BCSJ Award Article

Total Synthesis and Biological Evaluation of Auripyrones A and B

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The total synthesis of auripyrones was achieved by using a novel aldol-type reaction of γ-pyrone as a key step. From this synthetic work, we have established the stereostructure and absolute configuration of auripyrone B. Furthermore, the cytotoxicities of auripyrones against a panel of 39 human cancer cell lines (termed JFCR39) at the Japanese Foundation for Cancer Research were investigated. The patterns of the differential cytotoxicities of auripyrones were COMPARE negative, suggesting that they inhibit cancer cell proliferation through a novel mechanism.

A number of significant biologically active γ-pyrone-containing compounds from marine animals have been reported.[1] The structural features of these γ-pyrone-containing compounds are asymmetric centers at the neighboring positions of the γ-pyrone part. In 1996, Yamada and co-workers reported the isolation of auripyrones A (**1**) and B (**2**) from the sea hare *Dolabella auricularia* (Aplysiidae), which exhibit cytotoxicity against HeLa S_3 cells with IC_{50} values of 0.26 and 0.48 μg mL^{-1}, respectively (Figure 1).[2] The relative stereochemistry of the core unit of auripyrones A (**1**) and B (**2**) was determined by an extensive analysis of coupling constants and the NOESY correlations. The main structural features of auripyrones are a γ-pyrone ring and a spiroacetal moiety. The unique structures of auripyrones, in conjunction with their biological activities, have made them attractive synthetic targets. Several groups have reported approaches to the synthesis of auripyrones. In 2006, Perkins and Lister were the first to achieve the total synthesis of auripyrone A (**1**), featuring spiroacetalization.[3] This synthesis established the absolute configuration of auripyrone A (**1**). In 2009, Jung and Salehi-Rad achieved the total synthesis of auripyrone A (**1**) by using a tandem non-aldol aldol/Paterson aldol process.[4] The next year, we preliminarily reported the total synthesis of auripyrones A (**1**) and B (**2**) by using a novel diastereoselective aldol-type reaction of 2,6-diethyl-3,5-dimethyl-4-pyrone (**8**).[5] From this synthetic work, we determined the absolute configuration of auripyrone B (**2**). Very recently, Jung and co-workers reported the total synthesis of auripyrone B (**2**) using their previous strategy.[6] We describe herein the detailed synthesis of auripyrones A (**1**) and B (**2**) and their cytotoxicities against a panel of 39 human cancer cell lines.

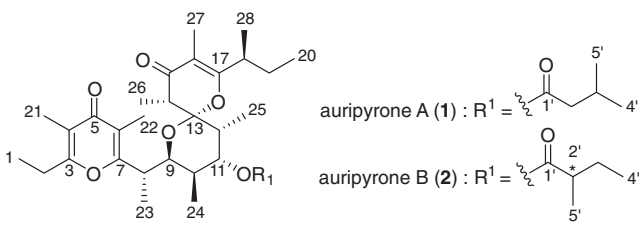

Figure 1. Structures of auripyrones A (**1**) and B (**2**).

Results and Discussion

Our retrosynthetic analyses of auripyrones A (**1**) and B (**2**) are shown in Scheme 1. Auripyrones A (**1**) and B (**2**) can be obtained from triketone **3** by using spiroacetalization. Triketone **3** can be derived from C1–C13 segment **4** and C14–C20 segment **5** by using the aldol coupling reaction. Asymmetric centers at C11 and C12 of C1–C13 segment **4** can be constructed from aldehyde **7** by asymmetric crotylboration. Aldehyde **7**, which possesses an asymmetric center at the neighboring position of γ-pyrone, can be synthesized from 2,6-diethyl-3,5-dimethyl-4-pyrone (**8**) and the optically active aldehyde **9** by diastereoselective aldol-type reaction as a key step.[7,8]

Synthesis of C1–C13 Segment. Previously, we reported diastereoselective aldol-type reaction of γ-pyrone (**8**) with NaHMDS[7] and the Mukaiyama aldol-type reaction of silyl enol

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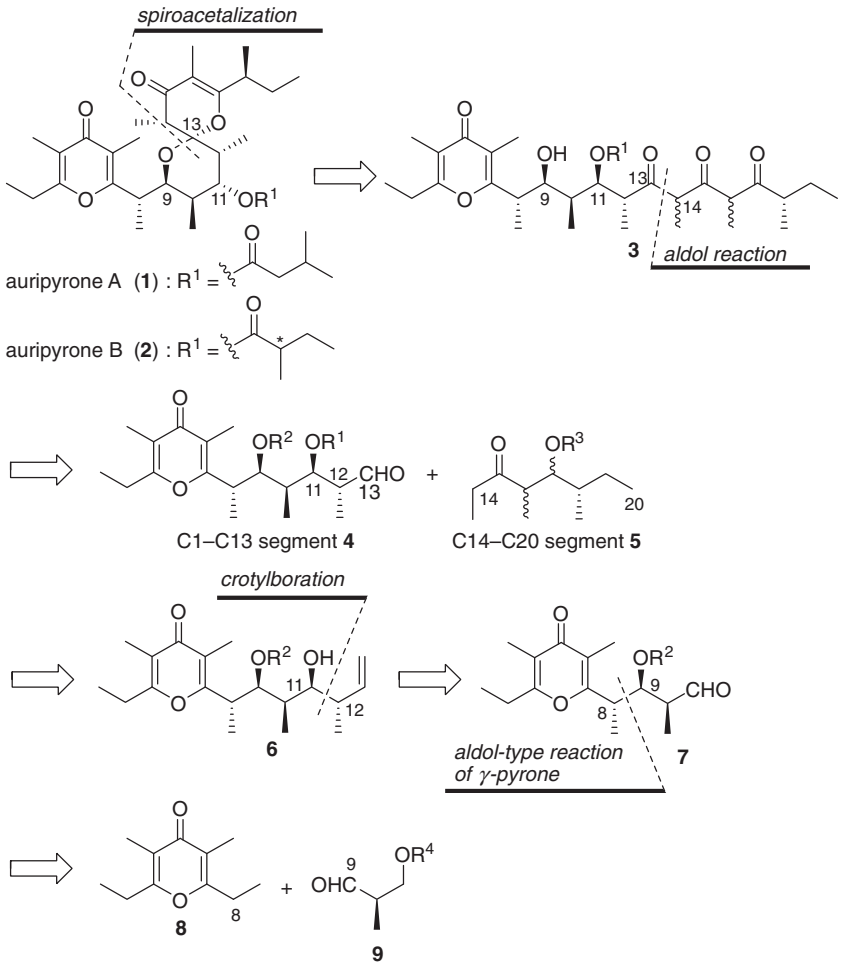
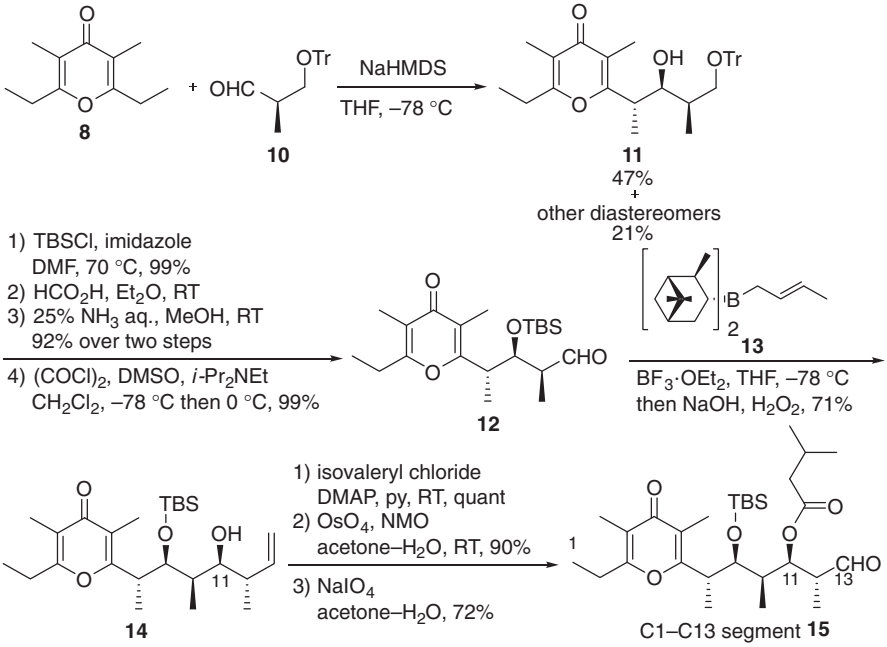


Scheme 1. Retrosynthetic analyses of auripyrones A (**1**) and B (**2**).

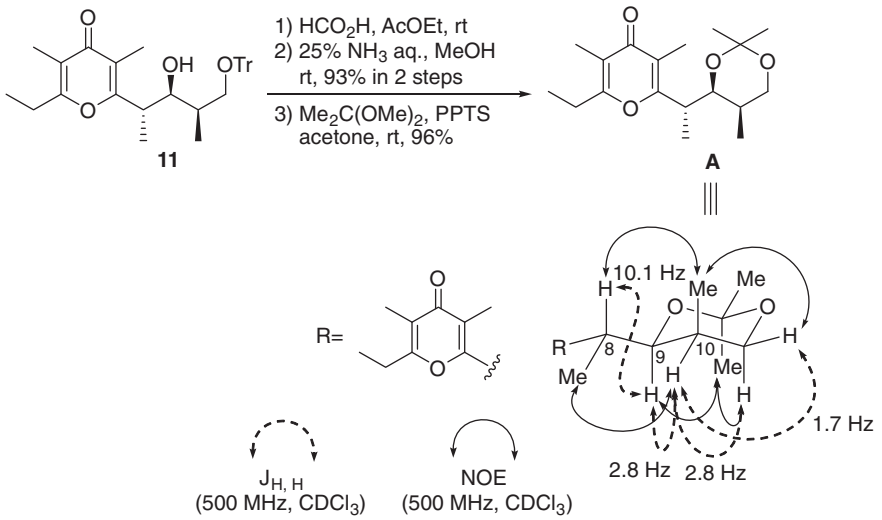
ether of γ-pyrone **8**.[8] These approaches have the benefits of straightforward access even to complex molecules and of the construction of two stereogenic centers at once. Therefore, we planned the synthesis of auripyrones A (**1**) and B (**2**) starting from this aldol-type reaction between γ-pyrone (**8**) and optically active aldehyde **10**.[9] First, we tried the aldol-type reaction with NaHMDS to afford the desired compound **11** in 47% yield along with other diastereomers (21%) (Scheme 2). Although we attempted a Mukaiyama aldol-type reaction between the silyl enol ether of γ-pyrone **8** and aldehyde **10** by using $TiCl_4$ to give the desired aldol adduct **11**, the yield and diastereoselectivity were low (desired aldol adduct **11**: 17% yield, other diastereomers: 21%). The configuration of **11** was determined from ^{1}H NMR of the corresponding acetonide derivative **A** including NOESY correlations (Scheme 3). Protection of the secondary hydroxy group in aldol adduct **11** gave a TBS ether, which was transformed into aldehyde **12** by removal of the trityl group and oxidation of the resulting primary hydroxy group. Aldehyde **12** was converted into homoallylic alcohol **14** as a single diastereomer via Brown crotylation using the (*E*)-crotyl boronate **13**.[10] The stereochemistry of **14** was determined as follows. Homoallylic alcohol **14** was converted into 1,3-acetonide **B**, the stereochemistry of which was confirmed to be *syn* by the ^{13}C chemical shifts of two acetonide methyls (δ_C 19.2 and 29.8) (Scheme 4).[11] Furthermore, 1,3-acetonide **B** was converted into 1,3-acetonide **C**, and the configuration at C11 and C12 in **C** was determined by ^{1}H–^{1}H coupling constants and NOESY correlations. Introduction of the isovaleryl group at C11 in homoallylic alcohol **14** and dihydroxylation of the terminal olefin afforded a diol, which was converted into aldehyde **15** as a C1–C13 segment. This two-step procedure was superior to the direct Lemieux–Johnson conditions[12] in both yield and reproducibility because of the instability of aldehyde **15**.

Synthesis of C14–C20 Segment. Next, we prepared C14–C20 segment **17** (Scheme 5). Oxidation of commercially available (*S*)-2-methy-1-butanol gave aldehyde **16**.[13] The aldol reaction of aldehyde **16** and 3-pentanone with LDA followed by the protection of the resulting secondary hydroxy group as the TES ether gave C14–C20 segment **17** as a diastereomeric mixture. This segment **17** was used for the next reaction without separation of diastereomers because the configurations of these newly generated stereocenters were lost by oxidation and epimerization in subsequent steps.

Total Synthesis of Auripyrone A. With C1–C13 segment **15** and C14–C20 segment **17** in hand, we next tried the aldol coupling reaction between two segments. First, we attempted the aldol coupling reaction between model compounds **18** and **17** with LDA, LHMDS, and NaHMDS, but the yields were low (9–43%) (Table 1). We then examined the deuteration of C14–



Scheme 2. Synthesis of C1–C13 segment **15**.

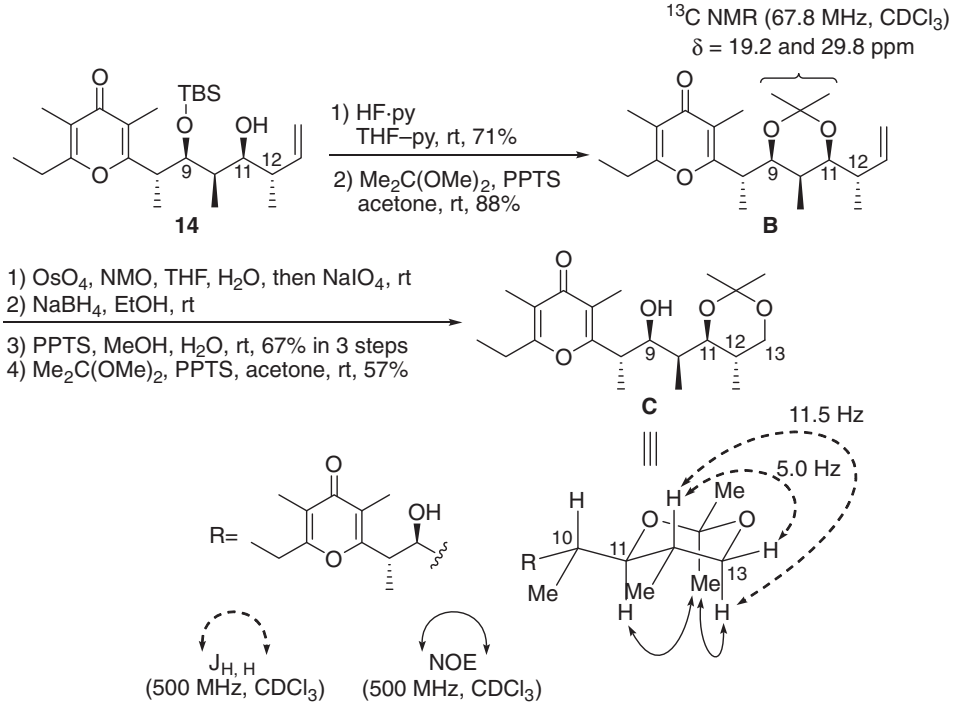


Scheme 3. Determination of stereochemistry of **11**.

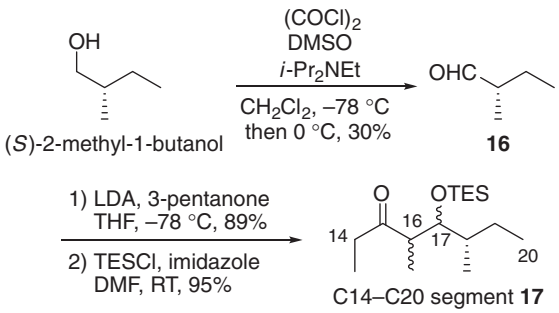
C20 segment **17**, as depicted in Table 2. Interestingly, treatment of **17** with LDA or LHMDS, followed by the addition of D_2O, did not give the deuterated compound **20** (Entries 1 and 2). In Entries 3 and 4, the enolate of **17** prepared with KHMDS and NaHMDS, respectively, gave a deuterated compound **20** in 70% yields in both cases. However, as we reported that γ-pyrone **8** is easily deprotonated by using metal bis(trimethylsilyl)amides (deuteration yield: >95%),[7,8] model compound **18** (C2 position) was expected to be more easily deprotonated at the C2 position of γ-pyrone than C14–C20 segment **17** was at the C14 position, reducing the yield of the aldol adduct. Therefore, we attempted an aldol reaction with a weaker base. The Mukaiyama Sn(II)-promoted aldol reaction[14] between C1–C13 segment **15** and C14–C20 segment **17** using $Sn(OTf)_2$ and Et_3N afforded coupling compound **21** in 99% yield as a diastereomeric mixture (Scheme 6).

Next, we tried to synthesize auripyrone A (**1**) from coupling compound **21** (Scheme 7). Selective removal of the TES group in **21** gave a diol, which was oxidized into triketone **22** as an equilibrium mixture of the keto and enol forms. Removal of the TBS group in triketone **22** by HF·py was accompanied by spiroacetalization to give auripyrone A (**1**) as a single isomer. The synthetic auripyrone A (**1**) is identical in all respects to the natural product.[2]

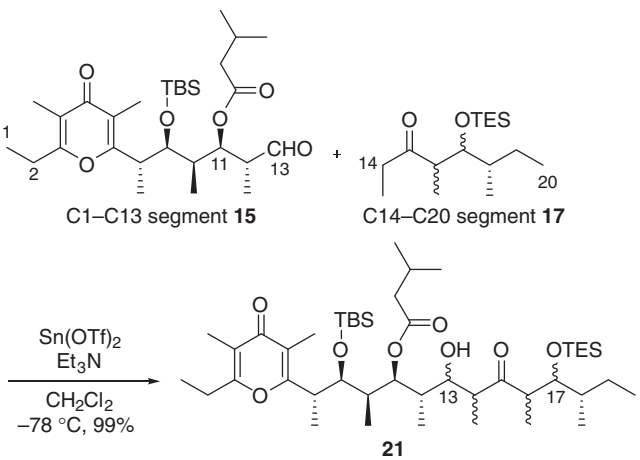
Stereocontrol in the spiroacetalization to auripyrone A (**1**) can be explained as follows (Figure 2). Triketone **22** was converted into hemiacetals **23a** and **23b**. The stereochemistry of spiro carbon (C13) in **23a** and **23b** was controlled by the double anomeric effect. The C14 methyl group in hemiacetal **23a** was epimerized into the equatorial position (hemiacetal **23b**) so as to avoid a 1,3-diaxial interaction between the C12 and C14 methyl groups in **23a** via β-diketone form **22**.



Scheme 4. Determination of stereochemistry of **14**.

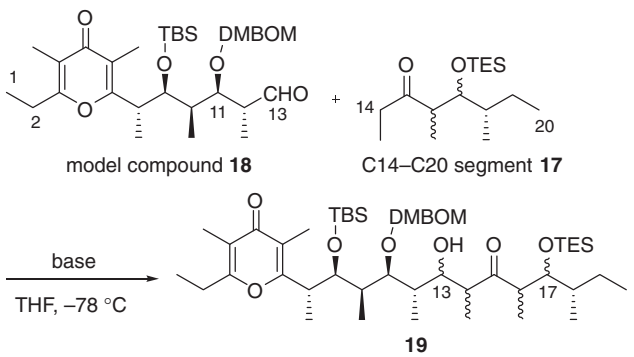


Scheme 5. Synthesis of C14–C20 segment **17**.



Scheme 6. Aldol coupling reaction between C1–C13 segment **15** and C14–C20 segment **17**.

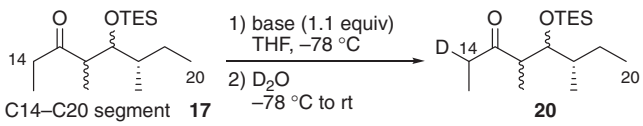
Table 1. Study of Aldol Coupling Reaction[a)]



Entry	Base	Yield/%
1	LDA	9
2	LHMDS	17
3	NaHMDS	43

a) DMBOM: [(3,4-dimethoxybenzyl)oxy]methyl.

Table 2. Deuteration of Ketone **17**

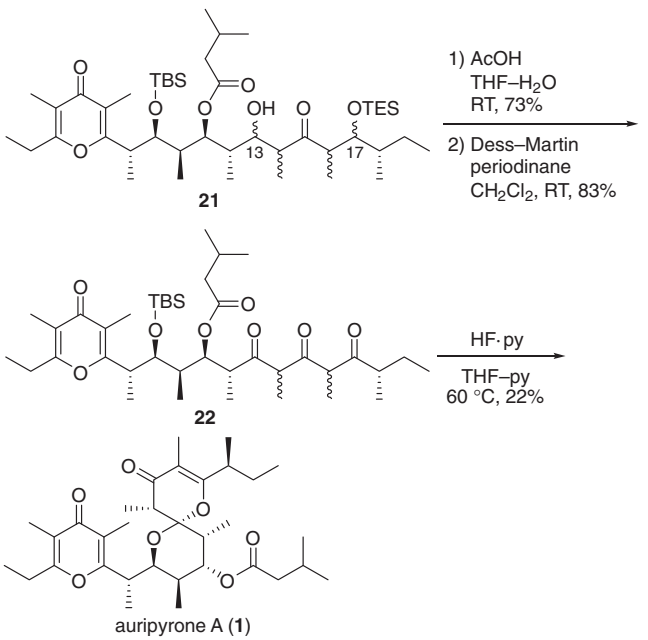


Entry	Base	Recovered ketones	Yield of deuterated compound **20**/%[a)]
1	LDA	quant.	0
2	LHMDS	quant.	0
3	KHMDS	quant.	70
4	NaHMDS	quant.	70

a) The deuteration yield was calculated by ^{1}H NMR.

Total Synthesis of (2′*S*)- and (2′*R*)-Auripyrones B. We next tried the synthesis of (2′*S*)- and (2′*R*)-auripyrones B to determine the absolute structure of auripyrones B (**2**). Therefore, we planned the conversion of auripyrone A (**1**) into B (**2**) by removal of the isovaleryl group at C11 in auripyrone A (**1**) and subsequent esterification with optically active 2-methylbutanoic acid. Thus, hydrolysis of the isovaleryl group of auripyrone A (**1**) with LiOH in aqueous methanol was attempted (Scheme 8). However, we could not obtain the desired deacyl derivative **24**, but a bis(pyrone) compound **25**. Bis(pyrone) compound **25** was thought to be produced by deprotonation at C14 and elimination.

On the other hand, Jung and co-workers reported that the hydrolysis of auripyrone A (**1**) under similar conditions (KOH(aq)/THF) gave the C14-epimerized elimination compounds **26** and **27** (Scheme 9).[6] From these results, auripyrone A (**1**) was shown to be easily deprotonated at the C14 position under basic conditions, causing side reactions.



Scheme 7. Total synthesis of auripyrone A (**1**).

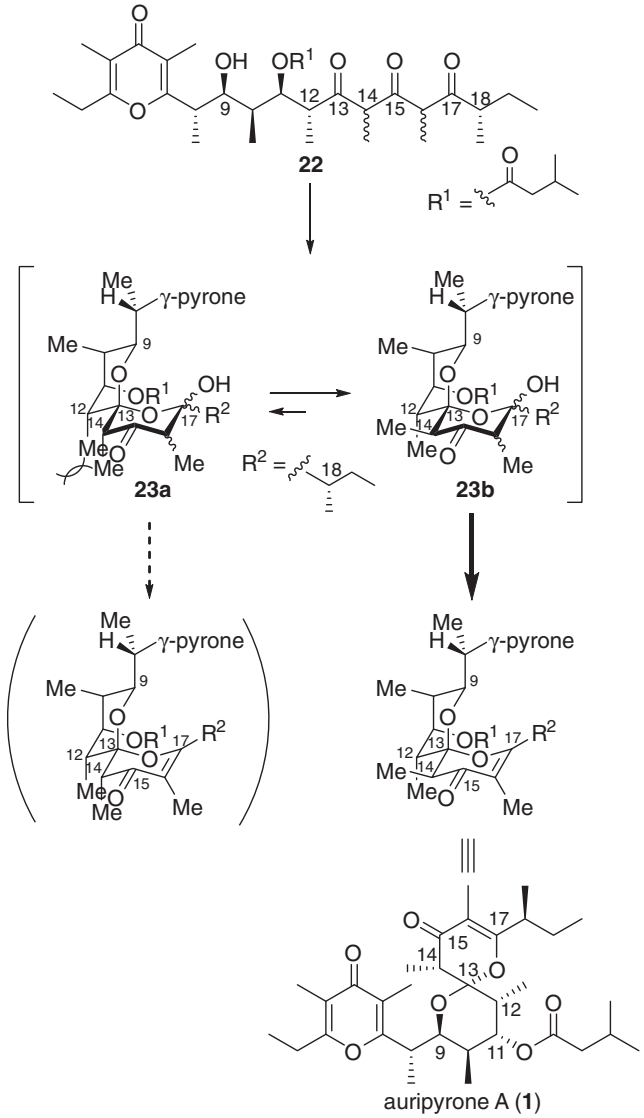
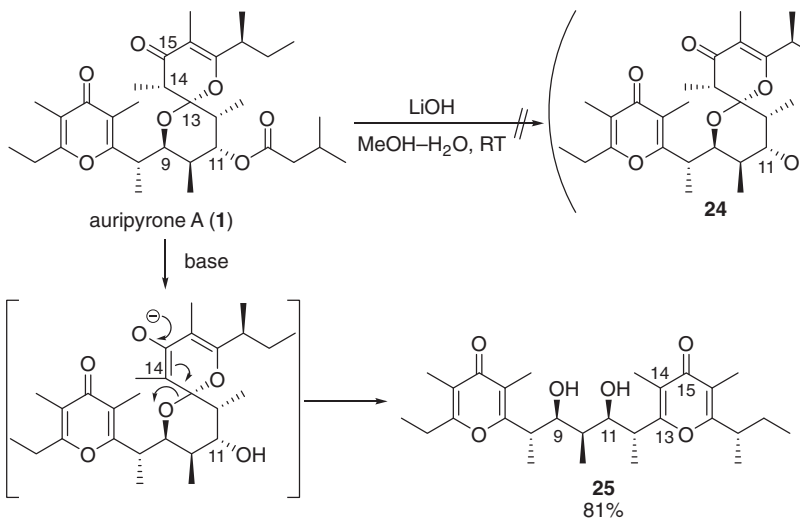
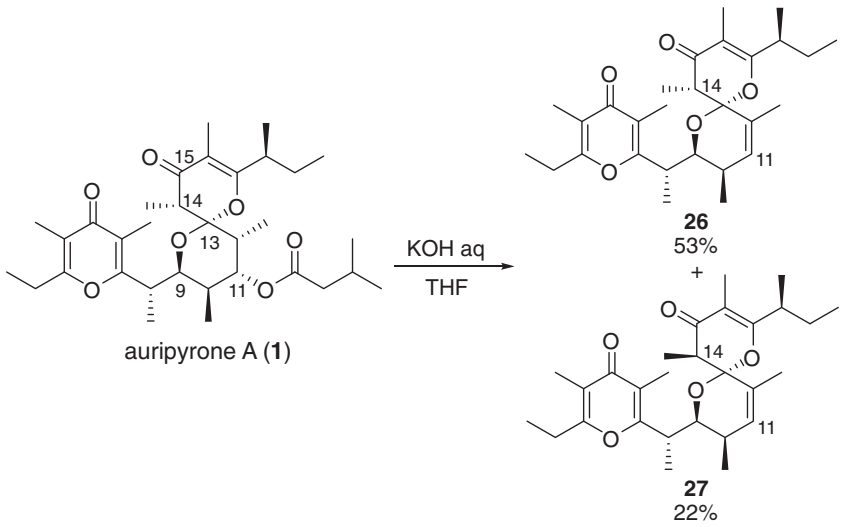


Figure 2. Spiroacetalization of triketone **22**.



Scheme 8. Hydrolysis of auripyrone A (**1**).



Scheme 9. Hydrolysis of auripyrone A (**1**) by Jung and co-workers.

Therefore, we attempted the synthesis of auripyrone B (**2**) by using our synthetic strategy for auripyrone A (**1**) (Scheme 10). Esterification between homoallylic alcohol **14** and (*S*)-2-methylbutanoic (**28**)[15] by using Yamaguchi conditions[16] gave compound **29**. The terminal olefin in **29** was transformed into a diol, which was oxidatively cleaved to afford aldehyde **30**. The coupling reaction between aldehyde **30** and C14–C20 segment **17** via the Mukaiyama Sn(II)-promoted aldol reaction[14] gave the coupling product **31** as a diastereomeric mixture. Removal of the TES group in **31** and subsequent oxidation of the diol group afforded triketone **32** as a mixture of the keto and enol forms, a precursor of spiroacetalization. Removal of the TBS group in triketone **32** by HF·py and a spontaneous spiroacetalization gave (2′*S*)-auripyrone B (**33**).

Also, (2′*R*)-auripyrone B (**36**) was synthesized from homoallylic alcohol **14** in the same manner with (*R*)-2-methylbutanoic (**34**) (Scheme 11).

Determination of the Absolute Configuration of Auripyrone B. With both diastereomers (2′*S*)-auripyrone B (**33**) and (2′*R*)-auripyrone B (**36**) in hand, the determination of configuration of C2′ in auripyrone B was determined by comparing the ^{1}H NMR spectra of synthetic samples with those reported for the natural auripyrone B (**2**) (Figure 3). The chemical shifts of protons in the acyl group (H4′, H5′) in (2′*S*)-auripyrone B (**33**) were different from those of (2′*R*)-auripyrone B (**36**). The ^{1}H NMR data of (2′*S*)-auripyrone B (**33**) were in good agreement with those of the natural one. Furthermore, comparison of the optical rotations of synthetic (2′*S*)-auripyrone B (**33**) and natural auripyrone B (**2**) determined the absolute configuration of auripyrone B (**2**): The optical rotation of synthetic (2′*S*)-auripyrone B (**33**) $\{[\alpha]_D^{25} = +43$ ($c = 0.29$, $CHCl_3$)$\}$ was in accordance with that of the natural one[2] $\{[\alpha]_D^{25} = +39$ ($c = 0.14$, $CHCl_3$)$\}$ to clarify the absolute configuration of auripyrone B (**2**) as depicted in Figure 4.

Biological Evaluation of Auripyrones A and B. Table 3 shows the cytotoxic activities of auripyrones A (**1**) and B (**2**), 2′-*epi* auripyrone B (**36**), and bis(pyrone) compound **25** against HeLa S_3 cells. Auripyrones A (**1**) showed an IC_{50} value of cytotoxic activity equivalent to that of auripyrone B (**2**). The IC_{50} values of synthetic auripyrones A (**1**) and B (**33**) were about 10-fold larger (less cytotoxic) than the reported IC_{50} values of natural auripyrones,[2] maybe because of the condition of the HeLa S_3 cells. 2′-*epi* Auripyrone B (**36**) showed cytotoxicity, with an IC_{50} of 3.4 μg mL^{-1}. From these results, the structure of the O^{11}-acyl group in auripyrones was shown to be unimportant for cytotoxicity. On the other hand, bis(pyrone) compound **25** showed no cytotoxicity even at 10 μg mL^{-1}. This result suggested that the spiro structure of auripyrones is essential for their cytotoxicity.

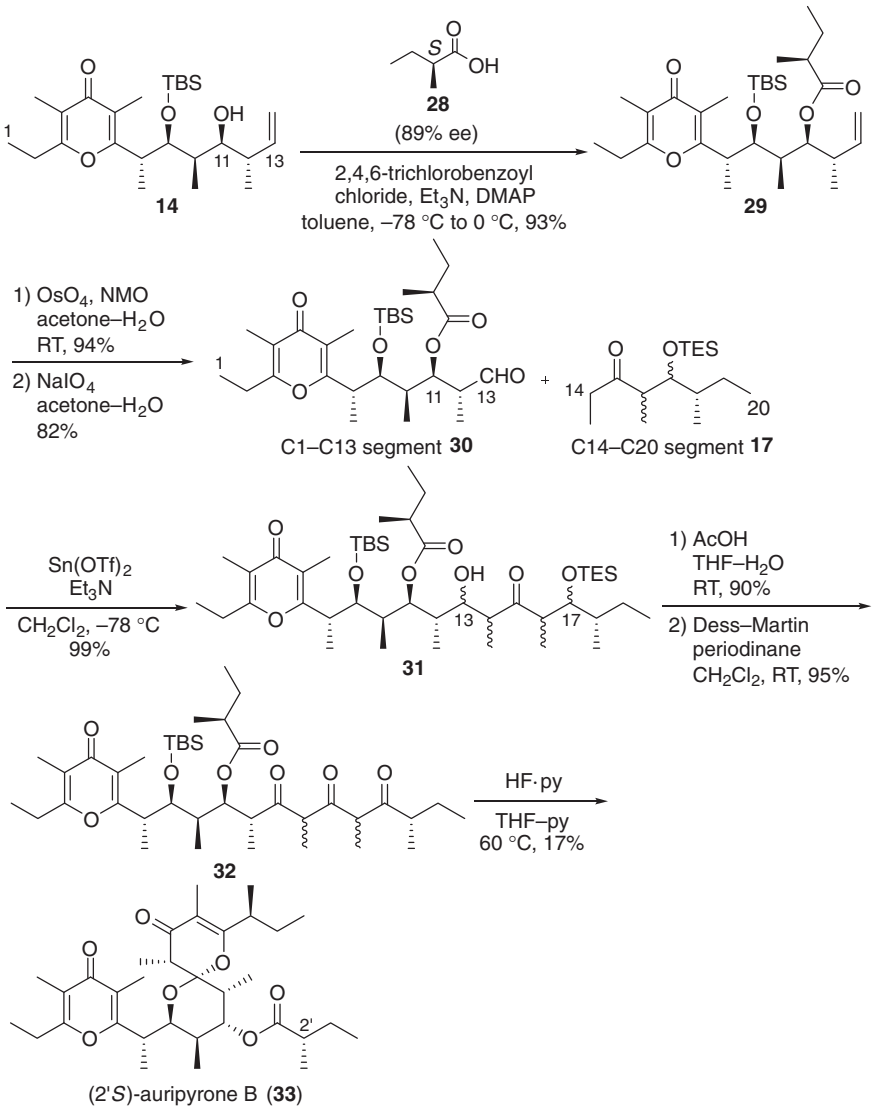
The cytotoxicities of synthetic auripyrones A (**1**) and B (**33**) were evaluated against a panel of 39 human cancer cell lines (termed JFCR39) at the Japanese Foundation for Cancer Research (Table 4). Auripyrones A (**1**) and B (**33**) each showed broad cytotoxicity in the panel, respectively. On the basis of the COMPARE analysis,[17] the patterns of the differential cytotoxicities of auripyrones A (**1**) and B (**33**) suggested that they inhibited cancer cell proliferation through a novel mechanism.

Conclusion

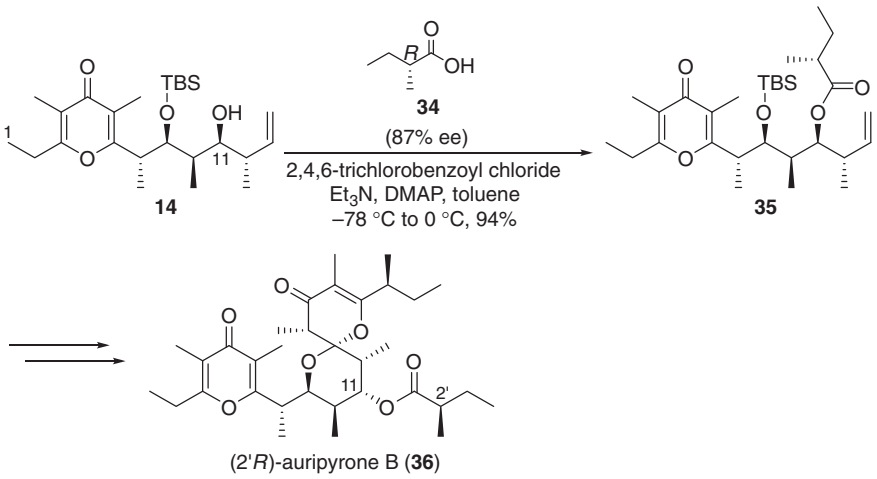
In conclusion, we have achieved the total synthesis of auripyrones A (**1**) (2.6% overall yield in 13 steps) and B (**2**) (2.8% overall yield in 13 steps), featuring a diastereoselective aldol-type reaction between 2,6-diethyl-3,5-dimethyl-4-pyrone (**8**) and optically active aldehyde **10** to construct three contiguous stereocenters. From this synthetic work, we have established the stereostructure and absolute configuration of auripyrone B (**2**). Furthermore, we have investigated the cytotoxicities of auripyrones against a panel of 39 human cancer cell lines. Auripyrones A (**1**) and B (**2**) were COMPARE-negative, suggesting that they inhibit cancer cell proliferation through a novel mechanism. Further studies on the synthesis of O^{11}-modified probe molecules of auripyrones for use in the search for target biomolecules are currently in progress.

Experimental

General. All reagents and dry solvents were used as obtained from commercial supplies unless otherwise noted. Organic solvents for moisture-sensitive reactions were distilled



Scheme 10. Total synthesis of (2′*S*)-auripyrone B (**33**).



Scheme 11. Total synthesis of (2′*R*)-auripyrone B (**36**).

by standard procedure. Column chromatography was performed using silica gel (75–200 or 45–75 μm). All moisture-sensitive reactions were performed under an atmosphere of argon or nitrogen, and the starting materials were azeotropically dried with benzene before use. Optical rotations were measured on digital polarimeter at room temperature, using

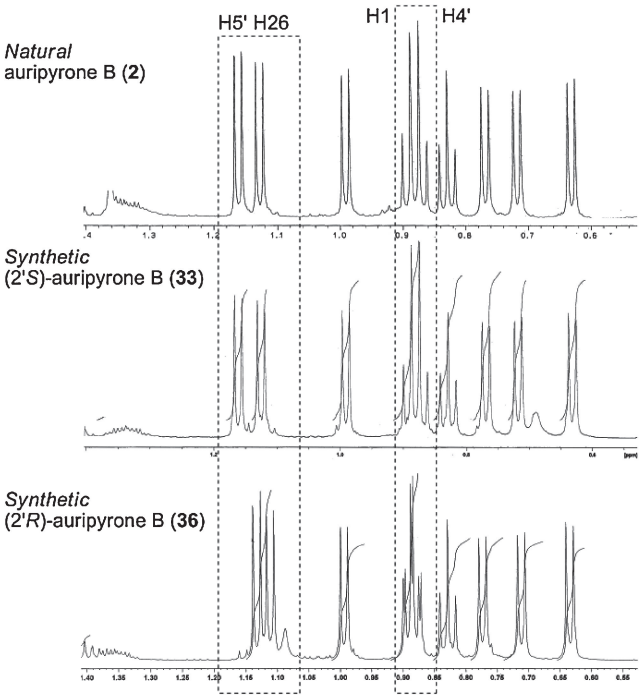
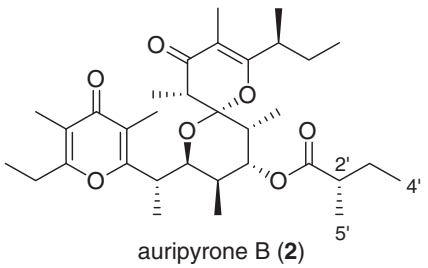


Figure 3. Partial ^{1}H NMR spectra (600 MHz, C_6D_6) of synthetic auripyrone B and of the natural one.



auripyrone B (**2**)

Figure 4. Absolute stereochemistry of auripyrone B (**2**).

Table 3. Cytotoxicities of Auripyrones and Their Analogues Against HeLa S_3 Cells

	IC_{50} values/μg mL^{-1}
Auripyrone A (**1**)	3.1 (lit. 0.26)
Auripyrone B (**33**)	3.1 (lit. 0.48)
2′-*epi* Auripyrone B (**36**)	3.4
Bis(pyrone) compound **25**	>10

the sodium D line. Infrared (IR) spectra were recorded on a FT IR system and only selected peaks are reported. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were run at various field strengths as indicated. The ^{1}H and ^{13}C chemical shifts (δ) are reported in parts per million (ppm) downfield relative to tetramethylsilane (TMS), $CDCl_3$ (δ_H 7.26 and δ_c 77.0) or C_6D_6 (δ_H 7.16 and δ_c 128.0). Coupling constants (J) are reported in Hz. Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. High-resolution mass spectra (HRMS) were recorded by electrospray ionization (ESI)/time-of-flight (TOF) experiments. Melting points are uncorrected.

Table 4. GI_{50} Values of Auripyrones A (**1**) and B (**33**) against 39 Human Cancer Cell Lines

	Cell line	GI_{50}[a),b)]/μM	
		Auripyrone A (**1**)	Auripyrone B (**33**)
Breast	HBC-4	4.3	3.5
	BSY-1	2.0	1.9
	HBC-5	5.2	3.6
	MCF-7	4.5	3.7
	MDA-MB-231	4.3	2.5
Central nervous system	U251	4.5	3.0
	SF-268	15>	4.5
	SF-295	3.9	2.9
	SF-539	12	2.4
	SNB-75	3.1	2.0
	SNB-78	8.5	3.4
Colon	HCC2998	2.6	1.8
	KM-12	3.4	2.6
	HT-29	3.3	2.8
	HCT-15	4.6>	2.6
	HCT-116	3.4	2.3
Lung	NCI-H23	3.5	2.9
	NCI-H226	4.6	3.8
	NCI-H522	2.4	1.8
	NCI-H460	4.7	3.2
	A549	5.1	3.2
	DMS273	3.5	2.4
	DMS114	3.5	2.2
Melanoma	LOX-IMVI	5.5	2.2
Ovary	OVCAR-3	2.9	2.1
	OVCAR-4	3.6	2.8
	OVCAR-5	10>	3.7
	OVCAR-8	6.7	3.6
	SK-OV-3	13	3.7
Kidney	RXF-631L	7.3	3.0
	ACHN	5.7	3.5
Stomach	St-4	4.4	3.7
	MKN1	2.8	2.5
	MKN7	2.1	2.3
	MKN28	3.0	2.5
	MKN45	2.8	2.3
	MKN74	2.6	2.6
Prostate	DU-145	20>	4.4
	PC-3	3.5	2.9
MG-MID[c)]		−5.35	−5.55
Delta[d)]		0.36	0.19
Range[e)]		1	0.4

a) Concentrations for the inhibition of cell growth at 50% relative to control. b) Cell growth was determined according to the sulforhodamine B assay. c) Mean GI_{50} value in all of the cell lines tested. d) Difference in the GI_{50} value between the most-sensitive cells and the MG-MID value. e) Difference in the log GI_{50} value between the most- and least-sensitive cells.

Aldol 11. To a stirred solution of 2,6-diethyl-3,5-dimethyl-4-pyrone (**8**) (200 mg, 1.11 mmol) in THF (1.5 mL) was added NaHMDS (1.0 M solution in THF, 1.15 mL, 1.15 mmol) at −78 °C. After being stirred at −78 °C for 1.5 h, a solution of

aldehyde **10** (275 mg, 0.832 mmol) in THF (1.5 mL) was added via cannula. The mixture was stirred at −78 °C for 2.3 h, diluted with saturated aqueous NH_4Cl (10 mL), and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (30 g, hexane–EtOAc 7:1 → 3:1) to give a diastereomeric mixture of aldols (290 mg, 68%) and recovered 2,6-diethyl-3,5-dimethyl-4-pyrone (**8**) (74.5 mg, 37%). Further purification of the diastereomeric mixture of aldols by column chromatography on silica gel (FL-60D, 26 g, benzene–acetone 20:1; FL-60D, 12 g, benzene–acetone 20:1) gave aldol **11** (199 mg, 47%) and an inseparable mixture of undesired diastereomers (90.6 mg, 21%) as colorless powder, respectively: $R_f = 0.33$ (1:1 hexane/EtOAc); mp 136–138 °C; $[\alpha]_D^{23}$ −7.2 (*c* 0.90, $CHCl_3$); IR ($CHCl_3$): 3500 (br), 1655, 1595 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 7.45–7.40 (m, 6H), 7.34–7.20 (m, 9H), 4.10 (dd, $J = 9.7$, 3.2 Hz, 1H), 3.36–3.19 (m, 2H), 3.07 (dq, $J = 9.7$, 7.2 Hz, 1H), 2.62 (q, $J = 7.6$ Hz, 2H), 2.10–1.80 (m, 1H), 1.96 (s, 3H), 1.93 (s, 3H), 1.22 (t, $J = 7.6$ Hz, 3H), 1.12 (d, $J = 7.2$ Hz, 3H), 1.02 (d, $J = 7.1$ Hz, 3H), A signal due to one proton (OH) was not observed; ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 179.5, 164.7, 163.7, 143.6 (3C), 128.4 (6C), 127.7 (6C), 126.9 (3C), 119.1, 117.6, 86.7, 74.1, 67.2, 38.8, 34.8, 24.7, 14.7, 11.2, 9.6, 9.5, 9.2; HRMS (ESI): *m/z* 533.2664, calcd for $C_{34}H_{38}O_4Na$ $[M + Na]^+$ 533.2668.

Aldehyde 12. To a stirred solution of aldol **11** (1.61 g, 3.16 mmol) in DMF (3 mL) were added imidazole (2.10 g, 30.1 mmol) and *tert*-butyldimethylsilyl chloride (2.40 g, 15.9 mmol) at room temperature. The mixture was stirred at 70 °C for 22 h, diluted with H_2O (30 mL) at room temperature, and extracted with Et_2O (3 × 50 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (60 g, hexane–EtOAc 10:1 → 5:1 → 1:1) to give *tert*-butyldimethylsilyl ether **11a** (1.95 g, 99%) as a yellow amorphous solid; $R_f = 0.73$ (1:1 hexane/EtOAc); mp 37–39 °C; $[\alpha]_D^{25}$ +4.1 (*c* 0.405, $CHCl_3$); IR ($CHCl_3$): 1655, 1595 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 7.45–7.36 (m, 6H), 7.35–7.20 (m, 9H), 4.06 (d, $J = 8.9$ Hz, 1H), 3.20–3.00 (m, 3H), 2.68 (dq, $J = 15.2$, 7.6 Hz, 1H), 2.56 (dq, $J = 15.2$, 7.6 Hz, 1H), 2.05–1.88 (m, 1H), 1.94 (s, 3H), 1.94 (s, 3H), 1.25 (t, $J = 7.6$ Hz, 3H), 1.13 (d, $J = 7.0$ Hz, 3H), 0.94 (d, $J = 6.8$ Hz, 3H), 0.63 (s, 9H), −0.35 (s, 3H), −0.48 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 179.6, 164.7, 163.6, 144.1 (3C), 128.5 (6C), 127.5 (6C), 126.7 (3C), 119.3, 117.9, 86.5, 73.6, 66.6, 40.3, 36.8, 25.8 (3C), 24.7, 18.1, 15.1, 11.3, 10.1, 9.8, 9.5, −4.6, −4.7; HRMS (ESI): *m/z* 647.3532, calcd for $C_{40}H_{52}O_4SiNa$ $[M + Na]^+$ 647.3533; Anal. Found: C, 76.47; H, 8.47%. Calcd for $C_{40}H_{52}O_4$: C, 76.88; H, 8.39%.

To a stirred solution of *tert*-butyldimethylsilyl ether **11a** (165 mg, 0.265 mmol) in Et_2O (3 mL) was added formic acid (6 mL) at room temperature. The mixture was stirred at room temperature for 10 min, poured into saturated aqueous $NaHCO_3$ (150 mL) at 0 °C, and extracted with Et_2O (3 × 20 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated to afford a crude formate. The crude formate was dissolved in methanol (9 mL), and 25% aqueous NH_3 (3 mL) was added to the mixture at room temperature. The mixture was stirred at room temperature for 20 min, concentrated, diluted with half-saturated brine (10 mL), and extracted with EtOAc (3 × 10 mL). The combined extracts were dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (10 g, hexane–EtOAc 5:1 → 3:1 → 1:1) to give alcohol **11b** (92.7 mg, 92%) as a colorless oil: $R_f = 0.37$ (1:1 hexane/EtOAc); $[\alpha]_D^{24}$ −2.2 (*c* 0.815, $CHCl_3$); IR ($CHCl_3$): 3416, 1653, 1592, 1463, 1378 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 4.12 (dd, $J = 9.0$, 1.6 Hz, 1H), 3.62–3.45 (m, 2H), 3.20 (dq, $J = 9.0$, 7.0 Hz, 1H), 2.68 (dq, $J = 15.2$, 7.6 Hz, 1H), 2.55 (dq, $J = 15.2$, 7.6 Hz, 1H), 2.05–1.85 (m, 1H), 1.97 (s, 3H), 1.95 (s, 3H), 1.23 (t, $J = 7.4$ Hz, 3H), 1.15 (d, $J = 6.8$ Hz, 3H), 0.93 (d, $J = 7.0$ Hz, 3H), 0.80 (s, 9H), 0.02 (s, 3H), −0.40 (s, 3H), A signal due to one proton (OH) was not observed; ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 179.8, 165.0, 163.9, 119.3, 117.9, 73.1, 65.0, 39.9, 38.6, 25.9 (3C), 24.7, 18.1, 15.2, 11.4, 9.8, 9.5, 9.4, −4.8 (2C); HRMS (ESI): *m/z* 405.2461, calcd for $C_{21}H_{38}O_4SiNa$ $[M + Na]^+$ 405.2437.

To a stirred solution of oxalyl chloride (70.0 μL, 0.800 mmol) in CH_2Cl_2 (0.4 mL) was added DMSO (4.0 M solution in CH_2Cl_2, 0.500 mL, 2.00 mmol) at −78 °C. The mixture was stirred at −78 °C for 30 min, and a solution of alcohol **11b** (151 mg, 0.394 mmol) in CH_2Cl_2 (1.0 mL) was added via cannula. The mixture was stirred at −78 °C for 15 min, and diisopropylethylamine (0.280 mL, 1.61 mmol) was added. The resulting mixture was stirred at −78 °C for 15 min, warmed to 0 °C, and stirred for an additional 15 min. The mixture was diluted with pH 6.8 phosphate buffer (5 mL) and extracted with EtOAc (3 × 10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (6.5 g, hexane–EtOAc 3:1 → 1:1) to give aldehyde **12** (149 mg, 99%) as a colorless oil: $R_f = 0.53$ (1:1 hexane/EtOAc); $[\alpha]_D^{25}$ +29.0 (*c* 0.813, $CHCl_3$); IR ($CHCl_3$): 2827, 2786, 1728, 1655, 1595, 1463, 1426, 1377 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 9.71 (s, 1H), 4.54 (dd, $J = 8.9$, 1.9 Hz, 1H), 3.20 (dq, $J = 8.9$, 7.1 Hz, 1H), 2.70 (dq, $J = 15.2$, 7.6 Hz, 1H), 2.57 (dq, $J = 15.2$, 7.6 Hz, 1H), 2.52 (dq, $J = 1.9$, 6.8 Hz, 1H), 1.97 (s, 3H), 1.95 (s, 3H), 1.26 (t, $J = 7.4$ Hz, 3H), 1.22 (d, $J = 6.8$ Hz, 3H), 1.17 (d, $J = 7.1$ Hz, 3H), 0.74 (s, 9H), −0.09 (s, 3H), −0.34 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 203.9, 179.6, 163.9, 163.5, 119.8, 118.2, 72.3, 49.8, 40.1, 25.7 (3C), 24.8, 18.0, 15.1, 11.5, 9.9, 9.6, 6.4, −4.4, −4.9; HRMS (ESI): *m/z* 403.2275, calcd for $C_{21}H_{36}O_4SiNa$ $[M + Na]^+$ 403.2281.

Homoallylic Alcohol 14. To a stirred solution of potassium *tert*-butoxide (455 mg, 4.05 mmol) in THF (1.3 mL) were added *trans*-2-butene (1.20 mL, 12.9 mmol) and *n*-BuLi (1.57 M solution in hexane, 2.55 mL, 4.00 mmol) at −78 °C. After the mixture was stirred at −40 °C for 1 h, a solution of (−)-*B*-methoxydiisopinocampheylborane (2.10 g, 6.64 mmol) in THF (2.1 mL) was added via cannula at −78 °C. After 40 min, boron trifluoride diethyl etherate (0.754 mL, 6.00 mmol) and a solution of aldehyde **12** (780 mg, 2.05 mmol) in THF (2.3 mL) were added successively. The mixture was stirred at −40 °C for 8.3 h and diluted with a 1:1 mixture of Et_2O and EtOH (10 mL). The mixture was warmed up to room temperature and treated with a 1:1 mixture of 20% H_2O_2 and 20% NaOH (10 mL). After being

stirred for 13 h, the mixture was extracted with EtOAc (3 × 15 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (FL-60D, 25 g, hexane–EtOAc 7:1; FL-60D, 25 g, hexane–EtOAc 7:1; FL-60D, 25 g, hexane–EtOAc 7:1 → 5:1 → 3:1) to give homoallylic alcohol **14** (636 mg, 71%) as colorless powder: R_f = 0.57 (1:1 hexane/EtOAc); mp 24–26 °C; $[\alpha]_D^{26}$ +9.7 (*c* 0.600, $CHCl_3$); IR ($CHCl_3$): 3429, 1653, 1593, 1463, 1428, 1378 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 5.76 (ddd, J = 17.0, 10.5, 8.6 Hz, 1H), 5.15–5.05 (m, 2H), 4.03 (dd, J = 8.1, 2.4 Hz, 1H), 3.40 (t, J = 6.0 Hz, 1H), 3.28 (dq, J = 8.1, 7.0 Hz, 1H), 2.75–2.50 (m, 2H), 2.45–2.30 (m, 1H), 2.05–1.90 (m, 1H), 1.97 (s, 3H), 1.95 (s, 3H), 1.24 (t, J = 7.6 Hz, 3H), 1.17 (d, J = 7.0 Hz, 3H), 1.02 (d, J = 7.0 Hz, 3H), 1.01 (d, J = 7.0 Hz, 3H), 0.81 (s, 9H), 0.02 (s, 3H), −0.28 (s, 3H), A signal due to one proton (OH) was not observed; ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 179.6, 164.7, 163.6, 139.7, 119.2, 117.9, 116.2, 75.3, 75.0, 41.6, 40.9, 39.0, 26.0 (3C), 24.8, 18.1, 17.5, 14.9, 11.4, 9.9, 9.6, 9.0, −4.1, −4.6; HRMS (ESI): m/z 459.2922, calcd for $C_{25}H_{44}O_4SiNa$ $[M + Na]^+$ 459.2907.

C1–C13 Segment 15. To a stirred solution of homoallylic alcohol **14** (120 mg, 0.275 mmol) in pyridine (1 mL) were added dimethylaminopyridine (3.70 mg, 30.3 μmol) and isovaleryl chloride (0.200 mL, 1.64 mmol) at room temperature. The mixture was stirred at room temperature for 18 h, poured into saturated aqueous $NaHCO_3$ (50 mL) at 0 °C, and extracted with EtOAc (3 × 10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (10 g, hexane–EtOAc 10:1 → 5:1 → 3:1; 10 g, hexane–EtOAc 10:1 → 5:1) to give ester **14a** (143 mg, quant) as a colorless oil: R_f = 0.77 (1:1 hexane/EtOAc); $[\alpha]_D^{27}$ +19.7 (*c* 1.445, $CHCl_3$); IR ($CHCl_3$): 1727, 1654, 1594, 1463, 1377 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 5.73 (ddd, J = 17.5, 10.1, 6.8 Hz, 1H), 5.10–4.95 (m, 3H), 4.04 (d, J = 8.4 Hz, 1H), 3.16 (dq, J = 8.4, 7.1 Hz, 1H), 2.70–2.50 (m, 3H), 2.30–2.05 (m, 3H), 2.10–1.90 (m, 1H), 1.96 (s, 3H), 1.93 (s, 3H), 1.26 (t, J = 7.6 Hz, 3H), 1.09 (d, J = 7.1 Hz, 3H), 0.98 (d, J = 6.2 Hz, 9H), 0.89 (d, J = 7.0 Hz, 3H), 0.83 (s, 9H), 0.07 (s, 3H), −0.34 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 179.6, 172.5, 164.5, 163.6, 138.7, 119.4, 118.0, 115.9, 76.4, 72.6, 43.5, 40.6, 40.2, 37.9, 26.0 (3C), 25.4, 24.8, 22.6, 22.5, 18.2, 18.1, 15.4, 11.3, 9.9, 9.5, 9.3, −3.9, −4.5; HRMS (ESI): m/z 543.3486, calcd for $C_{30}H_{52}O_5SiNa$ $[M + Na]^+$ 543.3482.

To a stirred solution of ester **14a** (143 mg, 0.186 mmol) in acetone (1 mL) and H_2O (1 mL) were added *N*-methylmorpholine oxide (103 mg, 0.879 mmol) and osmium tetroxide (0.1 M solution in *tert*-butanol, 0.500 mL, 50.0 μmol) at room temperature. The mixture was stirred at room temperature for 17 h, diluted with saturated aqueous $NaHSO_3$ (5 mL) at 0 °C, and extracted with EtOAc (3 × 10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (10 g, hexane–EtOAc 1:1 → 0:1) to give a diastereomeric mixture of diol **14b** (ca. 6:1) (138 mg, 90%) as a colorless oil: R_f = 0.20 (major), 0.13 (minor) (1:1 hexane/EtOAc); IR ($CHCl_3$): 3421, 1726, 1651, 1592, 1464, 1378 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) for major isomer: δ 5.05 (dd, J = 8.4, 6.8 Hz, 1H), 4.07 (dd, J = 7.5, 2.4 Hz, 1H), 3.75–3.64 (m, 2H), 3.47–3.40 (m, 1H), 3.23 (dq, J = 7.5, 7.3 Hz, 1H), 2.70–2.55 (m, 3H), 2.30–2.05 (m, 6H), 1.99 (s, 3H), 1.95 (s, 3H), 1.24 (t, J = 7.6 Hz, 3H), 1.22 (d, J = 7.3 Hz, 3H), 0.97 (d, J = 6.2 Hz, 6H), 0.92 (d, J = 7.0 Hz, 3H), 0.86 (s, 9H), 0.83 (d, J = 6.8 Hz, 3H), 0.06 (s, 3H), −0.23 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 180.0, 172.6, 164.8, 164.4, 119.5, 118.0, 77.0, 73.4, 72.0, 64.3, 43.6, 40.9, 38.0, 37.6, 26.0 (3C), 25.4, 24.8, 22.5 (2C), 18.2, 14.9, 12.9, 11.4, 10.2, 10.0, 9.6, −3.9, −4.3; HRMS (ESI): m/z 577.3533, calcd for $C_{30}H_{54}O_7SiNa$ $[M + Na]^+$ 577.3537.

To a stirred solution of diol **14b** (138 mg, 0.249 mmol) in acetone (1 mL) and H_2O (1 mL) was added $NaIO_4$ (103 mg, 0.390 mmol). The mixture was stirred at room temperature for 15 min, diluted with half-saturated brine (5 mL), and extracted with EtOAc (3 × 10 mL). The combined extracts were dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (8 g, hexane–EtOAc 3:1 → 2:1 → 1:1) to give C1–C13 segment **15** (94.3 mg, 72%) as a colorless oil and recovered diol **14b** (18.1 mg, 13%); **15**: R_f = 0.66 (1:1 hexane/EtOAc); $[\alpha]_D^{26}$ +17.7 (*c* 0.951, $CHCl_3$); IR ($CHCl_3$): 1725, 1653, 1594, 1463, 1427, 1377 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 9.67 (d, J = 3.2 Hz, 1H), 5.26 (dd, J = 8.9, 3.2 Hz, 1H), 4.06 (dd, J = 8.4, 2.1 Hz, 1H), 3.19 (dq, J = 8.4, 6.8 Hz, 1H), 2.80–2.55 (m, 3H), 2.26–2.04 (m, 4H), 1.97 (s, 3H), 1.95 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H), 1.15 (d, J = 6.5 Hz, 3H), 1.13 (d, J = 6.8 Hz, 3H), 0.98 (d, J = 6.2 Hz, 6H), 0.96 (d, J = 6.8 Hz, 3H), 0.82 (s, 9H), 0.03 (s, 3H), −0.32 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 202.8, 179.5, 172.3, 164.0, 163.8, 119.5, 118.1, 75.1, 73.4, 47.6, 43.3, 40.5, 38.8, 26.0 (3C), 25.5, 24.8, 22.5 (2C), 18.1, 15.3, 11.8, 11.4, 10.1, 9.9, 9.6, −3.9, −4.5; HRMS (ESI): m/z 545.3268, calcd for $C_{29}H_{50}O_6SiNa$ $[M + Na]^+$ 545.3274.

C14–C20 Segment 17. To a stirred solution of LDA (5.21 mmol) prepared from diisopropylamine (0.730 mL, 5.21 mmol) and *n*-BuLi (1.63 M solution of in hexane, 3.20 mL, 5.22 mmol) in THF (6.0 mL) was added 3-pentanone (0.5 mL, 4.73 mmol) at −78 °C. After the mixture was stirred at −78 °C for 40 min, a solution of (*S*)-2-methylbutyraldehyde **16** (493 mg, 5.72 mmol) in THF (3.0 mL) was added via cannula. The mixture was stirred at −78 °C for 1 h, diluted with saturated aqueous NH_4Cl (10 mL), and extracted with Et_2O (3 × 10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (FL-60D, 50 g, hexane–Et_2O 10:1 → 7:1) to give a diastereomeric mixture of aldol **16a** (728 mg, 89%) as a colorless oil: R_f = 0.63, 0.38 (1:1 hexane/EtOAc); IR ($CHCl_3$): 3494, 1699, 1603, 1460, 1409, 1380 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 3.69 (ddd, J = 8.1, 5.9, 3.0 Hz, 0.51H), 3.61 (ddd, J = 6.7, 2.8, 2.8 Hz, 0.26H), 3.26 (ddd, J = 7.6, 5.9, 5.9 Hz, 0.23H), 2.88 (d, J = 3.0 Hz, 0.3H), 2.87–2.63 (m, 1.2H), 2.63–2.36 (m, 2H), 2.27 (d, J = 5.9 Hz, 0.5H), 1.88–1.65 (m, 0.6H), 1.65–1.38 (m, 1.7H), 1.38–1.20 (m, 0.7H), 1.20–1.10 (m, 6H), 0.96–0.75 (m, 6H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 217.1, 216.6, 216.5, 78.3, 75.7, 74.4, 48.6, 47.4, 47.0, 37.7, 36.8, 36.6, 36.2, 36.0, 34.8, 26.8, 24.9, 23.3, 16.1, 14.9, 14.1, 12.3, 11.8, 11.6, 10.9, 9.2, 7.7, 7.5, 7.5; HRMS (ESI): m/z 195.1359, calcd for $C_{10}H_{20}O_2Na$ $[M + Na]^+$ 195.1361.

To a stirred solution of aldol **16a** (322 mg, 1.87 mmol) and imidazole (389 mg, 5.71 mmol) in DMF (4.6 mL) was added triethylsilyl chloride (0.470 mL, 2.81 mmol) at room temperature. The mixture was stirred at room temperature for 75 min, diluted with H_2O (15 mL), and extracted with Et_2O (2 × 10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (15 g, hexane–Et_2O 200:1 → 100:1 → 20:1) to give a diastereomeric mixture of C14–C20 segment **17** (507 mg, 95%) as a yellow oil: $R_f = 0.78$ (3:1 hexane/EtOAc); IR ($CHCl_3$): 1712, 1459, 1412, 1380 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 3.89 (dd, $J = 8.5$, 1.8 Hz, 0.21H), 3.88 (dd, $J = 6.8$, 1.9 Hz, 0.66H), 3.84 (dd, $J = 8.9$, 5.4 Hz, 0.13H), 2.86–2.65 (m, 1H), 2.65–2.35 (m, 2H), 1.55–1.30 (m, 2H), 1.30–1.10 (m, 1H), 1.10–0.80 (m, 21H), 0.65–0.45 (m, 6H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 214.4, 214.2, 214.0, 78.6, 77.5, 77.0, 49.9, 49.7, 49.3, 40.3, 38.3, 37.9, 37.1, 36.8, 35.4, 26.9, 24.7, 23.7, 15.8, 14.2, 14.0, 13.4, 12.7, 12.5, 12.4, 12.3, 7.8, 7.5, 7.4, 7.1, 7.1, 5.5, 5.4, 5.3; HRMS (ESI): m/z 309.2206, calcd for $C_{16}H_{34}O_2SiNa$ $[M + Na]^+$ 309.2226.

Aldol 21. To a stirred solution of $Sn(OTf)_2$ (75.0 mg, 0.180 mmol) in CH_2Cl_2 (0.6 mL) were added triethylamine (27.0 μL, 0.200 mmol) and a solution of C14–C20 segment **17** (40.0 mg, 0.140 mmol) in CH_2Cl_2 (0.4 mL) at −78 °C, and the mixture was stirred at −78 °C for 1.3 h. After a solution of C1–C13 segment **15** (21.9 mg, 0.042 mmol) in CH_2Cl_2 (0.4 mL) was added via cannula, the reaction mixture was stirred at −78 °C for 3 h and diluted with pH 6.8 phosphate buffer (5 mL). The mixture was filtered through a pad of Celite, and the Celite was rinsed with EtOAc (4 × 5 mL). The filtrate and rinses were combined, and the layers were separated. The aqueous layer was extracted with EtOAc (3 × 10 mL). The organic layer and extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (4 g, hexane–EtOAc 10:1 → 3:1 → 2:1) to give a diastereomeric mixture of aldol **21** (33.6 mg, 99%) as a colorless oil: $R_f = 0.73$, 0.70, 0.64 (1:1 hexane/EtOAc); IR ($CHCl_3$): 3503, 1725, 1653, 1592, 1462, 1426, 1378 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 5.12 (d, $J = 9.5$ Hz, 1H), 4.38 (d, $J = 8.4$ Hz, 1H), 4.04 (d, $J = 9.5$ Hz, 1H), 3.93–3.75 (m, 2H), 3.74–3.70 (m, 1H), 3.33–2.55 (m, 7H), 2.25–2.05 (m, 4H), 1.96 (s, 3H), 1.94 (s, 3H), 1.30–1.19 (m, 6H), 1.18–1.06 (m, 6H), 1.05–0.92 (m, 21H), 0.90–0.80 (m, 15H), 0.59 (q, $J = 8.1$ Hz, 6H), 0.02 (s, 3H), −0.38 (s, 3H), A signal due to one proton (OH) was not observed; ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 220.0, 219.1, 216.5, 179.7 (3C), 179.6, 172.7 (2C), 172.6, 165.3 (2C), 165.2, 164.4, 164.1, 163.4, 119.6, 119.2 (2C), 117.9 (2C), 79.2, 78.5, 78.1, 77.2, 76.5, 75.7, 74.3, 73.0 (2C), 71.8, 71.1, 70.2, 69.6, 51.2, 49.0, 48.9, 48.3, 48.0, 46.8, 43.6, 43.5 (2C), 41.3, 41.2, 40.0, 39.9, 38.6, 38.1, 38.0 (2C), 37.9, 35.6, 35.3 (2C), 35.0, 26.8, 26.2, 26.0, 25.5 (2C), 25.4, 24.9, 24.7, 24.4, 22.6, 18.3, 18.2 (2C), 16.4, 15.9, 15.6 (2C), 15.3, 15.1, 15.0, 14.9, 14.8, 14.2, 14.1, 13.8, 13.5 (2C), 12.6, 12.5, 12.3, 11.7, 11.1 (2C), 10.0, 9.9 (2C), 9.8, 9.6, 9.0, 8.7, 7.8, 7.1, 7.0, 5.5, 5.4 (3C), 5.2, −3.7, −3.9, −4.1, −4.3; HRMS (ESI): m/z 831.5604, calcd for $C_{45}H_{84}O_8Si_2Na$ $[M + Na]^+$ 831.5602.

Triketone 22. Aldol **21** (122 mg, 0.151 mmol) was treated with a 4:4:1 mixture of acetic acid, H_2O, and THF (4.5 mL) at room temperature for 6.5 h. The mixture was poured into saturated aqueous $NaHCO_3$ (70 mL) at 0 °C and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (6 g, hexane–EtOAc 3:1 → 2:1 → 1:1) to give a diastereomeric mixture of diol **21a** (76.4 mg, 73%) as a colorless oil: $R_f = 0.74$, 0.65, 0.58, 0.48 (1:1 hexane/EtOAc); IR ($CHCl_3$): 3503, 1724, 1653, 1593, 1463, 1427, 1378 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 5.12 (d, $J = 9.1$ Hz, 1H), 4.28 (d, $J = 8.4$ Hz, 1H), 3.94 (d, $J = 9.5$ Hz, 1H), 3.70–3.55 (m, 1H), 3.20–3.10 (m, 1H), 3.15–2.80 (m, 3H), 2.70–2.50 (m, 4H), 2.30–2.05 (m, 5H), 1.96 (s, 3H), 1.95 (s, 3H), 1.55–1.40 (m, 2H), 1.30–1.20 (m, 6H), 1.20–1.10 (m, 9H), 1.05–0.95 (m, 9H), 0.95–0.80 (m, 15H), 0.04 (s, 3H), −0.31 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 220.7, 219.5, 179.7, 179.5, 173.1, 172.6, 165.0, 164.0, 163.9, 163.6, 119.5, 119.3, 119.2, 118.0, 117.9 (2C), 77.2, 76.4, 76.3 (2C), 74.7, 74.1, 73.1, 72.6, 70.4, 51.1, 49.1, 47.0, 45.7, 43.7, 43.6, 43.4, 41.2, 40.5, 37.9, 37.8, 37.3, 36.3, 36.1, 34.7, 26.8, 26.7, 26.0 (2C), 25.5 (2C), 25.4, 24.9, 24.7, 22.6, 22.5 (2C), 18.3, 18.2, 18.1 (2C), 15.4, 15.3, 15.2, 14.9, 13.6, 12.0 (2C), 11.9, 11.5, 11.2, 11.1, 10.0 (2C), 9.9, 9.8, 9.5, 9.3, 9.1, 8.7, 7.1, −3.9, −4.0, −4.2, −4.3, −4.5; HRMS (ESI): m/z 717.4735, calcd for $C_{39}H_{70}O_8SiNa$ $[M + Na]^+$ 717.4738.

To a stirred solution of diol **21a** (76.4 mg, 0.110 mmol) in CH_2Cl_2 (3.0 mL) was added Dess–Martin periodinane (184 mg, 0.434 mmol) at room temperature. The mixture was stirred at room temperature for 20 min; diluted with a 1:1:2 mixture of saturated aqueous $NaHCO_3$, saturated aqueous $Na_2S_2O_3$, and H_2O (4 mL); and extracted with Et_2O (2 × 10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (6 g, hexane–EtOAc 5:1 → 3:1 → 1:1) to give a keto–enol equilibrium mixture of triketone **22** (63.7 mg, 83%) as a colorless amorphous solid: $R_f = 0.61$ (1:1 hexane/EtOAc); mp 26–28 °C; $[\alpha]_D^{25}$ +16.9 (c 0.586, $CHCl_3$); IR ($CHCl_3$): 1724, 1653, 1593, 1463, 1378 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 16.93 (s, 0.06H), 16.80 (s, 0.04H), 16.66 (s, 0.10H), 5.50–5.39 (m, 0.3H), 5.32–5.22 (m, 0.4H), 5.20–5.08 (m, 0.3H), 4.15–3.66 (m, 2H), 3.50–3.30 (m, 0.5H), 3.25–3.00 (m, 1.5H), 2.80–2.50 (m, 2.8H), 2.25–1.80 (m, 13H), 1.40–0.70 (m, 39H), 0.10–0.05 (m, 3H), {(−0.10)–(−0.32)} (m, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 210.1, 207.9, 206.2, 203.9, 202.8, 198.9, 198.4, 197.6, 195.0, 193.6, 193.5, 191.7, 191.4, 190.2, 189.5, 179.6, 179.5 (2C), 174.1, 172.3 (2C), 172.1, 172.0 (2C), 171.8, 171.7, 166.2, 165.7, 164.7, 164.6, 164.5 (2C), 164.4, 164.2 (2C), 164.0 (2C), 163.9, 128.1, 119.6 (2C), 119.5 (2C), 119.4 (2C), 117.8 (3C), 117.7, 109.5, 108.4, 105.8, 105.4, 105.0, 104.4, 104.2, 103.8, 103.5, 75.5, 75.4, 74.8, 74.6, 74.5, 74.3, 74.1, 73.9, 73.8, 73.6, 73.5, 58.2, 58.1, 57.7, 57.1, 53.2, 52.6, 51.8, 50.5, 47.3, 47.2, 46.9, 46.6, 46.5, 46.2, 46.0, 45.9 (2C), 45.8, 44.7, 43.4, 43.3 (2C), 43.2, 41.9, 40.3, 40.2 (2C), 40.1, 39.9, 39.8, 39.7, 39.5, 39.4, 39.3, 38.7, 38.6, 38.4, 38.3, 26.8, 26.7, 26.1, 25.9, 25.7 (2C), 25.4, 25.3 (2C), 25.0, 24.9, 22.5, 22.4, 20.9, 18.2, 18.1, 18.0, 16.9, 16.3, 16.0, 15.9, 15.8, 15.6, 15.4, 15.2, 14.4, 14.2, 14.1, 14.0, 13.9, 13.8, 13.5, 13.3, 13.2 (2C), 13.0, 12.5, 12.2 (2C), 12.1, 11.7, 11.6, 10.7, 10.4, 10.3,

10.0, 9.5, 9.3, 9.0, 7.6, −3.7, −3.9, −4.0, −4.2, −4.7; HRMS (ESI): m/z 713.4419, calcd for $C_{39}H_{66}O_8SiNa$ $[M + Na]^+$ 713.4425.

Auripyrone A (1). A solution of triketone **22** (32.5 mg, 47.0 μmol) in a 5:3:7 mixture of HF·pyridine, pyridine, and THF (5.0 mL) was stirred at 60 °C for 14.3 h. The mixture was poured into saturated aqueous $NaHCO_3$ (150 mL) at 0 °C and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (5 g, hexane–EtOAc 5:1 → 2:1 → 1:1) and by preparative HPLC [Develosil ODS–HG–5 (250 × 20 mm), flow rate 5 mL min^{-1}; detection, UV 215 nm, solvent 80% aqueous MeOH] to give auripyrone A (**1**) (5.9 mg, 22%) as a colorless solid: $R_f = 0.37$ (1:1 CH_2Cl_2/Et_2O); $[\alpha]_D^{25}$ +47.3 (c 0.390, $CHCl_3$); IR ($CHCl_3$): 1725, 1655, 1623, 1598, 1462, 1387 cm^{-1}; ^{1}H NMR (600 MHz, C_6D_6): δ 4.92 (dd, $J = 3.3$, 3.3 Hz, 1H), 3.96 (dd, $J = 10.3$, 2.1 Hz, 1H), 2.75 (dq, $J = 10.3$, 7.0 Hz, 1H), 2.32 (q, $J = 7.0$ Hz, 1H), 2.31 (dq, $J = 15.0$, 7.5 Hz, 1H), 2.25 (ddq, $J = 7.5$, 7.5, 3.8 Hz, 1H), 2.21–2.16 (m, 1H), 2.16–2.11 (m, 2H), 2.09 (dq, $J = 15.0$, 7.5 Hz, 1H), 2.03 (s, 3H), 1.98 (s, 3H), 1.85–1.80 (m, 2H), 1.64 (s, 3H), 1.56–1.48 (m, 1H), 1.40–1.33 (m, 1H), 1.12 (d, $J = 7.0$ Hz, 3H), 0.99 (d, $J = 6.8$ Hz, 3H), 0.91 (d, $J = 6.2$ Hz, 3H), 0.90 (d, $J = 6.5$ Hz, 3H), 0.89 (t, $J = 7.6$ Hz, 3H), 0.83 (t, $J = 7.5$ Hz, 3H), 0.77 (d, $J = 7.0$ Hz, 3H), 0.73 (d, $J = 7.0$ Hz, 3H), 0.63 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (150 MHz, C_6D_6): δ 191.8, 178.5, 172.0, 166.2, 162.1, 161.5, 121.3, 118.1, 107.8, 105.0, 75.2, 70.5, 44.5, 44.0, 37.2, 36.6, 34.1, 31.7, 26.4, 26.3, 24.7, 22.5, 22.3, 16.0, 12.1, 12.0, 11.9, 11.0, 10.8, 9.7, 9.5, 9.0, 8.1; HRMS (ESI): m/z 581.3446, calcd for $C_{33}H_{50}O_7Na$ $[M + Na]^+$ 581.3454.

Bis(pyrone) Compound 25. To a stirred solution of auripyrone A (**1**) (2.5 mg, 4.5 μmol) in MeOH (2 mL) was added 1 M aqueous LiOH (2 mL) at room temperature. The mixture was stirred at room temperature for 3.5 h, diluted with saturated aqueous NH_4Cl (5 mL) at 0 °C, and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (0.6 g, hexane–EtOAc 1:1 → 0:1) to give bis(pyrone) compound **25** (1.7 mg, 81%) as colorless crystals: $R_f = 0.38$ (1:1 hexane/acetone); $[\alpha]_D^{25}$ +21.7 (c 0.138, $CHCl_3$); IR ($CHCl_3$): 3422, 1653, 1593, 1460, 1426, 1381 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.01 (dd, $J = 13.8$, 9.7 Hz, 2H), 3.23–3.16 (m, 2H), 3.02 (br s, 1H), 2.96–2.85 (m, 2H), 2.68 (dq, $J = 15.2$, 7.6 Hz, 1H), 2.62 (dq, $J = 15.2$, 7.6 Hz, 1H), 2.00–1.90 (m, 1H), 2.00 (s, 3H), 1.99 (s, 3H), 1.96 (s, 3H), 1.94 (s, 3H), 1.70–1.55 (m, 2H), 1.25 (t, $J = 7.6$ Hz, 3H), 1.23 (d, $J = 7.6$ Hz, 3H), 1.19 (d, $J = 7.0$ Hz, 3H), 1.18 (d, $J = 6.8$ Hz, 3H), 1.05 (d, $J = 6.8$ Hz, 3H), 0.90 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 179.7, 179.6, 165.9, 164.2, 163.5, 163.4, 120.1, 119.8, 118.3, 118.1, 79.0, 78.8, 39.3 (2C), 37.0, 34.5, 27.7, 24.8, 17.9, 14.6, 14.4, 11.9, 11.4, 9.7 (2C), 9.5 (2C), 3.8; HRMS (ESI): m/z 497.2882, calcd for $C_{28}H_{42}O_6Na$ $[M + Na]^+$ 497.2879.

Ester 29. To a stirred solution of homoallylic alcohol **14** (94.2 mg, 0.216 mmol), dimethylaminopyridine (1.00 g, 8.19 mmol), (*S*)-2-methylbutanoic acid (**28**) (0.234 mL, 2.15 mmol), and triethylamine (0.602 mL, 4.53 mmol) in toluene (18 mL) was added 2,4,6-trichlorobenzoyl chloride (0.742 mL, 4.75 mmol) at −78 °C. The mixture was stirred at 0 °C for 1.3 h, diluted with saturated aqueous $NaHCO_3$ (15 mL) at 0 °C, and extracted with EtOAc (3 × 10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (10 g, hexane–EtOAc 5:1 → 3:1) to give ester **29** (104 mg, 93%) as a colorless oil: $R_f = 0.77$ (1:1 hexane/EtOAc); $[\alpha]_D^{25}$ +21.5 (c 1.316, $CHCl_3$); IR ($CHCl_3$): 1724, 1654, 1594, 1462, 1426, 1378 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ 5.78 (ddd, $J = 17.3$, 10.0, 7.8 Hz, 1H), 5.12–4.99 (m, 3H), 4.08 (d, $J = 8.6$ Hz, 1H), 3.17 (dq, $J = 8.6$, 7.3 Hz, 1H), 2.72–2.52 (m, 3H), 2.45–2.30 (m, 1H), 2.00–1.92 (m, 1H), 1.97 (s, 3H), 1.96 (s, 3H), 1.73 (ddq, $J = 14.0$, 7.0, 7.0 Hz, 1H), 1.48 (ddq, $J = 14.0$, 7.0, 7.0 Hz, 1H), 1.26 (t, $J = 7.6$ Hz, 3H), 1.20 (d, $J = 7.3$ Hz, 3H), 1.09 (d, $J = 7.3$ Hz, 3H), 0.98 (d, $J = 6.8$ Hz, 3H), 0.94 (t, $J = 7.6$ Hz, 3H), 0.89 (d, $J = 6.8$ Hz, 3H), 0.83 (s, 9H), 0.07 (s, 3H), −0.33 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 179.6, 176.0, 164.4, 163.5, 138.7, 119.4, 118.0, 116.0, 76.2, 72.6, 41.6, 40.6, 40.3, 37.9, 26.6, 26.0 (3C), 24.8, 18.2, 18.1, 17.2, 15.5, 11.9, 11.4, 9.9, 9.5, 9.3, −3.8, −4.4; HRMS (ESI): m/z 543.3485, calcd for $C_{30}H_{52}O_5SiNa$ $[M + Na]^+$ 543.3482.

C1–C13 Segment 30. To a stirred solution of ester **29** (65.8 mg, 0.126 mmol) in acetone (1 mL) and H_2O (1 mL) were added *N*-methylmorpholine oxide (55.0 mg, 0.469 mmol) and osmium tetroxide (0.1 M solution in *tert*-butanol, 0.300 mL, 30.0 μmol) at room temperature. The mixture was stirred at room temperature for 14 h, diluted with saturated aqueous $NaHSO_3$ (10 mL) at 0 °C, and extracted with EtOAc (3 × 10 mL). The combined extracts were washed with saturated aqueous $NaHSO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (7 g, hexane–EtOAc 1:1 → 0:1) to give a diastereomeric mixture of diol **29a** (ca. 6:1) (65.5 mg, 94%) as a colorless oil: $R_f = 0.18$ (major), 0.10 (minor) (1:1 hexane/EtOAc); IR ($CHCl_3$): 3424, 1724, 1651, 1591, 1462, 1380 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) for major isomer: δ 5.07 (dd, $J = 8.6$, 3.5 Hz, 1H), 4.10 (dd, $J = 8.1$, 1.9 Hz, 1H), 3.80–3.62 (m, 2H), 3.50–3.38 (m, 1H), 3.24 (dq, $J = 8.1$, 7.3 Hz, 1H), 2.64 (dq, $J = 7.6$, 3.0 Hz, 2H), 2.63–2.55 (m, 1H), 2.43–2.05 (m, 4H), 1.99 (s, 3H), 1.95 (s, 3H), 1.72 (ddq, $J = 14.0$, 7.0, 7.0 Hz, 1H), 1.47 (ddq, $J = 14.0$, 7.0, 7.0 Hz, 1H), 1.24 (t, $J = 7.3$ Hz, 3H), 1.19 (d, $J = 7.3$ Hz, 3H), 1.18 (d, $J = 7.0$ Hz, 3H), 0.93 (t, $J = 7.0$ Hz, 3H), 0.91 (d, $J = 6.8$ Hz, 3H), 0.85 (s, 9H), 0.82 (d, $J = 7.3$ Hz, 3H), −0.18 (s, 3H), −0.24 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 179.9, 176.1, 164.8, 164.4, 119.5, 118.0, 76.9, 73.3, 71.9, 64.4, 41.6, 40.9, 38.0, 37.6, 26.6, 26.0 (3C), 24.8, 18.2, 17.1, 15.1, 12.9, 11.9, 11.4, 10.2, 10.0, 9.6, −3.9, −4.3; HRMS (ESI): m/z 577.3558, calcd for $C_{30}H_{54}O_7SiNa$ $[M + Na]^+$ 577.3537.

To a stirred solution of diol **29a** (88.2 mg, 0.159 mmol) in acetone (1 mL) and H_2O (1 mL) was added $NaIO_4$ (73.2 mg, 0.277 mmol). The mixture was stirred at room temperature for 15 min, diluted with half saturated brine (5 mL), and extracted with EtOAc (3 × 10 mL). The combined extracts were washed with saturated aqueous $NaHSO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified

by column chromatography on silica gel (8 g, hexane–EtOAc 3:1 → 2:1 → 1:1) to give C1–C13 segment **30** (68.0 mg, 82%) as a colorless oil: $R_f = 0.73$ (1:1 hexane/EtOAc); $[\alpha]_D^{25}$ +16.2 (*c* 1.000, $CHCl_3$); IR ($CHCl_3$): 1725, 1654, 1594, 1462, 1426, 1378 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 9.69 (d, $J = 3.2$ Hz, 1H), 5.26 (dd, $J = 9.5$, 3.5 Hz, 1H), 4.07 (dd, $J = 8.4$, 2.2 Hz, 1H), 3.20 (dq, $J = 8.4$, 7.0 Hz, 1H), 2.80–2.30 (m, 4H), 2.17–2.06 (m, 1H), 1.98 (s, 3H), 1.95 (s, 3H), 1.71 (ddq, $J = 14.4$, 7.2, 7.2 Hz, 1H), 1.47 (ddq, $J = 14.4$, 7.2, 7.2 Hz, 1H), 1.26 (t, $J = 7.6$ Hz, 3H), 1.19 (d, $J = 7.3$ Hz, 3H), 1.15 (d, $J = 8.1$ Hz, 3H), 1.12 (d, $J = 6.5$ Hz, 3H), 0.96 (d, $J = 7.0$ Hz, 3H), 0.94 (t, $J = 7.3$ Hz, 3H), 0.82 (s, 9H), 0.04 (s, 3H), −0.32 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 202.7, 179.5, 175.9, 164.0, 163.8, 119.6, 118.1, 75.0, 73.6, 47.7, 41.4, 40.4, 38.8, 26.5, 26.0 (3C), 24.8, 18.2, 17.1, 15.5, 11.8, 11.7, 11.4, 10.0, 9.9, 9.6, −3.9, −4.5; HRMS (ESI): *m/z* 523.3432, calcd for $C_{29}H_{50}O_6Si$ $[M + H]^+$ 523.3455.

Aldol 31. To a stirred solution of $Sn(OTf)_2$ (220 mg, 0.528 mmol) in CH_2Cl_2 (1.4 mL) were added triethylamine (0.0700 mL, 0.527 mmol) and a solution of C14–C20 segment **17** (110 mg, 0.384 mmol) in CH_2Cl_2 (0.7 mL) at −78 °C. After the mixture was stirred at −78 °C for 1.3 h, a solution of aldehyde **30** (68.0 mg, 0.130 mmol) in CH_2Cl_2 (0.7 mL) was added via cannula. The reaction mixture was stirred at −78 °C for 2.5 h, diluted with pH 6.8 phosphate buffer (10 mL), and filtrated through a pad of Celite. This Celite was rinsed with EtOAc (4 × 5 mL). The filtrate and rinses were combined, and the layers were separated. The aqueous layer was extracted with EtOAc (3 × 10 mL). The organic layer and extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (10 g, hexane–EtOAc 10:1 → 3:1 → 2:1) to give a diastereomeric mixture of aldol **31** (104 mg, 99%) as a colorless oil: $R_f = 0.83$, 0.77 (1:1 hexane/EtOAc); IR ($CHCl_3$): 3509, 1723, 1653, 1592, 1461, 1426, 1379 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 5.11 (d, $J = 10.3$ Hz, 1H), 4.39 (d, $J = 8.6$ Hz, 1H), 4.06 (d, $J = 9.5$ Hz, 1H), 4.02–3.80 (m, 1H), 3.76–3.65 (m, 1H), 3.20–3.05 (m, 1H), 2.95–2.25 (m, 6H), 2.13–2.06 (m, 1H), 1.95 (s, 3H), 1.93 (s, 3H), 1.80–1.60 (m, 1H), 1.52–1.33 (m, 2H), 1.30–1.00 (m, 15H), 1.00–0.85 (m, 18H), 0.85–0.70 (m, 15H), 0.60 (q, $J = 7.8$ Hz, 6H), 0.55–0.48 (m, 2H), 0.01 (s, 3H), −0.39 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 220.0, 179.7, 179.5, 176.1, 175.8, 165.2, 163.9, 163.8, 163.4, 119.5, 119.1, 118.0, 117.9, 79.0, 78.1, 77.2, 75.7, 75.6, 72.9, 70.1, 60.3, 48.9, 46.9, 41.6, 41.4, 41.3, 40.3, 40.0, 38.7, 37.8, 35.4, 26.8, 26.6, 26.5, 26.0, 25.9, 24.8, 24.7, 24.4, 21.0, 18.3, 18.1, 17.2, 16.4, 15.6, 15.5, 15.0, 14.2, 12.2, 11.9, 11.7, 11.4, 11.1, 10.0, 9.9, 9.8, 9.5, 8.6, 8.2, 7.1, 7.0, 5.5, 5.4, 5.3, 5.2, −3.9, −4.3, −4.5; HRMS (ESI): *m/z* 831.5596, calcd for $C_{45}H_{84}O_8Si_2Na$ $[M + Na]^+$ 831.5602.

Triketone 32. Aldol **31** (59.6 mg, 73.6 μmol) was treated with a 4:4:1 mixture of acetic acid, H_2O, and THF (4.5 mL) at room temperature for 13.3 h. The mixture was poured into saturated aqueous $NaHCO_3$ (70 mL) at 0 °C and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (10 g, hexane–EtOAc 3:1 → 2:1 → 1:1) to give a diastereomeric mixture of diol **31a** (45.9 mg, 90%) as a colorless oil: $R_f = 0.67$, 0.60, 0.50 (1:1 hexane/EtOAc); IR ($CHCl_3$): 3523, 1723, 1652, 1592, 1462, 1427, 1379 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 5.10 (d, $J = 9.5$ Hz, 1H), 4.32–4.24 (m, 1H), 3.95 (d, $J = 8.9$ Hz, 1H), 3.70–3.55 (m, 1H), 3.25–3.10 (m, 1H), 3.08–2.75 (m, 2H), 2.75–2.50 (m, 4H), 2.50–2.28 (m, 1H), 1.95 (s, 3H), 1.93 (s, 3H), 1.80–1.62 (m, 2H), 1.58–1.35 (m, 2H), 1.30–1.05 (m, 15H), 1.05–0.75 (m, 27H), 0.03 (s, 3H), −0.33 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 227.9, 220.8, 179.7, 176.1 (2C), 165.1, 165.0, 164.9, 163.6 (3C), 119.6, 119.2, 117.9, 117.7, 78.1, 77.2, 74.7, 74.3, 73.0, 70.2, 52.6, 50.2, 47.1, 46.9, 45.7, 45.5, 45.3, 44.7, 43.8, 41.6, 41.2, 41.1, 37.9, 37.3, 37.0, 36.4 (2C), 34.6, 33.7, 26.6, 26.1, 25.9, 25.0, 24.8, 18.3 (2C), 18.2, 17.2, 15.5, 15.4, 15.2, 15.0, 14.8, 12.5, 11.9, 11.2, 11.1 (2C), 10.0, 9.9 (2C), 9.6, 9.1, 8.7, −3.9, −4.2, −5.3; HRMS (ESI): *m/z* 717.4725, calcd for $C_{39}H_{70}O_8SiNa$ $[M + Na]^+$ 717.4738.

To a stirred solution of diol **31a** (34.0 mg, 48.9 μmol) in CH_2Cl_2 (1.5 mL) was added Dess–Martin periodinane (86.6 mg, 204 μmol) at room temperature. The mixture was stirred at room temperature for 25 min; diluted with a 1:1:2 mixture of saturated aqueous $NaHCO_3$, saturated aqueous $Na_2S_2O_3$, and H_2O (4 mL); and extracted with Et_2O (2 × 10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (10 g, hexane–EtOAc 5:1 → 3:1 → 1:1) to give a keto–enol equilibrium mixture of triketone **32** (32.1 mg, 95%) as a colorless amorphous solid: $R_f = 0.63$ (1:1 hexane/EtOAc); $[\alpha]_D^{25}$ +15.9 (*c* 1.325, $CHCl_3$); IR ($CHCl_3$): 1724, 1652, 1593, 1462, 1427, 1379 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 16.93 (s, 0.06H), 16.81 (s, 0.04H), 16.66 (s, 0.10H), 5.52–5.36 (m, 0.3H), 5.35–5.21 (m, 0.3H), 5.20–5.06 (m, 0.4H), 4.15–3.60 (m, 1.8H), 3.58–3.00 (m, 2H), 2.80–2.45 (m, 3H), 2.40–2.18 (m, 1H), 2.20–1.55 (m, 12H), 1.55–1.14 (m, 11H), 1.14–0.75 (m, 28H), {(0.10)–(−0.06)} (m, 3H), {(−0.10)–(−0.35)} (m, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 210.1, 206.1, 204.0, 203.9, 198.6, 197.6, 195.1, 194.0, 193.7, 191.4 (2C), 179.7, 179.6, 179.5, 177.8 (2C), 176.0, 175.9, 175.7 (2C), 175.6, 164.9, 164.8, 164.7 (2C), 164.6 (2C), 164.5 (2C), 164.4, 164.3 (2C), 164.2, 164.1, 164.0, 119.7, 119.6, 119.5 (2C), 119.4, 117.8 (3C), 109.4, 108.2, 106.0, 105.6, 105.1, 104.3, 104.0, 103.8, 103.5, 75.5, 75.4, 74.7, 74.4, 73.9, 73.7, 73.1, 57.6, 52.7, 50.4, 47.2, 46.8, 46.6, 46.2, 46.1, 46.0, 45.9, 44.8, 44.7, 42.0, 41.5, 41.4, 41.3 (2C), 41.2, 41.1, 40.3, 40.0, 39.8, 39.6 (2C), 39.5, 39.4 (2C), 39.3, 39.1, 38.7, 38.6, 38.5 (2C), 38.2, 26.9, 26.7 (2C), 26.5 (2C), 26.1, 26.0, 25.6, 24.9, 21.0, 18.4, 18.3, 18.2, 18.1, 16.9, 16.8, 16.4, 16.3, 16.1, 16.0, 14.6, 14.2, 14.0, 13.9, 13.8, 13.3, 13.2, 13.1, 13.0, 12.6, 12.2, 12.0, 11.9, 11.8 (2C), 11.6 (2C), 10.7, 10.5 (2C), 10.1 (2C), 10.0, 9.6, 9.3, 7.7, −3.5, −3.7, −3.8, −4.0, −4.4; HRMS (ESI): *m/z* 713.4432, calcd for $C_{39}H_{66}O_8SiNa$ $[M + Na]^+$ 713.4425.

(2′*S*)-Auripyrone B (Natural-Type Auripyrone B) (33). A solution of triketone **32** (26.5 mg, 38.3 μmol) in a 5:3:7 mixture of HF·pyridine, pyridine, and THF (10.0 mL) was stirred at 60 °C for 17 h. The mixture was poured into saturated aqueous $NaHCO_3$ (150 mL) at 0 °C and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered,

and concentrated. The residual oil was purified by column chromatography on silica gel (6 g, hexane–EtOAc 5:1 → 2:1 → 1:1) and by preparative HPLC [Develosil ODS–HG–5 (250 × 20 mm), flow rate 5 mL min^{-1}; detection, UV 215 nm, solvent 80% aqueous MeOH] to give (2′*S*)-auripyrone B (natural-type auripyrone B) (**33**) (3.6 mg, 17%) as colorless crystals: $R_f = 0.33$ (1:1 CH_2Cl_2/Et_2O); $[\alpha]_D^{25}$ +43.4 (*c* 0.293, $CHCl_3$); IR ($CHCl_3$): 1726, 1655, 1623, 1597, 1462, 1387 cm^{-1}; ^{1}H NMR (600 MHz, C_6D_6): δ 4.91 (dd, $J = 3.4$, 3.4 Hz, 1H), 3.97 (dd, $J = 10.3$, 2.1 Hz, 1H), 2.74 (dq, $J = 10.3$, 7.0 Hz, 1H), 2.43 (ddq, $J = 7.0$, 7.0, 7.0 Hz, 1H), 2.32 (q, $J = 7.0$ Hz, 1H), 2.32–2.24 (m, 2H), 2.09 (dq, $J = 15.0$, 7.5 Hz, 1H), 2.03 (s, 3H), 1.98 (s, 3H), 1.88–1.70 (m, 3H), 1.66 (s, 3H), 1.58–1.45 (m, 1H), 1.43–1.38 (m, 1H), 1.37–1.30 (m, 1H), 1.16 (d, $J = 7.0$ Hz, 3H), 1.13 (d, $J = 7.0$ Hz, 3H), 0.99 (d, $J = 6.8$ Hz, 3H), 0.89 (t, $J = 7.5$ Hz, 3H), 0.87 (t, $J = 7.6$ Hz, 3H), 0.83 (t, $J = 7.5$ Hz, 3H), 0.77 (d, $J = 7.0$ Hz, 3H), 0.72 (d, $J = 7.0$ Hz, 3H), 0.63 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (150 MHz, C_6D_6): δ 191.8, 178.5, 175.9, 166.2, 162.0, 161.5, 121.3, 118.1, 107.8, 105.1, 75.2, 70.6, 44.5, 41.6, 37.2, 36.6, 34.1, 31.7, 27.4, 26.4, 24.7, 16.9, 15.9, 12.1, 12.0, 11.8, 11.8, 10.8, 10.7, 9.7, 9.4, 9.0, 8.2; HRMS (ESI): *m*/*z* 581.3472, calcd for $C_{33}H_{50}O_7Na$ $[M + Na]^+$ 581.3454.

Ester 35. To a stirred solution of homoallylic alcohol **14** (149.5 mg, 0.342 mmol), dimethylaminopyridine (660 mg, 5.40 mmol), (*R*)-2-methylbutanoic acid (**34**) (0.123 mL, 1.13 mmol), and triethylamine (0.317 mL, 2.39 mmol) in toluene (9 mL) was added 2,4,6-trichlorobenzoyl chloride (0.374 mL, 2.39 mmol) at −78 °C. The mixture was stirred at 0 °C for 2.5 h, diluted with saturated aqueous $NaHCO_3$ (15 mL) at 0 °C, and extracted with EtOAc (3 × 10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (10 g, hexane–EtOAc 5:1 → 3:1) to give ester **35** (182 mg, quant) as a colorless oil: $R_f = 0.77$ (1:1 hexane/EtOAc); $[\alpha]_D^{25}$ +14.7° (*c* 1.228, $CHCl_3$); IR ($CHCl_3$): 1724, 1654, 1594, 1462, 1426, 1378 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ 5.73 (ddd, $J = 17.0$, 10.0, 7.0 Hz, 1H), 5.10–4.97 (m, 3H), 4.08 (d, $J = 8.4$ Hz, 1H), 3.16 (dq, $J = 8.1$, 7.6 Hz, 1H), 2.72–2.52 (m, 3H), 2.40 (q, $J = 6.8$ Hz, 1H), 2.00–1.90 (m, 1H), 1.96 (s, 3H), 1.94 (s, 3H), 1.75 (ddq, $J = 14.0$, 7.0, 7.0 Hz, 1H), 1.46 (ddq, $J = 14.0$, 7.0, 7.0 Hz, 1H), 1.25 (t, $J = 7.6$ Hz, 3H), 1.21 (d, $J = 7.6$ Hz, 3H), 1.08 (d, $J = 7.0$ Hz, 3H), 0.97 (d, $J = 6.5$ Hz, 3H), 0.94 (t, $J = 7.3$ Hz, 3H), 0.88 (d, $J = 6.8$ Hz, 3H), 0.82 (s, 9H), 0.06 (s, 3H), −0.35 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 179.6, 176.0, 164.4, 163.5, 138.7, 119.5, 118.1, 116.0, 76.3, 72.6, 41.6, 40.7, 40.2, 38.0, 26.8, 26.0 (3C), 24.8, 18.2, 18.1, 16.9, 15.5, 11.9, 11.4, 9.9, 9.5, 9.2, −3.8, −4.4; HRMS (ESI): *m*/*z* 543.3471, calcd for $C_{30}H_{52}O_5SiNa$ $[M + Na]^+$ 543.3482.

C1–C13 Segment 35b. To a stirred solution of ester **35** (93.5 mg, 0.180 mmol) in acetone (1 mL) and H_2O (1 mL) were added *N*-methylmorpholine oxide (70.0 mg, 0.598 mmol) and osmium tetroxide (0.1 M solution in *tert*-butanol, 0.400 mL, 40.0 μmol) at room temperature. The mixture was stirred at room temperature for 7 h, diluted with saturated aqueous $NaHSO_3$ (15 mL) at 0 °C, and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with saturated aqueous $NaHSO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (7 g, hexane–EtOAc 1:1 → 0:1) to give a diastereomeric mixture of diol **35a** (ca. 9:1) (84.5 mg, 85%) as a colorless oil: $R_f = 0.18$ (major), 0.10 (minor) (1:1 hexane/EtOAc); IR ($CHCl_3$): 3422, 1724, 1651, 1591, 1462, 1380 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ 5.05 (dd, $J = 8.9$, 3.5 Hz, 1H), 4.09 (dd, $J = 9.7$, 4.0 Hz, 1H), 3.75–3.64 (m, 2H), 3.47–3.38 (m, 1H), 3.23 (dq, $J = 7.6$, 7.6 Hz, 1H), 2.64 (dq, $J = 7.8$, 3.5 Hz, 2H), 2.50–2.25 (m, 2H), 2.20–2.05 (m, 1H), 1.99 (s, 3H), 1.95 (s, 3H), 1.75 (ddq, $J = 14.0$, 7.0, 7.0 Hz, 1H), 1.45 (ddq, $J = 14.0$, 7.0, 7.0 Hz, 1H), 1.20 (d, $J = 7.0$ Hz, 3H), 1.17 (d, $J = 8.1$ Hz, 3H), 1.14 (d, $J = 7.0$ Hz, 3H), 0.89 (d, $J = 7.3$ Hz, 3H), 0.87 (d, $J = 6.8$ Hz, 3H), 0.81 (s, 9H), 0.80 (d, $J = 8.4$ Hz, 3H), 0.04 (s, 3H), −0.28 (s, 3H), signals due to two protons (OH) were not observed; ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 180.0, 176.1, 164.9, 164.4, 119.5, 118.0, 76.9, 73.3, 71.9, 64.4, 41.5, 40.9, 38.0, 37.5, 26.7, 26.0 (3C), 24.8, 18.2, 16.9, 15.0, 13.0, 11.8, 11.3, 10.1, 9.9, 9.6, −3.9, −4.3; HRMS (ESI): *m*/*z* 555.3722, calcd for $C_{30}H_{55}O_7Si$ $[M + H]^+$ 555.3717.

To a stirred solution of diol **35a** (144 mg, 0.264 mmol) in acetone (1.5 mL) and H_2O (1.5 mL) was added $NaIO_4$ (120 mg, 0.445 mmol). The mixture was stirred at room temperature for 10 min, diluted with half saturated brine (5 mL), and extracted with EtOAc (3 × 10 mL). The combined extracts were dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (8 g, hexane–EtOAc 3:1 → 2:1 → 1:1) to give aldehyde **35b** (96.8 mg, 70%) as a colorless oil: $R_f = 0.73$ (1:1 hexane/EtOAc); $[\alpha]_D^{25}$ +11.0 (*c* 1.000, $CHCl_3$); IR ($CHCl_3$): 1726, 1654, 1594, 1462, 1426, 1378 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ 9.68 (d, $J = 3.5$ Hz, 1H), 5.26 (dd, $J = 9.1$, 5.8 Hz, 1H), 4.07 (dd, $J = 8.4$, 1.0 Hz, 1H), 3.19 (dq, $J = 8.4$, 7.0 Hz, 1H), 2.80–2.35 (m, 4H), 2.18–2.05 (m, 1H), 1.97 (s, 3H), 1.95 (s, 3H), 1.72 (ddq, $J = 14.4$, 7.2, 7.2 Hz, 1H), 1.49 (ddq, $J = 14.4$, 7.2, 7.2 Hz, 1H), 1.26 (t, $J = 7.6$ Hz, 3H), 1.18 (d, $J = 7.3$ Hz, 3H), 1.14 (d, $J = 7.0$ Hz, 3H), 1.12 (d, $J = 6.5$ Hz, 3H), 0.95 (d, $J = 7.6$ Hz, 3H), 0.94 (t, $J = 7.3$ Hz, 3H), 0.82 (s, 9H), 0.04 (s, 3H), −0.32 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 202.7, 179.5, 175.8, 163.9, 163.8, 119.5, 118.1, 75.0, 73.3, 47.6, 41.3, 40.4, 38.9, 26.7, 26.0 (3C), 24.8 (2C), 18.2, 16.7, 15.4, 11.8, 11.4, 10.0, 9.9, 9.5, −3.9, −4.5; HRMS (ESI): *m*/*z* 523.3436, calcd for $C_{29}H_{51}O_6Si$ $[M + H]^+$ 523.3455.

Aldol 35c. To a stirred solution of $Sn(OTf)_2$ (320 mg, 0.768 mmol) in CH_2Cl_2 (2 mL) were added triethylamine (0.100 mL, 0.753 mmol) and a solution of C14–C20 segment **17** (162 mg, 0.565 mmol) in CH_2Cl_2 (1 mL) at −78 °C. After the mixture was stirred at −78 °C for 1 h, a solution of aldehyde **35b** (96.8 mg, 0.185 mmol) in CH_2Cl_2 (1 mL) was added via cannula. The reaction mixture was stirred at −78 °C for 3.5 h, diluted with pH 6.8 phosphate buffer (15 mL), and filtered through a pad of Celite. This Celite was rinsed with EtOAc (4 × 5 mL). The filtrate and rinses were combined, and the layers were separated. The aqueous layer was extracted with EtOAc (3 × 10 mL). The organic layer and extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (10 g, hexane–EtOAc 10:1 → 3:1 → 2:1) to give a diastereomeric mixture of aldol **35c** (139 mg, 93%) as a

colorless oil: $R_f = 0.87$, 0.81 (1:1 hexane/EtOAc); IR ($CHCl_3$): 3507, 1723, 1694, 1653, 1592, 1462, 1426, 1379 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 5.12 (d, $J = 10.0$ Hz, 1H), 4.41 (d, $J = 8.4$ Hz, 1H), 4.06 (d, $J = 9.5$ Hz, 1H), 4.02–3.82 (m, 1H), 3.75–3.70 (m, 1H), 3.13 (t, $J = 7.6$ Hz, 1H), 3.00–2.25 (m, 5H), 2.12–2.05 (m, 1H), 1.96 (s, 3H), 1.94 (s, 3H), 1.82–1.65 (m, 1H), 1.52–1.30 (m, 2H), 1.30–1.00 (m, 15H), 1.00–0.70 (m, 36H), 0.58 (q, $J = 8.0$ Hz, 6H), 0.02 (s, 3H), −0.38 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 220.0, 217.1, 179.7 (2C), 176.1 (2C), 165.3, 165.1, 163.5 (2C), 119.2, 119.1, 117.9 (2C), 78.3, 78.1, 77.2, 75.7, 73.0, 72.9 (2C), 70.1, 49.7, 48.9, 48.6, 47.4, 46.9, 41.6, 41.3, 41.2, 40.0, 38.0, 37.8, 36.6, 36.2, 36.0, 35.3, 26.8, 26.2, 26.1, 26.0, 25.9, 24.7, 24.4, 23.3, 18.3, 16.9, 16.2, 15.6, 15.0, 14.9, 14.1 (2C), 12.4 (2C), 12.3, 12.2 (2C), 11.9, 11.1, 11.0, 9.8, 9.6, 7.6, 7.5, 7.4, 7.0, 6.9, 6.6, 5.9, 5.5, 5.4, 5.3, 5.3, −3.8, −4.3; HRMS (ESI): m/z 831.5591, calcd for $C_{45}H_{84}O_8Si_2Na$ $[M + Na]^+$ 831.5602.

Triketone 35e. Aldol **35c** (82.5 mg, 102 μmol) was treated with a 4:4:1 mixture of acetic acid, H_2O, and THF (4.5 mL) at room temperature for 13 h. The mixture was poured into saturated aqueous $NaHCO_3$ (70 mL) at 0 °C and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (10 g, hexane–EtOAc 3:1 → 2:1 → 1:1) to give a diastereomeric mixture of diol **35d** (60.2 mg, 84%) as a colorless oil: $R_f = 0.68$, 0.61, 0.45 (1:1 hexane/EtOAc); IR ($CHCl_3$): 3493, 1723, 1652, 1592, 1462, 1427, 1379 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 5.12 (d, $J = 9.5$ Hz, 1H), 4.32 (d, $J = 8.1$ Hz, 1H), 3.96 (d, $J = 8.9$ Hz, 1H), 3.70–3.55 (m, 1H), 3.25–3.10 (m, 1H), 3.05–2.75 (m, 2H), 2.70–2.30 (m, 4H), 2.20–2.00 (m, 1H), 1.97 (s, 3H), 1.94 (s, 3H), 1.80–1.65 (m, 2H), 1.60–1.35 (m, 2H), 1.30–1.05 (m, 15H), 1.05–0.75 (m, 27H), 0.04 (s, 3H), −0.31 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 220.8, 179.7, 176.2, 165.0, 163.6, 119.3, 118.0, 77.2, 74.8, 73.1, 70.3, 47.1, 47.0, 45.7, 41.6, 41.2, 39.9, 39.1, 38.1, 37.4, 36.3, 36.1, 34.4, 33.3, 30.6, 26.8 (2C), 26.1, 26.0, 25.9, 25.0, 24.8, 18.3 (3C), 17.1, 16.9, 16.8, 15.4, 15.2, 14.9, 14.8 (2C), 11.9 (2C), 11.2, 9.8, 9.6, −3.9, −4.2; HRMS (ESI): m/z 717.4747, calcd for $C_{39}H_{70}O_8SiNa$ $[M + Na]^+$ 717.4738.

To a stirred solution of diol **35d** (60.2 mg, 86.6 μmol) in CH_2Cl_2 (2 mL) was added Dess–Martin periodinane (260 mg, 471 μmol) at room temperature. The mixture was stirred at room temperature for 35 min; diluted with a 1:1:2 mixture of saturated aqueous $NaHCO_3$, saturated aqueous $Na_2S_2O_3$ and H_2O (4 mL); and extracted with Et_2O (2 × 10 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (6 g, hexane–EtOAc 5:1 → 3:1 → 1:1) to give a keto–enol equilibrium mixture of triketone **35e** (51.8 mg, 87%) as a colorless oil: $R_f = 0.66$ (1:1 hexane/EtOAc); $[\alpha]_D^{25}$ +23.4 (c 1.036, $CHCl_3$); IR ($CHCl_3$): 1724, 1653, 1593, 1462, 1427, 1379 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$): δ 16.94 (s, 0.07H), 16.81 (s, 0.06H), 16.67 (s, 0.18H), 5.55–5.39 (m, 0.3H), 5.32–5.25 (m, 0.4H), 5.20–5.08 (m, 0.3H), 4.15–3.60 (m, 1.69H), 3.55–3.30 (m, 0.7H), 3.30–3.00 (m, 1.3H), 2.80–2.45 (m, 3H), 2.45–2.20 (m, 1H), 2.20–1.55 (m, 12H), 1.50–1.05 (m, 18H), 1.05–0.70 (m, 21H), {(0.10)–(−0.05)} (m, 3H), {(−0.10)–(−0.40)} (m, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 210.1, 209.8, 198.5, 195.0, 193.7, 191.5 (2C), 190.5, 179.6, 179.5 (2C), 177.7 (2C), 175.7, 175.6, 164.8, 164.7, 164.6, 164.5, 164.4, 164.3, 164.2, 164.1, 119.7, 119.6 (2C), 119.5 (2C), 117.9 (2C), 117.8 (2C), 109.4, 108.3, 105.6, 105.1, 104.4, 104.0, 103.8, 103.5, 100.5, 77.7, 77.3, 77.2, 76.7, 74.8, 74.4, 47.0, 46.6, 46.1, 46.0, 45.9, 44.8, 41.4 (3C), 41.3, 40.4, 40.0, 39.9, 39.8, 39.7, 39.6, 39.7, 39.3, 38.7, 38.6, 38.4, 26.9, 26.6, 26.5, 26.3, 26.2, 26.1, 26.0, 25.7, 24.9, 18.4, 18.3, 18.1, 16.0, 11.7 (2C), 11.6, 10.0, 9.6, −3.7 (2C); HRMS (ESI): m/z 713.4423, calcd for $C_{39}H_{66}O_8SiNa$ $[M + Na]^+$ 713.4425.

(2′*R*)-Auripyrone B (2′-*epi*-Auripyrone B) (36). A solution of triketone **35e** (51.8 mg, 75.1 μmol) in a 5:3:7 mixture of HF•pyridine, pyridine, and THF (10.0 mL) was stirred at 60 °C for 19.5 h. The mixture was poured into saturated aqueous $NaHCO_3$ (150 mL) at 0 °C and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated. The residual oil was purified by column chromatography on silica gel (6 g, hexane–EtOAc 5:1 → 2:1 → 1:1) and by preparative HPLC [Develosil ODS–HG–5 (250 × 20 mm), flow rate 5 mL min^{-1}; detection, UV 215 nm, solvent 80% aqueous MeOH] to give (2′*R*)-auripyrone B (2′-*epi*-auripyrone B) (**36**) (10.3 mg, 25%) as colorless crystals: $R_f = 0.37$ (1:1 CH_2Cl_2/Et_2O); $[\alpha]_D^{25}$ +35.7 (c 0.837, $CHCl_3$); IR ($CHCl_3$): 1726, 1655, 1623, 1461, 1426, 1386 cm^{-1}; ^1H NMR (600 MHz, C_6D_6): δ 4.90 (dd, $J = 3.4$, 3.4 Hz, 1H), 3.95 (dd, $J = 10.3$, 2.2 Hz, 1H), 2.74 (dq, $J = 10.3$, 7.0 Hz, 1H), 2.43 (ddq, $J = 7.0$, 7.0, 7.0 Hz, 1H), 2.35–2.11 (m, 3H), 2.09 (dq, $J = 15.0$, 7.4 Hz, 1H), 2.02 (s, 3H), 1.97 (s, 3H), 1.88–1.65 (m, 3H), 1.64 (s, 3H), 1.58–1.48 (m, 1H), 1.43–1.32 (m, 2H), 1.13 (d, $J = 7.0$ Hz, 3H), 1.11 (d, $J = 7.0$ Hz, 3H), 0.99 (d, $J = 6.8$ Hz, 3H), 0.89 (t, $J = 7.4$ Hz, 3H), 0.88 (t, $J = 7.6$ Hz, 3H), 0.83 (t, $J = 7.5$ Hz, 3H), 0.77 (d, $J = 7.1$ Hz, 3H), 0.71 (d, $J = 7.0$ Hz, 3H), 0.63 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (150 MHz, C_6D_6): δ 191.9, 178.6, 175.8, 166.3, 162.2, 161.6, 121.4, 118.2, 107.9, 105.1, 75.1, 70.7, 44.6, 42.0, 37.3, 36.6, 34.1, 31.8, 27.0, 26.3, 24.8, 17.0, 16.0, 12.2, 12.0 (2C), 11.9, 11.0, 10.8, 9.8, 9.5, 9.0, 8.2; HRMS (ESI): m/z 581.3443, calcd for $C_{33}H_{50}O_7Na$ $[M + Na]^+$ 581.3454.

Cytotoxic Activity Assay. Stock cultures of HeLa S_3 cells were maintained in Eagle's Minimum Essential Medium containing Earle's Balanced Salts and 10% fetal bovine serum (DS Pharma Biomedical Co., Ltd.) and 1% antibiotic–antimycotic mixed stock solution {penicillin (10000 units mL^{-1}), streptomycin (10 mg mL^{-1}), and amphotericin B (25 μg mL^{-1})} at 37 °C under 5% CO_2.

For the purpose of the experiment, 2×10^3 cells suspended in 100 μL of medium per well were plated in a 96-well plate. After 12 h incubation at 37 °C under 5% CO_2 to allow cell attachment, compounds in 100 μL of medium were added to the wells at different concentrations and incubated for 96 h under the same conditions. After 3 h of the MTT (1.44 mg mL^{-1}, 50 μL) addition to each well, the medium/MTT mixtures were removed, and the formazan crystals formed were dissolved in 150 μL of DMSO per well. After 30 min, optical absorbance at 540 nm were measured with a microplate reader. The cytotoxic effects of each compound were obtained as IC_{50} values.

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Supporting Information

^{1}H and ^{13}C NMR spectra of all new compounds. This material is available free of charge on the Web at http://www.csj.jp/journals/bcsj/.

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