Stereoselective Approaches to the Total Synthesis of (6*R*,4′*S*,6′*R*)-Cryptofolione

Gowravaram Sabitha,* S. Siva Sankara Reddy, D. Vasudeva Reddy, Vangala Bhaskar, Jhillu S. Yadav

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500 007, India
Fax +91(40)27160512; E-mail: gowravaramsr@yahoo.com; E-mail: sabitha@iict.res.in

Received 4 June 2010; revised 23 June 2010

Abstract: Total syntheses of cryptofolione were accomplished by two different routes via a common intermediate that underwent a cross-metathesis (CM) reaction with a vinyl lactone. The intermediate was prepared by coupling of an acyl anion equivalent with a chiral allyl epoxide synthon, or by Prins cyclization of a *trans*-cinnamaldehyde with a chiral homoallylic alcohol. Goniothalamin was obtained as a cross-metathesis product of the diacetate and vinyl lactone.

Key words: lactones, total synthesis, heterocycles, cyclizations, cryptofolione

The α,β-unsaturated δ-lactone core unit (or 5,6-dihydro-2*H*-pyran-2-one moiety] is present in a variety of natural products.[1,2] Some of these compounds display important biological activities including antitumor activity.[3] One such lactone is cryptofolione, a 6-(ω-aralkenyl)-5,6-dihydro-α-pyrone isolated from the branches, leaves, and stem bark of two species of *Cryptocarya* (Lauraceae), *C. myrtifolia* and *C. moschata*, which are indigenous to South Africa and Brazil, respectively.[4,5] The structure of cryptofolione was elucidated on the basis of its circular dichroism and ^{13}C NMR spectra. *C. moschata* is an important food plant for primates such as the wooly spider monkey (*Brachyteles arachnoids*). Later, cryptofolione was also isolated from the fruits of *C. alba*, and its structure was confirmed by spectroscopic methods.[6] Cryptofolione is active against the trypomastigotes of *Trypanosoma cruzi*, reducing their number by 77% at 250 μg/mL; it is also moderately cytotoxic to both macrophages and *T. cruzi* amastigotes, and it displays a mild inhibitory effect on the promastigote form of *Leishmania* species.

Cryptofolione could be one of two possible stereoisomers (**1** and **2**; Figure 1). To determine the absolute configuration of cryptofolione, compounds **1** and **3** (an enantiomer of **2**) were synthesized in an enantioselective manner by using an asymmetric hetero-Diels–Alder reaction as the key step.[7] A comparison of the ^{1}H and ^{13}C NMR spectra, CD spectra, and specific rotations of the synthetic compounds with those reported in the literature established unequivocally that cryptofolione has the absolute configuration **1** (6*R*,4′*S*,6′*R*).

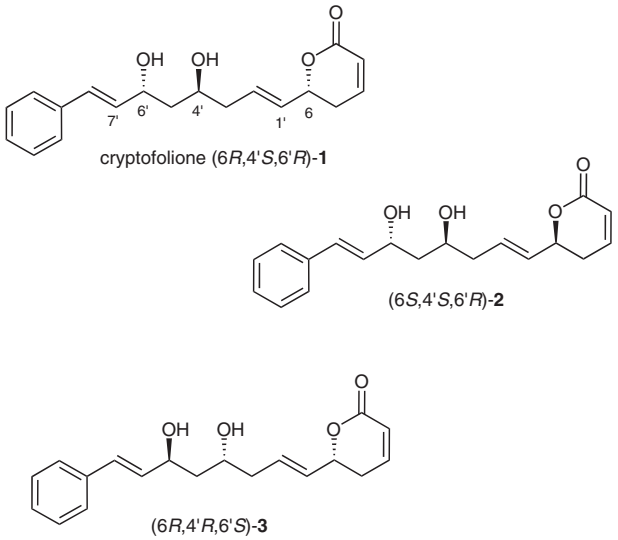


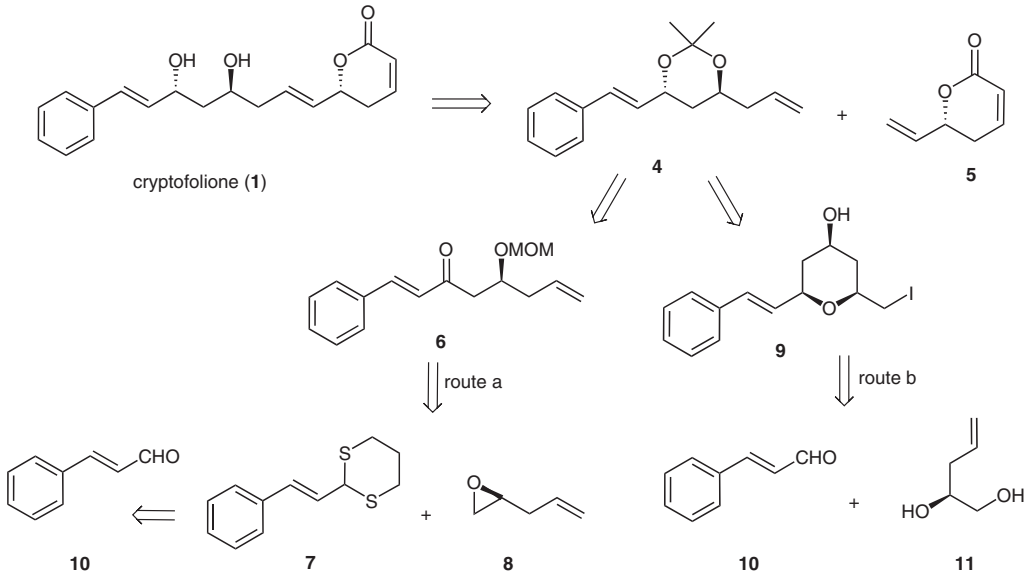
Figure 1 The absolute stereochemistry of cryptofolione

The main structural features of cryptofolione **1** are an *anti* 1,3-diol, two double bonds in the 1′- and 7′- positions, and a 6-substituted 5,6-dihydro-α-pyrone subunit. In the reported method for the synthesis of cryptofolione, the three chiral centers in **1** were fixed by means of two successive asymmetric hetero-Diels–Alder reactions of a Danishefsky diene with aldehydes by using second-generation salen complexes of chromium as catalysts.[7]

As a continuation of our interest on the synthesis of bioactive lactones,[8] we report two different strategies for the total synthesis of cryptofolione **1** that involve fewer steps than the original method. A retrosynthetic analysis (Scheme 1) suggested that the key intermediate **4** in route *a* might be synthesized by coupling of the acyl anion equivalent **7** with the chiral allyl epoxide **8**, whereas for route *b*, the analysis suggested that compound **4** might be prepared by a Prins cyclization of *trans*-cinnamaldehyde (**10**) with the homoallylic alcohol **11**. Finally, the target molecule **1** should be obtainable by a cross-metathesis reaction of **4** with the vinyl lactone **5**.[8p,t]

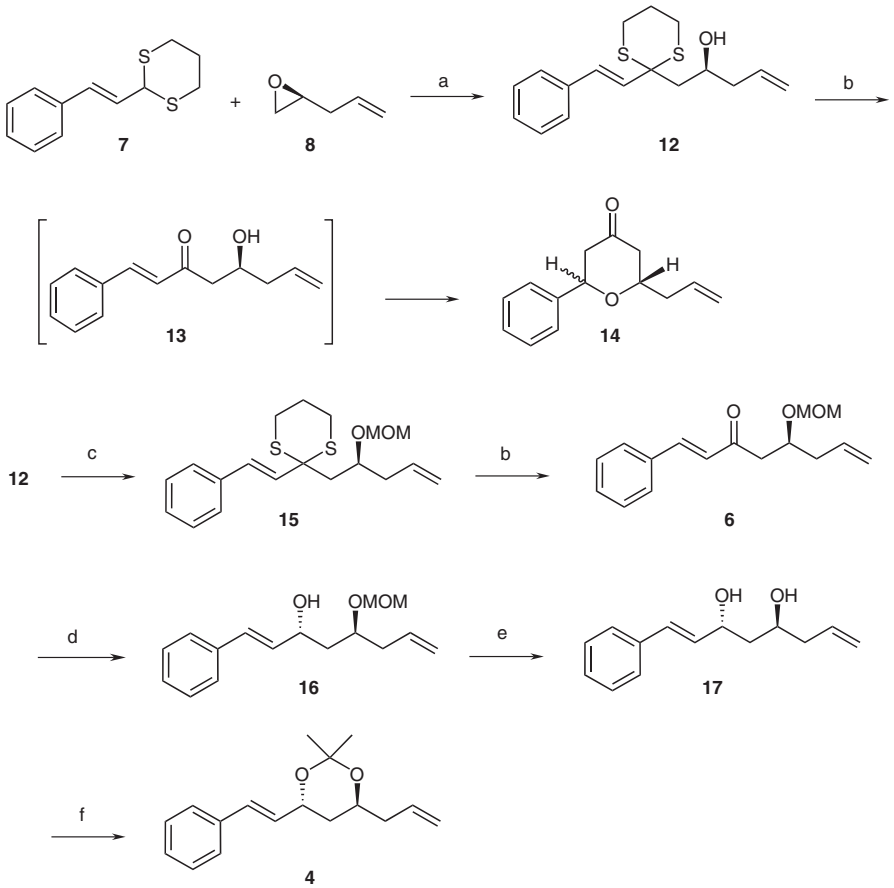
We began our synthesis of intermediate **4** by route *a* (Scheme 2) from commercially available *trans*-cinnamaldehyde (**10**). The aldehyde **10** was transformed into the thioacetal **7** in 85% yield by treatment with propane-1,3-dithiol in the presence of boron trifluoride etherate as a catalyst in dichloromethane.[9] Coupling of the known allyl epoxide **8** [prepared in one-step from (*S*)-epichlorohy-

SYNTHESIS 2010, No. 20, pp 3453–3460
Advanced online publication: 17.08.2010
DOI: 10.1055/s-0030-1258215; Art ID: Z14410SS



Scheme 1 Retrosynthetic analysis for cryptofolione (**1**)

drin][10] with the acyl anion equivalent **7** through metalation at –78 °C with one equivalent of butyllithium in the presence of boron trifluoride etherate gave the dithioketal **12** in 75% yield. Attempts to deprotect the dithioketal **12** under various conditions,[11] such as diacetyl(phenyl)-λ^3-iodane, potassium carbonate/iodomethane, mercury(II) chloride/calcium carbonate, or cerium(IV) ammonium nitrate/aqueous acetonitrile, failed to give the hydroxy ketone **13**; however, by using mercury(II) perchlorate hydrate/calcium carbonate,[12] the thioketal was deprotect-

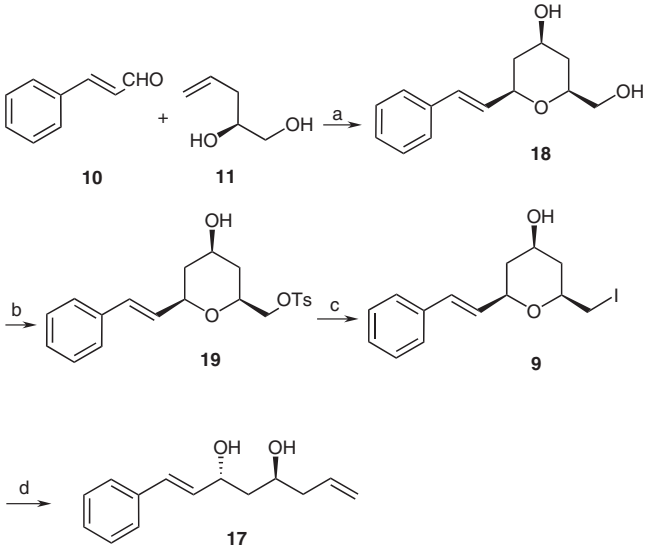


Scheme 2 *Reagents and conditions*: (a) BuLi, $BF_3{\cdot}OEt_2$, anhyd THF, –78 °C, 1 h, 75%; (b) $Hg(ClO_4)_2{\cdot}\times H_2O$), THF–$H_2O$ (5:1), $CaCO_3$, 0 °C, 0.5 h, 85%; (c) MOMCl, DIPEA, CH_2Cl_2, 0 °C to r.t. 0.5 h, 92%; (d) *S*-CBS catalyst, toluene, $BH_3{\cdot}$DMS, 0 °C, 0.5 h, 78%, 98% de; (e) $CeCl_3{\cdot}7H_2O$, MeCN–MeOH (1:1), reflux, 6 h, 91%; (f) $Me_2C(OMe)_2$, PPTS, CH_2Cl_2, 0 °C, 20 min, 89%.

ed to give **13**. This hydroxy ketone underwent cyclization onto the double bond in situ to give the pyranone **14**, which was characterized by means of ^{1}H NMR and mass spectroscopy (further studies on this core unit will be reported in a separate publication). The free hydroxy group in dithioketal **12** was therefore protected by formation of its methoxymethyl ether **15**, and this was subjected to deprotection of the thioketal with mercury(II) perchlorate hydrate to give the required ketone **6** in 85% yield. Diastereoselective reduction[13] of the ketone group was achieved by using the *S*-form of the Corey–Bakshi–Shibata catalyst (*S*-CBS) with borane–dimethyl sulfide adduct at 0 °C to give the protected *anti*-diol **16** in 78% yield. ^{1}H NMR analysis showed that the diastereomeric purity of the product (de) was >95%. Removal of the methoxymethyl group by using cerium(III) chloride heptahydrate in acetonitrile–methanol (1:1) gave the diol **17**. The relative stereochemistry of the 1,3-diol system in **17** was determined by using Rychnovsky's acetonide method.[14] Thus, treatment of diol **17** with 2,2-dimethoxypropane and pyridinium *p*-toluenesulfonate in dichloromethane gave the *anti*-acetonide **4**. The *anti* relationship of the two hydroxy groups in **4** was confirmed by the appearance in the ^{13}C NMR spectrum of the resonances for methyl carbons at δ = 24.8 and 25.5 ppm and for the acetal carbon at δ = 100.4 ppm.

In route *b*, cryptofolione was synthesized stereoselectively by means of a Prins cyclization (Scheme 3). Prins cyclization of the chiral homoallylic alcohol **11**[8r,s] with *trans*-cinnamaldehyde (**10**) in the presence of trifluoroacetic acid, followed by hydrolysis of the resulting trifluoroacetate, gave trisubstituted pyran **18**. The stereochemistry was assumed to be that shown in the scheme, as this has been well examined and previously established.[8r,s,15] (This was later proved to be the case by the conversion of the compound **18** into the target molecule **1**, which was identical to the reported compound in all respects.) Tosylation of **18** with 1.1 equivalents of tosyl chloride in the presence of triethylamine and catalytic amounts of dibutyltin(IV) oxide and 4-(*N*,*N*-dimethylamino)pyridine in dichloromethane gave the corresponding primary tosylate **19** in 90% yield. Treatment of tosylate **19** with sodium iodide in refluxing acetone gave the corresponding iodomethyl derivative **9**, which on treatment with nonactivated zinc in refluxing ethanol gave the open-chain key intermediate **17** with the *anti*-1,3-diol system in 85% yield. The properties of **17** exactly matched those of the sample of **17** prepared by route *a*, and both were diastereomerically pure (<95% de) and could be carried over to the next reaction.

The stage was now set to prepare cryptofolione (**1**) by an olefin cross-metathesis reaction. However, the cross-metathesis reaction[16] between the homoallylic alcohol **17** and the known vinyl lactone **5**[8p,t] in the presence of Grubbs' second-generation catalyst or Hoveyda's catalyst in dichloromethane gave only the product from homodimerization of the vinyl lactone in 90% yield within 15 min (Scheme 4); the nature of the product was confirmed from its mass spectrum. However, to our surprise, the cross-metathesis reaction of the diacetate **20**[17] with vinyl lactone **5** gave (*R*)-(+)-goniothalamin (**21**) in 80% yield, along with traces of the vinyl lactone homodimerized product (1–2%). The structure of **21** was established by spectroscopy and by comparison with an authentic sample that we had previously prepared.[8d]



Scheme 3 *Reagents and conditions*: (a) (i) TFA, CH_2Cl_2, 0 °C to r.t., 4 h; (ii) K_2CO_3, MeOH, r.t., 0.5 h, 55% (two steps); (b) TsCl, Et_3N, CH_2Cl_2, Bu_2SnO (cat.), DMAP (cat.), 0 °C to r.t., 4 h, 90%; (c) NaI, acetone, reflux, 7 h, 89%; (d) Zn dust, EtOH, reflux, 2 h, 85%.

However, the cross-metathesis reaction of acetonide-protected compound **4** with vinyl lactone **5** in the presence of Grubbs' second-generation catalyst in refluxing dichloromethane gave the desired cross-coupled product **22** in good yield (87%), along with a small amount of the vinyl lactone homodimerized product (4%) (Scheme 5).

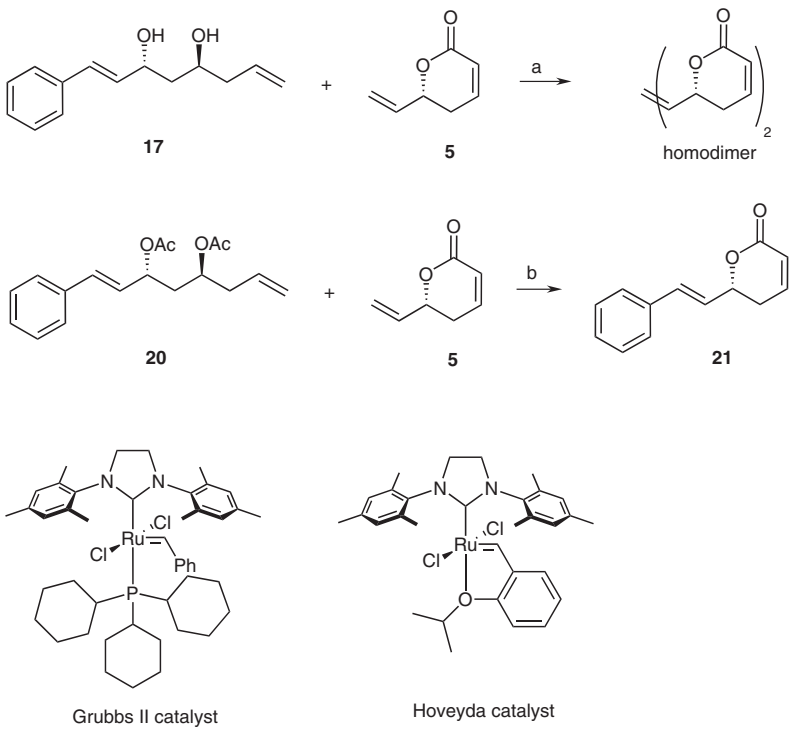
Several attempts to remove the acetonide group from the cross-coupled product **22** failed to give the target molecule **1**, as shown in Table 1.

Table 1 Attempts to Remove the Acetonide Group from Compound **22** under Various Conditions

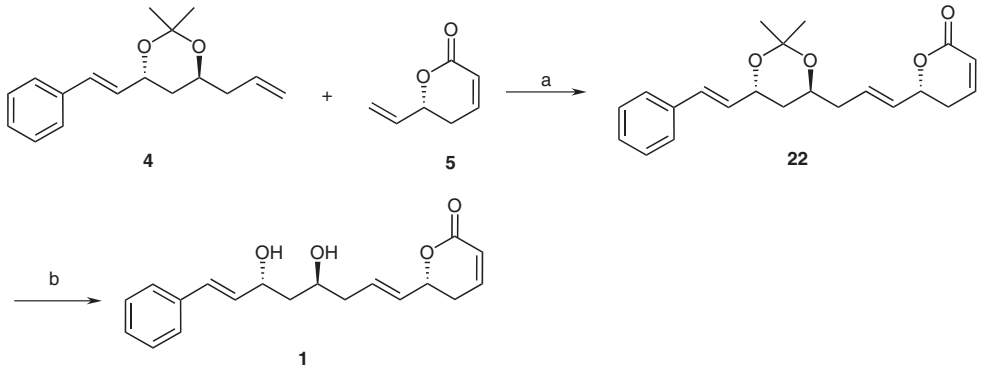
Catalyst	Solvent	Temp (°C)	Remarks
PTSA	MeOH	0	decomposed
PPTS	MeOH	0	decomposed
PTSA	CH_2Cl_2	0	decomposed

Fortunately, however, treatment with aqueous 4% hydrogen chloride at 0 °C did give cryptofolione (**1**) in 93% yield. The spectral and analytical data for the synthetic sample of **1** agreed well with the reported data for natural cryptofolione.

In conclusion, a convergent synthesis of cryptofolione (**1**) was devised by utilizing two different strategies. These protocols represent a second synthesis of cryptofolione



Scheme 4 *Reagents and conditions*: (a) Grubbs II catalyst or Hoveyda catalyst (10 mol%), CH_2Cl_2, reflux, 15 min, 90%; (b) Grubbs II catalyst (10 mol%), CH_2Cl_2, reflux, 4 h, 80%.



Scheme 5 *Reagents and conditions*: (a) Grubbs II catalyst (10 mol%), CH_2Cl_2, reflux, 6 h, 87%; (b) aq 4% HCl, MeCN, 0 °C, 0.5 h, 93%.

(**1**) by a short route that also provides access to the natural product goniothalamin (**21**).

Reactions were conducted under N_2 in anhyd solvents such as CH_2Cl_2, THF, or toluene. All reactions were monitored by TLC using silica-coated plates that were visualized under UV radiation. PE (bp 60–80 °C) was used. Yields refer to chromatographically and spectroscopically (^{1}H 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. ^{1}H and ^{13}C NMR spectra of samples in $CDCl_3$ were recorded on Varian FT-200MHz (Gemini) and Bruker UXNMR FT-300MHz (Avance) spectrometers. Chemical shifts (δ) are reported relative to TMS (δ = 0.0) as an internal standard. Mass spectra were recorded EI conditions at 70 eV on an LC-MSD (Agilent Technologies) spectrometer. Column chromatography was performed on silica gel (60–120 mesh; Acme Chemical Co., India). TLC was performed on Merck 60 F-254 silica gel plates. Optical rotations were measured with a Jasco DIP-370 polarimeter at 20 °C.

(2*S*)-1-{2-[(*E*)-2-Phenylvinyl]-1,3-dithian-2-yl}pent-4-en-2-ol (12)

A 2.5 M soln of BuLi in hexane (2.85 mL, 7.13 mmol) was added to a soln of dithiane **7** (300 mg, 3.57 mmol) and epoxide **8** (1.03 g, 4.63 mmol) in anhyd THF (20 mL) at –78 °C under N_2, and the mixture was stirred for 25 min. A soln of $BF_3{\cdot}OEt_2$ (0.23 mL) in anhyd THF (2 mL) was then added dropwise. After 1 h, the reaction was quenched by slow addition of MeOH (0.2 mL) followed by sat. aq NH_4Cl (2 mL). The mixture was then extracted with CH_2Cl_2 (3 × 10 mL). The extracts were washed with brine, dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash column chromatography [silica gel, PE–EtOAc (8:2)] to give a colorless oil; yield: 817 mg (75%); $[\alpha]_D^{25}$ +12.0 (*c* 0.25, $CHCl_3$); R_f = 0.6 (PE–EtOAc, 8:2).

IR (neat): 3449, 3071, 2920, 1639, 1421, 1275, 1062, 972, 913, 748, 694 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.43–7.18 (m, 5 H), 6.81 (d, *J* = 15.8 Hz, 1 H), 6.24 (d, *J* = 15.8 Hz, 1 H), 5.86–5.75 (m, 1 H), 5.12–

5.06 (m, 2 H), 4.11–4.01 (m, 1 H), 2.98–2.89 (m, 2 H), 2.81–2.72 (m, 2 H), 2.48–2.45 (br s, 1 H, OH), 2.28–1.90 (m, 6 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 136.1, 134.4, 133.1, 132.5, 128.7, 128.0, 126.6, 117.9, 67.7, 48.4, 42.1, 29.7, 27.4, 27.1, 24.9.

LCMS: *m/z* = 329 $[M + Na]^+$.

HRMS: *m/z* $[M + Na]^+$ calcd for $C_{17}H_{22}NaOS_2$: 329.1009; found: 329.1002.

(2*S*)-2-Allyl-6-phenyltetrahydro-4*H*-pyran-4-one (14)

A soln of enol **12** (70 mg, 0.22 mmol) and $CaCO_3$ (45 mg, 0.45 mmol) in 5:1 THF–H_2O (5 mL) was treated with $Hg(ClO_4)_2 \cdot \times H_2O$ (9 mg, 0.02 mmol) for 0.5 h at 0 °C. The mixture was then diluted with Et_2O (20 mL) and filtered through Celite. Concentration of the filtrate followed by flash chromatography [silica gel, PE–EtOAc (8:2)] gave a colorless liquid; yield: 41 mg (85%); R_f = 0.4 (PE–EtOAc, 8:2).

IR (neat): 2923, 2853, 1734, 1453, 1229, 1055, 918, 757, 698 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.36–7.12 (m, 5 H), 5.97–5.72 (m, 1 H), 5.22–5.08 (m, 2 H), 4.50–4.35 (m, 1 H), 3.40–3.08 (m, 1 H), 2.94–2.65 (m, 2 H), 2.61–2.32 (m, 2 H), 2.18–1.95 (m, 2 H).

LCMS: *m/z* = 239 $[M + Na]^+$.

HRMS: *m/z* $[M + Na]^+$ calcd for $C_{14}H_{16}NaO_2$: 239.1047; found: 239.1039.

2-[(2*S*)-2-(Methoxymethoxy)pent-4-en-1-yl]-2-[(*E*)-2-phenylvinyl]-1,3-dithiane (15)

DIPEA (1.18 mL, 9.14 mmol) and MOMCl (0.36 mL, 4.5 mmol) were added sequentially to a cooled (0 °C) soln of enol **12** (700 mg, 2.28 mmol) in CH_2Cl_2 (10 mL), and the mixture was stirred at r.t. for 0.5 h. The solvent was evaporated and the residue was purified by column chromatography [silica gel, PE–EtOAc (8:2)] to give a colorless liquid; yield: 736 mg (92%); $[\alpha]_D^{25}$ +19.4 (*c* 0.5, $CHCl_3$); R_f = 0.75 (PE–EtOAc, 8:2).

IR (neat): 2925, 1443, 1151, 1038, 915, 747, 694 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.42–7.17 (m, 5 H), 6.77 (d, *J* = 15.8 Hz, 1 H), 6.19 (d, *J* = 15.8 Hz, 1 H), 5.88–5.70 (m, 1 H), 5.10–5.02 (m, 2 H), 4.65 (d, *J* = 6.8 Hz, 1 H), 4.49 (d, *J* = 6.8 Hz, 1 H), 3.91–3.81 (m, 1 H), 3.30 (s, 3 H), 3.00–2.83 (m, 2 H), 2.73–2.59 (m, 2 H), 2.40–2.27 (m, 2 H), 2.18–1.81 (m, 4 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 136.4, 134.1, 132.9, 132.5, 128.6, 127.7, 126.5, 117.8, 96.5, 74.5, 55.7, 53.7, 47.2, 40.9, 27.2 (d, 2 C), 25.1.

LCMS: *m/z* = 373 $[M + Na]^+$.

HRMS: *m/z* $[M + Na]^+$ calcd for $C_{19}H_{26}NaO_2S_2$: 373.1271; found: 373.1286.

(1*E*,5*S*)-5-(Methoxymethoxy)-1-phenylocta-1,7-dien-3-one (6)

A soln of the dithiane **15** (700 mg, 1.99 mmol) and $CaCO_3$ (399 mg, 3.99 mmol) in 5:1 THF–H_2O (10 mL) was treated with $Hg(ClO_4)_2 \cdot \times H_2O$ (79 mg, 0.19 mmol) for 0.5 h at 0 °C. The mixture was then diluted with Et_2O (70 mL) and filtered through Celite. Concentration of the filtrate followed by flash chromatography [silica gel, PE–EtOAc (7:3)] gave a colorless liquid; yield: 441 mg, (85%); $[\alpha]_D^{25}$ –14.5 (*c* 0.55, $CHCl_3$); R_f = 0.7 (PE–EtOAc, 7:3).

IR (neat): 2926, 1659, 1610, 1448, 1331, 1038, 917, 751 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.55–7.34 (m, 6 H), 6.71 (d, *J* = 16.0 Hz, 1 H), 5.88–5.78 (m, 1 H), 5.16–5.06 (m, 2 H), 4.63 (q, *J* = 6.7 Hz, 2 H), 4.25–4.18 (m, 1 H), 3.32 (s, 3 H), 2.94 (dd, *J* = 16.0, 7.5 Hz, 1 H), 2.68 (dd, *J* = 16.0, 5.0 Hz, 1 H), 2.37 (t, *J* = 6.7 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 198.4, 142.9, 134.4, 134.0, 130.5, 128.9, 128.3, 126.6, 117.9, 95.9, 73.6, 55.6, 45.5, 39.3.

ESIMS: *m/z* = 283 $[M + Na]^+$.

HRMS: *m/z* $[M + Na]^+$ calcd for $C_{16}H_{20}NaO_3$: 283.1310; found: 283.1307.

(1*E*,3*R*,5*S*)-5-(Methoxymethoxy)-1-phenylocta-1,7-dien-3-ol (16)

A soln of BH_3·DMS (2 M in THF; 0.76 mL, 1.52 mmol) was added to a soln of *S*-CBS catalyst (1 M in toluene; 0.15 mL, 0.15 mmol) in toluene (2 mL) at 0 °C, and the mixture was stirred for 0.5 h. A concd soln of dienone **6** (400 mg, 1.53 mmol) in toluene (0.5 mL) was added, and the mixture was stirred for 0.5 h at 0 °C. The reaction was then quenched with MeOH (1 mL) and the mixture was allowed to warm to r.t. The solvent was then removed under reduced pressure and the residue was purified by column chromatography [silica gel, PE–EtOAc (7:3)] to give a colorless liquid; yield: 314 mg (78%); $[\alpha]_D^{25}$ +31.7 (*c* 0.5, $CHCl_3$); R_f = 0.6 (PE–EtOAc, 7:3).

IR (neat): 3446, 2926, 1641, 1445, 1147, 1036, 969, 916, 749, 694 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.36–7.14 (m, 5 H), 6.58 (d, *J* = 15.8 Hz, 1 H), 6.16 (dd, *J* = 15.8, 6.0 Hz, 1 H), 5.85–5.70 (m, 1 H), 5.13–5.04 (m, 2 H), 4.75 (d, *J* = 6.7 Hz, 1 H), 4.64 (d, *J* = 6.7 Hz, 1 H), 4.48–4.39 (m, 1 H), 3.94–3.83 (m, 1 H), 3.41 (s, 3 H), 2.40–2.32 (m, 2 H), 1.88–1.65 (m, 2 H).

^{13}C NMR ($CDCl_3$, 75 MHz): 136.8, 134.1, 132.1, 129.4, 128.5, 127.4, 126.3, 117.7, 96.3, 74.9, 68.8, 55.8, 41.4, 39.4.

LCMS: *m/z* = 285 $[M + Na]^+$.

HRMS: *m/z* $[M + Na]^+$ calcd for $C_{16}H_{22}NaO_3$: 285.1466; found: 285.1479.

(1*E*,3*R*,5*S*)-1-Phenylocta-1,7-diene-3,5-diol (17)

$CeCl_3 \cdot 7H_2O$ (3.98 g, 10.68 mmol) was added to a stirred soln of dienol **16** (280 mg, 1.06 mmol) in a mixture of MeOH (5 mL) and MeCN (5 mL) under N_2, and the mixture was stirred for 6 h at the reflux temperature. The reaction was quenched with solid $NaHCO_3$ (4.0 g) and the mixture was filtered. The solvent was removed under reduced pressure, and the residue was purified by column chromatography [silica gel, PE–EtOAc (7:3)] to give a colorless oil; yield: 211 mg (91%); $[\alpha]_D^{25}$ +32.0 (*c* 0.25, $CHCl_3$); R_f = 0.4 (PE–EtOAc, 7:3).

IR: 3370, 3075, 2924, 1641, 1443, 1066, 968, 917, 748, 694 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.36–7.16 (m, 5 H), 6.61 (d, *J* = 15.8 Hz, 1 H), 6.24 (dd, *J* = 15.8, 6.0 Hz, 1 H), 5.88–5.72 (m, 1 H), 5.18–5.09 (m, 2 H), 4.65–4.57 (m, 1 H), 4.06–3.95 (m, 1 H), 2.32–2.19 (m, 2 H), 1.81–1.70 (m, 2 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 136.6, 134.3, 131.9, 129.8, 128.5, 127.6, 126.4, 118.4, 70.3, 68.1, 42.1 (2 C).

LCMS: *m/z* = 241 $[M + Na]^+$.

HRMS: *m/z* $[M + Na]^+$ calcd for $C_{14}H_{18}NaO_2$: 241.1204; found: 241.1206.

(4*S*,6*R*)-4-Allyl-2,2-dimethyl-6-[(*E*)-2-phenylvinyl]-1,3-dioxane (4)

$Me_2C(OMe)_2$ (0.07 mL, 0.48 mmol) and a catalytic amount of PPTS were added to a soln of diol **17** (60 mg, 0.27 mmol) in anhyd CH_2Cl_2 (3 mL), and the mixture was stirred at r.t. for 20 min. Aq $NaHCO_3$ was then added to neutralize the PPTS and the mixture was filtered and concentrated. The residue was purified by column chromatography [silica gel, PE–EtOAc (9:1)] to give a clear liquid; yield: 63 mg (89%); $[\alpha]_D^{25}$ +45.5 (*c* 0.85, $CHCl_3$); R_f = 0.6 (PE–EtOAc, 9:1).

IR: 2926, 1642, 1376, 1223, 1072, 968, 747 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.35–7.14 (m, 5 H), 6.51 (d, *J* = 15.8 Hz, 1 H), 6.17 (dd, *J* = 15.8, 6.0 Hz, 1 H), 5.87–5.71 (m, 1 H),

5.13–5.00 (m, 2 H), 4.52–4.41 (m, 1 H), 3.97–3.86 (m, 1 H), 2.38–2.14 (m, 2 H), 1.88–1.69 (m, 2 H), 1.37 (d, J = 7.5 Hz, 6 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 136.7, 134.2, 130.4, 129.8, 128.5, 127.6, 126.4, 117.1, 100.4, 67.8, 66.0, 25.5, 24.8, 40.2, 37.4.

LCMS: m/z = 281 $[M + Na]^+$.

HRMS: m/z $[M + Na]^+$ calcd for $C_{17}H_{22}NaO_2$: 281.1517; found: 281.1521.

(2*S*,4*R*,6*R*)-2-(Hydroxymethyl)-6-[(*E*)-2-phenylvinyl]tetrahydro-2*H*-pyran-4-ol (18)

TFA (1.5 mL, 19.56 mmol) was added slowly to a soln of dioxane **11** (100 mg, 0.98 mmol) and *trans*-cinnamaldehyde (**10**; 323 mg, 2.44 mmol) in CH_2Cl_2 (20 mL) at r.t. under N_2. The mixture was stirred for 4 h before sat. aq $NaHCO_3$ (20 mL) was added and the pH was adjusted to >7 by addition of Et_3N. The aqueous layer was extracted with CH_2Cl_2 (4 × 10 mL) and the combined organic phase was concentrated. The residue was dissolved in MeOH (15 mL) and stirred with K_2CO_3 (3.2 g) for 0.5 h. The MeOH was then evaporated and H_2O (5 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic phase was dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography [silica gel, PE–EtOAc (1:1)] to give a gummy liquid; yield: 125 mg (55%); $[\alpha]_D^{25}$ +25.5 (*c* 0.35, $CHCl_3$); R_f = 0.2 (PE–EtOAc, 1:1).

IR (neat): 3373, 2936, 1649, 1354, 1061, 970, 748, 693 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.36–7.17 (m, 5 H), 6.55 (d, J = 15.8 Hz, 1 H), 6.16 (dd, J = 15.8, 6.0 Hz, 1 H), 4.07–3.98 (m, 1 H), 3.96–3.80 (m, 1 H), 3.70–3.49 (m, 3 H), 1.73–1.54 (br s, 2 H, 2 × OH), 1.50–1.20 (m, 4 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 136.4, 130.8, 129.1, 128.5, 127.7, 126.4, 76.2, 76.1, 67.5, 65.7, 41.0, 36.5.

LCMS: m/z = 257 $[M + Na]^+$.

HRMS: m/z $[M + Na]^+$ calcd for $C_{14}H_{18}NaO_3$: 257.1153; found: 257.1157.

{(2*S*,4*R*,6*R*)-4-Hydroxy-6-[(*E*)-2-phenylvinyl]tetrahydro-2*H*-pyran-2-yl}methyl Tosylate (19)

Et_3N (0.09 mL, 0.59 mmol), Bu_2SnO (cat.) and DMAP (cat.) were added to a soln of diol **18** (100 mg, 0.42 mmol) in anhyd CH_2Cl_2 (5.0 mL) at 0 °C. TsCl (81 mg, 0.42 mmol) was then added over 1 h. The resulting mixture was allowed to warm to r.t., stirred for 3 h, then treated with 1 M aq HCl (3 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The organic layer was washed sequentially with sat. aq $NaHCO_3$ (5 mL) and H_2O (5 mL), and the the combined organic phase was dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography [silica gel, PE–EtOAc (1:1)] to give a clear liquid; yield: 148 mg (90%); $[\alpha]_D^{25}$ –2.0 (*c* 1.25, $CHCl_3$); R_f = 0.5 (PE–EtOAc, 1:1).

IR (neat): 3411, 2924, 1722, 1598, 1358, 1176, 975, 818, 753, 668 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.79 (d, J = 8.1 Hz, 2 H), 7.35–7.15 (m, 7 H), 6.47 (d, J = 15.8 Hz, 1 H), 6.06 (dd, J = 15.8, 5.6 Hz, 1 H), 4.16–3.75 (m, 4 H), 3.73–3.58 (m, 1 H), 2.41 (s, 3 H), 2.09–1.89 (m, 2 H), 1.61 (br s, 1 H, OH), 1.40–1.11 (m, 2 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 144.8, 136.5, 132.8, 130.6, 129.8, 128.7, 128.5, 128.0, 127.7, 126.4, 76.0, 72.9, 71.8, 67.4, 40.7, 36.6, 21.6.

LCMS: m/z = 411 $[M + Na]^+$.

HRMS: m/z $[M + Na]^+$ calcd for $C_{21}H_{24}NaO_5S$: 411.1242; found: 411.1236.

(2*S*,4*R*,6*R*)-2-(Iodomethyl)-6-[(*E*)-2-phenylvinyl]tetrahydro-2*H*-pyran-4-ol (9)

NaI (463 mg, 3.08 mmol) was added to a soln of tosylate **19** (120 mg, 0.30 mmol) in acetone (20 mL), and the mixture was refluxed for 7 h. The acetone was evaporated H_2O (8 mL) and EtOAc (20 mL) were added to the residue. The organic layer was dried (Na_2SO_4) and concentrated, and the residue was purified by column chromatography [silica gel, PE–EtOAc (1:1)] to give a white solid; yield: 94 mg (89%); mp 105–107 °C; $[\alpha]_D^{25}$ +49.3 (*c* 0.8, $CHCl_3$); R_f = 0.8 (PE–EtOAc, 1:1).

IR (KBr): 3357, 2946, 1653, 1455, 1364, 1187, 1043, 965, 748, 693 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.38–7.15 (m, 5 H), 6.59 (d, J = 15.8 Hz, 1 H), 6.16 (dd, J = 15.8, 6.0 Hz, 1 H), 4.09–3.98 (m, 1 H), 3.97–3.80 (m, 1 H), 3.50–3.38 (m, 1 H), 3.32–3.17 (m, 2 H), 2.30–2.21 (m, 1 H), 2.08–1.98 (m, 1 H), 1.42–1.14 (m, 2 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 136.5, 130.8, 128.7, 128.5, 127.7, 126.5, 76.2, 74.9, 67.6, 40.7, 40.5, 8.6.

LCMS: m/z = 367 $[M + Na]^+$.

HRMS: m/z $[M + Na]^+$ calcd for $C_{14}H_{17}IO_2Na$: 367.0171; found: 367.0157.

(1*E*,3*R*,5*S*)-1-Phenylocta-1,7-diene-3,5-diol (17)

Commercial Zn dust (133 mg, 2.03 mmol) was added to a soln of iodide **9** (70 mg, 0.20 mmol) in EtOH (10 mL), and the mixture was refluxed for 2 h then cooled to 25 °C. Addition of solid NH_4Cl (150 mg) and Et_2O (30 mL) followed by stirring for 5 min gave a gray suspension. The suspension was filtered through Celite, and the filtrate was concentrated. The residue was purified by column chromatography [silica gel, PE–EtOAc (7:3)] to give a colorless oil; yield: 37 mg (85%); R_f = 0.4 (PE–EtOAc, 7:3).

The physical data for **17** exactly matched those of the sample of **17** prepared by route *a*.

(1*S*,3*R*,4*E*)-3-(Acetyloxy)-1-allyl-5-phenylpent-4-en-1-yl Acetate (20)

Pyridine (0.08 mL, 1.0 mmol) and Ac_2O (0.05 mL, 0.54 mmol) were added sequentially to a stirred soln of diol **17** (60 mg, 0.27 mmol) in anhyd CH_2Cl_2 (3 mL) at 0 °C. The mixture was stirred for 1 h and then diluted with CH_2Cl_2 (10 mL). The organic layer was washed sequentially with 5% aq $NaHCO_3$ (2 × 3 mL) and brine (2 × 3 mL) then dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by column chromatography [silica gel, PE–EtOAc (8:2)] to give a colorless liquid; yield: 52 mg, 65%); $[\alpha]_D^{25}$ +49.6 (*c* 0.95, $CHCl_3$); R_f = 0.8 (PE–EtOAc, 8:2).

IR (neat): 2922, 1738, 1371, 1240, 1022, 967, 749, 694 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.36–7.17, (m, 5 H), 6.59 (d, J = 15.8 Hz, 1 H), 6.06 (dd, J = 15.8, 7.1 Hz, 1 H), 5.82–5.65 (m, 1 H), 5.50–5.40 (m, 1 H), 5.14–4.98 (m, 3 H), 2.32 (t, J = 6.6 Hz, 2 H), 2.05 (s, 3 H), 2.0 (s, 3 H), 1.97–1.80 (m, 2 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.5, 170.2, 136.1, 133.0, 132.6, 128.5, 128.0, 127.1, 126.5, 118.2, 70.7, 68.9, 39.1, 38.4, 21.2, 21.0.

LCMS: m/z = 325 $[M + Na]^+$.

HRMS: m/z $[M + Na]^+$ calcd for $C_{18}H_{22}NaO_4$: 325.1415; found: 325.1401.

(6*R*)-6-[(*E*)-2-Phenylvinyl]-5,6-dihydro-2*H*-pyran-2-one (21; Goniothalamin)

A soln of Grubbs II catalyst (8 mg, 0.01 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise to a soln of diacetate **20** (30 mg, 0.09 mmol) and lactone **5** (18 mg, 0.14 mmol) in CH_2Cl_2 (0.5 mL) at r.t. The mixture was refluxed for 4 h, then the solvent was removed under reduced pressure and the crude product was purified by column

chromatography [silica gel, PE–EtOAc (8:2)] to give a white solid; yield: 15 mg (80%); mp 81–83 °C; $[\alpha]_D^{25}$ +161.3 (*c* 1.7, $CHCl_3$); R_f = 0.3 (PE–EtOAc, 8:2).

IR (KBr): 2923, 1720, 1382, 1245, 1024, 966, 814, 750.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.40–7.22 (m, 5 H), 6.94–6.86 (m, 1 H), 6.71 (d, *J* = 15.8 Hz, 1 H), 6.25 (dd, *J* = 15.8, 6.0 Hz, 1 H), 6.11–6.05 (m, 1 H), 5.12–5.04 (m, 1 H), 2.56–2.50 (m, 2 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 163.8, 144.6, 135.7, 133.1, 128.6, 128.3, 126.6, 125.6, 121.6, 77.9, 29.8.

LCMS: *m/z* = 201 $[M + H]^+$.

HRMS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{13}O_2$: 201.0915; found: 201.0921.

(6*R*)-6-((1*E*)-3-{(4*S*,6*R*)-2,2-Dimethyl-6-[(*E*)-2-phenylvinyl]-1,3-dioxan-4-yl}prop-1-en-1-yl)-5,6-dihydro-2*H*-pyran-2-one (22)

A soln of Grubbs II catalyst (13 mg, 0.01 mmol) in CH_2Cl_2 (1 mL) was added dropwise to a soln of the ketal **4** (42 mg, 0.16 mmol) and lactone **5** (30 mg, 0.24 mmol) in CH_2Cl_2 (1 mL) at r.t., and the mixture was refluxed for 1 h. The solvent was removed under reduced pressure and the crude product was purified by column chromatography [silica gel, PE–EtOAc (7:3)] to give a semi-solid; yield: 49 mg (87%); $[\alpha]_D^{25}$ +51.3 (*c* 0.9, $CHCl_3$); R_f = 0.4 (PE–EtOAc, 7:3).

IR (neat): 2924, 2856, 1718, 1378, 1242, 1020, 968, 816, 748 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.39–7.17 (m, 5 H), 6.90–6.82 (m, 1 H), 6.54 (d, *J* = 15.8 Hz, 1 H), 6.19 (dd, *J* = 15.8, 6.0 Hz, 1 H), 6.04 (dt, *J* = 9.8, 1.5 Hz, 1 H), 5.92–5.79 (m, 1 H), 5.68 (dd, *J* = 15.8, 6.0 Hz, 1 H), 4.89 (q, *J* = 6.7 Hz, 1 H), 4.49 (q, *J* = 6.7 Hz, 1 H), 4.01–3.87 (m, 1 H), 2.49–2.19 (m, 4 H), 1.92–1.47 (m, 2 H), 1.40 (d, *J* = 3.0 Hz, 6 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 164.0, 144.7, 130.9, 129.9, 129.6, 129.3, 128.9, 128.4, 127.6, 126.4, 121.5, 100.5, 77.9, 67.7, 65.8, 39.2, 38.5, 37.4, 25.5, 24.8.

LCMS: *m/z* = 377 $[M + Na]^+$.

HRMS: *m/z* $[M + Na]^+$ calcd for $C_{22}H_{26}NaO_4$: 377.1728; found: 377.1734.

6-[(1*E*,4*R*,6*S*,7*E*)-4,6-Dihydroxy-8-phenylocta-1,7-dien-1-yl]-5,6-dihydro-2*H*-pyran-2-one (1; Cryptofolione)

An aq 4% soln of HCl (0.5 mL) was added to a stirred soln of lactone **22** (28 mg, 0.07 mmol) in MeCN (5 mL) at 0 °C, and the mixture was stirred at 0 °C for 0.5 h. The reaction was quenched with solid $NaHCO_3$ (100 mg) and the mixture was filtered. The filtrate was concentrated under reduced pressure, and the crude product was purified by column chromatography [silica gel, PE–EtOAc (1:1)] to give an oil; yield: 22 mg (93%); $[\alpha]_D^{25}$ +44.3 (*c* 0.011, CH_2Cl_2); R_f = 0.25 (PE–EtOAc, 1:1).

IR (neat): 3406, 2924, 1707, 1385, 1253, 1051, 969, 818, 751, 696 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.37–7.14 (m, 5 H), 6.88–6.77 (m, 1 H), 6.59 (d, *J* = 15.8 Hz, 1 H), 6.23 (dd, *J* = 15.8, 6.0 Hz, 1 H), 5.98 (dt, *J* = 9.8, 1.5 Hz, 1 H), 5.94–5.81 (m, 1 H), 5.64 (dd, *J* = 15.8, 6.0 Hz, 1 H), 4.85 (q, *J* = 6.7 Hz, 1 H), 4.60 (q, *J* = 6.0 Hz, 1 H), 4.10–3.91 (m, 1 H), 3.51–3.01 (br s, 2 H, 2 × OH), 2.44–2.34 (m, 2 H), 2.31–2.20 (m, 2 H), 1.83–1.56 (m, 2 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 164.1, 144.9, 136.5, 131.7, 131.1, 129.9, 129.8, 128.5, 127.6, 126.4, 121.4, 77.8, 70.3, 68.1, 42.2, 40.3, 29.7.

LCMS: *m/z* = 337 $[M + Na]^+$.

HRMS: *m/z* $[M + Na]^+$ calcd for $C_{19}H_{22}NaO_4$: 337.1415; found: 337.1418.

Acknowledgment

S.S.S.R and D.V.R thank CSIR and V.B. thanks UGC, New Delhi, for awards of fellowships.

References

(1) (a) Negishi, E.; Kotora, M. *Tetrahedron* **1997**, *53*, 6707. For a review, see: (b) Collins, I. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1377. (c) Boucard, V.; Broustal, G.; Campagne, J. M. *Eur. J. Org. Chem.* **2007**, 225. (d) Marco, J. A.; Carda, M.; Murga, J.; Falomir, E. *Tetrahedron* **2007**, *63*, 2929 . For recent examples, see: (e) Pospíšil, J.; Markó, I. E. *Tetrahedron Lett.* **2006**, *47*, 5933. (f) Gobbini, M.; Cerri, A. *Curr. Med. Chem.* **2005**, *12*, 2343. (g) de Fátima, Â.; Pilli, R. A. *Tetrahedron Lett.* **2003**, *44*, 8721. (h) de Fátima, Â.; Pilli, R. A. *ARKIVOC* **2003**, *(x)*, 118. (i) Bruckner, R. *Curr. Org. Chem.* **2001**, *5*, 679. (j) Job, A.; Wolberg, M.; Muller, M.; Enders, D. *Synlett* **2001**, 1796.

(2) (a) Zhao, G.; Wu, B.; Wu, X. Y.; Zhang, Y. Z. *Mini-Rev. Org. Chem.* **2005**, *2*, 333. (b) Yet, L. *Chem. Rev.* **2003**, *103*, 4283. (c) Mereyala, H. B.; Joe, M. *Curr. Med. Chem.: Anti-Cancer Agents* **2001**, *1*, 293.

(3) Hoffmann, H. M. R.; Rabe, J. *Angew. Chem. Int. Ed.* **1985**, *24*, 94.

(4) Sehlapelo, B. M.; Drewes, S. E.; Scott-Shaw, R. *Phytochemistry* **1994**, *37*, 847.

(5) Cavalheiro, A. J.; Yoshida, M. *Phytochemistry* **2000**, *53*, 811.

(6) Schmeda-Hirschmann, G.; Astudillo, L.; Bastida, J.; Codina, C.; Rojas de Arias, A.; Ferreira, M. E.; Inchaustti, A.; Yaluff, G. *J. Pharm. Pharmacol.* **2001**, *53*, 563.

(7) Matsuoka, Y.; Aikawa, K.; Irie, R.; Katsuki, T. *Heterocycles* **2005**, *66*, 187.

(8) (a) Sabitha, G.; Sudhakar, K.; Reddy, N. M.; Rajkumar, M.; Yadav, J. S. *Tetrahedron Lett.* **2005**, *46*, 6567. (b) Sabitha, G.; Narjis, F.; Swapna, R.; Yadav, J. S. *Synthesis* **2006**, 2879. (c) Sabitha, G.; Reddy, E. V.; Yadagiri, K.; Yadav, J. S. *Synthesis* **2006**, 3270. (d) Sabitha, G.; Sudhakar, K.; Yadav, J. S. *Tetrahedron Lett.* **2006**, *47*, 8599. (e) Sabitha, G.; Bhaskar, V.; Yadav, J. S. *Tetrahedron Lett.* **2006**, *47*, 8179. (f) Sabitha, G.; Swapna, R.; Reddy, E. V.; Yadav, J. S. *Synthesis* **2006**, 4242. (g) Sabitha, G.; Bhikshapathi, M.; Yadav, J. S. *Synth. Commun.* **2007**, *37*, 561. (h) Sabitha, G.; Gopal, P.; Yadav, J. S. *Synth. Commun.* **2007**, *37*, 1495. (i) Sabitha, G.; Yadagiri, K.; Yadav, J. S. *Tetrahedron Lett.* **2007**, *48*, 1651. (j) Sabitha, G.; Yadagiri, K.; Yadav, J. S. *Tetrahedron Lett.* **2007**, *48*, 8065. (k) Sabitha, G.; Bhaskar, V.; Yadav, J. S. *Synth. Commun.* **2008**, *38*, 1. (l) Sabitha, G.; Bhaskar, V.; Reddy, S. S. S.; Yadav, J. S. *Tetrahedron* **2008**, *64*, 10207. (m) Sabitha, G.; Bhaskar, V.; Reddy, S. S. S.; Yadav, J. S. *Synthesis* **2009**, 3285. (n) Sabitha, G.; Gopal, P.; Reddy, C. N.; Yadav, J. S. *Tetrahedron Lett.* **2009**, *46*, 6298. (o) Sabitha, G.; Gopal, P.; Reddy, C. N.; Yadav, J. S. *Synthesis* **2009**, 3301. (p) Sabitha, G.; Fatima, N.; Gopal, P.; Reddy, C. N.; Yadav, J. S. *Tetrahedron: Asymmetry* **2009**, *20*, 184. (q) Sabitha, G.; Fatima, N.; Reddy, E. V.; Yadav, J. S. *Tetrahedron Lett.* **2008**, *49*, 6087. (r) Sabitha, G.; Prasad, M. N.; Shankaraiah, K. S.; Jadav, J. S. *Synthesis* **2010**, 1171. (s) Sabitha, G.; Reddy, N. M.; Prasad, M. N.; Yadav, J. S. *Helv. Chim. Acta* **2009**, *92*, 967. (t) Sabitha, G.; Bhaskar, V.; Reddy, S. S. S.; Yadav, J. S. *Helv. Chim. Acta* **2010**, *93*, 329.

(9) Mandal, P.; Roy, S. C. *Tetrahedron* **1995**, *51*, 7823.

(10) (a) Burova, S. A.; McDonald, F. E. *J. Am. Chem. Soc.* **2004**, *126*, 2495. (b) De Camp Schuda, A.; Mazzocchi, P. H.; Fritz, G.; Morgan, T. *Synthesis* **1986**, 309.

(11) $(F_3CCO_2)_2IPh$: (a) Smith, A. B. III; Beauchamp, T. J.; LaMarche, M. J.; Kaufman, M. D.; Qiu, Y.; Arimoto, H.; Jones, D. R.; Kobayashi, K. *J. Am. Chem. Soc.* **2000**, *122*, 8654. MeI/K_2CO_3: (b) Liu, J.-H.; Long, Y.-Q. *Tetrahedron Lett.* **2009**, *50*, 4592. $HgCl_2/CaCO_3$: (c) Corey, E. J.; Bock, M. G. *Tetrahedron Lett.* **1975**, *16*, 2643. CAN/aq MeCN: (d) Solladié, G.; Hutt, J. *Tetrahedron Lett.* **1987**, *28*, 797.

(12) $HgClO_4/CaCO_3$: Jiang, B.; Chen, Z. *Tetrahedron: Asymmetry* **2001**, *12*, 2835.

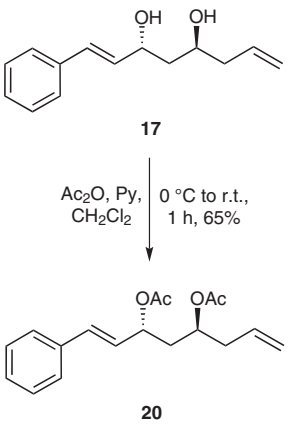
(13) Corey, E. J.; Helal, C. J. *Angew. Chem. Int. Ed.* **1998**, *37*, 1986.

(14) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945.

(15) (a) Bonini, C.; Chiummiento, L.; Lopardo, M. T.; Pullex, M.; Colobert, F.; Solladié, G. *Tetrahedron Lett.* **2003**, *44*, 2695. (b) Yadav, J. S.; Reddy, M. S.; Rao, P. P.; Prasad, A. R. *Tetrahedron Lett.* **2006**, *47*, 4397.

(16) For a recent review on cross-metathesis, see: (a) BouzBouz, S.; Simmons, R.; Cossy, J. *Org. Lett.* **2004**, *6*, 3465. (b) Comin, M. J.; Parrish, D. A.; Deschamps, J. R.; Marquez, V. E. *Org. Lett.* **2006**, *8*, 705. (c) Connon, S. J.; Blechert, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 1900. (d) Hoveyda, A. H.; Gillingham, D. G.; Van Veldhuizen, J. J.; Kataoka, O.; Garber, S. B.; Kingsbury, J. S.; Harrity, J. P. A. *Org. Biomol. Chem.* **2004**, *2*, 8. (e) Marsh, G. P.; Parsons, P. J.; McCarthy, C.; Corniquet, X. G. *Org. Lett.* **2007**, *9*, 2613. (f) Moura-Letts, G.; Curran, D. P. *Org. Lett.* **2007**, *9*, 5. (g) Bieniek, M.; Bujok, R.; Cabaj, M.; Lugan, N.; Lavigne, G.; Arlt, D.; Grela, K. *J. Am. Chem. Soc.* **2006**, *128*, 13652.

(17) Diacetate **20** was prepared from the diol **17** by acetylation (Scheme 6).



Scheme 6