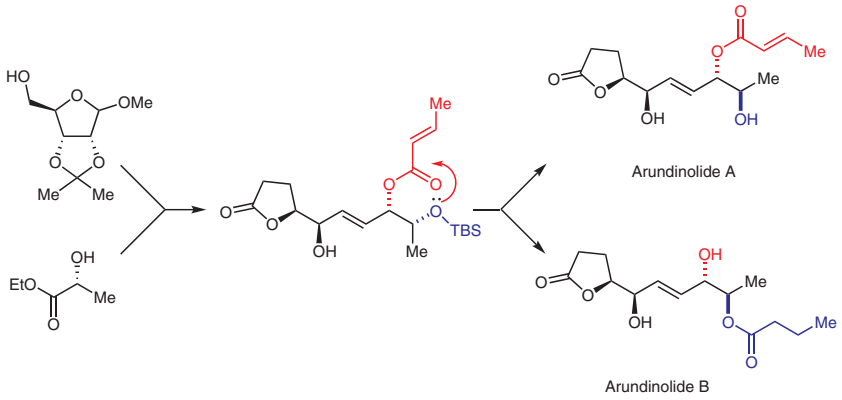
Synthesis C. Chang et al. Paper

Stereoselective Total Synthesis of Arundinolides A and B

Caizhu Chang[a,b]
Jialin Geng[a,c]
Yinxin Liu[a,c]
Yuguo Du[a,c]
Jun Liu*[a,c]
Zhi-Bing Dong*[a,b]

[a] State Key Laboratory of Environmental Chemistry and Eco-toxicology, Research Center for Eco-Environmental Sciences, Chinese Academy of Science, Beijing 100085, P. R. of China
junliu@rcees.ac.cn
[b] School of Chemistry and Environmental Engineering, Wuhan Institute of Technology, Wuhan 430205, P. R. of China
dzb04982@wit.edu.cn
[c] School of Chemical Sciences, University of Chinese Academy of Sciences, Beijing 100049, P. R. of China



Received: 07.12.2019
Accepted after revision: 09.01.2020
Published online: 05.02.2020
DOI: 10.1055/s-0039-1691699; Art ID: ss-2019-z0663-op

Abstract The efficient and enantioselective syntheses of arundinolides A and B have been accomplished for the first time from chiral pool methyl-2,3-*O*-isopropylidene-β-D-ribofuranoside and D-ethyl lactate. The key features of the total synthesis are intramolecular crotonyl migration and $NaBH_4$-CuCl catalyzed regioselective reduction and cross-metathesis reaction.

Key words arundinolides, total synthesis, chiral pool, regioselective reduction, crotonyl migration

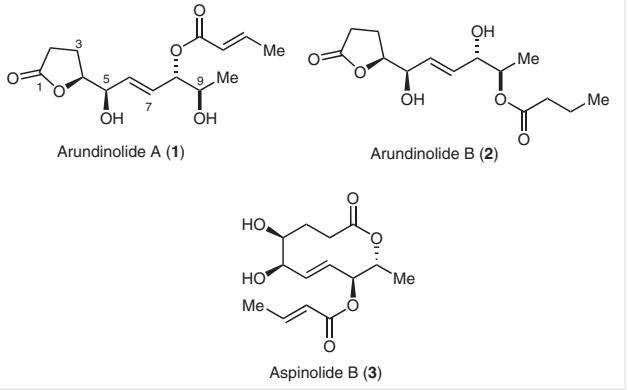


Figure 1 Chemical structures of arundinolides A (**1**), B (**2**) and aspinolide B (**3**)

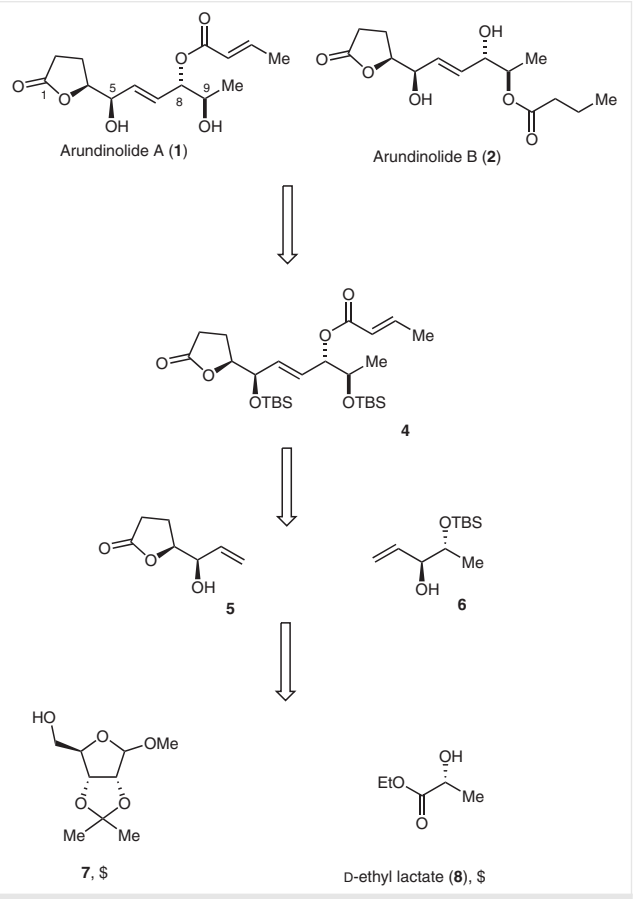
Trichoderma species are known for their ability to produce bioactive secondary metabolites, including terpenoids, alkaloids, polyketides and non-ribosomally biosynthesized peptides.[1] Among these *Trichoderma* species, *Trichoderma arundinaceum* has attracted increasing attention in recent years because it produces trichothecenes, which are sesquiterpenoid compounds that are harmful to plants and to the animals that consume contaminated food or feed stocks.[2] Arundinolides A (**1**) and B (**2**), which are two naturally occurring γ-lactones, were isolated as secondary metabolites from the fungus *Trichoderma arundinaceum gene tri4* (*TaΔTri4*) by Collado and co-workers very recently (Figure 1).[3]

The relative configurations of arundinolides A and B were established based on extensive spectroscopic analysis and electronic circular dichroism (ECD) experiments. The arundinolides A and B comprise similar γ-lactone skeletons with an extra side chain connecting C6 to C7. Architecturally, the backbone and stereochemistry of arundinolides are very close to the previously isolated natural product aspinolide B (**3**).[4] The absolute configuration of arundinolide A was further confirmed by treatment of aspinolide B (**3**) with a basic solution of K_2CO_3 (5%) and subsequent neutralization with a solution of HCl (0.1 M), which resulted in arundinolide A (**1**). Aspinolide B displayed good fungicidal activity and repressed SA-related genes, but the biological activities of arundinolides A and B were not fully evaluated. To date, no synthetic efforts have been reported toward the synthesis of arundinolides. In the context of our studies on the enantioselective synthesis of natural products based on the readily available natural carbohydrates,[5] we herein report a concise and efficient synthetic approach to arundinolides A and B.

The retrosynthetic analysis for arundinolides A (**1**) and B (**2**) is illustrated in Scheme 1. It was envisioned that the two natural arundinolides could be accessed from suitably functionalized intermediate **4** through an intramolecular crotonyl ester migration at C-8 and C-9 via *ortho* ester intermediates with retention of chirality. The *trans* double bond at C6-C7 could be installed by coupling subunit **5** with the olefinic side chain **6** through the olefin cross-metathesis (CM) strategy. The CM precursor **5** could be readily accessible

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

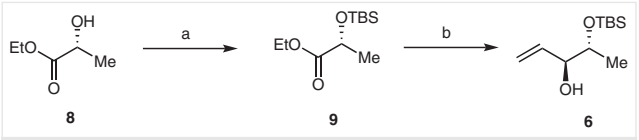
from commercially available methyl-2,3-*O*-isopropylidene-β-D-ribofuranoside (**7**). The TBS group protected allylic alcohol **6**, in which the desired *trans* diols are ready, could be obtained from D-ethyl lactate through reduction and Grignard addition in a one-pot sequence. Details of the studies thus undertaken are described below.



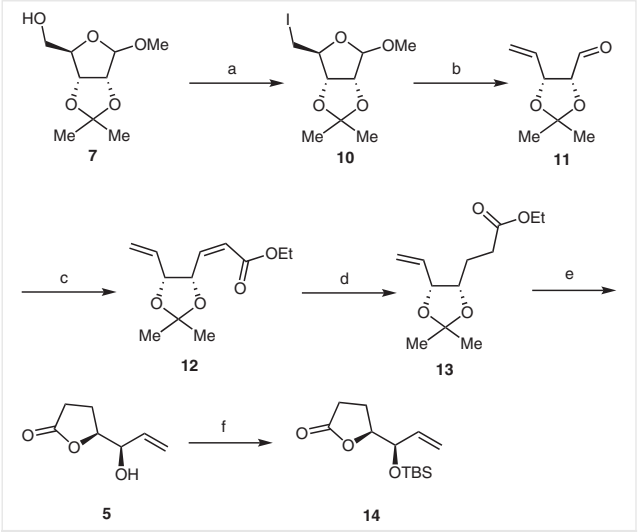
Scheme 1 Retrosynthetic analysis of arundinolides A and B (compounds **7** and **8** are commercially available)

We started the synthesis of arundinolides A and B by converting D-ethyl lactate **8** into silyl group protected allylic alcohol **6** in two steps by following a reported protocol,[6] as shown in Scheme 2. Reduction of the known TBS-protected ethyl lactate **9** with DIBAL-H to the corresponding aldehyde and subsequent treatment with vinyl magnesium chloride delivered the desired *trans* diol as a 7.8:1 mixture of diastereoisomers in a one-pot process. This approach afforded the desired allylic alcohol (3*S*,4*R*)-**6** in a yield of 80% over two steps from D-ethyl lactate.

The synthesis of the lactone fragment **5** began with conversion of commercially available methyl-2,3-*O*-isopropylidene-β-D-ribofuranoside (**7**) into the corresponding iodide **10** (Scheme 3). According to a modified literature procedure,[7] the resulting iodide **10** was further treated with active zinc in refluxing methanol to provide the desired aldehyde **11** in almost quantitative yield. Wittig olefination of the labile aldehyde **11** with (ethoxycarbonylmethylene) triphenylphosphorane in ethanol afforded predominantly (*Z*)-α,β-unsaturated ester **12** in 78% yield with 5:1 *Z*/*E* selectivity (J = 11.6 Hz for the *Z*-isomer, based on NMR analysis of the crude product).[8]

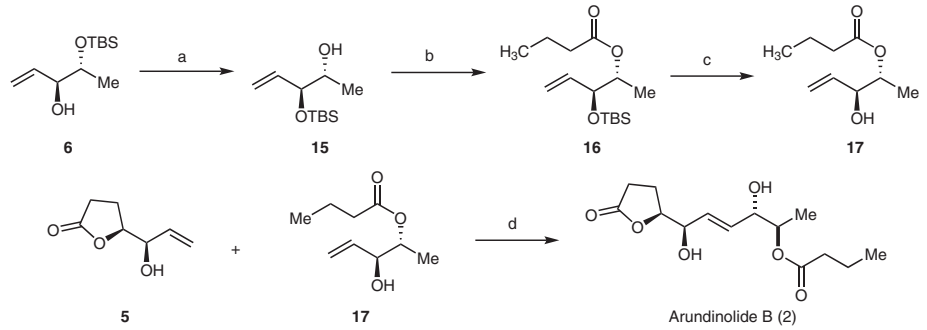


Scheme 2 Synthesis of **6**. *Reagents and conditions*: (a) TBDMSCl, imidazole, anhydrous DCM, 0 °C to r.t., 5 h; (b) DIBAL-H, anhydrous DCM, –98 °C, then vinylmagnesium chloride, –98 °C to r.t., 3 h, 80% over two steps.



Scheme 3 Synthesis of **14**. *Reagents and conditions*: (a) I_2, imidazole, PPh_3, THF, reflux, 30 min, 95%; (b) activated Zn, MeOH, reflux, 1 h; (c) $Ph_3P{=}CHCO_2Et$, EtOH, r.t., 12 h, 78% over two steps; (d) $NaBH_4$, CuCl, THF–EtOH (3:7), –40 °C, 1 h, 90%; (e) 4 M HCl, MeOH, r.t., 5 h, 82%; (f) TBDMSCl, imidazole, cat. DMAP, anhydrous DCM, r.t., 12 h, 93%.

Selective reduction of the conjugated double bond in the (*Z*)-α,β-unsaturated ester **12** with the $NaBH_4$-CuCl system in THF/EtOH at –40 °C provided the ester **13** in 90% yield.[9] It was found that the selectivity of the reduction was sensitive to the rate of addition of the sodium borohydride and to the reaction temperature. Other conditions using $NaBH_4$-$CoCl_2$,[10] $NaBH_4$-$CuCl_2$ and Mg-MeOH[11] did not show an acceptable yield improvement. Acidic hydrolysis of the acetonide group followed by lactonization was then effectively carried out in one pot by treating ester **13** with 4 M HCl in methanol. Blocking of the corresponding allylic alcohol with a TBS group provided **14** in 93% yield.

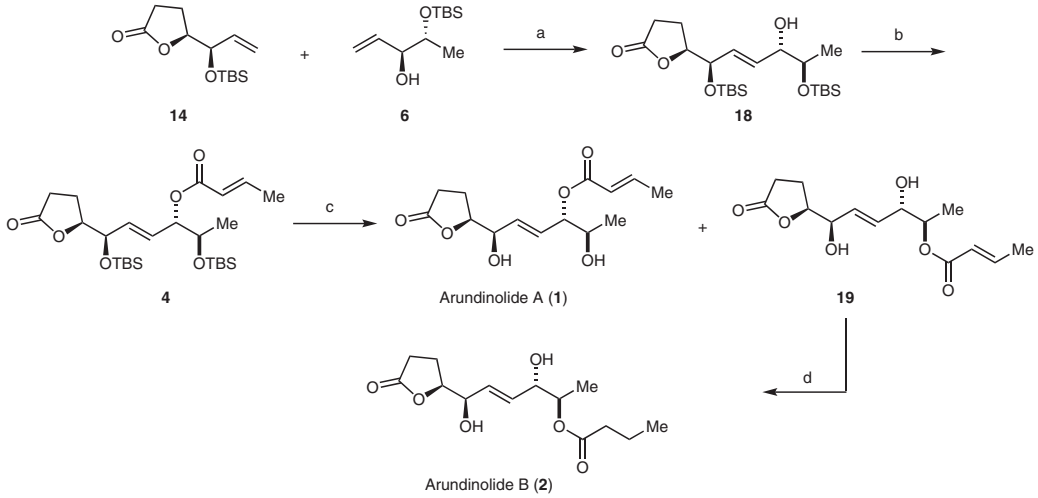


Scheme 4 Synthesis of arundinolide B. *Reagents and conditions*: (a) NaH, THF, r.t., 47% (73% BRSM); (b) *n*-Butyric anhydride, Py, DMAP, r.t., 90%; (c) HF-pyridine complex, THF, r.t., 52%. (d) Grubbs 2nd catalyst, anhydrous DCM, N_2, reflux, 28%.

With both key fragments in hand, we set out to synthesize arundinolide B (**2**) through the planned cross-metathesis strategy (Scheme 4). Thus, treatment of allylic alcohol **6** with excess NaH in anhydrous THF at ambient temperature resulted in the desired TBS-migration product **15**[12] in 47% and 73% yield based on recovered starting material. Presumably, the base-assisted 1,2-silyl migration took place via an intramolecular process and generated the thermodynamically more stable C-3 alkoxide **15** via a five-membered ring intermediate containing a pentacovalent silicon atom.[13] Esterification of the volatile alcohol **15** with *n*-butyric anhydride in pyridine gave **16** in better yield than the corresponding DCC-promoted coupling. It was also found that the TBS group in **15** was sensitive to *retro*-migration under the Keck procedure (DCC/ DMAP).[14] Deprotection of the TBS group was carried out with the hydrogen fluoride-pyridine (HF·Py) complex and gave the desired allylic alcohol **17** in a moderate yield of 52%. Finally, coupling of the lactone **5** with the excess alcohol **17** (2.0 equiv) under Grubbs second-generation catalyst[15] afforded the arundinolide B albeit in only 28% yield (Scheme 4). Based on previous reports, the low yield was probably due to the homodimerization and the undesired Ru-catalyzed intramolecular hydrogen-transfer isomerization of unprotected allylic alcohols into ethyl ketones.[16] Attempts to suppress the undesired isomerization by using benzoquinone or phenol as additives were fruitless.[17]

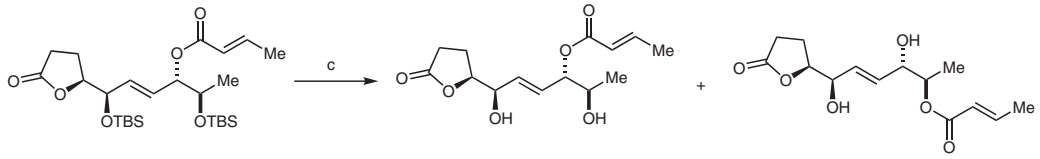
Although the synthesis of arundinolide B was short (six steps, the longest linear sequence) and efficient, it suffered from low yield in the NaH-mediated 1,2-silyl migration and the cross-metathesis process. Moreover, in view of the similar structural skeleton of arundinolides A and B, it is therefore highly desirable to develop a more efficient and divergent synthetic strategy for the total synthesis of both natural products.

To circumvent these problems, we therefore revised our synthetic plan. It was reported that some bulky silyl groups (e.g., TBS or TES) could prevent the Ru-catalyzed isomeriza-



Scheme 5 Synthesis of arundinolides **A** and **B**. *Reagents and conditions*: (a) Hoveyda–Grubbs second-generation catalyst, anhydrous DCM, reflux, 48 h, 81%; (b) Crotonic anhydride, cat. DMAP, Py, r.t., 4 h, 84%; (c) see Table 1, HF-pyridine complex, THF, r.t., 30 h, 60% for **1**; or PTSA, MeOH, r.t., 6 h, 43% for **19**; (d) $NaBH_4$, CuCl, THF–EtOH (3:7), –40 °C, 1 h, 78%.

Table 1 Conditions for Desilylation and Transesterification of **4**



4 Arundinolide A (**1**) **19**

Entry	Conditions	Yield of **1** (%)	Yield of **19** (%)
1	TBAF (2.5 equiv), THF, 50 °C, 1 h	40	26
2	HF·Py (15 equiv), THF, r.t., 30 h	47	0
3	HF·Py (20 equiv), THF, r.t., 30 h	60	0
4	HF·Py (30 equiv), THF, r.t., 30 h	58	trace
5	HF·Py (50 equiv), THF, r.t., 24 h	37	30
6	1 M HCl, MeOH, r.t., 30 h	49	17
7	PTSA, MeOH, r.t., 17 h	24	43
8	CSA (0.05 equiv), MeOH, r.t., 15 h	29	37

tion of allylic alcohols and inhibit homodimerization in cross-metathesis reactions.[18] Accordingly, we revised our synthetic expedition towards arundinolides A and B. To our delight, exposure of the TBS-substituted lactone **14** with the alcohol **6** (5.0 equiv) in the presence of Hoveyda–Grubbs second-generation catalyst, delivered compound **18** in good yield without any detectable isomerization product (Scheme 5).[19] Subsequently, esterification of the allyl alcohol **18** with crotonic anhydride in pyridine afforded **4** in 84% yield.

However, the envisaged desilylation and transesterification of **4** turned out to be more difficult than we expected. Therefore, various conditions of desilylation and crotonyl ester migration were investigated to deliver arundinolide A and the crotonyl migration product **19**, which would be subsequently regioselectively reduced to afford arundinolide B (Table 1).

Table 2 Comparison of ^{1}H and ^{13}C NMR Data of Natural[a] and Synthetic[b] Arundinolide A (**1**)

No	Proton	^{1}H NMR natural	^{1}H NMR synthetic	^{13}C NMR natural	^{13}C NMR synthetic
1	–	–	–	177.3	177.5
2	H-2α	2.60, ddd (18, 10.1, 6)	2.60, ddd (18, 10.1, 6.1)	28.4	28.4
	H-2β	2.48, ddd (18, 10.1, 7.6)	2.46, ddd (17.9, 10.2, 7.6)		
3	H-3α	2.21, m	2.21, m	21.0	21.0
	H-3β	2.12, m	2.12, m		
4		4.51, m	4.51, m	81.5	81.6
5		4.54, m	4.53, m		71.7
6		5.75, ddd (15.7, 5, 1.2)	5.75, dd (15.5, 4.6)	131.2	131.3
7		5.96, ddd (15.7, 7, 1.5)	5.95, ddd (15.6, 6.8, 1.2)	127.7	127.8
8		5.24, ddt (7, 3.9, 0.9)	5.23, dd (6.7, 3.9)	77.2	77.3
9		3.98, qd (6.5, 3.9)	3.97, qd (6.5, 4.0)	69.0	69.0
10		1.18, d (6.5)	1.18, d (6.4)	18.3	18.3
1′		–	–	165.6	165.6
2′		5.88, dq (15.6, 1.7)	5.88, dq (15.5, 1.7)	122.3	122.3
3′		7.02, dq (15.6, 6.9)	7.02, dq (15.6, 6.9)	145.9	145.9
4′		1.90, dd (6.9, 1.7)	1.90, dd (6.9, 1.6)	18.1	18.0

[a] Spectra were recorded at 500 MHz (^{1}H NMR) and 125 MHz (^{13}C NMR) in $CDCl_3$.
[b] Spectra were recorded at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR) in $CDCl_3$.

Table 3 Comparison of ^{1}H and ^{13}C NMR Data of Natural[a] and Synthetic[b] Arundinolide B (**2**)

No	Proton	^{1}H NMR natural	^{1}H NMR synthetic	^{13}C NMR natural	^{13}C NMR synthetic
1	–	–	–	177.2	177.3
2	H-2α	2.61, ddd (18.0, 10.1, 6)	2.61, ddd (18.1, 10.1, 6)	28.5	28.5
	H-2β	2.50, ddd (18.0, 10.1, 7.7)	2.49, ddd (17.8, 10.2, 7.6)		
3	H-3α	2.22, m	2.22, m	21.0	21.0
	H-3β	2.14, m	2.13, m		
4		4.52, m	4.50–4.54, m	81.6	81.7
5		4.55, m		71.8	71.8
6		5.78, ddd (15.5, 5.1, 1.4)	5.77, dd (15.6, 4.7)	129.0	129.2
7		5.91, ddd (15.5, 5.7, 1.4)	5.91, dd (15.6, 5.7)	131.1	131.1
8		4.28, m	4.27, t (4.4)	73.9	73.9
9		4.99, qd (6.5, 3.2)	4.98, qd (6.5, 3.2)	73.2	73.2
10		1.18, d (6.5)	1.18, d (6.4)	14.6	14.7
1′		–	–	173.6	173.6
2′		2.31, t (7.4)	2.31, t (7.4)	36.3	36.3
3′		1.66, sext (7.4)	1.66, dq (4.8, 7.4)	18.5	18.5
4′		0.96, t (7.4)	0.96, t (7.4)	13.6	13.6

[a] Spectra were recorded at 500 MHz (^{1}H NMR) and 125 MHz (^{13}C NMR) in $CDCl_3$.
[b] Spectra were recorded at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR) in $CDCl_3$.

In an initial experiment, attempted desilylation of **4** under basic conditions with TBAF in THF resulted in the formation of a separable mixture of the two isomers, arundinolide A (**1**) and the crotonyl migration product **19** (26%) (Table 1, entry 1). After screening a number of conditions, we were delighted to find that the use of a large excess of hydrogen fluoride-pyridine complex could effectively suppress crotonyl migration. It was found that the equivalent of HF-pyridine complex had a great effect on the crotonyl migration reaction in view of the yield (entry 2–5). When more loading of HF-pyridine complex was used, a dramatic improvement (up to 23%) and the highest yield (60%) for arundinolide A (**1**) was observed, without any detectable migration product. However, further increase in the number of equivalents of HF-pyridine to 50 equiv sharply decreased the yield of arundinolide A (**1**) and gave a mixture of two isomers (entry 5). We also attempted the desilylation using acidic hydrolysis (entry 6–8). The best result for the acid-promoted migration came from using *p*-toluenesulfonic acid (PTSA) in MeOH (entry 7) and provided the desired crotonyl migration product **19** with an acceptable reaction yield (43%). Finally, following the same regioselective reduction as described above, the synthesis of arundinolide B (**2**) was accomplished in 78% yield.

All the spectroscopic data and specific rotation data (^{1}H and ^{13}C NMR, Table 2 and Table 3) of our synthetic arundinolides **A** and **B** were in good agreement with the values reported for the natural product.[3] The observed optical rotation values for synthetic arundinolide A {$[\alpha]_D^{20}$ –4.2 (*c* 0.15, $CHCl_3$), lit. $[\alpha]_D^{20}$ –3.2 (*c* 0.15, $CHCl_3$)} and for synthetic arundinolide B {$[\alpha]_D^{20}$ +4.8 (*c* 0.32, $CHCl_3$), lit. $[\alpha]_D^{20}$ +15 (*c* 0.32, $CHCl_3$)} were comparable to those reported for the natural products.

In summary, we have succeeded in the first total synthesis of arundinolides A and B in 20.8% overall yield (9 steps) and 11.6% (10 steps) or 7.7% (6 steps) overall yields, respectively. The efficient combination of chiron approach, intramolecular crotonyl migration and $NaBH_4$-CuCl catalyzed regioselective reduction represent the key features of the total synthesis. Our work confirmed the complete structure and absolute stereochemistry of arundinolides. Further efforts on the synthesis of related arundinolides and aspinolides analogues and bioactivity evaluations are under way in our laboratory.

Unless noted otherwise, commercially available materials were used without further purification. All solvents were dried according to the established procedures ahead of use. All reactions under standard conditions were monitored by thin-layer chromatography (TLC) on gel F_{254} plates. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials. ^{1}H NMR, ^{13}C NMR were measured on 400 MHz or 100 MHz spectrometers (NMR in $CDCl_3$ with TMS as an internal standard). Chemical shifts (δ) are given in ppm relative to residual solvent (usually chloroform; δ 7.26 ppm for ^{1}H NMR or 77.0 ppm for proton decoupled ^{13}C NMR), and coupling constants (*J*) are in Hz. Multiplicity is tabulated as s for singlet, d for doublet, t for triplet, q for quadruplet, and m for multiplet. Flash chromatography (FC) was performed using silica gel (200–300 mesh) according to

the standard protocol. Optical rotations were measured with a polarimeter with a thermally jacketed 5 cm cell at approximately 20 °C. High-resolution mass spectrometry data (HRMS) were acquired with a Q-TOF analyzer in acetone or MeOH as solvent.

(3*S*,4*R*)-4-((*tert*-Butyldimethylsilyl)oxy)pent-1-en-3-ol (6)

To a solution of TBS-protected lactate **9**[6] (4.0 g, 17.2 mmol) in anhydrous DCM (80 mL) was added slowly DIBAL-H (1.0 M in hexane, 18.9 mL, 18.9 mmol) via syringe at –98 °C under N_2 atmosphere and the solution was stirred for 15 min. After completion of reaction (TLC), vinylmagnesium chloride (1.0 M in toluene, 43.0 mL, 43.0 mmol) was added dropwise into the mixture via syringe. The solution was then warmed to r.t. and stirred for 2 h. Upon completion, the reaction was quenched with saturated sodium potassium tartarate (40 mL) and stirred overnight. The aqueous layer was extracted with DCM (3 × 100 mL) and the combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated. The crude residue was purified by flash column chromatography (petroleum ether/EtOAc 80:1) to give **6**.

Yield: 2.97 g (80%); colorless oil; $[\alpha]_D^{20}$ +7.2 (*c* 0.39, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.81 (ddd, *J* = 17.1, 10.6, 6.2 Hz, 1 H), 5.31–5.17 (m, 2 H), 4.02 (ddt, *J* = 6.3, 3.6, 1.4 Hz, 1 H), 3.84 (qd, *J* = 6.3, 3.6 Hz, 1 H), 1.07 (d, *J* = 6.3 Hz, 3 H), 0.89 (s, 9 H), 0.08 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.5, 116.5, 76.6, 71.2, 25.8, 18.0, 17.6, –4.4, –4.9.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{24}O_2SiNa$: 239.1443; found: 239.1427.

(3a*S*,4*S*,6a*R*)-4-(Iodomethyl)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3] dioxole (10)

A stirred solution of methyl-2,3-*O*-isopropylidene-β-D-ribofuranoside (**7**) (8 g, 39.2 mmol), imidazole (4.8 g, 70.5 mmol), and triphenylphosphine (15.4 g, 58.8 mmol) in THF (100 mL), iodine (14.8 g, 58.8 mmol) was added portionwise. The solution was heated at reflux for 30 min. After completion of reaction (TLC), the mixture was decanted into excess saturated aqueous $Na_2S_2O_3$, and then extracted with EtOAc (3 × 200 mL). The combined organic phase was dried over Na_2SO_4, and concentrated under reduced pressure. The crude material was purified by flash column chromatography (petroleum ether/EtOAc 25:1) to give the known compound **10**.[7]

Yield: 11.7 g (95%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.05 (s, 1 H), 4.76 (dd, *J* = 5.9, 1.0 Hz, 1 H), 4.62 (d, *J* = 5.9 Hz, 1 H), 4.44 (ddd, *J* = 10.2, 6.0, 1.0 Hz, 1 H), 3.37 (s, 3 H), 3.28 (dd, *J* = 9.9, 6.1 Hz, 1 H), 3.16 (t, *J* = 10.0 Hz, 1 H), 1.48 (s, 3 H), 1.32 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 112.6, 109.6, 87.4, 85.3, 83.0, 55.2, 26.4, 24.9, 6.7.

Ethyl (*Z*)-3-((4*S*,5*R*)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)acrylate (12)

Activated zinc powder (819 mg, 12.6 mmol) was added to the above iodides **10** (2.0 g, 6.3 mmol) in MeOH (35 mL), and the mixture was heated at reflux for 1 h. After completion of reaction (TLC), the mixture was cooled to r.t., and filtered through a short plug of silica gel. The filtrate was concentrated under reduced pressure to provide a colorless oil, which was directly used in the following step without further purification. The crude aldehyde (**11**) was dissolved in EtOH (30 mL), then ethyl (triphenylphosphoranylidene)acetate (3.28 g, 9.4 mmol) was added at 0 °C and the resulting mixture was stirred at r.t. for 12 h. After completion of the reaction (TLC), the mixture was evaporated to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc 22:1) to furnish compound **12**.

Yield: 1.1 g (78% over two steps); $[\alpha]_D^{20}$ +31.2 (*c* 0.68, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.17 (dd, *J* = 11.6, 7.5 Hz, 1 H), 5.88 (dd, *J* = 11.7, 1.6 Hz, 1 H), 5.71–5.61 (m, 2 H), 5.27 (dt, *J* = 17.1, 1.4 Hz, 1 H), 5.15 (dt, *J* = 10.4, 1.3 Hz, 1 H), 4.86 (t, *J* = 7.1 Hz, 1 H), 4.16 (q, *J* = 7.1 Hz, 2 H), 1.54 (s, 3 H), 1.40 (s, 3 H), 1.28 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.6, 146.3, 133.9, 121.4, 117.8, 109.1, 79.6, 75.6, 60.4, 27.8, 25.2, 14.2.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{18}O_4Na$: 249.1103; found: 249.1100.

Ethyl 3-((4*S*,5*R*)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)propanoate (13)

To a stirred solution of ester **12** (1.0 g, 4.4 mmol) and cuprous chloride (305 mg, 3.08 mmol) in a mixture of THF (15 mL) and MeOH (35 mL), $NaBH_4$ (1.1 g, 29.5 mmol) was added portionwise at –40 °C. The reaction mixture was stirred at the same temperature for 1 h, then concentrated under reduced pressure. The residue was diluted with water, extracted with EtOAc (3 × 50 mL), and the organic layer was separated, washed with water, brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude material was purified by flash column chromatography (petroleum ether/EtOAc 20:1) to give **13**.

Yield: 903 mg (90%); colorless oil; $[\alpha]_D^{20}$ –4.6 (*c* 0.54, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.81 (ddd, *J* = 17.5, 10.3, 7.6 Hz, 1 H), 5.35–5.24 (m, 2 H), 4.53 (t, *J* = 6.9 Hz, 1 H), 4.17–4.10 (m, 3 H), 2.51–2.32 (m, 2 H), 1.77–1.71 (m, 2 H), 1.47 (s, 3 H), 1.35 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3, 133.8, 118.6, 108.4, 79.5, 77.2, 60.4, 30.9, 28.1, 26.1, 25.6, 14.2.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{20}O_4Na$: 251.1259; found: 251.1273.

(*S*)-5-((*R*)-1-Hydroxyallyl)dihydrofuran-2(3*H*)-one (5)

To a stirred solution of **13** (500 mg, 2.2 mmol) in MeOH (20 mL) was added a catalytic amount of 4 M HCl and the mixture was stirred at r.t. for 5 h. Upon completion of the reaction (TLC), the mixture was directly concentrated and the residue was extracted with EtOAc, then the organic layer was evaporated under reduced pressure to afford **5**.

Yield: 256 mg (82%); colorless oil; $[\alpha]_D^{20}$ +8.7 (*c* 0.6, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.79 (ddd, *J* = 17.2, 10.6, 5.2 Hz, 1 H), 5.43 (dt, *J* = 17.2, 1.6 Hz, 1 H), 5.29 (dt, *J* = 10.6, 1.5 Hz, 1 H), 4.55–4.47 (m, 2 H), 2.59 (ddd, *J* = 17.8, 10.2, 6.2 Hz, 1 H), 2.47 (ddd, *J* = 17.8, 10.2, 7.2 Hz, 1 H), 2.27–2.18 (m,1 H), 2.16–2.06 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.8, 134.6, 117.8, 82.0, 72.5, 28.5, 20.8.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_7H_{10}O_3Na$: 165.0528; found: 165.0521.

(*S*)-5-((*R*)-1-((*tert*-Butyldimethylsilyl)oxy)allyl)dihydrofuran-2(3*H*)-one (14)

To a stirred solution of **5** (120 mg, 0.84 mmol) and imidazole (171 mg, 2.52 mmol) in anhydrous DCM (10 mL), a catalytic amount of DMAP and TBDMSCl (317 mg, 2.1 mmol) were added at 0 °C, and the mixture was stirred at r.t. for 12 h. The reaction was quenched with saturated NH_4Cl solution. The organic phase was separated and the

aqueous phase was extracted with DCM (2 × 15 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude material was purified by flash column chromatography (petroleum ether/EtOAc 8:1) to give compound **14**.

Yield: 200 mg (93%); colorless oil; $[\alpha]_D^{20}$ –10.3 (*c* 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.72 (ddd, *J* = 17.2, 10.5, 5.0 Hz, 1 H), 5.35 (dt, *J* = 17.1, 1.6 Hz, 1 H), 5.22 (dt, *J* = 10.5, 1.5 Hz, 1 H), 4.47–4.42 (m, 2 H), 2.53 (ddd, *J* = 17.8, 10.5, 7.2 Hz, 1 H), 2.39 (ddd, *J* = 17.8, 10.5, 6.0 Hz, 1 H), 2.27–2.19 (m, 1 H), 2.07–1.97 (m, 1 H), 0.86 (s, 9 H), 0.05 (s, 3 H), 0.02 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.4, 135.9, 117.2, 81.8, 73.8, 28.4, 25.7 (3C), 20.2, 18.0, –4.9, –5.1.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{25}O_3Si$: 257.1573; found: 257.1564.

(2*R*,3*S*)-3-((*tert*-Butyldimethylsilyl)oxy)pent-4-en-2-ol (15)

A stirred solution of **6** (220 mg, 1.01 mmol) in THF (10 mL) was treated with sodium hydride (81.5 mg, 2.03 mmol) at 0 °C, then the mixture was stirred at r.t. for 2 h. Upon completion of the reaction (TLC), the reaction was neutralized with saturated NH_4Cl solution and extracted with EtOAc (3 × 20 mL). The combined organic phase was dried over Na_2SO_4, and concentrated under reduced pressure. The crude material was purified by flash column chromatography (petroleum ether/EtOAc 100:1) to give **15**.

Yield: 103 mg (47%); colorless oil; $[\alpha]_D^{20}$ –6.4 (*c* 0.05, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.80 (ddd, *J* = 17.3, 10.4, 6.8 Hz, 1 H), 5.24–5.17 (m, 2 H), 3.98 (ddt, *J* = 6.7, 4.0, 1.2 Hz, 1 H), 3.72 (qd, *J* = 6.4, 4.0 Hz, 1 H), 1.09 (d, *J* = 6.4 Hz, 3 H), 0.89 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.0, 117.0, 78.0, 70.6, 25.8 (3C), 18.1, 17.4, –4.3, –5.0.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{24}O_2SiNa$: 239.1443; found: 239.1451.

(2*R*,3*S*)-3-((*tert*-Butyldimethylsilyl)oxy)pent-4-en-2-yl Butyrate (16)

To a stirred solution of **15** (110 mg, 0.51 mmol) in pyridine (5 mL), *n*-butyric anhydride (0.26 mL, 1.78 mmol) and a catalytic amount of DMAP was added, and the mixture was stirred at r.t. for 4 h. Upon completion of the reaction (TLC), the reaction was quenched by the addition of MeOH (0.5 mL). The mixture was concentrated with toluene and poured into saturated aqueous $NaHCO_3$ and then extracted with EtOAc (2 × 15 mL). The combined organic phase was washed with saturated aqueous $CuSO_4$, water, and dried over Na_2SO_4, and concentrated under reduced pressure. The crude material was purified by flash column chromatography (petroleum ether/EtOAc 25:1) to give **16**.

Yield: 131 mg (90%); colorless oil; $[\alpha]_D^{20}$ +2.8 (*c* 0.5, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.77 (ddd, *J* = 17.1, 10.4, 5.7 Hz, 1 H), 5.28–5.13 (m, 2 H), 4.86 (qd, *J* = 6.4, 3.7 Hz, 1 H), 4.18 (ddt, *J* = 5.5, 3.5, 1.5 Hz, 1 H), 2.26 (td, *J* = 7.3, 1.3 Hz, 2 H), 1.69–1.60 (m, 2 H), 1.15 (d, *J* = 6.4 Hz, 3 H), 0.94 (t, *J* = 7.4 Hz, 3 H), 0.91 (s, 9 H), 0.06 (s, 3 H), 0.02 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3, 137.9, 116.3, 75.6, 73.2, 36.7, 26.0 (3C), 18.6, 18.4, 14.2, 13.9, –4.3, –4.7.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{31}O_3Si$: 287.2042; found: 287.2035.

(2*R*,3*S*)-3-Hydroxypent-4-en-2-yl Butyrate (17)

To a cooled (0 °C) solution of compound **16** (70 mg, 0.24 mmol) in THF (3 mL), HF-pyridine complex (0.5 mL, 3.6 mmol) was added dropwise and the solution was stirred at r.t. for 24 h. After completion of reaction (TLC), it was neutralized with saturated sodium bicarbonate solution, and the mixture was extracted with EtOAc (3 × 15 mL), washed with saturated aqueous $CuSO_4$ and dried over Na_2SO_4. The organic phases was evaporated under reduced pressure and purified by flash column chromatography (petroleum ether/EtOAc 12:1) to give **17**.

Yield: 21 mg (52%); colorless oil; $[\alpha]_D^{20}$ +2.7 (*c* 0.3, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.84 (ddd, *J* = 16.9, 10.5, 6.0 Hz, 1 H), 5.37–5.22 (m, 2 H), 4.97 (qd, *J* = 6.5, 3.4 Hz, 1 H), 4.20 (ddt, *J* = 6.0, 3.3, 1.4 Hz, 1 H), 2.29 (t, *J* = 7.4 Hz, 2 H), 1.70–1.60 (m, 2 H), 1.20 (d, *J* = 6.5 Hz, 3 H), 0.95 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.5, 135.7, 117.4, 74.9, 73.1, 36.4, 18.5, 14.5, 13.6.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_9H_{16}O_3Na$: 195.0997; found: 195.0991.

(*S*)-5-((5*R*,8*S*,9*R*,*E*)-8-Hydroxy-2,2,3,3,9,11,11,12,12-nonamethyl-4,10-dioxa-3,11-disilatridec-6-en-5-yl)dihydrofuran-2(3*H*)-one (18)

Hoveyda–Grubbs second generation catalyst (7 mg, 0.011 mmol) was added to a mixture of **14** (58 mg, 0.226 mmol) and **6** (244 mg, 1.13 mmol) in anhydrous DCM (10 mL) and the mixture was heated at reflux for 48 h. After completion of reaction (TLC), the solution was concentrated and purified by flash column chromatography (petroleum ether/EtOAc 6:1) to give **18**.

Yield: 81 mg (81%); colorless oil; $[\alpha]_D^{20}$ –30.6 (*c* 0.4, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.79 (dd, *J* = 15.7, 5.6 Hz, 1 H), 5.65 (dd, *J* = 15.6, 5.1 Hz, 1 H), 4.53–4.51 (m, 1 H), 4.46 (ddd, *J* = 8.3, 4.8, 2.4 Hz, 1 H), 4.07–4.05 (m, 1 H), 3.88 (qd, *J* = 6.3, 3.2 Hz, 1 H), 2.55 (ddd, *J* = 17.8, 10.5, 7.2 Hz, 1 H), 2.41 (ddd, *J* = 17.8, 10.5, 6.0 Hz, 1 H), 2.29–2.21 (m, 1 H), 2.08–1.98 (m, 1 H), 1.03 (d, *J* = 6.3 Hz, 3 H), 0.89 (s, 18 H), 0.081 (s, 3 H), 0.076 (s, 3 H), 0.07 (s, 3 H), 0.04 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.5, 130.9, 129.6, 82.0, 75.3, 73.2, 71.1, 28.5, 25.8 (3C), 25.7 (3C), 20.3, 18.1, 18.0, 17.7, –4.4, –4.7, –4.9, –5.0.

HRMS (ESI-TOF): *m*/*z* [M + K]$^+$ calcd for $C_{22}H_{44}O_5Si_2K$: 483.2364; found: 483.2360.

(5*R*,6*S*,9*R*,*E*)-2,2,3,3,5,11,11,12,12-Nonamethyl-9-((*S*)-5-oxotetrahydrofuran-2-yl)-4,10-dioxa-3,11-disilatridec-7-en-6-yl (*E*)-But-2-enoate (4)

To a stirred solution of **18** (440 mg, 0.99 mmol) in pyridine (10 mL), crotonic anhydride (0.74 mL, 4.95 mmol) and a catalytic amount of DMAP were added, and the mixture was stirred at r.t. for 4 h. The reaction was quenched by the addition of MeOH (2 mL). The solution was concentrated with toluene and poured into saturated aqueous $NaHCO_3$ (20 mL) and then extracted with EtOAc (2 × 20 mL). The combined organic phase was washed with saturated aqueous $CuSO_4$, water, dried over Na_2SO_4, and concentrated under reduced pressure. The crude material was purified by flash column chromatography (petroleum ether/EtOAc 7:1) to give **4**.

Yield: 425 mg (84%); colorless oil; $[\alpha]_D^{20}$ –5.8 (*c* 0.3, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.98 (dq, *J* = 15.6, 6.9 Hz, 1 H), 5.93 (ddd, *J* = 15.6, 7.4, 1.6 Hz, 1 H), 5.83 (dq, *J* = 15.5, 1.7 Hz, 1 H), 5.65 (ddd, *J* = 15.6, 5.0, 1.0 Hz, 1 H), 5.14 (dd, *J* = 7.4, 2.6 Hz, 1 H), 4.53 (dt,

J = 4.7, 2.0 Hz, 1 H), 4.45 (ddd, *J* = 8.4, 4.9, 2.4 Hz, 1 H), 4.00 (qd, *J* = 6.5, 2.8 Hz, 1 H), 2.56 (ddd, *J* = 17.8, 10.6, 7.2 Hz, 1 H), 2.41 (ddd, *J* = 17.7, 10.5, 5.9 Hz, 1 H), 2.31–2.23 (m, 1 H), 2.07–1.97 (m, 1 H), 1.89 (dd, *J* = 6.9, 1.8 Hz, 3 H), 1.08 (d, *J* = 6.4 Hz, 3 H), 0.88 (s, 18 H), 0.07 (s, 3 H), 0.05 (s, 3 H), 0.04 (s, 3 H), 0.03 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.5, 165.6, 145.0, 132.3, 127.4, 122.7, 81.8, 77.6, 72.9, 69.5, 28.5, 25.8 (3C), 25.7 (3C), 20.2, 19.9, 18.1, 18.03, 17.98, –4.7, –4.8 (2C), –5.1.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{48}O_6Si_2Na$: 535.2887; found: 535.2891.

(2*R*,3*S*,6*R*,*E*)-3,6-Dihydroxy-6-((*S*)-5-oxotetrahydrofuran-2-yl)hex-4-en-2-yl (*E*)-But-2-enoate (19)

To a solution of **4** (65 mg, 0.12 mmol) in MeOH (3.5 mL) was added PTSA (11 mg, 0.06 mmol) as a solid. The reaction mixture was stirred at r.t. for 6 h, then the reaction was directly concentrated under reduced pressure. The crude material was purified by flash column chromatography (hexane/EtOAc, 1:2) to give **19**.

Yield: 15 mg (43%); colorless oil; $[\alpha]_D^{20}$ –2.1 (*c* 0.1, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.01 (dq, *J* = 15.6, 6.9 Hz, 1 H), 5.92 (ddd, *J* = 15.6, 5.7, 1.4 Hz, 1 H), 5.86 (dq, *J* = 15.5, 1.8 Hz, 1 H), 5.77 (ddd, *J* = 15.6, 5.0, 1.3 Hz, 1 H), 5.02 (qd, *J* = 6.5, 3.4 Hz, 1 H), 4.58–4.48 (m, 2 H), 4.29 (t, *J* = 4.5 Hz, 1 H), 2.60 (ddd, *J* = 17.8, 10.1, 6.0 Hz, 1 H), 2.48 (ddd, *J* = 17.9, 10.2, 7.6 Hz, 1 H), 2.26–2.17 (m, 1 H), 2.16–2.06 (m, 1 H), 1.89 (dd, *J* = 6.9, 1.6 Hz, 3 H), 1.24 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.2, 166.3, 145.5, 131.0, 129.5, 122.4, 82.1, 73.8, 73.0, 71.6, 28.4, 20.9, 17.9, 14.8.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{20}O_6Na$: 307.1158; found: 307.1159.

Arundinolide A

To a cooled (0 °C) solution of **4** (17 mg, 0.033 mmol) in THF (1 mL), HF-pyridine complex (0.1 mL, 0.66 mmol) was added dropwise and the solution was stirred at r.t. for 30 h. After completion of the reaction (TLC), the mixture was neutralized with saturated sodium bicarbonate solution, extracted with EtOAc (2 × 10 mL), washed with saturated aqueous $CuSO_4$, and dried over Na_2SO_4. The organic phases was evaporated under reduced pressure and purified by flash column chromatography (petroleum ether/EtOAc 1:2) to give arundinolide A.

Yield: 5 mg (60%); colorless oil; $[\alpha]_D^{20}$ –4.2 (*c* 0.15, $CHCl_3$) {lit.[3] $[\alpha]_D^{20}$ –3.2 (*c* 0.15, $CHCl_3$)}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.02 (dq, *J* = 15.4, 6.9 Hz, 1 H), 5.95 (ddd, *J* = 15.6, 6.8, 1.3 Hz, 1 H), 5.88 (dq, *J* = 15.5, 1.7 Hz, 1 H), 5.75 (dd, *J* = 15.5, 4.6 Hz, 1 H), 5.23 (dd, *J* = 6.7, 3.9 Hz, 1 H), 4.53–4.49 (m, 2 H), 3.97 (qd, *J* = 6.5, 4.0 Hz, 1 H), 2.60 (ddd, *J* = 18, 10.1, 6.1 Hz, 1 H), 2.48 (ddd, *J* = 17.9, 10.2, 7.6 Hz, 1 H), 2.21 (m, 1 H), 2.11 (m, 1 H), 1.90 (dd, *J* = 6.9, 1.6 Hz, 3 H), 1.18 (d, *J* = 6.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.5, 165.6, 145.9, 131.3, 127.8, 122.3, 81.6, 77.3, 71.7, 69.0, 28.4, 21.0, 18.3, 18.0.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{20}O_6Na$: 307.1158; found: 307.1162.

Arundinolide B

Method A: To a stirred solution of **19** (13 mg, 0.046 mmol) and cuprous chloride (4 mg, 0.046 mmol) in a mixture of THF (0.6 mL) and EtOH (1.4 mL), $NaBH_4$ (17 mg, 0.46 mmol) was added portionwise at –40 °C. The reaction mixture was stirred at the same temperature for 1 h, then the reaction mixture was concentrated under reduced pressure, and the residue was diluted with water and extracted with EtOAc (3 × 10 mL). The organic layer was separated, washed with water, brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude material was purified by flash column chromatography (petroleum ether/EtOAc 1:2) to give arundinolide B (10 mg, 78%) as a colorless oil.

Method B: Grubbs' second generation catalyst (7 mg, 0.008 mmol) was added to a mixture of **5** (40 mg, 0.28 mmol) and **17** (96 mg, 0.56 mmol) in anhydrous DCM (10 mL) and the mixture was heated at reflux for 6 h. Upon completion of reaction (TLC), the solution was concentrated and purified by flash column chromatography (petroleum ether/EtOAc 1:2) to give arundinolide B.

Yield: 22 mg (28%); colorless oil; $[\alpha]_D^{20}$ +4.8 (*c* 0.32, $CHCl_3$) {lit.[3] $[\alpha]_D^{20}$ +15 (*c* 0.32, $CHCl_3$)}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.91 (dd, *J* = 15.6, 5.7 Hz, 1 H), 5.77 (dd, *J* = 15.6, 4.7 Hz, 1 H), 4.98 (qd, *J* = 6.5, 3.2 Hz, 1 H), 4.50–4.54 (m, 2 H), 4.27 (t, *J* = 4.4 Hz, 1 H), 2.61 (ddd, *J* = 18.1, 10.1, 6 Hz, 1 H), 2.49 (ddd, *J* = 17.8, 10.2, 7.6 Hz, 1 H), 2.31 (t, *J* = 7.4 Hz, 2 H), 2.22 (m, 1 H), 2.13 (m, 1 H), 1.66 (dq, *J* = 4.8, 7.4 Hz, 2 H), 1.21 (d, *J* = 6.5 Hz, 3 H), 0.96 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.3, 173.6, 131.1, 129.2, 81.7, 73.9, 73.2, 71.8, 36.3, 28.5, 21.0, 18.5, 14.7, 13.6.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{22}O_6Na$: 309.1314; found: 309.1311.

Funding Information

We thank the foundation support from the National Key Research and Development Program of China (2016YFA0203102), the Strategic Priority Research Program of Chinese Academy of Sciences (Grant XDB14040201), National Natural Science Foundation of China (Projects 21302150 and 21602082), Science and Technology Department of Hubei Province (2019CFB596), Chen-Guang program from Hubei Association for Science and Technology, Ministry-of-Education Key Laboratory for the Synthesis and Application of Organic Functional Molecules, Hubei University (KLSAOFM1810), Key Laboratory of Hubei Province for Coal Conversion and New Carbon Materials, Wuhan University of Science and Technology (WKDM202003).

Acknowledgment

We thank Dr. Miao Chen and Xinyi Zhang for HRMS measurements.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1691699.

References

(1) (a) Reino, J. L.; Guerrero, R. F.; Hernández-Galán, R.; Collado, I. G. *Phytochem. Rev.* **2008**, *7*, 89. (b) Mukherjee, P. K.; Horwitz, B. A.; Kenerley, C. M. *Microbiology* **2012**, *158*, 35. (c) Lorito, M.; Woo, S. L.; Harman, G. E.; Monte, E. *Annu. Rev. Phytopathol.* **2010**, *48*, 395.

(2) (a) Desjardins, A. E. *Fusarium Mycotoxins. Chemistry, Genetics and Biology*; The American Phytopathological Society: St. Paul, **2006**. (b) McCormick, S. P.; Stanley, A. M.; Stover, N. A.; Alexander, N. J. *Toxins* **2011**, *3*, 802.
(3) Izquierdo-Bueno, I.; Moraga, J.; Cardoza, R. E.; Lindo, L.; Hanson, J. R.; Gutiérrez, S.; Collado, I. G. *Org. Biomol. Chem.* **2018**, *16*, 2955.
(4) (a) Fuchser, J.; Zeeck, A. *Liebigs Ann./Recl.* **1997**, 87. For total synthesis of aspinolide B, see: (b) Chang, C.; Geng, J.; Du, Y.; Lv, Q.; Dong, Z.; Liu, J. *Tetrahedron* **2019**, *75*, 3933. (c) Krishna, P. R.; Narsingam, M. *Synthesis* **2007**, 3627. (d) Ghosh, S.; Rao, R. V. *Tetrahedron Lett.* **2007**, *48*, 6937. (e) Pilli, R. A.; Victor, M. M.; de Meijere, A. *J. Org. Chem.* **2000**, *65*, 5910.
(5) (a) Geng, J.; Ren, Q.; Chang, C.; Xie, X.; Liu, J.; Du, Y. *RSC Adv.* **2019**, *9*, 10253. (b) Gao, Y.; Liu, J.; Qiao, J.; Liu, Y.; He, P.; Du, Y. *Tetrahedron Lett.* **2018**, *59*, 291. (c) Liu, Y.; He, P.; Zhang, Y.; Zhang, X.; Liu, J.; Du, Y. *J. Org. Chem.* **2018**, *83*, 3897. (d) Gao, Y.; Liu, J.; Wang, L.; Xiao, M.; Du, Y. *Eur. J. Org. Chem.* **2014**, 2092.
(6) (a) Schmidt, B.; Biernat, A. *Chem. Eur. J.* **2008**, *14*, 6135. (b) Liu, J.; Gao, Y.; Wang, L.; Du, Y. *Tetrahedron* **2017**, *73*, 6443.
(7) Wender, P. A.; Bi, F. C.; Buschmann, N.; Gosselin, F.; Kan, C.; Kee, J.-M.; Ohmura, H. *Org. Lett.* **2006**, *8*, 5373.
(8) It is noteworthy that that the Wittig reaction of stabilized ylides with α- or β-alkoxy aldehyde can stereoselectively produce (*Z*)-α,β-unsaturated ester in alcoholic solvents, and the correlation between the stereoselectivity of the reaction and the structure of the starting aldehyde was also well established. For a comprehensive review, see: Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863.
(9) Narisada, M.; Horibe, I.; Watanabe, F.; Takeda, K. *J. Org. Chem.* **1989**, *54*, 5308.
(10) He, R.; Deng, M.-Z. *Tetrahedron* **2002**, *58*, 7613.
(11) Pak, C. S.; Lee, E.; Lee, G. H. *J. Org. Chem.* **1993**, *58*, 1523.
(12) The known (+)-**15** was prepared from L-ethyl lactate over nine steps, see: Sharma, G. V. M.; Babu, K. V. *Tetrahedron: Asymmetry* **2007**, *18*, 2175.
(13) It is well known that *tert*-butyldimethylsilyl (TBS) groups can migrate between vicinal diols under basic conditions. For selected examples of NaH-mediated TBS migration, see: (a) Lassaletta, J. M.; Meichle, M.; Weiler, S.; Schmidt, R. R. *J. Carbohydr. Chem.* **1996**, *15*, 241. (b) Furegati, S.; White, A. J. P.; Miller, A. D. *Synlett* **2005**, 2385. (c) Ashton, P. R.; Boyd, S. E.; Gattuso, G.; Hartwell, E. Y.; Königar, R.; Spencer, N.; Stoddart, J. F. *J. Org. Chem.* **1995**, *60*, 3898. (d) Phanumartwiwath, A.; Hornsby, T. W.; Jamalis, J.; Bailey, C. D.; Willis, C. L. *Org. Lett.* **2013**, *15*, 5734.
(14) Boden, E. P.; Keck, G. E. *J. Org. Chem.* **1985**, *50*, 2394.
(15) (a) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953. (b) Chatterjee, A. K.; Choi, T. L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360.
(16) Isomerization of allylic alcohols to ketones using catalytic or stoichiometric amounts of ruthenium complexes has been reported. For other reports of ethyl ketone formation from allylic alcohols under olefin metathesis reaction using Grubbs reagents, see: (a) Sworen, J. C.; Pawlowa, J. H.; Case, W.; Lever, J.; Wagener, K. B. *J. Mol. Catal. A: Chem.* **2003**, *194*, 69. (b) Nakashima, K.; Ito, R.; Sono, M.; Tori, M. *Heterocycles* **2000**, *53*, 301.
(17) Hong, S. H.; Sanders, D. P.; Lee, C. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2005**, *127*, 17160.
(18) For selected examples of homodimerization suppression by silyl group protection, see: (a) Nakashima, K.; Okamoto, S.; Sono, M.; Tori, M. *Molecules* **2004**, *9*, 541. (b) Sabitha, G.; Reddy, S. S. S.; Bhaskar, V.; Yadav, J. S. *Synthesis* **2010**, 1217.
(19) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168.