX) in DCM/DMSO at 0 °C to furnish the corresponding aldehyde



Scheme 4. Reagents and conditions: (a) $Ph_3P{=}CHCOOEt$, DCM, 0 °C, 2 h, 91%; (b) TBAF, THF, 2 h, rt, 82%; (c) benzaldehyde and potassium *tert*-butoxide, dry THF, 0 °C, 2 h, pH 7 phosphate buffer, 60%; (d) LAH, THF, 30 min, 0 °C, 85%; (e) (i) IBX, DCM/DMSO, 0 °C to rt, 3 h, (ii) $(F_3CCH_2O)_2POCH_2CO_2Me$, NaH, dry THF, −78 °C, 30 min, 76% (over two steps; (f) (i) 80% aq AcOH, 67 °C, 2 h; (ii) PTSA, benzene, rt, 1 h, 70%; (g) Ac_2O/pyridine, CH_2Cl_2, rt, 1 h, 73%.

in good yield, and the crude aldehyde was then chain-elongated via a Wittig reaction to give the corresponding α,β-unsaturated ester **25** {$(F_3CCH_2O)_2POCH_2COOMe$, NaH, dry THF, −78 °C, 76% over two steps} predominantly as the *Z*-isomer,[19] as characterized by ^1H and ^{13}C NMR spectroscopy. For example, the coupling constant (J=11.3 Hz) of the olefinic protons confirmed the (*Z*)-geometry of the olefin.

Finally, hydrolysis (80% aq AcOH at 60 °C for 2 h) of the benzylidene acetal followed by concomitant lactone cyclization with *p*-toluenesulfonic acid in benzene at room temperature yielded **19** in 70% yield and then acylated by the addition of acetic anhydride and pyridine in CH_2Cl_2 at room temperature for 1 h to afford the target compound **6** as a white solid (mp 127–129 °C) (reported as liquid in lit. 8) in 73% yield. The spectroscopic data of synthetic material were identical to the reported values.[8]

3. Conclusion

In conclusion, stereoselective reduction reactions were used as key steps for installing the chiral centers of the 1,3-polyol system and subsequent elaboration to the α,β-unsaturated-δ-lactone moiety affords target molecules, cryptocaryalactone **7** and *epi* cryptocaryalactone **6**. The stereoselective synthesis of **6** has also been achieved by a simple strategy wherein a benzylidene acetal reaction is utilized for installing the 1,3-*syn* polyol system.

4. Experimental

4.1. General

Reactions were conducted under N_2 in anhydrous solvents such as CH_2Cl_2, THF, and EtOAc. All reactions were monitored by TLC (silica-coated plates and visualizing under UV light). Light petroleum (bp 60–80 °C) was used. Yields refer to chromatographically and spectroscopically (^1H and ^{13}C NMR) homogeneous material. Air-sensitive reagents were transferred by syringe or double-ended needle. Evaporation of solvents was performed at reduced pressure on a Buchi rotary evaporator. ^1H and ^{13}C NMR spectra of samples in $CDCl_3$ were recorded on Varian FT-200 MHz (Gemini) and Bruker UXNMR FT-300 MHz (Avance) spectrometers. Chemical shift δ is reported relative to TMS (δ=0.0) as an internal standard. Mass spectra were recorded E1 conditions at 70 eV on an LC-MSD (Agilent technologies) spectrometers. All high-resolution spectra were recorded on QSTAR XL hybrid MS/MS system (Applied Biosystems/MDS sciex, foster city, USA), equipped with an ESI source (IICT, Hyderabad). Column chromatography was performed on silica gel (60–120 mesh) supplied by Acme Chemical Co., India. TLC was performed on Merck 60 F-254 silica gel plates. Optical rotations were measured with JASCO DIP-370 Polarimeter at 25 °C.

*4.1.1. Ethyl 2-(4S,6S)-2,2-dimethyl-6-[(E)-2-phenyl-1-ethenyl]-1,3-dioxan-4-ylacetate (**13**)*

To a stirred solution of tetramethylammonium triacetoxyborohydride (1.506 g, 5.724 mmol) in anhydrous acetonitrile (5.0 mL) was added acetic acid (5.0 mL) and the mixture was stirred at room temperature for 30 min. The mixture was cooled to 0 °C and acetonitrile solution of compound **11** (1.0 g, 3.816 mmol in 2 mL of acetonitrile) was added. The mixture was stirred at the same temperature for 3 h. The reaction was quenched with 0.5 N aqueous sodium potassium tartrate (5 mL), the mixture was diluted with CH_2Cl_2 (40 mL), and washed with saturated aqueous Na_2CO_3 solution (2×10 mL). The aqueous layer was back extracted with CH_2Cl_2 (2×20 mL) and the combined organic layers were washed with saturated aqueous Na_2CO_3 solution (2×20 mL). The aqueous layer was back extracted with CH_2Cl_2 (2×20 mL) and the combined organic layers were dried over Na_2SO_4 (3 g). After concentration in vacuo, the residue was purified by column chromatography (petroleum ether/ethyl acetate 1:1) to give a mixture of *syn*-and *anti*-dihydroxy ester **12** (*syn*/*anti* 1:9). The mixture fraction was purified by flash column chromatography (petroleum ether/ethyl acetate 1:1) and *anti*-dihydroxy ester **12** was isolated as a colorless oil (0.89 g, 79%); R_f=0.50 (petroleum ether/ethyl acetate 1:1). The enantiomeric excess of **12** was determined after conversion of **12** into the corresponding acetonide-protected compound **13**

[2,2-dimethoxypropane (0.8 g, 3.030 mmol), CH_2Cl_2, catalytic amount of PPTS (pyridinium *para*-toluenesulfonate) (0.02 mg)] as an oil (0.84 g, 91%); R_f=0.68 (petroleum ether/ethyl acetate 8:2). ^{1}H NMR data of acetonide-protected compound **13**: $[\alpha]_D^{25}$ +19.5 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ [ppm]=1.27 (t, *J*=6.8 Hz, 3H, –CH_2–CH_3), 1.38 (s, 3H, acetonide CH_3), 1.41 (s, 3H, acetonide CH_3), 1.66–1.82 (m, 1H, CH(O)–CH_aH_b–CH(O)), 1.87–2.03 (m, 1H, CH(O)–CH_aH_b–CH(O)), 2.35–2.42 (m, 1H, CH_aH_b–COOEt), 2.48–2.55 (m, 1H, CH_aH_b–COOEt), 4.14 (q, *J*=7.5 Hz, 2H, –OCH_2–CH_3), 4.26–4.39 (m, 1H, –CH(O)–CH_2–COOEt), 4.43–4.58 (m, 1H, –CH=CH–CH(O)), 6.17 (dd, *J*=15.8, 6.0 Hz, 1H, Ph–CH=CH), 6.53 (dd, *J*=15.8, 9.0 Hz, 1H, Ph–CH=CH), 7.15–7.42 (m, 5H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm]=14.1, 24.6, 25.2, 36.6, 40.8, 60.4, 63.3, 67.6, 100.7, 126.4, 127.6, 128.4, 129.4, 130.5, 136.5, 170.7. IR (Neat): 3040, 2987, 2925, 2855, 1737, 1599, 1495, 1455, 1378, 1312, 1222, 1199, 1166, 1089, 1024, 967, 747, 694 cm^{-1}; ESI-MS: *m*/*z* 327 $[M+Na]^+$. HRMS (ESI) $[M+Na]^+$ *m*/*z* calcd for $C_{18}H_{24}O_4Na$: 327.1572; found: 327.1566 (−1.9 ppm error).

4.1.2. Methyl (Z)-4-(4R,6S)-2,2-dimethyl-6-[(E)-2-phenyl-1-ethenyl]-1,3-dioxan-4-yl-2-butenoate (**14**)

To a stirred suspension of $LiAlH_4$ (0.0624 g, 1.644 mmol) in dry THF (20 mL) at 0 °C was added dropwise, a solution of compound **13** (0.5 g, 1.644 mmol) in dry THF (5 mL). The reaction mixture was allowed to warm to room temperature and stirred for 30 min. It was then cooled to 0 °C, diluted with ethyl acetate (20 mL), and quenched with dropwise addition of saturated aqueous Na_2SO_4 solution (2 mL). The solid material was filtered through a Celite pad (1 g) and washed thoroughly with hot ethyl acetate (4×20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 (2 g). The solvent was removed under vacuo and the crude residue was used for the next stage. To an ice-cooled solution of 2-iodoxybenzoic acid (0.92 g, 3.289 mmol) in DMSO (1.5 mL) was added a solution of the above crude alcohol in anhyd CH_2Cl_2 (10 mL). The mixture was stirred at room temperature for 2 h and then filtered through a Celite pad (1 g) and washed with CH_2Cl_2 (4×20 mL). The combined organic filtrates were washed with H_2O (2×10 mL) and brine (2×10 mL), dried (anhyd Na_2SO_4), and concentrated in vacuo to afford crude aldehyde, which was used for the next stage without further purification.

In a 25 mL RB flask NaH (0.079 g, 3.29 mmol) was taken and to it 5 mL of dry THF was added under N_2 atmosphere. After 5 min, bis-(2,2,2-trifluoromethyl)(methoxycarbonylmethyl)phosphonate (0.63 g, 1.97 mmol) in 2 mL of dry THF was added dropwise at 0 °C. It was allowed for stirring for 30 min. The reaction mixture was cooled to −78 °C and the above aldehyde in dry THF (3 mL) was added dropwise over a period of 10 min, and the resulting mixture was stirred for 60 min at −78 °C. The reaction mixture was quenched with saturated NH_4Cl (2 mL) and the product was extracted into ethyl acetate (4×10 mL), dried over anhydrous Na_2SO_4 (1 g), and evaporated in vacuo (water bath temperature should not exceed more than 30 °C) and the product was purified using silica gel (60–120 mesh) column chromatography (petroleum ether/ethyl acetate 8:2) with 20% EtOAc in hexane to afford (*Z*)-olefin ester **14** as viscous liquid (0.35 g, 67% yield, over three steps); R_f=0.62 (petroleum ether/ethyl acetate 8:2); $[\alpha]_D^{25}$ +8.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ [ppm]=1.39 (s, 3H, acetonide CH_3), 1.43 (s, 3H, acetonide CH_3), 1.63 (dt, *J*=12.5, 2.3 Hz, 1H, CH(O)–CH_aH_b–CH(O)), 1.84 (dd, *J*=9.3, 2.3 Hz, 1H, CH(O)–CH_aH_b–CH(O)), 2.57–2.85 (m, 1H, CH_aH_b–CH=CH–CO_2Me), 2.87–3.10 (m, 1H, –CH_aH_b–CH=CH–CO_2Me), 3.70 (s, 3H, OCH_3), 3.80–4.11 (m, 1H, –CH(O)–CH_2–CH=CH), 4.41–4.56 (m, 1H, Ph–CH=CH–CH(O)), 5.84 (dt, *J*=11.7, 1.5 Hz, 1H, –CH=CH–CO_2Me), 6.13 (dd, *J*=16.0, 6.2 Hz, 1H, Ph–CH=CH), 6.35 (dd, *J*=11.7, 4.6 Hz, 1H, –CH=CH–CO_2Me), 6.52 (dd, *J*=15.6, 4.6 Hz, 1H, Ph–CH=CH–), 7.07–7.42 (m, 5H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm]=24.8, 25.4, 35.4, 37.3, 50.9, 67.6, 69.9, 100.4, 120.7, 126.4, 127.5, 128.4, 129.7, 130.6, 136.6, 146.0, 166.6. IR (Neat): 3040, 2990, 2945, 1721, 1647, 1493, 1440, 1378, 1225, 1197, 1171, 1131, 1096, 1024, 967, 820, 746, 694 cm^{-1}; ESI-MS: *m*/*z* 339 $[M+Na]^+$. HRMS (ESI) $[M+Na]^+$ *m*/*z* calcd for $C_{19}H_{24}O_4Na$: 339.1572; found: 339.1579 (2.0 ppm error). ^{1}H NMR data of the corresponding trans compound: ^{1}H NMR ($CDCl_3$, 300 MHz): δ [ppm]=1.40 (s, 3H, acetonide CH_3), 1.43 (s, 3H, acetonide CH_3), 1.61 (dt, *J*=12.8, 2.2 Hz, 1H, CH(O)–CH_aH_b–CH(O)), 1.70–1.91 (m, 1H, CH(O)–CH_aH_b–CH(O)), 2.26–2.37 (m, 1H, CH_aH_b–CH=CH–CO_2Me), 2.38–2.51 (m, 1H, CH_aH_b–CH=CH–CO_2Me), 3.72 (s, 3H, OCH_3), 3.93–4.07 (m, 1H, –CH(O)–CH_2–CH=CH), 4.43–4.54 (m, 1H, Ph–CH=CH–CH(O)), 5.86 (dt, *J*=15.8, 1.5 Hz, 1H, –CH=$CH_{(trans)}$–CO_2Me), 6.13 (dd, *J*=15.8, 6.0 Hz, 1H, Ph–CH=CH), 6.52 (dd, *J*=15.8, 7.5 Hz, 1H, Ph–CH=CH), 6.91 (dt *J*=15.8, 7.5 Hz, 1H, –$CH_{(trans)}$=CH–CO_2Me), 7.15–7.35 (m, 5H).

4.1.3. (+)-(6R,2′S)-Cryptocaryalactone (**7**)

To a stirred solution of compound **14** (0.1 g, 0.316 mmol) in methanol (3 mL) was added catalytic amount of pyridinium *para*-toluenesulfonate (10 mg). The reaction mixture was stirred at room temperature for about 4 h and the solvent was removed under reduced pressure. To the crude CH_2Cl_2 (3 mL), pyridine (0.05 mL, 0.63 mmol) was added followed by acetic anhydride (0.047 mL, 0.474 mmol) at 0 °C. The reaction mixture was continued to stir for 2 h and then diluted with CH_2Cl_2 (10 mL). The organic layer was washed with 5% $NaHCO_3$ solution (2×5 mL) and brine (2×5 mL), and dried over anhydrous Na_2SO_4 (100 mg). Evaporation of the solvent under reduced pressure followed by column chromatography (petroleum ether/ethyl acetate 1:1) to give 0.05 g (56% yield) of (+)-(6*R*,2′*S*)-cryptocaryalactone **7** as crystals; R_f=0.64 (petroleum ether/ethyl acetate 1:1); mp 125–126 °C; $[\alpha]_D^{25}$ +17.8 (*c* 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ [ppm]=2.08 (s, 3H, OAc), 2.08 (m, 1H, H-1′$_a$), 2.20 (ddd, *J*=14.5, 8.1,4.5 Hz, 1H, H′$_b$), 2.34–2.42 (m, 2H, H-5), 4.53 (m, 1H, H-6), 5.65 (m, 1H, H-2′), 6.03 (dt, *J*=10.2, 2.0 Hz, 1H, H-3), 6.11 (dd, *J*=15.9, 7.4 Hz, 1H, H-3′), 6.66 (d, *J*=15.9 Hz, 1H, H-4′), 6.85 (dt, *J*=10.0, 4.5 Hz, 1H, H-4), 7.20–7.40 (m, 5H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm]=21.29 (OAc), 29.5 (C-5), 39.9 (C-11), 70.7 (C-2′), 74.2 (C-6), 121.5 (C-3), 126.5 (C-3′), 126.6, 128.1, 128.6, 135.9 (Ar–C), 133.3 (C-4′), 144.5 (C-4), 163.9 (CO), 169.9 (OCOMe); IR (Neat): 3040, 2925, 1730, 1492, 1425, 1375, 1240, 1075, 1034, 966 cm^{-1}; ESI-MS: *m*/*z* 309 $[M+Na]^+$. HRMS (ESI) $[M+Na]^+$ *m*/*z* calcd for $C_{17}H_{18}O_4Na$: 309.1102; found: 309.1115 (4.0 ppm error).

4.1.4. Ethyl 2-(4R,6S)-2,2-dimethyl-6-[(E)-2-phenyl-1-ethenyl]-1,3-dioxan-4-ylacetate (**17**)

A solution of compound **11** (1.0 g, 3.816 mmol) in dry tetrahydrofuran was chilled in a MeOH–ice bath (−10 °C) and charged with freshly distilled 1 M solution of catecholborane (1.22 mL, 11.45 mmol). After 4 h, the reaction mixture was quenched by the addition of 1 mL of anhydrous MeOH and 2 mL of a saturated aqueous solution of sodium potassium tartarate. This mixture was allowed to stir at room temperature for 1 h, layers were separated, and the aqueous layer was extracted with ethyl acetate (3×30 mL). The organic extracts were washed with brine (30 mL), dried over anhydrous Na_2SO_4, and the desired product was isolated by silica gel column chromatography (petroleum ether/ethyl acetate 1:1) to afford the diol **16** (0.85 g, 84%) (*syn*/*anti* >20:1) as a colorless liquid; R_f=0.50 (petroleum ether/ethyl acetate 1:1). The enantiomeric excess of **16** (0.7 g, 2.65 mmol) was determined after conversion of **16** into the corresponding acetonide-protected compound [(2,2-dimethoxypropane, 0.55 g, 5.303 mmol), CH_2Cl_2 (15 mL), catalytic amount of PPTS (pyridinium *para*-toluenesulfonate) (0.02 mg)] as a colorless oil (0.72 g, 89.35%); R_f=0.59 (petroleum ether/ethyl acetate 8:2). Acetonide-protected compound **17**: $[\alpha]_D^{25}$ −22.7 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ [ppm]=1.27 (t, *J*=6.8 Hz, 3H,

–CH_2–CH_3), 1.38 (s, 3H, acetonide CH_3), 1.41 (s, 3H, acetonide CH_3), 1.66–1.82 (m, 1H, CH(O)–CH_aH_b–CH(O)), 1.87–2.03 (m, 1H, CH(O)–CH_aH_b–CH(O)), 2.34 (dd, 1H, J=15.8, 6.0 Hz, CH_aH_b–COOEt), 2.53 (dd, J=15.8, 7.5 Hz, 1H, CH_aH_b–COOEt), 4.14 (q, J=7.5 Hz, 2H, –OCH_2–CH_3), 4.26–4.39 (m, 1H, –CH(O)–CH_2–COOEt), 4.43–4.58 (m, 1H, –CH=CH–CH(O)), 6.11 (dd, J=15.8, 6.0 Hz, 1H, Ph–CH=CH), 6.53 (dd, J=15.8, 9.0 Hz, 1H, Ph–CH=CH), 7.14–7.36 (m, 5H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm]=14.5, 19.7, 30.0, 37.3, 41.3, 60.4, 65.7, 69.8, 99.0, 126.4, 127.6, 128.4, 129.5, 130.7, 136.5, 170.8. IR (Neat): 3040, 2987, 2925, 2855, 1737, 1599, 1495, 1455, 1378, 1312, 1222, 1199, 1166, 1089, 1024, 967, 747, 694 cm^{-1}; ESI-MS: m/z 327 [M+Na]$^+$. HRMS (ESI) [M+Na]$^+$ m/z calcd for $C_{18}H_{24}O_4Na$: 327.1572; found: 327.1566 (−1.9 ppm error).

4.1.5. Methyl (Z)-4-(4S,6S)-2,2-dimethyl-6-[(E)-2-phenyl-1-ethenyl]-1,3-dioxan-4-yl-2-butenoate (**18**)

Ester **17** (0.6 g, 1.973 mmol) was dissolved in CH_2Cl_2 (20 mL) and cooled to −78 °C. To a solution was added a 1 M solution of DIBAL–H (4.93 mL) in CH_2Cl_2. After 60 min, the reaction was quenched with methanol (1 mL) and potassium sodium tartrate (2 mL), and stirred at room temperature for 30 min. The layers were separated and the aqueous layer extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (2×10 mL), dried over anhydrous Na_2SO_4 (1 g), filtered, and concentrated in vacuo to give the corresponding unstable aldehyde, which was used directly for further reaction. To a stirred solution of *O*,*O*′-bis-(2,2,2-trifluoroethyl)(methoxycarbonylmethyl)phosphonate (0.75 g, 2.366 mmol), in dry THF (10 mL) at 0 °C was added NaH (0.12 mg, 4.93 mmol) and stirred for 30 min at 0 °C. To the reaction mixture, the above aldehyde dissolved in dry THF (4 mL) was added and stirred for 60 min at −78 °C. The reaction mixture was quenched with satd NH_4Cl solution (3 mL) and stirred at room temperature for 10 min. The layers were separated and the aqueous layer extracted with EtOAc (2×30 mL). The combined organic layers were washed with brine (2×20 mL), dried over Na_2SO_4 (1 g), concentrated in vacuo, and the residue purified by column chromatography (petroleum ether/ethyl acetate 8:2) to afford the ester **18** (0.41 g, 66%) as a viscous liquid; R_f=0.63 (petroleum ether/ethyl acetate 8:2); $[\alpha]_D^{25}$ −5.5 (*c* 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz): δ [ppm]=1.39 (s, 3H, acetonide CH_3), 1.43 (s, 3H, acetonide CH_3), 1.63 (dt, J=12.5, 2.3 Hz, 1H, CH(O)–CH_aH_b–CH(O)), 1.75–1.91 (m, 1H, CH(O)–CH_aH_b–CH(O)), 2.64–2.85 (m, 1H, CH_aH_b–CH=CH–CO_2Me), 2.87–3.10 (m, 1H, –CH_aH_b–CH=CH–CO_2Me), 3.70 (s, 3H, OCH_3), 3.83–4.10 (m, 1H, –CH(O)–CH_2–CH=CH), 4.41–4.57 (m, 1H, Ph–CH=CH–CH(O)), 5.84 (dt, J=11.6, 1.6 Hz, 1H, –CH=CH–CO_2Me), 6.18 (dd, J=16.4, 6.2 Hz, 1H, Ph–CH=CH), 6.39 (dd, J=11.6, 7.4 Hz, 1H, –CH=CH–CO_2Me), 6.52 (dd, J=15.8, 4.1 Hz, 1H, Ph–CH=CH–), 7.08–7.40 (m, 5H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm]=19.8, 30.3, 35.0, 36.6, 50.9, 65.9, 68.1, 98.8, 120.7, 126.4, 127.5, 128.4, 129.7, 130.3, 136.6, 145.8, 166.6. IR (Neat): 2991, 2925, 2855, 1724, 1656, 1492, 1437, 1379, 1270, 1198, 1163, 1094, 1038, 969, 874, 748, 694. ESI-MS: m/z 339 [M+Na]$^+$. HRMS (ESI) [M+Na]$^+$ m/z calcd for $C_{19}H_{24}O_4Na$: 339.1572; found: 339.1579 (2.0 ppm error).

4.1.6. (6S)-6-[(2S,3E)-2-Hydroxy-4-phenyl-3-butenyl]-5,6-dihydro-2H-2-pyranone (**19**)

To a stirred solution of compound **18** (0.35 g, 1.107 mmol) in CH_2Cl_2 (30 mL) was added catalytic amount of PPTS (20 mg). The reaction mixture was stirred at room temperature for about 4 h. CH_2Cl_2 was removed under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/ethyl acetate 1:1) to give **19** (0.17 g, 63%) as a colorless oil; R_f=0.54 (petroleum ether/ethyl acetate 1:1); $[\alpha]_D^{25}$ −21.5 (*c* 0.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz): δ [ppm]=1.71–1.99 (m, 1H, *H*-1′$_a$), 2.00–2.23 (m, 1H, *H*-1′$_b$), 2.30–2.50 (m, 2H, *H*-5), 4.36–4.87 (m, 2H, *H*-6 and *H*-2′), 6.02 (dt, J=10.0, 1.6 Hz, 1H, *H*-3), 6.21 (dd, J=16.0, 7.0 Hz, 1H, *H*-3′), 6.64 (d, J=16.0 Hz, 1H, *H*-4′), 6.78–6.92 (m, 1H, *H*-4), 7.25–7.42 (m, 5H, Ar–*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm]=29.9 (C-5), 42.4 (C-1′), 69.7 (C-2′), 76.0 (C-6), 121.3 (C-3), 126.5, 128.0, 128.6 (Ar–C), 130.3 (C-3′), 131.4 (C-4′), 136.4 (Ar–C), 145.5 (C-4), 164.6 (C-2); IR (Neat): 3420, 3060, 2925, 1712, 1625, 1483, 1388, 1254, 1042, 917, 815, 756 cm^{-1}; ESI-MS: m/z 267 [M+Na]$^+$. HRMS (ESI) [M+Na]$^+$ m/z calcd for $C_{15}H_{16}O_3Na$: 267.0997; found: 267.0994 (−1.2 ppm error).

4.1.7. (−)-(6S,2′S)-epi Cryptocaryalactone **6**

To a stirred solution of compound **19** (0.12 g, 0.49 mmol) in dry CH_2Cl_2 (3 mL) was added pyridine (0.077 mL, 0.98 mmol) followed by acetic anhydride (0.073 mL, 0.737 mmol) at 0 °C. The reaction mixture was continued to stir for 1 h and then diluted with CH_2Cl_2 (10 mL). The organic layer was washed with 5% $NaHCO_3$ solution (2×3 mL), brine (2×3 mL), and dried over anhydrous Na_2SO_4 (100 mg). Evaporation of the solvent under reduced pressure followed by column chromatography (petroleum ether/ethyl acetate 1:1) afforded the acetate **6** (0.08 g, 57%) as white solid; R_f=0.64 (petroleum ether/ethyl acetate 5:5); mp 127–129 °C. $[\alpha]_D^{25}$ −75.4 (*c* 0.70, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz): δ [ppm]=2.08 (s, 3H, $OCOCH_3$), 2.08 (m, 1H, *H*-1′$_a$), 2.10–2.21 (m, 1H, *H*-1′$_b$), 2.34–2.42 (m, 2H, *H*-5), 4.44–4.57 (m, 1H, *H*-6), 5.54–5.65 (m, 1H, *H*-2′), 6.02 (dt, J=9.8, 1.5 Hz, 1H, *H*-3), 6.10 (dd, J=15.8, 7.5 Hz, 1H, *H*-3′), 6.65 (d, J=15.8 Hz, 1H, *H*-4′), 6.83 (dt, J=9.8, 4.5 Hz, 1H, *H*-4), 7.18–7.39 (m, 5H, Ar–*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm]=21.2 (OAc), 29.5 (C-5), 39.9 (C-1′), 70.7 (C-2′), 74.2 (C-6), 121.5 (C-3), 126.5 (C-3′), 126.6, 128.1, 128.6 (Ar–C), 133.3 (C-4′), 135.9 (Ar–C), 144.5 (C-4), 163.9 (CO), 169.9 (OCOMe); IR (Neat): 3040, 3000, 2950, 2925, 1730, 1499, 1427, 1375, 1237, 1072, 1035, 967, 815, 752 cm^{-1}; ESI-MS: m/z 309 [M+Na]$^+$. HRMS (ESI) [M+Na]$^+$ m/z calcd for $C_{17}H_{18}O_4Na$: 309.1102; found: 309.1115 (4.0 ppm error).

4.1.8. Ethyl (2E,5S,6E)-5-[1-(tert-butyl)-1,1-diphenylsilyl]oxy-7-phenyl-2,6-heptadienoate (**21**)

To a solution of the aldehyde **20** (2.0 g, 4.830 mmol) in CH_2Cl_2 (15 mL) was added PPh_3=CHCOOEt (2.0 g, 5.797 mmol) and the reaction mixture was stirred for 2 h at room temperature. After completion of the reaction, monitored by TLC, CH_2Cl_2 was removed under reduced pressure, residue was dissolved in ether, and petroleum ether was added to it. The triphenylphosphine oxide crystallized out was filtered off and the filtrate was concentrated to dryness. The crude product was purified by column chromatography (petroleum ether/ethyl acetate 9:1) to afford the pure ester **21** (2.14 g, 91% yield) as a colorless liquid; R_f=0.68 (petroleum ether/ethyl acetate 9:1); $[\alpha]_D^{25}$ −65.5 (*c* 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ [ppm]=1.08 (s, 9H, –CH(CH_3)$_3$), 1.27 (t, J=7.5 Hz, 3H, –CH_2–CH_3), 2.20–2.59 (m, 2H, –CH_2–CH=CH), 4.15 (q, J=7.5 Hz, 2H, –OCH_2–CH_3), 4.38 (q, J=7.0 Hz, 1H, –CH(OTBDPS)), 5.72 (d, J=15.8 Hz, 1H, –CH=CH–CO_2Et), 6.06 (dd, J=15.8, 6.8 Hz, 1H, Ph–CH=CH), 6.20 (d, J=15.8 Hz, 1H, Ph–CH=CH), 6.73–6.98 (m, 1H, –CH=CH–CO_2Et), 7.11–7.29 (m, 5H, Ar–*H*), 7.30–7.47 (m, 5H, Ar–*H*), 7.56–7.72 (m, 5H, Ar–*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm]=14.2, 19.3, 27.0, 41.0, 60.1, 73.3, 123.7, 126.5, 127.5, 127.6, 128.4, 129.6, 129.7, 130.6, 133.7, 134.8, 135.9, 144.6, 166.3; IR (Neat): 3068, 2932, 2857, 1720, 1654, 1467, 1427, 1265, 1109, 1048, 973, 741 cm^{-1}; LCMS: m/z 507.2 [M+Na]$^+$. HRMS (ESI) [M+Na]$^+$ m/z calcd for $C_{31}H_{36}O_3NaSi$: 507.2331; found: 507.2337 (1.1 ppm error).

4.1.9. Ethyl (2E,5S,6E)-5-hydroxy-7-phenyl-2,6-heptadienoate (**22**)

To compound **21** (2 g, 4.12 mmol) in dry THF (10 mL) was added TBAF (6.2 mL, 1 M solution in THF) dropwise at room temperature and the mixture was stirred for 2 h, water (2 mL) was added, and the mixture was extracted with ethyl acetate. The organic extracts were washed with brine and dried over anhydrous Na_2SO_4, the solvent was evaporated, and the residue was purified

by column chromatography (petroleum ether/ethyl acetate 7:3) to afford the product **22** (0.840 g, 82%) as a colorless oil; R_f=0.34 (petroleum ether/ethyl acetate 6:4); $[\alpha]_D^{25}$ −4.1 (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ [ppm]=1.29 (t, *J*=7.3 Hz, 3H, –CH_2–CH_3), 2.44–2.58 (m, 2H, –CH_2–CH=CH), 4.17 (q, *J*=7.3 Hz, 2H, –OCH_2–CH_3), 4.41 (q, *J*=6.9 Hz, 1H, –C*H*(OTBDPS)), 5.91 (dt, *J*=15.4, 1.5 Hz, 1H, –CH=C*H*–CO_2Et), 6.20 (dd, *J*=15.4, 6.6 Hz, 1H, Ph–CH=C*H*), 6.60 (d, *J*=16.1 Hz, 1H, Ph–C*H*=CH), 6.97 (dt, *J*=15.4, 7.3 Hz, 1H, –C*H*=CH–CO_2Et), 7.12–7.42 (m, 5H, Ar–*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm]=14.0, 40.0, 60.2, 71.2, 123.7, 126.4, 127.6, 128.4, 130.7, 131.0, 136.3, 144.6, 166.3; IR (Neat): 3439, 3065, 2927, 1715, 1631, 1651, 1383, 1040, 973, 753, 696 cm^{-1}; ESI-MS: *m*/*z* 269 $[M+Na]^+$. HRMS (ESI) $[M+Na]^+$ *m*/*z* calcd for $C_{15}H_{18}O_3Na$: 269.1153; found: 269.1158 (1.6 ppm error).

4.1.10. Ethyl 2-(4S,6S)-2-phenyl-6-[(E)-2-phenyl-1-ethenyl]-1,3-dioxan-4-ylacetate (**23**)

To a solution of alcohol **22** (0.8 g, 3.252 mmol) in dry THF (30 mL) at 0 °C was added distilled benzaldehyde (0.362 mL, 3.577 mmol) followed by *t*-BuOK (0.036 g, 0.325 mmol). The yellow solution was stirred for 15 min at 0 °C. The addition of benzaldehyde/*t*-BuOK was repeated twice and allowed to warm to room temperature after which the reaction was quenched with pH 7 phosphate buffer (25 mL). The layers were separated and the aqueous layer was extracted with ether (4×30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo and purified by column chromatography (petroleum ether/ethyl acetate 2:8) to obtain **23** (0.69 g, 60%) as a colorless oil; R_f=0.82 (petroleum ether/ethyl acetate 8:2); $[\alpha]_D^{25}$ −7.0 (*c* 0.25, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ [ppm]=1.28 (t, *J*=7.5 Hz, 3H, –CH_3), 1.64 (dd, *J*=12.8, Hz, 1H, CH(O)–C$H_a$$H_b$–CH(O)), 1.88 (dt, *J*=12.8, 2.2 Hz, 1H, CH(O)–C$H_a$$H_b$–CH(O)), 2.50 (dd, *J*=15.8, 6.0 Hz, 1H, –C$H_a$$H_b$–$CO_2$Et), 2.74 (dd, *J*=15.1, 6.8 Hz, 1H, –C$H_a$$H_b$–$CO_2$Et), 4.16 (q, *J*=7.5 Hz, 2H, –OCH_2–CH_3), 4.29–4.44 (m, 1H, –C*H*(O)–CH_2–COEt), 4.49–4.60 (m, 1H, –CH=CH–C*H*(O)), 5.63 (s, 1H, Ph–C*H*–), 6.23 (dd, *J*=16.6, 6.0 Hz, 1H, Ph–CH=C*H*–), 6.44 (d, *J*=16.6 Hz, 1H, Ph–C*H*=CH–), 7.13–7.56 (m, 10H, Ar–*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm]=14.1, 36.6, 40.8, 60.5, 73.0, 76.9, 100.6, 126.1, 126.4, 127.7, 128.0, 128.4, 128.7. 130.8, 132.4, 136.4, 138.2, 170.5; IR (Neat): 3031, 2922, 1734, 1635, 1495, 1451, 1212, 1161, 1099, 1022, 967, 754, 698 cm^{-1}; ESI-MS: *m*/*z* 375 $[M+Na]^+$. HRMS (ESI) $[M+Na]^+$ *m*/*z* calcd for $C_{22}H_{24}O_4Na$: 375.1572; found: 375.1579 (1.8 ppm error).

4.1.11. Methyl (Z)-4-(4S,6S)-2-phenyl-6-[(E)-2-phenyl-1-ethenyl]-1,3-dioxan-4-yl-2-butenoate (**25**)

To a stirred suspension of $LiAlH_4$ (0.07 g, 1.846 mmol) in dry THF (30 mL) at 0 °C was added dropwise a solution of compound **23** (0.65 g, 1.846 mmol mmol) in dry THF (10 mL). The reaction mixture was allowed to warm to room temperature and stirred for 30 min. It was then cooled to 0 °C, diluted with ethyl acetate (40 mL), and quenched with dropwise addition of saturated aqueous Na_2SO_4 solution (3 mL). The solid material was filtered through a Celite pad (1 g) and washed thoroughly with hot ethyl acetate (3×30 mL). The combined organic layers were dried over anhyd Na_2SO_4 (2 g). Removal of solvent under reduced pressure and purification on silica gel column chromatography (petroleum ether/ethyl acetate 1:1) afforded compound **24** (0.49 g, 85% yield) as a viscous liquid; R_f=0.47 (petroleum ether/ethyl acetate 1:1). To an ice-cooled solution of 2-iodoxybenzoic acid (0.885 g, 3.161 mmol) in DMSO (2.5 mL) was added a solution of the above alcohol (0.49 g, 1.580 mmol) in anhyd CH_2Cl_2 (15 mL). The mixture was stirred at room temperature for 2 h and then filtered through a Celite pad (1 g) and washed with CH_2Cl_2 (3×40 mL). The combined organic filtrates were washed with H_2O (3×10 mL) and brine (3×10 mL), dried (anhyd Na_2SO_4), and concentrated in vacuo to afford crude aldehyde, which was used for the next stage without further purification.

In a 25 mL RB flask NaH (0.0987 g, 4.116 mmol) was taken and 15 mL of dry THF was added under N_2 atmosphere. After 5 min, bis-(2,2,2-trifluoromethyl)(methoxycarbonylmethyl)phosphonate (0.603 g, 1.895 mmol) in 10 mL dry THF was added dropwise at 0 °C and was allowed to stir for 30 min. The reaction mixture was cooled to −78 °C and the above aldehyde in dry THF (3 mL) was added dropwise over a period of 10 min, and the resulting mixture was stirred for 60 min at −78 °C. The reaction mixture was quenched with saturated NH_4Cl (2 mL) and the product was extracted into ethyl acetate (4×20 mL). The extracted ethyl acetate was dried over anhyd Na_2SO_4 (1 g) and evaporated in vacuo (water bath temperature should not exceed more than 45 °C), and the product was purified using silica gel (60–120 mesh) column chromatography (petroleum ether/ethyl acetate 8:2) to afford (*Z*)-olefin ester **25** as viscous liquid (0.20 g, 76% yield); R_f=0.70 (petroleum ether/ethyl acetate 8:2); $[\alpha]_D^{25}$ −8.3 (*c* 1.05, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz): δ [ppm]=1.63–1.75 (m, 1H, –CH(O)–C$H_a$$H_b$–CH(O)), 1.77–1.86 (m, 1H, CH(O)–C$H_a$$H_b$–CH(O)), 2.88–3.01 (m, 1H, –C$H_a$$H_b$–CH=CH–$CO_2$Me), 3.08–3.22 (m, 1H, –C$H_a$$H_b$–CH=CH–$CO_2$Me), 3.74 (s, 3H, O$CH_3$), 3.96–4.17 (m, 1H, C*H*(O)–CH_2–CH=CH–), 4.48–4.60 (m, 1H, Ph–CH=CH–C*H*(O)), 5.62 (s, 1H, Ph–C*H*–), 5.91 (d, *J*=11.3 Hz, 1H, –CH=C*H*–CO_2Me), 6.26 (dd, *J*=15.8, 6.0 Hz, 1H, Ph–CH=C*H*–), 6.52 (td, *J*=11.3, 7.5 Hz, 1H, –C*H*=CH–CO_2Me), 6.66 (d, *J*=15.8 Hz, 1H, Ph–C*H*=CH–), 7.14–7.67 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm]=34.8, 36.5, 50.9, 75.7, 76.4, 100.6, 120.8, 126.0, 126.3, 127.5, 128.0, 128.3, 128.6, 128.7, 130.6, 136.4, 138.3, 145.3, 166.5; IR (Neat): 3033, 2949, 1720, 1648, 1494, 1440, 1402, 1199, 1174, 1103, 1015, 969, 753, 697 cm^{-1}; ESI-MS: *m*/*z* 387 $[M+Na]^+$. HRMS (ESI) $[M+Na]^+$ *m*/*z* calcd for $C_{23}H_{24}O_4Na$: 387.1572; found: 375.1582 (2.5 ppm error).

Acknowledgements

V.B. thanks UGC and S.S.R. thanks CSIR, New Delhi for the award of fellowships.

References and notes

1. (a) Yasui, K.; Tamura, Y.; Nakatani, T.; Kawada, K.; Ohtani, M. *J. Org. Chem.* **1995**, *60*, 7567–7574 and references cited therein; (b) Fang, X. P.; Jone, A.; Chang, C. J.; Mclaughlin, J. L. *J. Nat. Prod.* **1991**, *54*, 1034–1043; (c) Argoudelis, A. D.; Zieserl, J. F. *Tetrahedron Lett.* **1966**, *18*, 1969–1973; (d) For a review of 5,6-dihydro-2*H*-pyran-2-ones, see: Davies-Coleman, M. T.; Rivett, D. E. A. In *Progress in the Chemistry of Organic Natural Products*; Herz, W., Grisebach, H., Kirby, G. W., Tamm, Ch., Eds.; Springer: New York, NY, 1989; Vol. 55, pp 1–35.
2. Bohlmann, F.; Suwita, A. *Phytochemistry* **1979**, *18*, 677–679.
3. Juliawata, L. D.; Kitajima, M.; Takayama, H.; Achmad, S. A.; Aimi, N. *Phytochemistry* **2000**, *54*, 989–993.
4. Drewes, S. E.; Schlapelo, B. M.; Horn, M. M.; Scoltt Shaw, R.; Sander, O. *Phytochemistry* **1995**, *38*, 1427–1430.
5. Drewes, S. E.; Horn, M. M.; Shaw, R. S. *Phytochemistry* **1995**, *40*, 321–323.
6. Govindachari, T. R.; Parthasarathy, P. C.; Modi. *Indian J. Chem.* **1972**, *10*, 149–151.
7. Spencer, G. F.; England, R. E.; Wolf, R. B. *Phytochemistry* **1984**, *23*, 2499–2500.
8. Meyer, H. H. *Liebigs Ann. Chem.* **1984**, 977–981.
9. Zschocke, S.; van Staden, J. *J. Ethnopharmacol.* **2000**, *71*, 473–478.
10. Drewes, S. E.; Horn, M. H.; Mavi, S. *Phytochemistry* **1997**, *44*, 437–440.
11. Hawariah, A.; Stanslas, J. *Anticancer Res.* **1998**, *18*, 4383–4386.
12. Pihie, A. H. L.; Stanslas, J.; Din, L. B. *Anticancer Res.* **1998**, *18*, 1739–1744.
13. Ee, Y. S.; Lai, L. C.; Reimann, K.; Lim, P. K. C. *Oncol. Rep.* **1999**, *6*, 843–846.
14. Hawariah, L. P. A.; Munawer, M.; Din, L. B. *Asia-Pac J. Pharmacol.* **1994**, *9*, 273–277.
15. Mori, Y.; Furukawa, H. *Chem. Pharm. Bull.* **1994**, *42*, 2161–2163.
16. (a) Sabitha, G.; Sudhakar, K.; Reddy, N. M.; Rajkumar, M.; Yadav, J. S. *Tetrahedron Lett.* **2005**, *46*, 6567–6570; (b) Sabitha, G.; Narjis, F.; Swapna, R.; Yadav, J. S. *Synthesis* **2006**, *17*, 2879–2884; (c) Sabitha, G.; Reddy, E. V.; Yadagiri, K.; Yadav, J. S. *Synthesis* **2006**, *19*, 3270–3274; (d) Sabitha, G.; Sudhakar, K.; Yadav, J. S. *Tetrahedron Lett.* **2006**, *47*, 8599–8602; (e) Sabitha, G.; Bhaskar, V.; Yadav, J. S. *Tetrahedron Lett.* **2006**, *47*, 8179–8181; (f) Sabitha, G.; Swapna, R.; Reddy, E. V.; Yadav, J. S. *Synthesis* **2006**, *24*, 4242–4246; (g) Sabitha, G.; Bhikshapathi, M.;

Yadav, J. S. *Synth. Commun.* **2007**, *37*, 561–569; (h) Sabitha, G.; Gopal, P.; Yadav, J. S. *Synth. Commun.* **2007**, *37*, 1495–1502; (i) Sabitha, G.; Yadagiri, K.; Yadav, J. S. *Tetrahedron Lett.* **2007**, *48*, 1651–1652; (j) Sabitha, G.; Yadagiri, K.; Yadav, J. S. *Tetrahedron Lett.* **2007**, *48*, 8065–8068.
17. (a) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560–3578; (b) Evans, D. A.; Chapman, K. T. *Tetrahedron Lett.* **1986**, *27*, 5939–5942.
18. (a) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945–948; (b) Evans, D. A.; Rieger, D. L,; Gage, J. R. *Tetrahedron Lett.* **1990**, *31*, 7099–7103; (c) Rychnovsky, S. D.; Rogers, B.; Yang, G. *J. Org. Chem.* **1993**, *58*, 3511–3515.
19. Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405–4408.
20. Evans, D. A.; Hoveyda, A. H. *J. Org. Chem.* **1990**, *55*, 5190–5192.
21. Evans, D. A.; Gauchet-Prunet, J. A. *J. Org. Chem.* **1993**, *58*, 2446–2453.