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Article

Total Synthesis of Clostrienose

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Cite This: *ACS Omega* 2023, 8, 35382−35392

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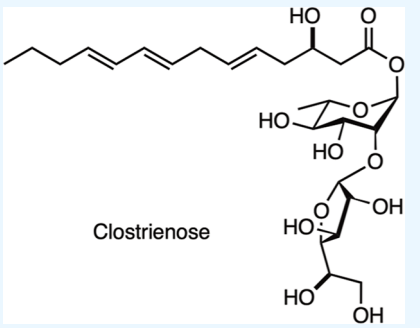
ABSTRACT: This paper considers the total synthesis of a cellular differentiation regulator of *Clostridium acetobutylicum*, clostrienose, which is a unique fatty-acid glycosyl ester consisting of clostrienoic acid, (3*R*,5*E*,8*E*,10*E*)-3-hydroxy-tetradeca-5,8,10-trienoic acid and α-D-galactofuranosyl-(1 → 2)-α-L-rhamnose. The key features of our synthesis include stereoselective construction of a skipped-triene system in clostrienoic acid and its esterification with a disaccharide residue. The partially protected clostrienoic acid employed for the coupling also served for the preparation of L-rhamnosyl clostrienoate, thus leading to confirmation of the proposed structure unambiguously.



INTRODUCTION

Polyketides constitute one of the major classes of natural products having diverse carbon structures. A number of polyketide natural products have been identified as biologically important molecules such as antibiotic, immunosuppressant, anticancer, and antiparasitic agents.[1] Some of these natural products serve as regulators to influence expression of specific genes of their producing organisms.[2] One source of such natural products is known to be aerobic organisms, and there have been few anaerobic organisms that produce polyketides.[3]

Clostridium acetobutylicum is an anaerobic bacterium well known for its historical use as an industrial producer of the organic solvents acetone, butanol, and ethanol (ABE). In 2017, Zhang *et al.* isolated three new polyketides **1**−**3** from the culture broth of *C. acetobutylicum* ATCC 824 (Figure 1).[4] Clostrienose (**1**) was one of the major constituents and was elucidated to have a unique glycosyl ester structure consisting of α-D-galactofuranosyl-(1 → 2)-α-L-rhamnosyl moiety and a tetradecatrienoic acid derivative termed clostrienoic acid (**2**) by extensive NMR, mass spectrometry (MS) and UV spectral analyses. The absolute configuration of **2** was deduced by correlation of its hydrogenation product with (*R*)-hydroxy-tetradecanoic acid.[5] The molecular structure of **3** was tentatively assigned based on the limited physical data [UV and liquid chromatography (LC)−MS] and thus remained inconclusive. The same authors demonstrated that these polyketides acted as chemical triggers of sporulation and granulose accumulation in this strain, suggesting them to be signaling molecules used by the strain to control cellular physiology and metabolism. Such biological significance coupled with the structural rarity[6] makes these natural products fascinating synthetic targets. Furthermore, development of an efficient method for preparation of an authentic sample might be quite useful for identification of a natural product obtained from the culture broth. Interest derived from these considerations has prompted us to prepare them. In this paper, we report the total synthesis of **1**−**3**.

RESULTS AND DISCUSSION

The structural feature of clostrienose (**1**) includes a chemically unstable skipped-triene system[7] in the fatty-acid moiety connected to an anomeric center of the disaccharide residue. In order to avoid destruction of the triene-ester system during the synthetic process, the proper choice of *O*-protecting groups in synthetic intermediates seemed to be a significantly important problem; usual protecting groups such as benzyl and benzoyl employed in oligosaccharide synthesis might be inappropriate. Therefore, we considered that the deprotection reaction at the final stage of the total synthesis should be performed under mild acidic conditions. In the successful synthesis plan, we have presumed that **1** would be accessible from a fatty acid **4** carrying an acid-labile *O*-protecting group and a silylated disaccharide **7**[8] (Scheme 1) and that the obligatory esterification would lead to the desired α-isomer predominantly by an anomeric effect. The triene system in **4** could be constructed by Migita−Kosugi−Stille coupling[9] of vinylstannane **5** and *E*,*E*-diene **6**, while disaccharide **7** would be synthesized from thioglycoside **8**[10] *via* a simple manipulation. In addition, this strategy would also enable us to prepare **3** by changing disaccharide **7** to monosaccharide **20** (see Scheme 4) for esterification.

Received: July 25, 2023
Accepted: August 22, 2023
Published: September 11, 2023

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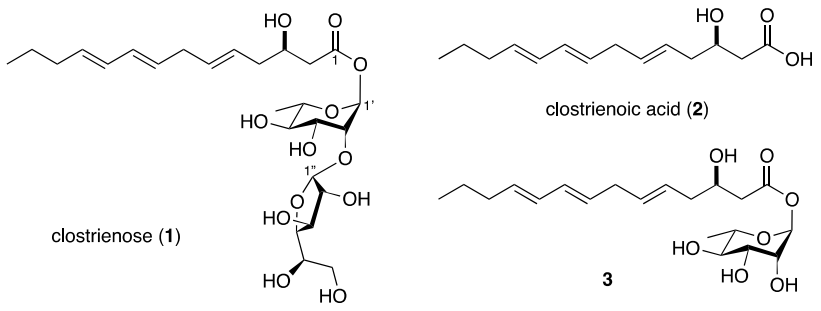
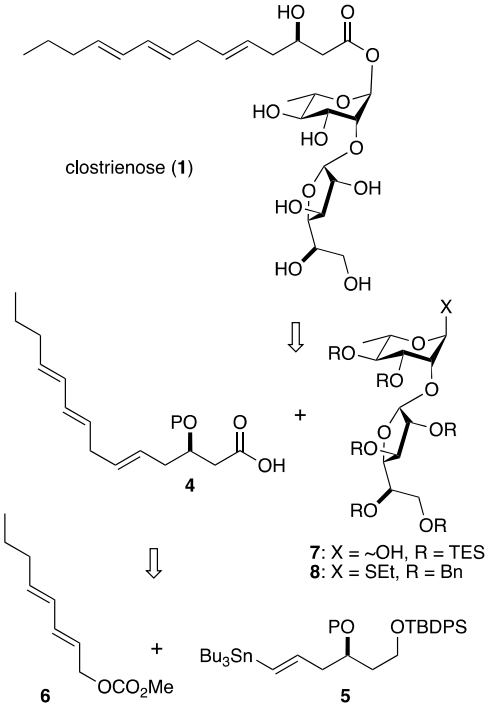


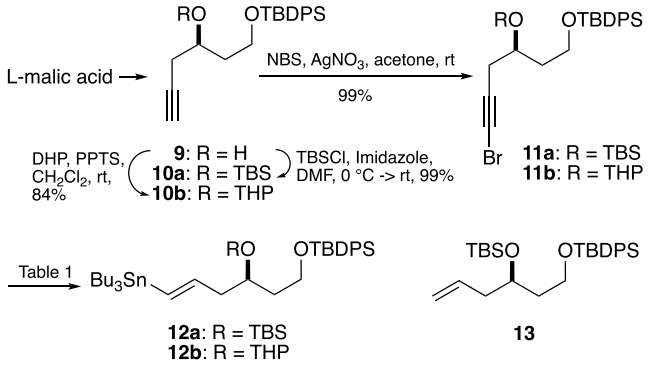
Figure 1. Structures of polyketides derived from *C. acetobutylicum* ATCC 824.

Scheme 1. Synthetic Plan of Clostrienose (1)



Our synthesis began with installation of an acid-cleavable protecting group into terminal acetylene **9**[11] which is readily obtainable from L-malic acid (Scheme 2). Treatment of **9** with TBSCl/imidazole or 2,3-dihydropyran/PPTS gave the corresponding tert-butyldimethylsilyl ether **10a** or 2-tetrahydropyranyl ether **10b**. Each compound was further transformed into bromide **11a** or **11b** by the action of *N*-bromosuccinimide-silver nitrate ($AgNO_3$).[12] Stereoselective hydrostannylation of the C−C triple bond in **10** or **11** was one of the key steps in this total synthesis and was investigated under several conditions (Table 1). Under conventional conditions (Bu_3SnH, AIBN, toluene, 100 °C),[13] a mixture of stereoisomers (*E*/*Z* = *ca.* 6/1−7/1) of 1-tributylstannyl-1-alkenes **12a,b** was obtained. Hydrostannylation using a palladium catalyst[14−18] suppressed formation of the corresponding *Z*-isomer, resulting in the production of terminal isomers in a variety of ratios. For silyl series **10a** and **11a**, a considerable amount (5−41%) of a protiodestannylation[19] product **13** was observed. Among the results, the reaction of **11b** with a combination of Bu_3SnH-tetrakis(triphenylphosphine)-palladium[20] (entry 9) afforded desired vinylstannane **12b** in high yield (>95% *E*-selectivity), and this compound, without separation of undesired regioisomers, was employed for the coupling reaction in Scheme 3.

Scheme 2. Preparation of Vinylstannane Derivatives

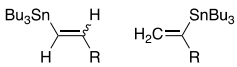


For the coupling partner, allyl carbonate **6**[21] was selected because it can be readily prepared as a geometrically pure form.[22,23] The Migita−Kosugi−Stille coupling of **12b** with **6** was investigated under several conditions (Table 2).[24−28] It was revealed that the coupling product **14** contained 8*Z*,10*E*- and 8*E*,10*Z*-isomers (8*Z*:10*Z* = *ca.* 1:1), whose ratio was determined by NMR analyses.[29] The best result was obtained by the use of tris(dibenzylideneacetone)dipalladium (0.03 equiv)[30] and lithium chloride (6.6 equiv) in dimethylformamide (DMF) to give **14** in high yield. As the separation of regioisomers was found to be difficult on a practical scale, this coupling product was employed for the next desilylation, and the minor cis-isomers (not shown) were removed by high-performance liquid chromatography (HPLC) separation. Alcohol **15** thus obtained was transformed into the corresponding carboxylic acid **16** *via* Dess−Martin oxidation, followed by Pinnick oxidation.[32] Finally, exposure of this to mild acidic conditions (acetic acid−water, rt) led to the formation of **2** after HPLC separation. The physical and spectral data were identical to those of the natural product.

Prior to the total synthesis of **1**, we embarked on the synthesis of **3** to optimize the reaction conditions of the esterification and a global deprotection at the final stage. Benzyl L-rhamnoside (**17**)[33] was selected as a starting material (Scheme 4), and preparation of **18** was attempted. However, hydrogenation of the *tri*-TES derivative obtained from **17** caused partial desilylation, resulting in a complex mixture.[34] This side reaction could not be reduced with several basic additives (*e.g.*, $NaHCO_3$). Therefore, we revised our protecting group strategy; the $C_{2,3}$-diol moiety of **17** was initially protected with acetonide and the remaining C_4-alcohol was transformed to the TES ether **19**. Its debenzylation proceeded without problems to give hemiacetal **20** in good yield. The crucial coupling[35] of **20** with **16** was affected by the action of

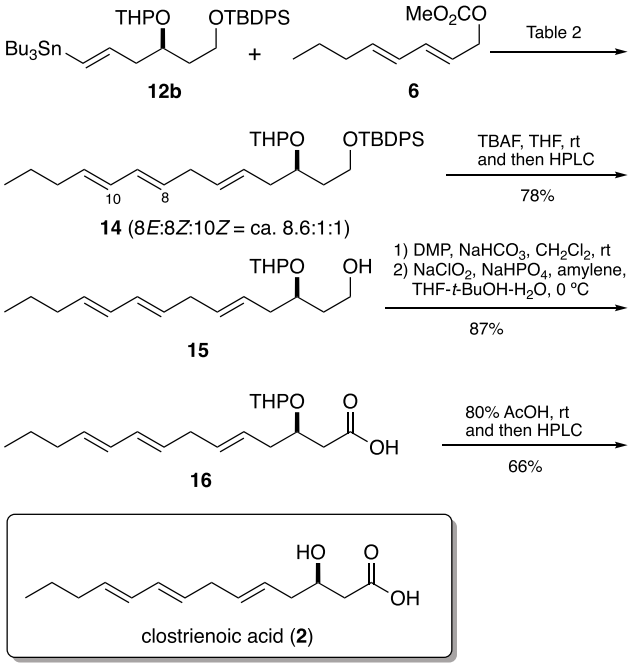
https://doi.org/10.1021/acsomega.3c05277
ACS Omega 2023, 8, 35382−35392

Table 1. Preparation of *E*-Vinylstannane 12a or 12b *via* Hydrostannylation of 10 or 11

entry	conditions	ratio[a] (*E*/*Z*/terminal)  *E* or *Z* terminal	yield[b] (%)
1	**10a**, Bu_3SnH (1.2 eq.), AIBN, 100 °C	84/15/1[c]	93
2	**10b**, Bu_3SnH (1.2 eq.), AIBN, 100 °C	85/14/1	90
3	**10a**, Bu_3SnH (1.2 eq.), $Pd_2(dba)_3$ (0.005 eq.), $(C_6H_{11})_3P{\cdot}HBF_4$ (0.2 eq.), Hünig's base (0.4 eq), CH_2Cl_2, 0 °C	80/2/18[c]	54
4	**10b**, Bu_3SnH (1.2 eq.), $Pd_2(dba)_3$ (0.005 eq.), $(C_6H_{11})_3P{\cdot}HBF_4$ (0.2 eq.), Hünig's base (0.4 eq), CH_2Cl_2, 0 °C	79/0/21	86
5	**10b**, Bu_3SnH (1.1 eq.), $Pd(PPh_3)_2Cl_2$ (0.02 eq.), CH_2Cl_2, rt	50/0/50	77
6	**11a**, Bu_3SnH (1.2 eq.), $Pd_2(dba)_3$ (0.005 eq.), Ph_3P (0.04 eq.), CH_2Cl_2, rt	94/1/5[c]	74
7	**11b**, Bu_3SnH (1.2 eq.), $Pd_2(dba)_3$ (0.005 eq.), Ph_3P (0.04 eq.), CH_2Cl_2, rt	87/5/8	82
8	**11a**, Bu_3SnH (3.0 eq.), $Pd(Ph_3P)_4$ (0.05 eq.), THF, -78 °C -> rt	95/2/3[c]	64
9	**11b**, Bu_3SnH (3.0 eq.), $Pd(Ph_3P)_4$ (0.05 eq.), THF, -78 °C -> rt	95/3/2	91

[a]Determined by ^1H NMR analysis. [b]Combined yield of olefin isomers after flash column chromatography. [c]As another product, terminal olefin **13** possibly arising from the protiodestannylation product was also detected.

Scheme 3. Synthesis of Clostrienoic Acid (2)



N,*N*′-dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridine (DMAP) in dichloromethane to give the desired product **22** in 86% yield along with the *β*-anomer **21** (5%). The stereochemistry of each isomer was assigned by comparison of the chemical shift of the anomeric proton [δ_H 6.19, 6.14 (each d, J = 2.6−2.7 Hz) for **21** *vs* δ_H 6.70, 6.69 (each s) for **22**] to those of 2,3-*O*-isopropylidene-L-rhamnopyranosyl benzoates reported in the literature[36] and by the difference NOE experiments of **21**; strong NOE was observed for the signal of H-5′ upon irradiation of $H_{1'}$ (see Supporting Information, S-31).[37] The *α*-isomer **22** underwent

Table 2. Migita−Kosugi−Stille Coupling of 12b and 6

entry	Conditions	ratio[a] 8*E*/(8*Z* + 10*Z*)	yield[b] (%)
1	$Pd_2(dba)_3{\cdot}CHCl_3$ (0.03 equiv), LiCl (6.6 equiv), DMF, 0 °C	69/31	53
2	$[Pd(\eta^3\text{-}C_3H_5)Cl_2]_2$ (0.03 equiv), DPPB (0.05 equiv), DMF, 0 °C	62/38	40
3	$Pd(OAc)_2$ (0.05 equiv), *n*-Bu_4NCl (1.1 equiv), Hünig's base (2.5 equiv), DMF, rt	83/17	31
4	$Pd_2(dba)_3$ (0.03 equiv), LiCl (6.6 equiv), Hünig's base (1.2 equiv), DMF, rt	77/23	63
5	$Pd_2(dba)_3$ (0.03 equiv), LiCl (7.0 equiv), Hünig's base (1.2 equiv), NMP, rt	76/24	61
6	$Pd_2(dba)_3$ (0.03 equiv), LiCl (6.6 equiv), DMF, rt	81/19	89
7	$Pd(PPh_3)_4$ (0.05 equiv), LiCl (6.6 equiv), DMF, rt	65/35	20[c]
8	$Pd(PPh_3)_4$ (0.05 equiv), CuI (4.0 equiv), DMF, rt	65/35	1[c]

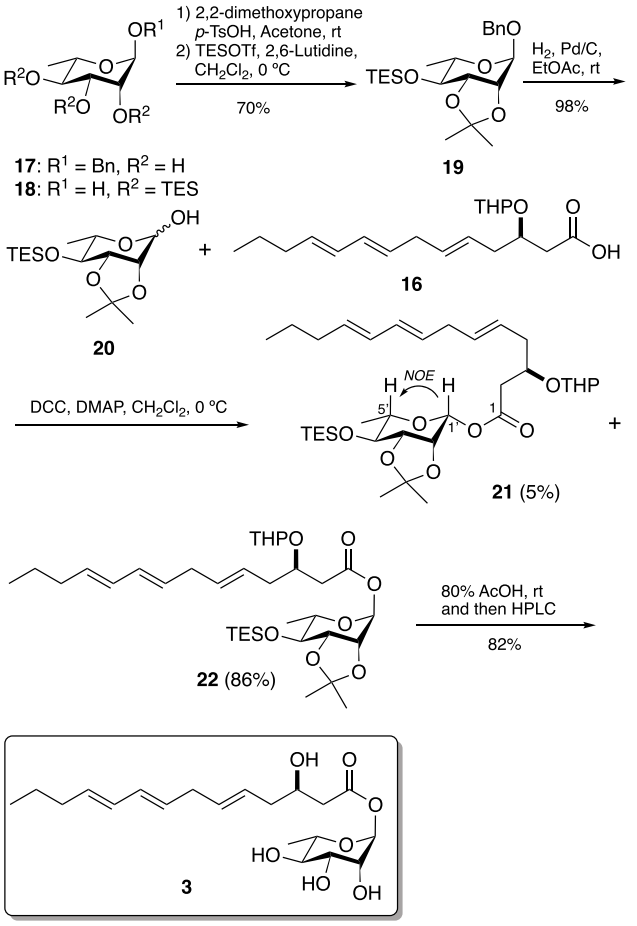
[a]Determined by ^1H NMR analysis. 8*Z* and 10*Z* mean 8*Z*, 10*E*- and 8*E*, 10*Z*-isomers, respectively. [b]Combined yield. [c]A mixture of homodimers derived from **12b** was obtained as major products (70~80%).[31]

hydrolysis under acidic conditions, affording **3**[38] after HPLC separation. The gross structure of **3** including the stereochemistry of the C-1 position was confirmed by extensive NMR analyses. In particular, the configuration of the anomeric position was also supported by the $^1J_{CH}$ coupling constant (173 Hz).[39] The other physical data for **3** showed agreement with those of the reported data for the natural product[4] (see Supporting Information, S-32).

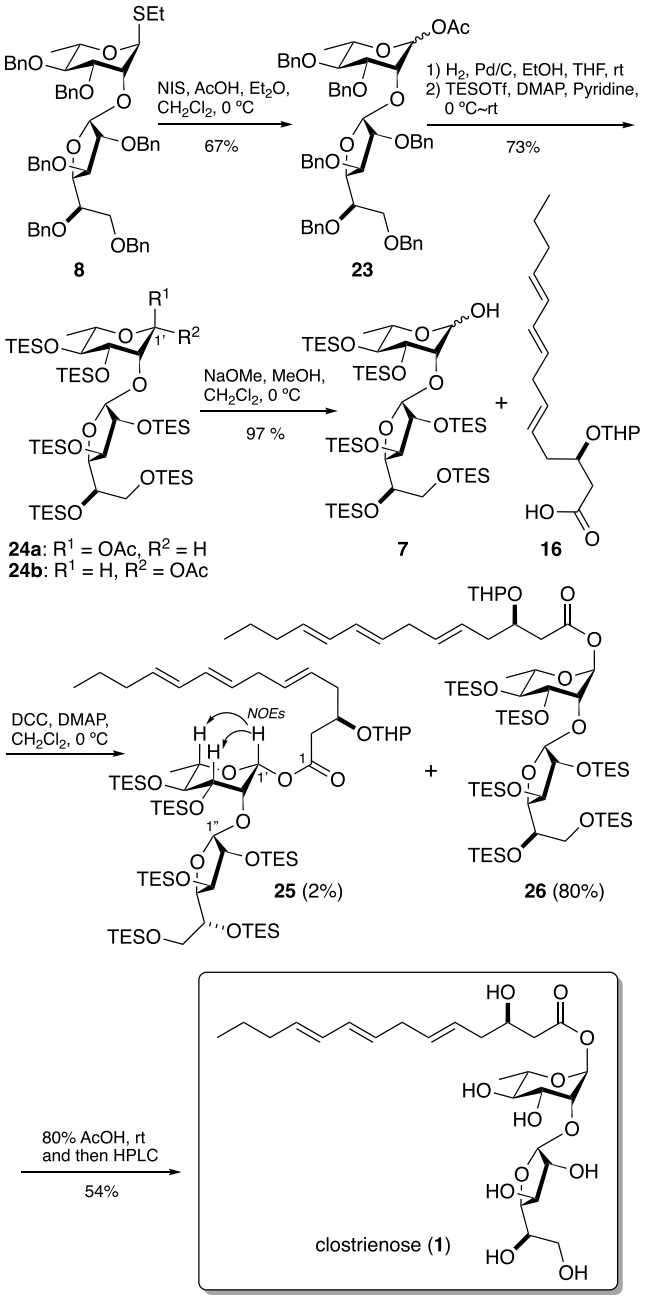
Having completed the stereoselective synthesis of **2** and **3**, we next turned our attention to the total synthesis of **1**. Disaccharide **7** was prepared from **8**, as summarized in Scheme 5. Treatment of **8** with *N*-iodosuccinimide in the presence of acetic acid[40] provided the corresponding glycosyl acetate **23** as an anomeric mixture. After hydrogenolysis of the benzyl

https://doi.org/10.1021/acsomega.3c05277
ACS Omega 2023, 8, 35382−35392

Scheme 4. Synthesis of L-Rhamnosyl Clostrienoate (3)



Scheme 5. Total Synthesis of Clostrienose (1)



groups, the resulting compound was silylated with TESOTf-DMAP in pyridine to afford fully protected disaccharides **24a,b** (major/minor = *ca.* 2/1) in high yield. To accurately assign **24a** and **24b** in ^{1}H NMR, a mixture of the diastereomers was separated into each isomer by HPLC. In the ^{1}H NMR spectra (C_6D_6), the anomeric proton at C-1′ of the major product was observed at 6.47 ppm as a broad singlet,[37] whereas the corresponding signal of the minor showed a sharp singlet (δ_H 5.78). The spectral broadening of the major product suggested that the anomer exists as several conformers in solution that have a relatively high barrier for interconversion. In order to suppress the reversible conformational changes, NMR measurements were performed using CD_2Cl_2 at −35 °C. As expected, a couple of signals derived from two conformers were observed in the ^{1}H NMR spectra, and the large coupling-constant value ($J_{1',2'}$ = 7.3 Hz) of the anomeric proton of the minor conformer at 5.84 ppm revealed the major product to be a 1′,2′-*trans* isomer **24a**. The structure of the minor product **24b** was supported by the difference NOE experiments (see Supporting Information, S-33).[37] Thus, irradiation of $H_{1'}$ caused enhancement of signals due to $H_{3'}$ and $H_{5'}$. These results became useful information for structural determination of the later esters (*vide infra*). Compounds **24a,b**, upon brief treatment with sodium methoxide, led to the formation of **7**. According to the procedure described above, **7** was coupled with **16**, affording **26** as a major product. In this reaction, a trace amount of **25** was also isolated. Concerning the assignment of stereochemistry, differentiation of the anomeric configuration newly created was conducted on the basis of the correlation of the chemical shift of H-1′ (δ_H 6.51 for **26** *vs* 5.84, 5.87 for **25**) with those of the corresponding acetates (δ_H 6.47 for **24a** *vs* 5.78 for **24b**) in the ^{1}H NMR spectra (C_6D_6).[37] Furthermore, the anomeric configuration of **25** was also confirmed by nuclear Overhauser effect spectroscopy spectra; there were cross peaks between $H_{1'}$ and $H_{3'}$, $H_{5'}$ in the L-rhamnose moiety (see Supporting Information, S-34). Finally, global deprotection of **26** was performed by treatment with aqueous acetic acid at rt, furnishing **1** after purification by HPLC.[38] The ^{1}H- and ^{13}C NMR spectral data of **1** were consistent with those of the natural product reported, thus confirming the structure of the natural product unambiguously.

In conclusion, clostrienoic acid (**2**) was synthesized *via* Migita−Kosugi−Stille coupling of octadienyl carbonate **6** and a chiral vinyltin derivative **12b** as a key step. By utilizing the

https://doi.org/10.1021/acsomega.3c05277
ACS Omega 2023, 8, 35382−35392

acid precursor **16** as a common key building block, total synthesis of a couple of fatty-acid glycosyl esters **1** and **3** was accomplished. Chemical preparation of these samples would be a useful tool for clarifying the metabolism of *C. acetobutylicum* and for improvement of ABE fermentation.

EXPERIMENTAL SECTION

General Experimental Procedures. Optical rotations were measured using a JASCO DIP-370 digital polarimeter. IR spectra were recorded by an attenuated total reflectance method using ZnSe prism on a JASCO FT/IR-4600 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded at 500 or 600 MHz with Agilent Technologies V500 or JEOL ECZ600 spectrometers. Chemical shifts were referenced to a residual signal of solvents [$CDCl_3$ (δ_H 7.26, δ_C 77.0), CD_2Cl_2 (δ_H 5.32, δ_C 53.8), C_6D_6 (δ_H 7.15, δ_C 128.0), and DMSO-d_6 (δ_H 2.62, δ_C 39.8)]. Electrospray ionization (ESI) MS was recorded on a JEOL JMS-T100 or Waters Synapt G2 mass spectrometer. Preparative HPLC was conducted on a Senshu SSC system with a Senshu Pak PEGASIL Silica 60−5 column (20 × 250 mm, SSC) or a Capcell Pak C_{18} column (20 × 250 mm, Shiseido). Merck precoated silica gel 60 F_{254} plates, 0.25 mm in thickness, were used for analytical thin-layer chromatography. Column chromatography was performed on Kanto Silica Gel 60N (spherical, neutral; 40−100 μm), and the columns were eluted in the flash mode.

*(R)-3-tert-Butyldimethylsilyloxy-1-tert-butyldiphenylsilyloxy-5-hexyne (**10a**).* To a stirred solution of **9** (3.52 g, 9.98 mmol) and imidazole (2.04 g, 29.9 mmol) in *N*,*N*-dimethylformamide (20 mL) was added *tert*-butyldimethylsilyl chloride (2.26 g, 15.0 mmol) at 0 °C, and the mixture was stirred at 0 °C—> rt for 16 h. After the addition of ice-water, the resulting mixture was stirred for 30 min and then extracted with ether. The combined organic layers were washed with cold HCl, water, saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ether = 100:1−>50:1) to give **10a** (4.29 g, 99%) as a syrup: $[\alpha]_D^{21}$ = −14.2 (*c* 1.1, $CHCl_3$); IR (ZnSe): ν_{max} 3311, 2928, 2856, 2117, 1471, 1254, 1086, 836, 701 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.70−7.63 (m, 4H), 7.44−7.36 (m, 6H), 4.07 (m, 1H), 3.78−3.73 (m, 2H), 2.37−2.35 (m, 2H), 1.98 (t, *J* = 2.7 Hz, 1H), 1.91 (m, 1H), 1.76 (m, 1H), 1.06 (s, 9H), 0.87 (s, 9H), 0.09 (s, 3H), 0.04 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 135.6, 133.9, 133.8, 129.6, 129.5, 127.6, 81.6, 70.0, 67.9, 60.4, 39.4, 27.6, 26.8, 25.8, 19.2, 18.0, −4.5, −4.8; HRMS (ESI): *m*/*z* 467.2782 $[M + H]^+$ (calcd for $C_{28}H_{43}O_2Si_2$, 467.2801).

*(R)-1-tert-Butyldiphenylsilyloxy-3-tetrahydropyranyloxy-5-hexyne (**10b**).* To a stirred solution of **9** (3.00 g, 8.52 mmol) and 3,4-dihydro-2*H*-pyran (1.32 mL, 14.5 mmol) in dichloromethane (25 mL) was added pyridinium *p*-toluenesulfonate (214 mg, 0.85 mmol) at rt. The mixture was stirred at rt for 5 h and then diluted with ether, washed with saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ether = 10:1−>5:1) to give **10b** (3.13 g, 84%) as a syrup: IR (ZnSe): ν_{max} 3313, 2926, 2117, 1235, 1087, 1022, 870, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.70−7.63 (m, 4H), 7.44−7.35 (m, 6H), 4.81 (brt, *J* = 3.6 Hz, 0.5H), 4.63 (brt, *J* = 3.9 Hz, 0.5H), 4.10−4.04 (m, 0.5H), 4.00−3.93 (m, 1H), 3.87−3.84 (m, 0.5H), 3.82−3.73 (m, 2H), 3.50−3.42 (m, 1H), 2.60 (ddd, *J* = 16.6, 4.4, 2.7 Hz, 0.5H), 2.52 (ddd, *J* = 16.6, 7.3, 2.7 Hz, 0.5H), 2.46 (ddd, *J* = 16.8, 6.1, 2.7 Hz, 0.5H), 2.38 (ddd, *J* = 16.8, 5.1, 2.7 Hz, 0.5H), 2.01−1.90 (m, 1.5H), 1.99 (t, *J* = 2.7 Hz, 0.5H), 1.96 (t, *J* = 2.7 Hz, 0.5H), 1.82−1.68 (m, 2H), 1.64−1.44 (m, 4.5H), 1.06, 1.05 (each s, total 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 135.5, 133.9, 133.8, 133.7, 129.6, 129.5, 127.60, 127.56, 100.0, 96.3, 81.4, 81.0, 73.6, 70.3, 69.9, 62.8, 62.2, 60.5, 60.0, 37.6, 36.6, 30.9, 30.7, 26.85, 26.81, 25.9, 25.4, 23.5, 19.8, 19.4, 19.2; HRMS (ESI): *m*/*z* 459.2326 $[M + Na]^+$ (calcd for $C_{27}H_{36}O_3SiNa$, 459.2331).

*(3R)-6-Bromo-3-tert-butyldimethylsilyloxy-1-tert-butyldiphenylsilyloxy-5-hexyne (**11a**).* To a stirred solution of **10a** (200 mg, 0.43 mmol) in acetone (2.0 mL) were added *N*-bromosuccinimide (83.7 mg, 0.47 mmol) and silver nitrate (7.3 mg, 43.0 μmol) at rt. The mixture was stirred at rt for 1 h and then diluted with ether, washed with water and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ether = 50:1) to give **11a** (235 mg, 99%) as a syrup: $[\alpha]_D^{23}$ = −13.8 (*c* 1.4, $CHCl_3$); IR (ZnSe): ν_{max} 2927, 2856, 1427, 1389, 1086, 890, 701 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.72−7.67 (m, 4H), 7.48−7.39 (m, 6H), 4.09 (m, 1H), 3.82−3.74 (m, 2H), 2.53−2.36 (m, 2H), 1.86 (m, 1H), 1.76 (m, 1H), 1.10 (s, 9H), 0.91 (s, 9H), 0.12 (s, 3H), 0.08 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 135.6, 135.5, 133.9, 133.8, 129.59, 129.56, 127.64, 127.63, 77.8, 67.9, 60.3, 39.6, 39.4, 28.8, 26.8, 25.8, 19.2, 18.0, −4.5, −4.8; HRMS (ESI): *m*/*z* 489.1127 [M-*t*-Bu]$^+$ (calcd for $C_{24}H_{32}O_2Si_2Br$, 489.1104).

*(3R)-6-Bromo-1-tert-butyldiphenylsilyloxy-3-tetrahydropyranyloxy-5-hexyne (**11b**).* To a stirred solution of **10b** (1.87 g, 4.27 mmol) in acetone (20 mL) were added *N*-bromosuccinimide (0.84 g, 4.70 mmol) and silver nitrate (72.5 mg, 0.43 mmol) at rt. The mixture was stirred at rt for 1 h and then diluted with ether, washed with water and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−benzene = 100:1 → 2:1 → 1:1) to give **11b** (2.20 g, 99%) as a syrup: IR (ZnSe): ν_{max} 3070, 2930, 2855, 2213, 1472, 1427, 1110, 1075, 1021, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.69−7.65 (m, 4H), 7.44−7.33 (m, 6H), 4.78 (brt, *J* = 3.2 Hz, 0.5H), 4.61 (brt, *J* = 3.7 Hz, 0.5H), 4.06 (m, 0.5H), 3.99−3.91 (m, 1H), 3.86 (m, 0.5H), 3.82−3.71 (m, 2H), 3.51−3.41 (m, 1H), 2.63 (dd, *J* = 16.6, 4.4 Hz, 0.5H), 2.53 (dd, *J* = 16.6, 7.6 Hz, 0.5H), 2.48 (dd, *J* = 16.9, 5.9 Hz, 0.5H), 2.41 (dd, *J* = 16.9, 5.1, 0.5H), 1.97−1.86 (m, 1.5H), 1.82−1.67 (m, 2H), 1.62−1.43 (m, 4.5H), 1.07, 1.06 (each s, total 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.52, 135.50, 133.85, 133.81, 133.7, 133.6, 129.6, 129.52, 129.50, 127.62, 127,59, 127.56, 100.0, 96.4, 77.4, 77.03, 73.5, 70.3, 62.7, 62.3, 60.4, 60.0, 39.3, 37.6, 36.7, 30.9, 30.7, 27.1, 26.82, 26.78, 25.4, 24.7, 19.8, 19.4, 19.1; HRMS (ESI): *m*/*z* 537.1431[M + Na]$^+$ (calcd for $C_{27}H_{35}O_3SiNaBr$, 537.1437).

*Hydrostannyllation of **10a**. Entry **8**.* To a stirred solution of **10a** (272 mg, 0.50 mmol) and tetrakis(triphenylphosphine) palladium {$Pd(Ph_3P)_4$} (31 mg, 26.8 mmol) in tetrahydrofuran (3 mL) was added dropwise tributyltin hydride (0.4 mL, 1.49 mmol) at −78 °C. The mixture was stirred at −78 °C for 1.2 h and rt for 1.8 h and then concentrated *in vacuo*. The residue was passed through a short column of silica gel (*n*-hexane → *n*-hexane/ether = 200/1 → 50/1) to give a 61:39 mixture of **12a** and **13** (340 mg). The latter was partly separated by preparative TLC. The yield of **12a** (*E*/*Z*/terminal = 95/2/3) was 64% by ^{1}H NMR analyses.

Entry 1. A mixture of **10a** (100 mg, 0.21 mmol), tributyltin hydride (0.07 mL, 0.26 mmol), and a trace amount of 2,2′-azo*bis*(isobutyronitrile) was heated at 100 °C with stirring for

https://doi.org/10.1021/acsomega.3c05277
ACS Omega 2023, 8, 35382−35392

1 h, cooled to rt, and then passed through a short column of silica gel (*n*-hexane) to give a 95:5 mixture of **12a** and **13** (156 mg). The former was obtained as an inseparable mixture (*E*/*Z*/terminal = 84/15/1), while the latter could be partly separated by preparative TLC. The yield of **12a** was 93% by ^{1}H NMR analyses.

12a. Syrup; IR (ZnSe): ν_{max} 2926, 2855, 1596, 1427, 1253, 1084, 1021, 773, 619 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.69−7.63 (m, 4H), 7.45−7.36 (m, 6H), 6.10−5.85 (m, 2H), 3.97 (m, 1H), 3.76−3.68 (m, 2H), 2.36−2.16 (m, 2H), 1.72−1.70 (m, 2H), 1.60−1.27 (m, 12H), 1.06 (s, 9H), 0.90 (s, 9H), 0.89−0.70 (m, 15H), 0.05 (s, 3H), 0.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 145.7, 135.6, 134.0, 133.9, 130.4 (J_{Sn-C} = 392.9 and 376.7 Hz), 129.49, 129.48, 127.6, 69.0, 60.8, 46.2, 39.7, 29.1 (J_{Sn-C} = 20.0 Hz), 27.3 (J_{Sn-C} = 54.4 Hz), 26.8, 25.8, 19.2, 18.1, 13.7, 9.4 (J_{Sn-C} = 341.5 and 326.2 Hz), −4.34, −4.63; HRMS (ESI): *m*/*z* 701.3244 [M-*t*-Bu]$^+$ (calcd for $C_{36}H_{61}O_2Si_2Sn$, 701.3232).

13. Syrup; $[\alpha]_D^{22}$ = −15.2 (*c* 0.1, $CHCl_3$); IR (ZnSe): ν_{max} 3069, 2856, 1639, 1474, 1428, 1235, 1086, 738, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.67−7.64 (m, 4H), 7.43−7.35 (m, 6H), 5.79 (m, 1H), 5.08−4.90 (m, 2H), 3.93 (ddd, *J* = 12.1, 6.1, 5.8 Hz, 1H), 3.75−3.68 (m, 2H), 2.27−2.15 (m, 2H), 1.72−1.63 (m, 2H), 1.04 (s, 9H), 0.85 (s, 9H), 0.04 (s, 3H), 0.01 (s, 3H); ^{13}C NMR ($CDCl_3$, 500 MHz): δ 135.5, 135.2, 133.9, 129.5, 127.6, 116.8, 68.8, 60.8, 42.0, 39.5, 26.8, 25.9, 19.2, 18.1, −4.4, −4.7; HRMS (ES): *m*/*z* 469.2955 [M + H]$^+$ (calcd for $C_{28}H_{45}O_2Si_2$, 469.2958).

*Hydrostannyllation of **11b**. Entry **9**.* To a stirred solution of **11b** (1.0 g, 1.94 mmol) and tetrakis(triphenylphosphine) palladium (115.6 mg, 0.1 mmol) in tetrahydrofuran (10 mL) was added dropwise tributyltin hydride (1.6 mL, 5.82 mmol) at −78 °C. The mixture was stirred at −78 °C for 1.5 h and then at rt for 1 h and concentrated. The residue was passed through a short column of silica gel (*n*-hexane−benzene = 2:1 → 1:1) to give **12b** (1.28 g, 91%) as an inseparable mixture of stereoisomers (*E*/*Z*/terminal = 95/3/2). This compound was employed to the next step without further purification.

12b. Syrup; IR (ZnSe): ν_{max} 2926, 2853, 1598, 1111, 1074, 1021, 997, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.70−7.65 (m, 4H), 7.43−7.35 (m, 6H), 6.10−5.88 (m, 2H), 4.73 (brt, *J* = 3.2 Hz, 0.5H), 4.65 (brt, *J* = 3.6 Hz, 0.5H), 3.97−3.71 (m, 4H), 3.49−3.37 (m, 1H), 2.65−2.21 (m, 2H), 1.92−1.41 (m, 14H), 1.31 (dq, *J* = 14.5, 7.1 Hz, 6H), 1.064, 1.060, 1.057 (each s, total 9H), 0.95−0.88 (m, 15H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 145.8, 145.2, 135.6, 135.5, 134.1, 134.0, 133.9, 133.8, 130.9, 130.3 (J_{Sn-C} = 394.8 and 375.9 Hz), 129.5, 129.4, 127.6, 127.53, 127.52, 98.6, 96.8, 74.1, 72.5, 62.5, 62.3, 60.9, 60.3, 44.5, 42.5, 37.9, 36.6, 30.9, 29.1 (J_{Sn-C} = 20.0 Hz), 27.3 (J_{Sn-C} = 54.0 Hz), 26.84, 26.81, 25.55, 25.50, 19.7, 19.6, 19.18, 19.15, 13.7, 9.38 (J_{Sn-C} = 340.5 and 324.3 Hz); HRMS (ESI): *m*/*z* 751.3545 [M + Na]$^+$ (calcd for $C_{39}H_{64}O_3SiSnNa$, 751.3544).

*(3R,5E,8E,10E)-1-tert-Butyldiphenylsilyoxy-3-tetrahydropyranyloxy-5,8,10-tetradecatriene (**14**).* To a stirred solution of **6** (229 mg, 1.24 mmol) and **12b** (1.13 g, 1.49 mmol) in *N*,*N*-dimethylformamide (10 mL) were added lithium chloride (347 mg, 8.18 mmol) and tris(dibenzylideneacetone)-dipalladium (34.1 mg, 37.2 μmol) at rt. The mixture was stirred at rt for 19 h. After the addition of ice water, the resulting mixture was extracted with ether. The combined organic layers were washed successively with water and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−benzene = 100:1 → 2:1 → 1:1) to give **14** (602 mg, 89%) as a syrup (5*E*,8*E*,10*E*/5*E*,8*Z*,10*E*/5*E*,8*E*,10*Z* = 8.6/1/1 by ^{1}H NMR analysis): IR (ZnSe): ν_{max} 2925, 2853, 1472, 1427, 1235, 1087, 871, 701 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): δ 7.81−7.71 (m, 4H), 7.23−7.20 (m, 6H), 6.09−5.99 (m, 2H), 5.63−5.39 (m, 4H), 4.73 (m, 1H), 4.04−3.95 (m, 1.5H), 3.91−3.85 (1H), 3.83−3.72 (m, 1.5H), 3.39 (m, 0.5H), 3.34 (m, 0.5H), 2.72−2.65 (m, 2H), 2.52−2.37 (m, 1H), 2.23−2.14 (m, 1H), 1.95−1.46 (m, 7H), 1.32−1.17 (m, 5H), 1.19, 1.15 (each s, total 9H), 0.83 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 500 MHz): δ 135.9, 134.51, 134.50, 134.4, 134.3, 133.2, 133.1, 131.4, 131.3, 131.1, 130.72, 130.68, 130.5, 130.4, 129.94, 129.87, 129.85, 128.0, 127.94, 127.93, 127.4, 99.2, 97.0, 74.7, 72.7, 62.9, 62.8, 61.4, 60.8, 39.3, 38.1, 37.2, 37.1, 36.0, 35.0, 31.5, 31.4, 27.00, 26.99, 25.98, 25.95, 22.9, 20.3, 20.2, 19.4, 13.8; HRMS (ESI): *m*/*z* 569.3411 [M + Na]$^+$ (calcd for $C_{35}H_{50}O_3SiNa$, 569.3427).

*(3R,5E,8E,10E)-3-Tetrahydropyranyloxy-tetradeca-5,8,10-trien-1-ol (**15**).* To a stirred solution of **14** (71.3 mg, 0.13 mmol) in tetrahydrofuran (1.5 mL) was added dropwise a 1.0 M solution of *n*-tetrabutylammonium fluoride in tetrahydrofuran (0.16 mL, 0.16 mmol) at rt. The mixture was stirred at rt for 4 h and then diluted with ethyl acetate, washed with brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane-ethyl acetate = 10:1 → 4:1) to give a syrup (40 mg) as a regioisomeric mixture. This was purified by HPLC using a Shiseido Capcell-Pak C_{18} column (20 × 250 mm) with a mobile phase of acetonitrile/water (80:20) to give **15** (31.3 mg, 78%) as a syrup: IR (ZnSe): ν_{max} 3417, 2923, 2870, 1432, 1383, 1235, 1076, 1022, 985, 868, cm^{-1}; ^{1}H NMR (C_6D_6, 500 MHz): δ 6.08−6.02 (m, 2H), 5.58−5.34 (m, 4H), 4.71 (t, *J* = 3.8 Hz, 0.5H), 4.40 (dd, *J* = 7.1, 2.5 Hz, 0.5H), 3.97 (m, 0.5H), 3.91 (m, 0.5H), 3.87−3.81 (m, 1H), 3.73 (m, 0.5H), 3.68 (m, 0.5H), 3.63 (m, 0.5H), 3.54 (m, 0.5H), 3.33 (m, 0.5H), 3.14 (m, 0.5H), 2.71 (brdt, *J* = 7,3, 6.4 Hz, 1H), 2.69 (brdt, *J* = 6,9, 6.1 Hz, 1H), 2.47 (m, 0.5H), 2.39 (m, 0.5H), 2.18−2.07 (m, 1H), 1.93 (brdt, *J* = 7.3, 7.1 Hz, 2H), 1.71−1.38 (m, 5H), 1.30−1.01 (m, 3H), 1.29 (brqd, *J* = 7.4, 7.3 Hz, 2H), 0.82 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (CD_2Cl_2,125 MHz): δ 133.25, 133.17, 131.5, 131.4, 131.3, 131.1, 130.64, 130.61, 130.3, 130.2, 127.6, 127.2, 100.4, 99.2, 76.8, 75.2, 65.4, 63.0, 60.3, 59.6, 39.0, 38.8, 37.4, 36.2, 35.9, 35.0, 31.61, 31.56, 25.9, 25.6, 22.9, 21.8, 20.2, 13.8; HRMS (ESI): *m*/*z* 331.2243 [M + Na]$^+$ (calcd for $C_{19}H_{32}O_3Na$, 331.2249).

*(3R,5E,8E,10E)-3-Tetrahydropyranyloxy-tetradeca-5,8,10-trienoic Acid (**16**).* To a stirred suspension of **15** (272 mg, 0.89 mmol) and $NaHCO_3$ (150 mg, 1.78 mmol) in dichloromethane (5.0 mL) was added Dess−Martin periodinane (560 mg, 1.32 mmol) at 0 °C, and the mixture was stirred at 0 °C for 1.5 h. After the addition of saturated aqueous $NaHCO_3$/$Na_2S_2O_3$ (1:1), the resulting mixture was extracted with ether. The combined organic layers were washed successively with water and brine, dried, and concentrated. The residue was passed through a short column of silica gel (*n*-hexane−ethyl acetate = 6:1) to give a syrup (241 mg) which was dissolved in tetrahydrofuran-2-methyl−2-propanol−water (8:3:1, 7.2 mL). To this solution were added $NaH_2PO_4{\cdot}2H_2O$ (417 mg, 2.67 mmol) and 2-methyl-2-butene (1.42 mL, 13.4 mmol). To a stirred solution of the above mixture was added dropwise a solution of sodium chlorite (242 mg, 2.67 mmol) in water (0.6 mL) at 0 °C, and the resulting mixture was stirred at the same temperature for 20 min. After the addition of saturated aqueous $Na_2S_2O_3$, the resulting mixture was extracted with

https://doi.org/10.1021/acsomega.3c05277
ACS Omega 2023, 8, 35382−35392

ethyl acetate. The combined organic layers were washed successively with water, brine, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 6:1 → 4:1) to give **16** (250 mg, 87%) as a syrup; IR (ZnSe): ν_{max} 3180, 3017, 2929, 2866, 1726, 1707, 1438, 1282, 1134, 1021, 984, 764 cm^{-1}; ^1H NMR (C_6D_6, 500 MHz): δ 6.09−6.00 (m, 2H), 5.54−5.29 (m, 4H), 4.83 (t, J = 3.5 Hz, 0.5H), 4.68 (t, J = 3.7 Hz, 0.5H), 4.23−4.19 (m, 1H), 3.87−3.80 (m, 1H), 3.39−3.31 (m, 1H), 2.68−2.60 (m, 2.5H), 2.48−2.33 (m, 2.5H), 2.19 (m, 1H), 1.95 (brdd, J = 7.4, 7.1 Hz, 2H), 1.69−1.62 (m, 1H), 1.60−1.54 (m, 1H), 1.55−1.50 (m, 1H), 1.31 (brqt, J = 7.4, 7.3 Hz, 2H), 1.28−1.19 (m, 3H), 0.84 (t, J = 7.3 Hz, 3H); ^{13}C NMR (500 MHz, C_6D_6): δ 178.1, 177.7, 132.77, 132.67, 131.9, 131.8, 131.7 (x2), 131.1, 131.07, 130.0, 129.9, 127.0, 126.5, 99.1, 97.7, 74.2, 73.3, 62.32, 62.27, 40.5, 39.3, 37.3, 35.97, 35.95, 35.0, 31.3, 31.1, 25.8, 25.7, 22.9, 19.80, 19.77, 13.8; HRMS (ESI): m/z 321.2069 $[M - H]^-$ (calcd for $C_{19}H_{29}O_4$, 321.2066).

*Clostrienoic Acid (**2**).* A solution of **16** (150 mg, 0.47 mmol) in 80% acetic acid (8.0 mL) was stirred at rt for 2 h and then concentrated. The residue was, after coevaporation with toluene (x2), purified by HPLC using a Shiseido Capcell-Pak C_{18} column (20 × 250 mm) with a mobile phase of acetonitrile: 0.1% formic acid−H_2O (40:60) to give **2** (74 mg, 66%) as an amorphous solid; $[\alpha]_D^{25}$ = −9.6 (c 0.55, $CHCl_3$) {lit.[4] $[\alpha]_D^{20}$ = −9.1 (c 1, $CHCl_3$)}; IR (ZnSe): ν_{max} 3379, 2959, 2924, 1710, 1235, 1086, 969, 873 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 6.02−5.95 (m, 2H), 5.55 (m, 2H), 5.47−5.37 (m, 2H), 3.82 (m, 1H), 2.72 (t, J = 4.8 Hz, 2H), 2.29 (dd, J = 14.9, 4.9 Hz, 1H), 2.17 (dd, J = 14.9, 8.3 Hz, 1H), 2.09 (t, J = 5.9 Hz, 2H), 1.99 (brdd, J = 7.1, 7.0 Hz, 2H), 1.34 (qd, J = 7.4, 7.1 Hz, 2H), 0.85 (t, J = 7.4 Hz, 3H); ^1H NMR (500 MHz, $CDCl_3$): δ 6.02−5.99 (m, 2H), 5.63−5.55 (m, 3H), 5.46−5.38 (m, 1H), 4.07 (m, 1H), 2.79 (t, J = 6.4 Hz, 2H), 2.58 (dd, J = 16.6, 3.5 Hz, 1H), 2.48 (dd, J = 16.6, 9.0 Hz, 1H), 2.26 (t, J = 6.4 Hz, 2H), 2.01−2.06 (brdd, J = 14.4, 7.1 Hz, 2H), 1.40 (qd, J = 7.3, 7.1 Hz, 2H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 173.0, 132.2, 130.7, 130.4, 130.1(x2), 127.5, 67.2, 41.9, 40.2, 34.9, 34.0, 22.0, 13.5; HRMS (ESI): m/z 237.1486 $[M - H]^-$ (calcd for $C_{14}H_{21}O_3$, 237.1491).

*Benzyl 2,3-O-isopropylidene-4-O-triethylsilyl-α-L-rhamnopyranoside (**19**).* To a stirred solution of **17** (1.88 g, 7.41 mmol) and 2,2-dimethoxypropane (1.09 mL, 8.90 mmol) in acetone (40.0 mL) was added *p*-toluenesulfonic acid monohydrate (141 mg, 0.74 mmol), and the mixture was stirred at rt for 12 h. After the addition of triethylamine, the resulting mixture was concentrated *in vacuo*. The residue was passed through a short column of silica gel (benzene−ethyl acetate = 6:1) to give the corresponding acetonide[29] (1.60 g, 73%) as a syrup. This compound was employed to the next step without further purification. To a stirred solution of the above acetonide (81.2 mg, 0.28 mmol) and 2,6-lutidine (48.0 μL, 0.41 mmol) in dichloromethane (2.0 mL) was added dropwise triethylsilyl trifluoromethanesulfonate (TESOTf) (76.9 μL, 0.34 mmol) at 0 °C, and the mixture was stirred at 0 °C ∼ rt for 8.5 h. After the addition of ice water, the resulting mixture was vigorously stirred for 10 min and then extracted with ether. The combined organic layers were washed successively with cold aqueous HCl, water, saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane → *n*-hexane-ether = 20:1) to give **19** (110 mg, 96%) as an amorphous solid; $[\alpha]_D^{21}$ = −46.4 (c 1.0, $CHCl_3$); IR (ZnSe): ν_{max} 2956, 2909, 2875, 1456, 1380, 1241, 1219, 1083, 865, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.35−7.29 (m, 4H), 5.03 (s, 1H), 4.69, 4.49 (each d, J = 11.8 Hz, total 2H), 4.15 (d, J = 5.5 Hz, 1H), 4.00 (dd, J = 7.1, 5.5 Hz, 1H), 3.68 (dq, J = 9.5, 6.1 Hz, 1H), 3.36 (dd, J = 9.5, 7.1 Hz, 1H), 1.51 (s, 3H), 1.33 (s, 3H), 1.26 (d, J = 6.1 Hz, 1H), 0.96 (t, J = 7.8 Hz, 9H), 0.66 (m, 6H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 137.2, 128.5, 128.2, 127.9, 108.9, 96.2, 79.1, 76.2, 75.9, 69.0, 66.1, 28.1, 26.4, 17.5, 6.8, 5.0; HRMS (ESI): m/z 431.2216 $[M + Na]^+$ (calcd for $C_{22}H_{36}O_5NaSi$, 431.2230).

*2,3-O-Isopropylidene-4-O-triethylsilyl-α-L-rhamnopyranose (**20**).* A mixture of **19** (200 mg, 0.49 mmol) and 10% Pd/C (40 mg) in ethyl acetate (4.0 mL) was stirred vigorously under a hydrogen atmosphere at rt for 1.5 h, filtered through a pad of Celite, and then concentrated. The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 4:1) to give **20** (153 mg, 98%) as an amorphous solid; IR (ZnSe): ν_{max} 3421, 2956, 2908, 2876, 1457, 1380, 1239, 1219, 1101, 1073, 844 cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2): δ 5.23 (d, J = 4.7 Hz, 0.89H), 4.92 (dd, J = 11.2, 2.5 Hz, 0.11H), 4.19 (dd, J = 5.8, 2.5 Hz, 0.11H), 4.14 (brd, J = 5.4 Hz, 0.89H), 4.05 (brt, J = 6.4 Hz, 1H), 3.83 (dq, J = 8.4, 6.3 Hz, 1H), 3.47 (d, J = 11.2 Hz, 0.11H), 3.46−3.36 (m, 1H), 3.00 (d, J = 4.7 Hz, 0.89H) 1.52 (s, 0.33H), 1.49 (s, 2.67H), 1.36 (s, 0.33H), 1.33 (s, 2.67H), 1.26 (d, J = 6.3 Hz, 0.33H), 1.23 (d, J = 6.3 Hz, 2.67H), 0.97 (t, J = 7.8 Hz, 8.01H), 0.96 (t, J = 7.8 Hz, 0.99H), 0.73−0.58 (m, 6H); ^{13}C NMR (500 MHz, CD_2Cl_2): δ 110.5 (β-anomer), 109.4 (α-anomer), 93.0 (β), 92.4 (α), 80.6 (β), 79.0 (α), 76.7 (α), 75.8 (α), 75.6 (β), 75.1 (β), 73.5 (β), 67.1 (α), 28.1 (α), 27.8 (β), 26.5 (β), 26.4 (α), 18.7 (β), 18.1 (α), 7.0 (α and β), 5.32 (α), 5.29 (β); HRMS (ESI): m/z 341.1754 $[M + Na]^+$ (calcd for $C_{15}H_{30}O_5NaSi$, 341.1760).

*(3R,5E,8E,10E)-2,3-O-Isopropylidene-4-O-triethylsilyl-β-L-Rhamnopyranosyl 3-(Tetrahydropyranyloxy)tetradeca-5,8,10-trienoate (**21**) and (3R,5E,8E,10E)-2,3-O-Isopropylidene-4-O-triethylsilyl-α-L-Rhamnopyranosyl 3-(Tetrahydropyranyloxy)tetradeca-5,8,10-trienoate (**22**).* To a stirred solution of **20** (30.0 mg, 93.5 μmol) and **16** (20.1 mg, 62.3 μmol) in dichloromethane (0.5 mL) were added DCC (15.4 mg, 74.8 μmol) and DMAP (0.8 mg, 6.23 μmol) at 0 °C. The mixture was stirred at 0 °C ∼ rt for 18 h and then concentrated. The residue was chromatographed on a column of silica gel (*n*-hexane−ether = 30:1 → 10:1) to give **22** (33.4 mg, 86%) as an amorphous solid. Further elution with *n*-hexane−ethyl acetate (10:1) afforded an oil which was purified by preparative TLC (*n*-hexane−ether = 10:1) to give **21** (2.0 mg, 5%) as an amorphous solid.

21. IR (ZnSe): ν_{max} 2956, 2934, 2874, 1749, 1377, 1112, 1088, 1022, 986, 727 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): δ 6.22 (d, J = 2.7 Hz, 0.51H), 6.17 (d, J = 2.7 Hz, 0.49H), 6.08−6.04 (m, 2H), 5.56−5.40 (m, 4H), 4.91, 4.75 (each t, J = 7.1 Hz, total 1H), 4.38−4.30 (m, 1H), 3.97−3.71 (m, 4H), 3.44−3.31 (m, 2H), 2.86−2.41 (m, 5H), 2.27 (m, 1H), 1.96 (brdd, J = 7.1, 7.1 Hz, 2H), 1.78−1.23 (m, 8H), 1.468, 1.465 (each s, total 3H), 1.35 (d, J = 6.1 Hz, 3H), 1.19 (s, 3H), 1.04 (t, J = 7.8 Hz, 9H), 0.84 (t, J = 7.4 Hz, 3H), 0.80−0.65 (m, 6H); ^{13}C NMR (125 MHz, CD_2Cl_2): δ 170.4, 170.2, 133.24, 133.20, 132,1, 131.9, 131.5, 130.6, 130.15, 130.11, 126.9, 126.4, 110.71, 110.69, 99.4, 97.9, 90.95, 90.92, 80.41, 80.38, 75.1, 74.4, 73.7, 73.41, 73.36, 73.1, 62.82, 62.78, 40.7, 39.7, 39.2, 37.2, 35.9, 35.0, 31.3, 31.2, 30.1, 27.6, 27.5, 26.00, 25.96, 25.90, 25.8, 22.9, 20.00, 19.98, 18.74, 18.71, 13.82, 6.9, 5.2; HRMS

https://doi.org/10.1021/acsomega.3c05277
ACS Omega 2023, 8, 35382−35392

(ESI): m/z 645.3794 $[M + Na]^+$ (calcd for $C_{34}H_{58}O_8NaSi$, 645.3799).

22. IR (ZnSe): ν_{max} 2956, 2921, 2874, 1749, 1380, 1118, 1083, 1022, 862 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): δ 6.74 (m, 0.46H), 6.72 (m, 0.54H), 6.09−6.02 (m, 2H), 5.57−5.35 (m, 4H), 4.87 (t, J = 3.4 Hz, 0.54H), 4.65 (t, J = 4.4 Hz, 0.46H), 4.29 (m, 0.46H), 4.23 (m, 0.54H), 4.17 (d, J = 5.2 Hz, 0.46H), 4.13−4.05 (m, 1.54H), 3.97−3.80 (m, 2H), 3.59−3.54 (m, 1H), 3.38−3.31 (m, 1H), 2.72−2.64 (m, 2.46H), 2.52−2.40 (m, 2H), 2.34 (dd, J = 15.4, 4.4 Hz, 0.56H), 2.25−2.19 (m, 1H), 1.95 (brdd, J = 7.4, 7.1 Hz, 2H), 1.72−1.19 (m, 11H), 1.45, 1.43 (each s, total 3H), 1.16, 1.18 (each s, total 3H), 1.039, 1.036 (each t, J = 7.8 Hz, total 9H), 0.84 (t, J = 6.4 Hz, 3H), 0.81−0.66 (m, 6H); ^{13}C NMR (125 MHz, C_6D_6): δ 169.5, 169.4, 132.8, 132.7, 131.9, 131.8, 131.78, 131.75, 131.10, 131.07, 129.94, 129.87, 127.0, 126.5, 109.5, 109.4, 99.5, 97.8, 91.8, 91.7, 79.33, 79.29, 76.3, 76.2, 75.93, 75.90, 74.5, 73.2, 69.1, 69.0, 62.7, 62.5, 40.5, 39.5, 39.4, 37.3, 36.01, 35.98, 35.0, 31.4, 31.3, 28.12, 28.10, 26.4, 26.3, 25.8, 25.7, 22.9, 20.2, 19.9, 18.0, 13.8, 7.1, 5.4; HRMS (ESI): m/z 645.3784 $[M + Na]^+$ (calcd for $C_{34}H_{58}O_8NaSi$, 645.3799).

*(3R,5E,8E,10E)-α-L-Rhamnopyranosyl Crostrienoate (**3**).* A solution of **22** (252 mg, 0.40 mmol) in 80% acetic acid (17.0 mL) was stirred at rt for 3 d, concentrated, and then coevaporated with toluene−ethanol. The residue was chromatographed on silica gel (dichloromethane-methanol = 100:1 → 50:1 → 10:1) to give a syrup (159 mg) which was purified by HPLC using a Shiseido Capcell-Pak C_{18} column (20 × 250 mm) with a mobile phase of acetonitrile: water (4:7) to give **3** (127 mg, 82%) as a white powder after lyophilization; $[\alpha]_D^{26}$ = −45.5 (c 1.0, MeOH); IR (ZnSe): ν_{max} 3353, 2956, 2930, 1734, 1258, 1134, 1057, 953, 804 cm^{-1}; ^1H NMR (500 MHz, CD_3OD): δ 6.03−5.97 (m, 2H), 5.95 (d, J = 1.7 Hz, 1H) 5.57−5.48 (m, 4H), 4.03 (m, 1H), 3.82 (m, 1H), 3.69−3.66 (m, 2H), 3.43 (t, J = 9.5 Hz, 1H), 2.77 (t, J = 6.0 Hz, 2H), 2.55 (dd, J = 15.4, 4.4 Hz, 1H), 2.40 (dd, J = 15.4, 8.8 Hz, 1H), 2.22 (m, 2H), 2.03 (brdd, J = 7.1, 7.0 Hz, 2H), 1.40 (dq, J = 7.1, 7.4 Hz, 2H), 1.24 (d, J = 6.1 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD): δ 171.5, 133.5, 132.9, 132.5, 131.8, 130.7, 127.6, 95.4, 73.4, 72.3, 72.1, 71.2, 69.3, 42.6, 41.4, 36.6, 35.7, 23.7, 18.1, 14.0; HRMS (ESI): m/z 407.2041 $[M + Na]^+$ (calcd for $C_{20}H_{32}O_7Na$, 407.2046).

*2,3,5,6-Tetra-O-benzyl-α-D-galactofuranosyl-(1 → 2)-1-O-acetyl-3,4-di-O-benzyl-L-rhamnopyranose (**23**).* To a stirred solution of **8** (300 mg, 0.33 mmol) in dichloromethane−ether (1:1; 2.0 mL) were added *N*-iodosuccinimide (90 mg, 0.40 mmol) and acetic acid (23 μL, 0.40 mmol) at 0 °C. After 3 h, aqueous saturated $NaHCO_3/Na_2S_2O_3$ (1:1) was added, and the resulting mixture was extracted with dichloromethane. The combined organic layers were washed with water and brine, dried, and concentrated. The residue was chromatographed on silica gel (benzene−ethyl acetate = 50:1 → 20:1) to give **23** (200 mg, 67%) as an anomeric mixture: syrup: IR (ZnSe): ν_{max} 3060, 3031, 2930, 2869, 1753, 1454, 1366, 1224, 1062, 1026, 735, 697 cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2): δ 7.47−7.20 (m, 30H), 6.17 (d, J = 2.4 Hz, 0.71H), 5.63 (d, J = 0.8 Hz, 0.29H), 5.53 (d, J = 4.1 Hz, 0.29H), 5.31 (d, J = 4.4 Hz, 0.71H), 4.94 (d, J = 11.4 Hz, 0.29H), 4.88 (d, J = 11.0 Hz, 0.29H), 4.82 (d, J = 10.8 Hz, 0.71H), 4.81 (d, J = 12.4 Hz, 0.29H), 4.75−4.08 (m, 13.42H), 3.98 (t, J = 6.6 Hz, 0.71H), 3.93 (t, J = 6.1 Hz, 0.29H), 3.86−3.46 (m, 6H), 2.06 (s, 0.87H), 2.04 (s, 2.13H), 1.26 (d, J = 6.1 Hz, 0.87H), 1.21 (d, J = 6.1 Hz, 2.13H); ^{13}C NMR (125 MHz, CD_2Cl_2): δ 169.5, 169.1, 139.53, 139.48, 139.0, 138.92, 138.89, 138.7, 138.5, 128.7, 128.61, 128.58, 128.50, 128.48, 128.43, 128.28, 128.25, 128.20, 128.17, 128.11, 128.08, 128.01, 127.95, 127.91, 127.86, 127.77, 127.74, 127.67, 127.64, 101.4, 99.2, 93.4, 91.2, 84.4, 83.6, 81.8, 81.4, 81.0, 80.5, 80.4, 80.3, 80.0, 79.9, 79.5, 78.3, 75.5, 75.3, 73.6, 73.5, 73.2, 72.8, 72.62, 72.61, 72.5, 72.44, 72.39, 72.2, 72.1, 71.4, 70.7, 70.4, 70.3, 21.3, 21.2, 18.33, 18.26; HRMS (ESI): m/z 931.4026 $[M + Na]^+$ (calcd for $C_{56}H_{60}O_{11}Na$, 931.4033).

*(2,3,5,6-Tetra-O-triethysilyl-α-D-galactofuranosyl)-(1 → 2)-1-O-acetyl-3,4-di-O-triethyl-silyl-α-L-rhamnopyranose (**24a**) and (2,3,5,6-Tetra-O-triethysilyl-α-D-galactofuranosyl)-(1 → 2)-1-O-acetyl-3,4-di-O-triethylsilyl-β-L-rhamnopyranose (**24b**).* A mixture of **23** (225 mg, 0.25 mmol) and 10% Pd/C (30 mg) in ethanol−tetrahydrofuran (1:1; 4.0 mL) was stirred vigorously under a hydrogen atmosphere at rt for 7 h, filtered through a pad of Celite, and then concentrated. The residue (118 mg) was dissolved in pyridine (12.0 mL). To the solution were added a catalytic amount of DMAP (one crystal) and TESOTf (0.57 mL, 2.52 mmol) at 0 °C with stirring, and the resulting mixture was stirred at 0 °C ∼ rt for 28 h. After the addition of ice water, the resulting mixture was vigorously stirred for 10 min and then extracted with ether. The combined organic layers were washed successively with cold aqueous HCl, water, saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane → *n*-hexane−benzene = 1:1) to give a mixture of anomeric isomers **24a** and **24b** (185 mg, 73%). For detailed NMR analyses, a small amount of the anomeric mixture was separated into each isomer by HPLC (Senshu-Pak 20 × 250 mm; *n*-hexane−ethyl acetate = 20:1).

24a. Syrup; $[\alpha]_D^{23}$ = +2.3 (c 0.52, $CHCl_3$); IR (ZnSe): ν_{max} 2952, 2876, 1759, 1459, 1414, 1235, 1089, 1006, 858, 726 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): δ 6.47 (brs, 1H), 5.30 (brs, 1H) 4.33 (brs, 1H), 4.23 (dt, J = 8.6, 3.4 Hz, 1H), 4.17 (brs, 1H), 4.12−3.97 (m, 4H), 4.10 (dd, J = 10.3, 3.2 Hz, 1H), 3.90 (brs, 1H), 3.75 (dd, J = 10.3, 7.8 Hz, 1H), 1.69 (brs, 3H), 1.42 (bd, J = 6.2 Hz, 3H) 1.19−1.05 (m, 54H), 0.90−0.74 (m, 36H): ^1H NMR (500 MHz, CD_2Cl_2): δ 5.96 (bd, J = 3.1 Hz, 1H), 4.98 (d, J = 2.4 Hz, 1H) 4.03 (brs, 1H), 3.92 (brs, 1H), 3.89 (m, 1H), 3.85 (brs, 1H), 3.80−3.75 (m, 2H), 3.73−3.65 (brs, 1H), 3.65−3.56 (brs, 1H), 3.60 (brt, J = 4.0 Hz, 1H), 3.43 (dd, J = 10.5, 8.1 Hz, 1H), 2.05 (s, 3H), 1.22 (brd, J = 4.9 Hz, 3H) 1.02−0.94 (m, 54H), 0.77−0.59 (m, 36H); ^{13}C NMR (125 MHz, CD_2Cl_2): δ 169.6, 102.5, 92.4, 85.0, 78.7, 78.0, 76.5, 74.0 (x2), 72.8 (x2), 64.7, 21.2, 18.6, 7.22, 7.19, 7.00, 6.97, 5.71, 5.69, 5.6, 5.5, 5.4, 5.3, 5.1, 5.0, 4.9, 4.8, 4.7; HRMS (ESI): m/z 1075.6400 $[M + Na]^+$ (calcd for $C_{50}H_{108}O_{11}Si_6Na$, 1075.6405).

24b. Syrup; $[\alpha]_D^{23}$ = +30.5 (c 0.22, $CHCl_3$); IR (ZnSe): ν_{max} 2952, 2875, 1758, 1458, 1231, 1131, 1092, 1051, 1006, 822, 725 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): δ 5.78 (br s, 1H), 5.16 (d, J = 2.2 Hz, 1H), 4.29 (ddd, J = 8.5, 4.4, 2.0 Hz, 1H), 4.24 (d, J = 1.9 Hz, 1H), 4.17 (dd, J = 10.5, 2.2 Hz, 1H), 3.98 (d, J = 2.2 Hz, 1H), 3.97 (dd, J = 9.8, 2.9 Hz, 1H), 3.95 (d, J = 2.2 Hz, 1H), 3.78 (t, J = 8.5 Hz, 1H), 3.70 (dd, J = 10.5, 8.8 Hz, 1H), 3.57 (dd, J = 8.8, 2.9 Hz, 1H), 3.24 (m, 1H), 1.79 (s, 3H), 1.37 (d, J = 6.4 Hz, 3H), 1.19−1.03 (m, 54H), 0.92−0.70 (m, 36H); ^1H NMR (500 MHz, CD_2Cl_2): δ 5.65 (br s, 1H), 4.88 (d, J = 2.4 Hz, 1H), 3.97−3.94 (m, 2H), 3.91 (brs, 1H), 3.83 (dd, J = 10.6, 2.2 Hz, 1H) 3.74 (d, J = 1.9 Hz, 1H), 3.63−3.59 (m, 2H), 3.56 (dd, J = 4.4, 1.2 Hz, 1H), 3.38 (dd, J = 10.6, 8.5 Hz, 1H), 3.35 (m, 1H), 2.05 (s, 3H), 1.27 (d, J = 6.3

https://doi.org/10.1021/acsomega.3c05277
ACS Omega 2023, 8, 35382−35392

Hz, 3H), 1.01−0.95 (m, 54H), 0.74−0.59 (m, 36H); ^{13}C NMR (125 MHz, CD_2Cl_2): δ 169.5, 105.5, 92.5, 85.5, 80.2, 78.0, 76.8, 74.63, 74.57, 74.2, 73.8, 64.8, 21.2, 18.6, 7.3, 7.2, 7.01, 6.99, 5.7, 5.5, 5.3, 5.24, 5.22, 5.20, 4.7; HRMS (ESI): m/z 1075.6400 $[M + Na]^+$ (calcd for $C_{50}H_{108}O_{11}Si_6Na$, 1075.6405).

*(2,3,5,6-Tetra-O-triethysilyl-α-D-galactofuranosyl)-(1 → 2)-3,4-di-O-triethylsilyl-L-rhamnopyranose (**7**).* A solution of **24a,b** (200 mg, 0.19 mmol) in dichloromethane (3.0 mL) was treated with a 1.0 M solution of sodium methoxide in methanol (0.3 mL, 0.3 mmol) at 0 °C for 2 min. After the addition of saturated aqueous NH_4Cl, the mixture was extracted with ether. The combined organic layers were washed with water and brine, dried and concentrated. The residue was chromatographed on silica gel (*n*-hexane−benzene = 1:1 → 1:2 → 1:4) to give **7** (187 mg, 97%) as an amorphous solid: IR (ZnSe): ν_{max} 3396, 2952, 2913, 2876, 1458, 1236, 1088, 1006, 860, 728 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): δ 5.26 (d, J = 4.2 Hz, 0.15H), 5.21 (d, J = 2.2 Hz, 0.85H), 5.20 (d, J = 10.0 Hz, 0.15H), 5.07 (brs, 0.85H), 4.68 (brd, J = 10.0 Hz, 0.15H), 4.54 (t, J = 6.4 Hz, 0.15H), 4.35 (t, J = 3.4 Hz, 0.85H), 4.23−3.73 (m, 8.55H), 3.52 (brd, J = 8.3 Hz, 0.15H), 3.16 (m, 0.15H), 2.01 (brs, 1H), 1.45 (d, J = 6.4 Hz, 0.45H), 1.43 (d, J = 5.9 Hz, 2.55H), 1.19−1.00 (m, 54H), 0.88−0.68 (m, 36H); ^{13}C NMR (125 MHz, C_6D_6): δ 103.7, 102.6, 93.9, 93.0, 84.7, 82.9, 80.7, 80.4, 79.7, 79.3, 77.1, 76.6, 75.4, 74.9, 74.2, 74.0, 73.2, 73.1, 73.0, 70.7, 64.9, 64.4, 19.0, 18.8, 7.5, 7.43, 7.40, 7.3, 7.19, 7.17, 7.1, 6.01, 5.98, 5.93, 5.88, 5.73, 5.69, 5.67, 5.6, 5.51, 5.45, 5.3, 4.9, 4.8; HRMS (ESI): m/z 1033.6307 $[M + Na]^+$ (calcd for $C_{48}H_{106}O_{10}Si_6Na$, 1033.6299).

*(2,3,5,6-Tetra-O-triethysilyl-α-D-galactofuranosyl)-(1 → 2)-3,4-di-O-triethylsilyl-β-L-rhamnopyranosyl (3R,5E,8E,10E)-3-(tetrahydropyranyloxy)tetradeca-5,8,10-trienoate (**25**) and (2,3,5,6-Tetra-O-triethysilyl-α-D-galactofuranosyl)-(1 → 2)-3,4-di-O-triethylsilyl-α-L-rhamnopyranosyl (3R,5E,8E,10E)-3-(tetrahydropyranyloxy)tetradeca-5,8,10-trienoate (**26**).* As described for the preparation of **21** and **22**, disaccharide **7** (152.5 mg, 0.151 mmol) and carboxylic acid **16** (72.9 mg, 0.226 mmol) was treated with DCC (37.3 mg, 0.181 mmol) and DMAP (1.84 mg, 15.1 μmol) in dichloromethane (8.0 mL) for 18 h. After evaporation, the residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 70:1) to give **26** (144.6 mg, 73%) as an amorphous solid and 35.8 mg of an anomeric mixture. The mixture was further separated by preparative TLC (*n*-hexane−ethyl acetate = 10:1 and then benzene−dichloromethane = 3:2) to give more **26** (13.2 mg, 7%) and **25** (3.0 mg, 2%) as an amorphous solid.

25. IR (ZnSe): ν_{max} 2952, 2909, 2875, 1757, 1458, 1414, 1236, 1128, 1088, 1053, 880, 826, 724 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): δ 6.15−6.05 (m, 2H), 5.87 (brs, 0.52H), 5.85 (brs, 0.48H), 5.66−5.45 (m, 4H), 5.27 (d, J = 2.0 Hz, 0.52H), 5.23 (d, J = 2.0 Hz, 0.48H), 4.93 (dd, J = 4.1, 3.4 Hz, 0.48H), 4.75 (dd, J = 4.1, 3.4 Hz, 0.52H), 4.43−3.74 (m, 9H), 3.81 (dd, J = 9.0, 9.0 Hz, 0.52H), 3.71 (dd, J = 11.0, 9.0 Hz, 0.48H), 3.59 (brdd, J = 9.0, 2.7 Hz, 1H), 3.48 (m, 0.52H), 3.42 (m, 0.48H), 3.27 (m, 1H), 2.92−2.32 (m, 6H), 1.97 (m, 2H), 1.80−1.05 (m, 65H), 1.04−0.72 (m, 39H); ^{13}C NMR (150 MHz, C_6D_6): δ 169.8, 169.6, 132.9, 132.7, 132.0, 131.9, 131.8, 131.7, 131.1, 131.0, 129.9, 129.8, 127.2, 126.6, 105.8 ($^1J_{CH}$ = 163.7 Hz, C-1″), 105.7 ($^1J_{CH}$ = 163.7 Hz, C-1″), 99.2, 97.7, 92.6 ($^1J_{CH}$ = 162.5 Hz, C-1′x2), 85.9, 85.8, 81.3, 81.1, 78.4, 78.3, 77.4, 77.2, 75.3, 75.2, 74.62, 74.58, 74.5, 74.4, 74.2, 74.0, 73.1, 65.1, 62.5, 62.4, 40.8, 39.7, 39.5, 37.6, 36.10, 36.08, 35.0, 31.4, 31.3, 25.9, 22.9, 19.93, 19.88, 18.7, 18.6, 13.8, 7.6, 7.5, 7.4, 7.3, 7.2, 5.98, 5.96, 5.68, 5.66, 5.6, 5.45, 5.42, 4.9; HRMS (ESI): m/z 1337.8335 $[M + Na]^+$ (calcd for $C_{67}H_{134}O_{13}Si_6Na$, 1337.8338).

26. IR (ZnSe): ν_{max} 2952, 2913, 2875, 1750, 1458, 1417, 1235, 1088, 1005, 866, 729 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6): δ 6.51 (br s, 1H), 6.06 (m, 2H), 5.64−5.35 (m, 4H), 5.31 (brs, 0.52H), 5.29 (brs, 0.48H), 4.86 (m, 0.52H), 4.66 (m, 0.48H), 4.36−3.85 (m, 10.52H), 3.84 (m, 0.48H), 3.73 (m, 1H), 3.43 (m, 0.52H), 3.38 (m, 0.48H), 2.70−2.15 (m, 6H), 1.97 (m, 2H), 1.76−1.20 (m, 11H), 1.18−1.03 (m, 54H), 0.89−0.71 (m, 39H); ^{13}C NMR (150 MHz, C_6D_6): δ 169.5, 132.7, 132.6, 131.9, 131.77, 131.73, 131.65, 131.13, 131.09, 130.0, 129.9, 127.1, 126.6, 103.4, 98.9, 97.8, 92.7, 92.5, 85.4, 85.3, 79.1, 78.92, 78.86, 77.82, 77.76, 74.41, 74.38, 74.0, 73.9, 73.2, 73.1, 72.8, 65.0, 62.5, 62.3, 40.6, 39.4, 39.3, 37.2, 36.03, 36.01, 35.0, 31.4, 31.2, 25.9, 22.9, 20.0, 19.9, 18.8, 13.8, 7.44, 7.40, 7.2, 7.1, 6.0, 5.7, 5.51, 5.47, 4.9; HRMS (ESI): m/z 1337.8333 $[M + Na]^+$ (calcd for $C_{67}H_{134}O_{13}Si_6Na$, 1337.8338).

*Clostrienose (**1**).* A solution of **26** (71.4 mg, 54.8 μmol) in 80% acetic acid (5.0 mL) was stirred at rt for 1 d, concentrated, and then coevaporated with toluene−ethanol. The residue was purified by HPLC using a Shiseido Capcell-Pak C_{18} column (20 × 250 mm) with a mobile phase of acetonitrile/water (7:15) to give **1** (10.9 mg, 54%) as a white powder after lyophilization; $[\alpha]_D^{23}$ = +13.7 (*c* 0.10, MeOH); IR (ZnSe): ν_{max} 3289, 2956, 2923, 1736, 1569, 1408, 1057, 1037, 985, 920 cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD): δ 6.00 (m, 2H), 5.97 (d, J = 1.7 Hz), 5.59−5.52 (m, 3H) 5.48 (dt, J = 15.4, 6.6 Hz, 1H), 4.94 (d, J = 4.4 Hz, 1H), 4.29 (dd, J = 8.3, 8.1 Hz, 1H), 4.03 (m, 1H), 3.96 (dd, J = 8.8, 4.9 Hz, 1H), 3.88 (dd, J = 3.4, 1.9 Hz, 1H), 3.82 (dd, J = 7.8, 1.7 Hz, 1H), 3.69 (dd, J = 9.8, 3.7 Hz, 1H), 3.68−3.57 (m, 4H) 3.41 (dd, J = 9.7, 9.6 Hz, 1H), 2.77 (t, J = 6.1 Hz, 1H), 2.56 (dd, J = 15.4, 4.2 Hz, 1H), 2.39 (dd, J = 15.4, 8.8 Hz, 1H), 2.25 (m, 2H), 2.04 (dt, J = 7.1, 7.1 Hz, 1H), 1.40 (tq, J = 7.4, 7.3 Hz, 1H), 1.26 (d, J = 6.3 Hz, 1H) 0.90 (t, J = 7.3 Hz, 1H); ^{13}C NMR (500 MHz, CD_3OD): δ 171.5, 133.5, 132.9, 132.5, 131.8, 130.7, 127.6, 103.5, 93.8, 82.6, 79.2, 78.4, 74.5, 73.5, 72.5, 71.5, 71.3, 69.3, 64.3, 42.6, 41.5, 36.6, 35.8, 23.7, 17.9, 14.0; HRMS (ESI): m/z 569.2575 $[M + Na]^+$ (calcd for $C_{26}H_{42}O_{12}Na$, 569.2574).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.3c05277.

^{1}H and ^{13}C{^{1}H} NMR spectra for **1**−**3** and their synthetic intermediates and (−)-HRMS and MS−MS spectra of natural and synthetic **3** (PDF)

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https://doi.org/10.1021/acsomega.3c05277
ACS Omega 2023, 8, 35382−35392

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to Dr. T. Nakamura and S. Mamada at RIKEN for the mass spectral measurements and technical assistance, respectively. We also thank Drs. T. Goto and H. Abe of the Bioplastic Research Team (RIKEN) for assistance with utilizing their freeze dryer. This work was supported by JSPS KAKENHI, grant number 19K05858 (S.T.).

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https://doi.org/10.1021/acsomega.3c05277
ACS Omega 2023, 8, 35382−35392