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Synthesis and antibacterial evaluation of a series of oligorhamnoside derivatives

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ABSTRACT

A series of novel oligorhamnoside derivatives (**1**–**10**) and naturally occurring cleistrioside-**5** were synthesized and evaluated for their in vitro antibacterial activities. Among them, dirhamnoside derivative **7** and cleistrioside-**5** displayed similar antibacterial profiles and exhibited moderate to good inhibitory activities on bacterial growth against a panel of Gram-positive bacteria (MICs $\leq$ 4–32 μg/mL). The results revealed that these two compounds showed selectivity towards bacterial species strictly, without being affected by the antibiotic-resistant/susceptible properties of one species, which suggested that they might have the potential to avoid antibiotic cross-resistance. In addition, the preliminary SARs of this type of oligorhamnoside derivatives on the antibacterial activities were determined.

1. Introduction

The rising incidence of infections caused by antibiotic-resistant microorganisms has become a major concern for clinicians and the public health system. However, despite a push for new antibiotic therapies there has been a continued decline in the number of newly approved drugs.[1] In this respect, new prototype antibacterial agents with unique chemical structures, dissimilar toxicities, broad spectrum of activities and cross-resistances with present drug therapies are desperately needed.

Oligosaccharides play an important role in biological systems, such as cell–cell interaction, cell adhesion, and immunogenic recognition.[2] Most of them are primary ingredients of the cell-wall polysaccharides of bacteria.[3] The polysaccharides of pathogenic bacteria are responsible for the immunogenic activities[4] and contribute to bacterial virulence.[5] Oligosaccharides that share similar chemical structure with primary ingredients of bacterial polysaccharides may disrupt the biosynthesis of bacterial polysaccharides and destroy their virulence.[4] Rhamnose-containing oligosaccharides are widely distributed in natural products, such as triterpenoid glycosides,[6] K-antigens,[7] and a series of glycolipids from mycobacteria.[8,9] Because rhamnose-containing oligosaccharides are not present in mammalian cells,[10] they may have the potential to overcome the lack of specificity and resistance encountered with currently used antibiotics.

Two series of partially acetylated dodecanyl tetra- and trirhamnoside derivatives cleistetrosides-**1**–**8**, and cleistriosides-**1**–**6** were previously isolated[11] from *Cleistopholis* spp. (Fig. 1). Among them several compounds have been shown to have significant in vitro antibacterial activities. For example, cleistetroside-**2**, cleistetroside-**8** and cleistriosides-**5** were found to possess significant antibacterial activities against the Gram-positive methicillin-resistant *S. aureus* ATCC 33591 and *S. aureus* 78-13607A with MICs of $\leq$16 μg/mL.[11a] Furthermore, cleistriosides-**5** and cleistetroside-**2** displayed significant antibacterial activities against an expanded panel of Gram-positive pathogens including either ATCC strains or well-characterized clinical isolates from the global SENTRY Antimicrobial Surveillance Program.[11a]

The ability of partially acetylated simple rhamnoside derivatives to have significant in vitro inhibition on bacterial growth is interesting. Whereas, not all compounds in these two series have antibacterial activities as efficient as those above mentioned. Because each series of compounds shares a same oligorhamnoside skeleton, the observed variety of antibacterial activities indicated that the acetyl groups might play an important role on the underlying mechanism of action. In addition, the sugar chain length of three and four seemed to have no influence on the antibacterial activities because both cleistriosides-**5** and cleistetroside-**2** had the best antibacterial profiles against the panel of bacteria. To elucidate the contribution of the acetyl groups on antibacterial activities, and also to further understand the correlation between the sugar chain length and inhibitory activities, structure–activity relationships (SARs) of these compounds are a particularly attractive

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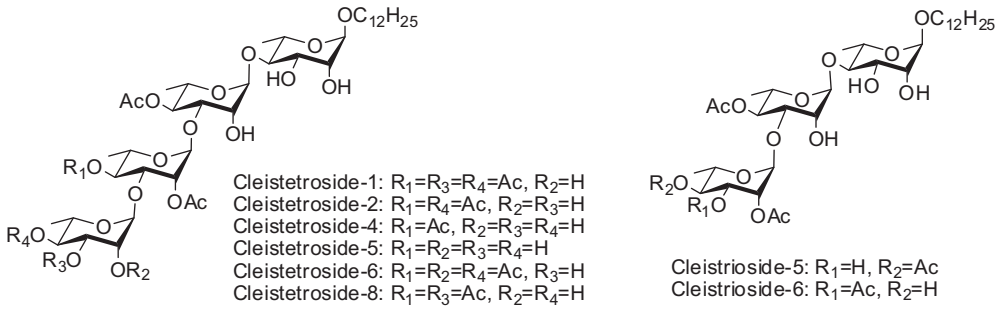


Figure 1. Eight partially acetylated oligorhamnosides from *Cleistopholis patens*.

direction. With our continuous interest in the biological activities of glycolipids[12] and to search for potential new antimicrobial agents, we decided to investigate the synthesis and in vitro biological evaluation of antibacterial activities of a series of dodecanyl oligorhamnoside derivatives. The results obtained render new clues on understanding of the antimicrobial profile for these types of compounds.

2. Results and discussion

Ten dodecanyl rhamnoside derivatives **1–10** with sugar chain length of 1–4 and none/partially/per acylated hydroxyls were designed and synthesized (Fig. 2). The natural product cleistrioside-**5**, which was reported to have significant in vitro antibacterial activities,[11a] was also synthesized for comparison during the antibacterial activity testing.

2.1. Chemistry

The total synthesis of cleistetroside-2 has been reported by us and others previously.[13] Following a similar strategy[13a] as that developed by us, the synthesis of cleistrioside-**5** and target compounds **1–10** were accomplished. As outlined in Scheme 1, most of the designed compounds as well as cleistrioside-**5** were synthesized from coupling of the key disaccharide building block **11**[13a] with appropriate glycosyl donors.

Cleistrioside-**5** was constructed via a '2+1' convergent strategy by glycosylation of **11** with thioglycoside **12**. The glycosylation was carried out smoothly in the presence of NIS–AgOTf to provide trisaccharide **13** in an 81% yield with exclusive α-glycosidic linkage. The α-configuration of the newly formed glycosidic bond in **13** was confirmed by HMBC spectrum ($^1J_{C\text{-}1'',H\text{-}1''}$ = 170.7 Hz). Deprotection of the Lev group in **13** with hydrazine acetate (81%), followed by removal of the isopropylidene group (70%) led to cleistrioside-**5**. Acetylation of cleistrioside-**5** with Ac_2O–Et_3N provided its peracetate **6** (90%).

Monosaccharide building blocks **18**[13a]**–20** were prepared by treating of **21** with corresponding acyl chlorides, respectively. With glycosyl acceptor **11** and donors **18–20** in hand, glycosylations were performed to provide three trisaccharides **22–24**. Removal of the Lev and isopropylidene protecting groups eventually gave desired compounds **3**, **4**, **5**, respectively.

Target disaccharide **7** was obtained by condensation of acceptor **25**[13a] with glycosyl donor **18** (74%), followed by cleavage of the isopropylidene group in compound **26** with 80% HOAc (81%).

Target disaccharide **8** was prepared from key intermediate **11** in three steps. Protection of 3′-OH in **11** with acetyl group followed by removal of the Lev group led to compound **27** (83% for two steps). Removal of the isopropylidene group (79%) afforded compound **8**.

Compounds **9** and **10** are known compounds and were synthesized according to our previously published procedures.[13a]

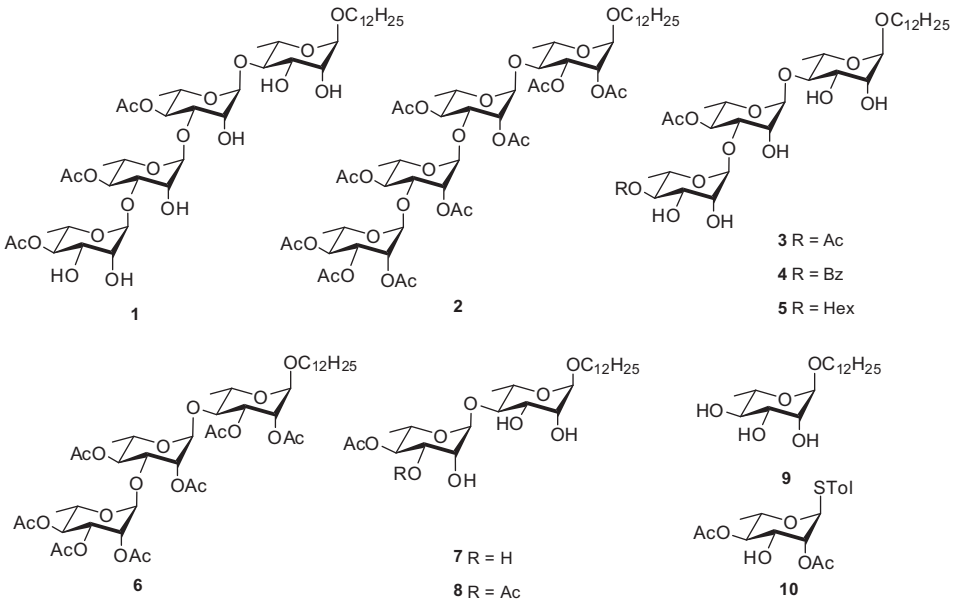
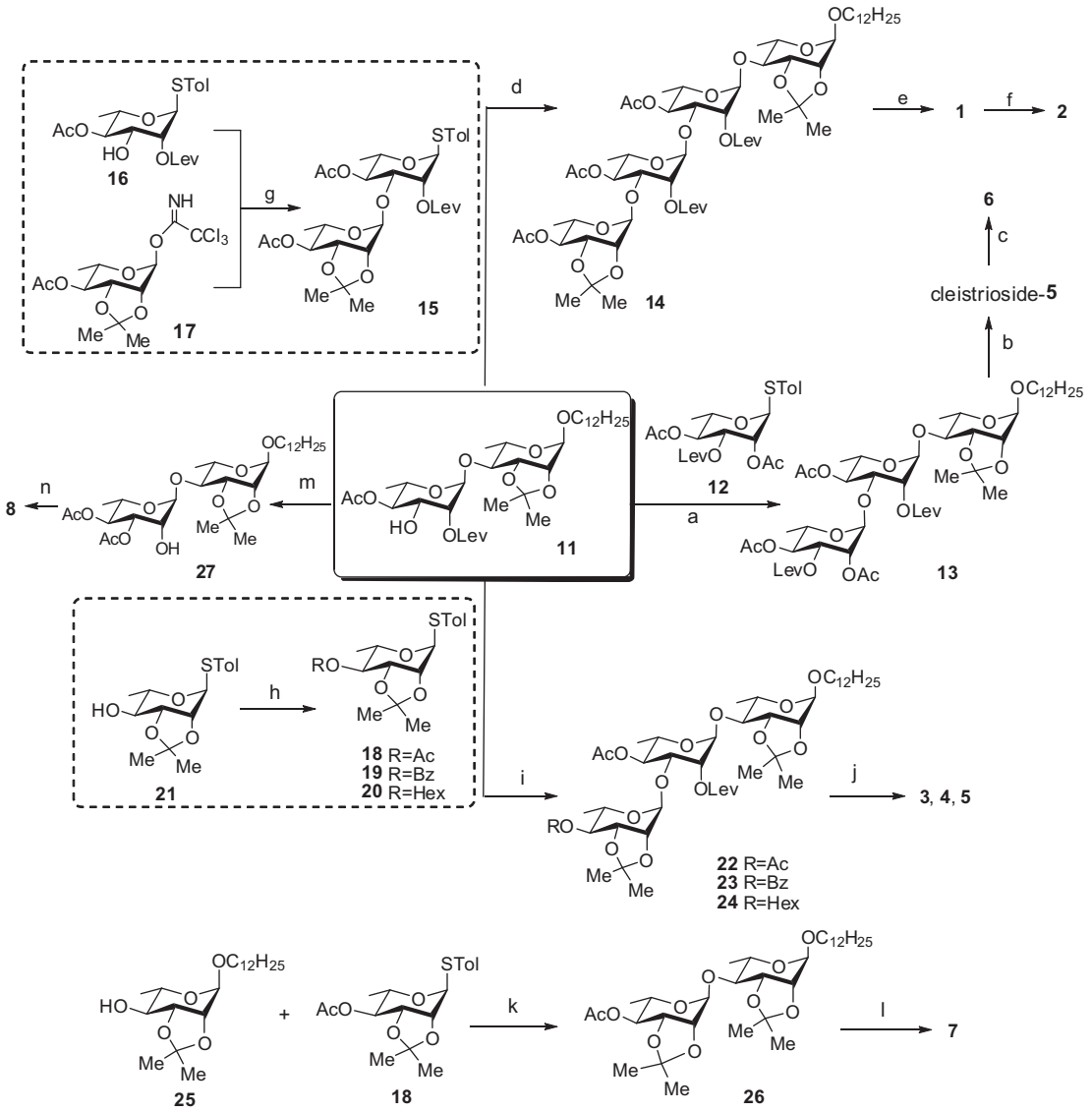


Figure 2. Designed compounds **1–10**.



Scheme 1. Synthesis of cleistrioside-**5** and target compounds **1–10**. Reagents and conditions: (a) **12**, NIS, AgOTf, CH_2Cl_2, 81%; (b) (i) $NH_2NH_2{\cdot}HOAc$, CH_2Cl_2–MeOH, 81%; (ii) 80% HOAc, 70%; (c) DMAP, Ac_2O, Et_3N, CH_2Cl_2, 90%; (d) **15**, NIS, AgOTf, CH_2Cl_2, 65%; (e) (i) $NH_2NH_2{\cdot}HOAc$, CH_2Cl_2–MeOH, 58%; (ii) 80% HOAc, 70%; (f) DMAP, Ac_2O, Et_3N, CH_2Cl_2, 99%; (g) TMSOTf, CH_2Cl_2, 77%; (h) BzCl, pyridine, 88% for **19**; *n*-hexanoyl chloride, pyridine, 68% for **20**; (i) **18**, **19**, or **20**, NIS, AgOTf, CH_2Cl_2, 99% for **22**, 55% for **23**, 49% for **24**; (j) (i) $NH_2NH_2{\cdot}HOAc$, CH_2Cl_2–MeOH, 72% from **25**, 87% from **26**, 90% from **27**; (ii) 80% HOAc, 81% for **3**, 83% for **4**, 63% for **5**; (k) NIS, AgOTf, CH_2Cl_2, 74%; (l) 80% HOAc, 81%; (m) (i) Ac_2O, Et_3N, DMAP, CH_2Cl_2; (ii) $NH_2NH_2{\cdot}HOAc$, CH_2Cl_2–MeOH, 83% for two steps; (n) 80% HOAc, 79%.

2.2. Antibacterial activities

Target compounds **1–10** and cleistrioside-**5** were evaluated for their in vitro antibacterial activities against a panel of bacteria including both antibiotic resistant and susceptible strains following a standard testing method.[14] The minimum inhibitory concentration (MIC) is defined as the concentration of the compound required to give 80% inhibition of bacteria growth. Selected MICs of the target compounds and cleistrioside-**5** along with those of Vancomycin and Oxacillin are presented in Table 1.

As expected, all the tested compounds showed no antibacterial activities against Gram-negative bacteria *E. coli.*, whereas the synthetic cleistrioside-**5** and compound **7** exhibited moderate to good inhibitory activities against a panel of Gram-positive bacteria with MICs of $\leq$32 μg/mL. Interestingly, these two compounds displayed similar antibacterial profiles in general and showed selectivity towards bacterial species. For instance, they had significant bacterial growth inhibitory activities against two strains of α-*haemolytic streptococci* with MICs of $\leq$4 μg/mL and good activities against five strains of *E. faecium* with MICs of $\leq$8 μg/mL. As for the tested six strains of *S. epidermidis* and six strains of *S. aureus*, the MICs were $\leq$16 μg/mL respectively.

More interestingly, the antibacterial activities of cleistrioside-**5** and compound **7** did not vary with the antibiotic-resistant/susceptible properties of a certain species. For example, they were effective in inhibiting the growth of both methicillin-resistant and susceptible *S. aureus* as well as *S. epidermidis* with MICs of $\leq$16 μg/mL, and inhibit the growth of both Vancomycin-resistant and susceptible *E. faecalis* with MICs of $\leq$8 μg/mL. These findings indicate cleistrioside-**5** and compound **7** might have the potential to avoid antibiotic cross-resistance, although their antibacterial activities are not at the same level as those of Vancomycin and Oxacillin in the current evaluation.

Comparing of the antibacterial activities of compounds **1–10** and cleistrioside-**5** with those of cleistrioside **1**–**6** and cleistetroside **1**–**8**, which have been reported previously,[11] preliminary SARs

Table 1
Selected antibacterial activities of the synthetic compounds and cleistrioside-**5**

Organism		Antibiotic resistant/susceptible (+)/(−)[a]	MIC[e] (μg/mL)				
			C5[b]	**7**	**10**	V[c]	O[d]
Escherichia coli	ATCC 25922		>32	>32	>32	—	4
Staphylococcus aureus	ATCC 43300	Methicillin (+)	>16	16	>32	2	2
	ATCC 29213	Oxacillin (−)	16	16	>32	2	1
	07L007	Methicillin (+)	16	16	>32	2	—
	07C089	Methicillin (+)	16	16	>32	2	—
	07C138	Methicillin (−)	16	16	>32	2	0.5
	07T083	Methicillin (−)	16	16	>32	2	0.5
Staphylococcus haemolyticus	07N024		32	>32	>32	2	0.5
	07G024		>32	>32	>32	2	0.5
Staphylococcus epidermidis	07T220	Methicillin (+)	16	16	>32	2	—
	07T030	Methicillin (+)	16	16	>32	2	—
	07N128	Methicillin (−)	16	16	>32	2	0.5
	07Q477	Methicillin (−)	16	16	>32	2	0.5
	07U273	Methicillin (−)	16	16	>32	2	1
Enterococcus faecalis	07K142	Vancomycin (−)	8	8	32	2	—
	ATCC 29212	Ampicillin (−) Vancomycin (−)	8	8	32	2	1
	07K019	Vancomycin (−)	8	8	32	2	—
	ZB11	Vancomycin (+)	8	8	>32	—	—
	ZB119	Vancomycin (+)	8	8	>32	—	—
α-Haemolytic streptococci	07H198		4	4	32	2	0.5
	07H219		4	4	32	2	0.5
β-Haemolytic streptococci	07U083		4	4	>32	2	0.5
	07U084		8	8	>32	—	0.5
	07U087		8	8	>32	—	0.5

[a] Antibiotic susceptibility was assessed by MIC method which was performed by the agar dilution method described by the NCCLS. Antibiotic resistant: (+), antibiotic susceptible: (−).
[b] **C5** = cleistrioside-**5**.
[c] V = Vancomycin.
[d] O = Oxacillin.
[e] —, No antibacterial activities was displayed when Vancomycin (2 μg/mL) and Oxacillin (0.5 μg/mL) were used.

could be concluded. The partial presence of acetyl groups on these rhamnoside derivatives is necessary for the antibacterial activities. For example, compounds **2** and **6**, which are the peracetates of active compounds cleistetroside-**2** and cleistrioside-**5**, lacked antibacterial activity. Additionally, the positions of acetyl groups are also important, especially for the 2-position of the third rhamnose unit and the 3-position of the terminal rhamnose. Removal of the acetyl moiety from the 2‴-OH group in active compounds cleistetroside-**2** and cleistrioside-**5** (resulting in compounds **1** and **3**, respectively) led to the loss of activity, whereas blocking the 3-OH group of the terminal rhamnose in compound **7** with an acetyl group (resulting in compound **8**) eliminated antibacterial activity.

In addition, the dirhamnoside derivative **7**, which exhibited antibacterial activities as good as cleistrioside-**5** against a panel of Gram-positive bacteria, suggest the sugar chain length could be reduced to two without affected the activity. This finding is attractive as dirhamnoside derivative **7** is easier to be accessed and modified by chemists, compared to longer structures. Further studies that focus on compound **7** are currently underway and will be reported later.

3. Conclusions

A series of novel oligorhamnoside derivatives (**1–10**) and cleistrioside-**5**, which was isolated from *Cleistopholis patens* were synthesized and evaluated for their in vitro antibacterial activities. Among them, dirhamnoside derivative compound **7** and cleistrioside-**5** displayed similar antibacterial profiles in general and exhibited moderate to good inhibitory activities on bacterial growth against a panel of Gram-positive bacteria. The results also revealed that these two compounds showed selectivity towards bacteria species without being affected by the antibiotic-resistant/susceptible properties of a certain species, which suggested they might have the potential to avoid antibiotic cross-resistance. In addition, preliminary SARs of this type of oligorhamnoside derivatives on the antibacterial activities were concluded. The rhamnoside derivative **7**, with a reduced sugar chain, was a potent lead compound to be further optimized as an antibacterial agent and these studies are currently underway.

4. Experimental

4.1. 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. 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. COSY, HMQC, and HMBC were routinely used to definitively assign the signals of ^{1}H NMR and ^{13}C NMR spectra. Mass spectra were measured using a HP5989A or VG Quattro MALDI-TOF-MS with α-cyano-4-hydroxycinnamic acid (CCA) as the matrix.

4.2. General method A for the glycosylation of disaccharide acceptor 11 with thioglycosides 12, 15, 18–20 and glycosylation of monosaccharide donor 18 with acceptor 25

To a solution of thioglycoside donor (1.2 mmol for **12**, **18**, **19**, **20**; 1.6 equiv for **15**) in dry CH_2Cl_2 (15 mL) 4 Å molecular sieves

and 1 mmol disaccharide acceptor **11** or **25** (1.0 mmol) were added. After stirred for 30 min at room temperature, the mixture was cooled to 0 °C and NIS (1.6 equiv), AgOTf (0.2 equiv) were added. The reaction mixture was kept at 0 °C for 30 min and then warmed to room temperature. When TLC showed complete conversion of **11**, the reaction mixture was filtered and concentrated. The residue was diluted with CH_2Cl_2 (50 mL) and washed with 5% aqueous $Na_2S_2O_3$ (25 mL), saturated aqueous $NaHCO_3$ (25 mL) and brine (2 × 25 mL). The organic layer were combined and dried over Na_2SO_4, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the product.

4.3. General method B for removal of the Lev protecting groups

To a stirred solution of Lev protected compound (1.0 mmol) in CH_2Cl_2 (10 mL) and CH_3OH (10 mL) was added NH_2NH_2·HOAc (19 mmol). After stirring at room temperature for 2 h, the reaction mixture was concentrated. The residue was purified by silica gel column chromatography to afford the product.

4.4. General method C for removal of the isopropylidene protecting groups

The isopropylidene protected compound (0.1 mmol) was dissolved in 80% HOAc (15 mL) and stirred for 1–2 h at 80 °C. The reaction mixture was concentrated and the residue was purified by silica gel column chromatography to give the product.

4.5. Dodecanyl 2,4-di-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranoside (cleistrioside-5)

The Lev protecting groups in compound **13** were removed following the general procedure B to afford dodecanyl 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. Yield: 83%; R_f 0.53 (1:2 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −54.7 (*c* 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 5.46 (d, 1H, *J* = 4.6 Hz, 2′-OH), 5.28 (d, 1H, *J* = 5.9 Hz, 3″-OH), 5.13 (s, 1H, H-1′), 4.94 (t, 1H, *J* = 9.9 Hz, H-4′), 4.91 (s, 1H, H-1), 4.78 (d, 1H, *J* = 3.8 Hz, H-2″), 4.74 (s, 1H, H-1″), 4.71 (t, 1H, *J* = 9.8 Hz, H-4″), 4.19–4.05 (m, 2H, H-2 and H-3), 3.95–3.90 (m, 2H, H-3″ and H-5″), 3.75 (br s, 1H, H-2′), 3.68 (dd, 1H, *J* = 10.1, 5.3 Hz, H-3′), 3.66–3.62 (m, 1H, H-5′), 3.59–3.53 (m, 2H, H-5 and OCH*H*), 3.41–3.35 (m, 2H, H-4 and OC*H*H), 2.07, 2.06, 2.05 (3s, each 3H, 3 × COCH_3), 1.54–1.49 (m, 2H, OCH_2CH_2), 1.43, 1.27 (2s, each 3H, 2 × CH_3), 1.24 (br s, 18H, $(CH_2)_9$), 1.17 (d, 3H, *J* = 6.4 Hz, 6-*Me*), 1.06 (d, 3H, *J* = 6.4 Hz, 6′-*Me*), 1.04 (d, 3H, *J* = 5.9 Hz, 6″-*Me*), 0.85 (t, 3H, *J* = 7.1 Hz, *Me*); ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.0, 169.9, 108.6, 99.6, 98.3, 96.1, 77.8, 76.9, 76.6, 75.6, 73.5, 72.3, 71.9, 69.9, 66.8, 66.6, 66.1, 65.6, 63.3, 31.3, 28.9–28.6, 27.7, 26.1, 25.6, 22.1, 20.9, 20.8, 20.5, 17.9, 17.2, 14.0; ESIMS: calcd for $[M+Na]^+$ *m*/*z* 813.4; found: 813.5.

The isopropylidene protecting group on the above compound was removed following the general procedure C to afford cleistrioside-**5**. Yield: 70%; R_f 0.48 (8:1, $CHCl_3$–MeOH); $[\alpha]_D^{20}$ −43.5 (*c* 0.04, MeOH); ^{1}H NMR (600 MHz, CD_3OD) δ 5.21 (d, 1H, *J* = 1.7 Hz, H-1′), 5.09 (t, 1H, *J* = 9.6 Hz, H-4′), 4.92 (dd, 1H, *J* = 3.8,1.6 Hz H-2″), 4.88 (t^{obsc}, 1H, H-4″), 4.86 (d, 1H, *J* = 1.7 Hz, H-1″), 4.63 (d, 1H, *J* = 1.1 Hz, H-1), 4.12 (dd, 1H, *J* = 9.9, 3.3 Hz, H-3″), 4.04 (dd, 1H, *J* = 2.8, 1.6 Hz, H-2′), 4.00–3.95 (m, 1H, H-5″), 3.87 (dd, 1H, *J* = 9.9, 3.2 Hz, H-3′), 3.90–3.85 (m, 1H, H-5′), 3.73 (dd, 1H, *J* = 9.0, 3.3 Hz, H-3), 3.72 (dd, 1H, *J* = 3.3, 1.7 Hz, H-2), 3.67–3.64 (m, 1H, OC*H*H), 3.64–3.60 (m, 1H, H-5), 3.50 (t, 1H, *J* = 9.1 Hz, H-4), 3.40–3.37 (m, 1H, OCH*H*), 2.12 (s, 3H, CH_3CO-4′), 2.11 (s, 3H, CH_3CO-2″), 2.08 (s, 3H, CH_3CO-4″), 1.62–1.53 (m, 2H, OCH_2CH_2), 1.37–1.34 (m, 2H, $OCH_2CH_2CH_2$), 1.29 (br s, 16H, $(CH_2)_8$), 1.27 (d, 3H, *J* = 6.4 Hz, 6-*Me*), 1.15 (d, 3H, *J* = 6.0 Hz, 6″-*Me*), 1.14 (d, 3H, *J* = 6.0 Hz, 6′-*Me*), 0.89 (t, 3H, *J* = 6.9 Hz, CH_2CH_3); ^{13}C NMR (150 MHz, CD_3OD) δ 172.3, 172.2, 172.1, 103.0, 101.4, 100.7, 81.3, 78.4, 75.3, 74.1, 73.9, 73.2, 72.8, 72.0, 68.6, 68.5, 68.03, 68.01, 68.0, 33.1, 30.7–30.4, 27.3, 23.7, 21.0, 20.9, 20.8, 18.7, 17.8, 17.6, 14.5; HRESIMS: *m*/*z* calcd for $C_{36}H_{62}O_{16}Na^+$ 773.3930; found 773.3919.

4.6. Dodecanyl 4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranoside (1)

The Lev protecting groups on compound **4** were removed following the general procedure B to afford dodecanyl 4-*O*-acetyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside. Yield: 58%; R_f 0.63 (1:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −40.4 (*c* 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 5.41 (d, 1H, *J* = 5.0 Hz, 2′-OH), 5.36 (d, 1H, *J* = 4.1 Hz, 2″-OH), 5.14 (s, 1H, H-1′), 4.99 (s, 1H, H-1″), 4.94 (t, 1H, *J* = 9.8 Hz, H-4′), 4.91 (s, 1H, H-1‴), 4.90 (t, 1H, *J* = 9.6 Hz, H-4″), 4.68 (s, 1H, H-1), 4.66 (dd, 1H, *J* = 10.6, 8.2 Hz, H-4″), 4.13–4.10 (m, 2H, H-3 and H-3‴), 4.06 (d, 1H, *J* = 5.9 Hz, H-2‴), 3.98–3.95 (m, 1 H, H-5″), 3.96 (d, 1H, *J* = 5.0 Hz, H-2), 3.92–3.89 (m, 1H, H-5‴), 3.88 (dd, 1H, *J* = 10.1, 3.2 Hz, H-3″), 3.78 (br s, 1H, H-2′), 3.68–3.65 (m, 2H, H-3′ and H-5′), 3.61 (br s, 1H, H-2″), 3.60–3.57 (m, 2H, H-5 and OCH*H*), 3.42–3.35 (m, 2H, H-4 and OC*H*H), 2.08, 2.04, 2.02 (3s, each 3H, 3 × CH_3CO), 1.53–1.51 (m, 2H, OCH_2CH_2), 1.43, 1.41, 1.28, 1.26 (4s, each 3H, 2 × C(CH_3)$_2$), 1.24 (br s, 18H, $(CH_2)_9$), 1.18 (d, 3H, *J* = 6.4 Hz, 6-*Me*), 1.06 (d, 3H, *J* = 6.0 Hz, 6′-*Me*), 1.03 (d, 3H, *J* = 6.4 Hz, 6″-*Me*), 1.01 (d, 3H, *J* = 6.4 Hz, 6‴-*Me*), 0.85 (t, 3H, *J* = 7.1 Hz, CH_2CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1, 170.0, 169.8, 109.8, 109.4, 100.7, 99.0, 98.0, 96.8, 78.4, 77.9, 77.7, 76.5, 76.3, 75.8, 75.4, 73.8, 72.4, 71.0, 70.9, 67.8, 67.1, 66.7, 65.2, 63.7, 31.9, 29.7–29.3, 27.9, 27.5, 26.3, 26.2, 26.1, 22.7, 21.0, 20.8, 18.0, 17.4, 17.3, 16.8, 14.1; ESIMS: calcd for $[M+Na]^+$ *m*/*z* 999.5; found: 999.6.

The isopropylidene protecting groups on the above compound were removed following the general procedure C to afford compound **1**. Yield: 70%; R_f 0.43 (8:1, $CHCl_3$–MeOH); $[\alpha]_D^{20}$ −80.2 (*c* 0.10, MeOH); ^{1}H NMR (600 MHz, CD_3OD) δ 5.21 (br s, 1H, H-1′), 5.09 (t, 1H, *J* = 9.9 Hz, H-4′), 5.05 (t, 1H, *J* = 9.9 Hz, H-4″), 4.92 (t, 1H, *J* = 7.8 Hz, H-4‴), 4.82 (br s, 1H, H-1″), 4.81 (br s, 1H, H-1‴), 4.63 (br s, 1H, H-1), 4.08 (br s, 1H, H-2′), 4.04 (dd, 1H, *J* = 10.1, 3.2 Hz, H-3″), 4.05–4.01 (m, 1H, H-5), 3.93–3.86 (m, 2H, H-5′ and H-5″), 3.91 (dd, 1H, *J* = 9.6, 3.2 Hz, H-3‴), 3.90 (dd, 1H, *J* = 9.6, 3.2 Hz, H-3′), 3.83 (br s, 1H, H-2″), 3.74 (br s, 1H, H-2‴), 3.73 (dd, 1H, *J* = 8.7, 2.8 Hz, H-3), 3.72 (d, 1H, *J* = 2.8 Hz, H-2), 3.68–3.62 (m, 2H, H-5 and OC*H*H), 3.51 (t, 1H, *J* = 9.2 Hz, H-4), 3.41–3.37 (m, 1H, OCH*H*), 2.07 (s, 9H, 3 × CH_3CO), 1.58–1.56 (m, 2H, OCH_2CH_2), 1.29 (br s, 18H, $(CH_2)_9$), 1.27 (d, 3H, *J* = 6.0 Hz, 6-*Me*), 1.15 (d, 3H, *J* = 6.0 Hz, 6′-*Me*), 1.14 (d, 3H, *J* = 6.0 Hz, 6″-*Me*), 1.13 (d, 3H, *J* = 6.0 Hz, 6‴-*Me*), 0.89 (t, 3H, *J* = 6.9 Hz, CH_2CH_3); ^{13}C NMR (150 MHz, CD_3OD) δ 172.5, 172.0, 171.7, 103.9, 103.8, 103.1, 101.4, 81.3, 78.8, 78.1, 75.5, 74.1, 74.0, 73.2, 72.8, 72.4, 72.1, 72.0, 70.1, 68.6, 68.5, 68.4, 68.1, 33.1, 30.8–30.5, 27.3, 23.8, 21.0, 21.0, 20.9, 18.7, 17.7, 17.7, 17.6, 14.5; HRESIMS: *m*/*z* calcd for $C_{36}H_{62}O_{16}Na^+$ 919.4509; found 919.4514.

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

To a solution of compound **1** (25 mg, 0.03 mmol) in dry CH_2Cl_2 (10 mL), Ac_2O (20.1 μL, 0.20 mmol), Et_3N (33.2 μL, 0.24 mmol) and

DMAP (2.0 mg, 0.016 mmol) were added under argon. The reaction mixture was stirred for 12 h and then quenched by the addition of MeOH (30 mL). The mixture was concentrated and the residue was purified by silica gel column chromatography (10:1→3:1 petroleum ether–EtOAc) to give **2** (32.5 mg, 99%) as a gummy solid: R_f 0.29 (3:2 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −33.2 (*c* 0.10, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.24 (dd, 1H, *J* = 9.7, 3.7 Hz, H-3), 5.21 (dd, 1H, *J* = 3.2, 1.8 Hz, H-2), 5.14 (dd, 1H, *J* = 10.1 3.2 Hz, H-3″), 5.07 (t, 1H, *J* = 9.8 Hz, H-4′), 5.06 (t, 1H, *J* = 10.1 Hz, H-4″), 5.02 (t, 1H, *J* = 9.8 Hz, H-4‴), 5.05 (dd, 1H, *J* = 3.2, 1.9 Hz, H-2‴), 5.01 (dd, 1H, *J* = 2.7, 2.0 Hz, H-2′), 4.97 (dd, 1H, *J* = 3.2, 1.8 Hz, H-2″), 4.94 (d, 1H, *J* = 1.4 Hz, H-1′), 4.85 (d, 1H, *J* = 1.4 Hz, H-1″), 4.84 (d, 1H, *J* = 1.4 Hz, H-1‴), 4.65 (d, 1H, *J* = 1.4 Hz, H-1), 3.98 (dd, 1H, *J* = 9.6, 3.2 Hz, H-3′), 3.91 (dd, 1H, *J* = 10.1, 3.2 Hz, H-3′), 3.91–3.86 (m, 1H, H-5′), 3.83–3.78 (m, 2H, H-5 and H-5‴), 3.73–3.68 (m, 1H, H-5″), 3.64 (t, 1H, *J* = 9.4 Hz, H-4), 3.66–3.64 (m, 1H, OCH*H*), 3.42–3.38 (m, 1H, OC*H*H), 2.18, 2.17, 2.14, 2.13, 2.12, 2.11, 2.07, 2.04, 1.97 (9s, each 3H, 9 × CH_3CO), 1.62–1.56 (m, 2H, OCH_2CH_2), 1.34 (d, 3H, *J* = 5.9 Hz, 6-*Me*), 1.26 (br s, 18H, $(CH_2)_9$), 1.20 (d, 3H, *J* = 6.4 Hz, 6′-*Me*), 1.17 (d, 3H, *J* = 5.9 Hz, 6‴-*Me*), 1.16 (d, 3H, *J* = 6.4 Hz, 6″-*Me*), 0.88 (t, 3H, *J* = 7.1 Hz, CH_2CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.5, 170.2–170.0, 169.7, 99.2, 99.1, 98.8, 97.3, 79.3, 75.3, 74.8, 72.0, 71.7, 71.6, 71.5, 71.4, 70.7, 70.2, 70.0, 68.5, 68.3, 67.5, 67.4, 67.1, 66.6, 31.9, 29.7–29.3, 26.0, 22.7, 21.0–20.7, 18.1, 17.2, 17.1, 17.0, 14.1; HRESIMS: *m*/*z* calcd for $C_{36}H_{62}O_{16}Na^+$ 1171.5143; found 1171.5144.

4.8. Dodecanyl 4-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranoside (3)

The Lev protecting group on compound **25** was removed following the general procedure B to afford dodecanyl 4-*O*-acetyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside. Yield: 72%; R_f 0.56 (1:2 petroleum ether–EtOAc,); $[\alpha]_D^{20}$ −60.4 (*c* 0.10, $CHCl_3$); ^1H NMR (600 MHz, DMSO-d_6) δ 5.36 (d, 1H, *J* = 4.6 Hz, 2′-OH), 5.13 (s, 1H, H-1″), 5.05 (s, 1H, H-1′), 4.93 (t, 1H, *J* = 9.8 Hz, H-4'), 4.91 (s, 1H, H-1), 4.61 (dd, 1H, *J* = 10.1, 7.7 Hz, H-4″), 4.12–4.08 (m, 2H, H-3 and H-3″), 4.06 (d, 1H, *J* = 5.5 Hz, H-2″), 3.96 (d, 1H, *J* = 5.5 Hz, H-2), 3.96–3.93 (m, 1H, H-5″), 3.79 (d, 1H, *J* = 4.6 Hz, H-2′), 3.78 (br d, 1H, *J* = 7.8 Hz, H-3′), 3.71–3.66 (m, 1H, H-5′), 3.60–3.54 (m, 2H, H-5 and OCH*H*), 3.42–3.38 (m, 1H, OC*H*H), 3.36 (dd, 1H, *J* = 9.7, 7.4 Hz, H-4), 2.07, 2.04 (2s, each 3H, 2 × $COCH_3$), 1.53–1.51 (m, 2H, OCH_2CH_2), 1.43, 1.41, 1.27, 1.26 (4s, each 3H, 4 × CH_3), 1.24 (br s, 18H, $(CH_2)_9$), 1.19 (d, 3H, *J* = 6.4 Hz, 6-*Me*), 1.06 (d, 3H, *J* = 6.4 Hz, 6′-*Me*), 1.02 (d, 3H, *J* = 6.4 Hz, 6″-*Me*), 0.85 (t, 3H, *J* = 6.9 Hz, CH_2CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.8, 108.8, 108.6, 98.5, 98.3, 96.1, 77.8, 76.9, 76.6, 75.5, 74.8, 73.9, 72.2, 70.0, 66.8, 66.6, 63.6, 63.3, 31.3, 28.9–28.6, 27.7, 27.5, 26.1, 25.6, 22.1, 20.7, 20.6, 17.9, 17.3, 16.6, 14.0; ESIMS: calcd for $[M+Na]^+$ *m*/*z* 811.5; found: 811.5.

The isopropylidene protecting groups on the above compound were removed following the general procedure C to afford compound **3**. Yield: 81%; R_f 0.56 (5:1, $CHCl_3$–MeOH); $[\alpha]_D^{20}$ −35.2 (*c* 0.10, MeOH); ^1H NMR (600 MHz, CD_3OD) δ 5.21 (d, 1H, *J* = 1.9 Hz, H-1′), 5.08 (t, 1H, *J* = 9.9 Hz, H-4′), 4.92 (t, 1H, *J* = 9.8 Hz, H-4″), 4.84 (d, 1H, *J* = 1.4 Hz, H-1″), 4.63 (d, 1H, *J* = 1.4 Hz, H-1), 4.07 (dd, 1H, *J* = 2.7, 1.8 Hz, H-2′), 3.98–3.94 (m, 1H, H-5″), 3.91–3.87 (m, 3H, H-3′, H-3″ and H-5″), 3.76–3.72 (m, 3H, H-2″, H-2 and H-3), 3.68–3.61 (m, 2H, H-5 and OC*H*H), 3.51 (t, 1H, *J* = 9.2 Hz, H-4), 3.41–3.40 (m, 1H, OCH*H*), 2.09, 2.07 (2s, each 3H, 2 × $COCH_3$), 1.61–1.55 (m, 2H, OCH_2CH_2), 1.39–1.34 (m, 2H, $OCH_2CH_2CH_2$), 1.29 (br s, 16H, $(CH_2)_8$), 1.27 (d, 3H, *J* = 6.4 Hz, 6-*Me*), 1.14 (d, 6H, *J* = 6.4 Hz, 6′-*Me* and 6″-*Me*), 1.02 (d, 3H, *J* = 6.4 Hz, 6‴-CH_3), 0.89 (t, 3H, *J* = 6.9 Hz, CH_2CH_3); ^{13}C NMR (150 MHz, CD_3OD) δ 1172.5, 171.9, 103.7, 103.1, 101.4, 81.3, 78.2, 75.4, 74.2, 73.2, 72.8, 72.4, 72.0, 70.0, 68.5, 68.1, 68.0, 33.1, 30.8–30.4, 27.3, 23.7, 21.0, 20.9, 18.7, 17.8, 17.7, 14.5; HRESIMS: *m*/*z* calcd for $C_{34}H_{60}O_{15}Na^+$ 731.3824; found 731.3826.

4.9. Dodecanyl 4-*O*-benzoyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranoside (4)

The Lev protecting group on compound **23** was removed following the general procedure B to afford Dodecanyl 4-*O*-benzoyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside. Yield: 87%; R_f 0.50 (2:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −61.6 (*c* 0.15, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 8.05 (d, 2H, *J* = 8.4 Hz, Ph), 7.58 (t, 1H, *J* = 7.3 Hz, Ph), 7.45 (t, 1H, *J* = 7.1 Hz, Ph), 5.40 (d, 1H, *J* = 1.4 Hz, H-1′), 5.19 (s, 1H, H-1″), 5.12 (t, 1H, *J* = 9.7 Hz, H-4′), 5.11 (t, 1H, *J* = 9.9 Hz, H-4″), 4.95 (s, 1H, H-1), 4.36 (dd, 1H, *J* = 7.7, 5.5 Hz, H-3″), 4.16 (dd, 1H, *J* = 7.3, 5.9 Hz, H-3), 4.14 (d, 1H, *J* = 5.5 Hz, H-2), 4.09 (d, 1H, *J* = 5.5 Hz, H-2″), 4.04 (dd, 1H, *J* = 2.9, 1.4 Hz, H-2′), 3.99 (dd, 1H, *J* = 9.5, 3.3 Hz, H-3′), 3.98–3.95 (m, 1H, H-5′), 3.86–3.82 (m, 1H, H-5″), 3.72–3.66 (m, 2H, OC*H*H and H-5), 3.51 (dd, 1H, *J* = 9.9, 7.3 Hz, H-4), 3.44–3.40 (m, 1H, OCH*H*), 2.12 (s, 3H, $COCH_3$), 1.60, 1.53, 1.34, 1.32 (4s, each 3H, 4 × CH_3), 1.58–1.55 (m, 2H, OCH_2CH_2), 1.29 (d, 3H, *J* = 6.2 Hz, 6-CH_3), 1.26 (br s, 18H, $(CH_2)_9$), 1.22 (d, 3H, *J* = 6.2 Hz, 6″-CH_3), 1.21 (d, 3H, *J* = 6.2 Hz, 6′-CH_3), 0.88 (t, 3H, *J* = 7.1 Hz, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1, 165.7, 133.3, 130.1, 129.8, 129.6, 128.4, 109.9, 109.5, 99.4, 98.0, 96.8, 78.4, 77.9, 76.2, 76.0, 75.5, 74.5, 72.7, 71.3, 67.8, 66.7, 65.1, 63.7, 60.4, 31.9, 29.6–29.3, 27.9, 27.6, 26.4, 26.3, 26.1, 22.7, 20.9, 18.0, 17.3, 17.1, 14.1; ESIMS: calcd for $[M+Na]^+$ *m*/*z* 873.4; found: 873.3.

The isopropylidene protecting groups on the above compound were removed following the general procedure C to afford compound **4**. Yield: 83%; R_f 0.55 (8:1, $CHCl_3$–MeOH); $[\alpha]_D^{20}$ −75.4 (*c* 0.05, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, 2H, *J* = 7.7 Hz, Ph), 7.56 (t-like, 1H, *J* = 7.7, 7.1 Hz, Ph), 7.42 (t-like, 1H, *J* = 7.4, 7.1 Hz, Ph), 5.28 (s, 1H, H-1″), 5.08 (t, 1H, *J* = 9.4 Hz, H-4′), 5.07 (t, 1H, *J* = 9.4 Hz, H-4″), 5.04 (s, 1H, H-1′), 4.73 (s, 1H, H-1), 4.19 (br s, 1H, H-2′), 4.17–4.09 (m, 2H, H-5′ and H-3″), 3.99 (dd, 1H, *J* = 9.4, 3.1 Hz, H-3′), 3.94 (br s, 1H, H-2″), 3.92–3.87 (m, 2H, H-5″ and H-3), 3.86 (s, 1H, H-2), 3.69–3.61 (m, 2H, H-5 and OC*H*H), 3.51 (t, 1H, *J* = 8.8 Hz, H-4), 3.39–3.35 (m, 1H, OCH*H*), 3.14–2.84 (m, 5H, 5 × OH), 2.08 (s, 3H, $COCH_3$), 1.56–1.53 (m, 2H, OCH_2CHH), 1.31 (d, 3H, *J* = 6.0 Hz, 6-*Me*), 1.26 (br s, 18H, $(CH_2)_9$), 1.18 (d, 6H, *J* = 6.0 Hz, 6″-*Me* and 6′-*Me*), 0.88 (t, 3H, *J* = 7.1 Hz, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 167.4, 133.5, 129.9, 129.3, 128.5, 103.3, 100.8, 100.7, 99.3, 75.5, 72.8, 72.6, 72.0, 71.6, 71.0, 70.7, 69.9, 67.9, 67.1, 66.9, 66.3, 65.8, 31.9, 29.6–29.3, 26.1, 22.7, 20.9, 18.1, 17.5, 17.3, 14.1; HRESIMS: calcd for $C_{39}H_{62}O_{15}Na^+$ 793.3981; found, 793.3958.

4.10. Dodecanyl 4-*O*-*n*-hexanoyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranoside (5)

The Lev protecting group on compound **24** was removed following the general procedure B to afford dodecanyl 4-*O*-*n*-hexanoyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside. Yield: 90%; R_f 0.48 (2:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −42.3 (*c* 0.08, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 5.25 (s, 1H, H-1′), 5.04 (t, 1H, *J* = 9.4 Hz, H-4′), 4.98 (s, 1H, H-1″), 4.83 (t, 1H, *J* = 9.4 Hz, H-4″), 4.74 (s, 1H, H-1), 4.13 (s, 1H, H-2), 3.99–3.87 (m, 7H), 3.70–3.63 (m, 2H), 3.50 (t, 1H, *J* = 9.4 Hz, H-4), 3.41–3.37 (m, 1H, OCH*H*), 2.96–2.82 (br s, 5H, OH), 2.41–2.29 (m, 2H, C*HH*CO), 2.09 (s, 3H, CH_3CO), 1.68–1.62 (m, 2H, C*HH*CH_2CO), 1.58–1.55 (m, 2H, OCH_2CHH), 1.31 (d, 3H, *J* = 6.0 Hz, 6-*Me*), 1.26

(m, 22 H), 1.21 (d, 3H, J = 6.4 Hz, 6′-*Me*), 1.19 (d, 3H, J = 6.3 Hz, 6″-*Me*), 0.93 (t, 3H, J = 7.0 Hz, C*H*$_3$); 0.88 (t, 3H, J = 6.7 Hz, C*H*$_3$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.9, 170.0, 109.7, 109.4, 99.2, 98.0, 96.8, 78.5, 77.9, 76.3, 75.9, 75.5, 73.6, 72.7, 71.3, 67.8, 66.7, 65.0, 63.7, 34.3, 31.9, 31.2, 29.6–29.3, 27.9, 27.6, 26.4, 26.3, 26.1, 24.5, 22.7, 22.3, 20.9, 18.0, 17.3, 17.1, 14.1, 13.9; ESIMS: calcd for [M+Na]$^+$ m/z 867.5; found: 867.7.

The isopropylidene protecting groups on the above compound were removed following the general procedure C to afford compound **5**. Yield: 63%; R_f 0.42 (8:1, $CHCl_3$–MeOH); $[\alpha]_D^{20}$ −64.9 (*c* 0.09, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 5.25 (s, 1H, H-1′), 5.04 (t, 1H, J = 9.4 Hz, H-4′), 4.98 (s, 1H, H-1″), 4.83 (t, 1H, J = 9.4 Hz, H-4″), 4.74 (s, 1H, H-1), 4.13 (s, 1H, H-2), 3.99–3.87 (m, 7H, H-2, H-3, H-2″, H-3″, H-3′, H-5′ and H-5″), 3.70–3.63 (m, 2H, H-5 and OC*H*H), 3.50 (t, 1H, J = 9.4 Hz, H-4), 3.41–3.37 (m, 1H, OCH*H*), 3.21–2.60 (m, 5H, 5 × O*H*), 2.41–2.29 (m, 2H, C*HH*CO), 2.09 (s, 3H, C*H*$_3$CO), 1.68–1.62 (m, 2H, C*HH*CH$_2$CO), 1.58–1.55 (m, 2H, OCH$_2$C*HH*), 1.31 (d, 3H, J = 6.0 Hz, 6-*Me*), 1.26 (br s, 22H, (C*H*$_2$)$_2$ and (C*H*$_2$)$_9$), 1.21 (d, 3H, J = 6.4 Hz, 6′-*Me*), 1.19 (d, 3H, J = 6.3 Hz, 6″-*Me*), 0.93 (t, 3H, J = 8.0 Hz, C*H*$_3$); 0.88 (t, 3H, J = 6.7 Hz, C*H*$_3$); ^{13}C NMR (150 MHz, C_5D_5N–CD_3OD, 6:1) δ 174.9, 170.4, 100.7, 100.6, 99.3, 80.4, 72.6, 72.3, 72.0, 71.6, 71.0, 70.9, 70.7, 67.9, 67.2, 66.7, 66.3, 34.3, 31.9, 31.2, 29.7–29.3, 26.1, 24.6, 22.7, 22.3, 20.9, 18.0, 17.4, 17.3, 14.1, 13.9; HRESIMS: calcd for $C_{38}H_{68}O_{15}Na^+$ 787.4450; found, 787.4449.

4.11. Dodecanyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-acetyl-α-L-rhamnopyranoside (6)

To a solution of cleistrioside-**5** (29.2 mg, 0.04 mmol) in dry CH_2Cl_2 (10 mL), Ac_2O (31.1 μL, 0.33 mmol), Et_3N (51.1 μL, 0.37 mmol) and DMAP (2.0 mg, 0.016 mmol) were added under argon. The reaction mixture was stirred for 12 h and then quenched by the addition of MeOH (30 mL). The mixture was concentrated and the residue was purified by silica gel column chromatography (1:1 petroleum ether–EtOAc) to give compound **6** (33.7 mg, 90%) as a syrup: R_f 0.37 (1:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −37.9 (*c* 0.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.24 (dd, 1H, J = 9.6, 3.2 Hz, H-3), 5.22 (d, 1H, J = 3.2 Hz, H-2), 5.14 (dd, 1H, J = 10.1 3.2 Hz, H-3″), 5.10 (t, 1H, J = 9.6 Hz, H-4″), 5.05 (t, 1H, J = 10.1 Hz, H-4′), 5.04 (br s, 2H, H-2′ and H-2″), 4.96 (br s, 1H, H-1′), 4.88 (br s, 1H, H-1″), 4.92 (dd, 1H, J = 3.8,1.6 Hz H-2″), 4.88 (t^{obsc}, 1H, H-4″), 4.86 (d, 1H, J = 1.7 Hz, H-1″), 4.66 (br s, 1H, H-1), 4.00 (dd, 1H, J = 9.7, 3.2 Hz, H-3′), 3.91–3.86 (m, 1H, H-5″), 3.85–3.79 (m, 2H, H-5 and H-5′), 3.65 (t, 1H, J = 9.6 Hz, H-4), 3.65–3.63 (m, 1H, OC*H*H), 3.42–3.38 (m, 1H, OCH*H*), 2.18, 2.14, 2.13, 2.12, 2.08, 2.05, 1.98 (7s, each 3H, 7 × C*H*$_3$CO), 1.62–1.57 (m, 2H, OCH$_2$C*H*$_2$), 1.34 (d, 3H, J = 6.0 Hz, 6-*Me*), 1.26 (br s, 18H, (CH$_2$)$_9$), 1.21 (d, 3H, J = 6.0 Hz, 6″-*Me*), 1.17 (d, 3H, J = 6.0 Hz, 6′-*Me*), 0.88 (t, 3H, J = 6.9 Hz, CH$_2$C*H*$_3$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.2–170.0, 169.7, 99.2, 98.5, 97.3, 79.2, 74.8, 72.0, 71.6, 71.3, 70.7, 70.2, 70.1, 68.5, 68.3, 67.4, 67.2, 66.6, 31.9, 29.6–29.3, 26.0, 22.7, 20.9–20.7, 18.1, 17.2, 17.1, 14.1; HRESIMS: m/z calcd for $C_{36}H_{62}O_{16}Na^+$ 941.4353; found 941.4332.

4.12. Dodecanyl 4-*O*-acetyl-2-*O*-levulinyl-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranoside (7)

The isopropylidene protecting groups on compound **26** were removed following the general procedure C to afford compound **7**. Yield: 81%; R_f 0.44 (6:1, $CHCl_3$–MeOH,); $[\alpha]_D^{20}$ −53.8 (*c* 0.06, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.17 (s, 1H, H-1′), 4.87 (m, 2H, H-4′and H-3′), 4.72 (s, 1H, H-1), 4.52 (br s, 1H, OH), 4.17 (br s, 1H, OH), 4.12 (br s, 1H, OH), 3.92 (br s, 1H, OH), 3.90–3.86 (m, 4H, H-2, H-2′ H-3 and H-5′), 3.65–3.60 (m, 2H, H-3′ and H-5′), 3.51 (dd, 1H, J = 9.7, 7.3 Hz, H-4), 3.43–3.40 (m, 2H, H-5 and OCH*H*), 3.51 (t, 1H, J = 9.2 Hz, H-4), 3.40–3.36 (m, 1H, OC*H*H), 2.11 (s, 3H, COC*H*$_3$), 158–1.53 (m, 2H, OCH$_2$C*H*$_2$), 1.30 (d, 3H, J = 6.0 Hz, 6-*Me*), 1.26 (br s, 18H, (CH$_2$)$_9$), 1.18 (d, 3H, J = 6.4 Hz, 6′-*Me*), 0.88 (t, 3H, J = 7.1 Hz, CH$_2$C*H*$_3$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.5, 101.9, 99.6, 81.2, 74.4, 72.1, 71.5, 70.9, 69.5, 67.7, 66.9, 66.6, 31.9, 29.7–29.3, 26.1, 22.7, 21.1, 17.9, 17.2, 14.1; HRESIMS: m/z calcd for $C_{26}H_{48}O_{10}Na^+$ 543.3140; found 543.3142.

4.13. Dodecanyl 3,4-di-*O*-acetyl-2-*O*-levulinyl-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranoside (8)

The isopropylidene protecting group on compound **27** was removed following the general procedure C to afford compound **8**. Yield: 79%; R_f 0.59 (6:1, $CHCl_3$–MeOH); $[\alpha]_D^{20}$ −64.6 (*c* 0.31, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.31 (s, 1H, H-1′), 5.15 (dd, 1H, J = 9.6, 2.8 Hz, H-3′), 5.14 (d, 1H, J = 2.8 Hz, H-2′), 5.11 (t, 1H, J = 9.4 Hz, H-4′), 4.73 (s, 1H, H-1), 4.19 (br s, 1H, 2′-OH), 3.98–3.93 (m, 1H, H-5′), 3.87 (br s, 2H, H-2 and H-3), 3.82 (br s, 1H, 2-OH), 3.74 (br s, 1H, 3-OH), 3.69–3.61 (m, 2H, H-5 and OC*H*H), 3.51 (t, 1H, J = 8.9 Hz, H-4), 3.40–3.36 (m, 1H, OCH*H*), 2.10, 2.04 (2s, each 3H, 2 × COC*H*$_3$), 1.59–1.55 (m, 2H, OCH$_2$C*H*$_2$), 1.31 (d, 3H, J = 6.0 Hz, 6′-*Me*), 1.26 (br s, 18H, (CH$_2$)$_9$), 1.20 (d, 3H, J = 6.0 Hz, 6-*Me*), 0.88 (t, 3H, J = 6.9 Hz, CH$_2$C*H*$_3$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.7, 170.1, 101.1, 99.5, 80.7, 72.1, 71.6, 71.5, 71.2, 69.3, 67.8, 67.1, 66.3, 31.9, 29.6–26.3, 26.1, 22.7, 21.0, 20.8, 18.0, 17.2, 14.2; HRESIMS: m/z calcd for $C_{28}H_{50}O_{11}Na^+$ 585.3245; found 585.3234.

4.14. *p*-Tolyl 3-*O*-levulinyl-2,4-di-*O*-acetyl-1-thio-α-L-rhamnopyranoside 12

To a solution of *p*-tolyl 2,4-di-*O*-acetyl-1-thio-α-L-rhamnopyranoside (2.0 g, 5.6 mmol) in dry CH_2Cl_2 (50 mL), levulinic acid (786.1 mg, 6.8 mmol), DCC (1.4 g, 6.8 mmol) and DMAP (68.9 mg, 0.6 mmol) were added under argon. The reaction mixture was stirred for 12 h and then the mixture was diluted with CH_2Cl_2 (150 mL) and washed with H_2O (100 mL), 1 M HCl (2 × 100 mL), saturated aqueous $NaHCO_3$ (2 × 100 mL) and brine (2 × 100 mL). The organic phase 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 **12** (2.13 g, 84%) as a white solid: R_f 0.44 (2:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −90.4 (*c* 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (d, 2H, J = 8.0 Hz, Ph*H*), 7.12 (d, 2H, J = 8.0 Hz, Ph*H*), 5.47 (dd, 1H, J = 3.2, 1.8 Hz, H-2), 5.33 (d, 1H, J = 1.4 Hz, H-1), 5.29 (dd, 1H, J = 10.1, 3.2 Hz, H-3), 5.15 (t, 1H, J = 9.9 Hz, H-4), 4.39–4.34 (m, 1H, H-5), 2.82–2.41 (m, 4H, COCH_2CH_2CO), 2.32 (s, 3H, PhC*H*$_3$), 2.18, 2.14, 2.13 (3s, each 3H, 3 × COC*H*$_3$), 1.24 (d, 3H, J = 6.0 Hz, 6-*Me*); ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.2, 171.6, 170.2, 170.0, 138.2, 132.4, 129.9, 129.4, 86.0, 71.2, 70.8, 69.6, 67.6, 37.6, 29.7, 27.8, 21.1, 20.9, 20.8, 17.3; ESIMS: calcd for [M+Na]$^+$ m/z 475.1; found: 475.1.

4.15. Dodecanyl 2,4-di-*O*-acetyl-3-*O*-levulinyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-levulinyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (13)

Compound **13** was prepared from donor 1**2** and acceptor **11** by method **A**. Yield: 81%; R_f 0.47 (1:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −31.8 (*c* 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.26 (s, 1H, H-1″), 5.25 (dd, 1H, J = 3.2, 1.8 Hz, H-2″), 5.18 (dd, 1H, J = 10.1, 3.7 Hz, H-3′), 5.07 (t, 1H, J = 10.1 Hz, H-4″), 5.06 (t, 1H, J = 9.8 Hz, H-4′), 4.99 (dd, 1H, J = 3.2, 1.9 Hz, H-2′), 4.94 (s, 1H, H-1), 4.89 (d, 1H, J = 1.9 Hz, H-1′), 4.16 (dd, 1H, J = 7.3, 5.5 Hz, H-3), 4.09 (dd, J = 5.5, 1.3 Hz, H-2), 4.02 (dd, 1H, J = 9.6, 3.2 Hz, H-3″), 3.99–3.96

(m, 1H, H-5′), 3.79–3.74 (m, 1H, H-5″), 3.70–3.65 (m, 2H, H-5 and OC*H*H), 3.46 (dd, 1H, *J* = 9.6, 7.3 Hz, H-4), 3.43–3.39 (m, 1H, OCH*H*), 2.90–2.40 (m, 8H, 2 × COCH_2CH_2CO), 2.22, 2.16, 2.13, 2.12, 2.11 (5s, each 3H, 5 × COCH_3), 1.60–1.55 (m, 2H, OCH_2CH_2), 1.53, 1.32 (2s, each 3H, 2 × CH_3), 1.26 (d, 3H, *J* = 5.9 Hz, 6-*Me*), 1.25 (br s, 18H, (CH_2)$_9$), 1.20 (d, 3H, *J* = 6.4 Hz, 6′-*Me*), 1.19 (d, 3H, *J* = 6.4 Hz, 6″-*Me*), 0.88 (t, 3H, *J* = 7.1 Hz, CH$_2$CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.6, 206.1, 172.1, 171.3, 170.4, 170.2, 170.1, 167.7, 132.4, 130.9, 128.8, 109.5, 98.7, 96.9, 95.9, 78.0, 77.5, 76.2, 74.4, 72.6, 71.8, 71.4, 70.6, 70.2, 68.6, 67.8, 67.1, 63.7, 38.0, 37.6, 31.9, 29.8–29.3, 28.4, 27.9, 27.8, 27.7, 26.4, 26.1, 22.7, 20.9, 20.8, 18.0, 17.4, 17.3, 14.1; ESIMS: calcd for $[M+Na]^+$ *m/z* 1009.5; found: 1009.5.

4.16. Dodecanyl 4-*O*-acetyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-levulinyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-levulinyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (14)

Compound **14** was prepared from donor **15** and acceptor **11** by method **A**. Yields: 65%; R_f 0.63 (1:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −20.1 (*c* 0.17, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.29 (dd, 1H, *J* = 3.2, 1.3 Hz, H-2′), 5.21 (s, 1H, H-1′), 5.20 (s, 1H, H-1″), 5.11 (s, 1H, H-1‴), 4.94 (s, 1H, H-1), 4.93 (t, 1H, *J* = 9.9 Hz, H-4″), 4.88 (t, 1H, *J* = 9.9 Hz, H-4′), 4.81 (dd, 1H, *J* = 10.3, 8.3 Hz, H-4‴), 4.75 (dd, 1H, *J* = 4.5, 2.6 Hz, H-2″), 4.22 (dd, 1H, *J* = 8.3, 5.8 Hz, H-3‴), 4.16 (dd, 1H, *J* = 7.0, 5.8 Hz, H-3), 4.12 (dd, 1H, *J* = 9.7, 4.5 Hz, H-3″), 4.07 (dd, 1H, *J* = 9.9, 3.2 Hz, H-3′), 4.06 (dd, 1H, *J* = 3.2, 1.9 Hz, H-2), 4.14 (d, 1H, *J* = 5.1 Hz, H-2‴), 3.99–3.96 (m, 1 H, H-5‴), 3.80–3.75 (m, 1 H, H-5′), 3.73–3.69 (m, 1 H, H-5), 3.68–3.64 (m, 1H, OC*H*H), 3.53–3.48 (m, 1H, H-5″), 3.45 (dd, 1H, *J* = 9.6, 7.1 Hz, H-4), 3.42–3.38 (m, 1H, OCH*H*), 2.88–2.75, 2.64–2.53, 2.50–2.45 (m, 8H, 2 × COCH_2CH_2CO), 2.19, 2.18, 2.13, 2.11, 2.10 (5s, each 3H, 5 × COCH_3), 1.60–1.57 (m, 2H, OCH_2CH_2), 1.55, 1.51, 1.33, 1.32 (4s, each 3H, 2 × C(CH_3)$_2$), 1.30 (d, 3H, *J* = 6.4 Hz, 6-*Me*), 1.26 (br s, 18H, (CH_2)$_9$), 1.20 (d, 3H, *J* = 6.4 Hz, 6″-*Me*), 1.16 (d, 6H, *J* = 6.4 Hz, 6′-*Me* and 6‴-*Me*), 0.88 (t, 3H, *J* = 6.9 Hz, CH$_2$CH_3); ESIMS: calcd for $[M+Na]^+$ *m/z* 1195.6; found: 1195.7.

4.17. *p*-Tolyl 4-*O*-acetyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-levulinyl-1-thio-α-L-rhamnopyranoside (15)

To a solution of compound **16** (40.5 mg, 0.10 mmol), **17** (46.1 mg, 0.12 mmol) and 4 Å molecular sieves in dry CH_2Cl_2 (5 mL) was added TMSOTf (2 μL, 0.02 mmol) at −20 °C under argon. The reaction mixture was stirred under −20 °C, until TLC indicated that the reaction was completed. The reaction was quenched by the addition of Et_3N and the mixture was concentrated. The residue was purified by silica gel column chromatography (3:1 petroleum ether–EtOAc) to give **15** (48.7 mg, 77%) as a syrup: R_f 0.33 (2:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −62.5 (*c* 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (d, 2H, *J* = 8.3 Hz, Ph*H*), 7.12 (d, 2H, *J* = 8.3 Hz, Ph*H*), 5.36 (d, *J* = 1.7 Hz, H-2), 5.30 (s, 1H, H-1), 5.11 (s, 1H, H-1′), 5.10 (t, 1H, *J* = 9.9 Hz, H-4), 4.82 (dd, 1H, *J* = 9.9, 8.2 Hz, H-4′), 4.32–4.27 (m, 1H, H-5), 4.21 (dd, 1H, *J* = 7.7, 5.5 Hz, H-3′), 4.14 (dd, 1H, *J* = 9.9, 3.3 Hz, H-3), 4.04 (d, 1H, *J* = 5.5 Hz, H-2′), 3.72–3.67 (m, 1H, H-5′), 2.77–2.61 (m, 4H, COCH_2CH_2CO), 2.33 (s, 3H, PhCH_3), 2.19, 2.12, 2.10 (s, each 3H, 3 × COCH_3), 1.54, 1.33 (s, each 3H, 2 × CH_3), 1.22 (d, 3H, *J* = 6.0 Hz, 6-*Me*), 1.14 (d, 3H, *J* = 6.0 Hz, 6′-*Me*); ^{13}C NMR (150 MHz, $CDCl_3$) δ 205.9, 171.7, 170.3, 170.0, 138.2, 132.3, 129.9, 129.3, 109.6, 99.4, 86.0, 76.0, 75.4, 74.3, 74.1, 73.3, 73.2, 67.7, 64.8, 37.8, 29.7, 28.1, 27.6, 26.4, 21.1, 20.9, 17.3, 16.7; ESIMS: calcd for $[M+Na]^+$ *m/z* 661.2; found: 661.1.

4.18. *p*-Tolyl 4-*O*-acetyl-2-*O*-levulinyl-1-thio-α-L-rhamnopyranoside (16)

To a stirred solution of *p*-tolyl 4-*O*-acetyl-2-*O*-levulinyl-3-*O*-*p*-methoxybenzyl-1-thio-α-L-rhamnopyranoside (500 mg, 0.9 mmol) in CH_2Cl_2 (30 mL) and H_2O (2 mL), was added DDQ (321.1 mg, 1.4 mmol) at room temperature. The reaction mixture was stirred until the reaction was completed indicated by TLC. The reaction mixture was poured into saturated aqueous $NaHCO_3$ solution (20 mL) and extracted with CH_2Cl_2 (2 × 50 mL). The combined organic phase was washed with saturated aqueous $NaHCO_3$ (2 × 50 mL) and brine (2 × 50 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (4:1 petroleum ether–EtOAc) to give **16** (294.0 mg, 76%) as a syrup: R_f 0.45 (1:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −122.9 (*c* 0.05, $CHCl_3$); ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.34 (d, 2H, *J* = 8.3 Hz, Ph*H*), 7.19 (d, 2H, *J* = 8.3 Hz, Ph*H*), 5.49 (d, *J* = 5.5 Hz, 3-OH), 5.31 (d, 1H, *J* = 1.1 Hz, H-1), 5.15 (dd, 1H, *J* = 3.3, 1.1 Hz, H-2), 4.79 (t, 1H, *J* = 9.9 Hz, H-4), 4.12–4.09 (m, 1H, H-5), 3.84 (ddd, 1H, *J* = 9.3, 5.5, 3.3 Hz, H-3), 2.73–2.50 (m, 4H, COCH_2CH_2CO), 2.29 (s, 3H, PhCH_3), 2.10, 2.08 (s, each 3H, 2 × COCH_3), 1.08 (d, 3H, *J* = 6.0 Hz, 6-*Me*); ^{13}C NMR (150 MHz, DMSO-d_6) δ 207.2, 172.0, 171.2, 138.0, 132.3, 132.0, 129.9, 129.6, 86.0, 74.7, 74.2, 69.3, 67.3, 38.2, 29.7, 28.1, 21.1, 21.0, 17.3; ESIMS: calcd for $[M+Na]^+$ *m/z* 433.1; found: 433.1.

4.19. *p*-Tolyl 4-*O*-benzoyl-2-*O*-levulinyl-1-thio-α-L-rhamnopyranoside (19)

Compound **21** (500 mg, 1.6 mmol) was dissolved in pyridine (20 mL). BzCl (0.4 mL, 3.2 mmol) was added dropwise at 0 °C. The solution was stirred for 2 h and then warmed to room temperature. After the reaction was completed indicated by TLC, the mixture was diluted with CH_2Cl_2 (100 mL), and washed consecutively with water (50 mL), HCl (3 × 50 mL), saturated aqueous $NaHCO_3$ solution (2 × 50 mL) and brine (50 mL). The organic layer was dried over Na_2SO_4 and concentrated. Purification of the residue on a silica gel column (20:1 petroleum ether–EtOAc) gave **19** (587.6 mg, 88%) as a syrup: R_f 0.55 (15:1 petroleum ether–EtOAc); $[\alpha]_D^{22}$ −202.4 (*c* 0.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13–7.15 (m, 9H, Ph*H*), 5.75 (s, 1H, H-1), 5.20 (dd, 1H, *J* = 10.1, 7.3 Hz, H-4), 4.42–4.33 (m, 3H, H-2, H-3 and H-5), 2.34 (s, 3H, PhCH_3), 1.63, 1.37 (s, each 3H, 2 × CH_3), 1.19 (d, 3H, *J* = 6.4 Hz, 6-*Me*); ^{13}C NMR ($CDCl_3$) δ 171.7, 165.7, 133.7–128.4, 101.1, 84.1, 76.5, 75.6, 75.1, 65.7, 27.7, 26.5, 21.1, 16.9; ESIMS: calcd for $[M+Na]^+$ *m/z* 437.1; found: 437.2.

4.20. *p*-Tolyl 4-*O*-*n*-hexanoyl-2-*O*-levulinyl-1-thio-α-L-rhamnopyranoside (20)

Compound **21** (516.9 mg, 1.7 mmol) was dissolved in pyridine (20 mL). *n*-Hexanoyl chloride (0.4 mL, 2.5 mmol) was added dropwise at 0 °C. The solution was stirred for 2 h and then warmed to room temperature. After the reaction was completed indicated by TLC, the mixture was diluted with CH_2Cl_2 (100 mL), and then washed consecutively with water (50 mL), HCl (3 × 50 mL), saturated aqueous $NaHCO_3$ solution (2 × 50 mL) and brine (50 mL). The organic layer was dried over Na_2SO_4 and concentrated. Purification of the residue on a silica gel column (20:1 petroleum ether–EtOAc) gave **20** (460.6 mg, 68%) as a syrup: R_f 0.65 (10:1 petroleum ether–EtOAc); $[\alpha]_D^{22}$ −174.5 (*c* 0.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 (d, 2H, *J* = 8.7 Hz, PhH), 7.13 (d, 2H, *J* = 7.8 Hz, PhH), 5.69 (s, 1H, H-1), 4.94 (dd, 1H, *J* = 10.1, 7.8 Hz, H-4), 4.35 (d, 1H, *J* = 5.9 Hz, H-2), 4.22–4.18 (m, 2H, H-3 and H-5), 2.40–2.32 (m, 5H, COCH_2 and PhCH_3), 1.67–1.64 (m, 2H, COCH$_2$CH_2), 1.57, 1.35 (s, each 3H, 2 × CH_3), 1.34–1.30 (m, 4H, 2 × CH_2), 1.12 (d, 3H,

J = 6.4 Hz, 6-*Me*); 0.90 (t, 3H, J = 6.8 Hz, *Me*); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.9, 138.0, 132.4, 129.9, 129.4, 110.0, 84.0, 76.4, 75.6, 74.3, 65.5, 34.3, 31.2, 27.7, 26.5, 24.6, 22.3, 21.1, 16.9, 13.9; ESIMS: calcd for $[M+Na]^+$ m/z 431.2; found: 431.2.

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

Compound **22** was prepared from donor **18** and acceptor **11** by method **A**. Yeild: 99%; R_f 0.60 (1:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −23.6 (c 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.25 (d, 1H, J = 0.9 Hz, H-1′), 5.20 (dd, 1H, J = 3.2, 1.4 Hz, H-2′), 5.08 (s, 1H, H-1″), 5.04 (t, 1H, J = 9.8 Hz, H-4′), 4.95 (s, 1H, H-1), 4.81 (dd, 1H, J = 10.1, 8.3 Hz, H-4″), 4.23 (dd, 1H, J = 7.8, 5.5 Hz, H-3″), 4.17 (dd, 1H, J = 7.3, 5.5 Hz, H-3), 4.09 (d, 1H, J = 5.5 Hz, H-2), 4.06 (dd, 1H, J = 9.7, 3.2 Hz, H-3′), 4.02 (d, 1H, J = 5.5 Hz, H-2″), 3.82–3.78 (m, 1H, H-5′), 3.76–3.72 (m, 1H, H-5″), 3.71–3.65 (m, 2H, H-5 and OCH*H*), 3.41 (dd, 1H, J = 9.6, 7.3 Hz, H-4), 3.43–3.39 (m, 1H, OC*H*H), 2.79–2.77 (m, 4H, $CO(CH_2)_2CO$), 2.20, 2.11, 2.10 (3s, each 3H, 3 × $COCH_3$), 1.60–1.56 (m, 2H, OCH_2CH_2), 1.54, 1.52, 1.32, 1.31 (4s, each 3H, 4 × CH_3), 1.28 (d, 3H, J = 5.9 Hz, 6-*Me*), 1.25 (br s, 18H, $(CH_2)_9$), 1.20 (d, 3H, J = 6.4 Hz, 6′-*Me*), 1.13 (d, 3H, J = 6.4 Hz, 6″-*Me*), 0.88 (t, 3H, J = 7.1 Hz, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 205.9, 171.6, 170.4, 170.0, 109.5, 109.4, 99.4, 96.9, 96.0, 78.0, 77.6, 76.3, 76.1, 75.5, 74.3, 74.1, 73.2, 71.8, 67.8, 66.9, 64.7, 63.7, 37.9, 31.9, 29.8–29.3, 28.2, 27.9, 27.6, 26.4, 26.1, 22.7, 21.1, 20.9, 18.1, 17.4, 16.7, 14.1; ESIMS: calcd for $[M+Na]^+$ m/z 909.5; found: 909.5.

4.22. Dodecanyl 4-*O*-benzoyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-levulinyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23)

Compound **23** was prepared from donor 1**9** and acceptor **11** by method **A**. Yield: 55%; R_f 0.53 (2:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −43.6 (c 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (d, 2H, J = 8.4 Hz, Ph), 7.56 (t, 1H, J = 7.3 Hz, Ph), 7.43 (t, 1H, J = 7.7 Hz, Ph), 5.26 (d, 1H, J = 1.4 Hz, H-1′), 5.25 (dd, 1H, J = 3.3, 1.4 Hz, H-2′), 5.13 (s, 1H, H-1″), 5.08 (t, 1H, J = 9.9 Hz, H-4′), 5.06 (dd, 1H, J = 10.1, 8.0 Hz, H-4″), 4.94 (s, 1H, H-1), 4.40 (dd, 1H, J = 7.7, 5.5 Hz, H-3″), 4.18 (dd, 1H, J = 7.3, 5.5 Hz, H-3), 4.09 (dd, 1H, J = 7.7, 3.3 Hz, H-3′), 4.08 (d, 2H, J = 5.5 Hz, H-2 and H-2″), 3.93–3.88 (m, 1H, H-5′), 3.84–3.79 (m, 1H, H-5″), 3.73–3.65 (m, 2H, H-5 and OC*H*H), 3.47 (dd, 1H, J = 9.9, 7.3 Hz, H-4), 3.43–3.39 (m, 1H, OCH*H*), 2.80–2.67 (m, 4H, $CO(CH_2)_2CO$), 2.20, 2.12 (2s, each 3H, 2 × $COCH_3$), 1.59, 1.52, 1.33, 1.31 (4s, each 3H, 4 × CH_3), 1.59–1.55 (m, 2H, OCH_2CH_2), 1.29 (d, 3H, J = 6.2 Hz, 6-CH_3), 1.26 (br s, 18H, $(CH_2)_9$), 1.21 (d, 3H, J = 6.2 Hz, 6″-CH_3), 1.18 (d, 3H, J = 6.2 Hz, 6′-CH_3), 0.88 (t, 3H, J = 7.1 Hz, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 205.7, 171.6, 170.0, 165.9, 133.1, 129.9, 128.3, 109.6, 109.4, 99.6, 96.8, 95.9, 77.9, 77.5, 76.2, 76.1, 75.6, 74.8, 74.3, 73.1, 71.8, 67.8, 66.9, 64.9, 63.7, 37.8, 31.9, 29.8–29.3, 28.1, 27.9, 27.7, 26.4, 26.3, 26.1, 22.7, 20.9, 18.0, 17.4, 16.8, 14.1; ESIMS: calcd for $[M+Na]^+$ m/z 971.5; found: 971.6.

4.23. Dodecanyl 4-*O*-*n*-hexanoyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-levulinyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (24)

Compound **24** was prepared from donor **20** and acceptor **11** by method **A**. Yield: 49%; R_f 0.50 (2:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −21.8 (c 0.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$,) δ 5.24 (d, 1H, J = 1.5 Hz, H-1′), 5.20 (dd, 1H, J = 3.3, 1.7 Hz, H-2′), 5.07 (s, 1H, H-1″), 5.04 (t, 1H, J = 9.9 Hz, H-4′), 4.94 (s, 1H, H-1), 4.81 (dd, 1H, J = 10.2, 8.2 Hz, H-4″), 4.21 (dd, 1H, J = 8.1, 5.5 Hz, H-3″), 4.17 (dd, 1H, J = 7.3, 5.7 Hz, H-3), 4.08 (d, 1H, J = 5.7 Hz, H-2), 4.06 (dd, 1H, J = 9.9, 3.3 Hz, H-3′), 4.01 (d, 1H, J = 5.5 Hz, H-2″), 3.80–3.66 (m, 4H, H-5′, H-5″, H-5 and OC*H*H), 3.46 (dd, 1H, J = 9.9, 7.3 Hz, H-4), 3.44–3.40 (m, 1H, OCH*H*), 2.78–2.68 (m, 4H, $COCH_2CH_2CO$), 2.35–2.34 (m, 2H, C*HH*CO), 2.19, 2.09 (2s, each 3H, 2 × CH_3CO), 1.64–1.60 (m, 2H, C*HH*CH_2CO), 1.58–1.56 (m, 2H, OCH_2CHH), 1.53, 1.52, 1.32, 1.31 (4s, each 3H, 4 × CH_3), 1.27 (d, 3H, J = 6.4 Hz, 6-CH_3), 1.26 (br s, 22H, $(CH_2)_2$ and $(CH_2)_9$), 1.19 (d, 3H, J = 6.6 Hz, 6″-CH_3), 1.12 (d, 3H, J = 6.3 Hz, 6′-CH_3), 0.89 (t, 3H, J = 7.1 Hz, CH_3); 0.88 (t, 3H, J = 7.2 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.8, 173.1, 171.6, 170.0, 133.9, 130.0, 109.5, 109.4, 99.9, 99.4, 96.8, 95.9, 78.0, 77.5, 74.1, 73.9, 73.2, 71.8, 67.8, 66.9, 64.7, 63.7, 37.9, 34.3, 31.9, 31.2, 29.8–29.3, 28.6, 28.2, 27.9, 27.6, 26.4, 26.3, 26.1, 24.5, 22.7, 22.3, 20.9, 18.0, 17.4, 16.7, 14.1, 13.9; ESIMS: calcd for $[M+Na]^+$ m/z 965.5; found: 965.7.

4.24. Dodecanyl 4-*O*-acetyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (26)

Compound **26** was prepared from donor **18** and acceptor **25** by method **A**. Yield: 74%; R_f 0.63 (5:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −27.3 (c 0.19, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.64 (s, 1H, H-1′), 4.95 (s, 1H, H-1), 4.88 (t, 1H, (dd, 1H, J = 10.1, 7.8 Hz, H-4′), 4.21 (dd, 1H, J = 7.3, 5.9 Hz, H-3), 4.17 (d, 1H, J = 5.5 Hz, H-2), 4.12 (dd, 1H, J = 7.7, 5.5 Hz, H-3′), 4.11 (d, 1H, J = 5.9 Hz, H-2′), 3.76–3.71 (m, 1H, H-5′), 3.69–3.64 (m, 2H, H-5 and OC*H*H), 3.57 (dd, 1H, J = 10.1, 7.3 Hz, H-4), 3.44–3.40 (m, 1H, OCH*H*), 2.10 (s, 3H, $COCH_3$), 1.57, 1.55, 1.35, 1.33 (4s, each 3H, 4 × CH_3), 1.26 (br s, 20H, $(CH_2)_{10}$), 1.25 (d, 3H, J = 6.0 Hz, 6-*Me*), 1.16 (d, 3H, J = 6.0 Hz, 6′-*Me*), 0.88 (t, 3H, J = 7.1 Hz, CH_2CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1, 109.6, 109.4, 96.8, 95.5, 78.5, 76.2, 75.6, 74.3, 67.7, 64.3, 63.7, 31.9, 29.6–29.3, 26.4, 26.3, 26.1, 22.7, 21.0, 17.9, 16.7, 14.1; ESIMS: calcd for $[M+Na]^+$ m/z 623.4; found: 623.4.

4.25. Dodecanyl 3,4-di-*O*-acetyl-2-*O*-levulinyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (27)

A suspension of **11** (150.0 mg, 0.23 mmol) in dry CH_2Cl_2 (10 mL) were placed in an ice bath with continuous stirring. To this cold suspension were added Ac_2O (64.5 μL, 0.68 mol) and Et_3N (94.1 μL, 0.68 mol) dropwise over a period of 30 min. The reaction mixture was stirred for another 30 min. DMAP (2.8 mg, 0.02 mmol) was added in one portion. The reaction mixture was stirred for 12 h at room temperature, and then reaction was quenched by the addition of CH_3OH (30 mL) and concentrated. The residue was diluted with CH_2Cl_2 (50 mL), washed with saturated aqueous $NaHCO_3$ (3 × 20 mL), brine (2 × 20 mL), dried over Na_2SO_4, filtered and concentrated under diminished pressure.

The above crude was treated with NH_2NH_2·HOAc (211.8 mg, 2.3 mmol) as described in general procedure B to give **27** (114.2 mg, 83% for two steps) as a syrup. R_f 0.48 (2:1 petroleum ether–EtOAc); $[\alpha]_D^{20}$ −54.9 (c 0.12, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.41 (d, 1H, J = 1.7 Hz, H-1′), 5.17 (dd, 1H, J = 9.9, 3.3 Hz, H-3′), 5.16 (d, 1H, J = 3.3 Hz, H-2′), 5.11 (t, 1H, J = 9.9 Hz, H-4′), 4.95 (s, 1H, H-1), 4.18 (dd, 1H, J = 7.1, 5.5 Hz, H-3), 4.09 (d, 1H, J = 5.5 Hz, H-2), 4.07 (br s, 1H, 2′-OH), 3.91–3.87 (m, 1H, H-5′), 3.72–3.68 (m, 1H, H-5), 3.68–3.65 (m, 1H, OC*H*H), 3.52 (dd, 1H, J = 9.9, 7.1 Hz, H-4), 3.43–3.40 (m, 1H, OCH*H*), 2.09, 2.05 (2s, each 3H, 2 × $COCH_3$), 1.60–1.56 (m, 2H, OCH_2CH_2), 1.53, 1.33 (2s, each 3H, 2 × CH_3), 1.30 (d, 3H, J = 6.4 Hz, 6-*Me*), 1.26 (br s, 18H, 9 × CH_2), 1.21 (d, 3H, J = 6.4 Hz, 6′-*Me*), 0.88 (t, 3H, J = 6.9 Hz,

CH_2CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1 170.0, 109.4, 97.9, 96.8, 78.4, 77.9, 76.2, 71.5, 71.3, 69.8, 67.8, 66.6, 63.7, 31.9, 29.6–29.3, 27.9, 26.3, 26.1, 22.7, 20.9, 20.8, 18.1, 17.4, 14.1; ESIMS: calcd for $[M+Na]^+$ *m/z* 625.4; found: 625.4.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2011.07.028.

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