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Total synthesis of cleistetroside-2, partially acetylated dodecanyl tetrarhamnoside derivative isolated from *Cleistopholis patens* and *Cleistopholis glauca*

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Abstract—The total synthesis of a partially acetylated dodecanyl tetrarhamnoside derivative, cleistetroside-**2**, which was isolated from *Cleistopholis patens* and *Cleistopholis glauca* and showed significant in vitro antibacterial activity against the Gram-positive bacteria, was achieved for the first time.

Keywords: Cleistetroside; Oligorhamnoside; Antibacterial; Gram-positive bacteria; Synthesis

1. Introduction

The rising incidence of infections caused by antibiotic-resistant bacteria has become a major concern for clinicians and the public health system. In the past several years, these types of infections have increased in severity, and their treatment has become far more complex and costly.[1,2] Therefore, searching for novel classes of antibiotics is critically important in order to effectively combat these and other complex antibiotic-resistant pathogens.[3] Carbohydrates are the most abundant species among the biopolymers and have recently been actively studied as important biological molecules.[4] It has been shown that the oligosaccharides have the ability to control the microbial infection.[5,6] The identification of the mycobacterial cell wall polysaccharides and the monosaccharides contained therein (particularly arabinofuranose, galactofuranose, and rhamnopyranose residue)[7] has focused interest on the putative glycosyltransferases required for biosynthesis.[8] These particular sugar units are not found in mammalian cells and their associated biosynthetic pathways could be targets for the development of novel inhibitors of mycobacterial cell wall elaboration.

As part of high-throughput natural products program directed toward the discovery of novel antibacterial agents from plants,[9] eight partially acetylated oligorhamnosides with significant in vitro antibacterial activity have been obtained recently from *Cleistopholis patens* by the Hu group.[10] One of the oligorhamnoside derivatives, cleistetroside-**2** (**1**, Scheme 1), initially isolated from the species *Cleistopholis glauca* by Tané et al.[11] in 1988 and subsequently found in *C. patens* by Waterman group[12] in 1999, showed the best in vitro antibacterial activity against the Gram-positive bacteria methicillin resistant *Staphylococcus aureus* ATCC 33591 and *S. aureus* 78-13607A with MICs of $\leqslant 1$ μg/mL.[10] Furthermore, it showed significant in vitro antibacterial activity against an expanded panel of Gram-positive pathogens including either ATCC strains or well-characterized clinical isolates from the global SENTRY Antimicrobial Surveillance Program.[10] Therefore a synthesis-driven mapping of their structure/activity profile is called for to probe these promising and diverse biological effects of partially acetylated oligorhamnosides in more detail. In this paper, we would like to

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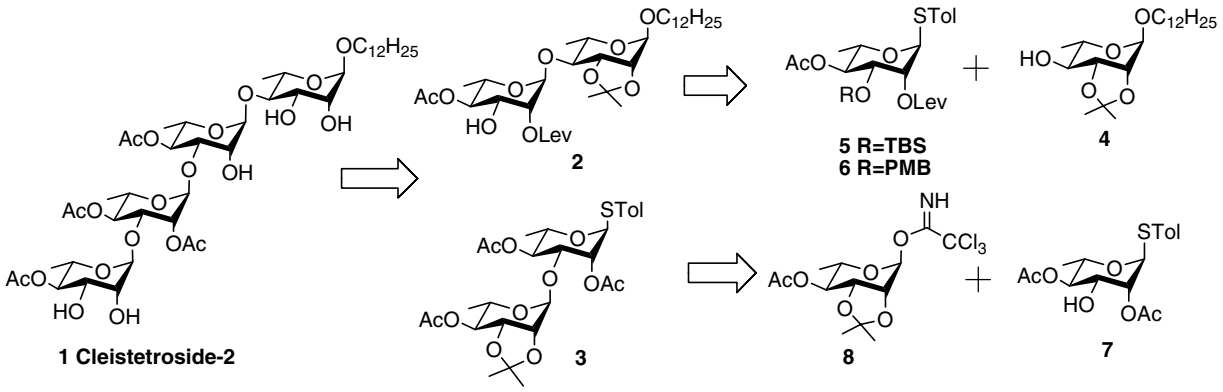


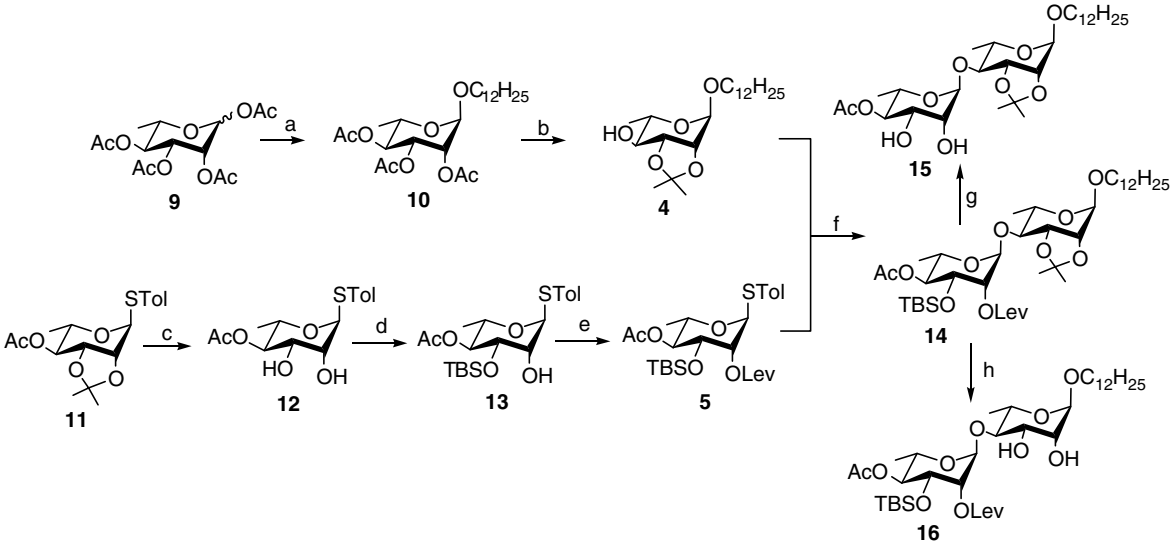
Scheme 1. Retrosynthetic analysis of cleistetroside-**2**.

report a facile synthesis of this partially acetylated dodecanyl tetrarhamnoside derivative cleistetroside-**2**, which would provide a facile approach to other structural analogues.

2. Results and discussion

The four acetyl groups in cleistetroside-**2** require attention in the convergent synthesis due to their O to O migration in some acidic or basic conditions. To address this issue, we chose isopropylidene and levulinoyl groups as hydroxy protecting groups, which could be selectively removed without affecting acetyl groups under mild conditions. Therefore the target compound **1** was retrosynthesized into two disaccharide building blocks **2** and **3** (Scheme 1). Building block **2** as a glycosyl acceptor could be derived from the glycosylation of monosaccharide acceptor **4** with monosaccharide donor **5** or **6**. While building block **3** as a glycosyl donor could be easily obtained by condensation of 2,4-di-*O*-acetyl acceptor **7** with trichloroacetimidate donor **8**. Although β-glycoside formation was observed occasionally, the good α-stereoselectivity in the glycosylation of rhamnopyranosyl donors that were either glycosylated at C-2 or blocked at this position with a non-participating group has been reported on several occasions in the literature.[13] Thus, we designed donor **8** with a non-participating isopropylidene group at C-2 and C-3.

First of all, building block **2** was synthesized by coupling of acceptor **4** with donor **5** or **6**. As outlined in Scheme 2, starting from readily available L-rhamnopyranosyl tetraacetate **9**,[14] the glycosylation with *n*-dodecyl alcohol using $SnCl_4$[15] as a catalyst was carried out smoothly to give pure α-isomer **10** in 70% yield. We had tried the glycosidic coupling of *p*-tolyl 2,3,4-tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside or 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl trichloroacetimidate under the



Scheme 2. Reagents and conditions: (a) $C_{12}H_{25}OH$, CH_3CN, $SnCl_4$, 69.8%; (b) (i) NaOMe, MeOH; (ii) 2,2-dimethoxylproprane, *p*-TsOH, DMF, 88.8% for two steps; (c) 80% HOAc, 93.1%; (d) TBSCl, imidazole, DMAP, pyridine, 99.0%; (e) levulinic acid, DCC, DMAP, CH_2Cl_2, 83.9%; (f) NIS, AgOTf, CH_2Cl_2, 83.4%; (g) TBAF, THF, 45.0%; (h) HF·pyridine, THF, 11.6%.

promotion of NIS/AgOTf, NIS/TfOH, trimethylsilyl trifluoromethanesulfonate (TMSOTf), $BF_3{\cdot}Et_2O$ or AgOTf, respectively, but compound **10** was not obtained in an acceptable yield. Removal of the acetyl groups in **10** with NaOMe in MeOH, followed by protecting the corresponding 2,3-positions with an isopropylidene group provided acceptor **4** ($^1J_{C\text{-}1,H\text{-}1} = 167.5$ Hz) in 89% good yield for two steps.

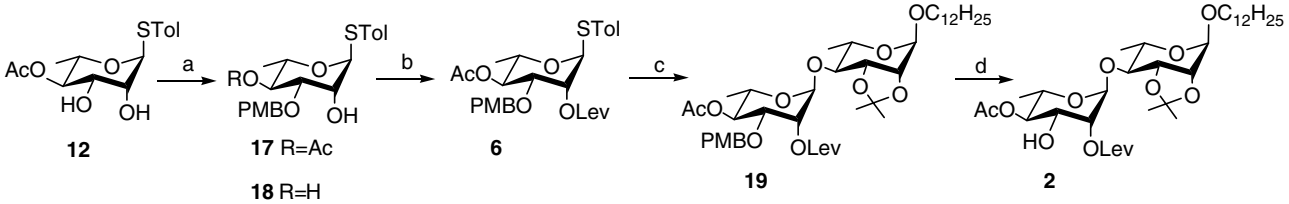
We first designed donor **5** with a *tert*-butyldimethylsilyl (TBS) group at C-3–OH for the construction of building block **2**. Thus, the known thioglycoside **11**[16] was subjected to removal of the 2,3-*O*-isopropylidene group (80% HOAc, 80 °C) to produce diol **12** (93%), which subsequently was silylated with *tert*-butyldimethylsilyl chloride in the presence of imidazole in pyridine (rt) to give an excellent yield of monosilylated compound **13** regioselectively (99%). It is worth noting that the high regioselectivity of the monosilylation was achieved only when pyridine was chosen as solvent in our experiment. Reaction of **13** with levulinic acid (LevOH) in the presence of *N*,*N*′-dicyclohexylcarbodiimide (DCC) and 4-*N*,*N*-dimethylaminopyridine (DMAP)[17] afforded the desired donor **5** in a good yield (84%). Regioselective substitution on C-3–OH of **13** was further confirmed from its levulinoyl ester **5**, that is, the chemical shifts of H-2 in **5** moved downfield to 5.32 ppm, from around 3.92 ppm in **13**. Finally, coupling of donor **5** with acceptor **4** was carried out in the presence of NIS and AgOTf to provide disaccharide **14** in 84% yield. However, removal of the silyl ether group from **14** by the usual reagent, 1.0 equiv TBAF in THF,[18] resulted in cleavage of the levulinoyl ester bond and formed side product **15** in 45% yield. When the deprotection was performed with HF·pyridine in THF,[19] leading to another side product **16** because of the lability of isopropylidene group to the acid condition. We had also examined other conditions for the desilylation, such as $BF_3{\cdot}Et_2O$,[20] pyridinium *p*-toluenesulfonate (PPTS),[21] TBAF-HOAc-THF,[22] $Pd(MeCN)_2Cl_2$,[23] TMSCI-KF·$2H_2O$,[24] and 2.3-dichloro-5,6-dicyanobenzoquinone (DDQ).[25] Unfortunately, they all failed to provide the desired building block **2**.

Alternatively we designed another monosaccharide donor **6** with a *p*-methoxybenzyl (PMB) group at C-3–OH. In Scheme 3: Diol **12** was refluxed with Bu_2SnO in toluene,[26] followed by reaction with *p*-methoxybenzyl chloride in the presence of CsF, and Bu_4NI in DMF (rt) to afford *p*-tolyl 4-*O*-acetyl-3-*O*-PMB-1-thio-α-L-rhamnopyranoside **17** in a favorable yield (74%). But employing toluene–MeOH as solvent diol **12** was converted to side product **18** due to removal of the acetyl group[27] in C-4–OH. Then treatment of compound **17** under the conditions for **5** gave levulinoyl ester **6** in an acceptable yield (57%). Glycosylation of donor **6** with acceptor **4** produced disaccharide **19** in an excellent yield (97%). And the α-configuration of the new glycosidic bond in **19** was confirmed by the HMBC spectrum ($^1J_{C\text{-}1',H\text{-}1'} = 171.8$ Hz). To our delight, deprotection of the 3′-*O*-PMB group with DDQ was conducted readily to form our expected building block **2** in 85% yield.

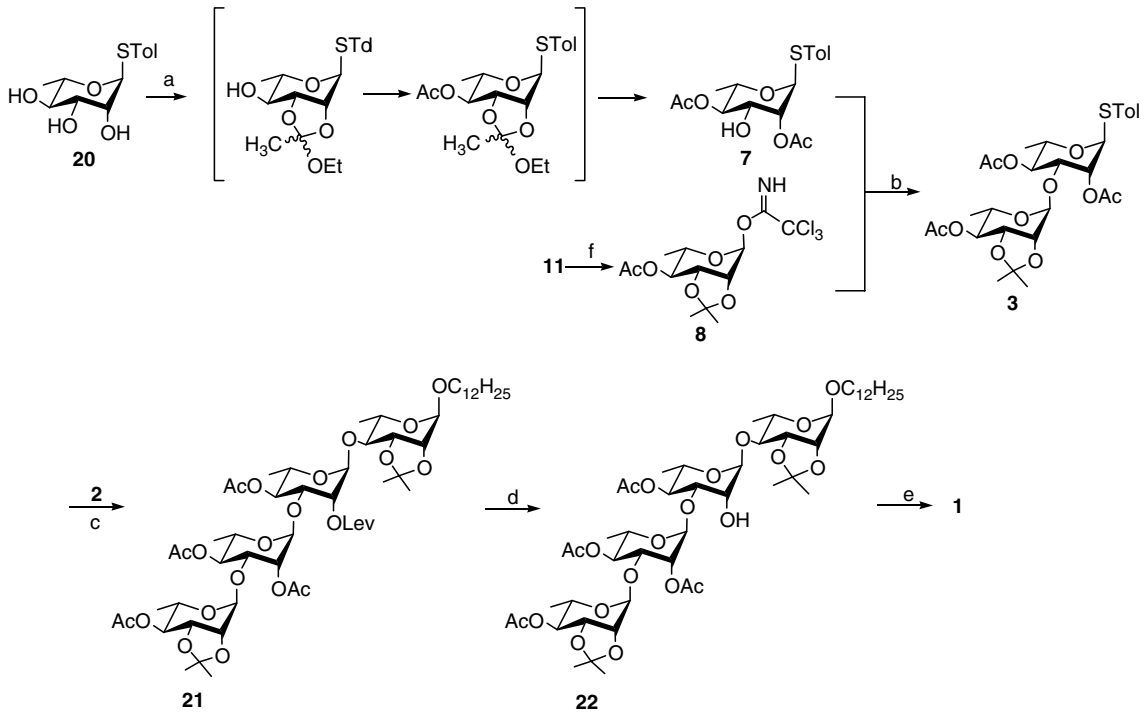
The next effort was to construct disaccharide building block **3**, which could be readily obtained by glycosylation of monosaccharide acceptor **7** with donor **8** (Scheme 4). Acceptor **7** was prepared from compound **20** in a simple one-pot method.[28] Treatment of **20** with triethylorthoacetate and a catalytic amount of (1*S*)-(+)-camphor-10-sulfonic acid (CSA) formed the corresponding orthoesters, which were directly acetylated in the same pot to protect the remaining hydroxy group. Then the reaction mixture was diluted with dichloromethane and shaken with 1 M HCl solution to effect orthoester rearrangement, giving the expected compound **7** in high yield (72%). And donor **8** was synthesized from thioglycoside **11** in two steps. Hydrolysis of **11** with *N*-bromosuccinimide (NBS) in acetone–H_2O, followed by treatment with CCl_3CN and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) gave trichloroacetimidate **8** in 73% yield for two steps. Then, donor **8** was coupled with acceptor **7** using TMSOTf as promoter to provide desired building block **3** in an excellent yield (99%).

With the acceptor **2** and donor **3** in hand, an NIS/AgOTf-promoted coupling was carried out to afford tetrasaccharide **21** in 62% good yield. Finally, deprotection of the Lev group with hydrazine acetate (82%) and the isopropylidene group with 80% HOAc (83%) smoothly furnished the target cleistetroside-**2** (**1**). The physical data obtained were full in agreement with those reported for the natural product.

In conclusion, we have successfully synthesized the partially acetylated dodecanyl tetrarhamnoside derivative cleistetroside-**2** in a convergent approach. The syntheses of its analogues and their bioactivities will be reported later.



Scheme 3. Reagents and conditions: (a) (i) Bu_2SnO, toluene; (ii) *p*-methoxybenzyl chloride, TBAI, DMF, 74.1% for two steps; (b) levulinic acid, DCC, DMAP, CH_2Cl_2, 56.9%; (c) NIS, AgOTf, CH_2Cl_2, 96.7%; (d) DDQ, CH_2Cl_2–MeOH, 85.0%.



Scheme 4. Reagents and conditions: (a) (i) $MeC(OEt)_3$, CSA, DMF; (ii) Ac_2O, DMAP, TEA, pyridine; (iii) 1 M HCl, 71.5% for three steps; (b) TMSOTf, CH_2Cl_2, 99.0%; (c) NIS, AgOTf, CH_2Cl_2, 61.6%; (d) hydrazine acetate, CH_2Cl_2–MeOH, 82.1%; (e) 80% HOAc, 82.7%; (f) (i) NBS, acetone–H_2O; (ii) DBU, $CNCCl_3$, CH_2Cl_2, 73.4% for two steps.

3. Experimental

3.1. General methods

Solvents were purified in a conventional manner. Thin-layer chromatography (TLC) was performed on precoated E. Merck Silica Gel 60 F254 plates. Flash column chromatography was performed on silica gel (200–300 mesh, Qingdao, China). Optical rotations were determined with a Perkin–Elmer Model 241 MC polarimeter. ^{1}H NMR and ^{13}C NMR spectra were taken on a JEOL JNM-ECP 600 spectrometer with tetramethylsilane as the internal standard, and chemical shifts are recorded in δ values. Mass spectra were recorded on a Q-TOF Global mass spectrometer.

3.2. 1-*O*-Dodecanyl-2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside (10)

To a solution of compound **9** (12.0 g, 36.1 mmol) in dry CH_3CN (100 mL) was added $SnCl_4$ (3.9 mL, 33.3 mmol) at 0 °C and the mixture was stirred for 30 min. To the cold solution, a *n*-dodecanol (5.2 g, 27.8 mmol) solution in CH_3CN was added dropwise over a period of 30 min. The reaction was stirred for an additional 30 min while warming to room temperature. After the reaction was completed as judged by TLC, the reaction was quenched with water (50 mL) and extracted with $CHCl_3$ (2×200 mL). The chloroform layer was washed with satd aq $NaHCO_3$ (3×100 mL), brine (2×100 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting crude oil was purified via silica gel column chromatography (10:1, petroleum ether–EtOAc) to yield **10** (8.90 g, 69.8%) as a colorless oil: R_f 0.53 (4:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −48.7 (*c* 0.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.30 (dd, 1H, $J = 10.1$, 3.7 Hz, H-3), 5.23 (dd, 1H, $J = 3.7$, 1.9 Hz, H-2), 5.06 (t, 1H, $J = 9.9$ Hz, H-4), 4.71 (d, 1H, $J = 1.4$ Hz, H-1), 3.9–3.85 (m, 1H, H-5), 3.68–3.64 (m, 1H, OC*H*H), 3.43–3.40 (m, 1H, OCH*H*), 2.15 (s, 3H, $COCH_3$), 2.05 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$), 1.63–1.56 (m, 2H, βCH_2), 1.33–1.30 (m, 2H, γCH_2), 1.28 (br s, 16H, $(CH_2)_8$), 1.22 (d, 3H, $J = 6.0$ Hz, CH_3-6), 0.88 (t, 3H, $J = 7.1$ Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 170.2, 170.0, 169.9, 97.4, 71.2, 70.0, 69.1, 68.2, 66.1, 31.9, 30.9, 29.7–29.3, 26.0, 22.6, 20.9, 20.8, 20.7, 17.4, 14.1. ESIMS: calcd for $[M+Na]^+$ *m*/*z* 481.3; found: *m*/*z* 481.2.

3.3. 1-*O*-Dodecanyl-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (4)

To a dry methanolic solution (25 mL) of compound **10** (1.66 g, 3.6 mmol) was added NaOMe (26.7 mg) at 0 °C. The reaction mixture was stirred at room temperature for 30 min, after which the reaction mixture was neutralized with Dowex $50 \times 8(H^+)$ resin until pH 7, filtered and concentrated. The residue was dried under vacuum to give a crude product. To a solution of the

crude product (1.17 g, 3.5 mmol) in dry DMF (10 mL) were added 2,2-dimethoxypropane (1.3 mL, 10.5 mmol) and *p*-toluenesulfonic acid (66.9 mg, 0.4 mmol) at room temperature. After 13 h stirring, Et_3N was added dropwise to attain pH 7.0. The solution was concentrated in vacuo. The resulting crude product via silica gel column chromatography (10:1, petroleum ether–EtOAc) gave **4** (1.16 g, 88.8% for two steps) as a white solid: R_f 0.50 (3:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −25.5 (*c* 0.10, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 5.20 (d, 1H, $J = 6.4$ Hz, 4-OH), 4.86 (s, 1H, H-1), 4.02 (d, 1H, $J = 5.9$ Hz, H-2), 3.84 (dd, 1H, $J = 7.4$, 5.5 Hz, H-3), 3.57 (td, 1H, $J = 9.7$, 6.4 Hz, H-4), 3.43–3.36 (m, 2H, H-5 and OC*H*H), 3.07–3.03 (m, 1H, OC*H*H), 1.53–1.48 (m, 2H, O CH_2), 1.40 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.24 (s, 16H, (CH_2)$_8$), 1.12 (d, 3H, $J = 6.0$ Hz, CH_3-6), 0.85 (t, 3H, $J = 7.1$ Hz, CH_3); ^{13}C NMR (DMSO-d_6) δ 108.1, 96.2, 78.1, 75.5, 73.4, 66.6, 65.5, 31.3, 29.0–28.7, 28.0, 26.2, 25.6, 22.1, 17.4, 13.9. ESIMS: calcd for $[M+Na]^+$ *m*/*z* 395.3; found: *m*/*z* 395.3.

3.4. *p*-Tolyl 4-*O*-acetyl-1-thio-α-L-rhamnopyranoside (12)

Compound **11** (6.2 g, 18.5 mmol) was dissolved in 80% HOAc (80 mL) and stirred for 1.5 h at 80 °C, then the reaction mixture was concentrated. The residue was purified by silica gel column chromatography (10:1, $CHCl_3$–MeOH) to give compound **12** (5.36 g, 93.1%) as a white solid: R_f 0.5 (1:2, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −273.6 (*c* 0.10, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 7.34 (d, 2H, $J = 8.0$ Hz, Ph), 7.17 (d, 2H, $J = 8.0$ Hz, Ph), 5.44 (d, 1H, $J = 4.1$ Hz, 2-OH), 5.29 (s, 1H, H-1), 5.09 (d, 1H, $J = 6.0$ Hz, 3-OH), 4.86 (t, 1H, $J = 9.6$ Hz, H-4), 4.06–4.01 (m, 1H, H-5), 3.94 (ddd, 1H, $J = 4.6$, 2.8, 1.4 Hz, H-2), 3.65 (ddd, 1H, $J = 9.6$, 5.9, 3.2 Hz, H-3), 2.29 (s, 3H, PhCH_3), 2.06 (s, 3H, COCH_3), 1.04 (d, 3H, $J = 6.0$ Hz, CH_3-6); ^{13}C NMR (DMSO-d_6) δ 169.9, 137.0, 131.6, 130.2, 129.8, 88.6, 73.8, 71.8, 68.8, 67.2, 20.9, 20.6, 17.3; ESIMS: calcd for $[M+Na]^+$ *m*/*z* 335.1; found: *m*/*z* 335.1.

3.5. *p*-Tolyl 4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-1-thio-α-L-rhamnopyranoside (13)

To a solution of compound **12** (500.0 mg, 1.6 mmol) in pyridine (10 mL) were added imidazole (272.3 mg, 4.0 mmol) and *tert*-butylchlorodimethylsilane (720.3 mg, 4.8 mmol) at 0 °C. The mixture was stirred under these conditions for 30 min and then at room temperature for another 12 h. After the reaction was complete as judged by TLC, the reaction mixture was diluted with cold water (50 mL) and extracted with EtOAc (3 × 50 mL). The organic phase was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Purification of the residue on a silica gel column (10:1, petroleum ether–EtOAc) gave **13** (682.7 mg, 99.9%) as a colorless oil: R_f 0.5 (4:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −171.5 (*c* 0.10, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 7.34 (d, 2H, $J = 7.8$ Hz, Ph), 7.17 (d, 2H, $J = 7.8$ Hz, Ph), 5.45 (d, 1H, $J = 4.6$ Hz, 2-OH), 5.29 (d, 1H, $J = 1.4$ Hz, H-1), 4.94 (t, 1H, $J = 9.6$ Hz, H-4), 4.07–4.02 (m, 1H, H-5), 3.92 (br s, 1H, H-2), 3.84 (dd, 1H, $J = 9.6$, 3.2 Hz, H-3), 2.28 (s, 3H, PhCH_3), 2.05 (s, 3H, COCH_3), 1.05 (d, 3H, $J = 6.0$ Hz, CH_3-6), 0.85 (s, 9H, (CH_3)$_3$C), 0.07 (s, 3H, CH_3), 0.05 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 169.9, 137.7, 131.8, 129.9, 86.9, 73.8, 72.9, 70.9, 67.3, 25.5, 21.1, 21.0, 17.8, 17.3. ESIMS: calcd for $[M+Na]^+$ *m*/*z* 449.2; found: *m*/*z* 449.1.

3.6. *p*-Tolyl 4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-2-*O*-levulinoyl-1-thio-α-L-rhamnopyranoside (5)

To a solution of compound **13** (0.5 g, 1.2 mmol) in dry CH_2Cl_2 (10 mL), levulinic acid (272.0 mg, 2.4 mmol), DCC (484.1 mg, 2.4 mmol), and DMAP (14.3 mg, 0.12 mmol) were added under argon. The mixture was stirred for 12 h, diluted with CH_2Cl_2 (100 mL), washed with H_2O (50 mL), 1 M HCl (2 × 50 mL), satd aq $NaHCO_3$ (2 × 50 mL), and brine (2 × 50 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (10:1, petroleum ether–EtOAc) to give **5** (516.0 mg, 83.9%) as a syrup: R_f 0.57 (3:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −68.9 (*c* 0.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.34 (d, 2H, $J = 8.2$ Hz, Ph), 7.12 (d, 2H, $J = 8.2$ Hz, Ph), 5.32 (dd, 1H, $J = 3.2$, 1.4 Hz, H-2), 5.30 (s, 1H, H-1), 5.02 (t, 1H, $J = 9.7$ Hz, H-4), 4.27–4.22 (m, 1H, H-5), 4.04 (dd, 1H, $J = 9.6$, 3.7 Hz, H-3), 2.79–2.62 (m, 4H, COCH_2CH_2CO), 2.33 (s, 3H, PhCH_3), 2.19 (s, 3H, COCH_3), 2.10 (s, 3H, COCH_3), 1.21 (d, 3H, $J = 6.4$ Hz, CH_3-6), 0.84 (s, 9H, (CH_3)$_3$C), 0.09, (s, 6H, 2CH_3); ^{13}C NMR ($CDCl_3$) δ 206.1, 171.8, 169.8, 138.0, 132.2, 129.9, 129.7, 86.2, 74.0, 73.8, 68.9, 67.7, 37.8, 30.9, 29.8, 28.0, 25.6, 25.4, 21.1, 21.0, 17.8, 17.4. ESIMS: calcd for $[M+Na]^+$ *m*/*z* 547.2; found: *m*/*z* 547.1.

3.7. 1-*O*-Dodecanyl-4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-2-*O*-levulinoyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (14)

To a solution of compound **4** (500.0 mg, 1.3 mmol), compound **5** (985.7 mg, 1.9 mmol) and 4 Å molecular sieves in dry CH_2Cl_2 (20 mL), NIS (484.5 mg, 2.1 mmol), and AgOTf (68.9 mg, 0.3 mmol) were added at 0 °C under argon. The reaction was stirred for an additional 12 h while warming to room temperature. After the reaction was complete as judged by TLC, the reaction mixture was filtered and concentrated. Then the residue was diluted with CH_2Cl_2 (100 mL), and washed with aqueous $Na_2S_2O_3$ (50 mL), satd aq $NaHCO_3$ (50 mL), brine (2 × 50 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced

pressure. The residue was purified by silica gel column chromatography (10:1, petroleum ether–EtOAc) to give **14** (865.4 mg, 83.4%) as a syrup: R_f 0.21 (4:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −41.5 (*c* 0.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.26 (d, 1H, $J = 1.4$ Hz, H-1′), 5.14 (dd, 1H, $J = 3.7$, 1.8 Hz, H-2′), 4.96 (t, 1H, $J = 9.4$ Hz, H-4′), 4.95 (s, 1H, H-1), 4.17 (dd, 1H, $J = 7.3$, 5.5 Hz, H-3), 4.09 (d, $J = 5.5$ Hz, H-2), 3.99 (dd, 1H, $J = 9.6$, 3.7 Hz, H-3'), 3.76–3.71 (m, 1H, H-5′), 3.70–3.65 (m, 2H, H-5 and OC*H*H), 3.46 (dd, 1H, $J = 10.1$, 7.3 Hz, H-4), 3.43–3.39 (m, 1H, OC*H*H), 2.78–2.67 (m, 4H, $COCH_2CH_2CO$), 2.20 (s, 3H, $COCH_3$), 2.07 (s, 3H, $COCH_3$), 1.60–1.56 (m, 2H, βCH_2), 1.53 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.31–1.28 (m, 2H, γCH_2), 1.27 (d, 3H, $J = 6.4$ Hz, CH_3-6), 1.26 (s, 16H, $(CH_2)_8$), 1.18 (d, 3H, $J = 6.4$ Hz, CH_3-6′), 0.88 (t, 3H, $J = 7.1$ Hz, CH_3), 0.83 (s, 9H, $3CH_3$), 0.07 (s, 3H, CH_3), 0.05 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 206.2, 171.7, 169.8, 109.4, 96.9, 96.0, 77.9, 76.2, 73.8, 72.3, 68.3, 67.7, 67.0, 63.8, 37.9, 31.9, 30.9, 29.8–29.3, 28.1, 27.9, 26.3, 26.1, 25.4, 22.6, 21.1, 18.0, 17.8, 17.5, 14.1. ESIMS: calcd for $[M+Na]^+$ *m*/*z* 795.5; found: *m*/*z* 795.4.

3.8. 1-*O*-Dodecanyl-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (15)

To a stirred solution of **14** (50.4 mg, 0.065 mmol) in THF (20 mL), TBAF (65.2 μL) was added at 0 °C under argon. The reaction mixture was stirring overnight while warming to room temperature. Then, the mixture was concentrated and the residue was purified by silica gel column chromatography (3:1, petroleum ether–EtOAc) to give compound **15** (16.5 mg, 45.0%) as a syrup: R_f 0.52 (1:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −76.4 (*c* 0.10, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 5.13 (d, 1H, $J = 1.9$ Hz, H-1′), 5.12(d, 1H, $J = 4.1$ Hz, 3′-OH), 4.90 (s, 1H, H-1), 4.85 (d, 1H, $J = 6.0$ Hz, 3′-OH), 4.79 (t, 1H, $J = 9.7$ Hz, H-4′), 4.10–4.05 (m, 2H, H-2 and H-3), 3.69 (br s, 1H, H-2′), 3.62–3.52 (m, 4H, H-3′, H-5′, H-5 and OC*H*H), 3.42–3.39 (m, 1H, OC*H*H), 3.35 (dd, 1H, $J = 10.1$, 6.8 Hz, H-4), 2.04 (s, 3H, $COCH_3$), 1.53–1.51 (m, 2H, βCH_2), 1.43 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.24 (s, 18H, $(CH_2)_9$), 1.16 (d, 3H, $J = 6.4$ Hz, CH_3-6), 1.04 (d, 3H, $J = 6.4$ Hz, CH_3-6′), 0.85 (t, 3H, $J = 7.1$ Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 171.9, 109.5, 98.1, 96.8, 78.4, 77.5, 76.2, 75.1, 71.2, 70.0, 67.7, 66.2, 63.8, 31.9, 29.6–29.3, 26.3, 26.1, 22.7, 21.1, 18.0, 17.3, 14.1. ESIMS: calcd for $[M+Na]^+$ *m*/*z* 583.3; found: *m*/*z* 583.3.

3.9. 1-*O*-Dodecanyl-4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-2-*O*-levulinoyl-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranoside (16)

To a stirred solution of **14** (207.8 mg, 1.2 mmol) in THF (20 mL), HF·pyridine (0.3 mL) was added at 0 °C under argon. The reaction mixture was stirring overnight while warming to room temperature. The mixture was diluted with EtOAc (100 mL), washed with satd aq $NaHCO_3$ (2×100 mL), brine (100 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Then, the crude reaction mixture was purified by silica gel column chromatography (3:1, petroleum ether–EtOAc) to give compound **16** (22.3 mg, 11.6%) as a white solid: R_f 0.30 (2:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −41.5 (*c* 0.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.09 (d, 1H, $J = 1.9$ Hz, H-1′), 4.99 (t, 1H, $J = 9.9$ Hz, H-4′), 4.97 (dd, 1H, $J = 3.7$, 1.8 Hz, H-2′), 4.95 (d, 1H, $J = 5.7$ Hz, 3-OH), 4.90 (d, 1H, $J = 6.4$ Hz, 2-OH), 4.52 (d, 1H, $J = 0.9$ Hz, H-1), 4.04 (dd, 1H, $J = 9.6$, 3.7 Hz, H-3′), 3.82–3.77 (m, 1H, H-5′), 3.56 (dd, 1H, $J = 6.4$, 3.2 Hz, H-2), 3.55–3.52 (m, 1H, OC*H*H), 3.51–3.47 (m, 1H, H-5), 3.41 (t, 1H, $J = 9.6$ Hz, H-4), 3.32–3.29 (m, 1H, OC*H*H), 2.70–2.67, 2.41–2.39 (m, 4H, $COCH_2CH_2CO$), 2.08 (s, 3H, $COCH_3$), 2.00 (s, 3H, $COCH_3$), 1.51–1.48 (m, 2H, βCH_2), 1.24 (s, 18H, $(CH_2)_9$), 1.16 (d, 3H, $J = 5.9$ Hz, CH_3-6), 1.06 (d, 3H, $J = 5.9$ Hz, CH_3-6′), 0.88 (s, 9H, $C(CH_3)_3$), 0.85 (t, 3H, $J = 6.8$ Hz, CH_3), 0.04 (s, 3H, CH_3), 0.03 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 171.9, 109.5, 98.1, 96.8, 78.4, 77.5, 76.2, 75.1, 71.2, 70.0, 67.7, 66.2, 63.8, 31.9, 29.6–29.3, 27.9, 26.3, 26.1, 22.7, 21.1, 18.0, 17.3, 14.1. ESIMS: calcd for $[M+Na]^+$ *m*/*z* 755.4; found: *m*/*z* 755.3.

3.10. *p*-Tolyl 4-*O*-acetyl-3-*O*-(*p*-methoxybenzyl)-1-thio-α-L-rhamnopyranoside (17)

A mixture of **12** (500 mg, 1.6 mmol) and Bu_2SnO (700 mg, 1.8 mmol) in toluene (20 mL) was refluxed for 6 h. Then the solution was concentrated. The residue was suspended in DMF (25 mL), and Bu_4NI (618.2 mg, 1.9 mmol) and PMBCl (258 μL, 1.9 mmol) were added. After being stirred at room temperature for 36 h, the mixture was diluted with CH_2Cl_2 (100 mL) and washed with H_2O (3×50 mL). The separated water phase was extracted with CH_2Cl_2 (2×100 mL). The combined organic phase was washed with ice water (2×100 mL), dried over Na_2SO_4, and then filtered through a short column of silica gel. The eluent was concentrated to a residue, which was purified by silica gel column chromatography (10:1, petroleum ether–EtOAc) to afford a white solid **17** (513.7 mg, 74.1%): R_f 0.27 (4:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −157.7 (*c* 0.10, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 7.32 (d, 2H, $J = 7.0$ Hz, Ph), 7.24 (dd, 2H, $J = 11.0$, 2.0 Hz, Ph), 7.17 (d, 2H, $J = 7.0$ Hz, Ph), 6.93 (dd, 2H, $J = 11.0$, 2.0 Hz, Ph), 5.50 (d, 1H, $J = 4.4$ Hz, 2-OH), 5.33 (d, 1H, $J = 1.3$ Hz, H-1), 4.97 (t, 1H, $J = 9.9$ Hz, H-4), 4.55 (d, 1H, $J = 11.9$ Hz, PhCH*H*), 4.38 (d, 1H, $J = 11.9$ Hz, PhC*H*H), 4.18 (ddd, 1H, $J = 4.4$, 3.2, 1.9 Hz, H-2), 4.05–4.00 (m, 1H, H-5), 3.75 (s, 3H, OCH_3), 3.54 (dd, 1H, $J = 9.6$, 3.2 Hz, H-3), 2.28 (s, 3H, $PhCH_3$), 2.04 (s, 3H, $COCH_3$),

1.04 (d, 3H, $J = 5.8$ Hz, CH_3-6); ^{13}C NMR (DMSO-d_6) δ 169.7, 158.7, 137.1, 131.7, 130.1, 130.0, 129.8, 129.2, 113.6, 88.5, 75.7, 72.1, 69.4, 68.0, 67.3, 55.0, 30.6, 20.8, 20.6, 17.2. ESIMS: calcd for $[M+Na]^+$ m/z 455.2; found: m/z 455.1.

3.11. *p*-Tolyl 3-*O*-(*p*-methoxybenzyl)-1-thio-α-L-rhamnopyranoside (18)

R_f 0.51 (1:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −140.8 (*c* 0.10, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 7.34 (d, 2H, $J = 8.3$ Hz, Ph), 7.30 (d, 2H, $J = 7.7$ Hz, Ph), 7.16 (d, 2H, $J = 8.3$ Hz, Ph), 6.91 (d, 2H, $J = 7.7$ Hz, Ph), 5.26 (d, 1H, $J = 1.4$ Hz, H-1), 5.18 (d, 1H, $J = 4.6$ Hz, 2-OH), 5.11 (d, 1H, $J = 5.9$ Hz, 4-OH), 4.59 (d, 1H, $J = 11.7$ Hz, PhC*H*H), 4.51 (d, 1H, $J = 11.7$ Hz, PhCH*H*), 4.07 (ddd, 1H, $J = 4.6$, 3.2, 1.9 Hz, H-2), 3.86–3.82 (m, 1H, H-5), 3.75 (s, 3H, OCH_3), 3.44 (td, 1H, $J = 9.6$, 5.9 Hz, H-4), 3.36 (dd, 1H, $J = 9.6$, 3.2 Hz, H-3), 2.28 (s, 3H, PhCH_3), 1.15 (d, 3H, $J = 6.4$ Hz, CH_3-6). ESIMS: calcd for $[M+Na]^+$ m/z 413.1; found: m/z 413.1.

3.12. *p*-Tolyl 4-*O*-acetyl-3-*O*-(*p*-methoxybenzyl)-2-*O*-levulinoyl-1-thio-α-L-rhamnopyranoside (6)

Reaction of compound **17** (5.0 g, 11.6 mmol), levulinic acid (4.0 g, 34.7 mmol), DCC (7.14 g, 34.7 mmol), and DMAP (141.5 mg, 1.2 mmol) in dry CH_2Cl_2 (100 mL) was essentially as described for **5** gave **6** (3.5 g, 56.9%) as a white solid: R_f 0.27 (4:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −30.7 (*c* 0.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.32 (d, 2H, $J = 8.0$ Hz, Ph), 7.21 (dd, 2H, $J = 8.6$, 4.6 Hz, Ph), 7.12 (d, 2H, $J = 8.0$ Hz, Ph), 6.88 (dd, 2H, $J = 8.6$, 4.6 Hz, Ph), 5.55 (dd, 1H, $J = 3.2$, 1.9 Hz, H-2), 5.35 (d, 1H, $J = 1.9$ Hz, H-1), 5.02 (t, 1H, $J = 9.9$ Hz, H-4), 4.56 (d, 1H, $J = 11.7$ Hz, PhC*H*H), 4.34 (d, 1H, $J = 11.7$ Hz, PhC*H*H), 4.25–4.21 (m, 1H, H-5), 3.81 (s, 3H, OCH_3), 3.75 (dd, 1H, $J = 9.6$, 3.2 Hz, H-3), 2.75–2.66 (m, 4H, COCH_2CH_2CO), 2.33 (s, 3H, PhCH_3), 2.16 (s, 3H, COCH_3), 2.04 (s, 3H, COCH_3), 1.19 (d, 3H, $J = 6.4$ Hz, CH_3-6); ^{13}C NMR ($CDCl_3$) δ 206.3, 171.8, 169.9, 159.3, 138.0, 132.3, 129.9, 129.6, 129.5, 113.7, 86.2, 74.1, 72.5, 70.7, 70.1, 67.6, 55.2, 38.0, 29.7, 28.2, 21.0, 20.9, 17.3. ESIMS: calcd for $[M+Na]^+$ m/z 553.2; found: m/z 553.1.

3.13. 1-*O*-Dodecanyl-4-*O*-acetyl-3-*O*-(*p*-methoxybenzyl)-2-*O*-levulinoyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (19)

Reaction of compound **4** (200.0 mg, 0.54 mmol), compound **6** (342.0 mg, 0.64 mmol), NIS (195.2 mg, 0.9 mmol), AgOTf (27.8 mg, 0.1 mmol), and 4 Å molecular sieves in dry CH_2Cl_2 (20 mL) was essentially as described for **14** gave **19** (388.4 mg, 92.9%) as a syrup: R_f 0.50 (2:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −22.4 (*c* 0.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.18 (d, 2H, $J = 8.7$ Hz, Ph), 6.85 (d, 2H, $J = 8.7$ Hz, Ph), 5.41 (dd, 1H, $J = 3.7$, 1.9 Hz, H-2′), 5.30 (d, 1H, $J = 1.8$ Hz, H-1′), 4.96 (t, 1H, $J = 9.8$ Hz, H-4′), 4.95 (s, 1H, H-1), 4.55 (d, 1H, $J = 11.5$ Hz, PhC*H*H), 4.29 (d, 1H, $J = 11.5$ Hz, PhC*H*H), 4.17 (dd, 1H, $J = 7.3$, 5.5 Hz, H-3), 4.10 (d, 1H, $J = 5.5$ Hz, H-2), 3.80 (s, 3H, OCH_3), 3.77–3.74 (m, 1H, H-5′), 3.71 (dd, 1H, $J = 9.6$, 3.2 Hz, H-3′), 3.68–3.64 (m, 2H, H-5 and OC*H*H), 3.45 (dd, 1H, $J = 9.7$, 7.3 Hz, H-4), 3.44–3.40 (m, 1H, OC*H*H), 2.79–2.65 (m, 4H, COCH_2CH_2CO), 2.15 (s, 3H, COCH_3), 2.01 (s, 3H, COCH_3), 1.61–1.56 (m, 2H, βCH_2), 1.54 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.27 (s, 18H, (CH_2)$_9$), 1.24 (d, 3H, $J = 6.4$ Hz, CH_3-6), 1.18 (d, 3H, $J = 6.0$ Hz, CH_3-6′), 0.88 (t, 3H, $J = 7.1$ Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 171.9, 169.9, 159.1, 130.0, 129.9, 129.4, 113.6, 109.5, 96.8, 96.1, 78.0, 76.2, 74.0, 72.2, 70.6, 68.5, 67.7, 67.0, 63.8, 55.2, 38.1, 31.9, 29.8–29.3, 28.5, 28.1, 27.9, 26.4, 26.1, 22.7, 21.0, 17.9, 17.5, 14.1. ESIMS: calcd for $[M+Na]^+$ m/z 801.4; found: m/z 801.3.

3.14. 1-*O*-Dodecanyl-4-*O*-acetyl-2-*O*-levulinoyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (2)

To a stirred mixture of **19** (81.1 mg, 0.1 mmol) in CH_2Cl_2 (5 mL) and H_2O (0.33 mL), was added DDQ (35.5 mg, 0.15 mmol) at room temperature. The reaction was stirred for 12 h until the reaction was complete as judged by TLC. The reaction mixture was poured into satd aq $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (2 × 50 mL). The combined organic phase was washed with satd aq $NaHCO_3$ (2 × 50 mL), and brine (2 × 50 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (10:1, petroleum ether–EtOAc) to give **2** (58.3 mg, 85.0%) as a syrup: R_f 0.33 (2:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −48.4 (*c* 0.10, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 5.24 (br s, 1H, 3′-OH), 5.08 (d, 1H, $J = 1.9$ Hz, H-1′), 4.97 (dd, 1H, $J = 3.7$, 1.9 Hz, H-2′), 4.91 (s, 1H, H-1), 4.72 (t, 1H, $J = 9.7$ Hz, H-4′), 4.08–4.05 (m, 2H, H-2 and H-3), 3.78 (dd, 1H, $J = 9.6$, 3.2 Hz, H-3′), 3.68–3.63 (m, 1H, H-5′), 3.60–3.55 (m, 2H, H-5 and OC*H*H), 3.42–3.38 (m, 1H, OC*H*H), 3.35 (dd, 1H, $J = 10.1$, 6.8 Hz, H-4), 2.72–2.70, 2.57–2.55, 2.51–2.50 (m, 4H, COCH_2CH_2CO), 2.12 (s, 3H, COCH_3), 2.05 (s, 3H, COCH_3), 1.53–1.50 (m, 2H, βCH_2), 1.41 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.24 (s, 18H, (CH_2)$_9$), 1.18 (d, 3H, $J = 6.4$ Hz, CH_3-6), 1.08 (d, 3H, $J = 6.4$ Hz, CH_3-6′), 0.85 (t, 3H, $J = 7.1$ Hz, CH_3); ^{13}C NMR (DMSO-d_6) δ 206.6, 171.6, 169.9, 108.7, 96.1, 95.3, 77.3, 76.6, 75.6, 73.4, 72.1, 66.8, 66.5, 66.0, 63.3, 37.4, 31.3, 29.6, 29.0–28.7, 27.7, 27.6, 26.2,

25.6, 22.1, 20.9, 17.8, 17.4, 14.0. ESIMS: calcd for $[M+Na]^+$ m/z 681.4; found: m/z 681.3.

3.15. *p*-Tolyl 2,4-di-*O*-acetyl-1-thio-α-L-rhamnopyranoside (7)

To a solution of compound **20** (5.1 g, 18.7 mmol) in dry DMF (50 mL), triethylorthoacetate (4.8 mL, 28.1 mmol) was added, followed by a catalytic amount of CSA (868.8 mg, 3.7 mmol). The mixture was stirred for 4 h. After complete conversion by thin-layer chromatography (TLC) (1:1, petroleum ether–EtOAc), Et_3N was added to neutralize the solution. Ac_2O (3.5 mL, 37.4 mmol), Et_3N (8 mL, 56.1 mmol), and DMAP (228.0 mg, 1.9 mmol) were added, and the mixture was allowed to stir for 1 h at room temperature. When TLC (2:1, petroleum ether–EtOAc) showed complete conversion, MeOH (1 mL) was carefully added to destroy excess Ac_2O, and the mixture was diluted with CH_2Cl_2 (200 mL). The organic layer was shaken with 1 M HCl (3 × 100 mL), followed by washing with satd aq $NaHCO_3$ (3 × 100 mL) and water (3 × 100 mL). Finally the organic layer was separated, dried over Na_2SO_4, and evaporated to syrup. The crude product was purified by silica gel column chromatography (6:1, petroleum ether–EtOAc) to give **7** (4.81 g, 71.5%) as a white solid: R_f 0.34 (2:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −144.3 (*c* 0.10, $CHCl_3$); ^1H NMR (DMSO-d_6) δ 7.35 (d, 2H, $J = 8.0$ Hz, Ph), 7.18 (d, 2H, $J = 8.0$ Hz, Ph), 5.51 (d, 1H, $J = 5.9$ Hz, 3-OH), 5.40 (d, 1H, $J = 1.4$ Hz, H-1), 5.18 (dd, 1H, $J = 3.7$, 1.4 Hz, H-2), 4.79 (t, 1H, $J = 9.9$ Hz, H-4), 4.12–4.09 (m, 1H, H-5), 3.85 (ddd, 1H, $J = 9.6$, 5.9, 3.7 Hz, H-3), 2.29 (s, 3H, PhCH_3), 2.08 (s, 3H, COCH_3), 2.07 (s, 3H, COCH_3), 1.07 (d, 3H, $J = 5.9$ Hz, CH_3-6); ^{13}C NMR (DMSO-d_6) δ 169.9, 169.8, 137.5, 131.8, 129.9, 129.2, 85.2, 73.5, 73.2, 67.2, 66.7, 20.9, 20.8, 20.6, 17.2. ESIMS: calcd for $[M+Na]^+$ m/z 377.1; found: m/z 377.1.

3.16. 4-*O*-Acetyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl trichloroacetimidate (8)

To a stirred solution of **11** (4.0 g, 11.3 mmol) in acetone (72 mL) and H_2O (8 mL) at −20 °C was added NBS (6.0 g, 34.1 mmol). After 5 min, the reaction was quenched with satd aq $NaHCO_3$ and concentrated. The residue was diluted with $CHCl_3$ (200 mL) and washed with satd aq $NaHCO_3$ (100 mL), brine (2 × 100 mL), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography (4:1, petroleum ether–EtOAc) to afford a white solid (2.4 g, 84.5%): R_f 0.48, 0.23 (2:1, petroleum ether–EtOAc). To a stirred solution of the white solid (150 mg, 0.6 mmol) and CCl_3CN (368.7 μL, 3.7 mmol) in CH_2Cl_2 (10 mL) at 0°C was added DBU (47 μL, 0.3 mmol). After 4 h, the solution was concentrated and the residue was purified by silica gel column chromatography (6:1, petroleum ether–EtOAc) to afford **8** (237.1 mg, 86.9%) as a white solid: R_f 0.42 (4:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −26.4 (*c* 0.10, $CHCl_3$); ^1H NMR (600 Hz, $CDCl_3$) δ 8.7 (s, 1H, N*H*), 6.49 (s, 1H, H-1), 4.97–4.93 (m, 2H, H-2 and H-4), 4.30 (dd, 1H, $J = 8.7$, 3.7 Hz, H-3), 3.96–3.92 (m, 1H, H-5), 2.12 (s, 3H, COCH_3), 1.60 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.20 (d, 3H, $J = 6.4$ Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 170.0, 160.1, 110.4, 95.0, 75.4, 74.6, 73.5, 67.2, 27.5, 26.4, 21.0, 17.0. ESIMS: calcd for $[M–CCl_3CN+Na]^+$ m/z 269.1; found: m/z 269.1.

3.17. *p*-Tolyl 4-*O*-acetyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-acetyl-1-thio-α-L-rhamnopyranoside (3)

To a solution of compound **8** (150.0 mg, 0.4 mmol), compound **7** (113.3 mg, 0.3 mmol) and 4 Å molecular sieves in dry CH_2Cl_2 (5 mL), TMSOTf (3 μL, 0.03 mmol) was added at −20 °C under argon. The reaction mixture was stirred under these conditions for 30 min, until TLC indicated that the reaction was complete. The reaction was quenched by Et_3N (two drops) and concentrated. The residue was purified by silica gel column chromatography (4:1, petroleum ether–EtOAc) to give **3** (186.3 mg, 99.9%) as a syrup: R_f 0.39 (2:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −63.4 (*c* 0.10, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.54 (d, 2H, $J = 8.0$ Hz, Ph), 7.13 (d, 2H, $J = 8.0$ Hz, Ph), 5.37 (dd, 1H, $J = 3.7$, 1.8 Hz, H-2), 5.32 (d, $J = 1.4$ Hz, H-1), 5.14 (t, 1H, $J = 9.8$ Hz, H-4), 5.13 (s, 1H, H-1′), 4.83 (dd, 1H, $J = 10.1$, 8.2 Hz, H-4′), 4.33–4.28 (m, 1H, H-5), 4.15 (dd, 1H, $J = 9.6$, 3.2 Hz, H-3), 4.09 (dd, 1H, $J = 8.2$, 5.5 Hz, H-3′), 4.04 (d, 1H, $J = 5.5$ Hz, H-2′), 3.73–3.68 (m, 1H, H-5′), 2.33 (s, 3H, PhCH_3), 2.15, 2.13, 2.10 (s, each 3H, 3 × COCH_3), 1.55 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.23 (d, 3H, $J = 6.4$ Hz, CH_3-6), 1.16 (d, 3H, $J = 6.4$ Hz, CH_3-6′); ^{13}C NMR ($CDCl_3$) δ 170.2, 170.0, 138.2, 132.4, 130.0, 129.4, 109.7, 99.4, 86.1, 76.0, 75.5, 74.4, 74.0, 73.3, 73.2, 67.8, 64.9, 27.6, 26.4, 21.1, 21.0, 20.9, 17.3, 16.7. ESIMS: calcd for $[M+Na]^+$ m/z 605.2; found: m/z 605.1.

3.18. 1-*O*-Dodecanyl-4-*O*-acetyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-levulinoyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (21)

Reaction of compound **2** (100.5 mg, 0.15 mmol), compound **3** (266.6 mg, 0.45 mmol), NIS (57.7 mg, 0.26 mmol), AgOTf (7.7 mg, 0.03 mmol), and 4 Å molecular sieves in dry CH_2Cl_2 (20 mL) was essentially as described for **16** gave **21** (105.0 mg, 61.6%) as a syrup: R_f 0.38 (2:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −42.5 (*c*

0.19, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 5.24 (d, 1H, $J = 1.4$ Hz, H-1′), 5.22 (s, 1H, H-1″), 5.21 (dd, 1H, $J = 3.2$, 1.9 Hz, H-2′), 5.05 (t, 1H, $J = 9.6$ Hz, H-4′), 5.04 (t, 1H, $J = 9.6$ Hz, H-4″), 4.94 (s, 1H, H-1‴), 4.92 (dd, 1H, $J = 3.2$, 1.9 Hz, H-2″), 4.84 (s, 1H, H-1), 4.79 (dd, 1H, $J = 10.1$, 8.3 Hz, H-4‴), 4.19 (dd, 1H, $J = 10.1$, 3.2 Hz, H-3″), 4.16 (dd, 1H, $J = 7.3$, 5.5 Hz, H-3), 4.09–4.07 (m, 2H, H-2 and H-3‴), 4.02 (d, 1H, $J = 5.5$ Hz, H-2‴), 3.99 (dd, 1H, $J = 10.1$, 3.2 Hz, H-3′), 3.92–3.87 (m, 1H, H-5″), 3.79–3.75 (m, 1H, H-5′), 3.68–3.65 (m, 2H, H-5 and OC*H*H), 3.64–3.59 (m, 1H, H-5‴), 3.46 (dd, 1H, $J = 9.6$, 7.3 Hz, H-4), 3.43–3.39 (m, 1H, OC*H*H), 2.89–2.69 (m, 4H, $COCH_2CH_2CO$), 2.24 (s, 3H, $COCH_3$), 2.14 (s, 3H, $COCH_3$), 2.13 (s, 3H, $COCH_3$), 2.12 (s, 3H, $COCH_3$), 2.09 (s, 3H, $COCH_3$), 1.60–1.55 (m, 2H, βCH_2), 1.53 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.27 (br s, 21H, CH_3-6 and $(CH_2)_9$), 1.19 (d, 6H, $J = 5.9$ Hz, CH_3-6′ and CH_3-6″), 1.10 (d, 3H, $J = 6.4$ Hz, CH_3-6‴), 0.88 (t, 3H, $J = 7.1$ Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 206.1, 171.7, 170.4, 170.3, 170.2, 170.1, 109.6, 109.5, 99.4, 99.2, 96.8, 95.8, 77.9, 77.5, 76.2, 76.0, 75.6, 74.7, 74.2, 74.1, 72.6, 72.4, 72.2, 71.5, 67.8, 67.3, 67.2, 64.6, 63.7, 37.8, 31.9, 29.8–29.3, 28.3, 27.9, 27.6, 26.4, 26.1, 23.8, 22.7, 21.1, 20.9, 20.7, 18.0, 17.4, 17.3, 16.5, 14.1. ESIMS: calcd for $[M+Na]^+$ m/z 1139.6; found: m/z 1139.5.

3.19. 1-*O*-Dodecanyl-4-*O*-acetyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (22)

To a stirred solution of **21** (77.0 mg, 0.07 mmol) in CH_2Cl_2 (5 mL) and CH_3OH (5 mL) was added NH_2NH_2·HOAc (63.5 mg, 0.70 mmol). After 2 h, the solution was concentrated. And the residue was purified by silica gel column chromatography (3:1, petroleum ether–EtOAc) to afford **22** (57.6 mg, 82.1%) as a syrup: R_f 0.38 (2:1, petroleum ether–EtOAc); $[\alpha]_D^{20}$ −44.8 (*c* 0.10, $CHCl_3$); ^1H NMR (DMSO-d_6) δ 5.46 (d, 1H, $J = 4.6$ Hz, 2′-OH), 5.15 (s, 1H, H-1′), 5.03 (s, 1H, H-1″), 4.96 (t, 1H, $J = 9.9$ Hz, H-4′), 4.91 (s, 1H, H-1‴), 4.89 (d, 1H, $J = 3.2$ Hz, H-2″), 4.84 (t, 1H, $J = 10.1$ Hz, H-4″), 4.80 (s, 1H, H-1), 4.64 (dd, 1H, $J = 9.7$, 8.3 Hz, H-4‴), 4.18 (dd, 1H, $J = 10.1$, 3.2 Hz, H-3″), 4.11–4.04 (m, 4H, H-2, H-3, H-5″, and H-3‴), 3.98 (d, 1H, $J = 5.0$ Hz, H-2‴), 3.78 (br s, 1H, H-2′), 3.71 (dd, 1H, $J = 10.1$, 2.7 Hz, H-3′), 3.68–3.64 (m, 1H, H-5′), 3.60–3.53 (m, 3H, H-5, H-5‴ and OCH_2), 3.42–3.39 (m, 1H, OCH_2), 3.36 (t^{obsc}, 1H, H-4), 2.10 (s, 3H, $COCH_3$), 2.08 (s, 3H, $COCH_3$), 2.07 (s, 3H, $COCH_3$), 2.05 (s, 3H, $COCH_3$), 1.53–1.51 (m, 2H, βCH_2), 1.43 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.24 (br s, 18H, $(CH_2)_9$), 1.18 (d, 3H, $J = 6.4$ Hz, CH_3-6), 1.08 (d, 3H, $J = 6.4$ Hz, CH_3-6″), 1.06 (d, 3H, $J = 6.4$ Hz, CH_3-6′), 1.01 (d, 3H, $J = 6.0$ Hz, CH_3-6‴), 0.85 (t, 3H, $J = 6.9$ Hz, CH_3); ^{13}C NMR (DMSO-d_6) δ 170.4, 170.3, 170.2, 170.1, 163.4, 109.3, 109.0, 99.2, 99.1, 98.6, 96.4, 78.0, 77.8, 75.8, 75.7, 74.8, 74.1, 73.9, 72.5, 72.0, 71.7, 70.2, 67.1, 66.9, 66.4, 64.3, 63.6, 31.5, 30.9, 29.2–28.9, 27.9, 27.7, 26.4, 26.3, 25.8, 22.4, 20.9, 20.8, 20.7, 20.7, 18.1, 17.5, 17.3, 16.4, 14.2. ESIMS: calcd for $[M+Na]^+$ m/z 1041.5; found: m/z 1041.6.

3.20. 1-*O*-Dodecanyl-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranoside (1)

Compound **22** (53.4 mg, 0.05 mmol) was dissolved in 80% HOAc (7.5 mL) and stirred for 2 h at 80 °C, then the reaction mixture was concentrated. The residue was purified by silica gel column chromatography (30:1-10:1, $CHCl_3$–MeOH) to give compound **1** (40.7 mg, 82.7%) as a gummy solid: $[\alpha]_D^{20}$ −63.9 (*c* 0.40, MeOH), (Ref. 10 $[\alpha]_D^{20}$ −59.5 (*c* 0.40, MeOH)); R_f 0.32 (8:1, $CHCl_3$–CH_3OH); ^1H NMR (CD_3OD) δ 5.22 (d, 1H, $J = 1.4$ Hz, H-1′), 5.11 (t, 1H, $J = 9.8$ Hz, H-4′), 5.04 (dd, 1H, $J = 3.2$, 1.4 Hz, H-2″), 4.97 (t, 1H, $J = 10.1$ Hz, H-4″), 4.89 (t^{obsc}, 1H), 4.87 (d, 1H, $J = 1.4$ Hz, H-1″), 4.82 (d, 1H, $J = 1.3$ Hz, H-1‴), 4.63 (d, 1H, $J = 1.3$ Hz, H-1), 4.25 (dd, 1H, $J = 10.1$, 3.7 Hz, H-3″), 4.05 (br d, 1H, $J = 3.2$ Hz, H-2′), 4.08–4.03 (m, 1H, H-5″), 3.90–3.86 (m, 1H, H-5′), 3.87 (dd, 1H, $J = 10.1$, 3.2 Hz, H-3′), 3.74–3.72 (m, 2H, H-2 and H-3), 3.70 (dd, 1H, $J = 3.2$, 1.9 Hz, H-2‴), 3.66 (dd, 1H, $J = 7.3$, 3.2 Hz, H-3‴), 3.67–3.60 (m, 3H, OC*H*H, H-5‴ and H-5), 3.51 (t, 1H, $J = 9.2$ Hz, H-4), 3.40–3.37 (m, 1H, OC*H*H), 2.13 (s, 3H, CH_3CO-4′), 2.12 (s, 3H, CH_3CO-2″), 2.08 (s, 3H, CH_3CO-4″), 2.10 (s, 3H, CH_3CO-4‴), 1.62–1.53 (m, 2H, βCH_2), 1.37–1.34 (m, 2H, γCH_2), 1.29 (br s, 16H, $(CH_2)_8$), 1.26 (d, 3H, $J = 6.4$ Hz, CH_3-6), 1.16 (d, 3H, $J = 6.4$ Hz, CH_3-6″), 1.14 (d, 3H, $J = 6.4$ Hz, CH_3-6′), 1.09 (d, 3H, $J = 6.4$ Hz, CH_3-6‴), 0.88 (t, 3H, $J = 7.1$ Hz, CH_3); ^{13}C NMR (6:1, C_5D_5N–CD_3OD) δ 171.6, 171.0, 170.5, 103.9, 103.5, 101.7, 100.6, 81.1, 80.5, 75.4, 75.3, 73.6, 73.4, 73.1, 73.0, 72.5, 71.9, 70.2, 68.4, 68.3, 68.1, 68.0, 67.6, 32.5, 30.3–30.0, 26.9, 23.3, 21.3, 21.2, 21.0, 20.9, 19.3, 18.1, 17.8, 14.6. HRESIMS: calcd for $C_{44}H_{74}O_{21}Na^+$ 961.4620; found, 961.4626, (Ref. 12 961.4739).

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