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Stereodivergent Total Synthesis of (+)-Aspergillide B and (+)-7-*epi*-Aspergillide A

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The stereoselective total syntheses of (+)-aspergillide B and (+)-7-epi-aspergillide A were achieved. The key reactions include Noyori's asymmetric transfer hydrogenation, an Achmatowicz rearrangement, a Ferrier-type alkynylation, a hydrosilylation–protodesilylation, a CBS (Corey–Bakshi–Shibata) oxazaborolidine reduction, a Yamaguchi macrolactonization, and a Mitsunobu macrolactonization.

Introduction

Nature produces a vast collection of natural products as new chemical entities that exhibit specific functions in biological systems. Most current drugs are derived from these natural products.[1] Marine microorganisms are a source for numerous natural products that exhibit interesting biological properties with wide therapeutic applications.[2] The work initiated by Kusumi and co-workers on the marine derived fungus *Aspergillus ostianus* strain 01F313 has led to the isolation of three new bicyclic 14-membered macrolides with 2,6-*cis*- and 2,6-*trans*-fused dihydro- or tetrahydropyan rings, namely aspergillides A, B, and C (**1**–**3**, see Figure 1).[3] These molecules showed modest cytotoxicity against mouse lymphatic leukemia cells. Further investigations showed these compounds to exhibit cytotoxicity toward a number of cancer cell lines including, HL-60 (human promyelocytic leukemia), MDA-MB-231 (human breast carcinoma), and HT1080 (human fibrosarcoma) cell lines.[4f] The striking structural complexity together with the biological activity of these macrolides has attracted several synthetic groups to target their total synthesis,[4–7] which would allow the confirmation/revision of the absolute stereostructure of the molecules and also make them available to further investigations of their biological properties. Although a specific stereoisomer with one or more stereogenic centers can be responsible for the biological activity, there are many times that the other isomer could cause side effects or may be more active than the parent isomer. This feature has increased the necessity from the synthetic community for stereoselective synthesis. With this feature in mind, we became interested in the syntheses of the enantiomers (both natural and unnatural isomers) of aspergillides to examine their activity.

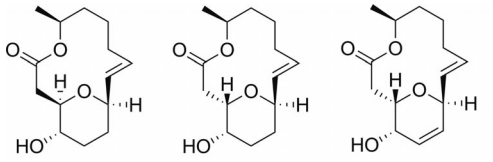

Figure 1. Structures of aspergillides A–C.

In continuation of our efforts towards the total syntheses of lactone-containing natural products,[8] we recently published the total synthesis of both enantiomers of aspergillide C and their C-4 epimers through a concise approach.[7a] Herein, we describe the total syntheses of (+)-aspergillide B and (+)-7-*epi*-aspergillide A.

Results and Discussion

We envisaged that both of the target macrolides (–)-aspergillide A (**1**) and (+)-aspergillide B (*ent*-**2**) could be prepared from the corresponding *seco* acids **4** and **5** by lactonization, removal of the *tert*-butyldimethylsilyl (TBS) group, and epimerization at C-7 (for **1**; see Scheme 1).

Both *seco* acids **4** and **5** could be synthesized from a common intermediate **6** through sequential reactions, that is, a reduction of the alkyne to a *trans* alkene, a chemoselective conjugate reduction of the α,β-unsaturated ketone to a ketone, and a stereoselective keto reduction that is followed by TBS protection and finally hydrolysis of the diester. Compound **6** can be obtained from acetal **7** by a Ferrier-type alkynylation with derivatized trimethylsilyl (TMS)-acetylene **8**. Acetal **7** could be obtained from chiral furfuryl

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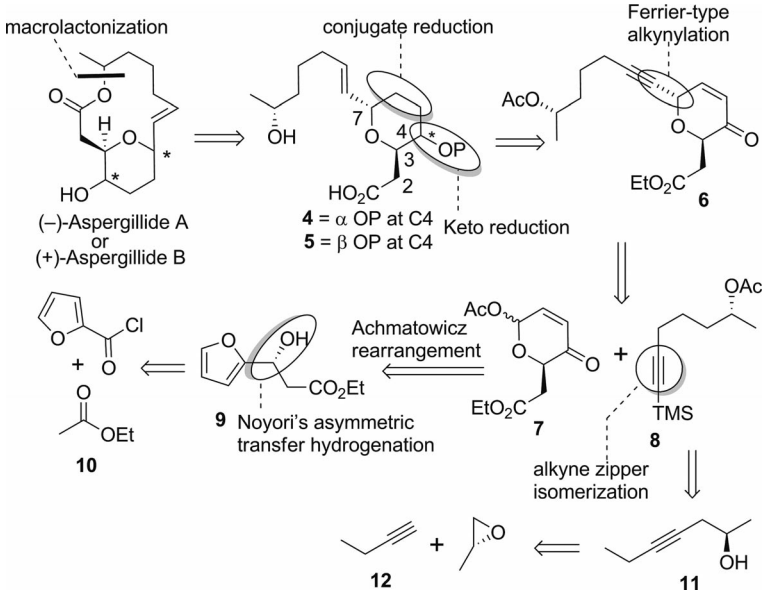


Scheme 1. Retrosynthetic analysis of aspergillides A and B.

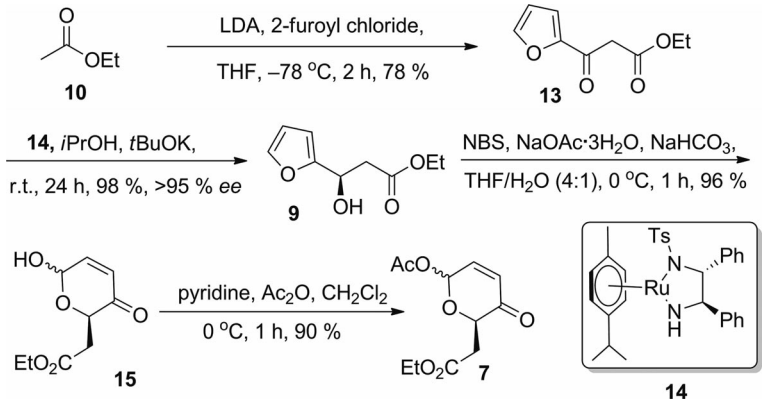
alcohol **9**, and the alkyne fragment **8** can be accessed from homopropargyl alcohol **11** through an alkyne zipper isomerization reaction, which in turn can be obtained from commercially available (*R*)-propylene oxide and 1-butyne (see Scheme 1) through an epoxide ring-opening reaction.

Our synthesis commenced by treating the lithium enolate of ethyl acetate (**10**) with 2-furoyl chloride to afford β-keto ester **13**. The ketone functionality was reduced chemo- and enantioselectively with Noyori's catalyst Ru[(1*R*,2*R*)-*p*-TsNCH(Ph)CH(Ph)NH](η^6-*p*-cymene) (**14**) in *i*PrOH.[9] Initially, our efforts towards the reduction of **13** to the corresponding β-hydroxy ester **9** were not fruitful under conventional Noyori's asymmetric transfer hydrogenation conditions. However, when a catalytic amount of *t*BuOK was used along with the catalyst, the reaction worked remarkably well affording **9** in 98% yield and >95% *ee*[10] (see Table 1, Entry 7). When subjected to an Achmatowicz oxidative rearrangement[11] under standard conditions, furyl alcohol **9** provided pyranone lactol **15** as an anomeric mixture (72:28), which was further activated through an acylation to give a mixture of the corresponding acetates **7** (see Scheme 2).

Table 1. Optimization of asymmetric transfer hydrogenation of β-keto ester **13**.

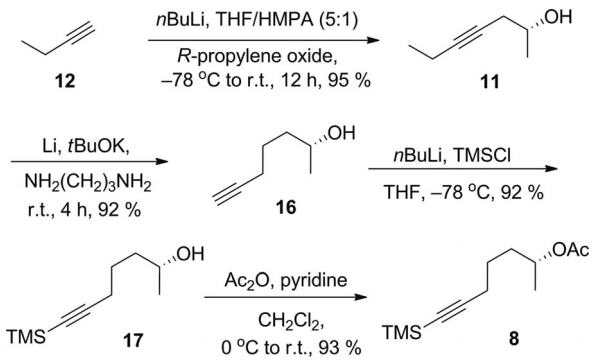
Entry	Hydrogen source	Solvent	Additive	*T* [°C]	Time [h]	Yield [%]	*ee* [%]
1	HCO_2H/Et_3N	–	–	25	48	00	–
2	HCO_2H/Et_3N	EtOAc	–	25 to reflux	48	00	–
3	HCO_2H/Et_3N	IPA[a]	–	25 to reflux	48	00	–
4	IPA	IPA	–	25 to reflux	48	00	–
5	IPA	IPA	KOH	25	24	00	–
6	IPA	IPA	KOH	reflux	24	96[b]	88
7	IPA	IPA	*t*BuOK	25	24	98	>95

[a] IPA = isopropyl alcohol. [b] Reduction with 100% transesterified product was formed.



Scheme 2. Synthesis of acetate **7** (LDA = lithium diisopropylamide).

The required alkyne fragment **8** was synthesized in four steps with an overall yield of 74.8%. Thus, (*R*)-propylene oxide was exposed to the lithium acetylide of 1-butyne (**12**) in the presence of HMPA (hexamethylphosphoramide) to give homopropargyl alcohol **11**. The internal alkyne of **11** was isomerized to terminal alkyne **16** through a zipper isomerization[12] by using Li-*t*BuOK in the presence of 1,3-diaminopropane. The resulting alkynol **16** was appropriately masked by treating it with TMSCl and Ac_2O to afford **8** (see Scheme 3). This sequence required a single column purification in the final step.



Scheme 3. Synthesis of alkyne **8**.

Acetate **7** was then subjected to a Ferrier-type alkynylation[13] by treatment with silylated alkyne **8** in the presence of $SnCl_4$ to give alkyne **6** as the only product in 85% yield.[14] The diastereoselectivity in this reaction can be explained by the formation during the course of reaction of a cyclic oxocarbenium ion (see Scheme 4). Because the cyclic oxocarbenium ion is almost planar in geometry with five sp^2-hybridized centers in the ring, it facilitates the incoming nucleophile to preferentially attack from the opposite face (i.e., α face) to that of ester substituent, which is present on the β face. The NOESY experiment for **6** did not reveal any spatial relationship between 3- and 7-H (δ = 4.85 and 5.08), which infers the 3,7-*anti* geometry of the product.

With the requisite stereochemical configuration set at C-3, C-7, and C-13, we further proceeded with the stereospecific reduction of the alkyne moiety in **6** to an (*E*) alkene. Initial attempts with Li in liquid NH_3 resulted in decomposition of starting material. However, the problem was later addressed by following Trost's protocol,[15] in which alkyne **6** was *trans* hydrosilylated by treatment with triethoxysilane in the presence of $[Cp^*Ru(MeCN)_3]PF_6$ followed by protodesilylation with HF/pyridine to yield *trans* olefin **18**, exclusively.[16]

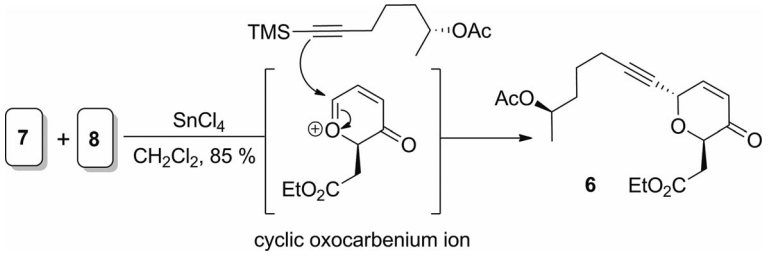
With the two olefins in the system, our attention then focused on the chemoselective reduction of the enone. Though the reaction was difficult in the beginning, we succeeded in the chemoselective reduction reaction by modifying Saegusa's method to yield the desired keto compound **19** (see Table 2). Thus, compound **18** was treated with a CuH complex, which was generated by treating $LiAlH_4$ with CuI in tetrahydrofuran THF/HMPA system, to afford compound **19** in 92% yield (see Scheme 5 and Table 2, Entry 6).[17]

Table 2. Conjugate reduction of **18**.

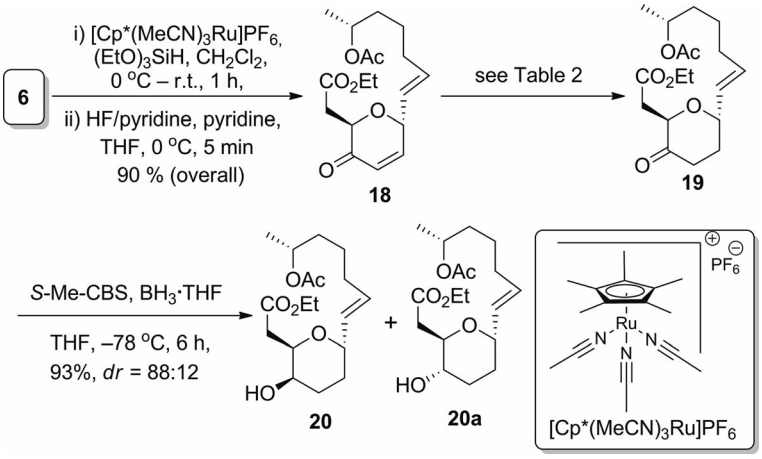
Entry	Reducing agent	Solvent	*T* [°C]	Time	Result
1	Mg	MeOH	0	10 min	decomp.
2	$NiCl_2{\cdot}6H_2O$, $NaBH_4$	MeOH	0, –40/–78	10 min	decomp.
3	PMHS, $B(C_6F_5)_3$	CH_2Cl_2	25	4 days	**18** recovered
4	Raney nickel	THF	25	24 h	30 % of **19**
5	$LiAlH_4$, CuI	THF	–78	10 min	complex mixture
6	$LiAlH_4$, CuI	THF/HMPA	–78	90 min	92 % of **19**

The next stage was to proceed further with a stereoselective reduction of the ketone functionality in **19**. This reaction was achieved by using (*S*)-Me-CBS[18] [(*S*)-2-methyl-CBS-oxazaborolidine] as the catalyst and BH_3–THF as the hydride ion source to provide the easily separable chiral allyl alcohols **20** and **20a** in 93% yield with a diastereomeric ratio (*dr*) of 88:12 (see Scheme 5).

Although the minor isomer **20a** could be further utilized for the synthesis of another analogue, the major alcohol **20** was utilized in the synthesis of (+)-aspergillide B. Thus, compound **20** was protected by treatment with TBSOTf (Tf = trifluoromethylsulfonyl) as the corresponding silyl ether **21**, and the resulting diester **21** was hydrolyzed with NaOH in $MeOH/H_2O$ to give *seco* acid **5**. Under Yamaguchi conditions,[19] *seco* acid **5** underwent lactonization to afford **22**, which contained the macrocyclic core of aspergillide B.

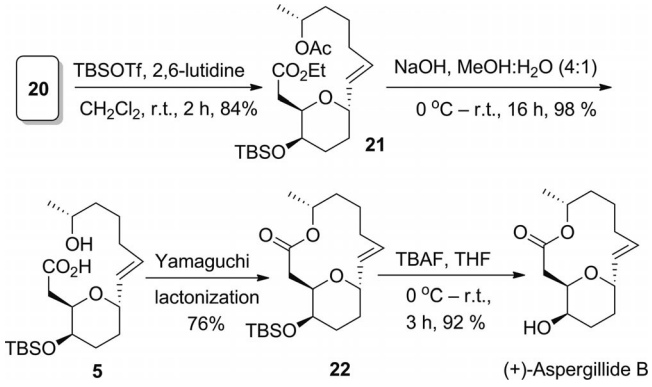


Scheme 4. Alkynylation of adduct **7**.



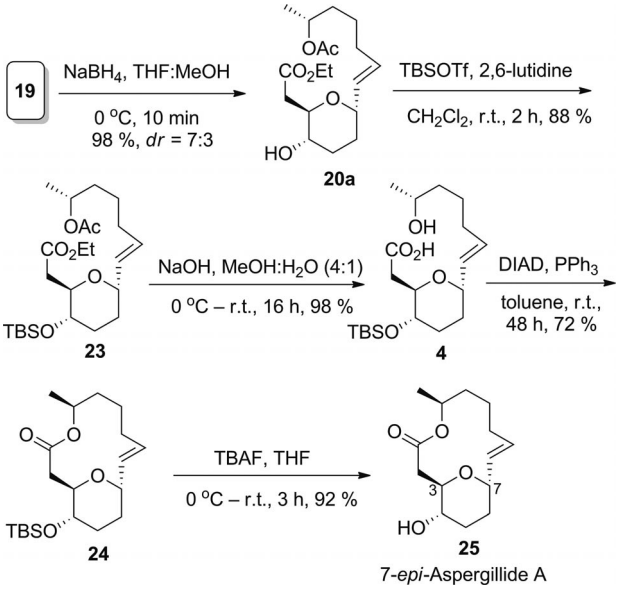
Scheme 5. Synthesis of alcohol **20**.

Compound **22** was further subjected to desilylation by treatment with TBAF (tetra-*n*-butylammonium fluoride) to give the target macrolide (+)-aspergillide B (see Scheme 6). The spectroscopic data of this synthetic compound was compared with previously known data and was identical with that of the enantiomeric natural product.

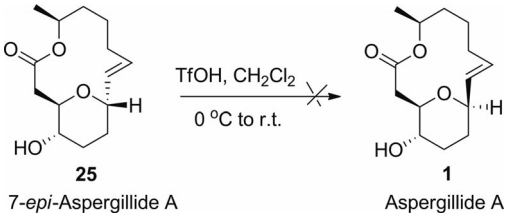


Scheme 6. Synthesis of (+)-aspergillide B.

By maneuvering the reaction conditions, we could also accomplish the total synthesis of aspergillide A. Compound **20a** (see Scheme 5) was also synthesized from **19** through a reduction with $NaBH_4$ to give a mixture of alcohols **20a** and **20** (7:3) that were easily separable by column chromatography (see Scheme 7). The major diastereomer **20a** was protected by treatment with TBSOTf to give the corresponding TBS ether **23**, and the diester was hydrolyzed by using NaOH in MeOH/H_2O to yield *seco* acid **4**. The resulting *seco* acid **4** was subjected to a Mitsunobu lactonization[20] to yield the macrocyclic core in **24**, which upon treatment with TBAF yielded 7-*epi*-aspergillide A (**25**, see Scheme 7). Our attempts to epimerize the vinyl-substituted anomeric carbon in **25** with TfOH[21] did not succeed and resulted in decomposition of the starting material (Scheme 8). Thus, we ended with the 7-*epi*-aspergillide A.



Scheme 7. Synthesis of 7-*epi*-aspergillide A.



Scheme 8. Attempted epimerization of 7-epi-aspergillide A to aspergillide A (**1**).

Conclusions

Herein, a facile strategy for the total syntheses of 7-*epi*-aspergillide A and the unnatural enantiomer of aspergillide B has been developed with an overall yield of 18.3 and 21.9%, respectively. Further employment of this strategy to

obtain several other analogues of these new 14-membered macrolides is currently being investigated.

Experimental Section

General Methods: The ^1H and ^{13}C NMR spectroscopic data were recorded with a 300 or 500 MHz spectrometer at ambient temperature. The samples were dissolved in either $CDCl_3$ or C_6D_6. The coupling constant (*J*) is given in Hz. The chemical shifts are reported in ppm on a scale downfield from TMS, which was used as an internal standard, and the signal patterns are indicated as s (singlet), d (doublet), t (triplet), q (quartet), sext (sextet), m (multiplet), and br. (broad). FTIR spectra were recorded by using KBr pellets (neat) or a $CHCl_3$ solution. The data are reported in wavenumbers (cm^{-1}). Optical rotations were measured with a digital polarimeter using a 1 mL cell with a 1 dm path length. For low MS and HRMS, *m*/*z* ratios are reported in atomic mass units. Mass analysis was carried out in ESI mode. All of the reagents were reagent grade and used without further purification unless otherwise specified. Solvents for the reactions were distilled prior to use. THF, toluene, and diethyl ether were distilled from Na and benzophenone ketyl. MeOH was distilled from Mg and I_2, and CH_2Cl_2 was distilled from CaH_2. All air- or moisture-sensitive reactions were conducted under nitrogen or argon in flame- or oven-dried glassware and were magnetically stirred. Column chromatography was carried out with silica gel (100–200 mesh) packed in glass columns. Technical grade ethyl acetate and petroleum ether, which were used for column chromatography, were distilled prior to use.

Ethyl 3-(Furan-2-yl)-3-oxopropanoate (13): To a solution of diisopropylamine (7.95 mL, 56.75 mmol) in THF (40 mL) was added *n*BuLi (1.60 M solution in hexane, 35.47 mL, 56.75 mmol) at –78 °C under argon. The stirring was continued for 1 h, and then anhydrous EtOAc (5.57 mL, 56.75 mmol) in THF (20 mL) was added at –78 °C. After 1 h, 2-furoyl chloride (5.61 mL, 56.75 mmol) in THF (20 mL) was slowly added over 30 min at –78 °C. The mixture was stirred for 1 h and then quenched with an aqueous saturated solution of NH_4Cl (20 mL). The reaction mixture was diluted with water (50 mL), and the resulting solution was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine (40 mL), dried with anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography (hexane/EtOAc, 9:1) to give **13** (8.06 g, 78%; keto/enol tautomers, 20:1) as a pale red oil; R_f = 0.55 (hexane/EtOAc, 4:1). IR (KBr): $\tilde{\nu}$ = 3135, 2984, 2939, 1739, 1679, 1570, 1468, 1325, 1154, 1026, 915, 769 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, keto tautomer): δ = 7.62 (dd, *J* = 1.6, 0.7 Hz, 1 H), 7.28 (dd, *J* = 3.6, 0.7 Hz, 1 H) 6.58 (dd, *J* = 3.6, 1.7 Hz, 1 H), 4.21 (q, *J* = 7.1 Hz, 2 H), 3.85 (s, 2 H), 1.26 (t, *J* = 7.1 Hz, 3 H) ppm. ^1H NMR (500 MHz, $CDCl_3$, visible resonances for enol tautomer): δ = 12.17 (s, 1 H), 7.50 (dd, *J* = 1.7, 0.7 Hz, 1 H), 6.94 (dd, *J* = 3.4, 0.6 Hz, 1 H), 6.51 (dd, *J* = 3.5, 1.8 Hz, 1 H), 5.61 (s, 1 H), 4.25 (q, *J* = 7.1 Hz, 2 H), 1.33 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, keto tautomer): δ = 180.9, 166.8, 151.8, 146.9, 118.2, 112.6, 61.3, 45.3, 13.9 ppm. ^{13}C NMR (75 MHz, $CDCl_3$, visible resonances for enol tautomer): δ = 172.9, 161.8, 148.1, 144.7, 111.9, 86.1, 60.2, 14.1 ppm. HRMS (ESI): calcd. for $C_9H_{10}O_4Na$ $[M + Na]^+$ 205.04713; found 205.04727.

(R)-Ethyl 3-(Furan-2-yl)-3-hydroxypropanoate (9): To a degassed solution of β-keto ester **13** (2.00 g, 10.99 mmol) and Ru[(1*R*,2*R*)-*p*-TsNCH(Ph)CH(Ph)NH](η^6-*p*-cymene) (0.14 g, 0.22 mmol) in *i*PrOH (20 mL) under argon was added *t*BuOK (1 M solution in *t*BuOH, 1.10 mL, 1.10 mmol) at room temperature. The stirring was continued until complete consumption of the starting material was observed (indicated by TLC, approximately 24 h.). Water (50 mL) was added to the reaction mixture, and the product was extracted with CH_2Cl_2 (4 × 20 mL). The combined extracts were washed with brine (40 mL) and dried with anhydrous Na_2SO_4. The solvents were removed in vacuo to give the ethyl ester, which was purified by column chromatography through a short pad of silica gel (hexane/EtOAc, 92:8) to give **9** (1.98 g, 98%) as a light yellow oil; R_f = 0.40 (hexane/EtOAc, 4:1). $[a]_D^{20}$ = +20.86 (*c* = 1.66, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3445, 2984, 2938, 1732, 1632, 1373, 1283, 1217, 1163, 1012, 741 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 1.8 Hz, 1 H), 6.30 (dd, *J* = 3.3, 1.8 Hz, 1 H), 6.25 (d, *J* = 3.3 Hz, 1 H), 5.09 (dt, *J* = 7.8, 4.5 Hz, 1 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 3.19 (br. s, OH), 2.86 (dd, *J* = 16.2, 7.5 Hz, 1 H), 2.79 (dd, *J* = 16.5, 4.5 Hz, 1 H), 1.28 (t, *J* = 7.2 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.6, 154.7, 141.9, 110.0, 106.0, 63.9, 60.7, 39.7, 13.8 ppm. MS (ESI): *m*/*z* = 207 $[M + Na]^+$.

(*R*)-Ethyl 2-(6-Hydroxy-3-oxo-3,6-dihydro-2*H*-pyran-2-yl)acetate (15): To a magnetically stirred solution of furfuryl alcohol **9** (2.00 g, 10.87 mmol) in THF/H_2O (24:6 mL) were added solid $NaHCO_3$ (1.83 g, 21.74 mmol), $NaOAc{\cdot}3H_2O$ (1.62 g, 11.96 mmol), and *N*-bromosuccinimide (NBS, 1.93 g, 10.87 mmol) at 0 °C. The stirring was continued at 0 °C until complete consumption of starting material was observed (as monitored by TLC, 1 h). The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (10 mL), and the resulting solution was extracted with EtOAc (2 × 20 mL). The combined extracts were washed with a saturated aqueous solution of $Na_2S_2O_4$ (20 mL) followed by brine (20 mL). The organic layer was dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue obtained was purified by silica gel column chromatography (hexane/EtOAc, 4:1) to give **15** (2.09 g, 96%; mixture of inseparable anomers, 72:28) as a yellow oil; R_f = 0.40 (hexane/EtOAc, 3:2). $[a]_D^{20}$ = +5.23 (*c* = 1.50, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3426, 2925, 1729, 1695, 1374, 1292, 1180, 1028 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, major anomer): δ = 6.88 (dd, *J* = 10.2, 3.3 Hz, 1 H), 6.09 (d, *J* = 10.2 Hz, 1 H), 5.56 (d, *J* = 3.3 Hz, 1 H), 4.97 (dd, *J* = 8.1, 3.6 Hz, 1 H), 4.14 (q, *J* = 7.2 Hz, 2 H), 2.98 (dd, *J* = 16.8, 3.9 Hz, 1 H), 2.65 (dd, *J* = 16.8, 8.1 Hz, 1 H), 1.27 (t, dd, *J* = 7.2 Hz, 3 H) ppm. ^1H NMR (300 MHz, $CDCl_3$, visible resonances for minor anomer): δ = 6.94 (dd, *J* = 10.5, 1.5 Hz, 1 H), 6.14 (dd, *J* = 10.5, 1.5 Hz, 1 H), 5.69 (br. s, 1 H), 4.52 (dd, *J* = 7.8, 3.6 Hz, 1 H), 4.15 (q, *J* = 7.2 Hz, 2 H), 2.74 (dd, *J* = 16.5, 8.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, major anomer): δ = 195.1, 170.9, 144.9, 126.7, 87.5, 70.5, 60.9, 35.1, 13.9 ppm. ^{13}C NMR (75 MHz, $CDCl_3$, visible resonances for minor anomer): δ = 194.5, 148.7, 128.1, 90.8, 75.1, 61.0, 35.8 ppm. HRMS (ESI): calcd. for $C_9H_{12}O_5Na$ $[M + Na]^+$ 223.0582; found 223.0579.

(*S*)-Ethyl 2-(6-Acetoxy-3-oxo-3,6-dihydro-2*H*-pyran-2-yl)acetate (7): To the magnetically stirred solution of lactol **15** (2.0 g, 10.0 mmol) in CH_2Cl_2 (20 mL) was added pyridine (1.61 mL, 20.0 mmol) at 0 °C followed by Ac_2O (1.12 mL, 11.0 mmol) at the same temperature. Within 1 h, the entire lactol was consumed, and the reaction was then quenched with HCl (1 N solution, 20 mL) at 0 °C. The resulting solution was extracted with CH_2Cl_2 (2 × 20 mL). The organic layer was washed with water (30 mL) followed by a saturated aqueous solution of $NaHCO_3$ (20 mL) and then dried with anhydrous Na_2SO_4. Evaporation of the CH_2Cl_2 in vacuo gave the crude product, which in turn was purified by column chromatography (hexane/EtOAc, 9:1) to give the desired product **7** (2.18 g, 90%; mixture of inseparable anomers, 75:25) as a yellow viscous oil; R_f = 0.5 (hexane/EtOAc, 7:3). $[a]_D^{20}$ = –20.56 (*c* = 1.10, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2984, 1747, 1701, 1375, 1216, 1104, 939, 763 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, major anomer): δ = 6.86 (dd, *J* = 10.8,

3.7 Hz, 1 H), 6.45 (d, *J* = 3.7 Hz, 1 H), 6.23 (d, *J* = 9.8 Hz, 1 H), 4.86 (dd, *J* = 6.6, 4.2 Hz, 1 H), 4.15 (q, *J* = 7.5 Hz, 2 H), 2.92 (dd, *J* = 17.7, 4.5 Hz, 1 H), 2.73 (dd, *J* = 16.5, 6.9 Hz, 1 H), 2.14 (s, 3 H), 1.27 (t, *J* = 7.8 Hz, 3 H) ppm. ^{1}H NMR (300 MHz, $CDCl_3$, visible resonances for the minor anomer): δ = 6.52 (d, *J* = 3.0 Hz, 1 H), 6.25 (d, *J* = 9.8 Hz, 1 H), 4.69 (dd, *J* = 8.3, 4.5 Hz, 1 H), 4.20 (q, *J* = 7.5 Hz, 2 H), 2.15 (s, 3 H), 1.28 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, major anomer): δ = 193.7, 169.7, 169.1, 141.2, 128.0, 86.4, 72.2, 60.6, 34.9, 20.6, 13.8 ppm. ^{13}C NMR (75 MHz, $CDCl_3$, visible resonances for the minor anomer): δ = 193.4, 169.3, 168.7, 143.7, 128.2, 87.2, 75.7, 60.7, 37.5, 20.7 ppm. HRMS (ESI): calcd. for $C_{11}H_{14}O_6Na$ $[M + Na]^+$ 265.0688; found 265.0701.

(*R*)-Hept-4-yn-2-ol (11): Into a 500 mL, two-necked round-bottomed flask was collected 1-butyne (**12**) (6.95 mL, 86.21 mmol), which was diluted with dry THF (80 mL). The reaction mixture was cooled to –78 °C and then treated with *n*BuLi (1.6 M solution in hexanes, 32.40 mL, 51.72 mmol). After 30 min, the reaction mixture was gradually warmed to 0 °C. The resulting grey solution was stirred at 0 °C for 30 min. Then, dry HMPA (dried with CaH_2, 8 mL) was added dropwise at 0 °C. After cooling the reaction mixture to –20 °C and stirring for 30 min, (*R*)-propylene oxide (3.01 mL, 43.10 mmol) in dry HMPA (8 mL) was added. The stirring was continued for 1 h, and then the reaction mixture was warmed to ambient temperature over 4 h and stirred for an additional 12 h. A saturated aqueous solution of NH_4Cl (50 mL) was added at 0 °C followed by water (50 mL). The reaction mixture was extracted with Et_2O (4 × 50 mL), and the combined extracts were washed with brine and dried with anhydrous Na_2SO_4. The solvents were removed in vacuo at room temperature to give alcohol **11** (4.67 g, 95%) as a pale yellow oil; R_f = 0.50 (hexane/EtOAc, 4:1). $[\alpha]_D^{20}$ = –17.48 (*c* = 2.20, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3385, 2968, 2928, 1905, 1530, 1350, 1249, 1083, 841, 760, 690 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.88–3.81 (m, 1 H), 2.34–2.20 (m, 2 H), 2.19–2.14 (m, 2 H), 2.00 (br. d, *J* = 3.2 Hz, OH), 1.22 (d, *J* = 6.4 Hz, 3 H), 1.14 (t, *J* = 7.5 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 84.0, 75.5, 66.3, 29.1, 21.9, 14.0, 12.2 ppm. $C_7H_{12}O$ (112.17): calcd. C 74.95, H 10.78; found C 74.73, H 10.33.

(*R*)-Hept-6-yn-2-ol (16): Lithium pieces (1.49 g, 21.43 mmol) were intermittently added to vigorously stirring anhydrous 1,3-diaminopropane (60 mL) at ambient temperature, and then the mixture was warmed to 70 °C and stirred for 3 h. During this time, the reaction mixture gradually changed from deep blue to grey. The reaction mixture was cooled to ambient temperature, and *t*BuOK (16.00 g, 14.29 mmol) was added under argon. The resulting pale yellow solution was stirred for 30 min. Then, alkyne **11** (4.00 g, 35.72 mmol) was added neat at ambient temperature, and the reaction mixture changed from pale yellow to purple to dark brown. After 30 min, the entire reaction mixture was poured into ice water (200 mL), and the resulting solution was extracted with Et_2O (4 × 50 mL). The combined extracts were washed with HCl (1 N solution, 2 × 50 mL) and a saturated aqueous solution of $NaHCO_3$ (50 mL) and then dried with anhydrous Na_2SO_4. The Et_2O was removed in vacuo at ambient temperature to give terminal alkyne **16** (3.68 g, 92%) as a pale yellow oil; R_f = 0.40 (hexane/EtOAc, 4:1). $[\alpha]_D^{20}$ = –12.40 (*c* = 0.99, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3453, 2922, 2851, 2180, 1128 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.84 (sext, *J* = 5.9 Hz, 1 H), 2.25–2.21 (m, 2 H), 1.95 (t, *J* = 2.7 Hz, 1 H), 1.71–1.54 (m, 4 H), 1.30 (br. s, OH), 1.21 (t, *J* = 6.2 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 84.3, 68.4, 67.4, 38.0, 24.6, 23.4, 18.3 ppm. $C_7H_{12}O$ (112.17): calcd. C 74.95, H 10.78; found C 74.60, H 10.45.

(*R*)-7-(Trimethylsilyl)hept-6-yn-2-ol (17): *n*BuLi (1.60 M solution in hexane, 36.83 mL, 58.93 mmol) was added dropwise to a magnetically stirred solution of alcohol **16** (3.00 g, 26.79 mmol) in THF (40 mL) at –78 °C. The stirring was continued for 1 h, and then freshly distilled TMSCl (7.49 mL, 58.93 mmol) was added at –78 °C. After 1 h, the reaction mixture was warmed to 0 °C. HCl (1 N aqueous solution, 50 mL) was added dropwise, and the stirring was continued at room temperature for 30 min. The reaction mixture was extracted with diethyl ether (2 × 10 mL). The combined organic extracts were washed with water (30 mL) followed by a saturated aqueous solution of $NaHCO_3$ (50 mL) and then dried with anhydrous Na_2SO_4. Evaporation of solvents in vacuo gave **17** (4.53 g, 92%) as a light yellow oil; R_f = 0.50 (hexane/diethyl ether, 4:1). $[\alpha]_D^{20}$ = –6.83 (*c* = 0.55, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3347, 2961, 2928, 2174, 1249, 841, 760 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.82 (sext, *J* = 7.0 Hz, 1 H), 2.23 (t, *J* = 7.0 Hz, 2 H), 1.69–1.49 (m, 4 H), 1.20 (d, *J* = 7.0 Hz, 3 H), 0.14 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 107.2, 84.8, 67.6, 38.3, 24.8, 23.5, 19.8, 0.12 ppm. $C_{10}H_{20}OSi$ (184.35): calcd. C 65.15, H 10.94; found C 64.52, H 10.56.

(*R*)-7-(Trimethylsilyl)hept-6-yn-2-yl Acetate (8): To a magnetically stirred solution of alcohol **17** (4.0 g, 21.74 mmol) in CH_2Cl_2 (40 mL) was added pyridine (3.50 mL, 43.48 mmol) at 0 °C followed by the addition of DMAP [4-(*N*,*N*-dimethylamino)pyridine, 0.66 g, 5.43 mmol] and Ac_2O (2.44 mL, 23.91 mmol) at the same temperature. The mixture was stirred for 3 h and then quenched with HCl (1 N aqueous solution, 60 mL) at 0 °C. The resulting solution was extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were washed with water (40 mL) and a saturated aqueous solution of $NaHCO_3$ (40 mL) and then dried with anhydrous Na_2SO_4. Evaporation of the CH_2Cl_2 in vacuo gave the crude product, which in turn was purified by column chromatography (hexane/diethyl ether, 9.5:0.5) through a short pad of silica gel to give **8** (4.57 g, 93%) as a colorless oil; R_f = 0.8 (hexane/diethyl ether, 9:1). $[\alpha]_D^{20}$ = –1.96 (*c* = 0.93, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2926, 2854, 2175, 1740, 1372, 1247, 842, 771 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.89 (sext, *J* = 6.0 Hz, 1 H), 2.21 (t, *J* = 6.9 Hz, 2 H), 2.02 (s, 3 H), 1.67–1.46 (m, 4 H), 1.23 (d, *J* = 6.3 Hz, 3 H), 0.14 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.2, 106.5, 84.5, 70.1, 34.7, 24.2, 20.9, 19.7, 19.4, 0.1 ppm. $C_{12}H_{22}O_2Si$ (226.39): calcd. C 63.66, H 9.80; found C 63.73, H 9.52.

Ethyl 2-{(2*S*,6*R*)-6-[(*S*)-6-Acetoxyhept-1-ynyl]-3-oxo-3,6-dihydro-2*H*-pyran-2-yl}acetate (6): To a magnetically stirred solution of acetate **7** (1.00 g, 4.13 mmol) and **8** (0.51 g, 4.55 mmol) in CH_2Cl_2 (20 mL) was added $SnCl_4$ (1 M solution in heptane, 1.24 mL, 1.24 mmol) at 0 °C. The ice bath was removed, and the stirring was continued at room temp. for 1 h. After that time, acetate **7** was entirely consumed (monitored by TLC), and the reaction mixture was quenched with a saturated aqueous solution of $NaHCO_3$ (20 mL) at 0 °C and then diluted with water (20 mL). The resulting mixture was stirred at room temp. for an additional 1 h and then extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with brine (20 mL) and dried with anhydrous Na_2SO_4. Evaporation of the CH_2Cl_2 in vacuo gave the crude product, which was subjected to silica gel column chromatography (hexane/EtOAc, 9:1) to give the desired product **6** (1.18 g, 85%) as a light yellow oil; R_f = 0.50 (hexane/EtOAc, 4:1). $[\alpha]_D^{20}$ = –142.60 (*c* = 0.83, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2933, 2190, 1735, 1696, 1373, 1247, 1175, 1024 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.90 (dd, *J* = 9.8, 4.5 Hz, 1 H), 6.04 (dd, *J* = 9.8, 1.5 Hz, 1 H), 5.08 (dt, *J* = 4.5, 2.3 Hz, 1 H), 4.90 (sext, *J* = 6.0 Hz, 1 H), 4.85 (dd, *J* = 7.3, 4.2 Hz, 1 H), 4.16 (qt, *J* = 4.7, 7.5 Hz, 2 H), 2.95 (dd, *J* = 16.6, 4.5 Hz, 1 H), 2.66 (dd, *J* = 16.8, 7.5 Hz, 1 H), 2.28 (td, *J* = 6.8, 2.3 Hz, 2

H), 2.01 (s, 3 H), 1.69–1.52 (m, 4 H), 1.28 (t, J = 6.9 Hz, 3 H), 1.22 (d, J = 6.6, Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.0, 170.3, 170.0, 146.7, 124.7, 88.5, 73.0, 72.6, 70.0, 63.0, 60.5, 35.0, 34.7, 24.0, 21.0, 19.7, 18.3, 13.9 ppm. HRMS (ESI): calcd. for $C_{18}H_{24}O_6Na$ $[M + Na]^+$ 359.1470; found 359.1475.

Ethyl 2-{(2*S*,6*S*)-6-[(*S*,*E*)-6-Acetoxyhept-1-enyl]-3-oxo-3,6-dihydro-2*H*-pyran-2-yl}acetate (18): To a degassed stirred solution of alkyne **6** (0.50 g, 1.49 mmol) and $(EtO)_3SiH$ (1.09 mL, 5.95 mmol) in CH_2Cl_2 (20 mL) was added $[Cp^*(MeCN)_3Ru]PF_6$ (7 mg, 0.014 mmol) at 0 °C under argon. The reaction mixture was warmed to room temperature, as it was stirred. After 1 h, alkyne **6** was entirely consumed (monitored by TLC), and the solvent was evaporated under reduced pressure to give the crude mixture, which was diluted with THF (20 mL). This mixture was cooled to 0 °C, and to it was added pyridine (1.19 mL, 14.88 mmol) and then HF/pyridine (70:30, 0.20 mL, 7.44 mmol) dropwise at 0 °C. After the entire vinyl siloxane was consumed (monitored by TLC, 5 min), the reaction mixture was quenched with water (5 mL) and then neutralized with HCl (0.5 N solution, 35 mL). The resulting solution was extracted with EtOAc (3 × 20 mL). The organic layers were washed with water (20 mL) and a saturated aqueous solution of $NaHCO_3$ (10 mL) and then dried with anhydrous Na_2SO_4. Evaporation of solvent in vacuo gave the crude product, which was subjected to silica gel column chromatography (hexane/EtOAc, 9:1) to give desired product **18** (0.45 g, 90%) as a colorless oil; R_f = 0.50 (hexane/EtOAc, 4:1). $[\alpha]_D^{20}$ = –78.42 (c = 1.88, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2982, 1745, 1698, 1375, 1246, 1104 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.96 (dd, J = 10.2, 3.9 Hz, 1 H), 6.10 (dd, J = 10.5, 1.8 Hz, 1 H), 5.76 (dt, J = 15.6, 6.6 Hz, 1 H), 5.58 (dd, J = 15.6, 5.1 Hz, 1 H), 4.81–4.92 (m, 2 H), 4.61 (dd, J = 8.1, 3.9 Hz, 1 H), 4.16 (q, J = 7.2, Hz, 2 H), 2.92 (dd, J = 16.2, 3.9 Hz, 1 H), 2.60 (dd, J = 16.5, 8.1 Hz, 1 H), 2.16–2.09 (m, 2 H), 2.0 (s, 3 H), 1.64–1.39 (m, 4 H), 1.27 (t, J = 7.2 Hz, 3 H), 1.20 (d, J = 6.3 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.5, 170.5, 170.4, 149.4, 136.3, 125.6, 124.0, 72.2, 72.0, 70.5, 60.5, 35.3, 35.1, 32.0, 24.5, 21.2, 19.8, 14.0 ppm. HRMS (ESI): calcd. for $C_{18}H_{26}O_6Na$ $[M + Na]^+$ 361.1627; found 361.1641.

Ethyl 2-{(2*R*,6*S*)-6-[(*R*,*E*)-6-Acetoxyhept-1-en-1-yl]-3-oxotetrahydro-2*H*-pyran-2-yl}acetate (19): Flame-dried CuI was dissolved in HMPA at 50 °C, and the solution was cooled to room temperature. To a vigorously stirred suspension of $LiAlH_4$ (0.08 g, 2.22 mmol) in anhydrous THF (20 mL) was added dropwise the solution of CuI (0.42 g, 2.22 mmol) in HMPA (8 mL) at –78 °C. The generated orange suspension gradually turned to brown. The stirring was continued for an additional 1 h, and then compound **18** (0.50 g, 1.48 mmol) in anhydrous THF (2 mL) was added dropwise at the same temperature. Within 15 min, the enone was entirely consumed. The reaction mixture was quenched with an aqueous saturated solution of NH_4Cl (5 mL) at –78 °C, and the resulting mixture was warmed to room temp. over 30 min. The reaction mass was filtered through a wet pad of silica gel (EtOAc), which was washed with EtOAc (4 × 10 mL). The combined filtrates were washed with water (2 × 20 mL) and brine (20 mL), dried with anhydrous Na_2SO_4, and filtered. The solvents were evaporated under reduced pressure to give the crude product, which was purified by column chromatography (hexane/EtOAc, 9:1) to give **19** (0.46 g, 92%) as a colorless oil; R_f = 0.50 (hexane/EtOAc, 4:1). $[\alpha]_D^{20}$ = +64.86 (c = 1.20, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2979, 2934, 2859, 1734 (br.), 1374, 1248, 1185, 1025, 757 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.76 (dtd, J = 15.6, 6.6, 1.4 Hz, 1 H), 5.59 (ddt, J = 15.6, 5.0, 1.0 Hz, 1 H), 4.89 (sext, J = 6.4 Hz, 1 H), 4.52–4.45 (m, 2 H), 4.15 (q, J = 7.2 Hz, 2 H), 2.82 (dd, J = 16.3, 4.5 Hz, 1 H), 2.67 (dd, J = 16.3, 7.3 Hz, 1 H), 2.63–2.46 (m, 2 H), 2.34–2.17 (m, 1 H), 2.14–1.93 (m, 3 H), 2.03 (s, 3 H), 1.66–1.35 (m, 4 H), 1.26 (t, J = 7.2, Hz, 3 H), 1.20 (d, J = 6.3, Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 209.5, 170.7, 170.6, 132.9, 128.5, 73.9, 72.2, 70.7, 60.7, 35.6, 35.3, 34.9, 32.0, 27.7, 24.8, 21.3, 19.8, 14.1 ppm. HRMS (ESI): calcd. for $C_{18}H_{29}O_6$ $[M + H]^+$ 341.19587; found 341.19560.

Ethyl 2-{(2*R*,3*R*,6*S*)-6-[(*R*,*E*)-6-Acetoxyhept-1-en-1-yl]-3-hydroxytetrahydro-2*H*-pyran-2-yl}acetate (20): To a magnetically stirred solution of (*S*)-Me-CBS (1 M solution in toluene, 0.88 mL, 0.88 mmol) in anhydrous THF (10 mL) was added dropwise BH_3–THF (1 M solution in THF, 0.88 mL, 0.88 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 30 min. The generated complex was cooled to –78 °C, and then a solution of ketone **19** (0.30 g, 0.88 mmol) in THF (2 mL) was added dropwise. The stirring was continued until there was complete consumption of starting material (indicated by TLC, approximately 6 h). The reaction mixture was quenched with a saturated aqueous solution of NH_4Cl and then diluted with water (10 mL). The resulting solution was extracted with EtOAc (3 × 10 mL). The combined extracts were washed with brine (10 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated to give the crude product. Purification by column chromatography (hexane/EtOAc, 85:15) gave **20** (0.246 g, 82%) and **20a** (0.034 g, 11%) as colorless oils; R_f = 0.40 (hexane/EtOAc, 3:2). $[\alpha]_D^{20}$ = +27.30 (c = 0.23, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3452, 2976, 2835, 1735, 1374, 1248, 1080, 1040, 981, 760 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.66 (dtd, J = 15.7, 6.5, 1.4 Hz, 1 H), 5.52 (ddt, J = 15.8, 4.6, 1.0 Hz, 1 H), 4.89 (sext, J = 6.20 Hz, 1 H), 4.30 (br. m, 1 H), 4.23 (td, J = 6.9, 2.6 Hz, 1 H), 4.15 (q, J = 7.14 Hz, 2 H), 3.74 (br. s, 1 H), 2.62 (dd, J = 7.4, 2.4 Hz, 2 H), 2.09–1.95 (m, 4 H), 2.02 (s, 3 H), 1.89–1.83 (m, 1 H), 1.79–1.70 (m, 1 H), 1.63–1.33 (m, 4 H), 1.26 (t, J = 7.1 Hz, 3 H), 1.20 (d, J = 6.3 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.8, 170.7, 132.8, 129.0, 72.0, 70.8, 70.3, 66.8, 60.6, 35.9, 35.4, 32.2, 26.4, 24.9, 24.2, 21.4, 19.9, 14.2 ppm. HRMS (ESI): calcd. for $C_{18}H_{30}O_6Na$ $[M + Na]^+$ 365.19346; found 365.19256.

Ethyl 2-{(2*R*,3*S*,6*S*)-6-[(*R*,*E*)-6-Acetoxyhept-1-en-1-yl]-3-hydroxytetrahydro-2*H*-pyran-2-yl}acetate (20a): To a magnetically stirred solution of ketone **19** (0.10 g, 0.29 mmol) in THF/MeOH (3:1, 4 mL) was added $NaBH_4$ (0.011 g, 0.29 mmol) portionwise at 0 °C. The stirring was continued until there was a complete consumption of starting material (monitored by TLC, approximately 10 min), and the reaction mixture was quenched with a saturated aqueous NH_4Cl solution and then diluted with water (10 mL). The resulting solution was extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with brine (5 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated to give the crude product. Purification by column chromatography (hexane/EtOAc, 85:15) gave **20a** (0.069 g, 69%) and **20** (0.029 g, 29%) as colorless oils; R_f = 0.40 (hexane/EtOAc, 3:2). $[\alpha]_D^{20}$ = +23.07 (c = 1.09, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3453, 2979, 2935, 1735, 1447, 1374, 1248, 1155, 1080, 981, 760 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.66 (dtd, J = 15.9, 6.6, 1.5 Hz, 1 H), 5.49 (dd, J = 15.7, 4.0 Hz, 1 H), 4.88 (sext, J = 6.2 Hz, 1 H), 4.34 (br. d, J = 2.8 Hz, 1 H), 4.17 (q, J = 7.2 Hz, 2 H), 3.95 (td, J = 8.1, 4.5 Hz, 1 H), 3.40 (td, J = 8.9, 3.8 Hz, 1 H), 2.79 (dd, J = 15.1, 4.3 Hz, 1 H), 2.52 (dd, J = 15.1, 8.50 Hz, 1 H), 2.18–2.01 (m, 4 H), 2.03 (s, 3 H), 1.95–1.78 (m, 2 H), 1.71–1.36 (m, 4 H), 1.27 (t, J = 7.2 Hz, 3 H), 1.22 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.8, 170.9, 132.6, 129.4, 72.5, 71.6, 71.0, 69.8, 60.5, 37.9, 34.9, 32.1, 27.8, 27.3, 24.6, 21.3, 19.7, 14.1 ppm. HRMS (ESI): calcd. for $C_{18}H_{31}O_6$ $[M + H]^+$ 343.21152; found 343.21096.

Ethyl 2-{(2*R*,3*R*,6*S*)-6-[(*R*,*E*)-6-Acetoxyhept-1-en-1-yl]-3-[(*tert*-butyldimethylsilyl)oxy]tetrahydro-2*H*-pyran-2-yl}acetate (21): To a

magnetically stirred solution of alcohol **20** (0.20 g, 0.58 mmol) in CH_2Cl_2 (5 mL) was added 2,6-lutidine (0.20 mL, 1.75 mmol) dropwise at 0 °C. After 10 min, TBSOTf (0.15 mL, 0.64 mmol) was added at the same temperature. The stirring was continued until there was complete consumption of starting material (monitored by TLC, approximately 2 h), and the reaction mixture was quenched with a saturated aqueous NH_4Cl solution and then diluted with water (10 mL). The resulting solution was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with brine (10 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by column chromatography (hexane/EtOAc, 95:5) gave **21** (0.22 g, 84%) as a colorless oil; R_f = 0.55 (hexane/EtOAc, 9:1). $[\alpha]_D^{20}$ = +18.25 (*c* = 0.84, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2933, 2858, 1737, 1465, 1372, 1248, 1103, 974, 838, 777 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.62 (dt, *J* = 15.2, 6.8 Hz, 1 H), 5.44 (dd, *J* = 15.1, 5.3 Hz, 1 H), 4.88 (sext, *J* = 6.3 Hz, 1 H), 4.30–4.27 (m, 1 H), 4.19–4.10 (m, 3 H), 3.85–3.81 (m, 1 H), 2.69 (dd, *J* = 15.0, 9.3 Hz, 1 H), 2.6 (dd, *J* = 15.2, 4.9 Hz, 1 H), 2.05–2.00 (m, 2 H), 2.02 (s, 3 H), 1.89–1.83 (m, 1 H), 1.81–1.73 (m, 1 H), 1.64–1.54 (m, 2 H), 1.51–1.31 (m, 4 H), 1.25 (t, *J* = 7.1 Hz, 3 H), 1.19 (d, *J* = 6.3 Hz, 3 H), 0.89 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.0, 170.7, 132.0, 130.1, 72.7, 70.8, 70.2, 67.7, 60.3, 35.3, 33.3, 32.1, 27.9, 27.4, 25.7, 24.8, 21.3, 19.9, 18.0, 14.2, –4.8, –4.9 ppm. HRMS (ESI): calcd for $C_{24}H_{44}O_6NaSi$ $[M + Na]^+$ 479.27994; found 479.27911.

Ethyl 2-{(2*R*,3*S*,6*S*)-6-[(*R*,*E*)-6-Acetoxyhept-1-en-1-yl]-3-[(*tert*-butyldimethylsilyl)oxy]tetrahydro-2*H*-pyran-2-yl}acetate (23): Following a similar procedure as that used for the preparation of compound **21**, alcohol **20a** (0.30 g, 0.87 mmol) afforded TBS ether **23** (0.35 g, 88%) as a colorless oil; R_f = 0.50 (hexane/EtOAc, 9:1). $[\alpha]_D^{20}$ = +24.93 (*c* = 0.80, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2934, 2858, 1737, 1371, 1249, 1102, 1046, 838, 775 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.65 (dt, *J* = 16.1, 5.7 Hz, 1 H), 5.5 (dd, *J* = 16.1, 4.2 Hz, 1 H), 4.90 (sext, *J* = 6.8 Hz, 1 H), 4.34 (br. s, 1 H), 4.16 (q, *J* = 7.2 Hz, 2 H), 3.89 (td, *J* = 9.3, 3.2 Hz, 1 H), 3.37 (td, *J* = 9.6, 4.0 Hz, 1 H), 2.78 (dd, *J* = 14.9, 3.0 Hz, 1 H), 2.32 (dd, *J* = 14.9, 9.6 Hz, 1 H), 2.13–2.02 (m, 2 H), 2.03 (s, 3 H) 1.95–1.70 (m, 2 H), 1.67–1.35 (m, 6 H), 1.27 (t, *J* = 7.2, Hz, 3 H), 1.21 (d, *J* = 6.2, Hz, 3 H), 0.87 (s, 9 H), 0.05 (s, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.8, 170.8, 132.7, 129.2, 72.4, 71.9, 71.0, 70.8, 60.3, 38.1, 35.3, 32.3, 28.8, 27.6, 25.7, 24.9, 21.3, 20.0, 17.9, 14.2, –4.1, –4.8 ppm. HRMS (ESI): calcd. for $C_{24}H_{44}O_6NaSi$ $[M + Na]^+$ 479.27994; found 479.27858.

2-{(2*R*,3*R*,6*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-6-[(*R*,*E*)-6-hydroxyhept-1-en-1-yl]tetrahydro-2*H*-pyran-2-yl}acetic Acid (5): To a vigorously stirred solution of diester **21** (0.20 g, 0.44 mmol) in MeOH/H_2O (4:1, 8 mL) was added NaOH (0.07 g, 1.75 mmol) at 0 °C. The stirring was continued until there was complete consumption of the starting material (indicated by TLC, for 16 h). The reaction mixture was neutralized by the addition of $KHSO_4$ (0.24 g, 1.75 mmol) at 0 °C and then diluted with water (10 mL). The resulting solution was extracted with CH_2Cl_2 (5 × 10 mL). The organic layers were separated, dried with anhydrous Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure to give *seco* acid **5** (0.165 g, 98%) as a colorless oil; R_f = 0.35 (hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = +28.58 (*c* = 1.00, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3424 (br.), 2931, 2858, 1724, 1601, 1456, 1255, 1107, 1032, 837, 757, 640 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.69 (dtd, *J* = 15.5, 6.6, 1.2 Hz, 1 H), 5.49 (br. dd, *J* = 15.5, 5.5 Hz, 1 H), 4.26–4.21 (m, 2 H), 3.77–3.83 (m, 2 H), 2.74 (dd, *J* = 15.5, 9.6 Hz, 1 H), 2.56 (dd, *J* = 15.4, 4.1 Hz, 1 H), 2.01–2.10 (m, 2 H), 1.93–1.99 (m, 1 H), 1.83–1.76 (m, 1 H), 1.70–1.59 (m, 1 H), 1.54–1.38 (m, 5 H), 1.18 (d, *J* = 6.20 Hz, 3 H), 0.89 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.9, 133.3, 129.5, 72.3, 70.9, 67.8, 38.3, 34.7, 32.0, 27.4, 27.0, 25.8, 25.0, 23.2, 18.0, –4.7, –4.9 ppm. HRMS (ESI): calcd. for $C_{20}H_{38}O_5NaSi$ $[M + Na]^+$ 409.23807; found 409.23727.

2-{(2*R*,3*S*,6*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-6-[(*R*,*E*)-6-hydroxyhept-1-en-1-yl]tetrahydro-2*H*-pyran-2-yl}acetic Acid (4): Following a similar procedure as that used for preparation of **5**, diester **23** (0.3 g, 0.66 mmol) afforded *seco* acid **4** (0.249 g, 98%) as a colorless oil; R_f = 0.35 (hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = +39.33 (*c* = 2.24, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3409 (br.), 2932, 2858, 1715, 1464, 1367, 1255, 1106, 1046, 838, 775, 668 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.77–5.62 (m, 2 H), 4.41–4.35 (m, 1 H), 3.91–3.78 (m, 2 H), 3.36 (td, *J* = 9.9, 4.4 Hz, 1 H), 2.83 (dd, *J* = 15.3, 2.8 Hz, 1 H), 2.33 (dd, *J* = 15.3, 9.8 Hz, 1 H), 2.22–1.98 (m, 2 H), 1.96–1.78 (m, 2 H), 1.75–1.55 (m, 2 H), 1.51–1.36 (m, 4 H), 1.19 (d, *J* = 6.19 Hz, 3 H), 0.88 (s, 9 H), 0.06 (s, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.0, 134.2, 128.5, 72.3, 72.2, 71.0, 68.2, 37.9, 37.7, 32.1, 29.0, 27.7, 25.7, 24.7, 22.9, 17.9, –4.1, –4.8 ppm. HRMS (ESI): calcd. for $C_{20}H_{39}O_5Si$ $[M + H]^+$ 387.25613; found 387.25600.

(1*R*,5*R*,11*S*,14*R*,*E*)-14-[(*tert*-Butyldimethylsilyl)oxy]-5-methyl-4,15-dioxabicyclo[9.3.1]pentadec-9-en-3-one (22): To a magnetically stirred solution of *seco* acid **5** (0.05 mg, 0.13 mmol) in THF (5 mL) was added Et_3N (0.11 mL, 0.78 mmol) at 0 °C followed by the addition of 2,4,6-trichlorobenzoyl chloride (0.06 mL, 0.39 mmol). The stirring was continued at 0 °C for 1 h and then at room temp. for an additional 1 h. The reaction mixture was diluted with toluene (20 mL), and the stirring was continued for an additional 1 h. The resulting mixture was added dropwise over 8 h by syringe pump to a solution of DMAP (0.395 g, 3.23 mmol) in toluene (40 mL) at 60 °C under argon. After the addition, the mixture was stirred for another 15 min. The toluene was evaporated under reduced pressure, and the residue was diluted with EtOAc (10 mL). The resulting mixture was neutralized with HCl (0.5 N aqueous solution, 6.50 mL) at 0 °C, and the solution was extracted with EtOAc (3 × 10 mL). The combined extracts were washed with water (20 mL) and brine (10 mL) and then dried with anhydrous Na_2SO_4. Evaporation of the solvents in vacuo gave the crude lactone. Purification by column chromatography (hexane/EtOAc, 95:5) afforded the desired lactone **22** (0.036 g, 76%) as a colorless oil; R_f = 0.60 (hexane/EtOAc, 9:1). $[\alpha]_D^{20}$ = +47.59 (*c* = 0.21, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2930, 2856, 1729, 1458, 1259, 1109, 837, 774, 668 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 6.16 (dddd, *J* = 15.6, 10.9, 4.7, 1.8 Hz, 1 H), 5.63 (dd, *J* = 15.6, 4.1 Hz, 1 H), 5.07–5.02 (m, 1 H), 4.45–4.40 (br. m, 1 H), 4.08 (br. d, *J* = 11.00 Hz, 1 H), 3.64 (t, *J* = 3.0 Hz, 1 H), 2.45 (dd, *J* = 13.7, 1.61 Hz, 1 H), 2.23–2.16 (m, 2 H), 2.14 (dd, *J* = 13.6, 11.1 Hz, 1 H), 1.99–1.90 (m, 1 H), 1.86–1.76 (m, 3 H), 1.72–1.66 (m, 1 H), 1.64–1.56 (m, 1 H), 1.45–1.37 (m, 1 H), 1.31–1.25 (m, 1 H), 1.18 (d, *J* = 6.5 Hz, 3 H), 0.96 (s, 9 H), 0.05 (s, 3 H), 0.03 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6, 137.6, 129.2, 71.1, 69.8, 69.7, 68.2, 40.2, 31.8, 30.6, 28.2, 26.0, 25.1, 22.7, 19.2, 18.3, –4.4, –4.8 ppm. HRMS (ESI): calcd. for $C_{20}H_{37}O_4Si$ $[M + H]^+$ 369.24556; found 369.24593.

(1*R*,5*R*,11*S*,14*S*,*E*)-14-[(*tert*-Butyldimethylsilyl)oxy]-5-methyl-4,15-dioxabicyclo[9.3.1]pentadec-9-en-3-one (24): To a vigorously stirred solution of PPh_3 (0.68 g, 2.59 mmol) in anhydrous toluene (50 mL) at 0 °C was added diisopropylazodicarboxylate (DIAD, 0.513 mL, 2.59 mmol). The yellowish solution was stirred for 30 min, and then a solution of *seco* acid **4** (0.10 g, 0.26 mmol) in anhydrous toluene (40 mL) was added dropwise at room temperature over 30 min. The reaction mixture was stirred for 48 h until there was complete consumption of the starting material (monitored by TLC). The toluene was evaporated under reduced pres-

sure, and the crude mass was purified by column chromatography (hexane/EtOAc, 95:5) to give lactone **24** as a colorless oil (0.069 g, 72%); R_f = 0.65 (hexane/EtOAc, 9:1). $[\alpha]_D^{20}$ = +85.52 (*c* = 0.22, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2929, 2856, 1728, 1458, 1259, 1109, 837, 774, 668 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 6.39 (dddd, *J* = 15.4, 11.1, 4.0, 1.5 Hz, 1 H), 5.64 (br. dd, *J* = 15.7, 4.5 Hz, 1 H), 4.66–4.60 (m, 1 H), 4.44–4.40 (br. m, 1 H), 3.76 (t, *J* = 9.1 Hz, 1 H), 3.33 (td, *J* = 9.9, 4.4 Hz, 1 H), 2.76 (d, *J* = 15.9 Hz, 1 H), 2.24 (dd, *J* = 15.9, 8.6 Hz, 1 H), 2.19–2.04 (m, 2 H), 2.00–1.88 (m, 3 H), 1.82–1.66 (m, 3 H), 1.63–1.55 (m, 2 H), 1.30 (d, *J* = 6.2 Hz, 3 H), 0.89 (s, 9 H), 0.09 (s, 3 H), 0.08 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.5, 138.4, 127.9, 73.2, 71.6, 71.4, 70.6, 37.9, 33.2, 32.1, 30.5, 28.5, 25.8, 25.6, 20.2, 18.0, –3.9, –4.7 ppm. HRMS (ESI): calcd. for $C_{20}H_{37}O_4Si$ $[M + H]^+$ 369.24556; found 369.24645.

(+)-Aspergillide B: To a magnetically stirred solution of silyl ether **22** (0.020 g, 54.34 μmol) in anhydrous THF (2 mL) was added tetrabutylammonium fluoride (1 M solution in THF, 0.11 mL, 108.70 μmol) at 0 °C. The ice bath was removed, and the stirring was continued until there was complete consumption of the starting material (indicated by TLC, approximately 3 h). Water was added (5 mL), and the resulting solution was extracted with EtOAc (3 × 5 mL). The combined extracts were washed with brine (5 mL) and dried with anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to give the crude product. Purification by column chromatography (hexane/EtOAc, 6:4) afforded (+)-**2** as a white amorphous solid (12.70 mg, 92%), m.p. 83–85 °C; R_f = 0.50 (hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = +96.97 (*c* = 0.33, MeOH); ref.[6c] $[\alpha]_D^{20}$ = +84 (*c* = 0.12, MeOH). IR (KBr): $\tilde{\nu}$ = 3440, 2924, 2853, 1732, 1452, 1254, 1190, 1026, 969 cm^{-1}. ^1H NMR (300 MHz, C_6D_6): δ = 6.18 (dddd, *J* = 15.7, 10.8, 4.8, 1.9 Hz, 1 H), 5.37 (br. dd, *J* = 15.7, 4.3 Hz, 1 H), 5.08–4.99 (m, 1 H), 4.32–4.25 (m, 1 H), 4.06 (br. d, *J* = 11.3 Hz, 1 H), 3.20 (br. s, 1 H), 2.70 (dd, *J* = 13.7, 11.3 Hz, 1 H), 2.12 (dd, *J* = 13.66, 1.75 Hz, 1 H), 2.09–1.93 (m, 1 H), 1.90–1.65 (m, 2 H), 1.61–1.41 (m, 3 H), 1.42–1.21 (m, 3 H), 1.05 (d, *J* = 6.40 Hz, 3 H), 0.96 (dddd, *J* = 13.8, 4.9, 2.6, 1.3 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 169.9, 138.2, 129.1, 71.6, 69.9, 69.6, 67.3, 39.9, 32.1, 30.8, 27.9, 25.3, 22.6, 19.2 ppm. HRMS (ESI): calcd. for $C_{14}H_{23}O_4$ $[M + H]^+$ 255.15909; found 255.15939.

(+)-7-*epi*-Aspergillide A (25): Following a similar procedure as that employed for product (+)-**2**, compound **24** (0.05 g, 0.135 mmol) afforded **25** (31.75 mg, 92%) as a colorless oil; R_f = 0.50 (hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = +91.68 (*c* = 0.80, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3430, 2926, 2854, 1724, 1454, 1265, 1078, 972, 757 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 6.44 (dddd, *J* = 15.5, 10.2, 3.6, 1.4 Hz, 1 H), 5.61 (br. dd, *J* = 15.8, 3.5 Hz, 1 H), 4.67–4.57 (m, 1 H), 4.49–4.42 (m, 1 H), 3.77 (t, *J* = 9.0 Hz, 1 H), 3.35 (td, *J* = 9.9, 3.9 Hz, 1 H), 2.83 (d, *J* = 16.1 Hz, 1 H), 2.34 (dd, *J* = 16.1, 8.2 Hz, 1 H), 2.20–2.03 (m, 2 H), 2.05–1.93 (m, 2 H), 1.90–1.77 (m, 2 H), 1.73–1.67 (m, 2 H), 1.59–1.51 (m, 2 H), 1.30 (d, *J* = 6.1 Hz, 3 H), 1.28–1.16 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.6, 138.4, 127.5, 73.4, 71.4, 71.3, 69.6, 37.9, 33.3, 32.2, 30.0, 28.4, 25.7, 20.3 ppm. HRMS (ESI): calcd. for $C_{14}H_{23}O_4$ $[M + H]^+$ 255.15909; found 255.15944.

Supporting Information (see footnote on the first page of this article): Copies of ^1H and ^{13}C NMR spectra.

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[1] For reviews on natural products in drug discovery, see: a) B. B. Mishra, V. K. Tiwari, *Eur. J. Med. Chem.* **2011**, *46*, 4769–4807; b) K. Kumar, H. Waldmann, *Angew. Chem.* **2009**, *121*, 3272; *Angew. Chem. Int. Ed.* **2009**, *48*, 3224–3242; c) R. M. Wilson, S. J. Danishefsky, *J. Org. Chem.* **2006**, *71*, 8329–8351; d) M. S. Butler, *J. Nat. Prod.* **2004**, *67*, 2141–2153; e) D. J. Newman, G. M. Cragg, K. M. Snader, *Nat. Prod. Rep.* **2000**, *17*, 215–234.

[2] For reviews on marine natural products, see: a) J. W. Blunt, B. R. Copp, M. H. G. Munro, P. T. Northcote, M. R. Prinsep, *Nat. Prod. Rep.* **2011**, *28*, 196–268; b) J. W. Blunt, B. R. Copp, M. H. G. Munro, P. T. Northcote, M. R. Prinsep, *Nat. Prod. Rep.* **2010**, *27*, 165–237; c) A. T. Tresa Remya, P. K. Devanand, A. L. Ponnapakkam, *Mar. Drugs* **2010**, *8*, 1417–1468; d) H. Burkhard, *Drug Discovery Today* **2003**, *8*, 536–544.

[3] a) K. Kito, R. Ookura, S. Yoshida, M. Namikoshi, T. Ooi, T. Kusumi, *Org. Lett.* **2008**, *10*, 225–228; b) R. Ookura, K. Kito, Y. Saito, T. Kusumi, T. Ooi, *Chem. Lett.* **2009**, *38*, 384.

[4] For the synthesis of aspergillide A, see: a) G. V. M. Sharma, V. Manohar, *Tetrahedron: Asymmetry* **2012**, *23*, 252–263; b) Z. Andrea, P. Manuel, G. Maria, G. Generosa, F. Yagamare, *Synthesis* **2011**, 3301–3306; c) Y. Izuchi, N. Kanomata, H. Koshino, Y. Hongo, T. Nakata, S. Takahashi, *Tetrahedron: Asymmetry* **2011**, *22*, 246–251; d) T. Nagasawa, T. Nukada, S. Kuwahara, *Tetrahedron* **2011**, *67*, 2882–2888; e) M. Kanematsu, M. Yoshida, K. Shishido, *Angew. Chem.* **2011**, *123*, 2666; *Angew. Chem. Int. Ed.* **2011**, *50*, 2618–2620; f) S. Díaz-Olta, C. A. Angulo-Pachón, J. Murga, E. Falomir, V. Carda, J. A. Marco, *Chem. Eur. J.* **2011**, *17*, 675–688; g) H. Fuwa, H. Yamaguchi, M. Sasaki, *Tetrahedron* **2010**, *66*, 7492–7503; h) G. Sabitha, D. V. Reddy, A. S. Rao, J. S. Yadav, *Tetrahedron Lett.* **2010**, *51*, 4195–4198; i) T. Nagasawa, S. Kuwahara, *Tetrahedron Lett.* **2010**, *51*, 875–877; j) S. Díaz-Oltra, C. A. Angulo-Pachón, J. Murga, M. Carda, J. A. Marco, *J. Org. Chem.* **2010**, *75*, 1775–1778; k) H. Fuwa, H. Yamaguchi, M. Sasaki, *Org. Lett.* **2010**, *12*, 1848–1851.

[5] For a review on the syntheses of aspergillides, see: T. Nagasawa, S. Kuwahara, *Heterocycles* **2012**, *85*, 587–613.

[6] For the synthesis of aspergillide B, see: a) B. M. Trost, M. J. Bartlett, *Org. Lett.* **2012**, *14*, 1322–1325; b) A. J. M. Hendrix, M. P. Jennings, *Tetrahedron Lett.* **2010**, *51*, 4260–4262; c) J. Liu, K. Xu, J. He, L. Zhang, X. Pan, X. She, *J. Org. Chem.* **2009**, *74*, 5063–5066; d) S. Diaz-Oltra, C. A. Angulo-Pachon, M. N. Kneeteman, J. Murga, M. Carda, J. A. Marco, *Tetrahedron Lett.* **2009**, *50*, 3783–3785; e) T. Nagasawa, S. Kuwahara, *Biosci. Biotechnol. Biochem.* **2009**, *73*, 1893–1894; f) S. M. Hande, J. Uenishi, *Tetrahedron Lett.* **2009**, *50*, 189–192; and also see ref.[4a,4e–4g,4k]

[7] For the synthesis of aspergillide C, see: a) P. Srihari, Y. Sridhar, *Eur. J. Org. Chem.* **2011**, 6690–6697; b) H. Kobayashi, M. Kanematsu, M. Yoshida, K. Shishido, *Chem. Commun.* **2011**, *47*, 7440–7442; c) M. Kanematsu, M. Yoshida, K. Shishido, *Tetrahedron Lett.* **2011**, *52*, 1372–1374; d) J. D. Panarese, S. P. Waters, *Org. Lett.* **2009**, *11*, 5086–5088; e) T. Nagasawa, S. Kuwahara, *Org. Lett.* **2009**, *11*, 761–764.

[8] For our recent contributions to natural products Synthesis see: a) G. Mehta, S. Ramesh, P. Srihari, *Tetrahedron Lett.* **2012**, *53*, 829–832; b) K. Vamshikrishna, P. Srihari, *Tetrahedron* **2012**, *68*, 1540–1546; c) P. Srihari, B. Mahankali, K. Rajendraprasad, *Tetrahedron Lett.* **2012**, *53*, 56–58; d) G. Mehta, S. Ramesh, P. Srihari, *Tetrahedron Lett.* **2011**, *52*, 1663–1666; e) P. Srihari, K. Satyanarayana, B. Ganganna, J. S. Yadav, *J. Org. Chem.* **2011**, *76*, 1922–1925.

[9] S. Hashiguchi, A. Fujii, J. Takehara, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1995**, *117*, 7562–7563.

[10] The optical purity was determined by chiral HPLC (Chiralpak OJ-H, 5% *i*PrOH/hexanes, λ = 210 nm, flow rate: 1.0 mL/min): t_R = 23.4 min.
[11] a) M. P. Georgiadis, E. A. Couladouros, *J. Org. Chem.* **1986**, *51*, 2725–2727; b) O. Achmatowicz, R. Bielski, *Carbohydr. Res.* **1977**, *55*, 165–176.
[12] S. R. Abrams, A. C. Shaw, *Org. Synth.* **1993**, *8*, 146–148.
[13] a) J. S. Yadav, A. K. Raju, V. Sunitha, *Tetrahedron Lett.* **2006**, *47*, 5269–5272; b) M. Isobe, W. Poosaha, R. Saeeng, K. Kira, C. Yenjai, *Org. Lett.* **2003**, *5*, 4883–4885; c) R. Saeeng, U. Sirion, P. Sahakitpichan, M. Isobe, *Tetrahedron Lett.* **2003**, *44*, 6211–6215; d) M. Isobe, R. Nishizawa, S. Hosokawa, T. Nishikawa, *Chem. Commun.* **1998**, 2665–2676.
[14] The single product was confirmed by LCMS analysis.
[15] B. M. Trost, Z. T. Ball, T. Joge, *J. Am. Chem. Soc.* **2002**, *124*, 7922–7923.
[16] Protodesilylation with the TBAF-CuI system resulted in decomposition of the vinyl siloxane. After screening several desilylating agents under different conditions, we were successful with HF/pyridine in presence of an excess amount of pyridine at 0 °C.
[17] T. Tsuda, T. Fujii, K. Kawasaki, T. Saegusa, *J. Chem. Soc., Chem. Commun.* **1980**, 1013–1014.
[18] a) E. J. Corey, R. K. Bakshi, S. Shibata, *J. Am. Chem. Soc.* **1987**, *109*, 5551–5553; b) E. J. Corey, R. K. Bakshi, *Tetrahedron Lett.* **1990**, *31*, 611–614; c) E. J. Corey, C. J. Helal, *Angew. Chem.* **1998**, *110*, 2092; *Angew. Chem. Int. Ed.* **1998**, *37*, 1986–2012.
[19] J. Inanaga, K. Hirata, H. Saeki, T. Katsuki, M. Yamaguchi, *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989–1993.
[20] a) O. Mitsunobu, M. Eguchi, *Bull. Chem. Soc. Jpn.* **1971**, *44*, 3427–3430; b) O. Mitsunobu, *Synthesis* **1981**, 1–28; c) D. L. Hughes, *Org. React.* **1992**, *42*, 335–656.
[21] A. S. Kendey, Y. Fujii, *Tetrahedron Lett.* **1991**, *32*, 2199–2202.

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