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A New Approach to Asymmetric Synthesis of Infectocaryone †

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A useful and flexible strategy for synthesis of (-)- and (+)-infectocaryone from commercial sugars is developed. Key step of the synthesis is an new-type Diels-Alder reaction with good chemselectivity and stereoselectivity, in which a mixture of alkene regioisomers in a dynamic equilibrium is employed as chiral dienophiles for the first time.

Introduction

Infectocaryone (**1**),[1] together with demethylinfectocaryone (**2**)[1b,2] and cryptocaryone (**3**)[1a,b,2,3], belongs to a special class of naturally occurring dihydrochalcones (Figure 1). Unlike most dihydrochalcones, as the hydrogenation occur not C2-C3 position but C5-C6 position, these dihydrochalcones bearing a reduced A-ring, such as **1**-**3**, are optically active. These chiral dihydrochalcone derivatives exist only in the plant genus Cryptocarya.[4] (+)-Infectocaryone (**1**) was first isolated in 2001 from the trunk bark of Cryptocarya infectoria.[1a] Subsequently, (+)-**1** was also obtained from the other two species in the genus, C. konishii[1b] and C. chinensis.[1c] As a member of bioactive flavonoid constituents[1-3,5] in the genus Cryptocarya, **1** showed strong cytotoxicities against KB, P-388, MCF-7, NCI-H460 and SF-268 cell lines,[1] and could be a promising lead compound for cancer treatment. Therefore the development of the efficient and short access to infectocaryone and its analogues is of importance.

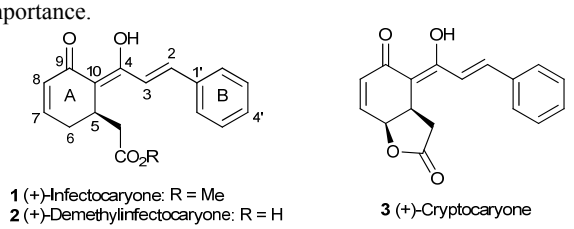
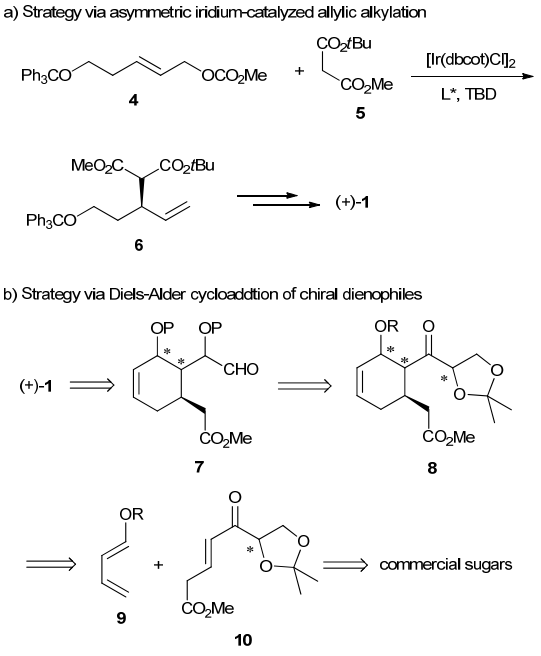


Figure 1. Examples of chiral dihydrochalcones from the plant genus *Cryptocarya*.

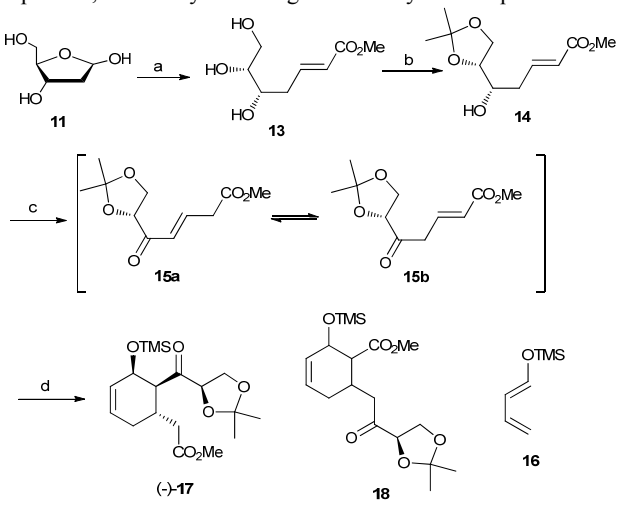
Up to now, only Helmchen group synthesized **1** from the trityl-protected allylic carbonate **4** in 14 steps.[6] In the strategy, an elegant regioselective iridium-catalyzed allylic alkylation of **4**, under the catalyst system they developed,[7] was used as a key step to synthesize terminal olefin **6** with the necessary chiral center (Scheme 1a). As a continuation of our interests in enantioselective synthesis of natural products[8] and heterocycle systems[9] using cheap chiral materials, we herein report a new asymmetric approach to **1** that starts from commercially available monosaccharides. Our retrosynthetic analysis of **1** is illustrated in Scheme 1b. Intermediate **7** would provide target compound **1** through Wittig reaction followed by functional group manipulations. Aldehyde **7** could be obtained by the oxidative cleavage of the diol derivative **8**. The substituted cyclohexene ring in **8** should be constructed through an asymmetric Diels-Alder reaction based on chiral dienophile **10**, which could be prepared conveniently from common sugars.



Scheme 1. Strategies for the enantioselective synthesis of infectocaryone (**1**).

Results and discussion

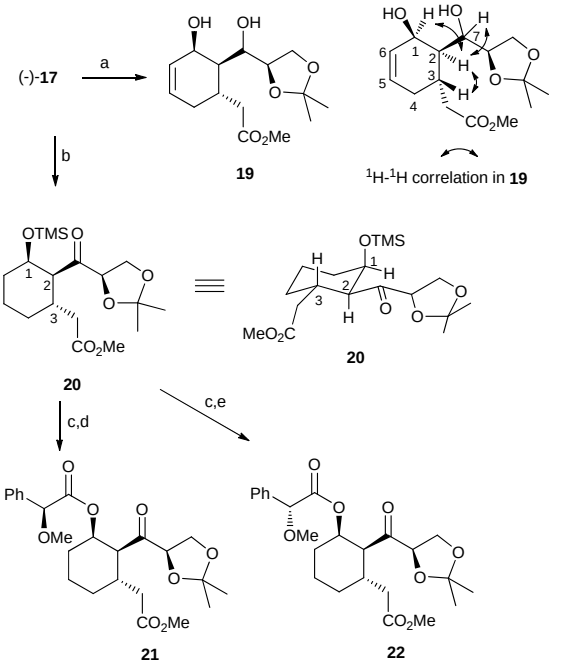
We began our synthesis with 2-deoxy-D-ribose (**11**) (Scheme 2). Treatment of **11** with (carbmethoxymethylene)triphenylphosphorane (**12**) and a trace of benzoic acid gave unsaturated ester **13** in high yield.[10] The terminal 1,2-diol functional group of **13** was selectively protected producing acetonide **14**, which was proposed to prepare dienophile **15a** by hydroxyl oxidation and double bond rearrangement. Interestingly, **14** was treated with IBX to furnish the unsaturated 1,5-keto ester **15a** and **15b** as a 1:1 mixture of regioisomers.[11] The two isomers can not be separated, and always exist together in a dynamic equilibrium.



Scheme 2. Synthesis of (-)-**17** from 2-deoxy-D-ribose (**11**): (a) $Ph_3P{=}CHCO_2Me$ (**12**), $PhCO_2H$, THF, 70℃, 95%; (b) $Me_2C(OMe)_2$, TsOH, acetone, RT, 92%; (c) IBX, AcOEt, 80℃, 40%; (d) **16**, toluene, 120℃, 43%.

To the best of our knowledge, Diels-Alder reactions employing this kind of tautomeric olefin isomers as mixed dienophiles have not been explored yet. In theory, both isomers **15a** and **15b** could react with 1-(trimethylsilyloxy)-1,3-butadiene (**16**) to yield the corresponding cycloaddition products **17** and **18** respectively. However, it is possible that the product from the reaction of more active dienophile isomer would be obtained preferably due to reactivity difference and dynamic equilibrium between two olefin isomers **15a** and **15b**. Indeed, heating of isomeric alkenes **15a**/**b** and diene **16** in toluene at 120℃ in a sealed tube gave **17** as major product in 43% yield, together with a mixture of two other cycloaddition isomers in small amount (9%, ca. 1:1), which could not be separated by routine chromatography to get pure compound for structural analysis.

To identify the structure of the major product, reduction of **17** with $NaBH_4$ and simultaneous removal of TMS group afforded diol **19** as a single isomer (Scheme 3). In its ^1H-^1H COSY spectrum, H-2 signal (δ = 1.76) correlated with H-1 (δ = 4.59), H-3 (δ = 2.45) and H-7 (δ = 3.63) signals respectively. It suggests that the major Diels-Alder product **17** is not derived from dienophile **15b** but from dienophile **15a**, for alkene isomer **15a** with a conjugate ketone carbonyl group is more electron-poor and active than its isomer **15b** with a conjugate ester carbonyl group. The next issue is the determination of stereochemistry of **17** contanining three new chiral centers. Catalytic hydrogenation of **17** smoothly furnished the corresponding 1,2,3-trisubstitued cyclohexane **20**, whose ^1H NMR spectrum was analyzed in detail. The presence of a large coupling constant in H-2 signal (dd, J = 11.1, 2.4 Hz) at 3.00 ppm means that H-2 should be in the axial position of the chair conformation. Meanwhile, the absence of any large J value from *trans* diaxial coupling on H-1 (δ = 4.53) attributes to its equatorial position. Therefore, the relative configuration of 1,2,3-trisubstitued cyclohexane **20** has 1,2-*cis* and 2,3-*trans* relationships. A useful method for establishment of absolute configuration of secondary alcohols utilizing the *O*-methylmandelate ester was developed,[12] and we recently applied the approach to establish the absolute configuration of natural lorneic acid B.[8a] Here we intend to examine further their applicability in more complicated alcohol. Thus, removal of TMS group in **20** gave the resulting secondary alcohol, which was converted to into both (*S*)- and (*R*)-*O*-methylmendelate derivatives **21** and **22** respectively. The proton shift differences between **21** and **22** (upfield H-2 signal at 3.07 ppm in **22** and upfield H-6 signals at 1.65 and 1.44 ppm in **21**) indicated *R* configuration of C-1 according to Mosher model extended by Trost (Figure 2).[12,13] Hence the absolute configuration of major isomer (-)-**17** is deduced to (*1R*, *2S*, *3S*).



Scheme 3. Transformation of (-)-**17** for structural determination: (a) $NaBH_4$, MeOH, RT, 88%; (b) 10% Pd/C, H_2, AcOEt, RT, 92%; (c) TBAF, AcOH, THF, RT; (d) (*S*)-*O*-methylmandelic acid, EDCI, DMAP, CH_2Cl_2, RT, 72% from **20**; (e) (*R*)-*O*-methylmandelic acid, EDCI, DMAP, CH_2Cl_2, RT, 70% from **20**.

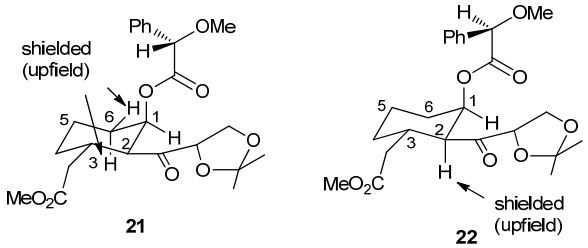
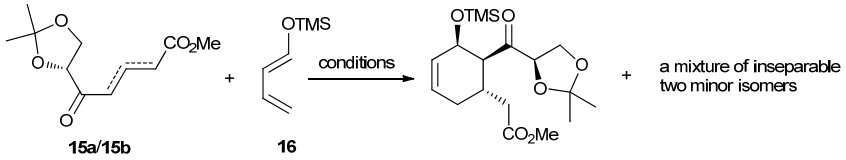


Figure 2. Establishment of absolute configuration of (-)-**17**.

We then focused on the optimization of reaction conditions to

improve the yield of **17**. Various Lewis acids including $Sc(OTf)_3$, $Yb(OTf)_3$, Et_2AlCl and $EtAlCl_2$ were investigated to promote the Diels-Alder cycloaddition. Unfortunately, these attempts gave poor yield or failed to proceed presumably due to instability of the reactants in the presence of these Lewis acids (Table 1, entry 2-8). To our delight, an appropriate increase in concentration of dienophile **15a**/**b** could facilitate the reactions performed in heating conditions (Table 1, entry 9-10). **17** was obtained in 65% yield when the concentration of **15a**/**b** was increased to 1M. However, higher concentrations, including solvent-free conditions, did not show a further improvement in the yield (Table 1, entry 11-12). While the amount of diene **16** was doubled, only a slight enhancement in yield was observed (Table 1, entry 13). Although the required reaction time could be efficiently shortened by elevating the reaction temperature, **17** was still obtained in a similar yield (Table 1, entry 14-15). It is worth noting that the selectivities of these reactions under heating conditions remain almost unaffected. **17** is always formed as a major product through a preferable transition state in which the ketone carbonyl unit of dienophile **15a** occupies the endo position. The configuration of the three new stereocenters is controlled well under induction of the chiral unit in **15**. As a chiral dienophile,[14] **15** is promising in development of new asymmetric Diels-Alder reactions and synthesis of some useful intermediates such as enantiomerically pure cyclohexenone derivatives[15,16] with control of stereochemistry.

Table 1. Optimization of the Diels-Alder reaction with **15a**/**15b** and **16**



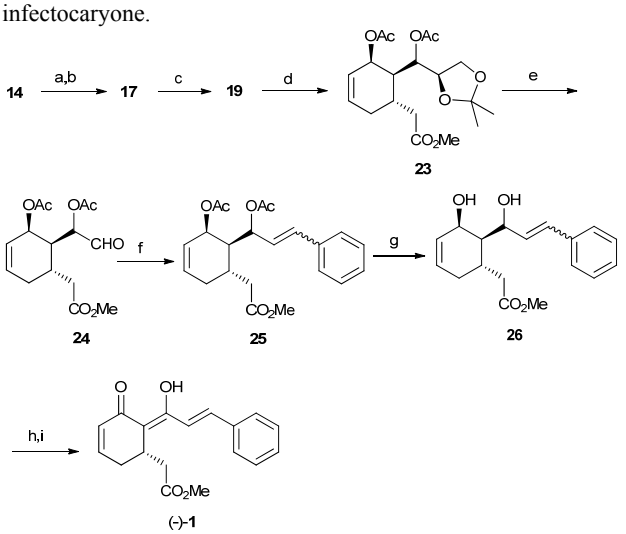
15a/15b **16** **17**

Entry	Concentration of **15** [M]	Amount of **16** [equiv.]	Solvent	Time [h]	Catalyst	Amount of catalyst [equiv.]	Temperature [℃]	Yield of **17** [%]	Yield of the mixture of two minor isomers [%]
1[a]	0.2	3	Toluene	65	--	--	120	43	9
2	0.2	3	CH_2Cl_2	24	$Sc(OTf)_3$	0.1	-78	0[b]	0
3	0.2	3	CH_2Cl_2	10	$Sc(OTf)_3$	0.1	0	Trace	0
4	0.2	3	CH_2Cl_2	20	$Yb(OTf)_3$	0.1	0	5	0
5	0.2	3	CH_2Cl_2	2	$EtAlCl_2$	1	0	Trace	0
6	0.2	3	CH_2Cl_2	20	Et_2AlCl	1	0	14	0
7	0.2	3	THF	20	Et_2AlCl	1	0	9	0
8	0.2	3	CH_2Cl_2	20	Et_2AlCl	1	-78	0[b]	0
9[a]	0.5	3	Toluene	48	--	--	120	55	12
10[a]	1	3	Toluene	40	--	--	120	65	14
11[a]	2	3	Toluene	40	--	--	120	64	16
12[a]	--	5	--[c]	45	--	--	120	58	15
13[a]	1	6	Toluene	35	--	--	120	67	15
14[a]	1	3	Xylene	22	--	--	160	64	16
15[a]	1	6	Xylene	18	--	--	160	66	17

[a] The reactions were heated in sealed tube. [b] Material **15** and **16** remained. [c] The reaction was performed with neat **15** and **16**.

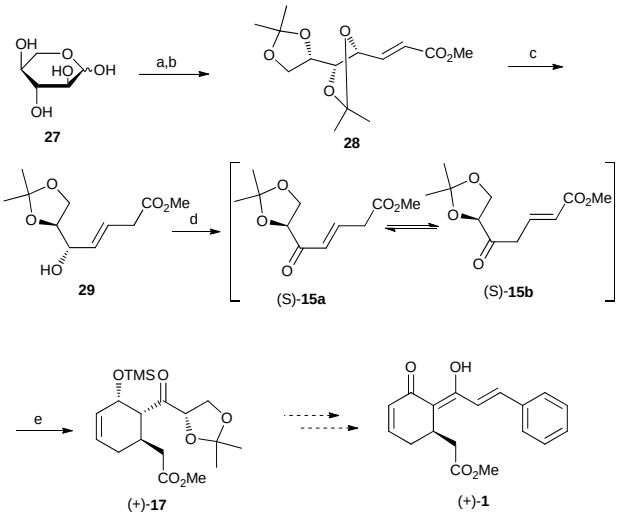
With the optimized Diels-Alder reaction conditions in hand, we continued to explore the synthesis of infectocaryone. However, in the purification of dienophile **15a**/**b**, a considerable mass loss occurred after column chromatography owing to partial decomposition of **15a**/**b** on silica column. Therefore, without further purification, the crude oxidation product of **14** with IBX was employed directly in the subsequent Diels-Alder reaction. By this modified procedure, **17** was obtained from in a better overall yield (50% for two steps). After treatment of **17** with $NaBH_4$, the resulting diol **19** was then acylated to give diacetate **23**. Sequential hydrolysis of acetonide **23** and oxidative cleavage of the resulting glycol with periodic acid[17] furnished the desired aldehyde **24**. The Wittig olefination of aldehyde **24** with the ylide generated by the treatment of benzyl triphenylphosphonium bromide with *n*-butyllithium[18] gave olefin **25** as an inseparable mixture of *E*/*Z* isomers. The *E*/*Z* ratio was determined by the ^{1}H NMR spectra and varied from 1:1.5 to 1:3. Deacetylation of the *E*/*Z* mixture **25** using potassium carbonate in aqueous methanol afforded the diol **26** in 71% yield with a small amount of the recovered **25** (20%). Prolonged reaction time for full consumption of diacetate **25** led to a drop in yield. Diol **26** was oxidized with Dess-Martin periodinane gave the resulting (*E*)- and (*Z*)-**1** mixture in a reverse *E*/*Z* ratio (ca. 2.5:1). Although *Z* alkene was partially

isomerized to more stable *E* alkene in the oxidation process, the *E*- and *Z*- isomers still could not be separated at this stage. After screening various conditions for Z- to E-alkene isomerization, the simple stirring of E/Z mixture in THF in the presence of $Pd(PPh_3)_4$ (0.1 equiv.) smoothly gave the desired E-isomer exclusively (Scheme 3). In comparison to the spectral data of the natural product,[1a,6] synthetic example **1** indicated identical NMR, IR and MS spectra except for the opposite sign in optical rotation. Thus, synthetic (-)-**1** from 2-deoxy-D-ribose was determined to be the enantiomer of the naturally occurring (+)-infectocaryone.



Scheme 4. Synthesis of (-)-**1** from **14**: (a) IBX, AcOEt, 80℃; (b) **16**, toluene, 120℃, 50% for two steps; (c) $NaBH_4$, MeOH, RT, 88%; (d) Ac_2O, DMAP, CH_2Cl_2, RT, 96%; (e) H_5IO_6, AcOEt, RT, 99%; (f) $[Ph_3PCH_2Ph]$·Br, *n*-BuLi, THF, 75%; (g) K_2CO_3, MeOH, H_2O, RT, 71% (89% brsm); (h) Dess-Martin periodinane, CH_2Cl_2, RT; (i) $Pd(PPh_3)_4$, THF, RT, 92% for two steps.

Theoretically, natural (+)-**1** can be synthesized via key intermediate (+)-**17** from 2-deoxy-L-ribose by the same synthetic route. However, an alternative strategy to preparation of (+)-**17** employing L-xylose or L-arabinose as cheaper chiral pool material should be much more practical. Thus, Wittig condensation of L-xylose (**27**) with stabilized ylide **12** in boiling THF followed by acetonation yielded diisopropylidenated (*E*)-unsaturated ester **28**.[19] Reductive cleavage of γ-functionalized α,β-unsaturated ester **28** mediated with Mg in MeOH,[20] gave allyl alcohol **29**. Oxidation of the hydroxyl group in **29** to ketone still afforded a mixture of (*S*)-**15a** and **15b**, ^{1}H NMR spectrum of which is same as that of the oxidation product of **14**. Without purification, crude mixture reacted with diene **16** under the optimal conditions to furnish the expected cycloaddition product (+)-**17** in 52% yield for two steps (Scheme 4). Following the same transformation to (-)-**1** as from (-)-**17**, (+)-**1** should be synthesized from (+)-**17**.



Scheme 5. Synthesis of (+)-**17** from L-xylose (**27**): (a) $Ph_3P{=}CHCO_2Me$, $PhCO_2H$, THF, reflux; (b) acetone, $CuSO_4$, H_2SO_4, RT, 91% for two steps; (c) Mg, MeOH, 0℃, 92%; (d) IBX, AcOEt, 80℃; (e) **16**, toluene, 120℃, 52% for two steps.

Conclusions

In summary, we have developed a new strategy for synthesis of optically pure infectocaryone featuring an asymmetric Diels-Alder reaction. From cheap 2-deoxy-D-ribose, (-)-infectocaryone was synthesized via key intermediate (-)-**17** in 11 steps with 17.9% overall yield. (+)-Infectocaryone can be obtained via (+)-**17** by this strategy using L-xylose as starting material. In our synthesis, the Diels-Alder reaction of chiral dienophile mixture such as **15a** and **15b** is explored for the first time, in which good chemselectivity and stereoselectivity is achieved to create the chiral centers on the ring of **17**. Efforts to utilize the practical strategy for the syntheses of other related dihydrochalcones are in progress.

Experimental section

General: IR spectra were recorded on a commercial spectrophotometer. Optical rotations were reported as follows: $[\alpha]_D^T$ (c: g/100 mL, in solvent). ^{1}H NMR spectra were recorded on commercial instruments (400 MHz) with TMS as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constants (Hz), integration. ^{13}C NMR data were collected on commercial instruments (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. HR-ESIMS spectra were recorded using a commercial apparatus and methanol was used to dissolve the sample. Solvents for reaction were distilled prior to use: tetrahydrofuran (THF) from sodium sand, toluene and dichloromethane from CaH_2, methanol from magnesium turnings. Ethyl acetate and other reagents were obtained from commercial suppliers unless otherwise stated.

Compound 13: To a solution of 2-deoxy-D-ribose (20.0 g, 0.15 mol) in THF (380 mL), Ph_3PCHCO_2Me (55.0 g, 0.16 mol) was

added. The resulting suspension was heated at 70℃ until TLC control showed complete conversion of the substrate. Then the mixture was concentrated under reduced pressure and the residue was subjected to flash column chromatography to yield triol ester **13** (26.9 g, 95%) as a white solid. m.p. 56–57℃; $[\alpha]_D^{26}$ = −24 (*c* = 1.71, CH_3OH); ^1H NMR (400 MHz, CD_3OD) δ 6.97 (dt, *J* = 15.6, 7.3 Hz, 1H), 5.85 (dt, *J* = 15.6, 1.2 Hz, 1H), 3.63 (dd, *J* = 11.4, 3.8 Hz, 1H), 3.61 (s, 3H), 3.55 (ddd, *J* = 8.3, 7.3, 3.3 Hz, 1H), 3.48 (dd, *J* = 11.3, 6.3 Hz, 1H), 3.36 (td, *J* = 6.6, 3.7 Hz, 1H), 2.51 (dddd, *J* = 14.7, 7.0, 3.2, 1.5 Hz, 1H), 2.26 (ddd, *J* = 15.0, 8.8, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 168.6, 148.2, 123.7, 75.8, 72.1, 64.5, 51.9, 37.1; IR (thin film): *v* 3371, 3208, 1712, 1658, 1382, 1209, 1159, 1117, 998 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_8H_{14}NaO_5$ $[M+Na]^+$ 213.0739, found 213.0736.

Compound 14: 2,2-Dimethoxypropane (15.7 mL, 0.13 mol) and TsOH (0.54 g, 3.16 mmol) were added to a solution of triol **13** (12.0 g, 0.06 mol) in acetone (450 mL). The resulting mixture was stirred at room temperature for 2 h. Then the reaction was quenched with moist $NaHCO_3$ and the solvent was removed under reduced pressure. Water (180 mL) was added, and the aqueous phase was extracted with dichloromethane (3 x 200 mL). The combined organic layers were dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The residue was subjected to column chromatography to yield **14** (13.4 g, 92%) as a colorless oil. $[\alpha]_D^{26}$ = +51 (*c* = 0.45, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 6.97 (dt, *J* = 15.6, 7.3 Hz, 1H), 5.92 (br d, *J* = 15.7 Hz, 1H), 4.03 – 3.97 (m, 2H), 3.94 – 3.90 (m, 1H), 3.87 – 3.79 (m, 1H), 3.72 (s, 3H), 2.45 (dddd, *J* = 14.6, 7.0, 4.1, 1.3 Hz, 1H), 2.41 – 2.22 (m, 2H), 1.41 (s, 3H), 1.34 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.9, 145.2, 123.5, 109.4, 78.1, 70.5, 65.6, 51.6, 36.1, 26.6, 25.2 ppm; IR (thin film): *v* = 3464, 2987, 2935, 1726, 1657, 1379, 1164, 1064, 852 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{11}H_{18}NaO_5$ $[M+Na]^+$ 253.1052, found 253.1054.

Compound 15a/b: To a stirred solution of alcohol **14** (0.35 g, 1.52 mmol) in ethyl acetate (10 mL) was added IBX (0.85 g, 3.04 mmol). The resulting suspension was refluxed for 4 h. The pale yellow precipitate was filtered through a pad of silica gel and concentrated under reduced pressure. The residue was subjected to column chromatography to yield a 1:1 mixture of **15a** and **15b** (0.14 g, 40%) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.08 – 7.00 (m, 1+1 H), 6.62 (d, *J* = 15.9 Hz, 1H), 5.91 (d, *J* = 15.8 Hz, 1H), 4.58 (dd, *J* = 7.3, 5.9 Hz, 1H), 4.45 (dd, *J* = 7.7, 5.3 Hz, 1H), 4.24 – 4.16 (m, 1+1 H), 4.05 (dd, *J* = 8.1, 5.3 Hz, 1H), 4.02 (dd, *J* = 8.7, 4.9 Hz, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.55 (t, *J* = 7.5 Hz, 2H), 3.28 (d, *J* = 7.1 Hz, 2H), 1.49 (s, 3H), 1.45 (s, 3H), 1.40 (s, 3H), 1.38 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 207.2, 197.8, 170.2, 166.3, 140.2, 139.8, 127.8, 124.9, 111.3, 111.2, 80.1, 79.6, 66.6 (x2), 52.4, 51.8, 41.6, 37.8, 26.2, 26.1, 25.3, 24.9 ppm; IR (thin film): *v* = 2990, 2951, 1727, 1630, 1380, 1270, 1213, 1066, 827 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{11}H_{16}NaO_5$ $[M+Na]^+$ 251.0895, found 251.0893.

Compound (-)-17: In a sealed tube, a mixture of **15a** and **15b** (0.26 g, 1.14 mmol) and diene **16** (1.0 mL, 5.70 mmol) in toluene (1.1 mL) was stirred at 120℃ for 40 h. Then the solvent was removed under reduced pressure and the residue was subjected to column chromatography to yield **(-)-17** (0.27 g, 65%) as a pale yellow oil, together with two other minor isomers (0.058g, 14%, ca. 1:1) as a inseparable mixture. **(-)-17**: $[\alpha]_D^{26}$ = −105 (*c* = 1.17, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 5.83 – 5.77 (m, 1H), 5.73 (dd, *J* = 9.8, 2.0 Hz, 1H), 4.75 – 4.71 (m, 1H), 4.44 – 4.39 (m, 1H), 4.16 (t, *J* = 8.2 Hz, 1H), 4.01 (dd, *J* = 8.5, 6.1 Hz, 1H), 3.62 (s, 3H), 3.25 (dd, *J* = 11.3, 4.0 Hz, 1H), 2.61 – 2.53 (m, 1H), 2.49 (dd, *J* = 15.1, 3.2 Hz, 1H), 2.32 (dd, *J* = 18.7, 5.0 Hz, 1H), 2.26 (dd, *J* = 14.8, 8.0, 1H), 1.81 (br dd, *J* = 18.2, 10.8 Hz, 1H), 1.42 (s, 3H), 1.37 (s, 3H), 0.05 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 208.9, 173.0, 129.4, 127.6, 110.9, 80.1, 66.5, 64.6, 52.3, 51.5, 37.8, 30.5, 26.2, 25.6, 25.2, 0.6 (x3) ppm; IR (thin film): *v* = 3029, 2988, 2955, 2819, 1735, 1380, 1255, 1159, 1065, 843 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{18}H_{30}NaO_6Si$ $[M+Na]^+$ 393.1709, found 393.1708.

Modified procedure for the preparation of (-)-17 from 14: To a stirred solution of **14** (0.98 g, 4.26 mmol) in ethyl acetate (28 mL) was added IBX (2.39 g, 8.52 mmol), The resulting suspension was refluxed for 4 h. The pale yellow precipitate was filtered through a pad of silica gel and concentrated under reduced pressure to afford the crude product as a yellow oil, which was used in the next step without further purification. In a sealed tube, a mixture of the above crude product and the diene **16** (2.2 mL, 12.78 mmol) in toluene (4.2 mL) was stirred at 120℃ for about 40 h. Then the solvent was removed under reduced pressure, and the residue was subjected to column chromatography to yield **(-)-17** (0.79 g, 50% over 2 steps) as a pale yellow oil.

Compound 19: $NaBH_4$ (0.15 g, 4.05 mmol) was added to a solution of ketone **17** (0.30 g, 0.81 mmol) in methanol (8.1 mL), the mixture was stirred at 0℃ for 2 h. Then the solvent was removed under reduced pressure. Water (25 mL) was added, and the aqueous phase was extracted with dichloromethane (3 x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was subjected to column chromatography to yield diol **19** (0.21 g, 88%) as a colorless oil. $[\alpha]_D^{26}$ = −68 (*c* = 0.98, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 5.89 (ddd, *J* = 9.6, 5.1, 1.8 Hz, 1H), 5.84 – 5.78 (m, 1H), 4.62 – 4.56 (m, 1H), 4.29 – 4.22 (m, 1H), 4.18 (dd, *J* = 8.4, 6.1 Hz, 1H), 4.02 (dd, *J* = 8.4, 4.7 Hz, 1H), 3.94 (d, *J* = 9.7 Hz, 1H), 3.67 (s, 3H), 3.63 (td, *J* = 9.5, 3.1 Hz, 1H), 2.72 (dd, *J* = 15.3, 4.8 Hz, 1H), 2.68 (d, *J* = 4.6 Hz, 1H), 2.51 – 2.40 (m, 1H), 2.31 (dd, *J* = 13.8, 6.6 Hz, 1H), 2.26 (t, *J* = 6.5 Hz, 1H), 1.96 – 1.86 (m, 1H), 1.76 (dt, *J* = 11.9, 3.2 Hz, 1H), 1.38 (s, 3H), 1.34 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.0, 131.2, 127.5, 109.5, 76.2, 72.9, 68.4, 66.3, 51.8, 42.1, 37.1, 32.3, 27.1, 26.6, 25.4 ppm; IR (thin film): *v* = 3442, 2987, 2930, 1737, 1436, 1376, 1254, 1217, 1068, 1057 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{15}H_{24}NaO_6$ $[M+Na]^+$ 323.1471, found 323.1470.

Compound 20: Under an atmosphere of hydrogen alkene **17** (70 mg, 0.19 mmol) was dissolved in ethyl acetate (5 mL) and

10% Pd/C (30 mg) was added to the solution. After being stirred 1 h at room temperature the reaction mixture was filtered through celite and the filter cake was washed with ethyl acetate. The organic layer was concentrated in vacuo and the residue was purified by column chromatography to give **20** (65 mg, 92%) as a colorless oil. $[\alpha]_D^{26}$ = +48 (*c* = 0.91, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.55 – 4.51 (m, 1H), 4.41 (dd, *J* = 7.6, 5.9 Hz, 1H), 4.16 (dd, *J* = 8.5, 7.7 Hz, 1H), 4.02 (dd, *J* = 8.6, 5.9 Hz, 1H), 3.63 (s, 3H), 3.00 (dd, *J* = 11.1, 2.4 Hz, 1H), 2.58 – 2.48 (m, 1H), 2.29 (dd, *J* = 14.7, 4.0 Hz, 1H), 2.04 (dd, *J* = 14.7, 8.3 Hz, 1H), 1.85 – 1.60 (m, 4H), 1.52 – 1.46 (m, 1H), 1.44 (s, 3H), 1.39 (s, 3H), 1.07 (ddd, *J* = 21.2, 12.8, 3.7 Hz, 1H), 0.04 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 209.4, 173.2, 110.9, 79.7, 67.0, 66.4, 55.2, 51.5, 39.0, 33.6, 30.7, 28.4, 26.2, 25.3, 19.0, 0.25 (x3) ppm; IR (thin film): *v* = 2940, 1738, 1380, 1253, 1155, 1072, 1038 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{18}H_{32}NaO_6Si$ $[M+Na]^+$ 395.1866, found 395.1864.

Compound 21: Tetrabutylammonium fluoride (TBAF) (81 uL of 1M in THF, 0.081 mmol) and acetic acid (7.3 uL, 0.12 mmol) was added to a solution of **20** (25 mg, 0.067 mmol) in THF (5.0 mL). After being stirred for 1 h, water (10 mL) was added, and the aqueous phase was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. After purification by column chromatography, the resulting alcohol was dissolved in dichloromethane (2.0 mL), and (*S*)-α-methoxyphenylacetic acid (17 mg, 0.10 mmol), DMAP (4.1 mg, 0.034 mmol) and EDCI (20 mg, 0.11 mmol) were added. The mixture was stirred for 12 h, and diluted with water (5 mL). The aqueous phase was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The crude product was subjected to column chromatography to yield **21** (22 mg, 72% over two steps) as a pale yellow oil. $[\alpha]_D^{26}$ = +50 (*c* = 0.34, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42 – 7.38 (m, 2H), 7.37 – 7.31 (m, 3H), 5.62 – 5.58 (m, 1H), 4.71 (s, 1H), 4.55 (dd, *J* = 7.7, 5.5 Hz, 1H), 4.11 (dd, *J* = 7.4, 2.6 Hz, 1H), 4.03 (dd, *J* = 8.7, 5.5 Hz, 1H), 3.65 (s, 3H), 3.37 (s, 3H), 3.19 (dd, *J* = 11.7, 2.4 Hz, 1H), 2.52 – 2.40 (m, 1H), 2.28 (dd, *J* = 15.0, 3.6 Hz, 1H), 2.04 (dd, *J* = 15.0, 8.5 Hz, 1H), 1.86 – 1.79 (m, 1H), 1.68 – 1.62 (m, 1H), 1.45 – 1.41 (m, 1H), 1.43 (s, 3H), 1.40 – 1.35 (m, 1H), 1.37 (s, 3H), 1.26 – 1.20 (m, 1H), 1.08 ppm (qd, *J* = 12.6, 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 209.4, 172.8, 170.4, 136.4, 128.8, 128.7 (x2), 127.2 (x2), 111.0, 82.1, 79.4, 69.7, 66.1, 57.5, 52.7, 51.6, 38.7, 30.4, 30.0, 28.9, 26.3, 25.0, 19.4 ppm; IR (thin film): *v* = 2937, 1739, 1452, 1377, 1257, 1154, 1118, 1069 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{24}H_{32}NaO_8$ $[M+Na]^+$ 471.1995, found 471.1992.

Compound 22: Tetrabutylammonium fluoride (TBAF) (86 uL of 1M in THF, 0.086 mmol) and acetic acid (7.7 uL, 0.129 mmol) was added to a stirred solution of **20** (27 mg, 0.072 mmol) in THF (5.0 mL). After being stirred for 1 h, water (10 mL) was added, and the aqueous phase was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. After purification by column chromatography, the resulting alcohol was dissolved in dichloromethane (2.0 mL), and (*R*)-(-)-α-methoxyphenylacetic acid (18 mg, 0.11 mmol), DMAP (4.4 mg, 0.036 mmol) and EDCI (22 mg, 0.12 mmol) were added. The solution was stirred for 12 h, and diluted with water (5 mL). The aqueous phase was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The crude product was subjected to column chromatography to yield **22** (23 mg, 70% over two steps) as a pale yellow oil. $[\alpha]_D^{26}$ = −19 (*c* = 0.38, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.39 – 7.32 (m, 5H), 5.54 (s, 1H), 4.69 (s, 1H), 3.94 (dd, *J* = 7.6, 5.3 Hz, 1H), 3.85 (d, *J* = 1.2 Hz, 1H), 3.84 (d, *J* = 3.6 Hz, 1H), 3.64 (s, 3H), 3.40 (s, 3H), 3.07 (dd, *J* = 11.5, 2.6 Hz, 1H), 2.37 (ddt, J = 20.0, 11.7, 3.7 Hz, 1H), 2.28 (dd, *J* = 15.1, 3.6 Hz, 1H), 2.07 – 2.02 (m, 1H), 2.01 (dd, *J* = 15.1, 8.4 Hz, 1H), 1.90 – 1.83 (m 1H), 1.60 – 1.50 (m, 3H) 1.36 (s, 3H), 1.30 (s, 3H), 1.15 – 1.07 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 208.2, 172.8, 170.5, 136.2, 128.8, 128.7 (x2), 127.3 (x2), 110.8, 82.5, 78.8, 70.5, 65.9, 57.5, 52.3, 51.6, 38.7, 30.4, 30.1, 28.9, 26.2, 25.0, 19.5 ppm; IR (thin film): *v* = 2988, 2936, 1736, 1379, 1257, 1213, 1156, 1112, 1072 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{24}H_{32}NaO_8$ $[M+Na]^+$ 471.1995, found 471.1994.

Compound 23: To a stirred solution of **19** (0.34 g, 1.13 mmol) and acetic anhydride (1.1 mL, 11.33 mmol) in anhydrous dichloromethane (22 mL) was added pyridine (1.4 mL, 17.0 mmol) followed by DMAP (21 mg, 0.17 mmol). When TLC control showed complete conversion of the substrate, the reaction mixture was quenched with saturated $NaHCO_3$ solution and was extracted with dichloromethane (3 x 45 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to yield diacetate **23** (0.42 g, 96%) as a colorless oil. $[\alpha]_D^{26}$ = −132 (*c* = 0.75, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.88 (ddd, *J* = 9.9, 4.1, 2.3 Hz, 1H), 5.83 – 5.76 (m, 1H), 5.67 – 5.62 (m, 1H), 5.17 (dd, *J* = 8.3, 3.8 Hz, 1H), 4.16 (dt, *J* = 8.2, 5.8 Hz, 1H), 3.95 (dd, *J* = 8.4, 5.9 Hz, 1H), 3.76 (dd, *J* = 8.4, 5.7 Hz, 1H), 3.66 (s, 3H), 2.63 (dd, *J* = 15.0, 3.5 Hz, 1H), 2.48 – 2.39 (m, 1H), 2.38 (dt, *J* = 18.0, 4.9 Hz, 1H), 2.16 (dd, *J* = 14.8, 9.6 Hz, 1H), 2.12 (dt, *J* = 10.9, 3.5 Hz, 1H), 2.04 (s, 3H), 2.03 (s, 3H), 1.87 ppm (br dd, *J* = 18.0, 9.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 172.9, 170.5 (x2), 131.4, 124.6, 109.7, 74.5, 71.9, 67.2, 66.2, 51.8, 41.6, 37.6, 32.1, 27.6, 26.9, 25.5, 21.6, 21.2 ppm; IR (thin film): *v* = 2987, 2952, 1731, 1436, 1374, 1250, 1160, 1066, 1019 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{19}H_{28}NaO_8$ $[M+Na]^+$ 407.1682, found 407.1684.

Compound 24: To a stirred solution of **23** (0.32 g, 0.83 mmol) in ethyl acetate (20 mL) was added H_5IO_6 (0.48 g, 2.08 mmol), and the resulting suspension was reacted for 2 h at room temperature. The reaction mixture was filtered through celite, and the filter cake was washed with ethyl acetate. The filtrate was washed with H_2O (25 mL) and the organic phase was separated. The aqueous layer was extracted with ethyl acetate (3 x 35 mL), and the combined organic extracts were washed with H_2O and brine, dried over anhydrous Na_2SO_4. Removal of all the solvent in vacuo gave the aldehyde **24** (0.26 g, 99%) as a yellow oil, which could be used without further purification in the next step. $[\alpha]_D^{26}$ = −114 (*c* = 1.34, $CHCl_3$); ^{1}H NMR (400

MHz, $CDCl_3$) δ = 9.60 (s, 1H), 5.91 (ddd, *J* = 9.9, 4.3, 2.9 Hz, 1H), 5.81 – 5.75 (m, 1H), 5.42 – 5.38 (m, 1H), 5.26 (d, *J* = 3.0 Hz, 1H), 3.67 (s, 3H), 2.53 – 2.44 (m, 3H), 2.37 – 2.23 (m, 2H), 2.16 (s, 3H), 2.07 (s, 3H), 1.97 – 1.88 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 197.9, 172.4, 170.2, 131.5, 124.2, 78.1, 67.2, 51.75 , 41.9, 37.4, 31.0, 28.4, 21.3, 20.7 ppm; IR (thin film): *v* = 3451, 3037, 2927, 2851, 1734, 1434, 1375, 1236, 1162, 1019 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{15}H_{20}NaO_7$ $[M+Na]^+$ 335.1107, found 335.1104.

Compound 25: To a THF solution (5.0 mL) of (benzyl)triphenylphosphonium bromide (0.27 g, 0.52 mmol) was added *n*-BuLi (0.22 mL of 2.4 M in hexene, 0.52 mmol) at 0 ℃ under argon. After stirred for 40 min, a solution of aldehyde **24** (65 mg, 0.21 mmol) in anhydrous THF (2.0 mL) was added. The suspension was warmed to room temperature and stirred for 16 h. Then the reaction was quenched with aqueous NaCl and extracted with ethyl acetate (3 x 30 mL). The organic layer was washed with H_2O and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography to give colorless oil **25** as a mixture of two stereoisomers (60.5 mg, 75%, *E*/*Z* = ca. 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38 –7.23 (m, 10H, 5*Z*+5*E* isomer), 6.65 (d, *J* = 15.9 Hz, 1H, *E* isomer), 6.59 (d, *J* = 11.9 Hz, 1H, *Z* isomer), 6.22 (dd, *J* = 15.9, 7.9 Hz, 1H, *E* isomer), 5.97 (dd, *J* = 9.0, 5.1 Hz, 1H, *Z* isomer), 5.91 (ddd, *J* = 9.8, 4.6, 2.5 Hz, 1H, *E* isomer), 5.84 (ddd, *J* = 9.8, 4.5, 2.3 Hz, 1H, *Z* isomer), 5.82 – 5.74 (m, 2H, *Z*+*E* isomer), 5.66 (dd, *J* = 11.9, 9.1 Hz, 1H, *Z* isomer), 5.63 (t, *J* = 6.9 Hz,, 1H, *E* isomer), 5.54 – 5.47 (m, 2H, *Z*+*E* isomer), 3.61 (s, 3H, *Z* isomer), 3.59 (s, 3H, *E* isomer), 2.65 (dd, *J* = 15.6, 4.1 Hz, 1H, *E* isomer), 2.56 – 2.44 (m, 3H, 2*Z*+*E* isomer), 2.32 – 2.22 (m 2H, *E*+*Z* isomer), 2.22 – 2.07 (m, 3H, 2*Z*+*E* isomer), 2.05 – 2.04 (m, *E* isomer), 2.03 (s, 3H, *E* isomer), 2.02 (s, 3H, *Z* isomer), 2.00 (s, 3H, *E* isomer), 1.99 (s, 3H, *Z* isomer), 1.96 – 1.88 (m, 1H, *E* isomer), 1.86 – 1.77 ppm (m, 1H, *Z* isomer); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 172.81, 172.80, 170.47, 170.44, 170.07, 169.91, 136.18, 136.10, 132.92, 131.55, 131.48, 128.68, 128.52, 128.24, 127.63, 126.71, 126.13, 124.50, 124.46, 73.83, 69.83, 67.34, 67.00, 51.61, 51.54, 44.90, 44.75, 31.58, 28.62, 28.22, 21.39, 31.37, 21.30, 21.25 ppm; IR (thin film): *v* = 3441, 2929, 1736, 1624, 1378, 1246, 1021 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{22}H_{26}NaO_6$ $[M+Na]^+$ 409.1627, found 409.1626.

Compound 26: Potassium carbonate (21.5 mg, 0.16 mmol) was added to a solution of **25** (30.0 mg, 0.08 mmol) in 3.3 mL mixture of methanol and H_2O (v/v = 10:1). The reaction was stirred for about 10 h at room temperature. Water (8 mL) was added and the aqueous phase was extracted with ethyl acetate (3 x 20 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was chromatographed on silica gel to give recovered **25** in a small amount (4.3 mg, 20%) and a mixture of *E*/*Z* stereoisomers of unsaturated diol **26** (11.9 mg, 71%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42 – 7.20 (m, 10H, 5*E* + 5*Z* isomer), 6.72 (d, *J* = 15.9 Hz, 1H, *E* isomer), 6.61 (d, *J* = 11.8 Hz, 1H, *Z* isomer), 6.38 (dd, *J* = 15.9, 5.1 Hz, 1H, *E* isomer), 6.00 (dd, *J* = 11.7, 9.2 Hz, 1H, *Z* isomer), 5.89 – 5.75 (m, 4H, 2*E* + 2*Z* isomer), 4.84 (br d, *J* = 5.5 Hz, 1H, *Z* isomer), 4.60 (br s, 2H, *E* + *Z* isomer), 4.48 (br s, 1H, *E* isomer), 4.07 (br s, 1H, *E* isomer), 3.87 (br s, 1H, *Z* isomer), 3.70 (s, 3H, *E* isomer), 3.64 (s, 3H, *Z* isomer), 3.22 – 3.05 (m, 1H, *Z* isomer), 3.04 – 2.89 (m, 1H, *E* isomer), 2.76 (dd, *J* = 15.3, 5.0 Hz, 1H, *E* isomer), 2.65 (dd, *J* = 15.4, 5.0 Hz, 1H, *Z* isomer), 2.60 – 2.45 (m, 2H, *E* + *Z* isomer), 2.41 (dd, *J* = 15.3, 7.7 Hz, 1H, *E* isomer), 2.35 – 2.29 (m, 1H, *E* isomer), 2.28 (dd, *J* = 15.3, 8.2 Hz, 1H, *Z* isomer), 2.18 (br d, *J* = 18.3 Hz, 1H, *Z* isomer), 1.89 (dd, *J* = 18.7, 10.1 Hz, 1H, *E* isomer), 1.84 (dd, *J* = 17.8, 10.0 Hz, 1H, *Z* isomer), 1.70 (dt, *J* = 10.9, 3.9 Hz, 1H, *Z* isomer), 1.65 ppm (dt, *J* = 11.5, 3.5 Hz, 1H, *E* isomer); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 173.95, 173.83, 136.92, 136.63, 133.00, 131.22, 130.97, 130.71, 130.54,, 130.22 (s), 128.77, 128.68, 128.43, 127.80, 127.95, 127.61, 127.35, 126.57, 72.04, 67.85, 66.56, 66.45, 51.87, 51.77, 47.00, 46.58, 37.28, 37.12, 32.02, 31.57, 27.67, 27.32 ppm; IR (thin film): *v* = 3357, 3025, 2924, 2854, 1735, 1438, 1258, 1159, 1055 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{18}H_{22}NaO_4$ $[M+Na]^+$ 325.1416, found 325.1410.

(-)-Infectocaryone ((-)-1): Dess-Martin periodinane (152 mg, 0.36 mmol) was added to a solution of diol **26** (36 mg, 0.12 mmol) in dichloromethane (10 mL), and the resulting white suspension was stirred overnight at room temperature. Saturated aqueous $NaHCO_3$ solution were added until the solids were dissolved, the aqueous phase was separated and extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was subjected to flash column chromatography to yield a mixture of **1** and its *Z*-isomer as a bright yellow oil. To a solution of the above mixture in THF (8 mL), $Pd(PPh_3)_4$ (13.8 mg, 0.012 mmol) was added, and the resulting suspension was stirred at room temperature for about 12 h. The mixture was filtered through celite, and the filter cake was washed with ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography afforded the (-)-**1** (32.7 mg, 92% over two steps) as a yellow gum. $[\alpha]_D^{26}$ = −123 (*c* = 0.38, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 16.15 (d, *J* = 1.1 Hz, 1H), 7.69 (d, *J* = 15.5 Hz, 1H), 7.60 – 7.56 (m, 2H), 7.42 – 7.36 (m, 3H), 7.01 (dd, *J* = 15.5, 1.0 Hz, 1H), 6.70 (dddd, *J* = 9.9, 6.3, 2.1,1.2 Hz, 1H), 6.18 (dd, *J* = 10.0, 2.6 Hz, 1H), 3.65 (s, 3H), 3.63 – 3.57 (m, 1H), 2.69 – 2.63 (m, 1H), 2.62 (dd, *J* = 15.0, 9.5 Hz, 1H), 2.43 (dd, *J* = 18.0, 5.9 Hz, 1H), 2.40 ppm (dd, *J* = 15.0, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 188.50, 172.64, 172.60, 144.16, 140.48, 135.55, 130.03, 129.42, 129.07, 128.19, 118.09, 108.95, 51.95, 40.00, 29.73, 29.67 ppm; IR (thin film): *v* = 3446, 3029, 2927, 2854, 1734, 1630, 1560, 1409, 1280, 1202 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{18}H_{18}NaO_4$ $[M+Na]^+$ 321.1103, found 321.1098.

Compound 28: A stirred mixture of L-xylose (1.0 g, 0.67 mmol), Ph_3PCHCO_2Me (2.67 g, 0.80 mmol) and catalytic amount of benzoic acid in THF (20 mL) was heated reflux overnight. The solvent was removed, and 15 mL water was added to the syrup which precipitated triphenylphosphine oxide. The precipitate was filtered and filtrate was washed with $CHCl_3$ (2 x 5 mL). The aqueous layer was evaporated to give a syrup,

which was dissolved in dry acetone (20 mL) containing 0.2% H_2SO_4. Then anhydrous Cu_2SO_4 (1.0 g) was added and stirred at ambient temperature for 20 h. Cu_2SO_4 was filtered off and washed with dry acetone. The filtrate rendered neutral by shaking with $Ca(OH)_2$ for 1 h. The inorganic salts were removed by filtration and washed with acetone. The combined filtrate was then evaporated to dryness under reduced pressure, and residue was purified by column chromatography to give **28** (1.73 g, 91%) as a colorless oil. $[\alpha]_D^{26}$ = +23 (*c* = 0.76, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.87 (dd, *J* = 15.6, 5.8 Hz, 1H), 6.13 (dd, *J* = 15.6, 1.2 Hz, 1H), 4.49 (ddd, *J* = 8.1, 5.8, 1.4 Hz, 1H), 4.19 (td, *J* = 6.8, 4.5 Hz, 1H), 4.02 (dd, *J* = 8.1, 7.0 Hz, 1H), 3.85 – 3.79 (m, 2H), 3.73 (s, 3H), 1.44 (s, 3H), 1.41 (s, 6H), 1.36 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.4, 144.3, 122.8, 110.6, 110.0, 80.5, 76.5, 74.6, 65.6, 51.9, 26.9, 26.2, 25.5 ppm; IR (thin film): *v* = 2989, 2939, 2892, 1729, 1663, 1437, 1377, 1217, 1164, 1070 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{14}H_{22}NaO_6$ $[M+Na]^+$ 309.1314, found 309.1312.

Compound 29: To a solution of **28** (1.50 g, 5.24 mmol) in dry MeOH (53 mL) was added magnesium turnings (0.38 g, 15.72 mmol) and the reaction mixture was stirred at 0 ºC for 1.5 h. Saturated NH_4Cl solution (150 mL) was then added and the mixture was extracted with ethyl acetate (2 x 200 mL). The organic layer was dried over Na_2SO_4, the solvent was then evaporated and the residue was chromatographed on silica gel column to give alcohol **29** (1.11 g, 92%) as a yellow oil. $[\alpha]_D^{26}$ = +7 (*c* = 1.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.91 (dt, *J* = 15.6, 7.0 Hz, 1H,), 5.60 – 5.50 (m, 1H), 4.07 – 4.00 (m, 2H), 4.00 – 3.95 (m, 1H), 3.76 (dd, *J* = 8.0, 5.1 Hz, 1H), 3.68 (s, 3H), 3.16 – 3.03 (m, 2H), 2.47 (d, *J* = 3.3 Hz, 1H), 1.43 (d, *J* = 4.6 Hz, 3H), 1.35 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.8, 132.1, 125.9, 109.9, 78.7, 73.5, 65.9, 51.9, 37.5, 26.8, 25.3 ppm; IR (thin film): *v* = 3470, 2988, 2952, 2891, 1739, 1436, 1378, 1212, 1066, 852 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{11}H_{18}NaO_5$ $[M+Na]^+$ 253.1052, found 253.1050.

Compound (+)-17: To a stirred solution of **29** (0.77 g, 3.34 mmol) in ethyl acetate (22 mL) was added IBX (1.87 g, 6.68 mmol), The resulting suspension was refluxed for 4 h. The pale yellow precipitate was filtered through a pad of silica gel and concentrated under reduced pressure to afford the crude product as a yellow oil, which was used in the next step without further purification. In a sealed tube, a mixture of the above crude product and the diene **16** (1.7 mL, 10.02 mmol) in toluene (3.3 mL) was stirred at 120℃ for 40 h. Then the solvent was removed under reduced pressure, and the residue was subjected to column chromatography to yield **(+)-17** (0.64 g, 52% over 2 steps) as a pale yellow oil. $[\alpha]_D^{26}$ = +109 (*c* = 1.04, $CHCl_3$); the other spectra (^{1}H, ^{13}C NMR, IR and MS) of **(+)-17** are same as those of **(-)-17**.

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