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Gold(I)-Catalyzed Glycosylation with Glycosyl *ortho*-Alkynylbenzoates as Donors: General Scope and Application in the Synthesis of a Cyclic Triterpene Saponin

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Dedicated to Professor Yongzheng Hui on the occasion of his 70th birthday

Abstract: Glycosyl *ortho*-alkynylbenzoates have emerged as a new generation of donors for glycosidation under the catalysis of gold(I) complexes such as $Ph_3PAuOTf$ and $Ph_3PAuNTf_2$ (Tf = trifluoromethanesulfonate). A wide variety of these donors, including 2-deoxy sugar and sialyl donors, are easily prepared and shelf stable. The glycosidic coupling yields with alcohols are generally excellent; even direct coupling with the poorly nucleophilic amides gives satisfactory yields. Moreover, excellent α-selective glycosylation with a 2-deoxy sugar donor and β-selective sialylation have been realized. Application of the present glycosylation protocol in the efficient synthesis of a cyclic triterpene tetrasaccharide have further demonstrated the versatility and efficacy of this new method, in that a novel chemoselective glycosylation of the carboxylic acid and a new one-pot sequential glycosylation sequence have been implemented.

Keywords: glycosylation · gold · homogeneous catalysis · sialylation · triterpene saponin

Introduction

Glycosylation to construct glycosidic linkages is the central theme in the synthesis of oligosaccharides and glycoconjugates, which play important roles in numerous biological processes.[1,2] In fact, chemists have studied glycosylation chemistry for over a century, and dozens of glycosylation protocols associated with hundreds of their variants have been developed.[1,2] However, it is still not an easy task in building many of the glycosidic linkages, especially compared to the synthesis of the phosphodiester and amide linkages occurring respectively in the other two fundamental biopolymers (i.e., nucleic acids and peptides). The limited accessibility to homogeneous oligosaccharides and glycoconjugates still remains as a major impediment to the study of the function of carbohydrates.[2]

The overwhelmingly applied glycosylation approach employs substitution of a leaving group on the anomeric carbon of a glycosyl donor with an acceptor (a nucleophile). Categorized by the leaving groups, which determine largely the glycosylation conditions, the major glycosylation protocols employ the following types of glycosyl donors: glycosyl halides;[3–5] thioglycosides;[6] trichloroacetimidates;[7] phosphate/phosphite derivatives;[8,9] sulfoxides;[10] glycals;[11] 1-acyl-,[12] 1-carbonates,[13] and variants; *n*-pentenyl glycosides;[14] orthoesters;[15] 1,2-anhydro sugars;[16] and glycosyl diazirines.[17] More recently, 1-hydroxyl sugars,[18] 1-(2′-carboxy)benzyl sugars,[19] glycosyl iodides,[20] and glycosyl thioimidates[21] have also attracted additional attention.

Most of these glycosyl donors demand, mechanistically, a stoichiometric amount of the promoter to assist the departure of the leaving group. Most of these promoters are expensive and toxic, such as the heavy metal salts for glycosyl

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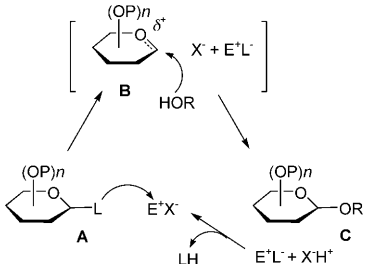
halides, thiophilic reagents for thioglycosides, and dehydrating reagents for 1-hydroxyl sugars. In addition, the stoichiometric promoter could be detrimental to a glycosylation reaction with multifunctional acceptors. In this regard, glycosyl trichloroacetimidates and phosphites are exceptional; in a wide scope, they are capable of being activated for glycosidation by a catalytic amount of a Lewis acid as promoter.

A speculation about the catalytic cycle of a glycosylation reaction is simplified as shown in Scheme 1, in which the re-



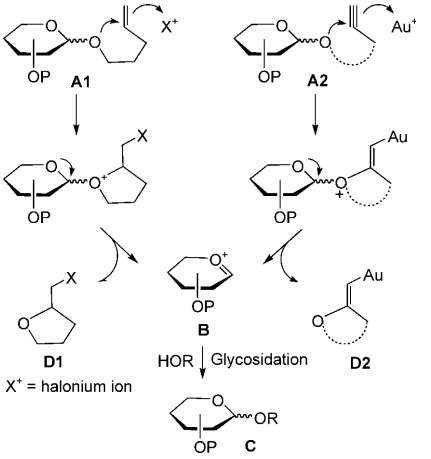
Scheme 1. A catalytic version of the glycosylation reaction (P = protecting group).

generation of the promoter E^+X^- requires the protonated leaving group (LH; the H^+ is from the acceptor HOR) to be an inert species that neither interferes with the promoter E^+X^- nor competes with the acceptor for glycosidation of the oxocarbenium **B**. Evidently, the LH generated from glycosyl trichloroacetimidates is $NH_2(C{=}O)CCl_3$, and from glycosyl phosphites $HOP(OR)_2$, which fulfill largely these requirements. Occasionally, $NH_2(C{=}O)CCl_3$ could still be competitive with poorly nucleophilic or highly stereo-demanding acceptors.[22,23d,l] In this circumstance, glycosyl *N*-phenyltrifluoroacetimidates demonstrate an advantage as glycosyl donors that generate $PhNH(C{=}O)CF_3$ instead.[23] A problem related to these donors that bear such leaving groups is their shelf stability. In fact, a few of the 'armed'[24] glycosyl trichloroacetimidates and phosphites could barely be purified and stored, and therefore could only be used directly after preparation.

We recently disclosed a novel catalytic glycosylation protocol with glycosyl *ortho*-hexynylbenzoates, which are stable, as donors, and $Ph_3PAuOTf$ (Tf = trifluoromethanesulfonate) as a catalyst,[25a] and which was highlighted in the total synthesis of *N*,*N*,*N*-trimethyl-D-glucosamine (TMG) chitotriomycin.[25b] In this full account, we demonstrate the great generality and versatility of this new glycosylation method.

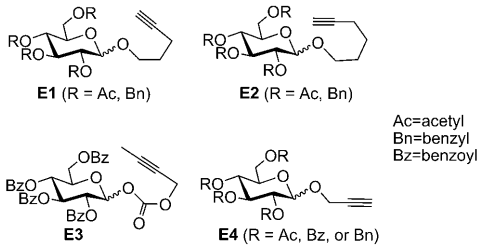
Results and Discussion

The evolution of glycosyl alkynylbenzoates as glycosylation donors: Recent studies have shown that cationic gold complexes are highly carbophilic Lewis acids that activate C–C multiple bonds (especially triple bonds) toward nucleophilic attack.[26] Meanwhile, these complexes, particularly gold(I) complexes, possess little oxophilic character, thus displaying good functional-group compatibility and low air and moisture sensitivity.[26] We envisioned that sugar derivatives analogous to *n*-pentenyl glycosides,[14,24] one of the major types of glycosyl donors or its variants (such as glycosyl pentenoates, 6-phenyl-5-hexynoates, and *gem*-dimethyl-4-pentenyl glycosides)[27–29] by positioning a C≡C triple bond in the leaving group (e.g., **E1**, **E2**, and **E3**) might be able to be activated by a gold complex to undergo glycosidation (Scheme 2). One obvious advantage of using a gold complex



Scheme 2. Analogy of the proposed new glycosylation protocol to the conventional glycosylation reaction with *n*-pentenyl glycosides as donors.

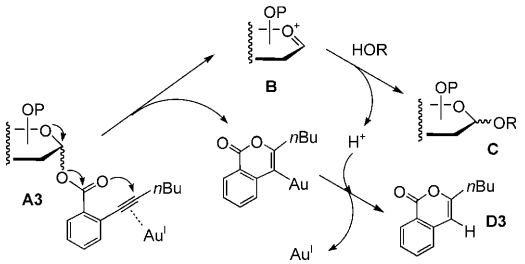
as promoter would be its inertness toward the oxo groups enriched in the carbohydrate substrates. In addition, protonation of the resulting Au species **D2** (by the acceptor HOR) would regenerate the active gold(I) to ensure a catalytic cycle of the glycosidation.



We then prepared several variants of the *n*-pentenyl glycosides, such as **E1**, **E2**, and **E3**, which possess a C≡C triple bond γ or δ to the *exo*-anomeric oxygen (data not shown). However, these glycosides stayed intact in the presence of an alcohol and a variety of the gold complexes (e.g., $AuCl_3$, PPh_3AuOTf, and PPh_3AuNTf_2) even at elevated temperatures (heated to reflux in CH_2Cl_2). Upon exposure to moisture, trace amounts of the methyl ketone products (from **E1** and **E2**) were detected, thus indicating that activation of the C≡C triple bond did take place but was not strong enough

for receiving a nucleophilic attack by the *exo*-anomeric oxygen.

From another viewpoint, we speculated that glycosidation of **E1**, **E2**, or **E3** would require the generation of an *exo*-methylene penta- or hexacyclic derivative (**D2**); this was unfavorable compared to the formation of a tetrahydrofuran **D1** from the *n*-pentenyl glycosides (Scheme 2). To force the glycosidation to proceed, the leaving group should be able to be converted into a more stable methylene derivative **D2**. We thus attempted to introduce aromaticity into the leaving group. Alkynylbenzoates turned out to be a good choice that would be converted into an isocoumarin derivative upon leaving behind a glycosyl oxocarbenium **B** for glycosidation (Scheme 3). Coincidentally, alkanol *ortho*-alkynylbenzoates have just been introduced as alkylating agents in the presence of $Hg(OTf)_2$ or $Ph_3PAuCl/AgOTf$.[30]

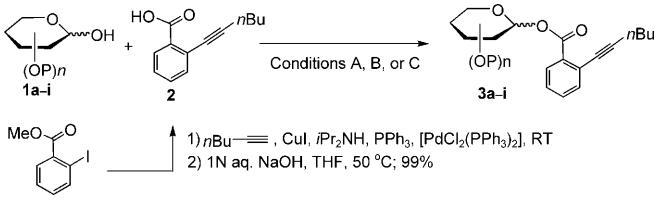


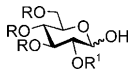
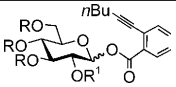
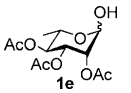
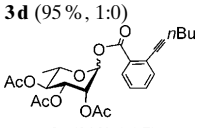
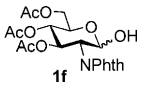
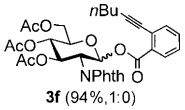
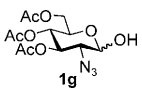
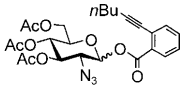
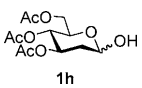
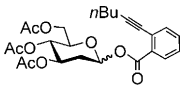
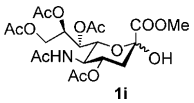
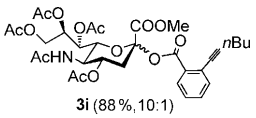
Scheme 3. The proposed new glycosylation reaction with glycosyl *ortho*-alkynylbenzoates as donors and gold(I) as catalyst.

It should be noted that Imagawa and co-workers have reported that perbenzylglucopyranosyl alkynoates could undergo glycosidation under the catalysis of $Hg(OTf)_2$.[31a] Hotha and co-workers have described that 'armed' propargyl glycosides such as **E4** (when R = Bn) could also undergo glycosidation in the presence of $AuCl_3$ (0.03 equiv $AuCl_3$, acetonitrile, 60 °C), whereas the 'disarmed' ones could not.[31b] More recently, they found that under stronger conditions (0.1 equiv $AuBr_3$, acetonitrile, 70 °C) 'armed' methyl glycosides could also undergo glycosidation,[31d] thereby implying the gold(III) catalyst activates the *exo*-anomeric oxygen instead of the C≡C triple bond.

Preparation of glycosyl *ortho*-alkynylbenzoates: 1-OH sugars (**1**) are common saccharide building blocks in preparative carbohydrate chemistry that are precursors to the widely applied glycosyl trichloroacetimidates and phosphites. *ortho*-Hexynylbenzoic acid (**2**) was easily prepared from the cheap methyl 2-iodobenzoate in two steps and in nearly quantitative yield (Table 1).[32] Condensation of lactol derivative **1** with benzoic acid **2** could be effected under many ester-forming conditions. Thus, a number of the glycosyl *ortho*-alkynylbenzoates (**3a–i**), including those of the 2-deoxyglucose and sialic acid derivatives (**3h** and **3i**), were readily prepared. Some selected preparative conditions and outcomes are given in Table 1.

Table 1. Preparation of glycosyl *ortho*-hexynylbenzoates **3a–i**.



Entry	Lactol	Conditions[a]	Glycosyl benzoate (yield, β/α)
			
1	**1a** (R = R^1 = Ac)	A	**3a** (97 %, 1:1.2)
2	**1b** (R = R^1 = Bz)	A	**3b** (98 %, 1.4:1)
3	**1b**	B	**3b** (97 %, 1:1.2)
4	**1c** (R = R^1 = Bn)	B	**3c** (97 %, 1:1.5)
5	**1d** (R = Bn, R^1 = Bz)	B	**3d** (95 %, 1:0)
6	 **1e**	B	 **3e** (96 %, 1:1.7)
7	 **1f**	A	 **3f** (94 %, 1:0)
8	 **1g**	B	 **3g** (99 %, 8.5:1)
9	 **1h**	B	 **3h** (95 %, 1.8:1)
10	 **1i**	C	 **3i** (88 %, 10:1)

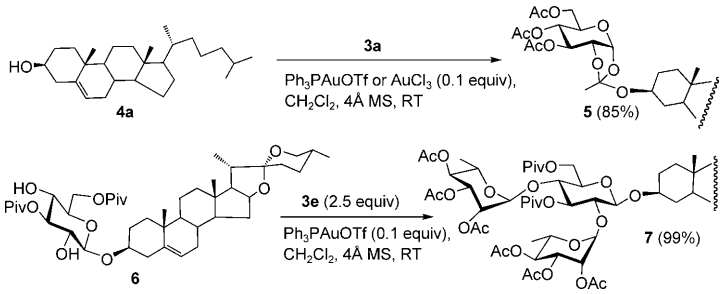
[a] Conditions A: DCC, DMAP, CH_2Cl_2, at RT. Conditions B: EDCI, DMAP, DIPEA, CH_2Cl_2, at RT. Conditions C: 2,4,6-trichlorobenzoyl chloride, DMAP, iPr_2NH, toluene, at RT.

The aldose derivatives **1a–h** were converted conveniently into the corresponding glycosyl *ortho*-hexynylbenzoates (**3a–h**) in excellent yields (>94 %) under the action of dicyclohexylcarbodiimide (DCC) (dimethylaminopyridine (DMAP), CH_2Cl_2, at RT) or 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI) (DMAP, *N,N*-diisopropylethylamine (DIPEA), CH_2Cl_2, at RT). Other conditions could also effect the condensation, but led to lower yields (≈80 %, data not shown), such as benzoyl chloride formation followed by acylation (**2**, $SOCl_2$, heated to reflux; then Et_3N, DMAP, CH_2Cl_2, at RT) or treatment of the glycosyl bromides with benzoic acid **2** under phase-transfer conditions ($BnEt_3N^+Cl^-$, K_2CO_3, H_2O, CH_2Cl_2, at RT). However, preparation of the sialyl *ortho*-hexynylbenzoate **3i** did not succeed under all these conditions. Finally, compound **3i** was obtained in a high yield of 88 % under the Yamaguchi conditions (2,4,6-trichlorobenzoyl chloride, DMAP,

iPr_2NH, toluene, at RT).[33] The α/β ratio in the glycosyl *ortho*-hexynylbenzoate products is mainly dependent on the nature of the starting sugars. Thus, for 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-D-glucose (**1d**), the 2-*N*-Phth- and 2-azido-glucose derivatives (**1f** and **1g**), and the *N*-acetylneuraminic acid (Neu5Ac) tetraacetate (**1i**), the β products were obtained exclusively or predominantly (Table 1, entries 5, 7, 8, and 10). Varying the condensation conditions could also affect slightly the α/β ratio in the products (entries 2 and 3). These α/β anomers are difficult to separate on a large scale; nevertheless, they behaved similarly well in the following glycosidation reactions. Also worth noting is the stability of these glycosyl *ortho*-hexynylbenzoates, including the 2-deoxyglucose derivative **3h**, which remained intact on the shelf for at least ten months.

With these glycosyl *ortho*-hexynylbenzoates (**3a–i**) readily available and well characterized,[32,34] we then examined their glycosidation reaction with a wide range of acceptors under a variety of conditions.

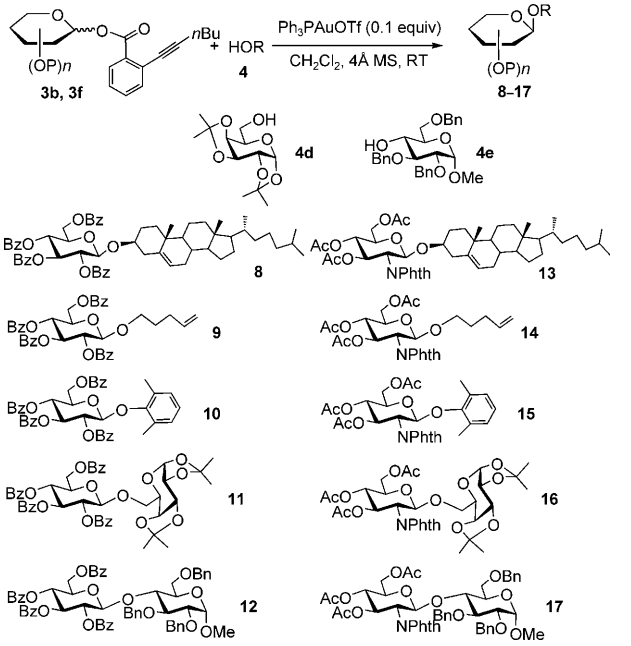
Glycosylation with donors bearing a neighboring participating group (3a, 3b, 3d–f): We first tried the glycosylation reaction of 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl *ortho*-hexynylbenzoate (**3a**) and cholesterol (**4a**) (Scheme 4). In the presence of $AuCl_3$ (0.1 equiv; CH_2Cl_2, 4 Å molecular sieves (MS), at RT), the major product turned out to be the orthoester **5** (85%). With PPh_3AuOTf as a catalyst instead, orthoester **5** was still the major product, but it decomposed readily afterwards. However, 2,3,4-tri-*O*-acetyl-L-rhamnopyranosyl *ortho*-hexynylbenzoate (**3e**) behaved as an excellent donor, which coupled with the β-glucopyranoside-2,4-diol **6**[35a,b] under the catalysis of PPh_3AuOTf (0.1 equiv; CH_2Cl_2, 4 Å MS, at RT) to provide trisaccharide **7** in nearly quantitative yield, which after deprotection is the natural saponin dioscin that possesses a variety of bioactivities.[35]



Scheme 4. Glycosylation with peracetyl glycosyl *ortho*-hexynylbenzoates **3a** and **3e**.

A ready alternative to avoid the orthoester formation in glycosylation is to replace the 2-*O*-acetyl group on the donor with a more sterically demanding acyl group,[36a] such as the benzoyl group.[36b] Indeed, glycosylation of cholesterol (**4a**) with 2,3,4,6-tetra-*O*-benzoyl-D-glucopyranosyl *ortho*-hexynylbenzoate (**3b**, 1.2 equiv) under the previous conditions (0.1 equiv PPh_3AuOTf, CH_2Cl_2, 4 Å MS, at RT) provided the desired β-glycoside **8** nearly quantitatively (Table 2, entry 1). Then a small panel of alcohols, including

Table 2. Glycosylation with glycosyl *ortho*-hexynylbenzoates **3b** and **3f**.



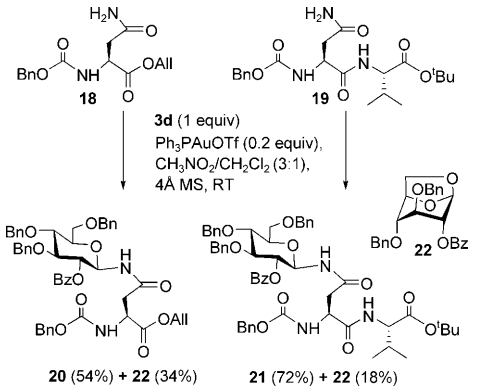
Entry	Donor	Acceptor	Product	Yield [%][b]
1	**3b**	cholesterol (**4a**)[a]	**8**	98
2	**3b**	4-penten-1-ol (**4b**)	**9**	98
3	**3b**	2,6-dimethylphenol (**4c**)	**10**	97
4	**3b**	**4d**	**11**	99
5	**3b**	**4e**	**12**	81 (98)[c]
6	**3f**	**4a**	**13**	99
7	**3f**	**4b**	**14**	99
8	**3f**	**4c**	**15**	91
9	**3f**	**4d**	**16**	99
10	**3f**	**4e**	**17**	63 (93)[c]

[a] A similar result was obtained with PPh_3AuNTf_2 as the catalyst. [b] Isolated yield. [c] Recovery yield.

n-pentenol (**4b**), 2,6-dimethylphenol (**4c**), glucose-6-OH derivative (**4d**), and glucose-4-OH derivative (**4e**), were tested as the representative acceptors for glycosylation with **3b** under similar conditions. All these coupling reactions proceeded cleanly within three hours. With **4b–4d** as acceptors the desired β-glycosides **9–11** were obtained in >97% yield (entries 2–4). With the sterically hindered **4e** as acceptor, the coupling product **12** was isolated in 81% yield and the remaining **4e** was recovered completely (entry 5). In comparison, in a recent report glycosylation of **4e** with methyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-D-glucopyranoside under a powerful promotion system (Me_2S_2/Tf_2O) provided the coupled disaccharide **12** in 67% yield.[37] By employing 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranosyl *ortho*-hexynylbenzoate (**3f**) as the donor, similar results were obtained for the glycosylation of the alcohols **4a–4e** (entries 6–10).[25a]

It should be noted that the coupling of **3b** and cholesterol (**4a**) as a model reaction could not proceed under the action of AgOTf, $Cu(OTf)_2$, $Pd(OAc)_2$, $PtCl_2$, TMSOTf (TMS = trimethylsilyl), $BF_3{\cdot}OEt_2$, TfOH, or $Bi(OTf)_3$, with the starting **3b** being fully recovered.[38]

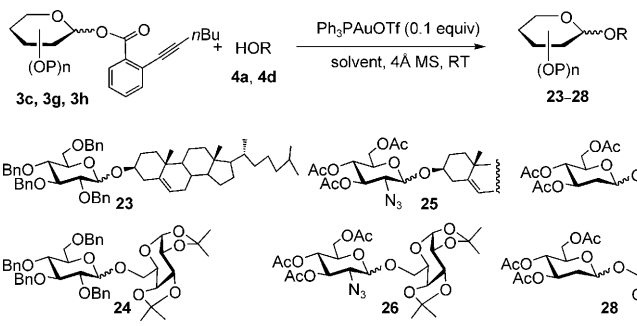
Construction of the *N*-glycosidic linkage of amides is important in the synthesis of *N*-glycopeptides; however, direct *N*-glycosylation is difficult due to the poor nucleophilicity of the amide nitrogen.[10,18b] Only recently, direct *N*-glycosylation of an amide was carried out by employing glycosyl trifluoroacetimidates as donors.[23d,m] To explore the efficiency of the present glycosylation protocol, we examined the direct *N*-glycosylation of the asparagine derivatives **18** and **19** with 3,4,6-tri-*O*-benzyl-2-*O*-benzoyl-D-glucopyranosyl *ortho*-hexynylbenzoate (**3d**). Under the catalysis of 0.2 equiv of $Ph_3PAuOTf$ (or $Ph_3PAuNTf_2$) in CH_3NO_2/CH_2Cl_2 (3:1) at RT, the glycosylation of amides **18** and **19** with **3d** (1.0 equiv) provided the corresponding β-*N*-glycosides **20** and **21** in a good yields of 54 and 72%, respectively.[23d] The major byproduct was the 1,6-anhydride **22** derived from the donor (Scheme 5).



Scheme 5. *N*-Glycosylation of amides with glycosyl *ortho*-hexynylbenzoate **3d**.

Glycosylation with donors without neighboring participating group (3c, 3g, and 3h): Donors without a neighboring participating group ('armed') are more active than those with a participating acyl group at 2-OH ('disarmed'), although they lead to α/β anomers by means of glycosidation of the corresponding sugar oxocarbenium **B** intermediate (Scheme 1). Thus, not surprisingly, coupling of cholesterol (**4a**) and sugar alcohol **4d** with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl *ortho*-hexynylbenzoate **3c** under the catalysis of $Ph_3PAuOTf$ (0.1 equiv) in CH_2Cl_2 at RT provided the corresponding glycosides **23** and **24** in nearly quantitative yields and 1:1 ratios of the α,β-anomers (Table 3, entries 1 and 3). It is well known that ether as a solvent, which might coordinate to the sugar oxocarbenium **B** to favorably form an equatorial oxonium ion (due to the reverse anomeric effect), leads to α-selective glycosylation.[1a,39] Evidently, coupling of alcohols **4a** and **4d** with *ortho*-hexynylbenzoate **3c** in Et_2O provided the corresponding glycosides **23** and **24** with good α selectivity (α/β = 4.4:1 and 5.3:1, respectively). Nevertheless, the present glycosylation reaction in Et_2O proceeded much less efficiently relative to the reaction in CH_2Cl_2, as it provided the coupled glycosides **23** and **24** in only around 70% yields, with complete recovery of the remaining acceptors (entries 2 and 4). This might be attributed to the transient coordination of Et_2O with the active gold(I) species. Similar results were obtained with 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-D-glucopyranosyl *ortho*-hexynylbenzoate **3g** as donors (entries 5–8). When 3,4,6-tri-*O*-acetyl-2-deoxy-D-glucopyranosyl *ortho*-hexynylbenzoate **3h** was used as donor to couple with alcohols **4a** and **4d** under similar conditions, all the reactions went smoothly (either in CH_2Cl_2 or Et_2O) and provided the corresponding glycosides **27** and **28** in excellent yields (98%) and similar α/β ratios (1.7:1 to 2.7:1, entries 9–12). These results demonstrate that the 2-deoxy sugar donors are more active than the corresponding 2-azido and 2-benzyloxy sugar donors for glycosidation.

Table 3. Glycosylation with glycosyl *ortho*-hexynylbenzoates **3c**, **3g**, and **3h**.

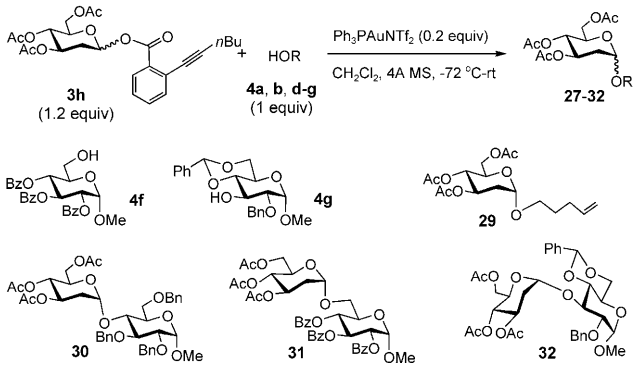


Entry	Donor	Acceptor	Product	Solvent	Yield [%][a] (α/β ratio)[b]
1	**3c**	**4a**	**23**	CH_2Cl_2	98 (1:1)
2				Et_2O	70 (4.4:1)
3	**3c**	**4d**	**24**	CH_2Cl_2	99 (1.2:1)
4				Et_2O	74 (5.3:1)
5	**3g**	**4a**	**25**	CH_2Cl_2	98 (2.5:1)
6				Et_2O	72 (8.8:1)
7	**3g**	**4d**	**26**	CH_2Cl_2	98 (2.7:1)
8				Et_2O	95 (10.2:1)
9	**3h**	**4a**	**27**	CH_2Cl_2	98 (2.5:1)
10				Et_2O	98 (1.7:1)
11	**3h**	**4d**	**28**	CH_2Cl_2	98 (2.7:1)
12				Et_2O	98 (2.0:1)

[a] Isolated yield. [b] The α/β ratio was determined by ^1H NMR spectroscopic measurements.

Moreover, we found that with $Ph_3PAuNTf_2$ (0.2 equiv) as the catalyst, the glycosidation of **3h** proceeded in CH_2Cl_2 (−72 °C to RT) with extremely high yields and α selectivity (Table 4). The coupling with both primary alcohols (cholesterol (**4a**), 4-penten-1-ol (**4b**), and sugar-6-ols **4d** and **4f**) and the sterically demanding secondary alcohols (sugar-4-ol **4e** and -3-ol **4g**) all afforded the corresponding coupled products (**27**–**32**) in nearly quantitative yields (>97%) and with nearly complete α selectivity (α/β > 30:1). The present superior results for α-selective glycosidation of 2-deoxy sugars are unprecedented.[40,41] In comparison, in a recent report the coupling of alcohol **4f** with 3,4,6-tri-*O*-acetyl-2-deoxy-D-glucopyranosyl trichloroacetimidate (TMSOTf, CH_2Cl_2, −78 °C) provided the disaccharide **31** in 90% yield and with an α/β ratio of 4:1.[41a] The α selectivity is known to be a result of the anomeric effect.[42] The present superior α selectivity suggests that the anomeric effect acts as the

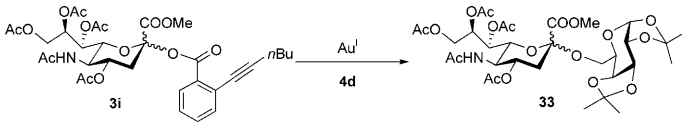
Table 4. Highly efficient α-selective glycosidation of **3h**.



Entry	Acceptor	Product	Yield [%][a] (α/β ratio)[b]
1	**4a**	**27α**	99 (α only)
2	**4b**	**29**	99 (α only)
3	**4d**	**28α**	99 (≈30:1)
4	**4e**	**30**	97 (α only)
5	**4f**	**31**	99 (≈30:1)
6	**4g**	**32**	99 (α only)

[a] Isolated yield. [b] The α/β ratio was determined by ^{1}H NMR spectroscopic measurements of the crude products.

Table 5. Sialylation of alcohol **4d** with **3i**.



Entry	Au^I (equiv)	Solvent	*T* [°C]	*t*	Yield [%][a] (α/β ratio)[b]
1	PPh_3AuOTf (0.1)	CH_2Cl_2	RT	5 min	83 (1:8.3)
2	PPh_3AuOTf (0.1)	CH_2Cl_2	−40	3 h	82 (1:6.3)
3	PPh_3AuOTf (0.2)	CH_2Cl_2	−78	6 h	79 (1:5.6)
4	PPh_3AuNTf_2 (0.1)	CH_2Cl_2	RT	5 min	80 (1:12.5)
5	PPh_3AuOTf (0.2)	CH_2Cl_2/CH_3CN (1:1)	RT	2 h	62 (5:4)
6	PPh_3AuOTf (0.4)	CH_2Cl_2/CH_3CN (1:1)	−78	7 h	72 (5:3)
7	PPh_3AuNTf_2 (0.4)	CH_2Cl_2/CH_3CN (1:1)	−78	7 h	77 (1:2)

[a] Isolated yield. [b] The α/β ratio was determined by ^{1}H NMR spectroscopic measurements.

sole or dominant element governing the stereoselectivity in the present reaction in that the oxocarbenium **B** is barely coordinated with other species, which include the solvent CH_2Cl_2, the isocoumarin **D3** derived from the leaving group, and the catalyst $Ph_3PAuNTf_2$ ($^-NTf_2$ is a more weakly coordinating anion than ^-OTf).[43]

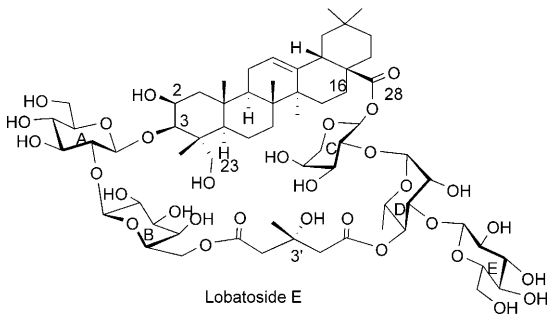
Sialylation: Sialylation to make the ketosidic linkages is one of the most challenging tasks in glycosylation chemistry.[44] The electron-withdrawing C1 carboxylic function, which disfavors the oxocarbenium formation, restricts glycosidation both electronically and sterically; moreover, an elimination to produce the 2,3-dehydroglycals can be a significant competing pathway. In fact, only limited glycosylation protocols are applicable for direct sialylation.[45] Those mainly include glycosylation with sialyl 2-sulfide,[46] xanthate,[47] phosphite,[48] and trifluoroacetimidate as donors.[49,50]

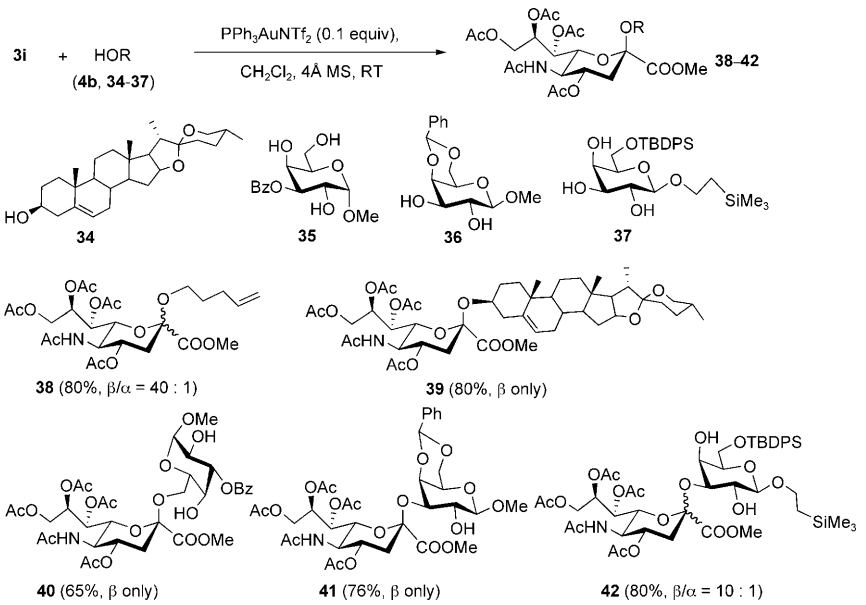
We found that sialyl 2-*ortho*-hexynylbenzoate **3i** behaved as an excellent donor in coupling with sugar alcohol **4d** in the presence of $Ph_3PAuOTf$ (0.1 equiv) in CH_2Cl_2 (Table 5). At room temperature, the reaction was completed in 5 min and provided the coupled disaccharide **33** in 83% yield in favor of the thermodynamically more stable β-anomer (α/β = 1:8.3, entry 1). With the commercially available and air-stable $Ph_3PAuNTf_2$ as catalyst, even better β selectivity was obtained (80%, α/β = 1:12.5, entry 4). At −78 °C, the reaction became sluggish; the formation of a comparable yield of the disaccharide **33** (79%) required 0.2 equiv of the catalyst for 6 h. The α/β selectivity was not much changed (α/β = 1:5.6, entry 3).

The α-selective sialylation with silalyl donors in the absence of a temporary directing group at the C3 position is usually affected by the nitrile solvent effect.[44,51] However, the present glycosylation protocol became inefficient when CH_3CN was introduced as a solvent. This might also be attributed to the coordination of CH_3CN with the gold(I) catalyst, although the α/β ratios was indeed remarkably increased (entries 5–7).

Since the excellent β-selective sialylation was observed in the coupling of the primary sugar alcohol **4d** with sialyl 2-*ortho*-hexynylbenzoate **3i** in the presence of $Ph_3PAuNTf_2$ in CH_2Cl_2, we then examined with more alcohols as acceptors, including *n*-pentenol (**4b**), the steroidal **34**, the galactose diol **36**, and the triols **35** and **37** (Scheme 6). All the reactions proceeded smoothly and provided the desired coupled products **38**–**42** in good yields (65–80%) and excellent β selectivity (α/β > 10:1). For the sialylation of galactose diol and triols (**35**–**37**), the reported regioselectivity as same as those with other types of the sialyl donors was obtained.[46a,e,47,49a,50a]

Application to the synthesis of a cyclic triterpene saponin: To further prove the usefulness of the present glycosylation protocol, we applied it to the total synthesis of a complex cyclic triterpene saponin **43**.[52] Cyclic triterpene saponins, such as Lobatoside E, constitute a very small family of the



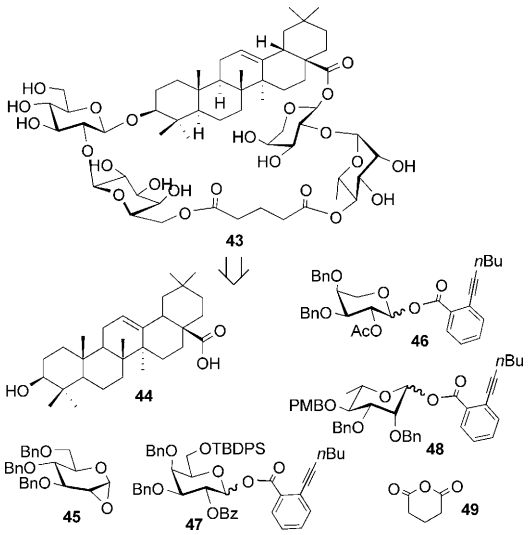


Scheme 6. β-Selective sialylation with sialyl 2-*ortho*-hexynylbenzoate **3i** as donor.

triterpene glycosides, which have two oligosaccharides flanking a pentacyclic triterpene bridged with 3-hydroxy-3-methyl glutarate. They show significant antitumor activities. We have recently achieved the first total synthesis of Lobatoside E,[53] in which a total of 73 steps were required and the five glycosidic linkages were constructed by the conventional methods with glycosyl trichloroacetimidates, glycosyl bromide, and thioglycoside as donors. Efficient synthesis toward simplified structures to decipher the structure–activity relationship and mechanism of action was an ongoing project in our lab. Compound **43** turned out naturally to be the first simplified structure to testify to the importance of the 2,23-dihydroxy group in the triterpene aglycone, the 3′-hydroxy and -methyl groups in the acyl moiety, and the terminal glucose (cf. Lobatoside E) to the antitumor activity. Removal of these structural elements would greatly shorten the synthetic steps relative to the total synthesis of the natural Lobatoside E.

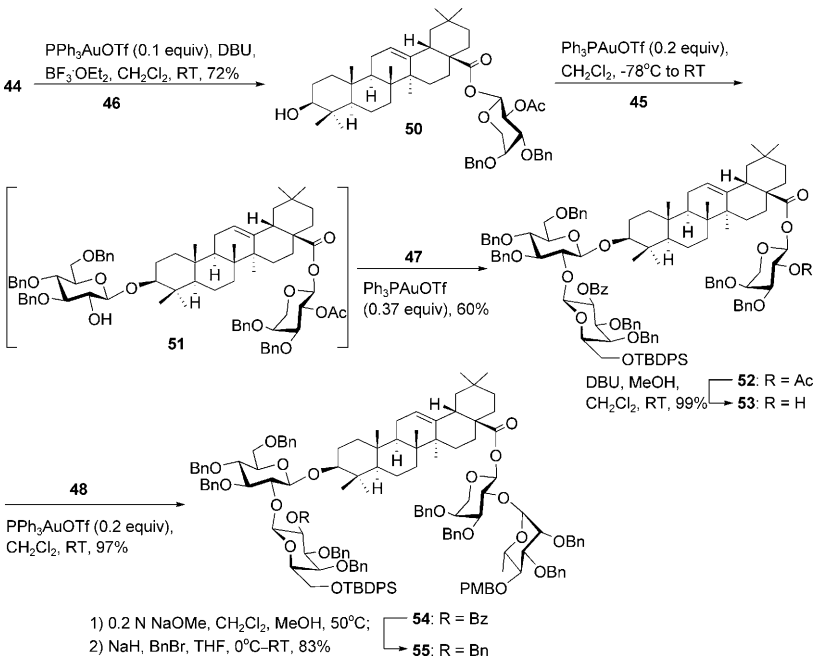
To realize a whole gold-catalyzed approach to the assembly of the sugar units in **43**, four sugar donors **45**–**48** were designed (Scheme 7). The arabinosyl, galactosyl, and rhamnosyl *ortho*-hexynylbenzoates **46**–**48** were readily prepared by condensation of the corresponding lactols with *ortho*-hexynylbenzoic acid **2** in excellent yields (>87%) in a manner similar to the preparation of donors **3a**–**h**.[32] 1,2-Anhydro-3,4,6-tri-*O*-benzyl-D-glucose (**45**)[54] was used as a donor because we have recently found that 1,2-anhydro sugar could undergo glycosidation smoothly under the catalysis of $Ph_3PAuOTf$,[55] and the resulting 2-OH would be subsequently glycosylated in a one-pot fashion with a glycosyl *ortho*-hexynylbenzoate under the action of the same gold catalyst. The global protecting-group strategy was adopted from the previous total synthesis of Lobatoside E,[53] thus the benzyl group was chosen as the permanent protecting group, and the acetyl, benzoyl, *tert*-butyldiphenylsilyl, and 4-methoxybenzyl groups were temporary protecting groups to facilitate the sequential assembly of the units.

Thus, the assembly of the cyclic triterpene saponin **43** commenced with a successful chemoselective glycosylation of the 28-carboxylic acid of the abundant oleanolic acid (**44**) with the arabinosyl *ortho*-hexynylbenzoate **46** ($Ph_3PAuOTf$ (0.1 equiv), $BF_3{\cdot}OEt_2$ (3.0 equiv), 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU; 2.0 equiv), CH_2Cl_2, 4 Å MS, at RT), thereby providing ester α-L-arabinoside **50** predominantly in a satisfactory 72% yield (Scheme 8). Such a chemoselective glycosylation of carboxylic acid in the presence of an alcohol has only been achieved with glycosyl bromides under phase-transfer conditions;[56] the corresponding 2-*O*-acetyl-3,4-di-*O*-benzyl-L-arabinopyranosyl bromide was unstable, thus was used uncharacterized after preparation.[53]

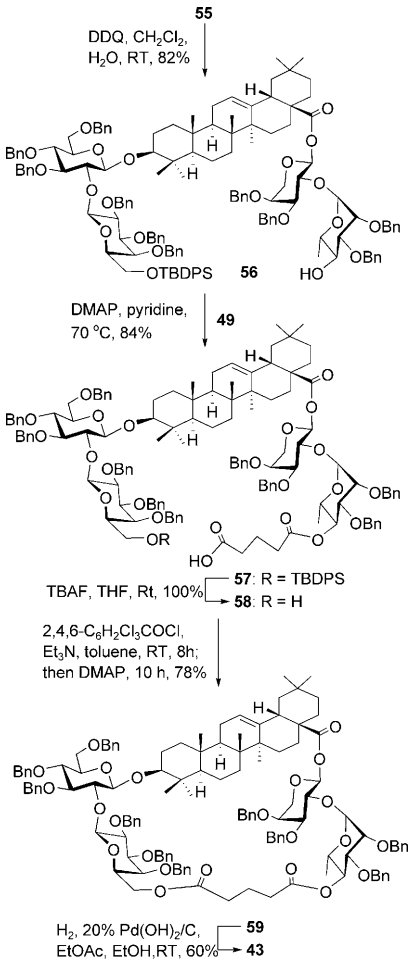


Scheme 7. The simplified cyclic triterpene saponin **43** and its retrosynthesis.

Then we examined the gold-catalyzed one-pot sequential glycosylation with the 1,2-anhydroglucose **45** and galactosyl *ortho*-hexynylbenzoate **47** to assemble the left-handed disaccharide. As expected, treatment of **50** with 1,2-anhydroglucose **45** in the presence of PPh_3AuOTf (0.2 equiv) (CH_2Cl_2, −78°C to RT) gave the desired 3-*O*-β-glucoside **51**. Subsequent addition of the *ortho*-hexynylbenzoate **47** and an addi-



Scheme 8. Assembly of tetrasaccharide **55**.



Scheme 9. Elaboration of the cyclic saponin **43**.

tional portion of PPh_3AuOTf (0.37 equiv) led to the desired trisaccharide **52** in a good 60% yield.

Removal of the 2-*O*-acetyl group on the arabinose unit in **52** with DBU (MeOH, CH_2Cl_2, at RT) gave **53**.[57] Glycosylation of the resulting 2-OH with the rhamnosyl *ortho*-hexynylbenzoate **48** under the standard gold-catalyzed conditions (0.2 equiv PPh_3AuOTf, 4 Å MS, CH_2Cl_2, at RT) proceeded smoothly and provided the tetrasaccharide **54** in nearly quantitative yield. Exchange of the 2-*O*-benzoyl group on the galactose unit in **54** with a benzyl group led to **55** (83% for two steps).

Tetrasaccharide **55** possesses two orthogonal protecting groups (*tert*-butyldiphenylsilyl (TBDPS) and *p*-methoxybenzyl (PMB)) at the two ends. Alternatively, deprotection of the 4-*O*-PMB group of the rhamnose unit with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) gave **56** (82%, Scheme 9). Treatment of alcohol **56** with glutaric anhydride **49** in the presence of DMAP in pyridine at 70°C provided ester **57** (84%). The 6-*O*-TBDPS group of the galactose unit in **57** was then cleaved with tertabutylammonium fluoride (TBAF) in THF to afford alcohol acid **58** (100%), which was subjected to macrocyclization under Yamaguchi conditions[33] to provide the cyclic glycoconjugate **59** in a satisfactory 78% yield. Finally, removal of the Bn groups by hydrogenolysis over $Pd(OH)_2/C$ furnished the target cyclic triterpene saponins **43** cleanly in 60% yield.

Thus, the cyclic triterpene saponin **43** was assembled with only 11 steps and in around 11% overall yield from six readily available building blocks by employing the present gold-catalyzed glycosylation as key steps.

Conclusion

Glycosyl *ortho*-alkynylbenzoates have been introduced as a new generation of donors for glycosidation under the catalysis of gold(I) complexes, such as $Ph_3PAuOTf$ and $Ph_3PAuNTf_2$. This new glycosylation protocol has shown significant merits: 1) the donors are easily prepared and shelf stable; 2) the glycosidic coupling yields are generally excellent; 3) the promotion is catalytic; 4) the promotion conditions are orthogonal to the conventional ones; 5) the reaction conditions are mild and neutral; and therefore 6) side reactions are minimal. The versatility of the present method has been demonstrated by the successful glycosylation of

amides, superior α-selective glycosidation of 2-deoxy sugars, and β-selective sialylation. Further evidence of the efficacy of the present method is provided by its application to the efficient synthesis of the complex cyclic triterpene glycoside **43**, in that a novel chemoselective glycosylation of carboxylic acid and a new one-pot sequential glycosylation sequence have been realized. However, the working mechanism of this new glycosylation protocol has not yet been validated, nor has a new solution for the general issue of the α/β selectivity been provided.

Experimental Section

General procedures: Please see the Supporting Information.

Preparation of compound 2: $[PdCl_2(PPh_3)_2]$ (4.20 g, 6.0 mmol), CuI (1144 mg, 6.0 mmol), and PPh_3 (3.14 g, 12.0 mmol) were added to methyl 2-iodobenzoate (18.0 mL, 120.0 mmol) in dry iPr_2NH (180 mL). After stirring at RT for 1 h under an Ar atmosphere, 1-hexyne (20.8 mL, 180.0 mmol) was slowly added at 0 °C. The mixture was allowed to stir at RT for 18 h (or at 60 °C for 6 h) and saturated NH_4Cl (400 mL) was added. After vigorously stirring for 30 min, petroleum ether (400 mL) was added and the phases separated. The aqueous layer was extracted with hexane/EtOAc (100:1), the combined organic layers were washed with H_2O and brine, dried over Na_2SO_4, then concentrated. The crude product was purified by column chromatography on silica gel (hexane/EtOAc 50:1) to provide methyl 2-hex-1-ynyl benzoate as a yellow oil (25.9 g, 99%). This oil was dissolved in THF (500 mL) and aqueous NaOH (1 N, 500 mL) was added. After stirring at 50 °C for 12 h, the solution was cooled to 0 °C and then acidified with concentrated HCl. After removal of THF by rotary evaporation, the residue was contracted with CH_2Cl_2 five times. The combined organic layers were dried over Na_2SO_4 and then concentrated to give **2**[58] as a yellow oil (24.2 g, 100%), which became a light yellow solid when stored at −18 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, J = 7.8 Hz, 1H), 7.57–7.44 (m, 2H), 7.36 (t, J = 7.2 Hz, 1H), 2.50 (t, J = 6.6 Hz, 2H), 1.70–1.45 (m, 4H), 0.96 ppm (t, J = 6.9 Hz, 3H).

Typical procedures for the preparation of glycosyl *ortho*-hexynylbenzoates

*Compound **3b** (Conditions A)*: A solution of lactol **1b** (1.08 g, 2.0 mmol), **2** (485 mg, 2.4 mmol), DMAP (366 mg, 3.0 mmol), and DCC (618 mg, 3.0 mmol) in dry CH_2Cl_2 (3 mL) was stirred for 3 h at RT, and was then diluted with CH_2Cl_2. The resulting mixture was filtered through Celite. The filtrates were washed with saturated $NaHCO_3$ solution and then concentrated in vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate 10:1) to provide **3b** as a white solid (1.42 g, 98%; β/α = 1.4:1). A small portion of the α,β-anomers were separated and characterized. Compound **3bα**: $[\alpha]_D^{27}$ = 98.3 (c = 4.1 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09–7.22 (m, 24H), 6.93 (d, J = 3.3 Hz, 1H), 6.32 (t, J = 10.2 Hz, 1H), 5.90 (t, J = 9.9 Hz, 1H), 5.73 (dd, J = 10.2, 2.7 Hz, 1H), 4.75–4.64 (m, 2H), 4.52 (dd, J = 12.3, 3.9 Hz, 1H), 2.49 (m, 2H), 1.58 (m, 2H), 1.45 (m, 2H), 0.91 ppm (t, J = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.0, 165.7, 165.3, 165.1, 163.9, 135.0, 133.5, 133.4, 133.3, 133.1, 132.4, 130.7, 129.9, 129.8, 129.7 (3C), 129.4, 128.8, 128.6, 128.5, 128.4, 128.3 (2C), 127.3, 125.3, 97.2, 90.0, 79.5, 70.6, 70.4, 70.4, 68.8, 62.3, 30.6, 22.0, 19.5, 13.6 ppm; HRMS (MALDI): m/z: calcd for $C_{47}H_{40}O_{11}$ $[M+Na]^+$: 803.2463; found: 803.2462. Compound **3bβ**: $[\alpha]_D^{27}$ = 54.2 (c = 4.5 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06–7.22 (m, 24H), 6.35 (d, J = 7.8 Hz, 1H), 6.03 (t, J = 9.3 Hz, 1H), 5.84 (m, 2H), 4.69 (dd, J = 12.3, 2.1 Hz, 1H), 4.53 (dd, J = 12.0, 4.2 Hz, 1H), 4.44 (m, 1H), 2.46 (t, J = 6.6 Hz, 2H), 1.61 (m, 2H), 1.49 (m, 2H), 0.94 ppm (t, J = 7.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.0, 165.6, 165.0 (2C), 163.3, 134.5, 133.4 (2C), 133.2, 133.0, 132.4, 130.8, 129.7 (2C), 129.4, 129.0, 128.6, 128.5, 128.3 (2C), 128.2, 127.1, 125.8, 97.3, 92.4, 78.9, 73.0, 72.8, 70.8, 68.9, 62.6, 30.5, 22.0, 19.4, 13.6 ppm; HRMS (MALDI): m/z: calcd for $C_{47}H_{40}O_{11}$ $[M+Na]^+$: 803.2463; found: 803.2479.

*Compound **3b** (Conditions B)*: A solution of lactol **1b** (2.16 g, 4.0 mmol), **2** (970 mg, 4.8 mmol), DMAP (488 mg, 4.0 mmol), EDCI (955 mg, 5.0 mmol), and DIPEA (1.3 mL, 7.2 mmol) in dry CH_2Cl_2 (4 mL) was stirred for 3 h at RT, and was then diluted with CH_2Cl_2. The resulting mixture was washed with saturated $NaHCO_3$ and brine, respectively. The filtrates were concentrated. The residue was purified by silica gel column chromatography (hexane/ethyl acetate 10:1) to provide **3b** as a white solid (2.82 g, 97%; β/α = 1:1.2).

*Compound **3i** (Conditions C)*: Triethylamine (0.58 mL, 4.18 mmol) and 2,4,6-trichlorobenzoylchloride (0.52 mL, 3.34 mmol) were added to a solution of **2** (338 mg, 1.67 mmol) in toluene at RT. After stirring at RT for 2 h, compound **1i** (820 mg, 1.67 mmol) in toluene was added, followed by the addition of DMAP (510 mg, 4.18 mmol) in toluene. After stirring for an additional 1 h, the mixture was concentrated. The residue was subjected to flash chromatography on silica gel (CH_2Cl_2/methanol 120:1) to provide **3i** as a white solid (992 mg, 88%; β/α = 10:1). A small portion of the α,β-anomers were separated and characterized. Compound **3iβ**: $[\alpha]_D^{20}$ = −12.5 (c = 0.6 in CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92–7.91 (m, 1H), 7.55–7.53 (m, 1H), 7.50–7.47 (m, 1H), 7.38–7.37 (m, 1H), 5.41–5.36 (m, 3H), 5.13–5.10 (m, 1H), 4.52 (dd, J = 13.0, 2.67 Hz, 1H), 4.22–4.15 (m, 3H), 3.82 (s, 3H), 2.73 (dd, J = 13.6, 5.1 Hz, 1H), 2.45 (t, J = 7.1 Hz, 2H), 2.20 (dd, J = 13.5, 11.6 Hz, 1H), 2.16 (s, 3H), 2.03 (s, 3H), 1.88 (s, 3H), 1.87 (s, 3H), 1.62–1.58 (m, 2H), 1.51–1.46 (m, 2H), 0.95 ppm (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.9, 170.6, 170.2, 170.0, 166.3, 163.4, 134.7, 132.4, 130.4, 130.0, 127.3, 125.2, 98.2, 97.0, 79.0, 72.9, 71.1, 68.6, 67.6, 62.1, 53.2, 49.5, 36.1, 30.6, 23.1, 22.0, 20.8, 20.7, 19.5, 13.6 ppm; HRMS (ESI): m/z: calcd for $C_{33}H_{41}NO_{14}Na$ $[M+Na]^+$: 698.2419; found 698.2426. Compound **3iα**: $[\alpha]_D^{20}$ = +3.1 (c = 1.2 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92–7.91 (m, 1H), 7.52–7.51 (m, 1H), 7.48–7.44 (m, 1H), 7.36–7.32 (m, 1H), 5.82 (d, J = 9.8 Hz, 1H), 5.41 (dd, J = 6.3, 2.2 Hz, 1H), 5.27–5.24 (m, 1H), 5.17 (td, J = 11.8, 5.0 Hz, 1H), 4.69 (dd, J = 10.8, 2.3 Hz, 1H), 4.42 (dd, J = 12.4, 2.8 Hz, 1H), 4.25 (q, J = 10.2 Hz, 1H), 4.13 (dd, J = 12.4, 6.0 Hz, 1H), 3.80 (s, 3H), 2.78 (dd, J = 13.3, 5.0 Hz, 1H), 2.47 (t, J = 7.1 Hz, 2H), 2.27 (dd, J = 13.2, 11.2 Hz, 1H), 2.11 (s, 3H), 2.10 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 1.91 (s, 3H), 1.64–1.58 (m, 2H), 1.53–1.47 (m, 2H), 0.95 ppm (t, J = 7.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.8, 170.5, 170.3, 170.0, 168.3, 163.5, 134.3, 132.1, 130.8, 130.1, 127.1, 125.0, 96.6, 96.4, 78.7, 73.8, 70.4, 68.8, 67.6, 62.1, 52.8, 49.0, 36.7, 30.6, 23.1, 22.0, 20.8, 20.7, 20.6, 19.4, 13.5 ppm; HRMS (ESI): m/z: calcd for $C_{33}H_{41}NO_{14}Na$ $[M+Na]^+$: 698.2419; found: 698.2416.

Typical procedure for the glycosylation with glycosyl *ortho*-hexynylbenzoates as donors (3b+4a→8): A freshly prepared solution of PPh_3AuOTf in CH_2Cl_2 (0.05 N, 0.2 mL) was added to a mixture of *o*-hexynylbenzoate **3b** (94 mg, 0.12 mmol), cholesterol **4a** (39 mg, 0.10 mmol), and 4 Å MS in dry CH_2Cl_2 (2 mL).[32,59] After stirring at RT for 3 h, the mixture was filtered through Celite. The filtrates were concentrated. The residue was purified by silica gel column chromatography (hexane/ethyl acetate 10:1) to provide **8**[60] as a white solid (95 mg, 98%).

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*Chemoselective glycosylation (**44**+**46**→**50**)*: DBU (0.85 mL, 5.82 mmol) was added to a stirred mixture of glycosyl benzoate **46** (1.62 g, 2.91 mmol), oleanolic acid **44** (1.57 g, 3.44 mmol), and 4 Å MS in CH_2Cl_2 (25 mL) at RT. After stirring for 20 min, $BF_3{\cdot}Et_2O$ (1.01 mL, 8.73 mmol) and a freshly prepared solution of $Ph_3PAuOTf$ in CH_2Cl_2 (0.06 M, 5 mL) was added sequentially. After stirring overnight, the mixture was filtered through Celite, and the filtrates were concentrated. The resulting residue was purified by silica gel column chromatography (toluene/EtOAc 30:1) to afford **50** (1.70 g, 72%) as a white foam. $[\alpha]_D^{20}$ = 30.3 (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.16 (m, 10H), 5.63 (d, J = 4.5 Hz, 1H), 5.30 (d, J = 3.3 Hz, 1H), 5.25 (t, J = 5.1 Hz, 1H), 4.66 (s, 2H), 4.59 (s, 2H), 4.13–4.07 (m, 1H), 3.76–3.68 (m, 2H), 3.52 (dd, J = 2.4, 11.4, 1H), 3.20 (br s, 1H), 2.85 (dd, J = 5.1, 14.4 Hz, 1H), 2.04, 1.12, 0.99, 0.90, 0.87, 0.78, 0.76 ppm (s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.8, 169.1, 143.3, 138.0, 137.9, 128.3, 128.2, 127.8, 127.7, 127.6, 127.4, 122.7, 91.2, 78.9, 75.1, 72.1, 71.7, 71.3, 69.3, 61.2, 55.3, 47.6, 46.9, 45.8, 41.8, 41.1,

39.3, 38.7, 38.5, 37.0, 33.8, 33.0, 32.0, 30.6, 28.1, 27.8, 27.2, 25.7, 23.5, 22.7, 20.8, 18.3, 17.0, 15.5, 15.3 ppm; HRMS (MALDI): *m/z*: calcd for $C_{51}H_{70}O_8Na$ $[M+Na]^+$: 833.4963; found: 833.4959.

*One-pot glycosylation (**50**+**45**+**47**→**52**)*: A freshly prepared solution of $Ph_3PAuOTf$ in CH_2Cl_2 (0.06 M, 0.45 mL) was added to a stirred mixture of **50** (105 mg, 0.129 mmol) and 4 Å MS in dry CH_2Cl_2 (5 mL). The mixture was stirred at RT for 30 min and was then cooled to −78 °C. A cooled solution (0 °C) of 1,2-anhydroglucose **45** in CH_2Cl_2 (5 mL), freshly prepared from 3,4,6-tri-*O*-benzyl-D-glucal (65 mg, 0.156 mmol),[54] was then added slowly by syringe. The resulting mixture was allowed to warm up naturally. After stirring overnight, a freshly prepared solution of $Ph_3PAuOTf$ in CH_2Cl_2 (0.06 M, 1.6 mL) and a solution of **47** in CH_2Cl_2 (230 mg, 5 mL, 0.26 mmol) were added sequentially. After stirring overnight, the mixture was filtered through Celite and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc 7:1) to afford **52** (148 mg, 60%) as a white foam. $[\alpha]_D^{24}=156.8$ ($c=1.1$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.87$ (d, $J=7.2$ Hz, 2H), 7.60 (t, $J=6.9$ Hz, 4H), 7.47–7.20 (m, 42H), 7.04 (brs, 2H), 5.68 (d, $J=4.5$ Hz, 1H), 5.65 (m, 1H), 5.08 (d, $J=10.8$ Hz, 1H), 4.97 (d, $J=8.1$ Hz, 1H), 4.69–4.38 (m, 13H), 4.24 (d, $J=8.1$ Hz, 1H), 4.14 (m, 2H), 3.96 (t, $J=9.6$ Hz, 1H), 3.75–3.48 (m, 12H), 2.97 (dd, $J=3.6$, 10.8 Hz, 1H), 2.86 (d, $J=10.8$ Hz, 1H), 2.09, 1.25, 1.09, 1.02, 0.92, 0.88, 0.87, 0.83, 0.77, 0.54 (s, each 3H), 1.08 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=175.8$, 169.2, 165.0, 143.3, 137.9, 135.5, 135.4, 129.7, 128.3, 128.2 (2C), 127.9, 127.7 (2C), 127.6 (2C), 127.4 (2C), 127.3, 100.5, 85.7, 77.3, 77.1, 74.6, 74.5, 73.2, 72.7, 72.0, 71.6, 71.5, 71.3, 69.2, 46.8, 41.6, 39.3, 39.0, 36.6, 33.0, 30.5, 27.5, 26.9, 25.6, 23.5, 20.8, 19.1, 17.0, 16.0, 15.2 ppm; HRMS (MALDI): *m/z*: calcd for $C_{121}H_{142}O_{19}SiNa$ $[M+Na]^+$: 1949.9807; found: 1949.9827.

*Standard glycosylation (**53**+**48**→**54**)*: A freshly prepared solution of $Ph_3PAuOTf$ in CH_2Cl_2 (0.06 M, 0.23 mL) was added to a stirred mixture of the glycosyl benzoate **48** (43 mg, 0.066 mmol), trisaccharide saponin **53** (85 mg, 0.045 mmol), and 4 Å MS in CH_2Cl_2 (5 mL) at RT. After stirring overnight, the mixture was filtered through Celite and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc 5:1) to afford **54** (102 mg, 97%) as a white foam. $[\alpha]_D^{25}=130.9$ ($c=1.1$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.88$ (d, $J=7.5$ Hz, 2H), 7.60 (t, $J=8.1$ Hz, 4H), 7.48–7.15 (m, 54H), 7.07–7.03 (m, 2H), 6.83 (d, $J=8.4$ Hz, 2H), 5.81 (d, $J=1.8$ Hz, 1H), 5.66 (dd, $J=9.9$, 8.1 Hz, 1H), 5.30 (brs, 1H), 5.10 (d, $J=11.1$ Hz, 1H), 4.99 (d, $J=7.8$ Hz, 1H), 4.82 (d, $J=10.8$ Hz, 2H), 4.71–4.39 (m, 18H), 4.26 (d, $J=7.8$ Hz, 1H), 4.16 (brs, 1H), 4.09 (t, $J=9.9$ Hz, 1H), 3.98 (t, $J=9.3$ Hz, 1H), 3.93 (br, 1H), 3.85–3.33 (m, 19H), 3.75 (s, 3H), 2.98 (dd, $J=4.2$, 10.8 Hz, 1H), 2.87 (dd, $J=12.9$, 3.0 Hz, 1H), 1.38 (d, $J=6.6$ Hz, 3H), 1.08 (s, 9H), 1.07, 0.94 (s, each 3H), 0.87 (s, 6H), 0.84, 0.77, 0.56 ppm (s, each 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=175.7$, 165.0, 159.1, 143.4, 138.9, 138.6, 138.5, 138.3, 138.2, 138.0, 137.9, 137.8, 135.5, 135.4, 133.3, 133.0, 132.6, 130.7, 130.2, 129.7, 129.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 126.9, 122.5, 104.2, 100.5, 97.9, 91.7, 90.8, 85.7, 80.1, 80.0, 79.8, 75.3, 75.1, 74.8, 74.6, 74.5, 74.4, 74.3, 73.3, 72.8, 72.6, 72.2, 72.1, 71.6, 71.2, 69.2, 68.8, 61.4, 59.5, 55.6, 55.2, 47.5, 46.8, 45.8, 41.6, 41.2, 39.3, 39.0, 38.5, 36.6, 33.8, 33.0, 32.8, 32.1, 30.6, 27.8, 27.5, 26.9, 25.9, 25.6, 23.5, 22.5, 19.1, 18.1, 17.9, 17.1, 16.0, 15.2 ppm; HRMS (MALDI): *m/z*: calcd for $C_{147}H_{170}O_{23}SiNa$ $[M+Na]^+$: 2354.1794; found: 2354.1760.

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[1] For seminal reviews on glycosylation chemistry, see: a) G. Wulff, G. Röhle, *Angew. Chem.* **1974**, *86*, 173–187; *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 157–170; b) H. Paulsen, *Angew. Chem.* **1982**, *94*, 184–201; *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 155–173; c) R. R. Schmidt, *Angew. Chem.* **1986**, *98*, 213–236; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 212–235; d) H. Kunz, *Angew. Chem.* **1987**, *99*, 297–311; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 294–308; e) K. Toshima, K. Tatsuta, *Chem. Rev.* **1993**, *93*, 1503–1531; f) C.-H. Wong, R. L. Halcomb, Y. Ichikawa, T. Kajimoto, *Angew. Chem.* **1995**, *107*, 569–593; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 521–546; g) G. J. Boons, *Tetrahedron* **1996**, *52*, 1095–1121; h) S. J. Danishefsky, M. T. Bilodeau, *Angew. Chem.* **1996**, *108*, 1482–1522; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1380–1419; i) B. G. Davis, *J. Chem. Soc. Perkin Trans. 1* **2000**, 2137–2160; j) P. H. Seeberger, W.-C. Haase, *Chem. Rev.* **2000**, *100*, 4349–4394; k) K. C. Nicolaou, H. Mitchell, *Angew. Chem.* **2001**, *113*, 1624–1672; *Angew. Chem. Int. Ed.* **2001**, *40*, 1576–1624.

[2] For recent reviews on glycosylation chemistry, see: a) A. V. Demchenko, *Synlett* **2003**, 1225–1240; b) D. P. Galonic, D. Y. Gin, *Nature* **2007**, *446*, 1000–1007; c) P. H. Seeberger, D. B. Werz, *Nature* **2007**, *446*, 1046–1051; d) X. Zhu, R. R. Schmidt, *Angew. Chem.* **2009**, *121*, 1932–1967; *Angew. Chem. Int. Ed.* **2009**, *48*, 1900–1934.

[3] Glycosyl chlorides and bromides: W. Koenigs, E. Knorr, *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 957–981.

[4] Glycosyl iodides: a) E. Fischer, H. Fisher, *Ber. Dtsch. Chem. Ges.* **1910**, *43*, 2521–2536; b) J. Thiem, B. Meyer, *Chem. Ber.* **1980**, *113*, 3075–3085.

[5] Glycosyl fluorides: T. Mukaiyama, Y. Murai, S. Shoda, *Chem. Lett.* **1981**, 431–432.

[6] Thioglycosides: R. J. Ferrier, R. W. Hay, N. Vethaviyasar, *Carbohydr. Res.* **1973**, *27*, 55–61.

[7] Glycosyl trichloroacetimidates: R. R. Schmidt, J. Michel, *Angew. Chem. Int. Ed. Eng.* **1980**, *19*, 731–732.

[8] Glycosyl phosphates: S. Hashimoto, T. Honda, S. Ikegami, *J. Chem. Soc. Chem. Commun.* **1989**, 613–619.

[9] Glycosyl phosphites: a) H. Kondo, Y. Ichikawa, C. H. Wong, *J. Am. Chem. Soc.* **1992**, *114*, 8748–8750; b) T. J. Martin, R. R. Schmidt, *Tetrahedron Lett.* **1992**, *33*, 6123–6126.

[10] Glycosyl sulfoxides: D. Kahne, S. Walker, Y. Cheng, D. van Engen, *J. Am. Chem. Soc.* **1989**, *111*, 6881–6882.

[11] Glycals: R. U. Lemieux, S. Levine, *Can. J. Chem.* **1962**, *40*, 1926–1932.

[12] 1-Acyl sugars: B. Helferich, E. Schmitz-Hillebrecht, *Chem. Ber.* **1933**, *66*, 378–383.

[13] 1-Carbonate sugars: S. Inaba, M. Yamada, T. Yoshino, Y. Ishido, *J. Am. Chem. Soc.* **1973**, *95*, 2062–2063.

[14] *n*-Pentenyl glycosides: B. Fraser-Reid, P. Konradsson, D. R. Mootoo, U. Udodong, *J. Chem. Soc. Chem. Commun.* **1988**, 823–825.

[15] Sugar orthoesters: a) N. K. Kochetkov, A. J. Khorlin, A. F. Bochkov, *Tetrahedron* **1967**, *23*, 693–707; b) N. K. Kochetkov, A. F. Bochkov, T. A. Sokolovsakaya, *Carbohydr. Res.* **1971**, *16*, 17–27.

[16] 1,2-Anhydro sugars: a) R. U. Lemieux, G. Huber, *J. Am. Chem. Soc.* **1953**, *75*, 4118–4119; b) R. U. Lemieux, G. Huber, *J. Am. Chem. Soc.* **1956**, *78*, 4117–4119.

[17] Glycosyl diazirines: K. Briner, A. Vasella, *Helv. Chim. Acta* **1989**, *72*, 1371–1382.

[18] a) H. M. Nguyen, Y. Chen, S. G. Duron, D. Y. Gin, *J. Am. Chem. Soc.* **2001**, *123*, 8766–8772; b) B. A. Garcia, D. Y. Gin, *J. Am. Chem. Soc.* **2000**, *122*, 4269–4279; c) B. A. Garcia, J. L. Poole, D. Y. Gin, *J. Am. Chem. Soc.* **1997**, *119*, 7597–7598; d) K. S. Kim, F. D. Baburao, J. Y. Baek, B.-Y. Lee, H. B. Jeon, *J. Am. Chem. Soc.* **2008**, *130*, 8537–8547.

[19] a) K. S. Kim, J. Park, Y. J. Lee, Y. S. Seo, *Angew. Chem.* **2003**, *115*, 475–478; *Angew. Chem. Int. Ed.* **2003**, *42*, 459–462; b) K. S. Kim, J. H. Kim, Y. J. Lee, Y. J. Lee, J. Park, *J. Am. Chem. Soc.* **2001**, *123*, 8477–8481.

[20] a) M. H. El-Badri, D. Willenbring, D. J. Tantillo, J. Gervay-Hague, *J. Org. Chem.* **2007**, *72*, 4663–4672; b) S. N. Lam, J. Gervay-Hague, *J. Org. Chem.* **2005**, *70*, 8772–8779; c) W. Du, J. Gervay-Hague, *Org. Lett.* **2005**, *7*, 2063–2065; d) S. N. Lam, J. Gervay-Hague, *Org. Lett.* **2002**, *4*, 2039–2042.

[21] a) A. V. Demchenko, N. N. Malysheva, C. De Meo, *Org. Lett.* **2003**, *5*, 455–458; b) A. V. Demchenko, P. Pornsuriyasak, C. De Meo,

N. N. Malysheva, *Angew. Chem.* **2004**, *116*, 3131–3134; *Angew. Chem. Int. Ed.* **2004**, *43*, 3069–3072; c) J. T. Smoot, P. Pornsuriyasak, A. V. Demchenko, *Angew. Chem.* **2005**, *117*, 7285–7288; *Angew. Chem. Int. Ed.* **2005**, *44*, 7123–7126.

[22] For examples, see: a) K. Larsen, C. E. Olsen, M. S. Motawia, *Carbohydr. Res.* **2008**, *343*, 383–387; b) G. J. S. Lohman, P. H. Seeberger, *J. Org. Chem.* **2004**, *69*, 4081–4093; c) L. A. Mulard, C. Corina, P. J. Philippe, *J. Carbohydr. Chem.* **2000**, *19*, 849–877; d) T. Zhu, G.-J. Boons, *Carbohydr. Res.* **2000**, *329*, 709–715; e) K. i. Shohda, T. Wada, M. Sekine, *Nucleosides Nucleotides* **1998**, *17*, 2199–2210; f) X. X. Zhu, M.-S. Cai, R.-L. Zhou, *Carbohydr. Res.* **1997**, *303*, 261–266; g) R. R. Schmidt, J. Michel, *J. Carbohydr. Chem.* **1985**, *4*, 141–169.

[23] For examples, see: a) B. Yu, H. Tao, *Tetrahedron Lett.* **2001**, *42*, 2405–2407; b) M. Adinolfi, G. Barone, A. Iadonisi, M. Schiattarella, *Tetrahedron Lett.* **2002**, *43*, 5573–5577; c) M. Li, X. Han, B. Yu, *J. Org. Chem.* **2003**, *68*, 6842–6845; d) H. Tanaka, Y. Iwata, D. Takahashi, M. Adachi, T. Takahashi, *J. Am. Chem. Soc.* **2005**, *127*, 1630–1631; e) E. Bedini, A. Carabellese, G. Barone, M. Parrilli, *J. Org. Chem.* **2005**, *70*, 8064–8070; f) S.-I. Tanaka, M. Takashina, H. Tokimoto, Y. Fujimoto, K. Tanaka, K. Fukase, *Synlett* **2005**, 2325–2328; g) B. S. Komarova, Y. E. Tsvetkov, Y. A. Knirel, U. Zahringer, G. B. Pier, N. E. Nifantiev, *Tetrahedron Lett.* **2006**, *47*, 3583–3587; h) M. Thomas, J.-P. Gesson, S. Papot, *J. Org. Chem.* **2007**, *72*, 4262–4264; i) D. B. Werz, B. Castagner, P. H. Seeberger, *J. Am. Chem. Soc.* **2007**, *129*, 2770–2771; j) D. Crich, O. Vinogradova, *J. Am. Chem. Soc.* **2007**, *129*, 11756–11765; k) N. Ding, C. Li, Y. Liu, Z. Zhang, Y. Li, *Carbohydr. Res.* **2007**, *342*, 2003–2013; l) M. Vasan, J. Rauvolfova, M. A. Wolfert, C. Leoff, E. L. Kannenberg, C. P. Quinn, R. W. Carlson, G.-J. Boons, *ChemBioChem* **2008**, *9*, 1716–1720; m) K. Tanaka, T. Miyagawa, K. Fukase, *Synlett* **2009**, 1571–1574.

[24] For the concept of 'armed'/'disarmed' donors, see: a) D. R. Mootoo, P. Konradsson, U. Udodong, B. Fraser-Reid, *J. Am. Chem. Soc.* **1998**, *120*, 5583–5584; b) B. Fraser-Reid, U. Udodong, Z. F. Wu, H. Ottosson, J. R. Merritt, C. S. Rao, C. Roberts, R. Madsen, *Synlett* **1992**, 927–942.

[25] a) Y. Li, Y. Yang, B. Yu, *Tetrahedron Lett.* **2008**, *49*, 3604–3608; b) Y. Yang, Y. Li, B. Yu, *J. Am. Chem. Soc.* **2009**, *131*, 12076–12077.

[26] For some recent reviews on gold-catalyzed reactions, see: a) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*, 3351–3378; b) A. Arcadi, *Chem. Rev.* **2008**, *108*, 3266–3325; c) Z. Li, C. Brouwer, C. He, *Chem. Rev.* **2008**, *108*, 3239–3265; d) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211; e) R. A. Widenhoefer, X. Han, *Eur. J. Org. Chem.* **2006**, 4555–4563.

[27] a) H. Kunz, P. Wernig, M. Schultz, *Synlett* **1990**, 631–632; b) J. C. Lopez, B. Fraser-Reid, *J. Chem. Soc. Chem. Commun.* **1991**, 159–161; c) T. J. Choi, J. Y. Baek, H. B. Jeon, K. S. Kim, *Tetrahedron Lett.* **2006**, *47*, 9191–9194.

[28] C. Murai, T. Itoh, M. Hanaoka, *Tetrahedron Lett.* **1997**, *38*, 4595–4598.

[29] M. Fortin, J. Kaplan, K. Pham, S. Kirk, R. B. Andrade, *Org. Lett.* **2009**, *11*, 3594–3597.

[30] a) H. Yamamoto, G. Pandey, Y. Asai, M. Nakano, A. Kinoshita, K. Namba, H. Imagawa, M. Nishizawa, *Org. Lett.* **2007**, *9*, 4029–4032; b) N. Asao, H. Aikawa, S. Tago, K. Umetsu, *Org. Lett.* **2007**, *9*, 4299–4302.

[31] a) H. Imagawa, A. Kinoshita, T. Fukuyama, H. Yamamoto, M. Nishizawa, *Tetrahedron Lett.* **2006**, *47*, 4729–4731; b) S. Hotha, S. Kashyap, *J. Am. Chem. Soc.* **2006**, *128*, 9620–9621; c) G. Sureshkumar, S. Hotha, *Tetrahedron Lett.* **2007**, *48*, 6564–6568; d) S. R. Vidadala, S. Hotha, *Chem. Commun.* **2009**, 2505–2507.

[32] See the Supporting Information for details.

[33] a) J. Inanaga, K. Hirata, H. Saeki, T. Kattsuki, M. Yamaguchi, *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989–1993; b) L. Thijs, D. M. Egenberger, B. Zwanenburg, *Tetrahedron Lett.* **1989**, *30*, 2153–2156.

[34] CCDC-746019 (**3aβ**), 746017 (**3gα**), and 746018 (**3hβ**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[35] a) B. Li, B. Yu, Y. Hui, M. Li, X. Han, K.-P. Fung, *Carbohydr. Res.* **2001**, *331*, 1–7; b) B. Yu, H. Tao, *J. Org. Chem.* **2002**, *67*, 9099–9102; c) Y. Wang, Y. Zhang, B. Yu, *ChemMedChem* **2007**, *2*, 888–891; d) Y. Wang, Y. Zhang, Z. Zhu, S. Zhu, Y. Li, M. Li, B. Yu, *Bioorg. Med. Chem.* **2007**, *15*, 2528–2532.

[36] a) T. Nukada, A. Berces, M. Z. Zgierski, D. M. Whitfield, *J. Am. Chem. Soc.* **1998**, *120*, 13291–13295; b) S. Deng, B. Yu, J. Xie, Y. Hui, *J. Org. Chem.* **1999**, *64*, 7265–7266.

[37] J. Tatai, P. Fugedi, *Org. Lett.* **2007**, *9*, 4647–4650.

[38] It has been well proved that Au^{I} activates the C≡C triple bond more strongly than Cu^{I} and Ag^{I}. See: H. V. R. Dias, J. A. Flores, J. Wu, P. Kroll, *J. Am. Chem. Soc.* **2009**, *131*, 11249–11255.

[39] For examples, see: a) A. Demchenko, T. Stauch, G.-J. Boons, *Synlett* **1997**, 818–819; b) M. Adinolfi, A. Iadonisi, A. Ravida, M. Schiattarella, *Tetrahedron Lett.* **2004**, *45*, 4485–4488; c) M. A. Oberli, P. Bindschadler, D. B. Werz, P. H. Seeberger, *Org. Lett.* **2008**, *10*, 905–908.

[40] a) C. H. Marzabadi, R. W. Frank, *Tetrahedron* **2000**, *56*, 8385–8417; b) D. Hou, T. L. Lowary, *Carbohydr. Res.* **2009**, *344*, 1911–1909.

[41] For recent examples, see: a) J. Park, T. J. Boltje, G.-J. Boons, *Org. Lett.* **2008**, *10*, 4367–4370; b) Y.-S. Lu, Q. Li, L.-H. Zhang, X.-S. Ye, *Org. Lett.* **2008**, *10*, 3445–3448.

[42] a) P. Deslongchamps, *Stereoelectronic Effects in Organic Chemistry*, Pergamon Press, Oxford, **1983**; b) E. Juaristi, G. Cuevas, *The Anomeric Effect*, CRC, Boca Raton, **1995**.

[43] a) S. M. Cornet, I. May, M. P. Redmond, A. J. Selvage, C. A. Sharrad, O. Rosnel, *Polyhedron* **2009**, *28*, 363–369; b) M. J. Muldoon, C. M. Gordon, I. R. Dunkin, *J. Chem. Soc. Perkin Trans. 2* **2001**, 433–435; c) D. J. Liston, Y. J. Lee, W. R. Scheidt, C. A. Reed, *J. Am. Chem. Soc.* **1989**, *111*, 6643–6648.

[44] a) K. Okamoto, T. Goto, *Tetrahedron* **1990**, *46*, 5835–5857; b) M. P. DeNinno, *Synthesis* **1991**, 583–593; c) G. J. Boons, A. V. Demchenko, *Chem. Rev.* **2000**, *100*, 4539–4566.

[45] Indirect sialylation mostly involves modified sialyl donors that have a participating functionality at C3, thus additional steps are required for installation and removal. See also ref. [44].

[46] For earlier reports, see: a) T. Murase, H. Ishida, M. Kiso, A. Hasegawa, *Carbohydr. Res.* **1988**, *184*, c1–c4; b) E. Kirchner, F. Thiem, R. Dernick, J. Heukeshoven, J. Thiem, *J. Carbohydr. Chem.* **1988**, *7*, 453–486; c) O. Kanie, M. Kiso, A. Hasegawa, *J. Carbohydr. Chem.* **1988**, *7*, 501–506; d) Y. Ito, T. Ogawa, *Tetrahedron Lett.* **1988**, *29*, 1061–1064; e) Y. Ito, T. Ogawa, *Carbohydr. Res.* **1990**, *202*, 165–175; f) A. Hasegawa, T. Nagahama, H. Ohki, K. Hotta, H. Ishida, M. Kiso, *J. Carbohydr. Chem.* **1991**, *10*, 493–498; g) R. Roy, F. O. Andersson, M. Letellier, *Tetrahedron Lett.* **1992**, *33*, 6053–6056.

[47] For earlier reports, see: a) A. Marra, P. Sinaÿ, *Carbohydr. Res.* **1990**, *195*, 303–308; b) W. Birberg, H. Lönn, *Tetrahedron Lett.* **1991**, *32*, 7453–7456; c) V. Martichonok, G. M. Whitesides, *J. Org. Chem.* **1996**, *61*, 1702–1706.

[48] For earlier reports, see ref. [9].

[49] a) S. Cai, B. Yu, *Org. Lett.* **2003**, *5*, 3827–3830; b) H. Tanaka, H. Ando, H. Ishida, M. Kiso, H. Ishihara, M. Koketsu, *Tetrahedron Lett.* **2009**, *50*, 4478–4481; c) H. Tanaka, Y. Fujii, H. Tokimoto, Y. Mori, S.-I. Tanaka, G.-M. Bao, A. Nakayabu, K. Fukase, *Chem. Asian J.* **2009**, *4*, 574–580; d) Y. Liu, X. Ruan, X. Li, Y. Li, *J. Org. Chem.* **2008**, *73*, 4287–4290; e) B. Sun, B. Srinivasan, X. Huang, *Chem. Eur. J.* **2008**, *14*, 7072–7081; f) K. Tanaka, T. Goi, K. Fukase, *Synlett* **2005**, 2958–2962.

[50] Recently, sialylation by means of dehydrative coupling of C2-hemiketal sialyl donors has also received attention, see: a) J. M. Haberman, D. Y. Gin, *Org. Lett.* **2003**, *5*, 2539–2541; b) D. Ye, W. Liu, D. Zhang, E. Feng, H. Jiang, H. Liu, *J. Org. Chem.* **2009**, *74*, 1733–1735.

[51] R. R. Schmidt, M. Behrendt, A. Toepfer, *Synlett* **1990**, 694–696.

[52] For recent reviews on the chemical synthesis of saponins, see: a) B. Yu, J. Sun, *Chem. Asian J.* **2009**, *4*, 642–654; b) B. Yu, Y. Zhang, P. Tang, *Eur. J. Org. Chem.* **2007**, 5145–5161; c) H. Pellissier, *Tetrahedron* **2004**, *60*, 5123–5162.

[53] C. Zhu, P. Tang, B. Yu, *J. Am. Chem. Soc.* **2008**, *130*, 5872–5873.

[54] R. L. Halcomb, S. J. Danishefsky, *J. Am. Chem. Soc.* **1989**, *111*, 6661–6666.
[55] Y. Li, P. Tang, Y. Chen, B. Yu, *J. Org. Chem.* **2008**, *73*, 4323–4325.
[56] a) C. Bliard, G. Massiot, S. Nazabadioko, *Tetrahedron Lett.* **1994**, *35*, 6107–6108; b) W. Peng, X. Han, B. Yu, *Synthesis* **2004**, 1641–1647.
[57] L. H. B. Baptistella, J. F. dos Santos, K. C. Ballabio, A. J. Marsaioli, *Synthesis* **1989**, 436–438.
[58] H. Sashida, A. Kawamukai, *J. Heterocycl. Chem.* **1998**, *35*, 165–168.
[59] C. G. Yang, C. He, *J. Am. Chem. Soc.* **2005**, *127*, 6966–6967.
[60] M. Trujillo, E. Q. Morales, J. T. Vazquez, *J. Org. Chem.* **1994**, *59*, 6637–6642.

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