FULL PAPER

Carbohydrate-Based Studies Toward the Synthesis of Hamigeromycin E: A Stereoselective Total Synthesis of an Isomer of Zeaenol

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A stereoselective synthesis of 14-membered macrolide hamigeromycin E (**6**) has been studied by employing *ortho*-lithiated formylation, *Barbier* allylation, *Julia–Kocienski* olefination, *Mitsunobu* esterification, and ring-closing metathesis (RCM) reactions. The final RCM reaction did not provide the target molecule. This study has prompted us to synthesize a stereoisomer of zeaenol and accomplish the total synthesis with the above protocols.

Keywords: Macrolides, *Mitsunobu* reaction, *Wittig* homologation, *Julia–Kocienski* olefination, Metathesis.

Introduction

β-Resorcylic acid lactones (RALs) are fungal polyketide metabolites possessing a C_{10} side chain to form 14-membered benzannulated macrolides (*Fig. 1*) [1]. RALs have been known for decades, with the first isolation of radicicol in 1953 [2]. *Sugawara et al.* [3] isolated the zearalenone derivatives, such as zeaenol, LL-Z1640-1, and LL-Z1640-2, from the extract of *Drechslera portulacae* and these macrolides have shown potent kinase inhibitory properties. Caryospomycins were isolated from the fungus of *Caryospora callicarpa* YMF1.01026 [4]. Further, *Isaka et al.* isolated a series of new 14-membered lactones (nonaketide macrolides) from the soil fungus *Hamigera avellanea* BCC 17816. Scale-up fermentation and chemical studies led to the isolation of macrolides, such as hamigeromycin A – F. Hamigeromycins A, C, D, and E are stereoisomers that differ in the absolute configurations of the 4,5-diol moiety [5]. These macrolides have received considerable attention due to their potential biological properties [6 – 10]. Hamigeromycins are interesting molecules; however, there is no report available on their total synthesis. The synthesis of zeaenol and cochliomycin A were reported by *Jana* and *Nanda* [11a], however, the synthesis of zeaenol and cochliomycin B were reported by *Du et al.* [11b]. *Mohapatra et al.* [11c] reported the synthesis of zeaenol, 7-*epi*-zeaenol, and its analogs by diastereoselctive *Nozaki–Hiyama–Kishi* (NHK) reaction. Our long-term interest on total synthesis of natural products [12] and biologically active heterocyclic compounds [13] prompted us to study the synthesis of hamigeromycin E and zeaenol starting from readily available chemicals.

Results and Discussion

Our retrosynthetic strategy of hamigeromycin E (**6**) was depicted in *Scheme 1*. The conjugate enone **7** can be synthesized from substituted aromatic acid **8** and alcohol **10** by employing *Mitsunobu* esterification, ring-closing metathesis, and allylic oxidation. Further, the aromatic acid **8** can be accomplished from commercially available 2,4,5-trimethoxybenzoic acid **9** using *ortho*-lithiated formylation and one-carbon *Wittig* homologation protocols. The secondary alcohol **10** could be obtained from aldehyde **11** and sulfone **12** using *Julia–Kocienski* olefination. The aldehyde **11** can be prepared from commercially available D-mannitol **13** using *Barbier* allylation and the sulfone **12** from commercially available ethyl (–)-(*R*)-3-hydroxybutyrate (**14**).

Synthesis of Aromatic Acid **8**

The aromatic acid **8** was synthesized starting from 2,4,5-trimethoxybenzoic acid (**9**) (*Scheme 2*) as per the literature reported methods described below. 2,4,5-Trimethoxybenzoic acid (**9**) in the presence of oxalyl chloride with diethylamine provided amide **15** [14a]. Regioselective *ortho*-lithiated formylation of amide **15** with DMF in the presence of *sec*-BuLi and TMEDA at −78 °C afforded *N*,*N*-diethyl-2-formyl-3,4,6-trimethoxybenzamide (**16**) [14b]. The obtained benzamide **16** upon hydrolysis with 10% HCl under reflux conditions furnished 3-hydroxy-4,5,7-trimethoxyisobenzofuran-1(3*H*)-one (**17**) [14b]. Next, the one-carbon *Wittig* homologation of lactol **17** with methyltriphenylphosphonium bromide afforded 3,4,6-trimethoxy-2-vinylbenzoic acid (**8**) [14c].

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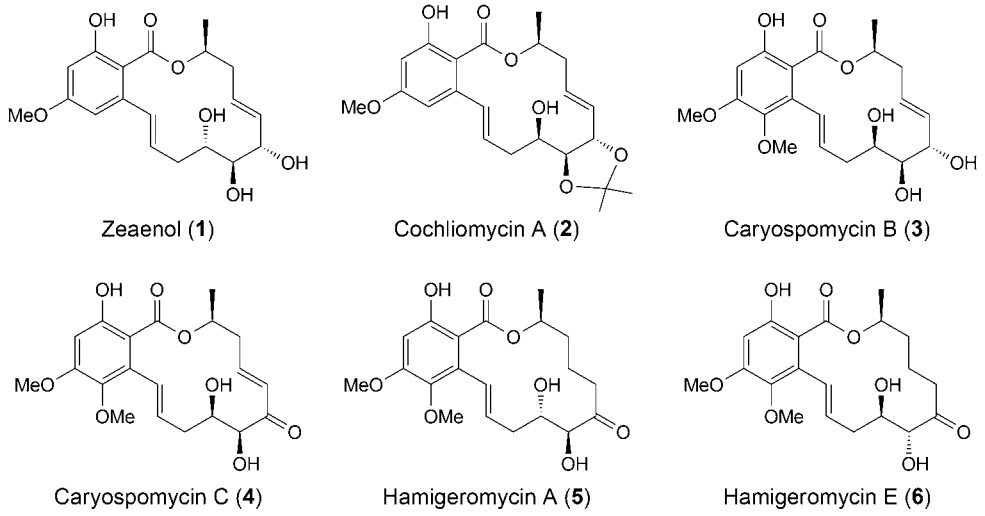
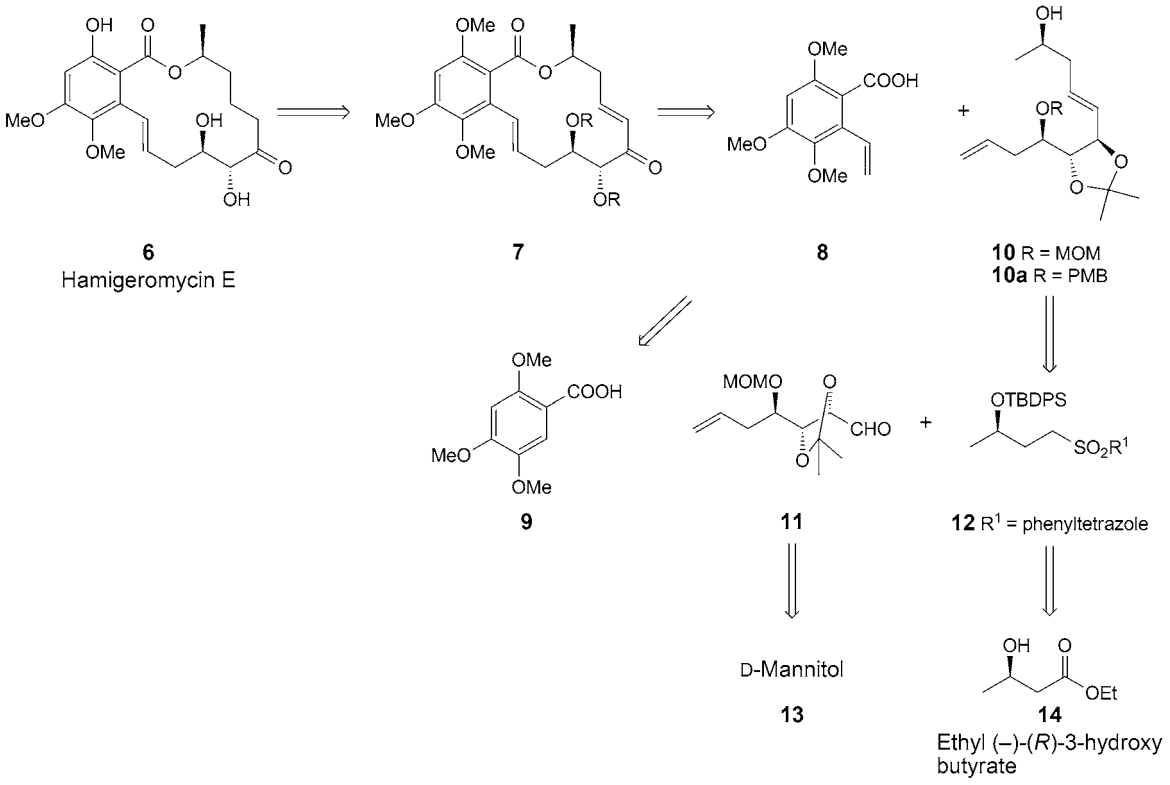


Fig. 1. Structures of 14-membered macrolides.

Scheme 1. Retrosynthetic analysis of hamigeromycin E.



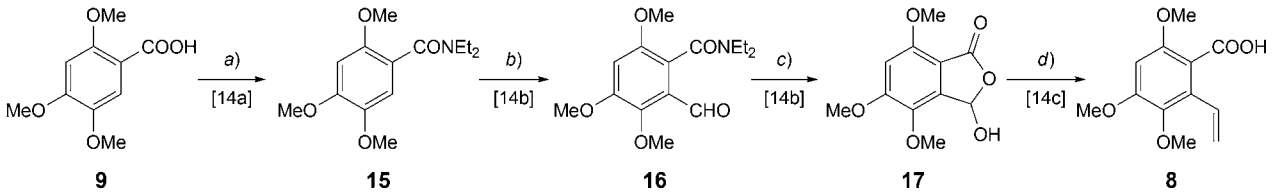
Synthesis of Sulfone **12**

The sulfone **12** was prepared starting from ethyl (–)-(*R*)-3-hydroxybutyrate (**14**) as depicted in *Scheme 3*. The OH group **14** was protected as TBDPS ether **18** using TBDPSCl in the presence of imidazole [15]. The ester **18** upon reduction with DIBAL-H in dry CH_2Cl_2 at −78 °C afforded the corresponding alcohol **19** [15]. The OH group **19** was converted to its corresponding 1-phenyl-5-mercapto-1*H*-tetrazole under *Mitsunobu* conditions (DIAD/TPP) at −20 °C to give sulfide **20** [11a]. The oxidation of sulfide **20** with $(NH_4)_6Mo_7O_{24} \cdot 4\ H_2O$ in the presence of H_2O_2 afforded the sulfone **12** [11a].

Synthesis of Aldehyde **11**

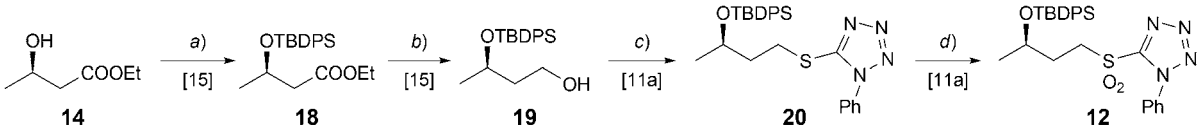
Synthesis of aldehyde **11** was accomplished from D-mannitol as depicted in *Scheme 4*. Acetonide protection of

Scheme 2. Synthesis of compound **8**.



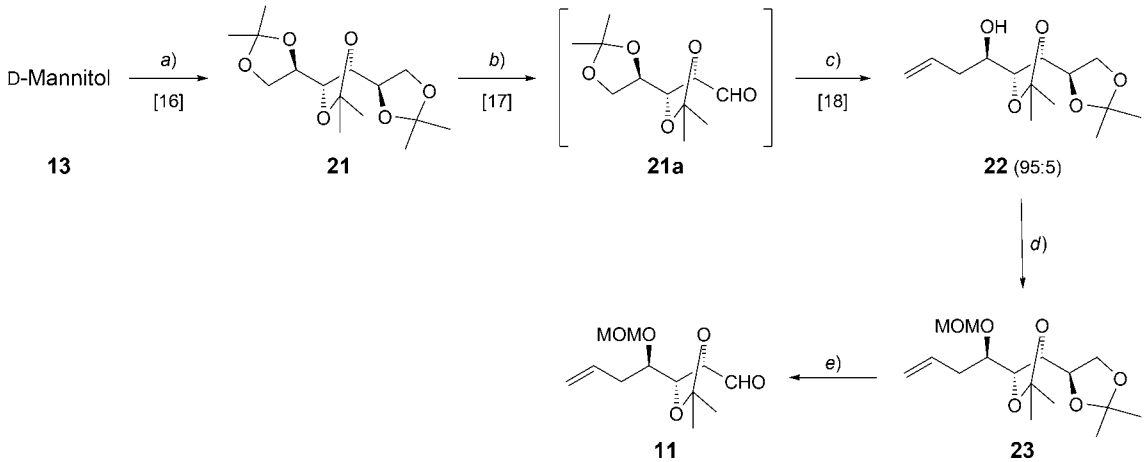
a) $(COCl)_2$, Et_2NH, dry DCM, 12 h; 80%. *b*) *sec*-BuLi, TMEDA, dry DMF, −78 °C, 2 h; 68%. *c*) 10% HCl, reflux, 24 h; 54%. *d*) CH_3PPh_3Br, KO^{t}Bu, dry THF, 0 °C, 5 h; 60%.

Scheme 3. Synthesis of compound **12**.



a) Imidazole, TBDPSCl, DCM, 0 °C to r.t., 6 h; 80%. *b*) DIBAL-H, dry DCM, −78 °C, 2 h; 90%. *c*) PTSH, PPh_3, DIAD, dry THF, −20 °C to r.t.; 85%. *d*) $(NH_4)_6Mo_7O_{24} \cdot 4\ H_2O$, H_2O_2, C_2H_5OH, 0 °C to r.t. 6 h; 88%.

Scheme 4. Synthesis of compound **11**.



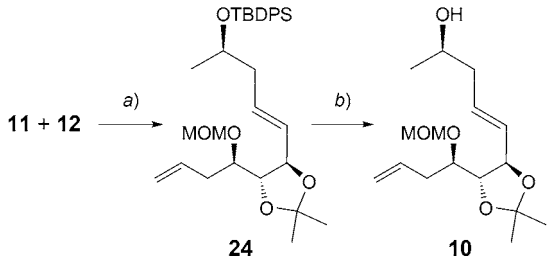
a) 2,2-Dimethoxypropane, *p*-TsOH, dry DMSO, 0 °C to r.t., 24 h; 80%. *b*) H_5IO_6, AcOEt, 3 h. *c*) Allyl bromide, Zn, NH_4Cl, THF, 2 h; 76%. *d*) DIPEA, MOMCl, dry CH_2Cl_2, 0 °C to r.t., 12 h; 80%. *e*) H_5IO_6, AcOEt, 0 °C to r.t., 6 h; 56%.

D-mannitol **13** with 2,2-dimethoxypropane in the presence of *p*-TsOH afforded **21** [16]. Oxidative cleavage [17] and *Barbier* allylation [18] of compound **21** provided the secondary alcohol **22** (^{1}H-NMR, *anti*/*syn* 95:5) [19]. The OH group of **22** was protected as MOM ether **23** using MOMCl in the presence of DIPEA [20]. The oxidative cleavage of **23** with H_5IO_6 afforded the corresponding aldehyde **11**.

Synthesis of Alcohol **10**

After the successful synthesis of aldehyde **11** and sulfone **12**, the *Julia–Kocienski* olefination reaction of **11** with **12** has been carried out with KHMDS in the presence of 18-crown-6 at −78 °C. This provided olefin derivative **24** (^{1}H-NMR, *E*/*Z* = 94:6, *Scheme 5*) [21]. The ^{1}H-NMR spectrum showed a *doublet–doublet* at δ(H) 5.40 (J = 7.8, 15.4) and a *multiplet* at δ(H) 5.78 – 5.86 indicating the formation of (*E*)-configured olefin C=C bond. The

Scheme 5. Synthesis of compound **10**.



a) KHMDS, 18-Crown-6, dry THF, −78 °C to r.t., 2 h; 75%. *b*) TBAF, dry THF, 24 h; 85%.

TBDPS ether **24** was freed using TBAF in dry THF at 0 °C to give the corresponding alcohol **10** [22].

RCM Reaction of Aromatic Acid **8** *and Alcohol* **10**

Mitsunobu esterification [23] of 3,4,6-trimethoxy-2-vinylbenzoic acid (**8**) and alcohol **10** in dry toluene provided ester **25** in 88% yield (*Scheme 6*). Next, we proceeded the RCM reaction to achieve macrocyclization to complete the target molecule hamigeromycin E. Accordingly, the RCM reaction of **25** has been carried out with *Grubbs*' *I* catalyst (10 mol-%) in dry CH_2Cl_2 at room temperature [24] as well as in toluene under reflux conditions. However, these reactions did not give the cyclized product **26**. Next, the RCM reaction was carried out with *Grubbs*' *II* catalyst (5 mol-%) in CH_2Cl_2 at room temperature [25]. The progress of the reaction was monitored by TLC, and after completion of the reaction (6 h), the solvent was removed under reduced pressure and the obtained residue was purified by column chromatography. This provided compound **27** as colorless liquid in 62% yield instead of the cyclized compound **26**. Compound **27** was well characterized by spectroscopic data. The IR spectrum showed the stretching frequency at 1723 cm^{-1} correspond to the ester C=O and 1588, 1264, and 1204 cm^{-1} for C=C, C–C, and C–O stretching frequencies. The ^{1}H-NMR spectrum of compound **27** showed a *doublet* at δ(H) 1.30 (J = 15.7) corresponds to Me H-atoms and a *multiplet* at δ(H) 2.28 – 2.54 corresponds to allylic CH_2 H-atoms. The three aromatic MeO groups appeared as three *singlet*s at δ(9) 3.71, 3.81 and 3.88. The two olefin H-atoms appeared as *multiplet* at δ(2) 5.07 – 5.15. The *quartet* appeared at δ(H) 5.18 corresponds to olefin H-atom. The CH H-atom appeared as *multiplet* at δ(H) 5.77 – 5.88. The ESI-MS spectrum showed the molecular ion peak at m/z 329 $[M + Na]^+$ and further the compound confirmed by HR-MS.

Next, we have carried out the RCM reaction of **25** with *Hoveyda–Grubbs* catalyst (5 mol-%). This also furnished **27** instead of **26**. The reason could be that the ruthenium regioselectively complexing with C=C bond instead terminal C=C bonds due to the steric effect of MeO group present on aromatic ring at *ortho*-position to vinylic carbon.

The synthetic studies on hamigeromycin E prompted us to synthesize the isomer of zeaenol, a 14-membered resorcylic acid lactone without MeO group on aromatic ring at *ortho*-position to vinylic carbon depicted below.

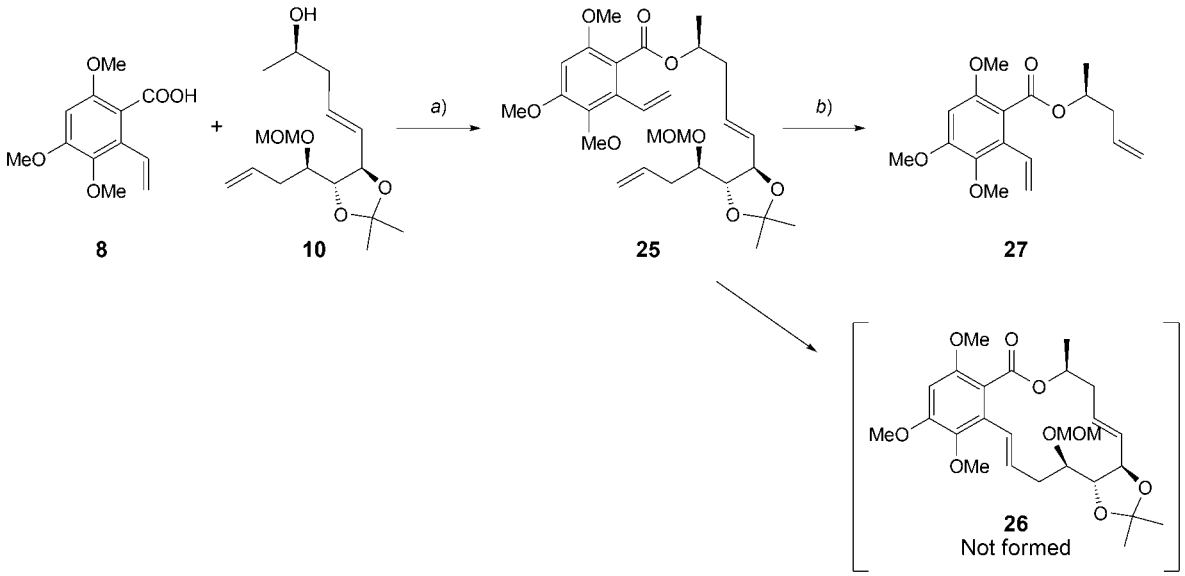
Stereoselective Total Synthesis of a Stereoisomer of Zeaenol **28**

The retrosynthetic approach for the synthesis of stereoisomer of zeaenol [26] can be accomplished from aromatic acid **29** and alcohol **10a** (*Scheme 7*). 2-Hydroxy-4-methoxy-6-vinylbenzoic acid (**29**) could be accomplished from commercially available 2,4,6-trihydroxybenzoic acid (**30**). The secondary alcohol **10a** with PMB ether was prepared as per the *Schemes 3 – 5*.

Synthesis of Styrene Acid **29**

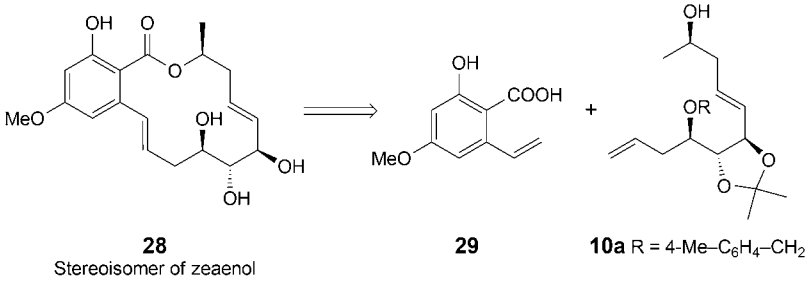
The synthesis of styrene acid **29** (*Scheme 8*) has been carried out as per the reported method [27]. Acetonide protection of 2,4,6-trihydroxybenzoic acid (**30**) with acetone in the presence of TFA and TFAA provided **31**.

Scheme 6. RCM reaction of compound **25**.

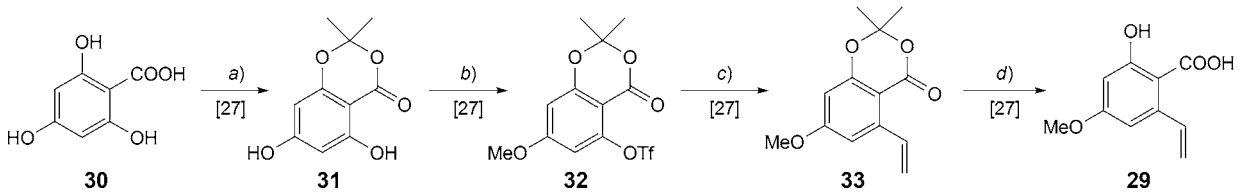


a) DIAD, TPP, dry toluene, 0 °C to r.t., 88%. *b*) Second-generation *Grubbs*' catalyst (5 mol-%), dry CH_2Cl_2, 6 h; 62%.

Scheme 7. Retrosynthetic analysis of compound **28**.



Scheme 8. Synthesis of compound **29**.



a) TFA, TFAA, Acetone, r.t., 48 h; 52%. *b*) *i*) PPh_3, DIAD, dry MeOH, dry THF, 0 °C to r.t., 80%. *ii*) Tf_2O, Pyridine, 0 °C, 3 h; 78%. *c*) Vinyl tributylstannane, LiCl, PPh_3, dry DMF, r.t., 4 h; 80%. *d*) $LiOH.H_2O$, THF:H_2O (2:1), r.t., 20 h; 75%.

Regioselective methylation under *Mitsunobu* conditions furnished the MeO derivative and protection of OH group with trifluoromethanesulfonic anhydride in the presence of catalytic amount of pyridine provided **32**. *Stille* coupling of triflate **32** with vinyl tributylstannane in the presence of $Pd(PPh_3)_4$, LiCl, and PPh_3 at room temperature afforded styrene **33**. Deprotection of acetonide **33** with $LiOH \cdot H_2O$ in the presence of THF/H_2O (2:1) provided **29**.

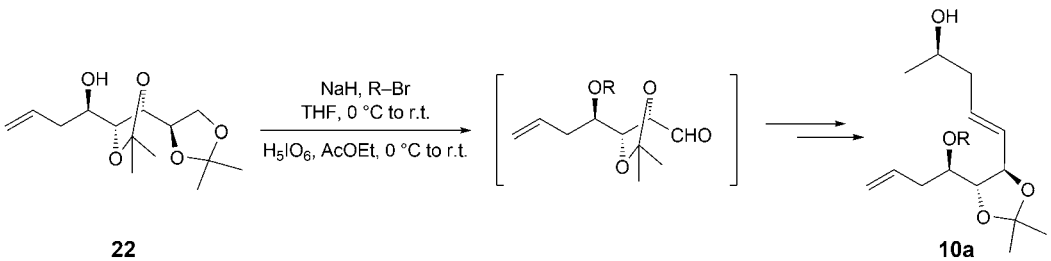
Synthesis of Compound **10a**

The secondary alcohol **10a** (*Scheme 9*) was prepared according to the synthetic path utilized for the synthesis of alcohol **10** as depicted in *Schemes 3 – 5*.

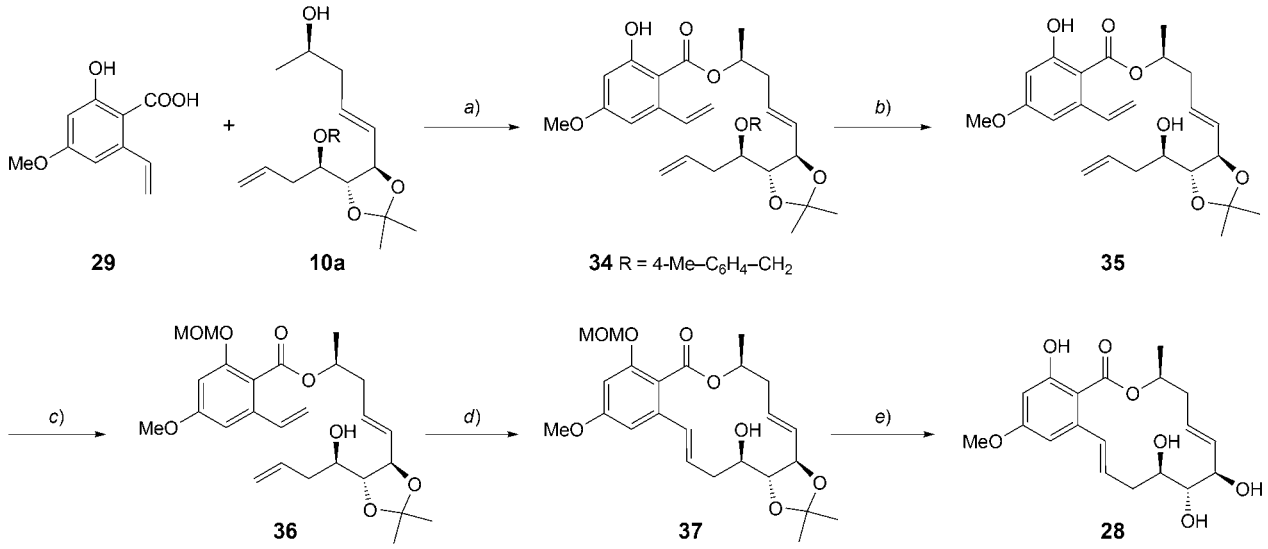
RCM Reaction of Acid **29** and Alcohol **10a**

Mitsunobu esterification of vinylbenzoic acid **29** and alcohol **10a** in dry toluene afforded the ester **34** (*Scheme 10*) [23]. Deprotection of PMB ether **34** with DDQ in CH_2Cl_2/H_2O (9:1) medium furnished alcohol **35** [28]. The phenolic OH group **35** was protected as MOM ether with MOMCl in the presence of DIPEA at 0 °C in dry CH_2Cl_2 provided **36**. The RCM reaction of **36** has been carried out with *Grubbs*' *II* catalyst (5 mol-%) in dry CH_2Cl_2 under reflux conditions. The reaction was monitored by TLC (8 h), and after column chromatography purification, lactone **37** was furnished as yellow liquid in 66% yield. The MOM ether and the acetonide group of **37** was removed using 2N HCl at room temperature (20 h) to afford the corresponding stereoisomer of zeaenol (3*S*,5*E*,7*R*,8*R*,9*R*,11*E*)-7,8,9,16-tetrahydroxy-14-methoxy-3-methyl-3,4,7,8,9,10-hexahydro-1*H*-benzo[*c*][1]oxacyclotetradecin-1-one (**28**) as colorless solid in 52% yield. The IR spectrum of **28** showed absorption bands at 3432 cm^{-1} corresponds to 4-OH groups, and 1253 and 1160 cm^{-1} correspond to C–C and C–O stretching frequencies. The ^{1}H-NMR spectrum of **28** showed four olefin H-atoms appeared as *doublet* at δ(H) 6.89 (J = 15.7), *multiplet* at δ (H) 5.89 – 6.03, and *doublet–doublet* at δ(H) 5.76, 5.79 (J = 7.2, 15.7). The two aromatic H-atoms showed *doublet*

Scheme 9. Synthesis of compound **10a**.



Scheme 10. Synthesis of stereoisomer of zeaenol **28**.



a) DIAD, TPP, dry toluene, 2 h; 80%. *b*) DDQ, CH_2Cl_2:H_2O (9:1) 2 h; 80%. *c*) DIPEA, MOMCl, dry CH_2Cl_2, 0 °C to r.t. 80%. *d*) *Grubbs*' *II* catalyst, dry CH_2Cl_2, reflux, 8 h; 66%. *e*) 2N HCl, THF, 20 h; 52%.

at δ(H) 6.45 (J = 2.1) and *doublet* at δ(H) 6.39 (J = 2.4). The C(7), C(8) CH H-atoms showed *triplet* at δ(H) 4.23 (J = 7.8) and *triplet* at δ(H) 4.04 (J = 5.8), and C(9) CH H-atom showed a *multiplet* at δ(H) 3.64. The C(3) CH H-atom showed *multiplet* at δ(H) 5.39 – 5.46. The four CH_2 H-atoms appeared as *multiplet* at δ(H) 2.39 – 2.54, 2.28 – 2.37, and 2.66 – 2.74. The Me resonated as *doublet* at δ(H) 1.39 (J = 6.4) and OCH_3 H-atoms resonated as *singlet* at δ(H) 3.82. The ^{13}C-NMR spectrum showed a signal at δ(C) 170.8 corresponds to the C=O. The signals at δ(C) 35.7 and 36.6 correspond to C(4) and C(10). The signals at δ(C) 55.4 and 18.7 ppm correspond to OCH_3 and CH_3. The signals at δ(C) 72.8, 77.2, and 72.5 are correspond to C(7), C(8), and C(9). The C(5), C(6), C(11), and C(12) olefin carbons resonated at δ(C) 127.5, 128.3, 132.6, and 133.4. Finally, the compound was confirmed by HR-ESI-MS spectrum (calcd. for $C_{19}H_{24}O_7Na$ [M + Na] 387.1414; found 387.1423).

Conclusions

In conclusion, a stereoselective synthesis of hamigeromycin E has been studied by employing *ortho*-lithiated formylation, *Barbier* allylation, *Julia–Kocienski* olefination, *Mitsunobu* esterification, and RCM reactions. The final RCM reaction did not provide the target molecule. This study has prompted us to synthesize a stereoisomer of zeaenol and accomplish the total synthesis with the above protocols.

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Supporting Information

Additional Supporting Information (compound spectra) may be found in the online version of this article.

Experimental Part

General

The chemicals were purchased from *Sigma–Aldrich* (St. Louis, MO, USA). The solvents and reagents were purified by standard techniques. Anal. TLC: precoated SiO_2 *60F*$_{254}$ (0.5 mm) glass plates; visualization of the spots on TLC plates was achieved by exposure to UV light. Column chromatography (CC): silica gel (SiO_2; 60 – 120 mesh, *Acme Synthetic Chemicals*, Mumbai, India). Optical rotations: *HORIBA SEPA*-300 digital polarimeter (*Horiba*, Kyoto, Japan). M.p.: *Mettler-Temp* apparatus (*Mettler–Toledo*, Mumbai, India); uncorrected. IR Spectra: *PerkinElmer*-1600 FT-IR spectrometer (*PerkinElmer*, Waltham, MS, USA); in KBr; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra: *Bruker*-300 and *Avance*-500 spectrometer (*Bruker Corp*. Fällanden, Switzerland); in $CDCl_3$; chemical shifts, δ, in ppm rel. to Me_4Si as internal standard; J in Hz. ESI-MS: *7070H* spectrometer (*Micromass UK Ltd*., Manchester, UK) with a direct inlet system; in *m*/*z* (rel. %). HR-ESI-MS: *Agilent 6510 Q-TOF* LC/MS instrument (*Agilent Technologies*, Waldbronn, Germany).

***N,N*-Diethyl-2-formyl-3,4,6-trimethoxybenzamide (16)** [14b]. *Sec*-BuLi (1.3M, 33 ml, 39 mmol) was added dropwise to the

soln. of TMEDA (5.9 ml, 39 mmol) in anh. THF at −78 °C under N_2 atmosphere. The mixture was continued at the same temp. for 30 min. Amide **15** (7.0 g, 26.2 mmol) in dry THF was added dropwise to the reaction mixture (20 min) and stirring was continued for another 2 h. After completion of the reaction, the DMF (8.0 ml, 104 mmol) was added to the reaction mixture at −78 °C and then allowed to r.t. After completion of the reaction, sat. NH_4Cl (15 ml) was added to the reaction mixture at 0 °C and diluted with AcOEt (80 ml). The org. layer was separated, and dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by CC affording **16** (5.25 g, 68%) as colorless solid. IR (KBr): 2967, 2930, 2860, 1688, 1629, 1594, 1328, 1276, 1218, 944. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.00 (*t*, 3 H, *J* = 7.2, CH_3); 1.30 (*t*, 3 H, *J* = 7.2, CH_3); 3.08 (*q*, 2 H, *J* = 7.2, *N*CH_2); 3.42 – 3.50 (*m*, 1 H, *N*CH_2); 3.68 – 3.76 (*m*, 1 H, *N*CH_2); 3.82 (*s*, 3 H, OCH_3); 3.91 (*s*, 3 H, OCH_3); 3.94 (*s*, 3 H, OCH_3); 6.75 (*s*, 1 H, aromatic); 10.40 (*s*, 1 H, CHO). ^{13}C-NMR (75 MHz, $CDCl_3$): 12.1; 13.3; 38.6; 42.5; 56.2; 56.4; 62.5; 102.6;117.8; 126.8; 146.4; 151.9; 153.6; 166.5; 190.0. ESI-MS: 296 $[M + H]^+$. HR-ESI-MS: calcd. for $C_{15}H_{22}NO_5$ $[M + H]$ 296.1492; found 296.1486.

2-Ethenyl-3,4,6-trimethoxybenzoic Acid (**8**) [14c]. To the mixture of methyltriphenylphosphonium iodide (16.9 g, 41.6 mmol) and potassium *tert*-butoxide (3.36 g, 30 mmol) was added dry THF (60 ml) at 0 °C under N_2 atmosphere. The mixture was allowed to r.t. and stirring was continued for 1 h. The mixture was again cooled to 0 °C, the lactol **17** (1.5 g, 6.25 mmol) in dry THF (15 ml) was added dropwise to the mixture over 15 min. The mixture was allowed to warm to r.t. and stirring was continued for another 5 h. After completion of the reaction, H_2O (20 ml) was added and the mixture extracted with AcOEt (3 × 50 ml). The org. layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by CC affording **8** (0.89 g, 60%) as colorless solid. M.p. 106 – 108 °C. IR (KBr): 2940, 2847, 1694, 1584, 1464, 1332, 1299, 1205, 1047, 1024, 742. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.71 (*s*, 3 H, OCH_3); 3.89 (*s*, 3 H, OCH_3); 3.92 (*s*, 3 H, OCH_3); 5.50 (*d*, 1 H, *J* = 11.3, olefin); 5.75 (*d*, 1 H, *J* = 18.9, olefin); 6.48 (*s*, 1 H, aromatic); 6.86 (*dd*, 1 H, *J* = 11.3, 18.9, aromatic). ^{13}C-NMR (75 MHz, $CDCl_3$): 55.9; 56.7; 60.4; 96.4; 113.9; 120.4; 130.4; 131.7; 140.9; 153.5; 154.7; 171.5. ESI-MS: 239 $[M + H]^+$. HR-ESI-MS: calcd. for $C_{12}H_{14}NaO_5$ $[M + Na]$ 261.0739; found 261.0736.

(1*R*)-1-[(4*S*,4′*R*,5*S*)-2,2,2′,2′-Tetramethyl-4,4′-bi-1,3-dioxol-5-yl]but-3-en-1-ol (**22**) [17,18]. To a stirred soln. of 1,2:3,4:5,6-tri-*O*-isopropylidene-D-mannitol **21** (6.2 g, 20.7 mmol) in AcOEt (90 ml) was added periodic acid (6.1 g, 27 mmol) portion wise at 0 °C under N_2 atmosphere. After stirring for 3 h at r.t., the mixture was filtered through *Celite*, and the filtrate was concentrated *in vacuo* to give crude aldehyde **21a**, which was used in the next step without further purification.

A soln. of aldehyde **21a** (3.6 g, 15.5 mmol) in dry THF (12 ml) was added to a stirred suspension of Zn (3.0 g, 46.5 mmol) in dry THF (30 ml) at 0 °C under N_2 atmosphere. Allyl bromide (4 ml, 46.5 mmol) was added dropwise to the mixture. After stirring at 0 °C for 15 min, sat. NH_4Cl was added slowly to the mixture at 0 °C and the resulting mixture was further stirred for another 2 h. After completion of the reaction, the mixture was filtered through *Celite*, the filtrate was diluted with $CHCl_3$, washed with brine, and the org. layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by CC (hexane/AcOEt, 9:1) affording **22** (3.2 g, 76%) as colorless liquid. $[\alpha]_D^{25}$ = +12.67 (*c* = 1.1, $CHCl_3$). IR (KBr): 2924, 2851, 1495, 1452, 1266, 1177, 1125, 776. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.38 (*s*, 6 H, CH_3); 1.40 (*s*, 3 H, CH_3); 1.44 (*s*, 3 H, CH_3); 2.20 – 2.42 (*m*, 4 H, allylic); 2.50 – 2.52 (*m*, 1 H, OH); 3.68 – 3.80 (*m*, 3 H, CH); 3.92 – 4.22 (*m*, 2 H, CH); 4.26 – 4.32 (*dd*, 1 H, *J* = 3.8, 6.9, CH); 5.10 – 5.24 (*m*, 2 H, olefin); 5.88 – 6.08 (*m*, 1 H, olefin). ^{13}C-NMR (75 MHz, $CDCl_3$): 25.1; 26.3; 26.7; 26.8; 37.9; 67.8; 71.6; 76.3; 80.9; 82.7; 109.1; 110.1; 117.4; 134.6. ESI-MS: 295 $[M + Na]^+$.

(4*S*,4′*R*,5*S*)-5-[(1*R*)-1-(Methoxymethoxy)but-3-en-1-yl]-2,2,2′,2′-tetramethyl-4,4′-bi-1,3-dioxolane (**23**). Diisopropyl ethylamine (1.5 ml, 8.82 mmol) was added to a stirred soln. of alcohol **22** (2.0 g, 7.3 mmol) in dry CH_2Cl_2 (20 ml) at 0 °C under N_2 atmosphere. MOMCl (0.66 ml, 8.82 mmol) was added slowly to the mixture at the same temp. The reaction was stirred at r.t. for 12 h. After completion of the reaction (TLC), the mixture was diluted with H_2O and extracted with CH_2Cl_2 (3 × 40 ml). The combined org. layers were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by CC (hexane/AcOEt, 96:4) affording **23** in 80% yield as yellow color liquid. $[\alpha]_D^{20}$ = +7.5 (*c* = 2.0, $CHCl_3$). IR (KBr): 2987, 2935, 1641, 1380, 1371, 1247, 1214, 1155, 1067, 1041, 848. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.35 (*s*, 3 H, CH_3); 1.38 (*s*, 3 H, CH_3); 1.40 (*s*, 3 H, CH_3); 1.42 (*s*, 3 H, CH_3); 2.41 – 2.45 (*m*, 2 H, allylic); 3.40 (*s*, 3 H, OCH_3); 3.81 – 3.85 (*m*, 1 H, CH); 3.92 – 3.99 (*m*, 2 H, OCH_2); 4.06 (*dd*, 1 H, *J* = 3.9, 6.7, CH); 4.12 (*dd*, 2 H, *J* = 2.1, 6.7, CH); 4.72 (*dd*, 2 H, *J* = 7.0, 12.8, CH); 5.06 – 5.17 (*m*, 2 H, olefin); 5.89 – 5.93 (*m*, 1 H, olefin). ^{13}C-NMR (75 MHz, $CDCl_3$): 25.3; 26.5; 27.2; 34.8; 55.8; 67.1; 77.0; 77.2; 78.3; 81.3; 96.4; 109.6; 117.3; 134.8. ESI-MS: 317 $[M + H]^+$. HR-ESI-MS: calcd. for $C_{16}H_{29}O_6$ $[M + H]$ 317.1959; found 317.1956.

5-[1-(Methoxymethoxy)but-3-en-1-yl]-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde (**11**). Periodic acid (1.6 g, 7.1 mmol) was added portion wise to a stirred soln. of **23** (1.5 g, 4.75 mmol) in AcOEt (20 ml) at 0 °C under N_2 atmosphere. The stirring was continued for 6 h at r.t. After completion of the reaction, the mixture was filtered through *Celite*, and the filtrate was washed with water and brine. The org. layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by CC affording **11** (648 mg, 56%) as yellow syrup. $[\alpha]_D^{20}$ = +5.5 (*c* = 1.2,

$CHCl_3$). IR (KBr): 2924, 2851, 1690, 1456, 1267, 1189, 1129, 776. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.38 (*s*, 3 H, CH_3); 1.49 (*s*, 3 H, CH_3); 1.09 (*d*, 3 H, *J* = 6.0, CH_3); 2.34 – 2.40 (*m*, 2 H, allylic); 3.36 – 3.42 (*m*, 1 H, CH); 3.40 (*s*, 3 H, OCH_3); 3.86 (*q*, 1 H, *J* = 5.8, CH); 4.17 (*dd*, 1 H, *J* = 4.7, 6.5, CH); 4.41 (*dd*, 1 H, *J* = 1.6, 6.5, OCH_2); 4.73 (*q*, 2 H, *J* = 6.8, OCH_2); 5.10 – 5.18 (*m*, 2 H, olefin); 5.80 – 5.88 (*m*, 1 H, olefin); 9.77 (*d*, 1 H, *J* = 1.8, CHO). ESI-MS: 245 $[M + H]^+$.

5-{[(3*R*)-3-{[*tert*-Butyl(diphenyl)silyl]oxy}butyl]sulfonyl}-1-phenyl-1*H*-tetrazole (**12**) [11a]. $(NH_4)_6Mo_7O_{24} \cdot 4\ H_2O$ (0.430 g, 0.348 mmol) and H_2O_2 soln. (30%, 3.0 ml) were sequentially added to the stirred soln. of sulfide **20** (1.7 g, 3.48 mmol) in dry EtOH (20 ml) at 0 °C under N_2 atmosphere. The mixture was slowly allowed to r.t. and stirred for 6 h. After completion of the reaction, the reaction was diluted with $Na_2S_2O_3$ soln. (10%) and extracted with AcOEt. The org. layer was washed with sat. $NaHCO_3$ soln. and brine. The org. layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by CC affording **12** in 88% yield as a colorless liquid. $[\alpha]_D^{20}$ = +15.5 (*c* = 2.2, $CHCl_3$). IR (KBr): 2931, 2857, 1497, 1342, 1151, 1108, 762, 704. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.08 (*s*, 9 H, CH_3); 1.14 (*d*, 3 H, *J* = 6.4, CH_3); 1.98 – 2.16, (*m*, 2 H, CH_2); 3.68 – 3.72 (*m*, 1 H, CH_2); 3.82 – 3.92 (*m*, 1 H, CH_2); 4.02 – 4.18 (*m*, 1 H, CH); 7.34 – 7.48 (*m*, 6 H, aromatic); 7.58 – 7.70 (*m*, 9 H, aromatic). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.2; 22.9; 26.9; 30.9; 52.6; 67.2; 125.0; 127.6; 127.8; 129.6; 129.7; 129.9; 131.4; 132.9; 133.3; 133.8; 135.7; 135.8; 153.3. ESI-MS: 543 $[M + Na]^+$.

***tert*-Butyl{[(2*R*,4*E*)-5-{(4*R*,5*R*)-5-[(1*R*)-1-(methoxymethoxy)but-3-en-1-yl]-2,2-dimethyl-1,3-dioxolan-4-yl}pent-4-en-2-yl]oxy}diphenylsilane** (**24**). KHMDS (0.5M, 1.6 ml, 0.8 mmol) was added to a stirred soln. of sulfone **12** (419 mg, 0.8 mmol) and 18-crown-6 (319 mg, 1.20 mmol) in dry THF (40 ml) at −78 °C under N_2 atmosphere. A soln. of aldehyde **11** (195 mg, 0.8 mmol) in THF (10 ml) was added. The mixture was allowed to warm to r.t. and stirred for 2 h. After completion of the reaction (TLC), sat. NH_4Cl soln. was added and the mixture was extracted with AcOEt. The org. layer was washed with sat. $NaHCO_3$ soln., and dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by CC affording **24** (324 mg, 75%) as colorless oil. $[\alpha]_D^{20}$ = +8.6 (*c* = 2.2, $CHCl_3$). IR (KBr): 2983, 2929, 1642, 1374, 1244, 1160, 1033, 918. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.05 (*s*, 9 H, CH_3); 1.06 (*d*, 3 H, *J* = 6.7, CH_3); 1.38 (*s*, 3 H, CH_3); 1.40 (*s*, 3 H, CH_3); 2.18 – 2.38 (*m*, 4 H, allylic); 3.38 (*s*, 3 H, OCH_3); 3.78 – 3.92 (*m*, 3 H, CH); 4.38 (*t*, 1 H, *J* = 7.8, CH); 4.66 (*d*, 1 H, *J* = 6.8, OCH_2); 4.74 (*d*, 1 H, *J* = 6.8, CH_3); 5.04 – 5.10 (*m*, 2 H, olefin); 5.40 (*dd*, 1 H, *J* = 7.8, 15.4, olefin); 5.78 – 5.86 (*m*, 2 H, olefin); 7.34 – 7.44 (*m*, 6 H, aromatic); 7.65 – 7.70 (*m*, 4 H, aromatic). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.1; 22.9; 26.9; 27.0; 27.1; 35.9; 42.4; 55.8; 69.0; 76.0; 78.2; 81.9; 96.6; 108.6; 117.5; 127.5; 127.6; 129.5; 129.6; 130.4; 132.1; 134.5; 135.8. ESI-MS: 561 $[M + Na]^+$.

(2*R*,4*E*)-5-{(4*R*,5*R*)-5-[(1*R*)-1-(Methoxymethoxy)but-3-en-1-yl]-2,2-dimethyl-1,3-dioxolan-4-yl}pent-4-en-2-ol (**10**). TBAF (1M, 0.6 ml, 0.6 mmol) was added to stirred soln. of **24** (150 mg, 0.3 mmol) in dry THF (5 ml) at 0 °C under N_2 atmosphere. The mixture was stirred for 24 h at r.t. After completion of the reaction (TLC), solvent was removed under *in vacuo*, H_2O (5 ml) was added and the mixture was extracted with AcOEt (50 ml). The org. layer was washed with brine, and dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by CC affording **10** (62 mg, 85% yield) as yellow color liquid. $[\alpha]_D^{20}$ = +8.4 (*c* = 1.2, $CHCl_3$). IR (KBr): 3444, 2926, 2851, 1639, 1371, 1241, 1217, 1057, 1034, 771. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.20 (*d*, 3 H, *J* = 7.8 Hz, CH_3); 1.41 (*s*, 6 H, CH_3); 2.21 – 2.38 (*m*, 4 H, allylic); 3.38 (*s*, 3 H, OCH_3); 3.80 – 3.90 (*m*, 3 H, CH); 4.42 (*t*, 1 H, *J* = 7.8, CH); 4.68 (*d*, 1 H, *J* = 6.7, OCH_2); 4.75 (*d*, 1 H, *J* = 6.7, OCH_2); 5.07 – 5.13 (*m*, 3 H, CH); 5.60 (*ddd*, 1 H, *J* = 0.9, 7.8, 15.4, olefin); 5.78 – 5.90 (*m*, 2 H, olefin). ^{13}C-NMR (75 MHz, $CDCl_3$): 22.86; 26.88; 27.01; 35.86; 42.12; 55.78; 67.09; 76.12; 78.31; 81.79; 96.52; 108.72; 117.53; 131.47; 131.53; 134.35. ESI-MS: 323 $[M + Na]^+$. HR-ESI-MS: calcd. for $C_{16}H_{28}NaO_5$ $[M + Na]$ 323.1834; found 323.1846.

(2*S*,4*E*)-5-{(4*R*,5*R*)-5-[(1*R*)-1-(Methoxymethoxy)but-3-en-1-yl]-2,2-dimethyl-1,3-dioxolan-4-yl}pent-4-en-2-yl 2-Ethenyl-3,4,6-trimethoxybenzoate (**25**). Triphenylphosphine (88 mg, 0.336 mmol) and DIAD (0.06 ml, 0.336 mmol) were sequentially added to a stirred soln. of acid **8** (40 mg, 0.168 mmol) and alcohol **10** (50 mg, 0.168 mmol) in dry toluene (6 ml) at 0 °C under N_2 atmosphere. After completion of the reaction (TLC, 2 h) the solvent was removed *in vacuo*. The residue was purified by CC (AcOEt/petroleum ether 20:80) affording **25** as yellow color liquid (76 mg, 88%). $[\alpha]_D^{20}$ = +8.7 (*c* = 1.4, $CHCl_3$). IR (KBr): 2982, 2933, 1724, 1231, 1109, 1042, 770. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.30 (*d*, 3 H, *J* = 6.4, CH_3); 1.40 (*s*, 3 H, CH_3); 1.42 (*s*, 3 H, CH_3); 2.26 – 2.50 (*m*, 4 H, allylic); 3.37 (*s*, 3 H, OCH_3); 3.71 (*s*, 3 H, OCH_3); 3.80 (*m*, 1 H, CH); 3.82 (*s*, 3 H, OCH_3); 3.89 (*s*, 3 H, OCH_3); 4.42 (*t*, 1 H, *J* = 7.6, CH); 4.68 (*d*, 3 H, *J* = 6.7, OCH_2); 4.74 (*d*, 1 H, *J* = 6.7, OCH_2); 4.94 – 5.00 (*m*, 1 H, CH); 5.04 – 5.12 (*m*, 1 H, olefin); 5.16 (*dd*, 1 H, *J* = 6.4, 12.5, olefin); 5.44 (*dd*, 1 H, *J* = 1.3, 11.5, olefin); 5.56 – 5.62 (*m*, 1 H, olefin); 5.70 (*dd*, 1 H, *J* = 1.5, 17.8, olefin); 5.78 – 5.90 (*m*, 2 H, olefin); 6.44 (*s*, 1 H, aromatic); 6.76 (*dd*, 1 H, *J* = 11.6, 17.8, olefin). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.14; 26.79; 26.94; 35.78; 38.39; 55.68; 55.97; 56.38; 60.36; 71.03; 75.93; 77.99; 81.69; 96.45; 108.60; 113.69; 115.67; 117.47; 120.38; 130.18; 130.46; 130.92; 131.17; 134.28; 140.60; 153.02; 153.89; 167.13. ESI-MS: 521 $[M + H]^+$. HR-ESI-MS: calcd. for $C_{28}H_{41}O_9$ $[M + H]$ 521.2745; found 521.2725.

(2*S*)-Pent-4-en-2-yl 2-Ethenyl-3,4,6-trimethoxybenzoate (**27**). The aromatic ester **25** (30 mg, 0.058 mmol) was dissolved in dry CH_2Cl_2 (300 ml), and degasified under Ar atmosphere. The second-generation *Grubbs*' catalyst (2.4 mg,

5 mol-%) in dry CH_2Cl_2 was added to the mixture and stirred at r.t. for 6 h. After completion of the reaction, the mixture was filtered through *Celite* and the solvent was removed under *in vacuo* to give crude residue. The residue was purified by CC affording **27** (10 mg, 62%) as colorless liquid. $[\alpha]_D^{20}$ = +2.1 (*c* = 0.6, $CHCl_3$). IR (KBr): 2925, 2853, 1723, 1588, 1463, 1333, 1264, 1204, 1025, 770. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.30 (*d*, 1 H, *J* = 6.0, aromatic); 2.28 – 2.54 (*m*, 2 H, allylic); 3.72 (*s*, 3 H, OCH_3); 3.80 (*s*, 3 H, OCH_3); 3.89 (*s*, 3 H, OCH_3); 3.90 – 4.00 (*m*, 1 H, CH); 5.06 – 5.22 (*m*, 2 H, olefin); 5.44 (*dd*, 1 H, *J* = 1.5, 11.3, olefin); 5.72 (*dd*, 1 H, *J* = 1.5, 17.3, olefin); 5.78 – 5.90 (*m*, 1 H, olefin); 6.46 (*s*, 1 H, aromatic); 6.76 (*dd*, 1 H, *J* = 11.3, 17.3, aromatic). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.26; 40.07; 56.08; 56.44; 60.42; 71.21; 96.65; 116.00; 117.59; 120.44; 130.24; 130.52; 133.80; 140.75; 153.07; 153.93; 167.28. ESI-MS: 329 $[M + Na]^+$. HR-ESI-MS: calcd. for $C_{17}H_{22}O_5Na$ $[M + Na]$ 329.1365; found 329.1351.

2-Ethenyl-6-hydroxy-4-methoxybenzoic Acid (**29**) [27]. $LiOH \cdot H_2O$ (126 mg, 3 mmol) was added to the stirred soln. of **33** (300 mg, 1.28 mmol) in THF: H_2O (2:1) at r.t. The mixture was heated to 60 °C and stirred for 20 h. After completion of the reaction, dil. HCl was added and the mixture extracted with AcOEt. The org. layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by CC affording **29** as colorless solid (186 mg, 75%). M.p. 130 – 132 °C. IR (KBr): 2924, 1639, 1462, 1259, 1161, 844. ^{1}H-NMR (300 MHz, $CDCl_3$ + (D_4) MeOH): 3.84 (*s*, 3 H, OCH_3); 5.7 (*d*, 1 H, *J* = 11.0, olefin); 5.48 (*d*, 1 H, *J* = 1.5, 18.0, olefin); 6.41 (*d*, 1 H, *J* = 3.0, aromatic); 6.52 (*d*, 1 H, *J* = 3.0, aromatic); 7.35 (*dd*, 1 H, *J* = 11.0, 18.0, olefin); 11.40 (*s*, 1 H, OH). ^{13}C-NMR (75 MHz, $CDCl_3$ + (D_4)MeOH): 54.30; 99.32; 105.52; 113.97; 137.66; 142.64; 162.31; 164.29. ESI-MS: 195 $[M + H]^+$.

(2*R*,4*E*)-5-[(4*R*,5*R*)-5-{(1*R*)-1-[(4-Methoxybenzyl)oxy]but-3-en-1-yl}-2,2-dimethyl-1,3-dioxolan-4-yl]pent-4-en-2-ol (**10a**). TBAF (1M, 0.6 ml, 0.6 mmol) was added to the stirred soln. of (4*S*,5*R*)-5-((*R*)-1-((4-methoxybenzyl)oxy)but-3-en-1-yl)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde (200 mg, 0.3 mmol) in dry THF (5 ml) at 0 °C under N_2 atmosphere. The mixture was stirred for 24 h at r.t. After completion of the reaction (TLC), solvent was removed under *in vacuo*. The residue was purified by CC affording **10a** (101 mg, 82% yield) as colorless liquid. $[\alpha]_D^{20}$ = +7.82 (*c* = 1.1, $CHCl_3$). IR (KBr): 2982, 2933, 1718, 1432, 1345, 1232, 1042, 778. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.16 (*d*, 3 H, *J* = 6.0, CH_3); 1.40 (*s*, 3 H, CH_3); 1.42 (*s*, 3 H, CH_3); 1.69 (br. *s*, 1 H, OH); 2.19 (*t*, 2 H, *J* = 6.8, allylic); 2.34 (*t*, 2 H, *J* = 6.8, allylic); 3.65 (*q*, 1 H, *J* = 5.2, CH); 3.76 – 3.84 (*m*, 2 H, CH); 3.80 (*s*, 3 H, OCH_3); 4.42 (*t*, 1 H, *J* = 7.5, CH); 4.57 (*s*, 2 H, OCH_2); 5.04 – 5.16 (*m*, 2 H, olefin); 5.58 (*dd*, 1 H, *J* = 7.5, 15.1, olefin); 5.74 – 5.90 (*m*, 2 H, olefin); 6.87 (*d*, 2 H, *J* = 9.0, aromatic); 7.25 (*d*, 2 H, *J* = 7.5, aromatic). ESI-MS: 399 $[M + Na]^+$. HR-ESI-MS: calcd. for $C_{22}H_{32}NaO_5$ $[M + Na]$ 399.2147; found 399.2145.

(2*S*,4*E*)-5-[(4*R*,5*R*)-5-{(1*R*)-1-[(4-Methoxybenzyl)oxy]but-3-en-1-yl}-2,2-dimethyl-1,3-dioxolan-4-yl]pent-4-en-2-yl 2-Ethenyl-6-hydroxy-4-methoxybenzoate (**34**). Triphenylphosphine (266 mg, 1.2 mmol) and DIAD (0.2 ml, 1.2 mmol) were added sequentially to a stirred soln. of acid **29** (100 mg, 0.510 mmol) and alcohol **10a** (96 mg, 0.510 mmol) in dry toluene (14 ml) at 0 °C under N_2 atmosphere. After completion of the reaction (TLC, 2 h), the solvent was removed under *in vacuo*. The residue was purified by CC affording **34** as colorless syrup (228 mg, 80%). $[\alpha]_D^{20}$ = +8.9 (*c* = 1.2, $CHCl_3$). IR (KBr): 3420, 2982, 2933, 1716, 1651, 1342, 1212, 786. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.24 (*d*, 3 H, *J* = 6.6, CH_3); 1.38 (*s*, 3 H, CH_3); 1.40 (*s*, 3 H, CH_3); 2.22 – 2.34 (*m*, 4 H, allylic); 3.46 – 3.62 (*m*, 1 H, CH); 3.79 (*s*, 3 H, OCH_3); 3.81 (*s*, 3 H, OCH_3); 4.40 (*t*, 1 H, *J* = 7.5, CH); 4.48 (*m*, 2 H, OCH_2); 5.00 – 5.22 (*m*, 3 H, olefin); 5.40 (*d*, 1 H, *J* = 15.4, olefin); 5.58 – 5.64 (*dd*, 1 H, *J* = 7.6, 15.4, olefin); 5.70 – 5.82 (*m*, 2 H, olefin); 6.40 (*d*, 1 H, *J* = 2.6, aromatic); 6.42 (*d*, 2 H, *J* = 2.6, aromatic); 6.82 (*d*, 2 H, *J* = 7.8, aromatic); 7.16 – 7.24 (*m*, 3 H, aromatic); 11.74 (*s*, 1 H, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.7; 26.9; 29.7; 35.6; 38.7; 55.2; 55.4; 71.9; 72.4; 78.1; 78.5; 81.9; 100.2; 103.9; 108.3; 108.7; 113.6; 115.4; 117.3; 129.4; 130.4; 132.1; 134.4; 138.6; 143.7; 159.1; 164.0; 165.0; 170.6. ESI-MS: 575 $[M + Na]^+$.

(2*S*,4*E*)-5-{(4*R*,5*R*)-5-[(1*R*)-1-Hydroxybut-3-en-1-yl]-2,2-dimethyl-1,3-dioxolan-4-yl}pent-4-en-2-yl 2-Ethenyl-6-hydroxy-4-methoxybenzoate (**35**). DDQ (122 mg, 0.554 mmol) was added to a stirred soln. of **34** (150 mg, 0.272 mmol) in CH_2Cl_2/H_2O (10 ml, 9:1) at 0 °C. The mixture was allowed to r.t. and stirred for 2 h. After completion of the reaction (TLC), the mixture was filtered through *Celite*, and the filtrate was washed with 5% $NaHCO_3$ soln., water, and brine. The org. layer was separated, and dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified by CC affording **35** (93 mg, 80%) as colorless liquid. $[\alpha]_D^{20}$ = +21.43 (*c* = 0.8, $CHCl_3$). IR (KBr): 3482, 2927, 1648, 1609, 1257, 1213, 1161, 1055, 767. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.38 (*d*, 3 H, *J* = 6.2, CH_3); 1.40 (*s*, 3 H, CH_3); 1.41 (*s*, 3 H, CH_3); 2.10 – 2.16 (*m*, 1 H, allylic); 2.18 (br. *s*, 1 H, OH); 2.42 – 2.52 (*m*, 2 H, allylic); 3.64 – 3.68 (*m*, 1 H, CH); 3.76 – 3.82 (*m*, 1 H, CH); 3.82 (*s*, 3 H, OCH_3); 4.44 (*t*, 1 H, *J* = 7.8, CH); 5.06 – 5.10 (*m*, 2 H, olefin); 5.20 – 5.28 (*m*, 2 H, olefin); 5.44 (*dd*, 1 H, *J* = 1.5, 17.0, olefin); 5.58 – 5.66 (*m*, 1 H, olefin); 5.74 – 5.84 (*m*, 2 H, olefin); 6.40 (*d*, 1 H, *J* = 2.6, aromatic); 6.44 (*d*, 1 H, *J* = 2.6 Hz, aromatic); 7.24 – 7.28 (*m*, 2 H, olefin). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.8; 26.8; 26.9; 37.2; 38.8; 55.4; 70.3; 71.8; 77.8; 82.5; 100.2; 103.9; 108.4; 108.8; 115.5; 118.2; 130.2; 131.3; 132.0; 134.0; 138.7; 143.7; 164.1; 165.0; 170.6. ESI-MS: 455 $[M + Na]^+$. HR-ESI-MS: calcd. for $C_{24}H_{32}NaO_7$ $[M + Na]$ 455.2046; found 455.2036.

(2*S*,4*E*)-5-{(4*R*,5*R*)-5-[(1*R*)-1-Hydroxybut-3-en-1-yl]-2,2-dimethyl-1,3-dioxolan-4-yl}pent-4-en-2-yl 2-Ethenyl-4-methoxy-6-(methoxymethoxy)benzoate (**36**). Diisopropylethylamine (0.03 ml, 0.178mmol) was added to the stirred soln. of **35** (70 mg, 0.162 mmol) in dry CH_2Cl_2 (4 ml) at 0 °C under N_2 atmosphere. After 10 min, MOMCl (14 mg in CH_2Cl_2, 0.178 mmol) was added slowly to the mixture and allowed to r.t. and stirred for 24 h. After completion of the reaction (TLC), diluted with H_2O and extracted with $CHCl_3$. The org. layer was separated, and dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by CC affording **36** (61 mg, 80% yield) as colorless liquid. $[\alpha]_D^{20}$ = +11.43 (*c* = 0.7, $CHCl_3$). IR (KBr): 3430, 2922, 2852, 2364, 1702, 1562, 1358, 1218, 788. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.34 (*d*, 3 H, *J* = 6.4, CH_3); 1.42 (*s*, 3 H, CH_3); 1.43 (*s*, 3 H, CH_3); 2.16 – 2.30 (*m*, 2 H, allylic); 2.36 – 2.52 (*m*, 2 H, allylic); 3.48 (*s*, 3 H, OCH_3); 3.68 – 3.74 (*m*, 1 H, CH); 3.82 (*s*, 3 H, OCH_3); 3.83 – 3.88 (*m*, 1 H, CH); 4.44 (*t*, 1 H, *J* = 7.7, CH); 5.06 – 5.16 (*m*, 1 H, olefin); 5.16 (*s*, 2 H, OCH_2); 5.22 (*t*, 1 H, *J* = 6.2, olefin); 5.34 (*d*, 1 H, *J* = 11.5, olefin); 5.56 – 5.66 (*m*, 1 H, olefin); 5.70 (*d*, 1 H, *J* = 15.4, olefin); 5.76 – 5.96 (*m*, 2 H, olefin); 6.64 (*d*, 1 H, *J* = 2.0, aromatic); 6.70 – 6.78 (*d*, 1 H, *J* = 2.4, aromatic); 6.70 – 6.78 (*m*, 1 H, olefin). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.5; 26.9; 26.9; 37.2; 38.6; 55.4; 56.1; 70.3; 71.1; 77.7; 82.4; 94.6; 101.1; 103.4; 108.7; 117.0; 118.1; 130.4; 131.3; 133.6; 134.1; 137.5; 155.4; 161.1; 167.1. ESI-MS: 499 $[M + Na]^+$. HR-ESI-MS: calcd. for $C_{26}H_{36}NaO_8$ $[M + Na]$ 499.2308; found 499.2302.

(3a*S*,4*E*,7*R*,14*E*,17*R*,17a*S*)-17-Hydroxy-12-methoxy-10-(methoxymethoxy)-2,2,7-trimethyl-3a,6,7,16,17,17a-hexahydro-9*H*-[1,3]dioxolo[4,5-*g*][2]benzoxacyclotetradecin-9-one (**37**). The aromatic ester **36** (50 mg, 0.10 mmol) was taken in dry CH_2Cl_2 (400 ml) and degasified under Ar atmosphere. The second-generation *Grubbs*' catalyst (4.4 mg, 5 mol-%) dissolved in dry CH_2Cl_2 was added to the mixture, and stirred under reflux conditions for 8 h. After completion of the reaction (TLC), the mixture was filtered through *Celite* and the solvent was removed under *in vacuo* to give crude material. The residue was purified by CC affording **37** (31 mg, 66%) as yellow liquid. $[\alpha]_D^{20}$ = −40.87 (*c* = 0.6, $CHCl_3$). IR (KBr): 3471, 2925, 1723, 1601, 1260, 1155, 1049, 760. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.38 (*s*, 3 H, CH_3); 1.41 (*d*, 3 H, *J* = 6.0, CH_3); 1.46 (*s*, 3 H, CH_3); 2.30 – 2.56 (*m*, 4 H, allylic); 2.70 – 2.82 (br. *s*, 1 H, OH); 3.46 (*s*, 3 H, OCH_3); 3.80 (*s*, 3 H, OCH_3); 4.00 (*dd*, 1 H, *J* = 2.2, 6.8, CH); 4.10 – 4.20 (*m*, 1 H, CH); 4.56 (*t*, *J* = 8.3, 1 H, CH); 5.10 – 5.20 (*m*, 3 H, OCH_2 & CH); 5.60 – 5.70 (*m*, 1 H, olefin); 5.86 (*ddd*, 1 H, *J* = 4.8, 8.8, 15.1, olefin); 6.08 (*ddd*, 1 H, *J* = 4.8, 10.0, 14.5, olefin); 6.22 – 6.34 (*m*, 1 H, olefin); 6.60 (*d*, 1 H, *J* = 2.0, aromatic); 6.66 (*dd*, 1 H, *J* = 2.4, aromatic). ^{13}C-NMR (75 MHz, $CDCl_3$): 20.5; 26.9; 27.0; 36.5; 39.4; 55.5; 56.1; 69.1; 70.9; 75.5; 81.5; 94.5; 100.9; 102.2; 108.8; 117.8; 125.7; 130.2; 130.5; 133.4; 135.6; 154.9; 161.0; 167.6. ESI-MS: 471 $[M + Na]^+$. HR-ESI-MS: calcd. for $C_{24}H_{32}NaO_8$ $[M + Na]$ 471.1995; found 471.1990.

(3*S*,5*E*,7*R*,8*R*,9*R*,11*E*)-7,8,9,16-tetrahydroxy-14-methoxy-3-methyl-3,4,7,8,9,10-hexahydro-1*H*-2-benzoxacyclotetradecin-1-one (**28**). 2N HCl (2 ml) was added dropwise to a soln. of **37** (20 mg, 0.198 mmol) in THF (2 ml) at 0 °C, and the mixture was stirred for 20 h at r.t. After completion of the reaction, aq. $NaHCO_3$ soln. was added and the mixture extracted with AcOEt. The org. layer was separated and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the crude product was purified by CC affording **28** (8.4 mg, 52% yield) as a colorless solid. M.p. 82 – 84 °C. $[\alpha]_D^{20}$ = −10.67 (*c* = 0.6, $CHCl_3$). IR (KBr): 3432, 2926, 1610, 1253, 1202, 1160, 1053, 959. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.39 (*d*, 3 H, *J* = 6.4 Hz, CH_3); 2.28 – 2.54 (*m*, 3 H, allylic); 2.66 – 2.74 (*m*, 1 H, allylic); 3.60 (*m*, 1 H, CH); 3.82 (*s*, 3 H, OCH_3); 4.00 – 4.06 (*m*, 1 H, CH); 4.18 – 4.26 (*m*, 1 H, CH); 5.38 – 5.46 (*m*, 1 H, CH); 5.77 (*dd*, 1 H, *J* = 7.2, 15.7, olefin); 5.88 – 6.02 (*m*, 2 H, olefin); 6.39 (*d*, 1 H, *J* = 2.4, aromatic); 6.44 (*d*, 1 H, *J* = 2.4, aromatic); 6.88 (*d*, 1 H, *J* = 15.7, olefin). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.7; 35.7; 36.6; 55.4; 71.3; 72.5; 72.8; 77.2; 99.9; 104.4; 107.6; 127.5; 128.3; 132.6; 133.4; 142.3; 163.9; 164.6; 170.8. ESI-MS: 363 $[M - H]^+$. HR-ESI-MS: calcd. for $C_{19}H_{24}NaO_7$ $[M + Na]$ 387.1422; found 387.1423.

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