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Total Syntheses of the Proposed Structure for Ieodoglucomides A and B

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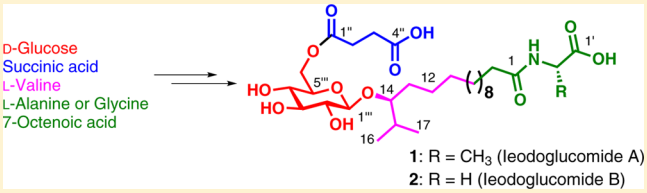
Supporting Information

ABSTRACT: The first enantioselective total synthesis of new glycolipopeptides, ieodoglucomides A and B, has been accomplished along with synthetic elaboration to their C14-epimers starting from D-glucose using β-glycosylation and Grubbs olefin cross-metathesis reactions as the key steps. The present synthetic study has indicated the ambiguity in proposed absolute stereochemistry for the natural product.



INTRODUCTION

Ieodoglucomide A (**1**) and B (**2**) are two unique glycopeptides isolated from a marine-derived bacterium *Bacillus licheniformis* (strain 09IDYM23) in 2012 by Shin et al.[1] The preliminary biological evaluation revealed that natural products **1** and **2** were found to exhibit moderate antimicrobial activity against Gram-positive, Gram-negative bacteria and fungi. Further studies on the cytotoxicity against six human cancer cell lines indicated that ieodoglucomide B (**2**) exhibited cancer cell growth inhibition against lung cancer (NCI-H23) and stomach cancer (NUGC-3) cell lines with GI_{50} values of 25.18 and 17.78 μg/mL, respectively. Structurally, ieodoglucomides A and B possess a C_{30} and C_{29} skeleton, respectively, with a glycolipid backbone, which is an unprecedented component of any natural product. In addition, their structures have represented the unique features consisting of an amino acid (L-alanine for **1** and glycine for **2**), a new fatty acid (14-hydroxy-15-methylhexadecanoic acid), a sugar (β-D-glucose) and a succinic acid unit. The absolute stereochemistry of **1** and **2** was determined by Marfey's method for the amino acid, Mosher's method for C14 of 14-hydroxy-15-methylhexadecanoic acid and comparison of specific rotation as well as R_f value with an authentic compound for β-D-glucose. The interesting bioactivities together with the distinctive structural framework have prompted us to undertake the total synthesis of ieodoglucomides A and B. As part of our continuing studies toward the total synthesis of bioactive molecules,[2] we describe herein the first total syntheses of **1** and **2** as well as their C14-epimers.

RESULTS AND DISCUSSION

According to our retrosynthetic analysis (Scheme 1), ieodoglucomides A and B were envisioned through a convergent process involving construction of the complete carbon skeleton through an intermolecular metathesis reaction of a sugar-linked olefin **3a** or **3b** and an amino acid-appended olefin **4** (for **1**) and **5** (for **2**). Synthesis of the olefin **3** was anticipated starting from readily available D-glucose, succinic acid and L-valine via a β-glycosylation reaction precursor alcohol. Other required olefins **4** and **5** would be easily prepared from the commercially available 7-octenoic acid and the related amino acids (L-alanine or glycine).

First Generation Strategy. Our initial synthetic expedition toward ieodoglucomide A and B began with the preparation of desired alcohol **7**, a precursor for glycosylation reaction from L-valine, which was initially converted to the epoxide **6** using literature procedures in three-steps.[3] A copper-catalyzed ring-opening of the epoxide **6** with the Grignard reagent, generated from 6-bromo-1-hexene and magnesium in THF, furnished the alcohol **7** in 78% yield with 96% ee (Scheme 2).[4,5]

The sugar precursor for glycosylation reaction toward the olefin **3a** was achieved from D-glucose (Scheme 3). First, D-glucose was transformed to the allyl glycoside **8** via a three-step sequence.[6] Next esterification of **8** with succinic anhydride in the presence of pyridine followed by benzylation of the resulting free-carboxylic acid using $BnBr/Cs_2CO_3$ in acetonitrile at 45 °C provided the succinate derivative **9** in 80% yield over two steps. Palladium-mediated deallylation of **9** using $PdCl_2/AcOH$[7] offered the desired sugar lactol **10** in 83% yield. After having prepared both the precursors, glycosylation of **10** with the alcohol **7** was performed to produce the olefin **3a** with exclusive β-anomeric selectivity. This was accomplished under Schmidt condensation[8] reaction conditions of lactol **10** in the presence of trimethylsilyltriflate (TMSOTf) at −15 °C, with the alcohol **7** as its perbenzoylated α-trichloroacetimidate ester (prepared using CCl_3CN/DBU in dichloromethane).

Olefins **4** and **5** were easily prepared via amide formation between the 7-octenoic acid and amino benzyl ester **11** (obtained from L-alanine) or **12** (from glycine), under standard reaction conditions (EDCI/HOBt/DIPEA in dichloromethane) (Scheme 4).

Having both the fragments, now the stage was set for the cross-metathesis reaction (Scheme 5). To our delight, the

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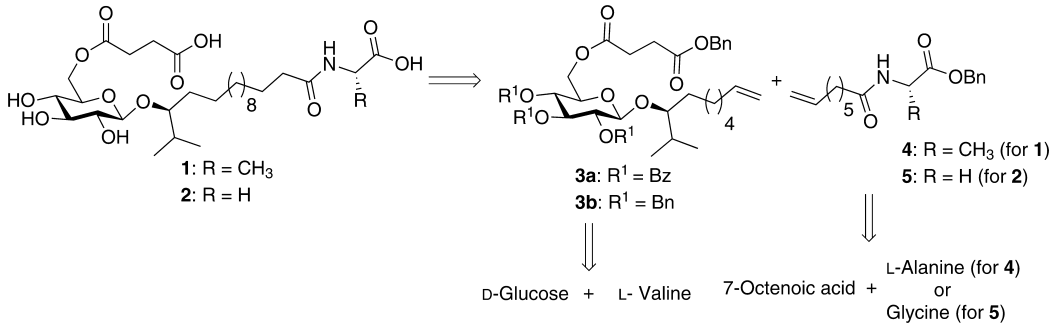
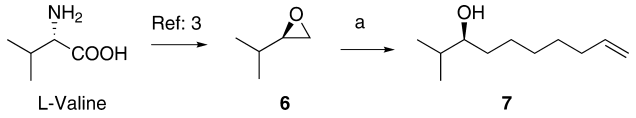
Scheme 1. Retrosynthesis of Ieodoglucomide A and B



Scheme 2. Synthesis of Alcohol 7[a]

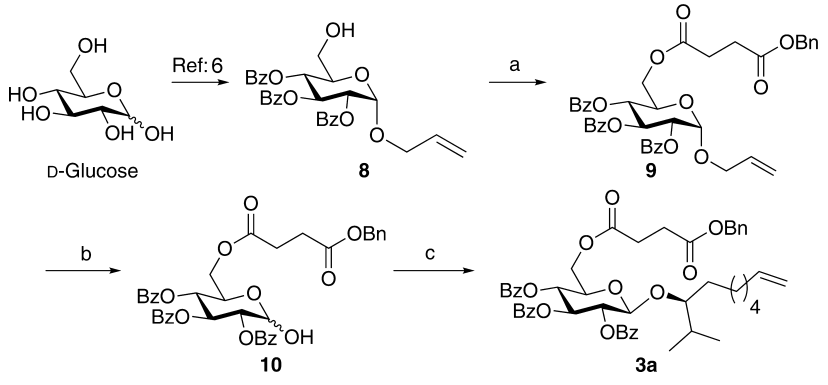


[a]Reagents and conditions: (a) 6-Bromo-1-hexene, Mg, THF, CuI, −10 °C, 3 h, 78%.

intermolecular metathesis reaction between **3a** and **4** proceeded smoothly in the presence of Grubbs second generation (G-II) catalyst[9] in dichloromethane at reflux temperature to give the fully protected glycopeptide **13** in 84% yield. Then, reduction of the double bond, debenzylation and ethanolysis of the benzoyl ester were planned in a one-pot operation under hydrogenation reaction conditions using 10% Pd/C−H_2 (g) in EtOH in the presence of K_2CO_3 to obtain the target molecule **1**. However, to our disappointment the above reaction provided the desuccinyl glycopeptide **14**, instead of the target molecule **1**. Similarly, metathesis reaction between **3a** and **5** provided the glycopeptide **15**, which upon treatment with hydrogenation conditions gave **16**, instead of the target molecule **2**. All the attempts for selective succinylation of the resulting primary alcohol **14** or **16** gave an inseparable mixture of compounds.[10]

Second Generation Strategy. The above failure led us to change our strategy to the one depicted in Scheme 6, wherein no base-mediated solvolysis was involved after introducing the succinyl group with suitable protecting groups on the sugar for β-glycosylation reaction as well as for one-pot olefin reduction and debenzylation. Thus, the revised approach for **1** and **2** commenced with the preparation of hemiacetal **17** from D-glucose in a two-step sequence involving acetylation followed by selective removal of the anomeric acetyl group.[11] Subsequent treatment of the hemiacetal **17** with trichloroacetonitrile in the presence of DBU in dichloromethane for 3 h afforded the thermodynamically stable α-trichloroacetimidate, which was immediately subjected to TMSOTf-promoted glycosylation[12] with the alcohol **7** to provide the corresponding β-glycoside **18** in 67% yield over two steps. The next task was to introduce the requisite succinyl group on to the sugar to give the metathesis precursor **3b**. Removal of the acetyl groups of glycoside **18** was achieved using the Zemplen method (0.02 M NaOMe/MeOH) to get the tetraol **19** in 78% yield.[13] Conversion of **19** to the compound **3b** with a free 4-hydroxyl group was carried out in a three-step sequence involving (i) 4,6-*O*-benzylidene formation (1,3-dioxane) with benzaldehyde dimethyl acetal/CSA to give **20** in 95% yield, (ii) benzylation of the remaining two hydroxyl groups using NaH/BnBr in DMF, followed by (iii) regioselective reductive ring-opening by treatment with $LiAlH_4$ in the presence of $AlCl_3$ provided the desired **21** in 67% yield.[14] Installation of the succinyl group was achieved via esterification of **21** with succinic anhydride/pyridine followed by benzylation of the resulting free-carboxylic acid using $BnBr/Cs_2CO_3$ in acetonitrile to provide the succinate derivative **3b** in 83% yield. Next, exposure of the alkene **3b** to the key cross-metathesis (CM) with the olefin partner **4** in the presence of G-II catalyst in dichloromethane at reflux temperature delivered the fully protected glycopeptide **22** in 86% yield. Finally, hydrogenation of **22** using 10% Pd/C in EtOH was successful in reduction of the double bond as well as removal of all five benzyl groups in one pot to produce the ieodoglucomide A (**1**) in 92% yield. Similarly, CM reaction of

Scheme 3. Synthesis of 3a[a]



[a]Reagents and conditions: (a) (i) Succinic anhydride, Py, rt, 12 h; (ii) BnBr, Cs_2CO_3, CH_3CN, 45 °C, 6 h, 80% (two steps); (b) $PdCl_2$, AcOH, H_2O, rt, 11 h, 83%; (c) (i) CCl_3CN, DBU, CH_2Cl_2, rt, 3 h; (ii) **7**, TMSOTf, CH_2Cl_2, −15 °C, 2 h, 65% (two steps).

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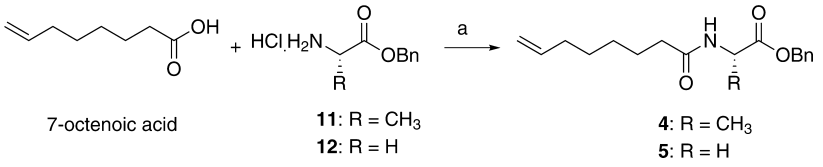
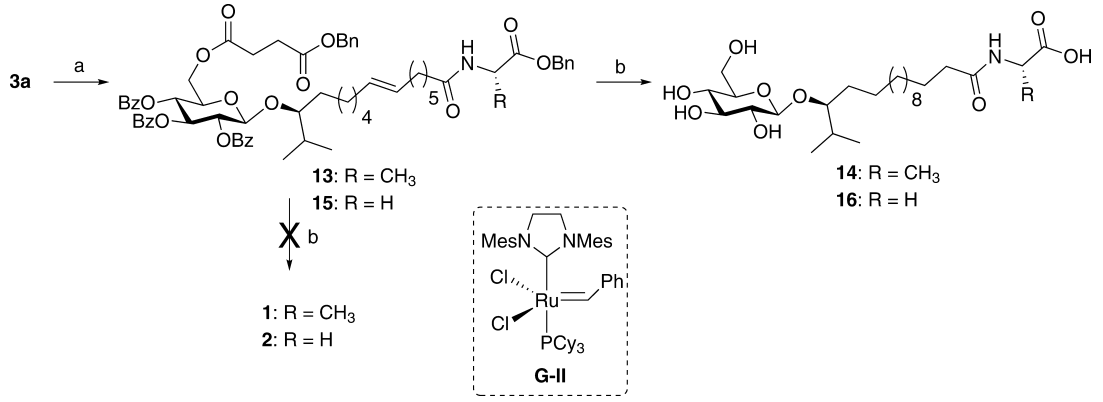
Scheme 4. Synthesis of 4 and 5[a]



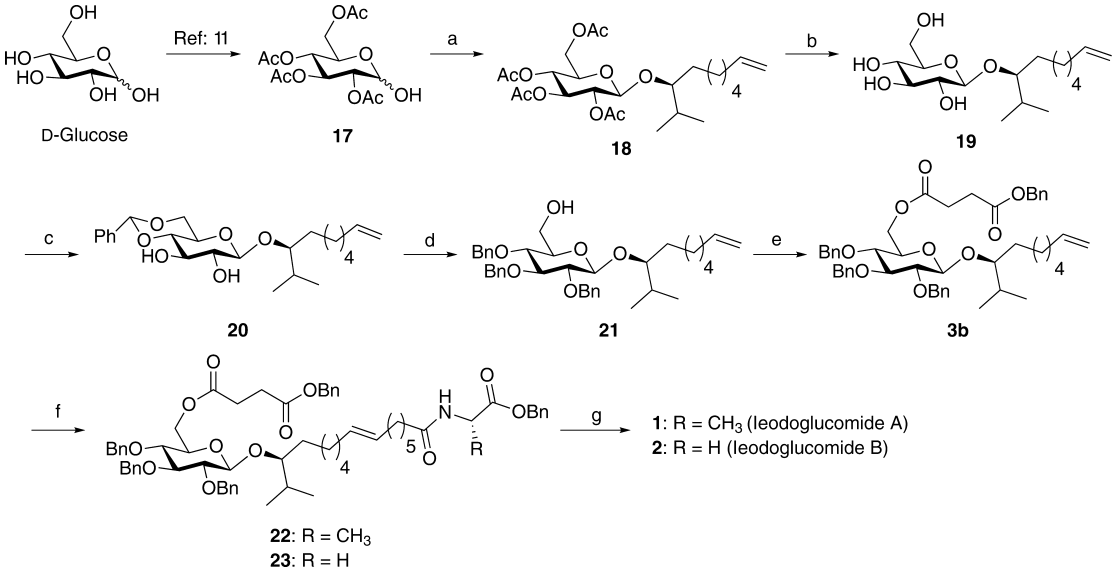
[a]Reagents and conditions: (a) HOBt, EDCI, DIPEA, CH_2Cl_2, 0 °C to rt, 12 h, **4**: 85%, **5**: 87%.

Scheme 5[a]



[a]Reagents and conditions: (a) **4** for **13** or **5** for **15**, benzoquinone, **G-II**, CH_2Cl_2, reflux, 5 h, **13**: 84%, **15**: 85%; (b) (i) 10% Pd/C, H_2 (g) (1 atm), EtOH, 2 h, rt; (ii) K_2CO_3, rt, 1 h, **14**: 80%, **16**: 82%.

Scheme 6. Synthesis of 1 and 2[a]



[a]Reagents and conditions: (a) (i) CCl_3CN, DBU, CH_2Cl_2, rt, 3 h; (ii) **7**, TMSOTf, CH_2Cl_2, −15 °C, 2 h, 67% (two steps); (b) NaOMe, MeOH, rt, 1 h, 78%; (c) $PhCH(OMe)_2$, CH_3CN, CSA, rt, 2 h, 95%; (d) (i) NaH, BnBr, DMF, 0 °C to rt, 3 h; (ii) $LiAlH_4$, $AlCl_3$, CH_2Cl_2, Et_2O, 2 h, 67% (two steps); (e) (i) succinic anhydride, Py, rt, 12 h; (ii) BnBr, Cs_2CO_3, CH_3CN, 45 °C, 6 h, 83% (two steps); (f) **4** for **22** or **5** for **23**, benzoquinone, **G-II**, CH_2Cl_2, reflux, 5 h, **22**: 86%, **23**: 85%; (g) 10% Pd/C, H_2 (g) (1 atm), EtOH, 6 h, rt, **1**: 92%, **2**: 90%.

3b with olefin **5** followed by hydrogenation of the resulting alkene **23** delivered the ieodoglucomide B (**2**) in 90% yield.

All the spectroscopic data (^1H, ^{13}C NMR, mass and IR) including NOE analysis for synthetic **1** and **2** were in full agreement with those reported for the natural product. But, the specific rotations were observed with the opposite sign as $[\alpha]^{20}_D = -16.9$ (c = 0.75, MeOH) for **1** and $[\alpha]^{20}_D = -8.9$ (c = 0.80, MeOH) for **2**, whereas for isolated compounds it was reported as $[\alpha]^{23}_D = +22$ (c = 0.2, MeOH) for **1** and $[\alpha]^{23}_D = +24$ (c = 0.2, MeOH) for **2**. This discrepancy prompted us to analyze the absolute configuration assignment of the natural product. The absolute stereochemistry of the natural ieodoglucomides A and B was entirely on comparison with the authentic samples except for the C14-hydroxyl group of 14-hydroxy-15-methylhexadecanoic acid, wherein we found the inconsistency between the given structure having "*S*" configuration and the reported $\Delta\delta_H$ ($\delta_S - \delta_R$) values obtained for (*S*)- and (*R*)-MTPA esters.[1] From these $\Delta\delta_H$ values, the

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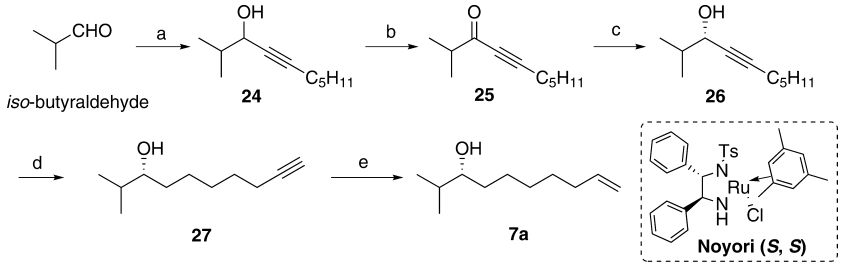
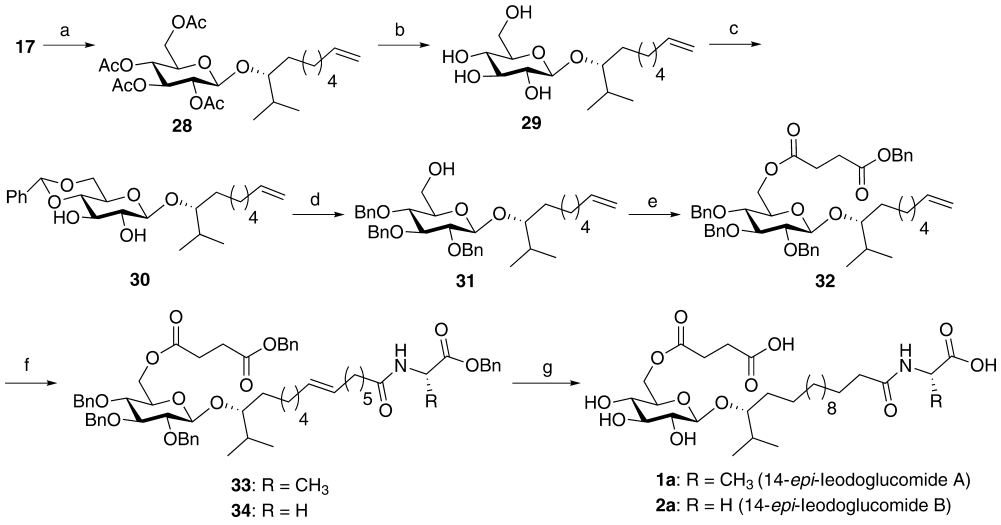
Scheme 7. Synthesis of Alcohol 7a[a]



[a]Reagents and conditions: (a) *n*-BuLi, 1-heptyne, THF, −78 °C, 3 h, 95%; (b) MnO_2, toluene, 50 °C, 2 h, 90%; c) (*S*,*S*)-Noyori catalyst, HCOOH, Et_3N, 10 h, rt, 80% (95% ee); (d) 1,3-diamino propane, KH, rt, 3 h, 78%; (e) Pd-$CaCO_3$, EtOAc, 1 h, rt, 84%.

Scheme 8. Synthesis of 1a and 2a[a]



[a]Reagents and conditions: (a) (i) CCl_3CN, DBU, CH_2Cl_2, rt, 3 h; (ii) **7a**, TMSOTf, CH_2Cl_2, −15 °C, 2 h, 65% (two steps); (b) NaOMe, MeOH, rt, 1 h, 80%; (c) $PhCH(OMe)_2$, CH_3CN, CSA, rt, 2 h, 95%; (d) (i) NaH, BnBr, DMF, 0 °C to rt, 3 h; (ii) $LiAlH_4$, $AlCl_3$, CH_2Cl_2, Et_2O, 2 h, 65% (two steps); (e) (i) succinic anhydride, Py, rt, 12 h; (ii) BnBr, Cs_2CO_3, CH_3CN, 45 °C, 6 h, 85% (two steps); (f) **4** for **33** or **5** for **34**, benzoquinone, **G-II**, CH_2Cl_2, reflux, 5 h, **33**: 85%, **34**: 87%; (g) 10% Pd/C, H_2 (g) (1 atm), EtOH, 6 h, rt, **1a**: 90%, **2a**: 88%.

Table 1. Comparison of ^1H and ^{13}C NMR Data of Natural and Synthetic Ieodoglucomides[a]

		ieodoglucomide **A**			ieodoglucomide **B**		
position	NMR	natural	*S*-isomer (**1**)	*R*-isomer (**1a**)	natural	*S*-isomer (**2**)	*R*-isomer (**2a**)
16	^1H	0.93 d (6.5)	0.93 d (6.4)	0.89 t (6.2)	0.93 d (7.0)	0.93 d (6.9)	0.90 t (6.2)
	^{13}C	18.3	18.3	18.7	18.3	18.3	18.7
17	^1H	0.93 d (6.5)	0.93 d (6.4)	0.89 t (6.2)	0.93 d (7.0)	0.93 d (6.9)	0.90 t (6.2)
	^{13}C	18.7	18.6	18.8	18.7	18.6	18.8

[a]Signals of all the other positions are in accordance with the reported values for natural product.

absolute configuration at C14 in the natural product should be "*R*". On the basis of this observation, we decided to synthesize ieodoglucomides A (**1a**) and B (**2a**) with the "*R*" configuration at the C14 stereocenter (C14-epimers of **1** and **2**).

Toward the C14-epimers of ieodoglucomide A and B, first, synthesis of the alcohol **7a** was considered from readily available isobutyraldehyde (Scheme 7). Addition of lithiated 1-heptyne on to isobutyraldehyde produced the propargylic alcohol **24** in 95% yield. Oxidation of the corresponding alcohol with MnO_2 in toluene at 50 °C for 2 h provided the propargylic ketone **25** in 90% yield. Asymmetric reduction of **25** using the (*S*,*S*)-Noyori catalyst in the presence of HCOOH/Et_3N[15] delivered the alcohol **26** in 80% yield with 95% ee.[16] The alkynol **26** was subjected to potassium 3-aminopropylamide (KAPA)-mediated alkyne zipper reaction, in which the alkyne functionality shifted from the center to the terminus of a chain to give the alkyne **27** in 78% yield,[17] which upon treatment under Lindlar's hydrogenation conditions (5% Pd-$CaCO_3$ in EtOAc) provided the desired alcohol **7a** in 84% yield.

Having the alcohol **7a** in hand, the stage was set for the synthesis of the C14-epimer of **1** and **2** (Scheme 8). Thus, glycosylation of the hemiacetal **17** with **7a** was carried out via the α-trichloroacetimidate followed by TMSOTf-mediated glycosylation to afford the corresponding β-glycoside **28** in 65% yield. Compound **28** was transformed to the targeted C14-epimers **1a** and **2a** through the intermediates **29** to **34**, following the similar sequence of reactions used for the

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conversion of **18** to **1** and **2**. The obtained **1a** and **2a** were fully characterized and found that the specific rotations for these compounds were also observed with a "negative" sign as $[\alpha]^{20}_{D}$ = −13.57 (*c* = 1.12, MeOH) for **1a** and $[\alpha]^{20}_{D}$ = −7.25 (*c* = 0.8, MeOH) for **2a**. At this stage, comparison of ^{1}H and ^{13}C NMR spectral data of all four synthetic compounds with the reported data revealed that the data of synthetic **1** and **2** are in accordance with the natural product, whereas **1a** and **2a** have a slight difference at the C16 and C17 positions (Table 1). This data suggests that the absolute configuration at the C14-stereocenter is most likely "*S*" as proposed for the natural products **1** and **2**. To elucidate this, a direct comparison of synthetic compound with the natural product sample is essential. Considering the chemical reliability of the synthetic products, confirmed by a range of analytical data, the observation of opposite sign for specific rotation values between the synthetic products and that reported for the natural products may be due to the erroneously reported specific rotation for the natural product.[18,19]

In summary, the efficient syntheses of ieodoglucomide A and B along with their C14-epimers have been achieved on the basis of the proposed structures. The synthetic sequence notably features *β*-glycosylation and Grubbs olefin cross-metathesis reactions as the key steps starting from D-glucose.

EXPERIMENTAL SECTION

General Methods. All solvents and reagents were purified by standard techniques. All of the reactions were performed in oven-dried round-bottom flasks. Crude products were purified by column chromatography either on silica gel (60−120 mesh) or silica gel 90 C18-reversed phase (for fully deprotected compounds). Thin layer chromatography plates were visualized by exposure to ultraviolet light and/or to a methanolic acidic solution of *p*-anisaldehyde or an aqueous solution of potassium permanganate ($KMnO_4$) or an ethanolic solution of ninhydrin followed by heating (<1 min) on a hot plate (∼250 °C). Organic solutions were concentrated on a rotary evaporator at 35−40 °C. FTIR spectra were recorded KBr thin films (for liquids) and disks (for solids). Specific rotations were measured with an automatic digital polarimeter at 20 °C. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ and CD_3OD solvent on 300, 400, and 500 MHz NMR spectrometers. Chemical shifts are reported in parts per million (ppm). ^{1}H NMR spectra were recorded at 300 or 500 MHz, and chemical shifts are referenced to either TMS (δ = 0.0) or CD_3OD (δ = 4.83). ^{13}C NMR spectra were recorded at 75 or 100 MHz, and chemical shifts are referenced to internal $CDCl_3$ (δ = 77.0) or CD_3OD (δ = 49.17). Coupling constants (*J*) are quoted in hertz (Hz). HRMS were recorded on quadrupole time-of-flight (Q-TOF) mass spectrometer equipped with an ESI source.

(*S*)-2-Methyldec-9-en-3-ol (7). To a solution of (*R*)-2-isopropyloxirane **6** (2.0 g, 23.2 mmol) in dry tetrahydrofuran (30 mL), cuprous iodide (441 mg, 2.3 mmol) was added, and the mixture was cooled to −10 °C. Hex-5-enylmagnesium bromide (1.5 M in tetrahydrofuran, 23.2 mL, 35.0 mmol) was added slowly at −10 °C. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. Reaction mixture was cooled to 0 °C, quenched with saturated aq. NH_4Cl (50 mL), allowed to warm to room temperature and extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4, filtered and evaporated under reduced pressure. The obtained crude was purified by silica gel column chromatography (4% EtOAc in hexanes) to afford the desired alcohol **7** (3.0 g, 78%) as a colorless liquid: $[\alpha]^{20}_{D}$ = −20.26 (*c* = 0.54, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87−5.76 (m, 1H), 5.00 (d, *J* = 17.4 Hz, 1H), 4.93 (d, *J* = 9.9 Hz, 1H), 3.38−3.32 (m, 1H), 2.10−2.01 (m, 2H), 1.70−1.59 (m, 1H), 1.54−1.27 (m, 8H), 0.96−0.85 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.0, 114.1, 76.6, 34.0, 33.7, 33.4, 29.1, 28.8, 25.8, 18.8, 17.0; IR (KBr) υ_{max} 3392, 3031, 2922, 2846, 1218, 772 cm^{-1}. Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.29; H, 12.93.

(*S*)-2-Methyldec-9-en-3-yl 4-nitrobenzoate (7′). To a solution of chiral alcohol **7** (100 mg, 0.6 mmol) in CH_2Cl_2 (5 mL), were added *p*-nitrobenzoic acid (118 mg, 0.7 mmol), DCC (242 mg, 1.2 mmol) and DMAP (catalytic), and the mixture was stirred for 2 h at room temperature. The reaction mixture was filtered and evaporated, and the crude was purified by silica gel column chromatography (2% EtOAc in hexanes) to afford the ester product **7′** (171 mg, 91%) as a yellow liquid: $[\alpha]^{20}_{D}$ = −16.42 (*c* = 0.95, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (d, *J* = 9.0 Hz, 2H), 8.22 (d, *J* = 9.0 Hz, 2H), 5.85−5.70 (m, 1H), 5.09−4.98 (m, 2H), 4.96−4.87 (m, 1H), 2.08−1.92 (m, 3H), 1.79−1.62 (m, 2H), 1.44−1.27 (m, 6H), 1.04−0.94 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 150.3, 138.8, 136.0, 130.6, 123.4, 114.2, 80.4, 33.6, 31.4, 31.0, 28.9, 28.6, 25.4, 18.6, 17.5; IR (KBr) υ_{max} 3078, 2956, 2931, 1720, 1528, 1272, 1101, 718 cm^{-1}. Anal. Calcd for $C_{18}H_{25}NO_4$: C, 67.69; H, 7.89; N, 4.39. Found: C, 67.90; H, 7.91; N, 4.41.

Allyl 2,3,4-tri-*O*-benzoyl-6-*O*-(3-benzyloxycarbonylpropanoyl)-*α*-D-glucopyranoside (9). 4-(*N*,*N*-Dimethylamino)-pyridine (110 mg, 0.9 mmol) and succinic anhydride (1.38 g, 18.7 mmol) were added to a stirred solution of the alcohol **8** (5.0 g, 9.3 mmol) in dry pyridine (50 mL) at room temperature under a nitrogen atmosphere. The reaction mixture was stirred for 12 h at room temperature. Upon completion, the reaction mixture was concentrated under reduced pressure, and the residue was dissolved in EtOAc (100 mL) and washed with 1 N HCl (50 mL) and brine (50 mL). The organic phase was dried over Na_2SO_4 and concentrated in vacuo. The obtained acid residue in acetonitrile (50 mL), cesium carbonate (6.1 g, 18.7 mmol) and benzyl bromide (3.2 g, 18.7 mmol) was stirred for 6 h at 45 °C. The reaction mixture was cooled to room temperature, diluted with EtOAc (100 mL), and washed with water (50 mL) and brine (25 mL). The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue obtained was purified by column chromatography on silica gel (30% EtOAc in hexanes) to afford compound **9** (5.4 g, 80%) as a yellow liquid: $[\alpha]^{20}_{D}$ = +45.95 (*c* = 1.31, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.9 Hz, 2H), 7.92 (d, *J* = 7.4 Hz, 2H), 7.85 (d, *J* = 7.4 Hz, 2H), 7.54−7.46 (m, 2H), 7.44−7.23 (m, 12H), 6.17 (t, *J* = 9.4 Hz, 1H), 5.92−5.81 (m, 1H), 5.57 (t, *J* = 9.4 Hz, 1H), 5.40−5.26 (m, 3H), 5.18 (d, *J* = 10.4 Hz, 1H), 5.14 (s, 2H), 4.37−4.23 (m, 4H), 4.15−4.05 (m, 1H), 2.74−2.63 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 171.7, 165.6, 165.2, 136.0, 135.7, 133.35, 133.30, 133.1, 133.0, 129.8, 129.7, 129.5, 129.1, 128.9, 128.8, 128.4, 128.3, 128.19, 128.15, 117.9, 95.1, 71.8, 70.3, 69.2, 68.9, 67.7, 66.4, 62.6, 29.0, 28.9; IR (KBr) υ_{max} 3067, 3034, 2957, 2929, 1733, 1601, 1452, 1262, 1159, 1102, 1028, 711 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{41}H_{38}O_{12}Na$ $(M + Na)^+$ 745.2261, found 745.2252.

2,3,4-Tri-*O*-benzoyl-6-*O*-(3-benzyloxycarbonylpropanoyl)-D-glucopyranoside (10). To a mixture of compound **9** (2.0 g, 2.7 mmol) in AcOH (20 mL) was added water (1 mL), NaOAc (522 mg, 6.3 mmol) and $PdCl_2$ (585 mg, 3.3 mmol), and the mixture was stirred for 11 h at room temperature. The reaction mixture was diluted with EtOAc (50 mL) and washed with water (25 mL), saturated aq. $NaHCO_3$ (25 mL) and brine (25 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated, and the resulting residue was purified by flash column chromatography (40% EtOAc in hexanes) to yield compound **10** (1.5 g, 83%) as a yellow viscous liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07−7.79 (m, 6H), 7.59−7.22 (m, 14H), 6.30−6.11 (m, 1H), 5.72 (br s, 1H), 5.65−5.47 (m, 1H), 5.41−5.24 (m, 1H), 5.13 (s, 2H), 4.64−4.50 (m, 1H), 4.38−4.21 (m, 2H), 3.86 (br s, 1H), 2.77−2.61 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 171.9, 165.7, 165.3, 133.4, 133.3, 133.1, 133.0, 129.9, 129.86, 129.81, 129.6, 129.0, 128.9, 128.7, 128.5, 128.4, 128.29, 128.24, 128.1, 96.4, 95.8, 72.1, 70.0, 69.3, 67.3, 66.6, 62.7, 29.2, 28.9; IR (KBr) υ_{max} 2921, 2852, 1729, 1451, 1262, 1219, 1098, 1069, 772, 710 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{38}H_{34}O_{12}Na$ $(M + Na)^+$ 705.1948, found 705.1940.

(3*S*)-2-Methyl-9-en-3-yl-2,3,4-tri-*O*-benzoyl-6-*O*-(3-benzyloxycarbonylpropanoyl)-*β*-D-glucopyranoside (3a). To a mixture of compound **10** (1.0 g, 1.4 mmol) in CH_2Cl_2 (15 mL), was added trichloroacetonitrile (2.1 g, 14.6 mmol) and DBU (30 *μ*L). The

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mixture was stirred at room temperature for 3 h and then concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (30% EtOAc in hexanes) to yield the imidate derivative as a yellow liquid. The imidate and alcohol **7** (249 mg, 1.4 mmol) were coevaporated three times with toluene, dissolved in dry CH_2Cl_2 (20 mL), and stirred over freshly activated 4 Å molecular sieves for 30 min and then cooled to −15 °C. TMSOTf (18 μL, 0.08 mmol) was added, and the mixture was stirred for 2 h at −15 °C. Then triethylamine (0.1 mL) was added, stirring was continued for 10 min, and the mixture was filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (20% EtOAc in hexanes) to afford compound **3a** (794 mg, 65%) as a yellow liquid: $[\alpha]^{20}_D$ = −14.06 (*c* = 0.32, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.0, 2H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 7.5 Hz, 2H), 7.49 (t, *J* = 7.0 Hz, 2H), 7.44−7.31 (m, 9H), 7.30−7.23 (m, 3H), 5.87−5.75 (m, 2H), 5.55−5.46 (m, 2H), 5.13 (s, 2H), 4.99 (d, *J* = 17.0 Hz, 1H), 4.92 (d, *J* = 9.5 Hz, 1H), 4.78 (d, *J* = 8.0 Hz, 1H), 4.34−4.28 (m, 2H), 3.96−3.89 (m, 1H), 3.43−3.37 (m, 1H), 2.70−2.58 (m, 4H), 2.08−2.00 (m, 2H), 1.78−1.69 (m, 1H), 1.53−1.23 (m, 8H), 0.73 (d, *J* = 6.5 Hz, 3H), 0.65 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 171.7, 165.7, 165.2, 164.9, 139.1, 135.7, 133.4, 133.1, 133.0, 129.7, 129.67, 129.63, 129.3, 128.7, 128.5, 128.3, 128.2, 114.0, 101.1, 72.9, 72.0, 71.6, 69.7, 66.4, 63.0, 33.7, 30.9, 30.7, 29.1, 29.0, 28.8, 25.2, 17.5, 17.3; IR (KBr) υ_{max} 3067, 2930, 2856, 1734, 1601, 1452, 1280, 1262, 1157, 1097, 772, 710 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{49}H_{54}O_{12}Na$ (M + Na)$^+$ 857.3513, found 857.3509.

(*S*)-Benzyl 2-oct-7-enamidopropanoate (4). To a solution of **11** (1.5 g, 7.0 mmol) in CH_2Cl_2 (10 mL) was added DIPEA (1.36 g, 10.5 mmol) at 0 °C, and the mixture was stirred for 30 min. Separately the oct-7-enoic acid (500 mg, 3.5 mmol) in CH_2Cl_2 (10 mL), HOBt (475 mg, 3.5 mmol) was added at 0 °C and stirred for 10 min. Then EDCI (1.3 g, 7.0 mmol) was added, and the mixture was stirred for 30 min at 0 °C. The above prepared amine solution was added to the reaction mixture at 0 °C, allowed to warm to room temperature and stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2 (25 mL) and washed with 1 N HCl (10 mL), followed by saturated aq. $NaHCO_3$ (20 mL) and brine (20 mL). The combined organic layers were dried over Na_2SO_4, filtered and evaporated under reduced pressure. The residue obtained was purified by silica gel column chromatography (20% EtOAc in hexanes) to give **4** (906 mg, 85%) as a yellow colored liquid: $[\alpha]^{20}_D$ = −3.02 (*c* = 1.02, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.30 (m, 5H), 6.00 (d, *J* = 4.9 Hz, 1H), 5.84−5.74 (m, 1H), 5.20 (d, *J* = 12.3 Hz, 1H), 5.15 (d, *J* = 12.3 Hz, 1H), 4.99 (d, *J* = 17.3 Hz, 1H), 4.93 (d, *J* = 9.8 Hz, 1H), 4.69−4.61 (m, 1H), 2.19 (t, *J* = 7.4 Hz, 2H), 2.07−2.01 (m, 2H), 1.67−1.60 (m, 2H), 1.44−1.29 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 172.6, 138.7, 135.2, 128.5, 128.4, 128.0, 114.3, 67.1, 47.9, 36.4, 33.5, 28.6, 28.5, 25.3, 18.5; IR (KBr) υ_{max} 3291, 2929, 1744, 1647, 1539, 1157, 910, 772 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{18}H_{26}NO_3$ (M + H)$^+$ 304.1907, found 304.1906.

Benzyl 2-oct-7-enamidoacetate (5). Compound **5** was prepared from oct-7-enoic acid (500 mg, 3.5 mmol) and **12** (1.4 g, 7.0 mmol) by using the procedure described for amide **4**, yielding **5** (885 mg, 87%) as a yellow liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.29 (m, 5H), 5.99 (br s, 1H), 5.84−5.73 (m, 1H), 5.18 (s, 2H), 4.98 (d, *J* = 17.3 Hz, 1H), 4.93 (d, *J* = 9.8 Hz, 1H), 4.08 (d, *J* = 4.9 Hz, 2H), 2.23 (t, *J* = 7.4 Hz, 2H), 2.07−2.01 (m, 2H), 1.68−1.61 (m, 2H), 1.45−1.30 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 169.9, 138.7, 135.0, 128.59, 128.51, 128.3, 114.3, 67.1, 41.3, 36.2, 33.4, 28.6, 28.5, 25.3; IR (KBr) υ_{max} 3300, 2929, 1749, 1654, 1539, 1184 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{17}H_{24}NO_3$ (M + H)$^+$ 290.1751, found 290.1749.

Compound 13. To a solution of **3a** (100 mg, 0.11 mmol) and **4** (72.6 mg, 0.23 mmol) in dry CH_2Cl_2 (20 mL), was added benzoquinone (3 mg, 0.02 mmol) in dry CH_2Cl_2 (1 mL). After stirring for 10 min Grubb's second generation (G-II) catalyst (5.0 mg, 5 mol %) was added to the resulting mixture, and the mixture was refluxed for 5 h. The reaction mixture was cooled to room temperature and filtered over Celite. The filtrate was concentrated in vacuo, and the resulting crude was purified by silica gel column chromatography (30% EtOAc in hexanes) to afford **13** (111 mg, 84%) as a yellow liquid: $[\alpha]^{20}_D$ = −11.92 (*c* = 0.92, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.9 Hz, 2H), 7.90 (d, *J* = 7.9 Hz, 2H), 7.81 (d, *J* = 7.7 Hz, 2H), 7.49 (t, *J* = 6.9 Hz, 2H), 7.43−7.23 (m, 17H), 6.02 (d, *J* = 6.2 Hz, 1H), 5.83 (t, *J* = 9.7 Hz, 1H), 5.54−5.46 (m, 2H), 5.40−5.27 (m, 3H), 5.21−5.15 (m, 1H), 5.13 (s, 2H), 4.78 (d, *J* = 7.7 Hz, 1H), 4.68−4.61 (m, 1H), 4.33−4.27 (m, 2H), 3.96−3.90 (m, 1H), 3.44−3.37 (m, 1H), 2.69−2.57 (m, 4H), 2.22−2.14 (m, 2H), 2.04−1.91 (m, 2H), 1.78−1.69 (m, 1H), 1.68−1.50 (m, 8H), 1.39 (d, *J* = 6.9 Hz, 3H), 1.36−1.23 (m, 8H), 0.73 (d, *J* = 6.7 Hz, 3H), 0.66 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 172.6, 171.8, 171.7, 165.7, 165.2, 164.9, 135.7, 135.2, 133.4, 133.1, 133.0, 130.3, 130.1, 129.7, 129.67, 129.65, 129.3, 128.7, 128.57, 128.53, 128.3, 128.2, 128.0, 101.2, 85.8, 72.9, 72.0, 71.6, 69.7, 67.0, 66.4, 63.0, 47.9, 36.4, 32.4, 30.8, 30.6, 29.66, 29.60, 29.3, 29.0, 28.83, 28.80, 25.5, 24.8, 18.4, 17.6, 17.3; IR (KBr) υ_{max} 3383, 3065, 2929, 2855, 1735, 1665, 1453, 1278, 1261, 1157, 1099, 772, 710 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{65}H_{75}NO_{15}Na$ (M + Na)$^+$ 1132.5034, found 1132.5022.

Compound 14. To the compound **13** (50 mg, 0.04 mmol) dissolved in methanol (10 mL), was added 10% Pd on carbon catalyst (5 mg, 10% w/w), and the mixture was stirred in a hydrogen atmosphere for 2 h at room temperature. The hydrogen gas was removed, potassium carbonate (18.6 mg, 0.13 mmol) was added, and then the mixture was stirred for 1 h at room temperature, filtered and concentrated under reduced pressure. The resulting crude was purified by Silica gel 90 C18-reversed phase column chromatography (3:2 MeOH:H_2O) to afford the compound **14** (18.7 mg, 80%) as a yellow liquid: $[\alpha]^{20}_D$ = −20.53 (*c* = 0.75, CH_3OH); ^{1}H NMR (500 MHz, CD_3OD) δ 4.38−4.29 (m, 2H), 3.85 (dd, *J* = 5.9, 11.9 Hz, 1H), 3.72−3.66 (m, 1H), 3.52−3.47 (m, 1H), 3.38−3.29 (m, 2H), 3.26−3.15 (m, 2H), 2.22 (t, *J* = 6.9 Hz, 2H), 1.95−1.86 (m, 1H), 1.65−1.57 (m, 2H), 1.55−1.42 (m, 2H), 1.37 (dd, *J* = 6.9 Hz, 3H), 1.35−1.24 (m, 18H), 0.97−0.90 (m, 6H); ^{13}C NMR (75 MHz, CD_3OD) δ 176.0, 104.1, 85.4, 78.4, 77.9, 75.7, 72.0, 63.2, 49.4, 37.1, 33.2, 32.1, 31.1, 31.0, 30.9, 30.7, 30.5, 27.1, 26.8, 18.7, 18.4, 18.3; IR (KBr) υ_{max} 3690, 2926, 2862, 1647, 1371, 1219, 1054, 1033, 772 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{26}H_{49}NO_9Na$ (M + Na)$^+$ 542.3305, found 542.3303.

Compound 15. Compound **15** was obtained from **3a** (100 mg, 0.11 mmol) and **5** (69.3 mg, 0.23 mmol) by using the procedure described for compound **13**, which gave the product as a yellow liquid (111 mg, 85%): $[\alpha]^{20}_D$ = −20.02 (*c* = 0.80, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.9 Hz, 2H), 7.90 (d, *J* = 7.9 Hz, 2H), 7.81 (d, *J* = 7.9 Hz, 2H), 7.49 (t, *J* = 6.9 Hz, 2H), 7.44−7.30 (m, 14H), 7.29−7.24 (m, 3H), 5.99 (br s, 1H), 5.83 (t, *J* = 9.9 Hz, 1H), 5.54−5.46 (m, 2H), 5.40−5.27 (m, 2H), 5.18 (s, 2H), 5.13 (s, 2H), 4.78 (d, *J* = 7.7 Hz, 1H), 4.30 (d, *J* = 3.9 Hz, 2H), 4.07 (d, *J* = 4.9 Hz, 2H), 3.96−3.90 (m, 1H), 3.44−3.38 (m, 1H), 2.68−2.57 (m, 4H), 2.22 (t, *J* = 6.9 Hz, 2H), 2.03−1.92 (m, 2H), 1.78−1.69 (m, 1H), 1.68−1.40 (m, 8H), 1.38−1.23 (m, 8H), 0.74 (d, *J* = 6.9 Hz, 3H), 0.66 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 171.8, 171.7, 169.9, 165.7, 165.2, 164.9, 135.8, 135.7, 133.4, 133.1, 133.0, 130.3, 130.1, 129.7, 129.67, 129.65, 129.3, 128.7, 128.59, 128.53, 128.39, 128.33 128.2, 101.1, 85.8, 72.9, 72.0, 71.6, 69.7, 67.1, 66.4, 63.1, 41.2, 36.3, 32.4, 30.8, 30.6, 29.5, 29.3, 29.0, 28.8, 28.6, 27.1, 25.5, 24.8, 17.6, 17.3; IR (KBr) υ_{max} 3372, 2928, 2855, 1736, 1452, 1260, 1097, 772, 710 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{64}H_{73}NO_{15}Na$ (M + Na)$^+$ 1118.4878, found 1118.4899.

Compound 16. Compound **16** was prepared from **15** (50 mg, 0.04 mmol) by using the procedure described for the preparation of **14**, yielding **16** (18.9 mg, 82%) as a yellow liquid: $[\alpha]^{20}_D$ = −16.04 (*c* = 0.96, CH_3OH); ^{1}H NMR (500 MHz, CD_3OD) δ 4.31 (d, *J* = 7.9 Hz, 1H), 3.89−3.82 (m, 3H), 3.70 (dd, *J* = 6.9, 11.9 Hz, 1H), 3.52−3.47 (m, 1H), 3.38−3.29 (m, 2H), 3.26−3.16 (m, 2H), 2.25 (t, *J* = 6.9 Hz, 2H), 1.95−1.86 (m, 1H), 1.66−1.59 (m, 2H), 1.55−1.42 (m, 2H), 1.36−1.25 (m, 18H), 0.97−0.91 (m, 6H); ^{13}C NMR (75 MHz, CD_3OD) δ 176.8, 104.1, 85.4, 78.4, 77.8, 75.7, 72.0, 63.2, 42.7, 37.1, 32.2, 32.1, 31.1, 31.0, 30.9, 30.7, 30.5, 27.1, 26.8, 18.7, 18.3; IR (KBr) υ_{max} 3668, 3386, 2940, 2866, 1647, 1371, 1219, 1054, 1032, 772 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{25}H_{47}NO_9Na$ (M + Na)$^+$ 528.3149, found 528.3181.

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(3*S*)-2-Methyl-9-en-3-yl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (18). Compound **18** was prepared from **17** (3.0 g, 8.6 mmol) and **7** (1.5 g, 8.6 mmol) by using the procedure described for the preparation of **3a**, yielding the title compound **18** (2.8 g, 67%) as a white solid: mp 84−86 °C; $[\alpha]^{20}_{D}$ = −14.06 (*c* = 0.32, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89−5.68 (m, 1H), 5.25−5.12 (m, 1H), 5.11−4.85 (m, 3H), 4.50 (d, *J* = 7.9 Hz, 1H), 4.26−4.00 (m, 3H), 3.72−3.59 (m, 1H), 3.39−3.28 (m, 1H), 2.15−1.91 (m, 14H), 1.86−1.70 (m, 1H), 1.69−1.18 (m, 8H), 0.89−0.80 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 170.3, 169.4, 169.2, 138.9, 114.1, 100.8, 85.7, 72.9, 71.6, 71.3, 68.6, 62.2, 33.6, 30.9, 30.7, 28.8, 24.7, 20.69, 20.66, 20.60, 17.7, 17.3; IR (KBr) υ_{max} 2926, 2856, 1756, 1370, 1226, 1039, 772 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{25}H_{40}O_{10}Na$ (M + Na)$^+$ 523.2513, found 523.2498.

(3*S*)-2-Methyl-9-en-3-yl-β-D-glucopyranoside (19). A solution of **18** (2.0 g) in anhydrous MeOH (20 mL) was treated with a catalytic amount of NaOMe and stirred for 1 h, neutralized with Dowex H$^+$ resin, filtered, and concentrated under reduced pressure, and the resulting crude was purified by flash column chromatography on silica gel (70% EtOAc in hexanes) to afford the compound **19** (1.0 g, 78%) as a colorless liquid: $[\alpha]^{20}_{D}$ = −20.31 (*c* = 1.6, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 5.88−5.76 (m, 1H), 4.99 (d, *J* = 17.2 Hz, 1H), 4.92 (d, *J* = 9.7 Hz, 1H), 4.30 (d, *J* = 7.9 Hz, 1H), 3.85 (dd, *J* = 1.8, 11.6 Hz, 1H), 3.68 (dd, *J* = 5.5, 12.1 Hz, 1H), 3.53−3.46 (m, 1H), 3.40−3.28 (m, 2H), 3.26−3.15 (m, 2H), 2.09−2.03 (m, 2H), 1.96−1.87 (m, 1H), 1.56−1.47 (m, 2H), 1.45−1.27 (m, 6H), 0.92 (t, *J* = 7.4 Hz, 2 × 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 140.1, 114.7, 103.8, 85.1, 78.1, 77.6, 75.3, 71.7, 62.8, 34.8, 32.5, 31.4, 30.5, 30.0, 26.2, 18.6; IR (KBr) υ_{max} 3384, 2925, 2851, 1455, 1359, 1219, 772 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{17}H_{32}O_6Na$ (M + Na)$^+$ 355.2091, found 355.2090.

(3*S*)-2-Methyl-9-en-3-yl-4,6-*O*-benzylidine-β-D-glucopyranoside (20). Benzaldehyde dimethylacetal (824 mg, 5.4 mmol) and CSA (189 mg, 0.81 mmol) were added to the tetrol **19** (900 mg, 2.7 mmol) in acetonitrile (20 mL), and the mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with EtOAc (25 mL) and washed with saturated aq. $NaHCO_3$ (10 mL) and brine (10 mL). The organic layer was dried over Na_2SO_4 and evaporated, and the crude was purified by flash column chromatography (50% EtOAc in hexanes) to afford the diol **20** (1.08 g, 95%) as a white solid: mp 103−105 °C; $[\alpha]^{20}_{D}$ = −25.23 (*c* = 1.28, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53−7.46 (m, 2H), 7.41−7.33 (m, 3H), 5.90−5.74 (m, 1H), 5.54 (s, 1H), 5.05−4.91 (m, 2H), 4.43 (d, *J* = 7.7 Hz, 1H), 4.31 (dd, *J* = 4.9, 10.3 Hz, 1H), 3.86−3.74 (m, 2H), 3.61−3.38 (m, 4H), 2.76 (br s, 1H), 2.46 (br s, 1H), 2.10−2.00 (m, 2H), 1.97−1.83 (m, 1H), 1.68−1.24 (m, 8H), 0.90 (d, *J* = 6.7 Hz, 2 × 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.0, 136.9, 129.2, 128.2, 126.2, 114.1, 102.6, 101.8, 84.7, 80.5, 74.9, 73.1, 68.6, 66.2, 33.7, 30.7, 29.0, 28.8, 25.1, 17.9, 17.7; IR (KBr) υ_{max} 3424, 2927, 2861, 1736, 1640, 1458, 1382, 1097, 1028, 990, 912, 770 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{24}H_{36}O_6Na$ (M + Na)$^+$ 443.2404, found 443.2401.

(3*S*)-2-Methyl-9-en-3-yl-2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (21). To a solution of sodium hydride (60% oil suspension, 285 mg, 7.1 mmol) in DMF (10 mL), compound **20** (1.0 g, 2.3 mmol) dissolved in DMF (10 mL) was added at 0 °C, and the mixture was stirred for 45 min at the same temperature. Benzyl bromide (814 mg, 4.7 mmol) was added to the above mixture at 0 °C, and then it was allowed to warm to room temperature, and stirring was continued for 3 h. The reaction mixture was quenched by adding ice cold water (20 mL), and the mixture was extracted with EtOAc (2 × 25 mL). The combined organic layers were washed with brine (3 × 20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude obtained was purified by flash column chromatography (10% EtOAc in hexanes) to afford dibenzylated compound as a yellow residue. The residue in CH_2Cl_2:diethyl ether (1:1, 10 mL) was added to a solution of lithium aluminum hydride (542 mg, 14.2 mmol) in CH_2Cl_2/diethyl ether (1:1, 5.0 mL) at 0 °C under a nitrogen atmosphere. The reaction mixture was warmed to 50 °C, and then a solution of $AlCl_3$ (1.44 g, 10.9 mmol) in diethyl ether (10 mL) was added slowly. The mixture was stirred for 2 h at the same temperature and then cooled to 0 °C; EtOAc (10 mL) and water (10 mL) were added slowly. The resulting mixture was filtered through a pad of Celite, and the filtrate was washed with 1 M HCl (20 mL), followed by water (20 mL) and brine (20 mL). The organic layer was dried over Na_2SO_4 and evaporated in vacuo. The resulting crude was purified by flash chromatography (20% EtOAc in hexanes) to afford **21** (960 mg, 67%) as a white solid: mp 71−74 °C; $[\alpha]^{20}_{D}$ = −27.50 (*c* = 0.64, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.23 (m, 15H), 5.88−5.75 (m, 1H), 5.05−4.97 (m, 3H), 4.89−4.77 (m, 2H), 4.75−4.68 (m, 2H), 4.65−4.59 (m, 1H), 4.49 (d, *J* = 7.5 Hz, 1H), 3.90−3.83 (m, 1H), 3.72−3.61 (m, 2H), 3.57−3.50 (m, 1H), 3.48−3.36 (m, 3H), 2.09−1.98 (m, 2H), 1.92−1.81 (m, 1H), 1.57−1.37 (m, 2H), 1.35−1.18 (m, 6H), 0.97−0.87 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.0, 138.5, 138.4, 137.9, 128.6, 128.3, 128.2, 128.0, 127.8, 127.7, 127.5, 114.2, 102.3, 84.6, 84.2, 82.1, 77.8, 75.6, 74.9, 74.8, 74.4, 62.2, 33.7, 31.1, 30.9, 29.5, 28.7, 25.4, 18.6, 17.6; IR (KBr) υ_{max} 3387, 3031, 2925, 2856, 1454, 1375, 1070, 736, 697 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{38}H_{50}O_6Na$ (M + Na)$^+$ 625.3499, found 625.3492.

(3*S*)-2-Methyl-9-en-3-yl-2,3,4-tri-*O*-benzyl-6-*O*-(3-benzyloxycarbonylpropanoyl)-β-D-glucopyranoside (3b). Compound **3b** was obtained from **21** (500 mg, 0.8 mmol) by using the procedure described for the preparation of **9**, yielding **3b** (545 mg, 83%) as a white solid: mp 66−68 °C; $[\alpha]^{20}_{D}$ = −20.01 (*c* = 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.21 (m, 20H), 5.87−5.76 (m, 1H), 5.14 (s, 2H), 5.02−4.89 (m, 4H), 4.88−4.75 (m, 2H), 4.70 (d, *J* = 10.9 Hz, 1H), 4.56 (d, *J* = 10.9 Hz, 1H), 4.44−4.32 (m, 2H), 4.20 (dd, *J* = 4.9, 11.8 Hz, 1H), 3.65 (t, *J* = 8.6 Hz, 1H), 3.53−3.36 (m, 4H), 2.70−2.63 (m, 4H), 2.09−2.02 (m, 2H), 1.92−1.80 (m, 1H), 1.57−1.37 (m, 2H), 1.37−1.16 (m, 6H), 0.99−0.91 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 171.8, 139.1, 138.5, 138.4, 137.8, 135.7, 128.5, 128.4, 128.3, 128.26, 128.23, 128.17, 128.10, 127.9, 127.7, 127.5, 114.1, 102.4, 84.6, 84.0, 82.9, 77.7, 75.6, 74.9, 74.7, 72.4, 66.5, 63.6, 33.7, 31.1, 30.8, 29.5, 29.1, 29.0, 28.8, 28.7, 25.4, 18.4, 17.6; IR (KBr) υ_{max} 3483, 2924, 2853, 1737, 1454, 1156, 1062, 772, 697 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{49}H_{60}O_9Na$ (M + Na)$^+$ 815.4129, found 815.4121.

Compound 22. Compound **22** was obtained from **3b** (100 mg, 0.12 mmol) and **4** (76.5 mg, 0.25 mmol) by using the procedure described for compound **13**, to give **22** as a yellow liquid (115 mg, 86%): $[\alpha]^{20}_{D}$ = −14.88 (*c* = 0.86, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.23 (m, 25H), 6.04 (d, *J* = 6.2 Hz, 1H), 5.39−5.29 (m, 3H), 5.17 (s, 2H), 4.95 (d, *J* = 10.9 Hz, 2H), 4.88−4.75 (m, 2H), 4.73−4.53 (m, 4H), 4.45−4.32 (m, 2H), 4.20 (dd, *J* = 4.5, 11.5 Hz, 1H), 3.73−3.60 (m, 1H), 3.50−3.31 (m, 4H), 2.69−2.61 (m, 4H), 2.25−2.15 (m, 2H), 2.10−1.76 (m, 4H), 1.71−1.56 (m, 2H), 1.55−1.45 (m, 1H), 1.39 (d, *J* = 7.1 Hz, 3H), 1.37−1.19 (m, 12H), 0.89 (t, *J* = 6.2 Hz, 2 × 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 172.6, 172.4, 172.0, 138.5, 138.2, 135.6, 135.2, 130.8, 130.5, 129.9, 128.58, 128.50, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 103.2, 84.7, 84.0, 82.0, 77.1, 75.3, 74.9, 73.0, 70.1, 67.1, 66.5, 63.7, 47.9, 36.4, 32.5, 32.3, 31.2, 31.0, 29.6, 29.5, 29.2, 29.1, 28.9, 28.6, 25.4, 25.3, 18.5, 18.0, 17.8; IR (KBr) υ_{max} 2921, 2852, 1736, 1453, 1218, 1155, 1062, 772 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{65}H_{81}NO_{12}Na$ (M + Na)$^+$ 1090.5656, found 1090.5590.

Compound 23. Compound **23** was prepared from **3b** (100 mg, 0.12 mmol) and **5** (72.9 mg, 0.25 mmol) by using the procedure described for compound **13**, giving **23** as a yellow liquid (113 mg, 85%): $[\alpha]^{20}_{D}$ = −11.14 (*c* = 0.88, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44−7.23 (m, 25H), 5.98 (br s, 1H), 5.41−5.27 (m, 2H), 5.20−5.17 (m, 2H), 5.12 (s, 2H), 4.98−4.91 (m, 2H), 4.88−4.76 (m, 2H), 4.70 (d, *J* = 10.9 Hz, 1H), 4.56 (d, *J* = 10.7 Hz, 1H), 4.44−4.43 (m, 2H), 4.20 (dd, *J* = 4.7, 11.7 Hz, 1H), 4.11−4.04 (m, 3H), 3.65 (t, *J* = 8.6 Hz, 1H), 3.53−3.36 (m, 3H), 2.71−2.58 (m, 4H), 2.28−2.18 (m, 2H), 2.10−1.81 (m, 3H), 1.78−1.57 (m, 4H), 1.55−1.19 (m, 12 H), 0.89 (t, *J* = 6.2 Hz, 2 × 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 172.4, 172.0, 170.0, 138.5, 138.2, 135.6, 130.5, 129.9, 129.4, 128.6, 128.5, 128.34, 128.30, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 103.2, 84.8, 84.0, 81.9, 77.1, 75.3, 74.9, 73.0, 70.0, 67.1, 66.5, 63.7, 41.2, 36.2, 32.5, 32.3, 31.2, 31.0, 29.6, 29.5, 29.2, 29.0, 28.9, 28.6, 25.4, 25.3, 18.0, 17.8; IR (KBr) υ_{max} 3348, 2923, 2853, 1737, 1656, 1455, 1218, 1063, 772 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{64}H_{79}NO_{12}Na$ (M + Na)$^+$ 1076.5500, found 1076.5542.

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Compound 1. 10% Pd on carbon (5 mg, 10% w/w) was added to a solution of compound **22** (50 mg) in methanol (10 mL), and the mixture was stirred in a hydrogen atmosphere for 6 h at room temperature. The reaction mixture was filtered and concentrated under reduced pressure to afford compound **1** (26.6 mg, 92%) as a yellow liquid: $[\alpha]^{20}_{D}$ = −16.93 (*c* = 0.75, CH_3OH); ^1H NMR (500 MHz, CD_3OD) δ 4.44 (d, *J* = 11.4 Hz, 1H), 4.37 (dd, *J* = 6.9, 13.9 Hz, 1H), 4.29 (d, *J* = 7.4 Hz, 1H), 4.19 (dd, *J* = 6.4, 11.9 Hz, 1H), 3.46−3.39 (m, 2H), 3.37−3.25 (m, 2H), 3.19 (t, *J* = 7.9 Hz, 1H), 2.66−2.57 (m, 4H), 2.22 (t, *J* = 7.4 Hz, 2H), 1.92−1.84 (m, 1H), 1.65−1.57 (m, 2H), 1.51−1.44 (m, 2H), 1.38 (d, *J* = 6.9 Hz, 3H), 1.36−1.24 (m, 18H), 0.93 (d, *J* = 6.4 Hz, 2 × 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 176.5, 176.2, 176.0, 174.0, 104.1, 85.6, 78.1, 75.5, 75.1, 72.0, 65.2, 49.1, 36.9, 32.3, 32.2, 30.9, 30.8, 30.6, 30.4, 30.2, 29.9, 27.0, 26.6, 18.6, 18.3, 17.8; IR (KBr) υ_{max} 3690, 2926, 2862, 1647, 1371, 1219, 1054, 1033, 772 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{30}H_{53}NO_{12}Na$ $(M + Na)^+$ 642.3465, found 642.3521.

Compound 2. Compound **2** was obtained as a yellow liquid from **23** (50 mg) by using the procedure described for the preparation of **1**, yielding **2** (25.8 mg, 90%): $[\alpha]^{20}_{D}$ = −8.98 (*c* = 0.88, CH_3OH); ^1H NMR (500 MHz, CD_3OD) δ 4.44 (d, *J* = 11.4 Hz, 1H), 4.30 (d, *J* = 7.9 Hz, 1H), 4.18 (dd, *J* = 6.4, 11.9 Hz, 1H), 3.89 (s, 2H), 3.46−3.39 (m, 2H), 3.37−3.24 (m, 2H), 3.19 (t, *J* = 8.4 Hz, 1H), 2.67−2.57 (m, 4H), 2.25 (t, *J* = 7.4 Hz, 2H), 1.92−1.83 (m, 1H), 1.67−1.58 (m, 2H), 1.51−1.42 (m, 2H), 1.39−1.21 (m, 18H), 0.93 (d, *J* = 6.4 Hz, 2 × 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 176.9, 176.0, 174.1, 173.5, 104.1, 85.6, 78.1, 75.5, 75.1, 72.0, 65.2, 42.0, 36.9, 32.3, 32.2, 30.9, 30.8, 30.6, 30.4, 30.2, 29.9, 27.0, 26.6, 18.6, 18.3; IR (KBr) υ_{max} 3668, 3386, 2940, 2866, 1647, 1371, 1219, 1054, 1032, 772 cm^{-1}; HRMS (*m*/*z*) calcd for $C_{29}H_{51}NO_{12}Na$ $(M + Na)^+$ 628.3303, found 628.3306.

2-Methyldec-4-yn-3-ol (24). To a solution of 1-heptyne (7.3 g, 76.4 mmol) in dry tetrahydrofuran (100 mL) was added *n*-BuLi (28 mL, 2.5 M solution in hexane, 69.4 mmol) at −78 °C slowly under nitrogen. Then the reaction mixture was stirred at the same temperature for 1 h. Isobutyraldehyde (5.0 g, 69.4 mmol) in dry tetrahydrofuran (50 mL) was added slowly to the above mixture at −78 °C. The mixture was stirred for 1 h at the same temperature, and then it was quenched by adding saturated aq. NH_4Cl (100 mL). The mixture was allowed to warm to room temperature, and then it was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 and evaporated under a vacuum. The crude obtained was purified by silica gel column chromatography (2% EtOAc in hexanes) to afford the racemic alcohol **24** (11.0 g, 95%) as a yellow liquid: ^1H NMR (300 MHz, $CDCl_3$) δ 4.22−4.07 (m, 1H), 2.21 (td, *J* = 1.5, 6.7 Hz, 2H), 1.91−1.78 (m, 1H), 1.57−1.45 (m, 2H), 1.43−1.23 (m, 4H), 1.03−0.95 (m, 6H), 0.90 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 85.9, 79.7, 67.9, 34.5, 30.9, 28.3, 22.0, 18.5, 18.0, 17.2, 13.8; IR (KBr) υ_{max} 3424, 2956, 2923, 2852, 1736, 1219, 772 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.34; H, 11.94.

2-Methyldec-4-yn-3-one (25). To a solution of alcohol **24** (10.0 g, 59.5 mmol) in toluene (100 mL) was added activated manganese-(IV) oxide (41.4 g, 476.1 mmol) at room temperature. The mixture was heated to 50 °C and stirred for 2 h (monitored by TLC). The reaction mixture was cooled to room temperature, filtered and evaporated. The crude was purified by flash column chromatography (2% EtOAc in hexanes) to get the ketone **25** (8.9 g, 90%) as a yellow residue: ^1H NMR (300 MHz, $CDCl_3$) δ 2.61 (septet, *J* = 6.9 Hz, 1H), 2.38 (t, *J* = 6.9 Hz, 2H), 1.60 (quintet, *J* = 7.1 Hz, 2H), 1.46−1.26 (m, 4H), 1.18 (d, *J* = 6.9 Hz, 6H), 0.91 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.0, 94.8, 79.5, 42.7, 30.7, 27.2, 21.8, 18.6 (2), 17.7, 13.6; IR (KBr) υ_{max} 2958, 2927, 2856, 1736, 1379, 1260, 1022, 800 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.71; H, 10.95.

(*S*)-2-Methyldec-4-yn-3-ol (26). To the ketone **25** (8.0 g, 48.1 mmol) in CH_2Cl_2 (15 mL), were added formic acid (40 mL), triethylamine (40 mL) and (*S*,*S*)-Noyori asymmetric hydrogenation catalyst (746 mg, 2.5 mol %). The resulting mixture was stirred at room temperature for 10 h, diluted with EtOAc (200 mL), and washed with water (100 mL) followed by saturated aq. $NaHCO_3$ (50 mL) and brine (50 mL). The organic layer was dried over Na_2SO_4, filtered, and evaporated, and the crude product was purified by silica gel column chromatography (2% EtOAc in hexanes) to afford the chiral alcohol **26** (6.4 g, 80%) as a yellow liquid: $[\alpha]^{20}_{D}$ = +0.75 (*c* = 1.07, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.20−4.12 (m, 1H), 2.21 (td, *J* = 1.5, 6.7 Hz, 2H), 1.91−1.73 (m, 1H), 1.57−1.46 (m, 2H), 1.43−1.25 (m, 4H), 1.09−0.95 (m, 6H), 0.90 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.2, 79.7, 68.1, 34.6, 31.0, 28.3, 22.1, 18.6, 18.0, 17.3, 13.9; IR (KBr) υ_{max} 3392, 2958, 2927, 2856, 1736, 1462, 1379, 1260, 1022, 800 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.80; H, 12.02.

(*S*)-2-Methyldec-4-yn-3-yl-4-nitrobenzoate (26′). To a solution of chiral alkynol **26** (100 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) were added *p*-nitrobenzoic acid (119 mg, 0.7 mmol), DCC (245 mg, 1.1 mmol) and DMAP (catalytic), and the mixture was stirred for 2 h at room temperature. The reaction mixture was filtered and evaporated, and the crude was purified by silica gel column chromatography (2% EtOAc in hexanes) to afford the ester product **26′** (179 mg, 95%) as a yellow liquid: $[\alpha]^{20}_{D}$ = +4.76 (*c* = 1.05, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.33−8.27 (m, 2H), 8.26−8.21 (m, 2H), 5.49−5.45 (m, 1H), 2.23 (td, *J* = 2.2, 6.7 Hz, 2H), 2.18−2.07 (m, 1H), 1.56−1.46 (m, 2H), 1.42−1.24 (m, 4H), 1.13−1.04 (m, 6H), 0.88 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7, 150.5, 135.7, 130.7, 123.4, 87.7, 75.5, 71.1, 32.7, 30.9, 28.1, 22.0, 18.6, 18.2, 17.6, 13.9; IR (KBr) υ_{max} 2962, 2932, 2867, 2234, 1729, 1531, 1345, 1267, 1099, 970, 719, 629 cm^{-1}. Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.30; N, 4.41. Found: C, 68.38; H, 7.33; N, 4.42.

(*R*)-2-Methyldec-9-yn-3-ol (27). Potassium hydride (35% suspension in mineral oil, 14.2 g, 125.0 mmol) was weighed in an oven-dried round bottomed flask, washed with diethyl ether (3 × 25 mL) under a nitrogen atmosphere, and dried under a vacuum for 15 min. To this was added slowly 1,3-diaminopropane (125 mL) at room temperature, and the mixture was stirred for 1 h. Then, the alkynol **26** (6.0 g, 35.7 mmol) was added dropwise to the above mixture at 0 °C, and it was allowed to stir for 2 h at room temperature. After completion of the reaction (monitored by TLC), the mixture was cooled to 0 °C and quenched by slow addition of crushed ice. The aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with 1 N HCl (50 mL), brine (50 mL) and dried over Na_2SO_4. The organic layers were evaporated under reduced pressure, and the residue was purified by silica gel column chromatography (4% EtOAc in hexanes) to give **27** (4.6 g, 78%) as a yellow liquid: $[\alpha]^{20}_{D}$ = +15.61 (*c* = 0.98, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 3.42−3.30 (m, 1H), 2.20 (td, *J* = 2.6, 6.9 Hz, 2H), 1.95 (t, *J* = 2.8 Hz, 1H), 1.75−1.23 (m, 9H), 0.96−0.87 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 84.5, 76.5, 68.1, 33.8, 33.4, 28.7, 28.3, 25.4, 18.7, 18.2, 17.0; IR (KBr) υ_{max} 3308, 2935, 2863, 2115, 1463, 1220, 990, 772, 629 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.30; H, 11.94.

(*R*)-2-Methyldec-9-en-3-ol (7a). Compound **27** (4.0 g, 2.3 mmol) was treated with Lindlar's catalyst (5% Pd/$CaCO_3$) (10% w/w, 200 mg) and quinoline (0.1 mL) in EtOAc (50 mL). The reaction mixture was purged with hydrogen several times and stirred under a hydrogen atmosphere. After 1 h, the reaction mixture was filtered and concentrated. The crude product was purified by flash column chromatography (5% EtOAc in hexanes) to afford the desired product **7a** (3.4 g, 84%) as a colorless liquid: $[\alpha]^{20}_{D}$ = +17.09 (*c* = 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.91−5.73 (m, 1H), 5.08−4.89 (m, 2H), 3.43− 3.31 (m, 1H), 2.14−1.98 (m, 2H), 1.75−1.58 (m, 1H), 1.56−1.22 (m, 8H), 0.95−0.88 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9, 114.0, 76.5, 33.9, 33.6, 33.3, 29.1, 28.8, 25.8, 18.7, 17.0; IR (KBr) υ_{max} 3392, 3067, 2921, 2856, 1258, 1219, 772 cm^{-1}. Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.78; H, 12.98.

(3*R*)-2-Methyl-9-en-3-yl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (28). Compound **28** was prepared from **17** (3.0 g, 8.6 mmol) and **7a** (1.2 g, 6.8 mmol) by using the procedure described for the preparation of **3a**, yielding **28** (2.8 g, 65%) as a white solid: mp 88−90 °C; $[\alpha]^{20}_{D}$ = −11.65 (*c* = 0.85, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.88−5.72 (m, 1H), 5.24−5.14 (m, 1H), 5.08 (d, *J* = 9.8 Hz, 1H), 5.04−4.98 (m, 1H), 4.97−4.93 (m, 1H), 4.92−4.89 (m, 1H), 4.51 (d, *J*

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= 7.5 Hz, 1H), 4.26−4.18 (m, 1H), 4.17−4.08 (m, 1H), 3.70−3.62 (m, 1H), 3.38−3.29 (m, 1H), 2.10−1.98 (m, 14H), 1.86−1.67 (m, 1H), 1.59−1.22 (m, 8H), 0.90−0.81 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 170.3, 169.4, 169.2, 139.0, 114.1, 100.8, 85.8, 72.9, 71.6, 71.4, 68.6, 62.2, 33.7, 30.9, 30.8, 29.0, 28.8, 25.1, 20.68, 20.60, 17.8, 17.3; IR (KBr) υ_{max} 2926, 2856, 1756, 1370, 1226, 1039, 772 cm^{-1}; HRMS (m/z) calcd for $C_{25}H_{40}O_{10}Na$ $(M + Na)^+$ 523.2513, found 523.2498.

(3*R*)-2-Methyl-9-en-3-yl-β-D-glucopyranoside (29). Compound **29** was obtained from **28** (2.0 g, 4.0 mmol) by using the procedure described for the preparation of **19**, yielding **29** (1.06 g, 80%) as a colorless liquid: $[\alpha]^{20}_D$ = −13.13 (c = 1.15, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 5.88−5.76 (m, 1H), 4.99 (d, J = 17.2 Hz, 1H), 4.92 (d, J = 9.7 Hz, 1H), 4.30 (d, J = 7.9 Hz, 1H), 3.85 (dd, J = 1.8, 11.6 Hz, 1H), 3.68 (dd, J = 5.5, 12.1 Hz, 1H), 3.53−3.46 (m, 1H), 3.37 (t, J = 8.8 Hz, 1H), 3.34−3.28 (m, 1H), 3.26−3.15 (m, 2H), 2.09−2.02 (m, 2H), 1.96−1.87 (m, 1H), 1.56−1.47 (m, 2H), 1.45−1.27 (m, 6H), 0.92 (t, J = 7.4 Hz, 6H); ^{13}C NMR (75 MHz, CD_3OD) δ 140.1, 114.7, 103.8, 85.1, 78.1, 77.6, 75.3, 71.7, 62.8, 34.8, 32.5, 31.4, 30.5, 30.0, 26.2, 18.6; IR (KBr) υ_{max} 3384, 2925, 2851, 1455, 1359, 1219, 772 cm^{-1}; HRMS (m/z) calcd for $C_{17}H_{32}O_6Na$ $(M + Na)^+$ 355.2091, found 355.2090.

(3*R*)-2-Methyl-9-en-3-yl-4,6-*O*-benzylidine-β-D-glucopyranoside (30). Compound **30** was obtained from **29** (800 mg, 2.4 mmol) following the procedure described for the preparation of **20**, yielding the acetal **30** (961 mg, 95%) as a white solid: mp 96−98 °C; $[\alpha]^{20}_D$ = −33.20 (c = 1.01, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53−7.46 (m, 2H), 7.42−7.33 (m, 3H), 5.89−5.73 (m, 1H), 5.53 (s, 1H), 5.05−4.91 (m, 2H), 4.42 (d, J = 7.5 Hz, 1H), 4.31 (dd, J = 4.9, 10.3 Hz, 1H), 3.87−3.72 (m, 2H), 3.61−3.37 (m, 4H), 2.75 (br s, 1H), 2.47 (br s, 1H), 2.11−2.00 (m, 2H), 1.95−1.81 (m, 1H), 1.56−1.23 (m, 8H), 0.93−0.85 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9, 137.0, 129.1, 128.2, 126.2, 114.3, 102.4, 101.8, 84.6, 80.7, 74.8, 73.1, 68.7, 66.2, 33.6, 31.2, 30.3, 29.3, 28.7, 25.3, 18.1, 17.9; IR (KBr) υ_{max} 3424, 2927, 2861, 1736, 1640, 1458, 1382, 1097, 1028, 990, 912, 770 cm^{-1}; HRMS (m/z) calcd for $C_{24}H_{37}O_6$ $(M + H)^+$ 421.2584, found 421.2582.

(3*R*)-2-Methyl-9-en-3-yl-2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (31). Compound **31** was obtained from **30** (850 mg, 2.0 mmol) following the procedure described for preparation of **21**, yielding **31** (792 mg, 65%) as a white solid: mp 71−74 °C; $[\alpha]^{20}_D$ = −12.77 (c = 1.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.23 (m, 15H), 5.86−5.69 (m, 1H), 5.02−4.90 (m, 3H), 4.89−4.77 (m, 2H), 4.75−4.68 (m, 2H), 4.65−4.59 (m, 1H), 4.47 (d, J = 7.5 Hz, 1H), 3.91−3.79 (m, 1H), 3.72−3.61 (m, 2H), 3.57−3.48 (m, 1H), 3.47−3.29 (m, 3H), 2.06−1.93 (m, 2H), 1.92−1.81 (m, 1H), 1.57−1.37 (m, 2H), 1.35−1.18 (m, 6H), 0.97−0.87 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.0, 138.5, 138.4, 137.9, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 127.5, 114.1, 102.3, 84.7, 84.0, 82.3, 77.8, 75.6, 74.9, 74.8, 74.5, 62.2, 33.7, 31.1, 30.9, 29.5, 28.7, 25.4, 18.6, 17.6; IR (KBr) υ_{max} 3387, 3031, 2925, 2856, 1454, 1375, 1070, 736, 697 cm^{-1}; HRMS (m/z) calcd for $C_{38}H_{50}O_6Na$ $(M + Na)^+$ 625.3499, found 625.3492.

(3*R*)-2-Methyl-9-en-3-yl-2,3,4-tri-*O*-benzyl-6-*O*-(3-benzyloxycarbonylpropanoyl)-β-D-glucopyranoside (32). Compound **32** was obtained from **31** (600 mg, 0.8 mmol) by using the procedure described for the preparation of **9**, yielding **32** (671 mg, 85%) as a white solid: mp 66−68 °C; $[\alpha]^{20}_D$= −16.13 (c = 1.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.21 (m, 20H), 5.85−5.69 (m, 1H), 5.12 (s, 2H), 5.02−4.89 (m, 4H), 4.88−4.75 (m, 2H), 4.70 (d, J = 10.9 Hz, 1H), 4.56 (d, J = 10.9 Hz, 1H), 4.44−4.32 (m, 2H), 4.20 (dd, J = 4.9, 11.8 Hz, 1H), 3.65 (t, J = 8.6 Hz, 1H), 3.53−3.36 (m, 4H), 2.68−2.60 (m, 4H), 2.05−1.93 (m, 2H), 1.92−1.80 (m, 1H), 1.57−1.37 (m, 2H), 1.37−1.16 (m, 6H), 0.95−0.83 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 171.8, 139.0, 138.5, 138.4, 137.8, 135.7, 128.5, 128.4, 128.3, 128.26, 128.23, 128.17, 128.10, 127.9, 127.7, 127.5, 114.1, 102.4, 84.8, 84.0, 82.9, 77.7, 75.6, 74.9, 74.7, 72.4, 66.5, 63.4, 33.7, 31.1, 30.8, 29.5, 29.1, 29.0, 28.9, 28.7, 25.5, 18.4, 17.6; IR (KBr) υ_{max} 3060, 3032, 2929, 2857, 1740, 1454, 1354, 1214, 1155, 1069, 772, 698 cm^{-1}; HRMS (m/z) calcd for $C_{49}H_{64}NO_9$ $(M + NH_4)^+$ 810.4576, found 810.4550.

Compound 33. The compound **33** was obtained from the reaction of **32** (100 mg, 0.12 mmol) with **4** (76.5 mg, 0.25 mmol) following the procedure described for compound **13**, affording **33** as a yellow liquid (119 mg, 85%): $[\alpha]^{20}_D$= −13.00 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.23 (m, 25H), 6.05 (d, J = 6.2 Hz, 1H), 5.40−5.28 (m, 2H), 5.20−5.15 (m, 3H), 5.12 (s, 2H), 4.95 (d, J = 10.9 Hz, 1H), 4.88−4.75 (m, 2H), 4.73−4.53 (m, 3H), 4.45−4.32 (m, 2H), 4.20 (dd, J = 4.5, 11.5 Hz, 1H), 3.73−3.60 (m, 1H), 3.53−3.36 (m, 4H), 2.70−2.60 (m, 4H), 2.25−2.15 (m, 2H), 2.10−1.76 (m, 4H), 1.71−1.56 (m, 2H), 1.55−1.45 (m, 1H), 1.40 (d, J = 7.1 Hz, 3H), 1.37−1.19 (m, 12H), 0.89 (t, J = 6.2 Hz, 2 × 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 172.5, 171.9, 171.8, 138.4, 137.8, 135.7, 135.2, 130.4, 129.9, 128.57, 128.50, 128.39, 128.30, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 102.3, 84.8, 84.0, 82.2, 77.6, 75.5, 74.8, 74.7, 72.4, 67.1, 66.4, 63.3, 47.9, 36.4, 32.5, 32.3, 31.1, 30.8, 29.6, 29.4, 29.2, 29.0, 28.9, 28.7, 25.6, 25.3, 18.5, 18.4, 17.6; IR (KBr) υ_{max} 2921, 2852, 1736, 1650, 1453, 1349, 1218, 1155, 1062, 772 cm^{-1}; HRMS (m/z) calcd for $C_{65}H_{81}NO_{12}Na$ $(M + Na)^+$ 1090.5656, found 1090.5590.

Compound 34. The compound **34** was prepared from **32** (100 mg, 0.12 mmol) and **5** (72.9 mg, 0.25 mmol) by using the procedure described for compound **13**, giving **34** as a yellow liquid (120 mg, 87%): $[\alpha]^{20}_D$= −15.50 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.20 (m, 25H), 5.98 (br s, 1H), 5.40−5.27 (m, 2H), 5.20−5.17 (m, 2H), 5.12 (s, 2H), 4.98−4.91 (m, 2H), 4.88−4.76 (m, 2H), 4.70 (d, J = 10.9 Hz, 1H), 4.56 (d, J = 10.7 Hz, 1H), 4.44−4.43 (m, 2H), 4.20 (dd, J = 4.7, 11.7 Hz, 1H), 4.11−4.04 (m, 3H), 3.65 (t, J = 8.6 Hz, 1H), 3.53−3.36 (m, 3H), 2.69−2.60 (m, 4H), 2.28−2.18 (m, 2H), 2.10−1.81 (m, 4H), 1.78−1.57 (m, 3H), 1.55−1.19 (m, 12H), 0.89 (t, J = 6.2 Hz, 2 × 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 171.9, 171.8, 169.9, 138.7, 138.5, 138.4, 135.7, 135.0, 130.4, 129.9, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 102.3, 84.8, 84.0, 82.2, 77.7, 75.5, 74.8, 74.7, 72.4, 67.1, 66.4, 63.3, 41.3, 36.3, 33.4, 32.5, 32.3, 31.2, 30.9, 29.5, 29.4, 29.2, 29.0, 28.9, 28.7, 28.6, 28.5, 25.6, 25.3, 18.4, 17.6; IR (KBr) υ_{max} 2921, 2851, 1739, 1654, 1455, 1355, 1215, 1172, 1083, 1009, 772 cm^{-1}; HRMS (m/z) calcd for $C_{64}H_{79}NO_{12}Na$ $(M + Na)^+$ 1076.5500, found 1076.5542.

Compound 1a. Compound **1a** was obtained from **33** (30 mg, 0.02 mmol) following the procedure described for the preparation of **1**, yielding **1a** (15.6 mg, 90%) as a yellow liquid: $[\alpha]^{20}_D$= −13.57 (c = 1.12, CH_3OH); ^{1}H NMR (500 MHz, CD_3OD) δ 4.43 (d, J = 11.6 Hz, 1H), 4.36 (dd, J = 7.1, 14.3 Hz, 1H), 4.28 (d, J = 7.1 Hz, 1H), 4.20 (dd, J = 6.2, 11.6 Hz, 1H), 3.46−3.38 (m, 2H), 3.37−3.23 (m, 2H), 3.17 (t, J = 8.0 Hz, 1H), 2.64−2.57 (m, 4H), 2.22 (t, J = 7.1 Hz, 2H), 1.94−1.84 (m, 1H), 1.65−1.57 (m, 2H), 1.54−1.45 (m, 2H), 1.38 (d, J = 7.1 Hz, 3H), 1.36−1.26 (m, 18H), 0.89 (t, J = 6.2 Hz, 6H); ^{13}C NMR (75 MHz, CD_3OD) δ 176.1, 174.4, 174.1, 104.1, 85.9, 78.2, 75.5, 75.2, 72.2, 65.2, 49.1, 37.2, 32.8, 31.9, 30.9, 30.8, 30.6, 30.4, 27.1, 26.7, 18.8, 18.7 (2); IR (KBr) υ_{max} 3690, 2926, 2862, 1647, 1371, 1219, 1054, 1033, 772 cm^{-1}; HRMS (m/z) calcd for $C_{30}H_{53}NO_{12}Na$ $(M + Na)^+$ 642.3500, found 642.3521.

Compound 2a. Compound **2a** was obtained from **34** (25 mg, 0.02 mmol) following the procedure described for the preparation of **1**, yielding **2a** (12.6 mg, 88%) as a yellow liquid: $[\alpha]^{20}_D$= −7.25 (c = 0.8, CH_3OH); ^{1}H NMR (500 MHz, CD_3OD) δ 4.43 (d, J = 11.6 Hz, 1H), 4.29 (d, J = 7.1 Hz, 1H), 4.20 (dd, J = 7.1, 11.6 Hz, 1H), 3.84 (s, 2H), 3.45−3.38 (m, 2H), 3.38−3.24 (m, 2H), 3.18 (t, J = 8.0 Hz, 1H), 2.64−2.56 (m, 4H), 2.25 (t, J = 8.0 Hz, 2H), 1.93−1.85 (m, 1H), 1.66−1.54 (m, 2H), 1.54−1.46 (m, 2H), 1.39−1.26 (m, 18H), 0.90 (t, J = 6.2 Hz, 2 × 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 176.3, 176.2, 174.6, 173.5, 104.1, 85.8, 78.2, 75.5, 75.2, 72.1, 65.1, 41.8, 37.2, 32.7, 31.8, 31.8, 31.2, 30.9, 30.8, 30.6, 30.5, 27.0, 26.7, 18.8, 18.7; IR (KBr) υ_{max} 3668, 3386, 2940, 2866, 1647, 1371, 1219, 1054, 1032, 772 cm^{-1}; HRMS (m/z) calcd for $C_{29}H_{52}NO_{12}$ $(M + H)^+$ 606.3484, found 606.3488.

Compound **8**[6] and **17**[10] were prepared from D-glucose according to the literature procedure. The spectral data of **8** and **17** were in full agreement with the literature data.

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■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of all new compounds, COSY, HMBC, HSQC and ROESY spectra of **2** and **2a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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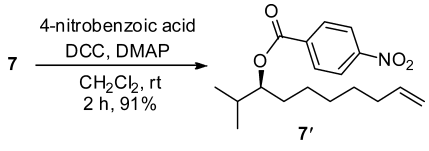
(5) The enantiomeric excess of (*S*)-2-methyldec-9-en-3-ol (**7**) was determined by converting it to *p*-nitrobenzoate derivative **7′** under DCC/DMAP reaction conditions using *p*-nitrobenzoic acid. Chiral HPLC: Chiral pack column (I 250 × 4.6 mm, 5 μ), mobile phase 3% isopropanol in hexanes, flow rate 1 mL/min, λ 210 nm. Retention time (min): 6.66 (2.1%), 7.22 (97.9%).



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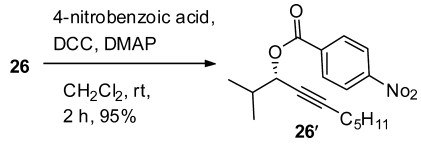
(16) The enantiomeric excess of (*S*)-2-methyldec-4-yn-3-ol (**26**) was determined by converting it to *p*-nitrobenzoate derivative **26′** under DCC/DMAP reaction conditions using *p*-nitrobenzoic acid. Chiral HPLC: Chiral pack column (I 250 × 4.6 mm, 5 μ), mobile phase 3% isopropanol in hexanes, flow rate 1 mL/min, λ 210 nm. Retention time (min): 8.0 (97.7%), 9.14 (2.3%).



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(19) We have requested Prof. Shin to provide the natural product samples for comparison with our synthetic compounds or to recheck the specific rotation of natural ieodoglucomides A and B. On the basis of our request, they have measured the specific rotation once again and found that their earlier reported values were incorrect and that the observed rotations are with a "negative" sign, as $[\alpha]^{23}_{D} = -22$ (c = 0.2, MeOH) for ieodoglucomide A (**1**) and $[\alpha]^{23}_{D} = -31$ (c = 0.2, MeOH) for ieodoglucomide B (**2**), which are in agreement with the identical sign of our observation.

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