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Synthesis of a group of diosgenyl saponins with combined use of glycosyl trichloroacetimidate and thioglycoside donors

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With the combined use of glycosyl trichloroacetimidates and thioglycosides, a group of natural diosgenyl saponins (**1**–**6**) are efficiently synthesized, in either a stepwise or a 'one-pot' manner. The trichloroacetimidate is employed as an efficient temporary hydroxy protecting group in glycosylation with the glycosyl trichloroacetimidate. The intermolecular alkylthio-group transfer is demonstrated to be a common side-reaction during glycosylation with thioglycosides.

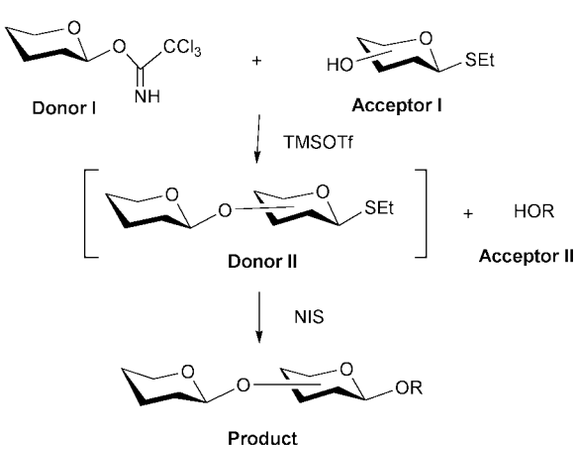
Introduction

Saponins, glycosides of steroids and triterpenes, are widely distributed in terrestrial plants and intimately involved in our daily lives.[1] They exist in relatively high quantities in many significant foods, beverage plants, and forage crops, including such familiar ones as oats, peanuts, soybeans, lentils, garlic, onions, spinach, asparagus, tea, alfalfa, *etc*. Saponins also figure prominently as active constituents in many commonly used herbal medicinal plants, especially those from the Orient – a number of the saponin preparations have long been used as pharmaceutical agents, such as those from ginseng, notoginseng, liquorice, horse chestnut, senega, and primula. Like the glycoconjugates occurring in animals, these plant glycosides exist as populations of glycosylated variants (glycoforms) of individual aglycones; these glycoforms result from the *in vivo* heterogeneous enzymic glycosylation processes. This heterogeneity not only makes the isolation of these compounds extremely difficult, but also leads to uncertainty concerning the saponin components in the same plant species but from different locations or seasons. The complicated existence of saponins has hampered further investigation of their biological functions, as well as quality control of the clinically used saponin preparations.

Saponins **1**–**6**[2] (Fig. 1) represent an example showing the heterogeneity of these compounds. They share a common aglycone, diosgenin, and possess oligosaccharides of similar form. The 'glycoforms' are made of β-D-glucopyranose and α-L-rhamnopyranose moieties, and each begins with a glucopyranose and elongates at its 4-OH through a rhamnopyranose. Some have a 2-rhamnopyranose branch (**1**, **2**) whereas others do not (**3**–**6**); this is the most visible difference within these two sets of 'glycoforms'.

In contrast to the difficulty in isolation of homogeneous saponins from plants, chemical synthesis would provide a realistic route to the availability of saponins. Our previous studies and those of others have shown that glycosylation of steroids and triterpenes is a rather difficult undertaking.[3] The use of 2-OAc glycosyl donors leads to the corresponding saponins in low to moderate yields, due to acetyl-group transfer and orthoester formation side-reactions. The use of glycosyl donors without the participation of a neighboring group commonly produces a mixture of α and β anomers. Nevertheless, as long as the glycosidic bond between an aglycone and a sugar moiety has been constructed, conventional carbohydrate chemistry can be successfully applied to extend the sugar chain.[4] The first monosaccharide moiety should therefore be attached to the aglycone first in preparing saponin 'glycoforms'.

In contemporary oligosaccharide synthesis, glycosyl trichloroacetimidates[5] and thioglycosides[6] are two of the most frequently used types of glycosyl donors – they have become many practitioners' first choice when confronting a glycosylation event.[7] Moreover, the combined use of glycosyl trichloroacetimidates and thioglycosides has recently been developed into a 'one-pot' procedure by Takahashi and co-workers.[8] (Scheme 1). The ready accessibility and the distinguishable



Scheme 1

activations of the glycosyl trichloroacetimidates and thioglycosides make this procedure rather attracting. Herein, we report the synthesis of saponins **1**–**6** with the combined use of glycosyl trichloroacetimidates and thioglycosides, in either a 'one-pot' or a stepwise manner.[4a]

Results and discussion

Preparation of donors and acceptors – the trichloroacetimidate as a hydroxy protecting group

According to the 'one-pot' strategy depicted in Scheme 1, each saponin **1**–**6** was retrosynthetically disconnected into three synthons (Fig. 2): a glycosyl trichloroacetimidate donor (Donor I, **7**,[9] **8**,[10] **9**), a thioglycoside acceptor (Acceptor I,

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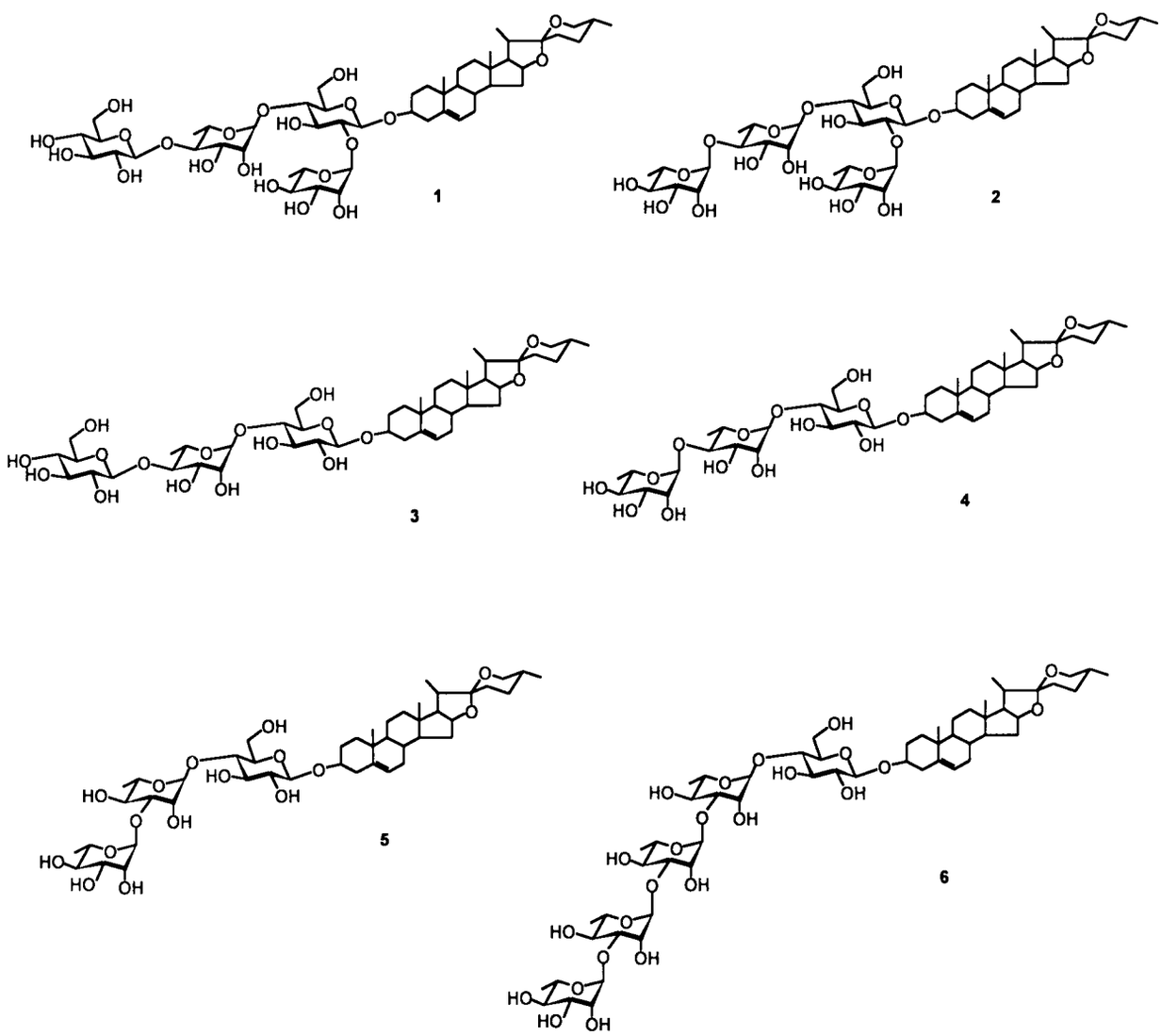
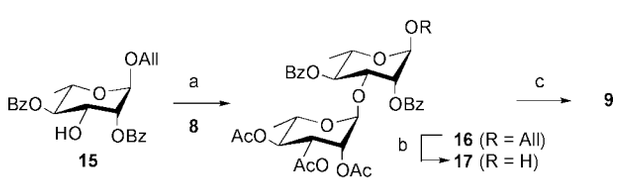


1 Glucβ-(1→4)-Rhaα-(1→4)-[Rhaα-(1→2)]-Glucβ→Diosgenin
2 Rhaα-(1→4)-Rhaα-(1→4)-[Rhaα-(1→2)]-Glucβ→Diosgenin
3 Glucβ-(1→4)-Rhaα-(1→4)-Glucβ→Diosgenin
4 Rhaα-(1→4)-Rhaα-(1→4)-Glucβ→Diosgenin
5 Rhaα-(1→3)-Rhaα-(1→4)-Glucβ→Diosgenin
6 Rhaα-(1→3)-Rhaα-(1→3)-Rhaα-(1→3)-Rhaα-(1→4)-Glucβ→Diosgenin

Fig. 1

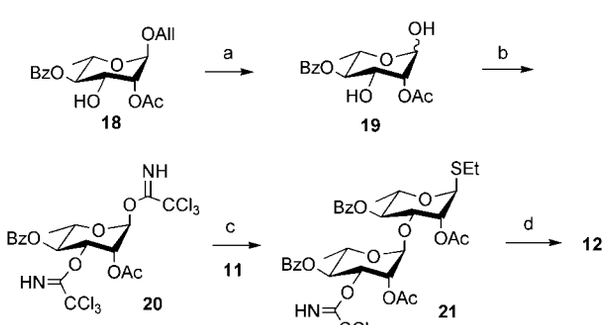
10,[11] **11**,[12] **12**), and a saponin acceptor (Acceptor II, **13**[4b,c] and **14**).

Disaccharide trichloroacetimidate **9** was prepared as shown in Scheme 2. Glycosylation of allyl 2,4-di-*O*-benzoyl-α-L-



Scheme 2 *Reagents and conditions* (*and yields*): (a) $BF_3{\cdot}OEt_2$ (0.25 equiv.), 4 Å MS, CH_2Cl_2, −78 °C, (88%); (b) $PdCl_2$ (0.25 equiv.), MeOH, rt (67%); (c) Cl_3CCN, DBU, CH_2Cl_2, rt (80%).

rhamnopyranoside[13] **15** with 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl trichloroacetimidate **8** under the promotion of $BF_3{\cdot}OEt_2$ provided the allyl disaccharide **16** (88%), which was then subjected to $PdCl_2$ in dry methanol[14] to remove the anomeric allyl group to give **17**. Hemiacetal **17** was then readily converted into the trichloroacetimidate **9** by addition with Cl_3CCN in the presence of DBU.



Scheme 3 *Reagents and conditions* (*and yields*): (a) $PdCl_2$ (0.2 equiv.), MeOH, rt (76%); (b) Cl_3CCN, DBU, CH_2Cl_2, rt (89%); (c) $BF_3{\cdot}OEt_2$, 4 Å MS, CH_2Cl_2, −78 °C (64%); (d) $TsOH{\cdot}H_2O$ (0.8 equiv.), MeOH, CH_2Cl_2, rt (81%).

Thiodisaccharide **12** was prepared using a novel procedure (Scheme 3).[15] The diol **19**, which was prepared from allyl glycoside **18**[12] by deallylation ($PdCl_2$, MeOH), was readily converted into 1,3-bis(trichloroacetimidate) **20**. Glycosylation of **11** with **20** under the promotion of $BF_3{\cdot}OEt_2$ at low temperature

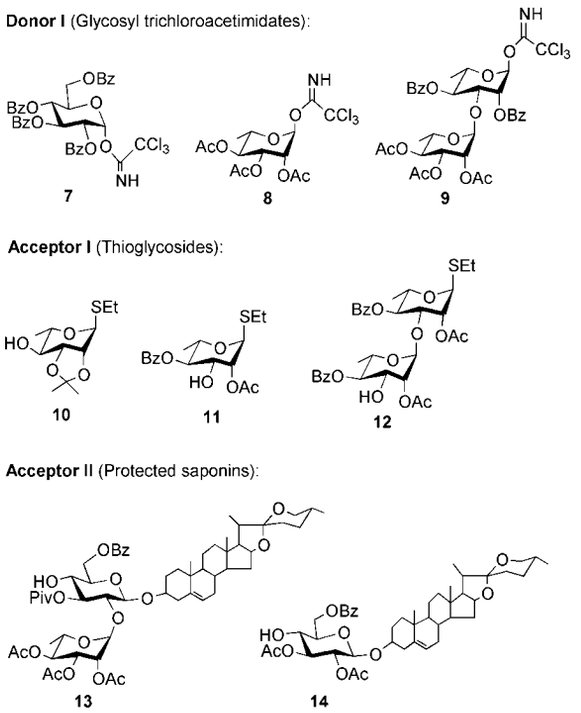


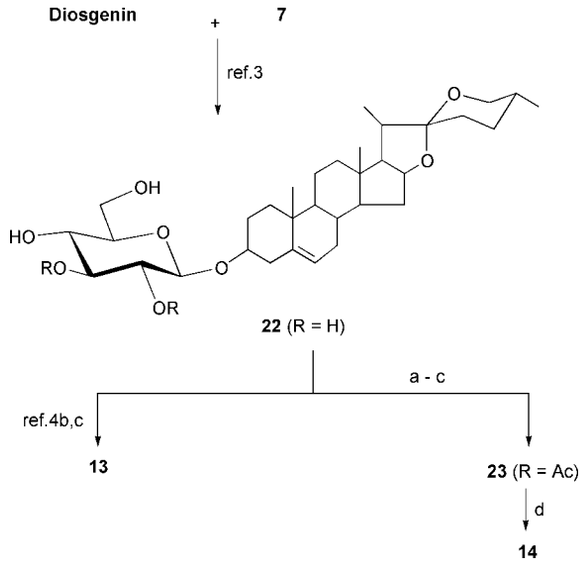
Fig. 2

(−78 °C) provided the coupling product **21** in good yield (64%). The 3-*O*-trichloroacetimidate, which remained intact in the glycosylation event, was conveniently removed under TsOH in methanol to provide the disaccharide acceptor **12** in good yield (81%). Herein, the 3-*O*-trichloroacetimidate was demonstrated to be an efficient temporary protecting group; otherwise, an additional step was needed to introduce a protecting group onto the 3-OH of **18**. It should be noted that two research groups have recently reported the similar usage of trichloroacetimidate as a hydroxy protecting group.[16] Further we have disclosed that trichloroacetimidate, as a protecting group of the hydroxy function, has orthogonal stability with both acetate and *tert*-butyldimethylsilyl (TBS) protection.[15]

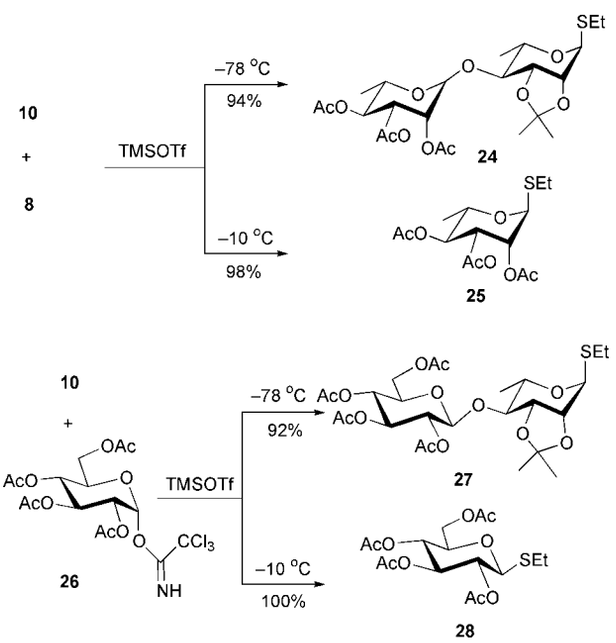
The protected diosgenyl saponins **13** and **14** were synthesized as shown in Scheme 4. We had previously disclosed that coupling of a glycosyl trichloroacetimidate donor bearing a neighboring 2-OBz with the 3-OH of a steroid and triterpene under the action of a catalytic amount of TMSOTf provided the corresponding 1,2-*trans* glycoside in excellent yield.[3] Glycosylation of diosgenin with 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl trichloroacetimidate **7**, after removal of the benzoates, gave diosgenyl β-D-glucopyranoside **22** (trillin) quantitatively.[3,4d] Trillin **22** was then readily converted into saponin acceptors **13**[4b,c] and **14** by routine transformations (Scheme 4).

Intermolecular ethylthio-group transfer of ethyl thioglycosides

With donors and acceptors at hand, we sought to effect the glycosylation reaction to furnish the target saponins. Before performing the 'one-pot' synthesis, each glycosylation event was carried out in a stepwise manner. In coupling of 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl trichloroacetimidate **8** with thioglycoside **10**, we found (surprisingly) that, although the normal coupling product **24** was produced in an excellent yield (94%) under conventional conditions (0.05 equiv. TMSOTf, 4 Å MS, CH_2Cl_2) at −78 °C, the intermolecular ethylthio-group transfer product **25**[17] was produced in 98% yield when the reaction was performed at −10 °C. Similar results were obtained in coupling of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate[18] **26** with thioglycoside **10** (Scheme 5). The normal coupling product **27** was produced (92%) at −78 °C, while the intermolecular ethylthio-group

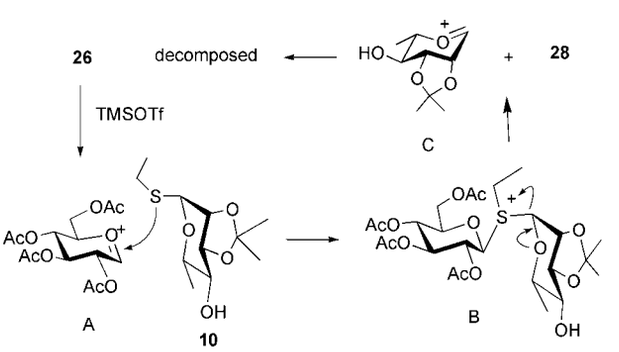


Scheme 4 *Reagents and conditions* (*and yields*): (a) $Bn(OMe)_2$, TsOH, DMF, 50 °C; (b) Ac_2O, pyridine, rt; (c) 80% HOAc, 70 °C (65% for 3 steps); (d) BzCl, pyridine, 0 °C (85%).



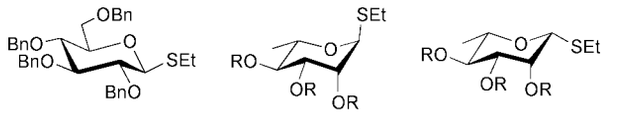
Scheme 5

transfer product **28** was formed (100%) at −10 °C. It is noted that this type of intermolecular transfer has been reported in glycosylation of ethyl or phenyl thioglycosides with glycosyl bromides or glycosyl trichloroacetimidates.[19] We envisaged that thioglycoside **28**,[20] as an example, might be produced following the path as shown in Scheme 6: glucopyranosyl oxycarbenium



Scheme 6

Table 1 Examination of the ethylthio group transfer[a,b]



29 **25**: R = Ac, **30**: R = Bn **31**: R = Ac, **32**: R = Bn

Thioglycoside	**29**	**25**	**30**	**31**	**32**
Yields of **28** (%)	87	0	77	0	74

[a] Conditions: **26** (1.2 equiv.), $BF_3{\cdot}OEt_2$ (0.5 equiv.), 4 Å MS, CH_2Cl_2, −78 °C ⟶ rt (naturally). [b] Isolated yields.

A, produced from trichloroacetimidate **26** under the action of Lewis acid TMSOTf, was attacked by the nucleophilic sulfur of the 1-SEt group in competition with the oxygen of 3-OH of the thiorhamnoside **10**, producing the sulfonium **B**; decomposition of **B** produced the thioglycoside **28** and a rhamnosyl oxycarbenium **C**. The reason why **A** + **10** generated **C** + **28**, rather than the reverse reaction occurring, was that the rhamnosyl moiety of **10** was more electron rich, or 'armed' (6-deoxy and isopropylidene protection), than the corresponding peracetylated glucopyranosyl moiety, which was 'disarmed' (acetyl protection).[21]

According to the above supposition, we thought that the transfer of the alkylthio group of a thioglycoside to a more electron-deficient sugar moiety should be a common side-reaction during glycosylation. Therefore, the following armed and disarmed thioglycosides **25**, **29**–**32** were examined: treatment of thioglycosides **25**, **29**–**32** with tetraacetylglucopyranosyl imidate **26** under the typical conditions for glycosylation with glycosyl trichloroacetimidate donors[5] would produce the tetraacetyl β-thioglucoside **28** once the intermolecular ethylthio-group transfer took place. As shown in Table 1, the corresponding ethylthio group was readily transferred from the 'armed' thioglycosides (**29**,[22] **30**,[17] **32**[17]) in a manner independent of the anomeric configuration (**30**, **32**), producing **28** as the major product; however, for the 'disarmed' thioglycosides (**25**, **31**[17]), the ethylthio-group transfer did not happen, with the corresponding starting thioglycosides remaining intact.

Synthesis of saponins 1–6 by the stepwise procedure

Coupling of trichloroacetimidates **7** and **8** with thioglycoside **10**, under the promotion of TMSOTf (4 Å MS, CH_2Cl_2) at −78 °C, afforded the corresponding disaccharides **33** and **24**, with a (1→4)-rhamnose linkage, in excellent yields (97% and 94%, respectively) (Table 2). Coupling of **8** with **11** and of disaccharide trichloroacetimidates **9** with thiodisaccharide **12**, under similar conditions, gave the expected saccharides **34** and **35**, with a (1→3)-rhamnose linkage, in 85% and 88% yield, respectively. Glycosylation of saponin acceptors **13** and **14** with thiodisaccharide donors **24**, **33**, and **34** under the promotion of NIS–AgOTf[23] provided the corresponding protected saponins **36**–**40**, with a newly constructed α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranoside linkage, in satisfactory yields (87–92%). Under similar conditions, pentasaccharide saponin **41** was obtained in 66% yield by coupling of thiotetrasaccharide **35** with **14**, whereas 20% of the acceptor **14** was recovered. Treatment of the fully protected saponins **36**–**39** with 80% HOAc to cleave the isopropylidene group, followed with NaOH to remove the acyl protecting groups (acetyl, benzoyl, and pivaloyl), afforded the desired saponins **1**–**4** in very good yields (81–87%). The Rha-(1→4)-Glu linkages, constructed by using donors (**33** and **24**) without a neighboring participating group, were confirmed to be α configurations by measuring the J_{C1-H1}-values (169.2, 169.7, 169.8, and 169.5 Hz, respectively) of the corresponding rhamnose residues in saponins **1**–**4**. Treatment of **40** and **41** with NaOMe in methanol to remove the acetyl and benzoyl groups provided saponins **5** and **6** in 90 and 82% yield, respectively. The synthetic saponins **1**–**6** gave satisfactory data compared with those reported for the natural compounds.[2]

Synthesis of saponins 36–41 by the 'one-pot' procedure

After fashioning the saponins by the stepwise manner, we sought to effect the two steps of glycosylation in one pot.[8] The results are listed in Table 3. After completion of the coupling of trichloroacetimidates with thioglycosides at −78 °C, the reaction temperature was elevated to −20 °C, and the saponin acceptor (**13** or **14**) was added, followed by addition of NIS. After 0.5 h at −20 °C, the second step of glycosylation, which was promoted by NIS and TfOH generated from the first step *via* TMSOTf hydrolysis, was completed, giving the expected protected saponins **36**–**41** in 61–98% yield. The yields for the final products achieved by the one-pot procedure were comparable to those obtained by the stepwise procedure; this demonstrated that the conditions for these two glycosylation steps were perfectly compatible.

Experimental

Solvents were purified in the usual way. TLC was performed on precoated plates of silica gel HF_{254} (0.5 mm, Yantai, Shandong, China). Flash-column chromatography was performed on silica gel H (10–40 μ, Yantai, Shandong, China). Optical rotations were determined with a Perkin-Elmer Model 241 MC polarimeter, and $[\alpha]_D$-values are in units of 10^{-1} deg cm^2 g^{-1}. NMR spectra were recorded on a Bruker AM 300 or a Bruker AM 400 spectrometer with Me_4Si as the internal standard. *J*-values are given in Hz. Mass spectra were obtained on a HP5989A or a VG Quatro mass spectrometer. Elemental analyses were performed on a Perkin-Elmer Model 2400 instrument. Petroleum spirit refers to the fraction with distillation range 60–90 °C.

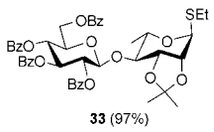
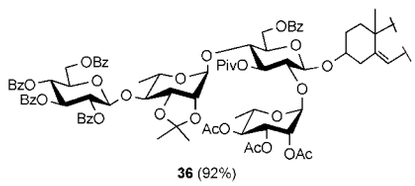
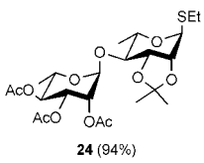
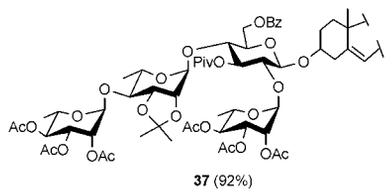
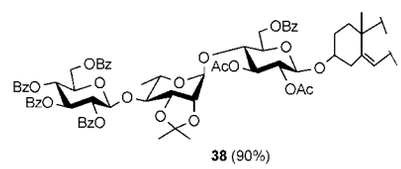
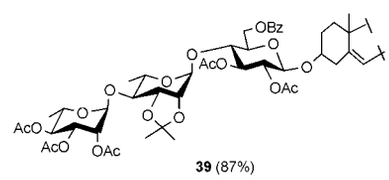
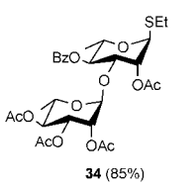
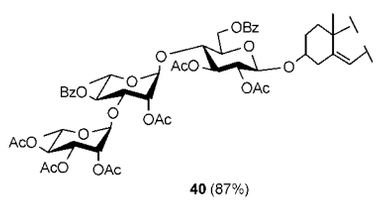
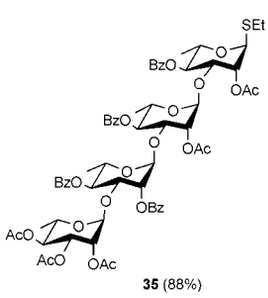
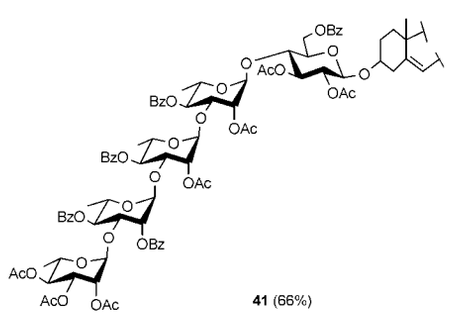
Allyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside 16

A mixture of the trichloroacetimidate **8** (3.10 g, 7.13 mmol), acceptor **15** (2.01 g, 4.87 mmol), and 4 Å MS (3.0 g) in dry CH_2Cl_2 (30 mL) was stirred at room temperature under argon for 30 min, cooled to −78 °C and a solution of $BF_3{\cdot}OEt_2$ (0.06 mL, 0.49 mmol) in CH_2Cl_2 (0.5 mL) was added. After being stirred for 30 min, the reaction mixture was quenched with Et_3N. The mixture was filtered through a pad of Celite, the filtrates were concentrated. The residue was purified by silica gel column chromatography (petroleum spirit–EtOAc, 3 : 1–2 : 1) to give **16** (2.93 g, 88%) as a white solid; $[\alpha]_D^{21}$ +28.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.17–7.43 (m, 10 H), 5.96 (m, 1 H), 5.51 (t, 1 H, *J* 9.8), 5.45 (dd, 1 H, *J* 1.6, 3.3), 5.36, 5.25 (m, 2 H), 5.07 (dd, 1 H, *J* 3.4, 9.8), 5.02 (d, 1 H, *J* 1.6), 4.92–4.85 (m, 3 H), 4.42 (dd, 1 H, *J* 3.4, 9.8), 4.24 (m, 1 H), 4.13–3.99 (m, 2 H), 3.90 (m, 1 H), 1.90, 1.87, 1.81 (3s, 3 × 3 H), 1.31 (d, 3 H, *J* 6.2), 1.05 (d, 3 H, *J* 6.2); EIMS *m*/*z* 684 (M^+, 0.1%), 628 (16.4), 539 (15.2), 273 (65.7), 105 (100) (Calc. for $C_{35}H_{40}O_{14}{\cdot}H_2O$: C, 59.82; H, 6.02. Found: C, 59.57; H, 5.79%).

2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranose 17

A mixture of allyl glycoside **16** (1.58 g, 2.31 mmol) and $PdCl_2$ (100 mg, 0.58 mmol) in dry MeOH (30 mL) was stirred at room temperature for 4 h, and then was filtered through a pad of Celite. The filtrate was concentrated. The residue was purified by silica gel column chromatography (petroleum spirit–EtOAc, 3 : 1–2 : 1) to give **17** (1.00 g, 67%) as a white solid, and recovered

Table 2 Synthesis of saponins **36**–**41** by the stepwise manner[a,b]

Entry	Donor **I**	Acceptor **I**	Product/Donor **II** (Yield)	Acceptor **II**	Product (Yield)	Yield (%) (2 steps)
1	**7**	**10**	 **33** (97%)	**13**	 **36** (92%)	89
2	**8**	**10**	 **24** (94%)	**13**	 **37** (92%)	86
3	**7**	**10**	**33**	**14**	 **38** (90%)	87
4	**8**	**10**	**24**	**14**	 **39** (87%)	82
5	**8**	**11**	 **34** (85%)	**14**	 **40** (87%)	74
6	**9**	**12**	 **35** (88%)	**14**	 **41** (66%)	58

[a] *Conditions*. Step 1: Donor **I** (1.2 equiv.), Acceptor **I** (1.0 equiv.), TMSOTf (0.2 equiv.), 4 Å MS, CH_2Cl_2, −78 °C. Step 2: Donor **II** (2.0 equiv.), Acceptor **II** (1.0 equiv.), NIS (2.0 equiv.), AgOTf (0.3 equiv.), 4 Å MS, CH_2Cl_2, −10 °C. [b] Isolated yields based on acceptors.

16 (0.5 g); $[a]_D^{21}$ +30.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.17–7.42 (m, 10 H), 5.75 (d, 1 H, *J* 2.9), 5.46 (t, 1 H, *J* 9.8), 5.00 (dd, 1 H, *J* 2.9, 9.9), 4.93–4.87 (m, 3 H), 4.64 (s, 1 H), 4.11 (dd, 1 H, *J* 3.1, 9.8), 3.98 (m, 1 H), 3.69 (m, 1 H), 1.97, 1.84, 1.81 (3s, 3 × 3 H), 1.40 (d, 3 H, *J* 6.1), 1.18 (d, 3 H, *J* 6.2); EIMS *m*/*z* 628 (2.0%), 382 (2.5), 273 (19.0), 105 (100) (Calc. for $C_{32}H_{36}O_{14}$: C, 59.62; H, 5.63. Found: C, 59.74; H, 5.78%).

2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl trichloroacetimidate 9

To a solution of **17** (1.01 g, 1.51 mmol) in dry CH_2Cl_2 (15 mL) at 0 °C added Cl_3CCN (1.0 mL, 9.97 mmol) and DBU (0.02 mL, 0.14 mmol). The mixture was stirred at room temperature for 4 h and then concentrated. The residue was purified by silica gel column chromatography (petroleum spirit–EtOAc, 3:1) to give **9** (1.99 g, 80%) as a white solid; $[a]_D^{21}$ +31.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.89 (s, 1 H), 8.17–7.44 (m, 10 H), 6.42 (s, 1 H), 5.61–5.55 (m, 2 H), 5.07 (dd, 1 H, *J* 2.8, 9.9), 4.92–4.86 (m, 3 H), 4.47 (dd, 1 H, *J* 3.3, 9.9), 4.21 (m, 1 H), 3.91 (m, 1 H), 1.92, 1.86, 1.82 (3s, 3 × 3 H), 1.34 (d, 3 H, *J* 6.3), 1.05 (d, 3 H, *J* 6.3); EIMS *m*/*z* 738 (0.1%), 628 (0.4), 382 (0.6), 273 (18.5), 105 (100) (Calc. for $C_{34}H_{36}Cl_3NO_{14}N$: C, 51.75; H, 4.60; N, 1.77. Found: C, 52.16; H, 4.29; N, 1.64%).

Table 3 Synthesis of saponins **36**–**41** by the 'one-pot' procedure[a,b]

Entry	Donor **I**	Acceptor **I**	Acceptor **II**	Product	Yield (%)
1	**7**	**10**	**13**	**36**	96
2	**8**	**10**	**13**	**37**	98
3	**7**	**10**	**14**	**38**	90
4	**8**	**10**	**14**	**39**	91
5	**8**	**11**	**14**	**40**	61
6	**9**	**12**	**14**	**41**	62

[a] Conditions: Donor **I** (2.3 equiv.), Acceptor **I** (2.0 equiv.), TMSOTf (0.3 equiv.), 4 Å MS, CH_2Cl_2, −78 °C; then Acceptor **II** (1.0 equiv.), NIS (2.0 equiv.), −20 °C. [b] Isolated yields based on Acceptor **II**.

Ethyl 2-*O*-acetyl-4-*O*-benzoyl-1-thio-α-L-rhamnopyranoside 11

A procedure similar to that for the preparation of allyl 2-*O*-acetyl-4-*O*-benzoyl-α-L-rhamnopyranoside[12] **18** was employed. $[a]_D^{16}$ −130.7 (*c* 0.92, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.06–7.45 (m, 5 H), 5.31 (s, 1 H), 5.23 (m, 1 H), 5.15 (t, 1 H, *J* 9.7), 4.35 (m, 1 H), 4.13 (dd, 1 H, *J* 9.8, 3.3), 2.67 (m, 2 H), 2.20 (s, 3 H), 1.35–1.28 (m, 6 H); ESIMS *m/z* 377 (M^+ + Na), 317 (Calc. for $C_{17}H_{22}O_6S$: C, 57.61; H, 6.28. Found: C, 57.42; H, 6.42%).

2-*O*-Acetyl-4-*O*-benzoyl-α-L-rhamnopyranose 19

A mixture of allyl glycoside **18** (1.27 g, 3.62 mmol) and $PdCl_2$ (126 mg, 0.73 mmol) in dry methanol (19 mL) was stirred at room temperature overnight, and then filtered through a pad of Celite. The filtrates were concentrated, and the residue was purified by silica gel column chromatography (petroleum spirit–EtOAc, 1:1) to afford **19** (α anomer dominated) (0.85 g, 76%) as a white solid; $[a]_D^{16}$ +23.8 (*c* 0.67, MeOH); ^{1}H NMR (300 MHz; $CDCl_3$) 8.05 (m, 2 H), 7.60 (m, 1 H), 7.46 (m, 2 H), 5.26 (m, 1 H), 5.16–5.09 (m, 2 H), 4.26 (m, 2 H), 3.23 (d, 1 H, *J* 4.1), 2.44 (d, 1 H, *J* 9.7), 2.19 (s, 3 H), 1.28 (d, 3 H, *J* 6.2); EIMS *m/z* 311 (M^+ + 1, 0.3%), 293 (28), 219 (6), 153 (10), 105 (100) (Calc. for $C_{15}H_{18}O_7$: C, 58.05; H, 5.84. Found: C, 57.92; H, 5.97%).

2-*O*-Acetyl-4-*O*-benzoyl-3-*O*-trichloroacetimidoyl-α-L-rhamnopyranosyl trichloroacetimidate 20

To a solution of diol **19** (125 mg, 0.36 mmol) in dry CH_2Cl_2 (4 mL) were added Cl_3CCN (0.39 mL, 3.91 mmol) and DBU (0.01 mL, 0.072 mmol). The mixture was stirred at room temperature overnight, and then concentrated. The residue was purified by silica gel column chromatography (petroleum spirit–EtOAc, 8:1) to afford **20** (190 mg, 89%) as a white solid; $[a]_D^{16}$ +11.4 (*c* 1.06, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.79 (s, 1 H), 8.57 (s, 1 H), 8.01 (m, 2 H), 7.60 (m, 1 H), 7.46 (m, 2 H), 6.47 (d, 1 H, *J* 1.6), 5.69–5.57 (m, 3 H), 4.26 (m, 1 H), 1.89 (s, 3 H), 1.32 (d, 3 H, *J* 6.3); EIMS *m/z* 404 (2%), 227 (3), 189 (14), 125 (23), 84 (100) (Calc. for $C_{19}H_{18}Cl_6N_2O_7$: C, 38.09; H, 3.03; N, 4.67. Found: C, 38.00; H, 3.05; N, 4.51%).

Ethyl 2-*O*-acetyl-4-*O*-benzoyl-3-*O*-trichloroacetimidoyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-benzoyl-1-thio-α-L-rhamnopyranoside 21

To a mixture of **11** (67 mg, 0.19 mmol) and 4 Å MS (150 mg) in dry CH_2Cl_2 (2 mL) under argon at −78 °C was added $BF_3{\cdot}OEt_2$ (0.025 mL, 0.02 mmol) followed by the addition of **20** (138 mg, 0.23 mmol) as a solution in CH_2Cl_2 (0.2 mL). After being stirred for 30 min, the reaction mixture was quenched by Et_3N (1 drop) and then filtered. The filtrates were concentrated, the residue was then purified by silica gel column chromatography (petroleum spirit–EtOAc, 5:1) to afford **21** (95 mg, 64%) as a colorless syrup, and recovered **11** (20 mg). Compound **21** $[a]_D^{16}$ −17.0 (*c* 0.71, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.02 (m, 4 H), 7.56 (m, 2H), 7.43 (m, 4 H), 5.48–5.26 (m, 5 H), 5.12 (m, 2 H), 4.37 (dd, 1 H, *J* 9.7, 3.4), 4.30 (m, 1 H), 4.12 (m, 1 H), 2.66 (m, 2 H), 2.29 (s, 3 H), 1.78 (s, 3 H), 1.27 (m, 9 H); EIMS *m/z* 793 (0.1%), 791 (M^+, 0.1), 733 (3), 732 (3), 731 (7), 730 (3), 729 (6), 438 (11), 436 (11), 293 (10), 153 (16), 105 (100) (Calc. for $C_{34}H_{38}Cl_3NO_{12}S$: C, 51.61; H, 4.85; N, 1.77. Found: C, 52.52; H, 4.75; N, 1.72%).

Ethyl 2-*O*-acetyl-4-*O*-benzoyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-benzoyl-1-thio-α-L-rhamnopyranoside 12

To a solution of **21** (169 mg, 0.14 mmol) in MeOH–CH_2Cl_2 (2 mL:2 mL) at room temperature was added *p*-TsOH·H_2O (21 mg, 0.11 mmol). After being stirred for 15 min, the reaction mixture was quenched with Et_3N (1 drop), and then concentrated. The residue was purified by silica gel column chromatography (petroleum spirit–EtOAc, 3:1) to afford **12** (112 mg, 81%) as a white solid; $[a]_D^{16}$ −39.6 (*c* 0.49, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.04 (m, 4 H), 7.57 (m, 2 H), 7.47 (m, 4 H), 5.44–5.38 (m, 2 H), 5.29–5.25 (m, 3 H), 4.95 (d, 1 H, *J* 1.5), 4.37–4.27 (m, 2 H), 4.04 (m, 1 H), 3.78 (m, 1 H), 2.63 (m, 2 H), 2.23 (s, 3 H), 1.89 (s, 3 H), 1.34–1.22 (m, 9 H); EIMS *m/z* 587 (2%), 586 (9), 585 (27), 396 (7), 334 (3), 293 (49), 105 (100) (Calc. for $C_{32}H_{38}O_{12}S{\cdot}H_2O$: C, 57.82; H, 6.06. Found: C, 58.02; H, 5.91%).

Diosgenyl 2,3-di-*O*-acetyl-β-D-glucopyranoside 23

To a solution of diosgenyl 4,6-*O*-benzylidene-β-D-glucopyranoside[4d] (1.07 g, 1.61 mmol, prepared as described previously) in dry pyridine (30 mL) at room temperature was added Ac_2O (5.0 mL). After being stirred overnight, the mixture was quenched with MeOH, diluted with EtOAc, and then washed successively with 1 M HCl, saturated aq. $NaHCO_3$, and water. The organic layer was dried over anhydrous Na_2SO_4, and then was filtered and concentrated. The residue was dissolved in 80% HOAc (30 mL). After being stirred at 70 °C for 4 h, the solution was concentrated. The residue was purified by silica gel column chromatography (petroleum spirit–EtOAc, 2:1) to give **23** (765 mg, 72%) as a white solid; $[a]_D^{18}$ −79.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 5.35 (d, 1 H, *J* 4.9), 5.03 (t, 1 H, *J* 9.4), 4.88 (dd, 1 H, *J* 7.9, 9.6), 4.60 (d, 1 H, *J* 7.9), 4.40 (m, 1 H), 3.91 (dd, 1 H, *J* 3.3, 12.0), 3.82 (dd, 1 H, *J* 4.4, 12.0), 3.75 (t, 1 H, *J* 9.4), 3.55–3.30 (m, 4 H), 2.09, 2.05 (2s, 2 × 3 H), 1.00 (s, 3 H), 0.96 (d, 3 H, *J* 6.9), 0.78 (d, 3 H, *J* 5.4), 0.78 (s, 3 H); EIMS *m/z* 397 (24.1%), 282 (0.9), 253 (27.3), 139 (100) (Calc. for $C_{37}H_{56}O_{10}{\cdot}0.5H_2O$: C, 66.34; H, 8.61. Found: C, 66.10; H, 8.38%).

Diosgenyl 2,3-di-*O*-acetyl-6-*O*-benzoyl-β-D-glucopyranoside 14

To a stirred solution of diol **23** (764 mg, 1.16 mmol) in dry pyridine (4 mL) and CH_2Cl_2 (4 mL) at 0 °C was added BzCl (0.16 mL, 1.38 mmol) dropwise. After being stirred at 0 °C for 30 min, the reaction mixture was quenched with MeOH, and then was concentrated. The residue was purified by silica gel column chromatography (petroleum spirit–EtOAc, 2:3) to give **14** (753 mg, 85%) as a white solid; $[a]_D^{18}$ −84.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.10–7.40 (m, 5 H), 5.33 (d, 1 H, *J* 4.9), 5.07 (t, 1 H, *J* 9.1), 4.91 (dd, 1 H, *J* 8.0, 9.5), 4.73 (dd, 1 H, *J* 3.6, 12.0), 4.60–4.52 (m, 2 H), 4.41 (m, 1 H), 3.69–3.58 (m, 2 H), 3.52–3.30 (m, 3 H), 2.08, 2.05 (2s, 2 × 3 H), 0.97 (s, 3 H), 0.96 (d, 3 H, *J* 5.6), 0.78 (d, 3 H, *J* 6.1), 0.77 (s, 3 H); *m/z* (EIMS) 765 (M^+, 0.2%), 396 (35.5), 282 (66.1), 105 (100) (Calc. for $C_{44}H_{60}O_{11}$: C, 69.09; H, 7.91. Found: C, 69.13; H, 8.11%).

Typical procedure for intermolecular ethylthio-group transfer

To a stirred mixture of trichloroacetimidate **26** (1.2 equiv.), thioglycoside (**25**, **29**–**32**) (≈50 mg, 1.0 equiv.), and 4 Å MS (50 mg) in CH_2Cl_2 at −78 °C, was added $BF_3{\cdot}OEt_2$ (0.5 equiv.). The mixture was allowed to warm to room temperature naturally

(*ca*. 30 min). The production of the thioglycoside **28** was then detected by TLC. The yield of **28** was calculated based on thioglycoside after normal work-up and purification by silica gel column chromatography.

Typical procedure for coupling of the trichloroacetimidates 7–9 with thioglycosides 10–12

To a mixture of a thioglycoside acceptor **10**–**12** (≈100 mg, 1.0 equiv.) and 4 Å MS (100 mg) in dry CH_2Cl_2 (8 mL) under argon at −78 °C, was added a solution of TMSOTf in CH_2Cl_2 (0.1 M, 0.2 equiv.) followed by addition of a solution of the trichloroacetimidate **7**–**9** (1.2 equiv.) in CH_2Cl_2 (1 mL). After being stirred for 30 min, the reaction mixture was quenched with Et_3N, and then filtered through a pad of Celite. The filtrate was concentrated. The residue was purified by silica gel column chromatography (petroleum spirit–EtOAc, 3 : 1–2 : 1) to afford the thioglycoside **24**, **33**–**35** as white solid. Yields were based on acceptors **10**–**12**.

Ethyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside 24. Yield 94%; $[a]_D^{22}$ −155.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 5.51 (s, 1 H), 5.33 (d, 1 H, *J* 1.7), 5.30 (dd, 1 H, *J* 1.9, 3.3), 5.22 (dd, 1 H, *J* 3.3, 10.1), 5.08 (t, 1 H, *J* 10.0), 4.21–4.13 (m, 2 H), 4.06 (m, 1 H), 3.89 (m, 1 H), 3.56 (dd, 1 H, *J* 7.1, 9.9), 2.61 (m, 2 H), 2.15, 2.05, 1.98, 1.53, 1.32 (5s, 5 × 3 H), 1.34–1.21 (m, 9 H); EIMS *m*/*z* 520 (M^+, 0.1%), 464 (0.5), 460 (2.3), 273 (100) (Calc. for $C_{23}H_{36}O_{11}S$: C, 53.06; H, 6.97. Found: C, 52.95; H, 6.93%).

Ethyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→4)-2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside 33. Yield 97%; $[a]_D^{22}$ −105.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.03–7.26 (m, 20 H), 5.93 (t, 1 H, *J* 9.7), 5.65 (t, 1 H, *J* 9.7), 5.50 (dd, 1 H, *J* 8.2, 9.7), 5.45 (s, 1 H), 4.66 (dd, 1 H, *J* 3.2, 12.1), 4.49 (dd, 1 H, *J* 5.5, 12.0), 4.14 (m, 1 H), 4.03 (d, 1 H, *J* 5.5), 3.96–3.88 (m, 2 H), 3.64 (dd, 1 H, *J* 7.3, 9.9), 2.53 (m, 2 H), 1.48–1.22 (m, 12 H); ESIMS *m*/*z* 1676 ($2M^+$ + Na, 11.0%), 866 (M^+ + K, 17.1), 850 (M^+ + Na, 100), 845 (M^+ + H_2O, 15.9) (Calc. for $C_{45}H_{46}O_{13}S{\cdot}0.5H_2O$: C, 64.65; H, 5.67. Found: C, 64.83; H, 5.41%).

Ethyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-benzoyl-1-thio-α-L-rhamnopyranoside 34. Yield 85%; $[a]_D^{22}$ −61.3 (*c* 0.9, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.04–7.42 (m, 5 H), 5.39 (t, 1 H, *J* 10.0), 5.36 (d, 1 H, *J* 1.8), 5.25 (s, 1 H), 5.10 (dd, 1 H, *J* 3.3, 9.9), 4.94 (t, 1 H, *J* 9.9), 4.91 (s, 1 H), 4.84 (s, 1 H), 4.29 (m, 1 H), 4.23 (dd, 1 H, *J* 3.6, 9.9), 3.89 (m, 1 H), 2.67 (m, 2 H), 2.24, 2.05, 1.88, 1.85 (4s, 4 × 3 H), 1.34–1.21 (m, 9 H); ESIMS *m*/*z* 672 (M^+ + 2Na, 6.2%), 649 (M^+ + Na, 100), 644 (22.7), 589 (23.4) (Calc. for $C_{29}H_{38}O_{13}S$: C, 55.58; H, 6.11. Found: C, 55.55; H, 6.22%).

Ethyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-benzoyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-benzoyl-1-thio-α-L-rhamnopyranoside 35. Yield 88%; $[a]_D^{22}$ −31.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.11–7.15 (m, 20 H), 5.45–5.27 (m, 7 H), 5.06–5.02 (m, 2 H), 4.95–4.85 (m, 3 H), 4.60 (d, 1 H, *J* 1.5), 4.37–4.25 (m, 3 H), 4.06–3.77 (m, 4 H), 2.69 (m, 2 H), 2.29, 1.94, 1.90, 1.89, 1.83 (5s, 5 × 3 H), 1.34–1.21 (m, 9 H), 1.04 (d, 3 H, *J* 6.3), 0.94 (d, 3 H, *J* 6.2); ESIMS *m*/*z* 1332 (M^+ + K + H_2O + 1, 100%), 1295 (M^+ + Na, 79.7), 1291 (M^+ + H_2O, 58.8), 1284 (23.4) (Calc. for $C_{64}H_{72}O_{25}S{\cdot}H_2O$: C, 59.52; H, 5.77. Found: C, 59.75; H, 5.63%).

Typical procedure for coupling of a thioglycoside 24, 33–35 with a saponin acceptor 13, 14

A suspension of the saponin acceptor (**13**, **14**) (≈100 mg, 1.0 equiv.), thioglycoside donor (**24**, **33–35**) (2.0 equiv.), and 4 Å MS (100 mg) in dry CH_2Cl_2 (6 mL) was stirred at room temperature under argon for 1 h, and then cooled to −10 °C. At this temperature, NIS (2.0 equiv.) was added followed by the immediate addition of a solution of AgOTf (0.3 equiv.) in dry toluene (0.5 mL). After being stirred for 30 min, the reaction mixture was quenched with Et_3N, and then filtered through a pad of Celite. The filtrate was concentrated. The residue was purified by silica gel column chromatography (petroleum spirit–EtOAc 1 : 3–1 : 2) to afford the fully protected saponin (**36**–**41**) as a white solid. Yields were based on the saponin acceptors (**13**, **14**).

Diosgenyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-[2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)]-6-*O*-benzoyl-3-*O*-pivaloyl-β-D-glucopyranoside 36. Yield 92%; $[a]_D^{22}$ −45.0 (*c* 1.54, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.06–7.26 (m, 25 H), 5.89 (t, 1 H, *J* 9.6), 5.63 (t, 1 H, *J* 9.8), 5.46 (dd, 1 H, *J* 8.0, 9.5), 5.34–5.27 (m, 3 H), 5.20–5.14 (m, 2 H), 5.04–5.01 (m, 2 H), 4.85 (s, 1 H), 4.66–4.37 (m, 7 H), 3.91–3.80 (m, 4 H), 3.71–3.37 (m, 6 H), 2.09, 2.01, 1.94 (3s, 3 × 3 H), 1.45–1.16 (m, 12 H), 1.07 (s, 9 H), 0.99 (d, 3 H, *J* 6.8), 0.94 (s, 3 H), 0.79 (d, 3 H, *J* 7.3), 0.77 (s, 3 H); ESIMS *m*/*z* 1823 (M^+ + 2Na, 41.4%), 1803 (M^+ + 1, 21.3), 1694 (9.2), 921 (100) (Calc. for $C_{100}H_{120}O_{30}$: C, 65.99; H, 6.75. Found: C, 66.01; H, 6.64%).

Diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-[2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)]-6-*O*-benzoyl-3-*O*-pivaloyl-β-D-glucopyranoside 37. Yield 92%; $[a]_D^{22}$ −45.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.05–7.40 (m, 5 H), 5.38–4.92 (m, 10 H), 4.87 (s, 1 H), 4.63–4.32 (m, 5 H), 4.13–3.68 (m, 7 H), 3.57–3.41 (m, 4 H), 2.12, 2.08, 2.01, 1.99, 1.94, 1.93 (6s, 6 × 3 H), 1.31–1.16 (m, 15 H), 1.16 (s, 9 H), 0.95 (d, 3 H, *J* 6.9), 0.93 (s, 3 H), 0.78 (d, 3 H, *J* 6.6), 0.77 (s, 3 H); ESIMS *m*/*z* 1519 (M^+ + Na, 24.7%), 1514 (M^+ + H_2O, 19.0), 649 (100) (Calc. for $C_{78}H_{110}O_{28}$: C, 62.63; H, 7.41. Found: C, 62.43; H, 7.39%).

Diosgenyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-acetyl-6-*O*-benzoyl-β-D-glucopyranoside 38. Yield 90%; $[a]_D^{22}$ +44.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.04–7.26 (m, 25 H), 5.90 (t, 1 H, *J* 9.1), 5.64 (t, 1 H, *J* 9.8), 5.46 (dd, 1 H, *J* 8.0, 9.7), 5.32–5.27 (m, 2 H), 5.12 (t, 1 H, *J* 9.33), 4.98 (s, 1 H), 4.84 (dd, 1 H, *J* 8.0, 9.7), 4.69–4.37 (m, 6 H), 4.11 (m, 1 H), 3.94–3.88 (m, 3 H), 3.64–3.33 (m, 6 H), 2.02, 1.94 (2s, 2 × 3 H), 1.21 (d, 3 H, *J* 6.7), 0.96 (d, 3 H, *J* 8.3), 0.95 (s, 3 H), 0.78 (d, 3 H, *J* 7.4), 0.77 (s, 3 H); ESIMS *m*/*z* 1854 (M^+ + H_2O, 26.2%), 1530 (M^+, 23.7), 538 (100), 479 (85.8), 413 (44.7) (Calc. for $C_{71}H_{92}O_{24}{\cdot}H_2O$: C, 67.51; H, 6.64. Found: C, 67.67; H, 6.44%).

Diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-acetyl-6-*O*-benzoyl-β-D-glucopyranoside 39. Yield 87%; $[a]_D^{22}$ −79.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.06–7.42 (m, 5 H), 5.33 (d, 1 H, *J* 3.8), 5.28–5.03 (m, 6 H), 4.88 (t, 1 H, *J* 8.9), 4.64–4.37 (m, 4 H), 4.13–3.70 (m, 6 H), 3.48–3.33 (m, 4 H), 2.17–1.96 (5s, 5 × 3 H), 1.44, 1.21 (2s, 2 × 3 H), 1.25 (d, 3 H, *J* 6.0), 1.20 (d, 3 H, *J* 6.8), 0.97 (s, 3 H), 0.96 (d, 3 H, *J* 5.8), 0.78 (d, 3 H, *J* 7.4), 0.77 (s, 3 H); ESIMS *m*/*z* 1241 (M^+ + H_2O, 100%), 1223 (M^+, 68.7), 538 (52.5) (Calc. for $C_{65}H_{90}O_{22}{\cdot}2H_2O$: C, 61.98; H, 7.52. Found: C, 61.77; H, 7.44%).

Diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-benzoyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-acetyl-6-*O*-benzoyl-β-D-glucopyranoside 40. Yield 87%; $[a]_D^{22}$ −43.9 (*c* 1.2, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.07–7.41 (m, 10 H), 5.34–5.23 (m, 3 H), 5.14 (dd, 1 H, *J* 2.0, 3.2), 5.11

(dd, 1 H, *J* 3.4, 10.0), 4.96–4.75 (m, 6 H), 4.64 (d, 1 H, *J* 8.0), 4.50–4.19 (m, 3 H), 3.95–3.84 (m, 3 H), 3.74 (m, 1 H), 3.52–3.42 (m, 3 H), 2.16, 2.07, 2.05, 2.02, 1.87, 1.86 (6s, 6 × 3 H), 1.21 (d, 3 H, *J* 6.2), 1.14 (d, 3 H, *J* 6.3), 0.96–0.79 (m, 12 H); ESIMS *m*/*z* 1376 (M^+ + 2Na + 1, 7.7%), 1353 (M^+ + Na + 1, 7.3), 647 (22.3), 301 (60.0), 105 (100) (Calc. for $C_{71}H_{92}O_{24}\cdot 2H_2O$: C, 62.44; H, 7.08. Found: C, 62.68; H, 7.05%).

Diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-benzoyl-α-L-rhamnopyranosyl-(1→3)-2-*O*-acetyl-4-*O*-benzoyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-acetyl-6-*O*-benzoyl-β-D-glucopyranoside 41. Yield 66% (recovered **14**, 20%); $[\alpha]_D^{22}$ −27.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$) 8.10–7.17 (m, 25 H), 5.44–5.21 (m, 9 H), 5.06–5.02 (m, 2 H), 4.94–4.74 (m, 6 H), 4.63 (d, 1 H, *J* 8.0), 4.60 (d, 1 H, *J* 1.5), 4.52–4.34 (m, 3 H), 4.22 (dd, 1 H, *J* 3.3, 9.5), 4.05–3.79 (m, 6 H), 3.49–3.34 (m, 3 H), 2.20, 2.07, 2.04, 1.94, 1.90, 1.89, 1.80 (7s, 7 × 3 H), 1.28–0.95 (m, 18 H), 0.79 (d, 3 H, *J* 8.2), 0.78 (s, 3 H); ESIMS *m*/*z* 2308 (M^+ + K + Na, 9.6%), 1976 (M^+, 17.0), 1008 (100), 479 (45.5), 414 (33.7) (Calc. for $C_{106}H_{126}O_{36}\cdot 2H_2O$: C, 63.27; H, 6.51. Found: C, 63.07; H, 6.50%).

Typical procedure for the one-pot synthesis of saponins 36–41

A mixture of a trichloroacetimidate **7**–**9** (≈100 mg, 2.3 equiv.), a thioglycoside **10**–**12** (2.0 equiv.), and 4 Å MS (100 mg) in dry CH_2Cl_2 (6 mL) was stirred at room temperature under argon for 0.5 h, and then cooled to −78 °C. At this temperature, a solution of TMSOTf (0.3 equiv.) in dry CH_2Cl_2 was added. The mixture was stirred for an additional 30 min and then warmed up to −20 °C. To the above mixture was added a solution of a saponin acceptor **13**, **14** (1.0 equiv.) in CH_2Cl_2 (2 mL) followed by NIS (2.0 equiv.). After being stirred for 1 h, the reaction mixture was quenched with Et_3N, and then filtered through a pad of Celite. The filtrate was concentrated. The residue was purified by silica gel column chromatography (petroleum spirit–EtOAc, 1 : 3–1 : 2) to afford the fully protected saponin **36**–**41** as a white solid. The amounts of the reactants and the yields of the products were calculated based on saponin acceptors **13**, **14**.

Typical procedure for removal of the protecting groups of saponins 36–39

A fully protected saponin **36**–**39** (≈100 mg) was dissolved in 80% HOAc (5 mL) and the solution was stirred at 80 °C for 3 h. The solvent was then coevaporated with toluene to give a residue, which was then suspended in MeOH–THF–H_2O (6 mL; 1 : 1 : 1). To the above suspension was added NaOH (40 mg) and the mixture was stirred at 40 °C overnight. The solution was neutralized with Dowex 50 (H^+) resin, and then filtered. The filtrate was concentrated. The residue was purified by silica gel column chromatography (MeOH–CH_2Cl_2, 1 : 4) to give the saponin **1**–**4** as a white solid.

Diosgenyl β-D-glucopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→4)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside 1. Yield 82%; $[\alpha]_D^{24}$ −70.5 (*c* 0.31, MeOH) {lit.,[2a] $[\alpha]_D^{24}$ −69.4 (*c* 0.11, pyridine)}; ^{1}H NMR (400 MHz; C_5D_5N) 6.35 (s, 1 H), 5.81 (s, 1 H), 5.24 (d, 1 H, *J* 4.7), 5.18 (d, 1 H, *J* 7.5), 4.99 (m, 1 H), 4.94–4.89 (m, 2 H), 4.82 (d, 1 H, *J* 2.9), 4.66–4.59 (m, 3 H), 4.48 (m, 1 H), 4.42–4.28 (m, 5 H), 4.25 (t, 1 H, *J* 9.0), 4.19–4.15 (m, 4 H), 4.07 (t, 1 H, *J* 8.5), 3.98 (d, 1 H, *J* 11.6), 3.82 (m, 1 H), 3.72 (m, 1 H), 3.57–3.43 (m, 3 H), 2.74 (dd, 1 H, *J* 4.1, 12.3), 2.66 (t, 1 H, *J* 12.0), 1.70 (d, 3 H, *J* 5.9), 1.60 (d, 3 H, *J* 5.9), 1.07 (d, 3 H, *J* 7.0), 0.98 (s, 3 H), 0.76 (s, 3 H), 0.63 (d, 3 H, *J* 5.3); ^{13}C NMR (100 MHz; C_5D_5N) 140.99, 121.99, 109.45, 107.02, 102.28, 102.16, 100.56, 85.56, 81.29, 78.75 (×2), 78.24, 78.16 (×2), 77.65, 77.20, 76.82, 74.32, 73.05, 72.74 (×2), 72.14, 71.52, 69.73, 68.79, 67.05, 63.08, 62.64, 61.45, 56.82, 50.48, 42.16, 40.64, 40.05, 39.16, 37.68, 37.32, 32.49 (×2), 32.01, 31.87, 30.79, 30.35, 29.45, 21.30, 19.59, 18.83, 18.56, 17.51, 16.52, 15.22; ESIMS *m*/*z* 1071 (M^+ + K + 1, 12.5%), 1054 (M^+ + Na, 100).

Diosgenyl α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→4)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside 2. Yield 81%; $[\alpha]_D^{24}$ −104.4 (*c* 0.32, MeOH) {lit.,[2b] $[\alpha]_D^{24}$ −104.7 (*c* 0.55, MeOH)}; ^{1}H NMR (400 MHz; C_5D_5N) 6.35 (s, 1 H), 6.23 (s, 1 H), 5.78 (s, 1 H), 5.25 (d, 1 H, *J* 3.4), 4.93–4.87 (m, 3 H), 4.85 (s, 1 H), 4.80 (s, 1 H), 4.59 (m, 1 H), 4.51–4.42 (m, 4 H), 4.40–4.20 (m, 5 H), 4.20–4.11 (m, 3 H), 3.98 (m, 1 H), 3.81 (m, 1 H), 3.56–3.43 (m, 3 H), 2.75–2.61 (m, 2 H), 1.71 (d, 3 H, *J* 6.5), 1.53 (d, 6 H, *J* 6.1), 1.07 (d, 3 H, *J* 6.8), 0.98 (s, 3 H), 0.76 (s, 3 H), 0.62 (d, 3 H, *J* 4.1); ^{13}C NMR (100 MHz; C_5D_5N) 141.97, 121.97, 109.44, 103.48, 102.39 (×2), 100.53, 81.28, 80.58, 78.24, 78.14, 77.91 (×2), 77.19, 74.32, 74.19, 73.46, 73.04 (×3), 72.82, 72.69, 70.59, 69.73, 68.51, 67.04, 63.07, 61.40, 56.81, 50.47, 42.15, 40.63, 40.03, 39.15, 37.67, 37.32, 32.49, 32.38, 31.99, 31.86, 30.77, 30.34, 29.44, 21.28, 19.58, 19.06, 18.83, 18.61, 17.50, 16.51, 15.21; ESIMS *m*/*z* 1055 (M^+ + K + 1, 61.7%), 1083 (M^+ + Na, 100).

Diosgenyl β-D-glucopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranoside 3. Yield 87%; $[\alpha]_D^{24}$ −69.1 (*c* 0.41, MeOH) {lit,.[2a] $[\alpha]_D^{24}$ −62.9 (*c* 0.17, pyridine)}; ^{1}H NMR (400 MHz; C_5D_5N) 5.86 (s, 1 H), 5.24 (d, 1 H, *J* 3.4), 5.21 (d, 1 H, *J* 7.8), 5.00 (m, 1 H), 4.90 (d, 1 H, *J* 7.7), 4.70–4.64 (m, 2 H), 4,49–4.41 (m, 3 H), 4,39–4.16 (m, 7 H), 4.09–4.00 (m, 2 H), 3.93 (t, 1 H, *J* 8.2), 3.81 (m, 1 H), 3.72 (m, 1 H), 3.63 (m, 1 H), 3.51 (dd, 1 H, *J* 2.7, 10.3), 3.43 (t, 1 H, *J* 10.3), 2.63 (dd, 1 H, *J* 2.7, 12.5), 2.37 (t, 1 H, *J* 12.0), 1.69 (d, 3 H, *J* 6.2), 1.07 (d, 3 H, *J* 6.9), 0.83 (s, 3 H), 0.76 (s, 3 H), 0.62 (d, 3 H, *J* 4.9); ^{13}C NMR (100 MHz; C_5D_5N) 141.03, 121.89, 109.42, 106.80, 102.64, 102.09, 85.27, 80.25, 78.74, 77.55, 78.40, 77.64, 77.30, 76.80, 76.60, 75.72, 72.80, 72.22, 71.56, 68.66, 67.02, 63.02, 62.70, 61.62, 56.81, 50.42, 42.12, 40.61, 40.03, 39.45, 37.59, 37.20, 32.42, 32.33, 31.96, 31.80, 30.74, 30.35, 29.41, 21.28, 19.55, 18.56, 17.49, 16.53, 15.20; ESIMS *m*/*z* 1809 ($2M^+$ + K, 18.2%), 1793 ($2M^+$ + Na, 9.3), 924 (M^+ + K, 100), 908 (M^+ + Na, 45.7).

Diosgenyl α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranoside 4. Yield 88%; $[\alpha]_D^{24}$ −96.5 (*c* 0.30, MeOH); ^{1}H NMR (400 MHz; C_5D_5N) 6.23 (s, 1 H), 5.79 (s, 1 H), 5.25 (d, 1 H, *J* 3.4), 4.96 (m, 1 H), 4.88 (d, 1 H, *J* 8.2), 4.82 (s, 1 H), 4.52–4.43 (m, 4 H), 4.39 (t, 2 H, *J* 8.8), 4.30 (m, 1 H), 4.23 (t, 1 H, *J* 8.9), 4.16 (m, 1 H), 4.14 (t, 1 H, *J* 8.9), 4.01 (dd, 1 H, *J* 2.7, 12.3), 3.91 (t, 1 H, *J* 8.9), 3.80 (m, 1 H), 3.61 (d, 1 H, *J* 8.9), 3.50 (dd, 1 H, *J* 2.7, 11.6), 3.42 (t, 1 H, *J* 11.0), 2.62 (dd, 1 H, *J* 2.7, 12.5), 2.37 (t, 1 H, *J* 12.0), 1.61 (d, 3 H, *J* 6.1), 1.52 (d, 3 H, *J* 6.1), 1.06 (d, 3 H, *J* 6.8), 0.84 (s, 3 H), 0.76 (s, 3 H), 0.62 (d, 3 H, *J* 4.8); ^{13}C NMR (100 MHz; C_5D_5N) 141.04, 121.88, 109.42, 103.34, 102.65, 102.29, 81.24, 80.44, 78.37, 77.84, 77.34, 76.68, 75.76, 74.13, 73.55, 73.15, 73.02, 72.78, 70.54, 68.42, 67.01, 63.02, 61.60, 56.80, 50.42, 42.12, 40.60, 40.02, 39.44, 37.59, 37.20, 32.41, 32.34, 31.96, 31.79, 30.74, 30.34, 29.41, 21.27, 19.55, 19.06, 18.60, 17.48, 16.52, 15.19; ESIMS *m*/*z* 1777 ($2M^+$ + K, 14.8%), 1761 ($2M^+$ + Na, 22.1), 908 (M^+ + K, 100), 892 (M^+ + Na, 92.3), 870 (M^+ + 1, 25.8).

Typical procedure for removal of the protecting groups of saponins 40–41

To a suspension of the fully protected saponin **40** or **41** (≈100 mg) in dry MeOH (8 mL) was added a catalytic amount of NaOMe (5 mg). After being stirred at room temperature overnight, the mixture was neutralized with Dowex 50 (H^+) resin, and then filtered. The filtrate was concentrated. The residue was purified by silica gel column chromatography (MeOH–CH_2Cl_2, 1 : 4) to give the saponin **5** or **6** as a white solid.

Diosgenyl α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranoside 5. Yield 90%; $[a]_D^{24}$ −99.9 (*c* 0.18, MeOH) {lit.,[2d] $[a]_D^{24}$ −93.6 (pyridine)}; ^{1}H NMR (400 MHz; C_5D_5N) 6.01 (s, 1 H), 5.83 (s, 1 H), 5.30 (d, 1 H, *J* 4.8), 4.98 (m, 1 H), 4.88 (d, 1 H, *J* 8.2), 4.79 (s, 1 H), 4.71 (br d, 1 H), 4.69–4.60 (m, 2 H), 4.56 (dd, 1 H, *J* 2.7, 9.5), 4.48–4.40 (m, 3 H), 4.24–4.11 (m, 4 H), 3.92 (t, 1 H, *J* 8.2), 3.84 (m, 1 H), 3.57 (m, 1 H), 3.51 (dd, 1 H, *J* 2.7, 11.6), 3.43 (t, 1 H, *J* 10.2), 2.67 (dd, 1 H, *J* 3.4, 12.9), 2.39 (t, 1 H, *J* 12.0), 1.62 (d, 3 H, *J* 6.1), 1.58 (d, 3 H, *J* 6.1), 1.07 (d, 3 H, *J* 6.8), 0.84 (s, 3H), 0.76 (s, 3 H), 0.62 (d, 3 H, *J* 4.8); ^{13}C NMR (100 MHz; C_5D_5N) 141.05, 121.92, 109.41, 104.43, 102.92, 102.51, 81.24, 79.87, 78.45, 78.33, 77.10, 76.81, 75.65, 74.34, 72.94 (×2), 72.57, 72.43, 70.85, 70.19, 67.01, 63.03, 61.65, 56.81, 50.41, 42.12, 40.61, 40.03, 39.43, 37.59, 37.22, 32.42, 32.35, 31.96, 31.79, 30.75, 30.34, 29.41, 21.27, 19.53, 18.76, 18.66, 17.48, 16.52, 15.19; ESIMS *m*/*z* 1761 ($2M^+ + Na$, 35.6%), 892 ($M^+ + Na$, 100), 870 ($M^+ + 1$, 97.7).

Diosgenyl α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranoside 6. Yield 82%; $[a]_D^{22}$ −87.0 (*c* 0.19, MeOH) {lit.,[2d] $[a]_D^{22}$ −85.4 (pyridine)}; ^{1}H NMR (400 MHz; C_5D_5N) 5.98 (s, 1 H), 5.91 (s, 2 H), 5.82 (s, 1 H), 5.29 (d, 1 H, *J* 3.4), 4.97 (m, 1 H), 4.93 (d, 1 H, *J* 8.2), 4.86 (s, 1 H), 4.72 (s, 2 H), 4.70–4.55 (m, 4 H), 4.53–4.30 (m, 8 H), 4.26–4.13 (m, 5 H), 3.94 (t, 1 H, *J* 8.2), 3.86 (m, 1H), 3.66 (m, 1 H), 3.51 (d, 1 H, *J* 9.5), 3.42 (t, 1 H, *J* 10.2), 2.68 (dd, 1 H, *J* 2.7, 12.9), 2.40 (t, 1 H, *J* 12.4), 1.62 (d, 3 H, *J* 6.0), 1.56 (d, 3 H, *J* 6.1), 1.51 (d, 3 H, *J* 6.1), 1.45 (d, 3 H, *J* 6.1), 1.07 (d, 3 H, *J* 6.8), 0.84 (s, 3 H), 0.76 (s, 3 H), 0.62 (d, 3 H, *J* 4.1); ^{13}C NMR (100 MHz; C_5D_5N) 141.07, 121.92, 109.44, 103.80 (×2), 102.88 (×2), 102.57, 81.27, 79.78, 78.77, 78.38 (×3), 77.20, 76.85, 75.68, 74.53, 74.32, 73.37, 72.90 (×2), 72.64, 72.51 (×2), 72.09, 70.88, 70.83, 70.21, 70.08, 67.03, 63.03, 61.73, 56.82, 50.43, 42.14, 40.62, 40.04, 39.46, 37.61, 37.23, 32.43, 32.36, 31.97, 31.81, 30.79, 30.34, 29.42, 21.28, 19.57, 18.78, 18.64 (×3), 17.49, 16.53, 15.20; ESIMS *m*/*z* 1200 ($M^+ + K$, 31.7%), 1184 ($M^+ + Na$, 100).

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References

1 (*a*) A. M. Rouhi, *Chem. Eng. News*, 1995, Sept. 11, p. 28; (*b*) K. Hosttetmann and A. Marston, *Saponins*, Cambridge University Press, 1995; (*c*) *Advances in Experimental Medicine and Biology*, Vol. 404: *Saponins Used in Traditional and Modern Medicine*, ed. G. R. Waller and K. Yamasaki, Plenum Press, New York, London, 1996.
2 (*a*) S. Chen and J. K. Snyder, *J. Org. Chem.*, 1989, **54**, 3679; (*b*) Y. Hirai, S. Sanada, Y. Ida and J. Shoji, *Chem. Pharm. Bull.*, 1986, **34**, 82; (*c*) K. Y. Jung, J. C. Do and K. H. Son, *Han'guk Yongyang Siklyong Hakhoechi*, 1993, **22**, 313 (*Chem. Abstr.*, 1994, **121**, 31075z); (*d*) S. B. Mahato, N. P. Sahu and B. C. Pal, *Indian J. Chem., Sect. B*, 1978, **16**, 350.
3 S. Deng, B. Yu, J. Xie and Y. Hui, *J. Org. Chem.*, 1999, **64**, 7265, and references cited therein.
4 (*a*) B. Yu, H. Yu, Y. Hui and X. Han, *Tetrahedron Lett.*, 1999, **40**, 8591; (*b*) S. Deng, B. Yu, Y. Hui, H. Yu and X. Han, *Carbohydr. Res.*, 1999, **317**, 53; (*c*) S. Deng, B. Yu and Y. Hui, *Tetrahedron Lett.*, 1998, **39**, 6511; (*d*) C. Li, B. Yu, M. Liu and Y. Hui, *Carbohydr. Res.*, 1998, 306, 189; (*e*) J. T. Randolph and S. J. Danishefsky, *J. Am. Chem. Soc.*, 1995, **117**, 5693.
5 R. R. Schmidt, (*a*) *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 212; (*b*) *Adv. Carbohydr. Chem. Biochem.*, 1994, **50**, 21.
6 P. J. Garegg, *Adv. Carbohydr. Chem. Biochem.*, 1995, **52**, 170.
7 (*a*) K. Toshima and K. Tatsuta, *Chem. Rev.*, 1993, **93**, 1503; (*b*) G.-J. Boons, *Contemp. Org. Synth.*, 1996, **3**, 173; (*c*) O. Hinsgaul, *J. Carbohydr. Chem.*, 1995, **14**, 1043.
8 (*a*) H. Yamada, T. Harada and T. Takahashi, *J. Am. Chem. Soc.*, 1994, **116**, 7919; (*b*) H. Yamada, T. Harada, H. Miyazaki and T. Takahashi, *Tetrahedron Lett.*, 1994, **35**, 3979; (*c*) H. Yamada, K. Tetsuya and T. Takahashi, *Tetrahedron Lett.*, 1999, **40**, 4581.
9 K. Fukase, H. Winarno and S. Kusumoto, *Chem. Express*, 1993, **8**, 409.
10 I. Kitagawa, N. I. Back, K. Ohashi, M. Sakagami, M. Yoshikawa and H. Shibuya, *Chem. Pharm. Bull.*, 1989, **37**, 1131.
11 A. M. P. van Steijn, M. Jetten, J. P. Kamerling and J. F. G. Vliegenthart, *Recl. Trav. Chim. Pays-Bas*, 1989, **108**, 374.
12 Thioglycoside **11** was prepared by a procedure similar to that for the preparation of allyl 2-*O*-acetyl-4-*O*-benzoyl-α-L-rhamnopyranoside **18**: F.-I. Auzanneau, F. Forooghian and B. M. Pinto, *Carbohydr. Res.*, 1996, **291**, 21.
13 G. O. Aspinall, A. M. Crane, D. M. Gammon, I. H. Ibrahim, N. K. Khare, D. Chatterjee, B. Rivoire and P. J. Brennan, *Carbohydr. Res.*, 1991, **216**, 337.
14 T. Ogawa and H. Yamamoto, *Agric. Biol. Chem.*, 1985, **49**, 475.
15 B. Yu, H. Yu, Y. Hui and X. Han, *Synlett*, 1999, 753.
16 (*a*) J. M. Lassaletta, K. Carlsson, P. J. Garegg and R. R. Schmidt, *J. Org. Chem.*, 1996, **61**, 6873; (*b*) D. Qiu and R. R. Koganty, *Tetrahedron Lett.*, 1997, **38**, 961.
17 A. K. Ray, U. B. Maddali, A. Roy and N. Roy, *Carbohydr. Res.*, 1990, **197**, 93.
18 R. R. Schmidt and J. Michel, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 731.
19 (*a*) D. A. Leigh, J. P. Smart and A. M. Truscello, *Carbohydr. Res.*, 1995, **276**, 417; (*b*) F. Belot and J.-C. Jacquinet, *Carbohydr. Res.*, 1996, **290**, 79.
20 M. O. Contour, J. Defaye, M. Little and E. Wong, *Carbohydr. Res.*, 1989, **193**, 283.
21 (*a*) D. R. Mootoo, P. Konradsson, U. Udodong and B. Fraser-Reid, *J. Am. Chem. Soc.*, 1988, **110**, 5583; (*b*) G. H. Veeneman and J. H. van Boom, *Tetrahedron Lett.*, 1990, **31**, 275; (*c*) Z. Zhang, I. R. Ollmann, X.-S. Ye, R. Wischnat, T. Baasov and C.-H. Wong, *J. Am. Chem. Soc.*, 1999, **121**, 734.
22 F. Weygand and H. Ziemann, *Justus Liebigs Ann. Chem.*, 1962, **657**, 179.
23 (*a*) K. Takeo, K. Nagayoshi, K. Nishimura and S. Kitamura, *J. Carbohydr. Chem.*, 1994, **13**, 1159; (*b*) O. Kanie, Y. Ito and T. Ogawa, *J. Am. Chem. Soc.*, 1994, **116**, 12073; (*c*) P. Konradsson, U. E. Udodong and B. Fraser-Reid, *Tetrahedron Lett.*, 1990, **31**, 4313; (*d*) G. H. Veeneman, S. H. van Leeuwan and J. H. van Boom, *Tetrahedron Lett.*, 1990, **31**, 1331.