Extended Alkenyl Glycosides by Ruthenium-Catalyzed Cross-Metathesis Reaction and Application toward Novel C-Linked Pseudodisaccharides

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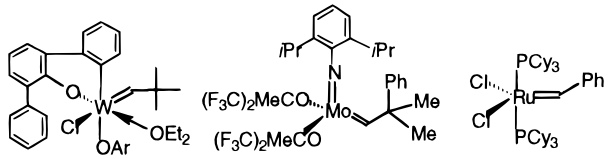
Grubbs's ruthenium benzylidene catalyst (**3**) has been successfully applied toward the cross-metathesis reactions of allyl α-D-galactopyranoside derivative (**4**) with a number of olefins. Terminal alkenes possessing a wide range of protecting groups were used as cross-metathetic partners to allow syntheses of glycosides having extended spacers and functionality in the aglycon moieties. The reaction is quite general and the cross-metathesis products (**14**−**21**) were obtained in high yields. The strategy has also been applied toward the synthesis of some C-linked pseudodisaccharides from allyl α-C-galactoside derivatives (**23**, **26**, and **28**) in good yields. In almost all cases, *trans*-stereoselectivity was found to be good to excellent.

Introduction

The extension of carbon skeletons by the construction of carbon−carbon bonds represents one of the most important areas in synthetic organic chemistry. Transition metal catalyzed olefin metathesis reaction is especially valuable in this regard. There are some early examples of olefin cross-metathesis[1] using a tungsten alkylidene catalyst **1**, but cross-metathesis reactions began to receive more attention after the discovery of the highly active but air-sensitive Schrock's molybdenum catalyst **2**.[2] It has been successfully used to synthesize cross-metathetic products of styrene,[3] acrylonitrile,[4] allyltrimethylsilane[5] with various olefins. The major drawbacks of these catalysts are that catalyst **1** cannot tolerate an allylic methyl group[6] and catalyst **2** is very air and moisture sensitive. After the development of the ruthenium benzylidene catalyst **3** by Grubbs's et al.,[7] olefin metathesis has experienced an important breakthrough. Catalyst **3** is air stable for a reasonable period of time and remains metathesis-active in the presence of a variety functional groups including carbonyl, alcohol, and amide.[8] Recently, we have reported an efficient method[9] for the synthesis of carbohydrate homodimers using catalyst **3**. Such sugar homodimers represent appealing tools to quickly titrate distances between carbohydrate binding sites in polyvalent recognition. Moreover, they may represent potent noncovalent cross-linking reagents.[10] In our continuing efforts toward the design and synthesis of neoglycoconjugates,[10] we required a convenient route to prepare differently functionalized spacers in the aglycon moiety that can be readily prepared from *O*- and *C*-allyl glycosides by cross-metathesis reaction. These extended glycosides can be further transformed by known methods (amidation, copolymerization) into useful neoglycoconjugates including, proteins, dendrimers, and polymers.[11]



1 **2** **3**

Although catalyst **3** has already been used in numerous recent syntheses[12] of biologically important natural products, there are very few examples for selective cross-

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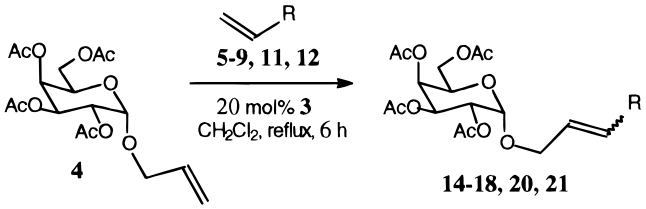
Scheme 1



metathesis.[13] Herein, we report the cross-metathesis of *O*- and *C*-allyl galactopyranoside derivatives with only 2−4 equiv of various aliphatic and aromatic olefins in good to excellent yields.

Results and Discussion

The starting material, allyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (**4**) was readily synthesized in multigram quantities from commercially available D-galactose by a known procedure.[14] The cross-metathesis of (**4**) with allyltrimethylsilane (**5**) is very interesting, since allylsilanes hold tremendous utility as reagent and reaction intermediates in organic syntheses.[15] Thus the reaction of 0.06 M solution of **4** in dry dichloromethane with 2 equiv of allyltrimethylsilane (**5**) under reflux conditions for 6 h gave the desired substituted allylsilane derivative (**14**) in 94% yield (based on allyl glycoside) as a mixture of *trans* and *cis* stereoisomers in a ratio of 4:1 which were assigned on the basis of ^{13}C NMR spectrum.[16] The chemical shift of the allylic carbon in the *Z* isomer appeared ca. 5 ppm upfield from that of the *E* isomer due to the γ-effect. Furthermore, the olefinic carbon of the *Z* isomer appeared ca. 1 ppm upfield from the *E*-isomer. When the reaction was repeated with 10 mol % of catalyst, the yield decreased to 50%. The remaining starting material was recovered along with 10% of homodimer **13**[9] resulting from self-metathesis of **4** (not shown). The use of 0.13 M solution of **4** in dichloromethane gave a lower yield of cross-metathesis product due to competitive homodimer formation. Stereoisomeric alkene mixture **14***E*/*Z* was further transformed into a single compound **14a** by reduction (H_2, 10% Pd−C, quant)

To investigate the protecting group compatibility of this cross-metathesis reaction, methyl 4-pentenoate (**6**) and allyloxy-*tert*-butyldimethylsilane (**7**) were synthesized using standard protecting group procedures. The reaction of **4** with **6** under the same reaction conditions gave 67% of the cross-metathesis product (**15**) with modest *trans*-selectivity (ca. 2:1) while treatment with **7** gave the cross-metathesis product **16** with high *trans*-selectivity without diminishing the overall yield (69% as unseparable isomers). The results with various alkenes are summarized in Scheme 1 and Table 1. Once the reaction conditions were optimized for aliphatic alkenes, the cross-metathesis was directed toward aromatic alkenes such as styrene (**8**) and 4-acetoxystyrene (**9**). The reaction between **4** and 2 equiv of styrene (**8**) gave 60% of the desired cross-metathesis product **17** but the use of 4 equiv of styrene was found to be more efficient and gave 80% of **17** with excellent *trans*-stereoselectivity (97:3). In a similar manner, treatment **4** with 4 equiv of **9** gave 75% of the cross-metathesis product **18**. In both cases, pure *trans* stereoisomers (**17***E*, **18***E*) were isolated. Though **9** contains an electron-withdrawing group, the yield and the stereoselectivity were found to be similar to that of styrene, implying that inductive effect does not play a role in this cross-metathesis reaction. The high *trans*-stereoselectivity observed with bulky substituents or styrene derivatives (see **7**, **8**, **9**, Table 1, entries 3−6) has been previously observed.[3,8d] To investigate the influence of disubstituted olefin in cross-metathesis, we prepared *cis*-2-butene-1,4-diol diacetate (**10**).[13d] The reaction between **4** and 2 equiv of **10** gave 70% of the cross-metathesis product **19** (*E*/*Z* = 5:1). In all cases mentioned above, 10−20% of self-metathized starting material (**13**) that can be easily recovered and recycled in the cross-metathesis step was formed.

Table 1. Isolated Yields and *E*/*Z* Ratios of Ruthenium-Catalyzed Cross-Metathesis of 4 with 5−12

entry	R	equiv	react. cond[a]	product	yield	*E*/*Z* ratio
1	CH_2SiMe_3 (**5**)	2	A	**14**	94	4:1
2	$CH_2CH_2CO_2Me$ (**6**)	2	A	**15**	67	2:1
3	CH_2OTBS (**7**)	2	A	**16**	69	95:5
4	Ph (**8**)	2	A	**17**	60	90:10
5	Ph (**8**)	4	A	**17**	80	97:3
6	*p*-AcOPh (**9**)	4	A	**18**	75	95:5
7	$(=CHCH_2OAc)_2$ (**10**)	2	A	**19**	70	5:1
8	CH_2NHBoc (**11**)	2	A	**20**	30	4:1
9	CH_2NHBoc (**11**)	2	B	**20**	57	4:1
10	CH_2NHCbz (**12**)	2	A	**21**	39	4:1
11	CH_2NHCbz (**12**)	2	B	**21**	65	4:1

[a] Method A: CH_2Cl_2, reflux, 6 h; method B: CH_2Cl_2; rt, 15 h.

To further explore the scope and generality of this method, the cross-metathesis reaction with amine-containing substrates was performed. When the cross-metathesis reaction was accomplished with allylamine and **4**, no cross-metathesis product was formed. The presence of a free amine group apparently poisoned catalyst **3**. This problem was, however, easily overcome by using Boc-protected allylamine (**11**), and the metathesis product provided a direct route to the corresponding protected allylic amine. Thus, treatment of 0.06 M solution of **4** in dry dichloromethane with 2 equiv of **11** at 40 °C gave **20** in only 30% yield. However, the yield could be improved by using 0.13 M solution of **4** and reached 57% when the reaction was carried out at room temperature. This is probably because the amide group deactivates the ruthenium catalyst at higher temperature (40 °C). The *trans*:*cis* ratio was again found to be 4:1 and pure *E*-isomer (**20***E*) was isolated. No improvement was observed when the catalyst was added incrementally (4 × 5%). In a similar manner, when 2 equiv of Cbz-protected allylamine (**12**) was treated with **4** (0.13 M solution), compound **21** was obtained in 65% yield, the overall yield and the *trans*-selectivity (4:1) were found to be similar to that of **11**.

Recently, *C*-glycosides have been the subject of considerable interest in carbohydrate chemistry.[17] In view

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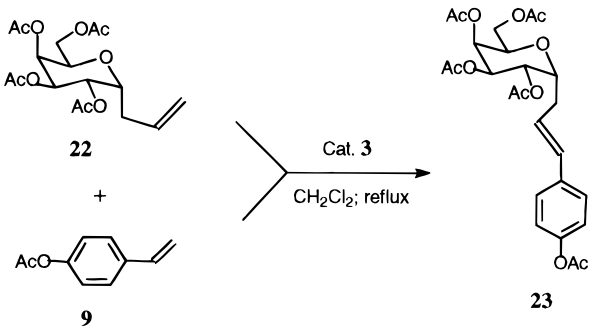
Scheme 2



of their importance, we planned to synthesize some *C*-glycoside derivatives by using the above strategy. Sequential reactions of peracetylated D-galactopyranose with allyltrimethylsilane in the presence of $BF_3 \cdot OEt_2$ gave the requisite *C*-allyl α-D-galactopyranoside (**22**).[18] The cross-metathesis reaction between **22** (0.06 M solution in dry dichloromethane) and 2 equiv of 4-acetoxystyrene (**9**) led to the formation of the cross-metathesis product **23** in 50% yield. The yield could be further improved to 75% by using 4 equiv of **9**. Compound **23** was obtained as a single *trans* isomer together with 19% of homodimer **24** (based on *C*-glycoside) (Scheme 2). When treatment of the *C*-galactoside **22** was extended to 6-*O*-allyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (**25**), the reaction provided **26** in 67% yield (*trans*:*cis*; 4:1) and 14% of homodimer **24** was isolated accordingly (Scheme 3). Another potentially powerful application of this methodology is to prepare *C*-linked pseudodisaccharides that can be used as glycomimetic precursors. For that, the other partner (**27**) of the cross-metathesis reaction was prepared from 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose by sequential oxidation and Wittig homologation.[19] The metathesis reaction between **22** and 2 equiv of **27** led to the formation of the cross product **28** (89%) together with 6% of homodimer **24** (not shown) resulting from self-metathesis of **22**. Each stereoisomer **28***E*/*Z* was obtained pure after silica gel column chromatography. The cross-metathized product was predominantly *trans* (*trans*:*cis* = 2:1), and the results are shown in Table 2. For control purposes, alkene **27** was separately homodimerized under the above conditions (CH_2Cl_2, reflux, 6 h). Dimer **27a** was obtained in 65% yield, and each stereoisomer was separated by silica gel column chromatography. A competitive experiment was also performed to compare the relative reactivity of **22** and **27** under homodimerization conditions. Preliminary results indicated that, despite being "apparently" more hindered, alkene **27** was reacting a little faster than **22**. Presumably, this observation may result from a decreased reactivity of the catalyst originating from a better "coordinating" ability of the acetate groups of **22**. In some ways, this may represent another example of "armed" and "disarmed" reactivity.[20]

Summary

In conclusion, it was shown that Grubbs's ruthenium benzylidene catalyzed cross-metathesis is a powerful synthetic method for the syntheses of various carbohydrate derivatives including some biologically active *C*-galactoside derivatives (compounds **26** and **28**). The main advantage of the cross-metathesis reaction for the preparation of substituted olefins over other methods is its operational simplicity, and the reaction proceeds under very mild and neutral conditions. It has also been shown that the catalyst remains highly active in the presence of a wide variety of functional groups. The reaction is general and high yielding with good to high *trans*-stereoselectivity.

Experimental Section

Materials. ^1H and ^{13}C NMR were recorded on an AMX500 spectrometer at 500 MHz for protons and 125.7 MHz for carbons, respectively. Spectral analyses were performed as first-order approximations and were based on shift correlation spectroscopy (COSY), heteronuclear multiple quantum coherence (HMQC), and one- and two-dimensional distortionless enhancement by polarization transfer (DEPT) experiments. Thin-layer chromatography (TLC) was performed using silica gel 60-F_{254} glass plates. Reagents used for developing plates include ceric sulfate (1% w/v) and ammonium sulfate (2.5% w/v) in 10% (v/v) aqueous sulfuric acid, iodine, dilute aqueous potassium permanganate, and UV light. TLC plates were heated to approximately 150 °C when necessary. Purifications were performed by gravity or flash chromatography on silica gel 60 (230−400 mesh; E. Merck No. 9385). Solvents were evaporated under reduced pressure using a Büchi rotary evaporator connected to a water aspirator. All chemicals used in experiments were of reagent grade. Solvents were purified by the published procedures.

General Procedure for Cross-Metathesis Reaction. To a 0.06 M solution of allyl glycoside **4** (50 mg, 0.129 mmol) in dry dichloromethane (2 mL) were added the appropriate alkene and Grubbs's catalyst (20 mol %), and the reaction mixture was heated at reflux under nitrogen for 6 h. The solution was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography using ethyl acetate and hexane as eluent.

4-(Trimethylsilyl)but-2-ene-1-yl 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranoside (14). Compound **14** was purified by silica gel column chromatography using ethyl acetate and hexane as eluent (2/1) and obtained as a syrup of unseparated *E*/*Z* stereoisomers (4:1); ^1H NMR ($CDCl_3$) δ 5.65 (ddd, J = 8.2, 9.3, 15.2 Hz, 1H, H-3′), 5.45 (dd, J = 1.4, 3.4 Hz, 1H, H-4), 5.35 (m, 2H, H-2′, H-3), 5.13 (dd, J = 3.7, 8.2 Hz, 1H, H-2), 5.12 (d, 1H, J = 3.7 Hz, H-1), 4.22 (t, J = 6.7 Hz, 1H, H-5), 4.10 (m, 3H, H-6a, H-6b, H-1′a), 3.93 (dd, J = 7.5, 11.9 Hz, 1H, H-1′b), 2.12, 2.05. 2.03, 2.00 (4s, 12H, OAc), 1.48 (d, 2H, J = 8.2 Hz, H-4′a, H-4′b), 0.00 (s, 9H, Me); ^{13}C NMR ($CDCl_3$) δ 170.4, 170.3, 170.2, 170.0 (CO), 133.4 (C-3′ *trans*), 131.3 (C-3′ *cis*), 122.9 (C-2′ *trans*), 121.8 (C-2′ *cis*), 94.5 (C-1), 68.7 (C-1′ *trans*), 68.2 (C-2), 68.1 (C-4), 67.7 (C-3), 66.2 (C-5), 63.4 (C-1′ *cis*), 61.8 (C-6), 23.0 (C-4′ *trans*), 20.8, 20.7, 20.6 (Me), 19.2 (C-4′ *cis*), −1.9 (Me). Anal. Calcd for $C_{21}H_{34}O_{10}Si$: C, 53.15; H, 7.22. Found: C, 52.99; H, 7.17.

4-(Trimethylsilyl)butane-1-yl 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranoside (14a). To a solution of compound **14** (100 mg, 0.21 mmol) in methanol (5 mL) was added 10 mg of Pd/C (10%). The reaction mixture was stirred under H_2 (1 atm) for 12 h at room temperature and then filtered through Celite. Removal of the solvent in vacuo and purification of the crude residue by silica gel column chromatography using ethyl acetate and hexane (2\1) as eluent gave the desired compound **14a** (100 mg, 100%) as a thick syrup; $[\alpha]^{20}_D$ = +82° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 5.45 (dd, J = 2.2, 3.3 Hz, 1H, H-4), 5.32−5.35 (m, 1H, H-3), 5.08−5.10 (m, 2H, H-1, H-2), 4.18−4.20 (m, 1H, H-5), 4.07 (dd, J = 3.4, 6.2 Hz, 1H, H-6), 3.66 (ddd, J = 6.5, 13.0 Hz, 1H, H-1′a), 3.40 (ddd, J = 6.5, 13.3 Hz, 1H, H-1′b), 2.12, 2.04, 2.02, 1.97 (4s, 12H), 1.56−1.60 (m, 2H, H-2′), 1.32−1.37 (m, 2H, H-3′), 0.48 (dd, J = 7.6, 9.4 Hz, 2H,

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Scheme 3

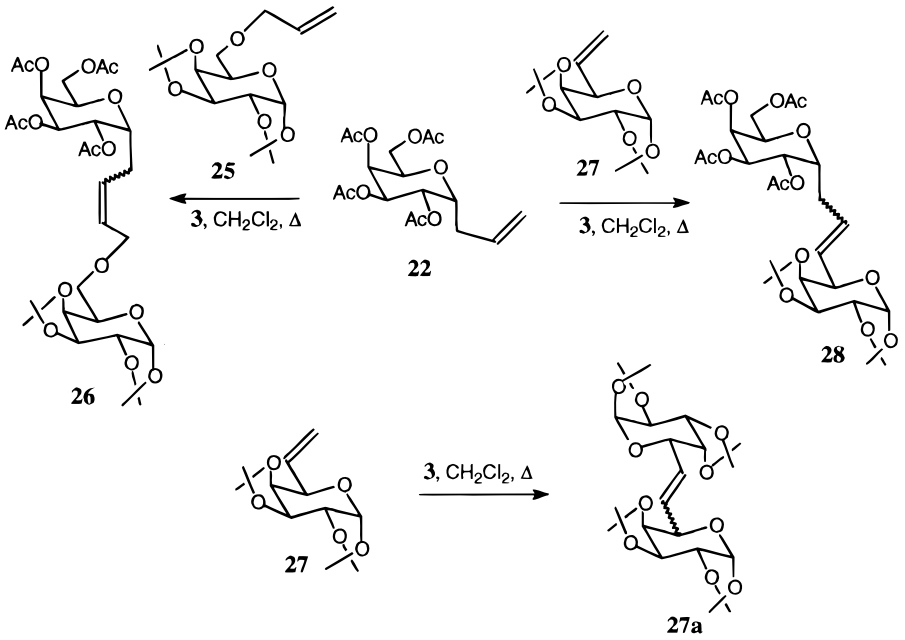

Table 2. Isolated Yields and *E*/*Z* Ratios of Ruthenium-Catalyzed Cross-Metathesis of *C*-Allyl Galactoside Derivative (22) with Alkenes 9, 25, and 27

entry	start. mater	equiv	react. cond.	product	yield	*E*/*Z* ratio
1	**9**	2	CH_2Cl_2, reflux	**23**	50	100:0
2	**9**	4	CH_2Cl_2; reflux	**23**	75	100:0
3	**25**	2	CH_2Cl_2; reflux	**26**	67	4:1
4	**27**	2	CH_2Cl_2; reflux	**28**	89	2:1

H-4′), −0.04 (s, 9H);^{13}C NMR ($CDCl_3$) δ 170.3, 170.3, 170.2, 170.0 (CO), 96.0 (C-1), 68.2 (C-4), 68.2 (C-1′), 68.1 (C-2), 67.7 (C-3), 66.1 (C-5), 61.7 (C-6), 32.9 (C-2′), 20.7, 20.6, 20.6, 20.6 (Me), 20.4 (C-3′), 16.3 (C-4′), −1.8 ($SiMe_3$); MS (FAB) *m*/*z*: 477.27 (M + 1).

Methyl 6-(2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyloxy)hex-4-enoate (15). Compound **15** was isolated by column chromatography using ethyl acetate and hexane (1\1) as a thick syrup of unseparated *E*/*Z* stereoisomers (2:1); ^{1}H NMR ($CDCl_3$) δ 5.70 (m, 1H, H-3′), 5.55 (m, 1H, H-2′), 5.40 (t, J = 3.4 Hz, 1H, H-4), 5.31 (dd, J = 3.4, 8.7 Hz, 1H, H-3), 5.10 (m, 2H, H-1, H-2), 4.25−3.90 (m, 5H, H-1′a, H-1′b, H-5, H-6a, H-6b), 3.64, 3.63 (2s, 3H, OMe), 2.35 (m, 4H, H-4′, H-5′), 2.09, 2.04, 2.01, 1.94 (4s, 12H); ^{13}C NMR ($CDCl_3$) δ 173.1, 170.3, 170.2, 170.1 (CO), 133.3 (C-3′ *trans*), 132.5 (C-3′ *cis*), 126.0 (C-2′ *trans*), 125.8 (C-2′ *cis*), 95.1 (C-1), 68.1 (C-1′ *trans*), 68.1 (C-4), 68.0 (C-2), 67.5 (C-3), 66.2 (C-5), 63.1 (C-1′ *cis*), 61.6 (C-6), 51.5 (OMe), 33.6 (C-5′), 27.4 (C-4′ *trans*), 22.9 (C-4′ *cis*), 20.7, 20.6, 20.5 (Me). Anal. Calcd for $C_{21}H_{30}O_{12}$: C, 53.16; H, 6.37. Found: C, 52.98; H, 6.49.

4-(*tert*-Butyldimethylsilyloxy)but-2-ene-1-yl 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranoside (16). Column chromatography was performed with ethyl acetate and hexane (2/1) as eluent to obtain syrupy compound **16** as an unseparated *E*/*Z* stereoisomeric mixture (95:5); ^{1}H NMR ($CDCl_3$) δ 5.79 (dt, J = 4.1, 15.5 Hz, 1H, H-2′), 5.70 (dt, J = 4.5, 15.5 Hz, 1H, H-3′), 5.41 (dd, J = 1.3, 3.3 Hz, 1H, H-4), 5.33 (dd, J = 3.3, 10.8 Hz, 1H, H-3), 5.12−5.08 (m, 2H, H-1, H-2), 4.21−4.14 (m, 4H, H-1′a, H-4′a, H-4′b, H-5), 4.06 (dd, J = 3.3, 6.4 Hz, 2H, H-6a, H-6b), 4.00−3.95 (m, 1H, H-1′b), 2.10, 2.03, 2.01, 1.94 (4s, 12H, OAc), 0.87 (s, 9H), 0.03 (s, 6H); ^{13}C ($CDCl_3$) δ 170.3, 170.3 170.2, 169.9 (CO), 133.6 (C-2′), 124.4 (C-3′), 95.1 (C-1), 68.1 (C-4), 68.0 (C-2), 67.8 (C-1′ *trans*), 63.7 (C-1′ *cis*), 67.6 (C-3), 66.3(C-5), 62.8 (C-4′ *trans*), 59.4 (C-4′ *cis*), 61.6 (C-6), 25.9, 20.7, 20.6, 20.6, −5.3 (Me). MS (FAB) *m*/*z*: 533.31 (M + 1).

3-Phenylprop-2-ene-1-yl 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranoside (17). After silica gel column chromatography with ethyl acetate and toluene as eluent (1/4), compound **17** was isolated as a thick syrup of *E*/*Z* mixture (97:3). The *E*-isomer was separated from the isomeric mixture. For *E*-isomer, $[\alpha]^{20}_D$ = +87° (*c* 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 7.38−7.15 (m, 5H, aromatic), 6.58 (d, J = 15.9 Hz, 1H, H-3′), 6.21 (ddd, J = 5.8, 6.6, 15.9 Hz, 1H, H-2′), 5.45 (dd, J = 1.4, 3.4 Hz, 1H, H-4), 5.38 (dd, J = 3.4, 10.8 Hz, 1H, H-3), 5.19 (d, J = 3.4 Hz, 1H, H-1), 5.14 (dd, J = 3.4, 10.8 Hz, 1H, H-2) 4.33 (ddd, J = 1.5, 5.7, 12.8 Hz, 1H, H-1′a), 4.27 (t, J = 6.5 Hz, 1H, H-5), 4.17 (ddd, J = 1.5, 6.6, 12.8 Hz, 1H, H-1′b) 4.08 (d, J = 6.5 Hz, 2H, H-6a, H-6b), 2.10, 2.05, 2.01, 2.00 (4s, 12H, OAc); ^{13}C NMR ($CDCl_3$) δ 170.3, 170.3, 170.2, 169.9 (CO), 136.3, 133.4, 128.6, 127.9, 126.5, 124.3 (aromatic and olefinic), 95.4 (C-1), 68.6 (C-1′), 68.1 (C-4), 68.1 (C-2), 67.6 (C-3), 66.4 (C-5), 61.7 (C-6), 20.7, 20.6, 20.6, 20.6 (Me). Anal. Calcd for $C_{23}H_{28}O_{10}$: C, 59.48; H, 6.08. Found: C, 59.38; H, 5.99.

3-(*p*-Acetoxyphenyl)prop-2-ene-1-yl 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranoside (18). Purification of syrupy *E*/*Z* mixture (95:5) **18** was performed by silica gel column chromatography using ethyl acetate and hexane (1/1) as eluent. The *E*-isomer was separated from the mixture. For *E*-isomer, $[\alpha]^{20}_D$ = +115° (*c* 4, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 7.36, 7.01 (2d, J = 8.5 Hz, 4H, aromatic), 6.58 (d, J = 15.9 Hz, 1H, H-3′), 6.16 (ddd, J = 5.8, 6.5, 15.9 Hz, 1H, H-2′), 5.44 (dd, J = 1.2, 3.3 Hz, 1H, H-4), 5.35 (dd, J = 3.3, 10.8 Hz, 1H, H-3), 5.18 (d, J = 3.7 Hz, 1H, H-1), 5.12 (dd, J = 3.7, 10.8 Hz, 1H, H-2), 4.31 (ddd, J = 1.5, 5.8, 12.9 Hz, 1H, H-1′a), 4.25 (ddd, J = 1.2, 6.5 Hz, 1H, H-5), 4.15 (ddd, J = 1.5, 6.4, 12.9 Hz, 1H, H-1′b), 4.09 (d, J = 6.5 Hz, 2H, H-6a, H-6b), 2.25, 2.11, 2.04, 2.01,1.95 (5s, 15H, OAc); ^{13}C ($CDCl_3$) δ 170.3, 170.3, 170.1, 169.9, 169.3 (CO), 150.3, 134.1, 132.3, 127.4, 124.6, 121.7 (aromatic and olefinic), 95.4 (C-1), 68.4 (C-1′), 68.1 (C-4), 68.0 (C-2), 67.6 (C-3), 66.4 (C-5), 61.7 (C-6), 21.0, 20.7, 20.6, 20.6 (Me). MS (FAB) *m*/*z*: 561.15 (M + K^+).

4-Acetoxybut-2-ene-1-yl 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranoside (19). Purification of **19**, as an unseparated mixture of *E*/*Z* stereoisomers (5:1), was performed by silica gel column chromatography (ethyl acetate:hexane = 1:1); ^{1}H NMR ($CDCl_3$) δ 5.82−5.68 (m, 2H, H-2′, H-3′), 5.39 (dd, J = 2.0, 3.4 Hz, 1H, H-4), 5.31 (dd, J = 3.4, 9.1 Hz, 1H, H-3), 5.07 (m, 2H, H-1, H-2), 4.57 (m, 2H, H-4′ *cis*), 4.52 (d, J = 4.4 Hz, 2H, H-4′ *trans*), 4.25−4.05 (m, 2H, H-5, H-1′a), 4.03 (d, J = 6.7 Hz, 2H, H-6a, H-6b), 3.98 (dd, J = 5.1, 13.5 Hz, 1H, H-1′b), 2.08, 2.03, 2.03, 2.00 (4s, 15H, OAc); ^{13}C NMR ($CDCl_3$) δ 170.5, 170.2, 170.2, 170.1, 169.9 (CO), 129.2, 127.4 (C-2′,C-3′), 95.5

(C-1), 68.0 (C-4), 67.9 (C-2), 67.5 (C-3), 67.4 (C-1′ *trans*), 66.4 (C-5), 63.9 (C-4′ *trans*), 63.2 (C-1′ *cis*), 61.7 (C-6), 59.8 (C-4′ *cis*), 20.8, 20.7, 20.6. 20.5, 20.5 (Me). Anal. Calcd for $C_{20}H_{28}O_{12}$: C, 52.17; H, 6.13. Found: C, 51.79; H, 6.07.

4-(*tert*-Butoxycarbonylamino)but-2-ene-1-yl 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranoside (20). Compound **20**, as a syrupy mixture of *E*/*Z* stereoisomers (4:1), was isolated by silica gel column chromatography using ethyl acetate and hexane (3/1). The *E*-isomer was separated from the isomeric mixture. $[\alpha]^{20}_D = +66°$ (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.71 (dt, $J = 5.4$, 15.5 Hz, 1H, H-3′), 5.62 (dt, $J = 5.4$, 15.5 Hz, 1H, H-2′), 5.41 (dd, $J = 1.4$, 3.3 Hz, 1H, H-4), 5.32 (dd, $J = 3.3$, 10.1 Hz, 1H, H-3), 5.10 (m, 2H, H-1, H-2), 4.70 (bs, 1H, NH), 4.24−3.90 (m, 5H, H-5, H-6a, H-6b, H-1′a, H-1′b), 3.70 (bs, 2H, H-4′a, H-4′b), 2.10, 2.04, 2.02, 1.95 (4s, 12H, OAc); ^{13}C NMR ($CDCl_3$) δ 170.4, 170.3, 170.3, 169.9 (CO), 155.7 (CO), 131.1, 126.4 (C-2′, C-3′), 95.4 (C-1), 68.1 (C-4), 68.0 (C-2), 67.9 (C-1′), 67.5 (C-3), 66.2 (C-5), 61.6 (C-6), 41.8 (C-4′), 28.3, 20.7, 20.6, 20.6, 20.5 (Me). HRMS (FAB): Calcd for $C_{23}H_{35}NO_{12}(K^+)$: 556.1796; Found: 556.1783 ($M + K^+$).

4-(Benzyloxycarbonylamino)but-2-ene-1-yl 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranoside (21). Silica gel column chromatography was performed using ethyl acetate and hexane (3/1) to give **21** as a thick syrup of an isomeric *E*/*Z* mixture (4:1); ^{1}H NMR ($CDCl_3$) δ 7.35−7.27 (m, 5H, aromatic), 5.73 (bdt, $J = 5.4$, 15.6 Hz, 1H, H-3′), 5.65 (bdt, $J = 5.4$, 15.6 Hz, 1H, H-2′), 5.41 (dd, $J = 1.3$,3.4 Hz, 1H, H-4), 5.32 (dd, $J = 3.5$, 10.2 Hz, 1H, H-3), 5.13−5.08 (m, 4H, H-1, H-2, H-6′a, H-6′b), 4.95 (bs, 1H, NH), 4.19 (bt, $J = 6.6$ Hz, 1H, H-5), 4.14−3.96 (m, 4 H, H-1′a, H-1′b, H-6a, H-6b), 3.81 (bt, $J = 5.2$ Hz, 2H, H-4′), 2.11, 2.04, 2.01, 1.96 (4s, 12H); ^{13}C ($CDCl_3$) δ 170.4, 170.4, 170.2, 169.9, 156.2 (CO), 136.5, 130.6, 128.5, 126.9 (ArH, =CHs), 95.4 (C-1), 68.1 (C-4), 68.0 (C-2), 67.8 (C-1′ *trans*), 67.5 (C-3), 66.8 (C-6′), 66.2 (C-5), 62.9 (C-1′ *cis*), 61.5 (C-6), 42.3 (C-4′), 20.8, 20.7, 20.6. Anal. Calcd for $C_{26}H_{33}NO_{12}$: C, 56.62; H, 6.03; N, 2.54. Found: C, 56.79; H, 6.14; N, 2.48.

Cross-Metathesis of 3-(2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl)propene (22) with 6-*O*-Allyl-1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (25). Compound **26** (*E*/*Z* mixture, 4:1) was isolated by silica gel column chromatography using ethyl acetate and hexane (1/1) as eluent; ^{1}H NMR ($CDCl_3$) δ 5.70−5.60 (m, 2H, H-8, H-9), 5.49 (d, $J = 5.0$ Hz, 1H, H-1), 5.37 (t, $J = 2.9$ Hz, 1H, H-4′), 5.21 (dd, $J = 1.3$, 9.2 Hz, 1H, H-3′), 5.16 (dd, $J = 4.3$, 9.2 Hz, 1H, H-2′), 4.55 (dd, $J = 2.4$, 7.9 Hz, 1H, H-3), 4.27−4.15 (m, 4H, H-1′, H-2, H-4, H-6′a), 4.08−4.03 (m, 2H, H-5′, H-6′b), 3.97−3.90 (m, 3H, H-5, H-7), 3.60 (dd, $J = 5.7$, 10.1 Hz, 1H, H-6a), 3.50 (dd, $J = 4.8$, 10.1 Hz, 1H, H-6b), 2.53−2.39 (m, 1H, H-10a), 2.27−2.20 (m, 1H, H-10b), 2.07, 2.03, 2.01, 1.99 (4s, 12H, OAc), 1.49, 1.40, 1.30, 1.29 (4s, 12H, Me); ^{13}C NMR ($CDCl_3$) δ 170.4, 169.9, 169.8, 169.7 (CO), 129.7, 128.2 (C-8, C-9), 109.1, 108.4 (*C*Me_2), 96.3 (C-1), 71.6 (C-7 *trans*), 71.4 (C-4), 71.2 (C-1′), 70.6 (C-3), 70.5 (C-2), 68.8 (C-6), 68.3 (C-5′), 68.2 (C-3′), 67.8 (C-2′), 67.4 (C-4′), 66.8 (C-7 *cis*), 66.8 (C-5), 61.2 (C-6′), 29.4 (C-10 *trans*), 26.0, 25.9, 25.0 (C-10 *cis*), 24.8, 24.4, 20.7, 20.6, 20.6 (Me). Anal. Calcd for $C_{30}H_{44}O_{15}$. C, 55.89; H, 6.88. Found: C, 55.86; H, 6.67.

Cross-Metathesis of 22 with 6,7-Dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-hept-6-enopyranose (27). Compound **28** was purified by silica gel column chromatography with ethyl acetate and hexane (3/1), and *E*/*Z* stereoisomers were separated in 2:1 ratio.

Z-Isomer: white solid, mp 50 °C; $[\alpha]^{20}_D = -6°$ (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.81 (bt, $J = 9.5$ Hz, 1H, H-6), 5.61 (ddd, $J = 9.5$, 10.5 Hz, 1H, H-7), 5.48 (d, $J = 5.2$ Hz, 1H, H-1), 5.37 (dd, $J = 1.6$, 3.3 Hz, 1H, H-4′), 5.29 (dd, $J = 5.4$, 9.9 Hz, 1H, H-2′), 5.21 (dd, $J = 3.3$, 9.9 Hz, 1H, H-3′), 4.58 (dd, $J = 2.2$, 7.9 Hz, 1H, H-3), 4.47 (bd, $J = 8.05$ Hz, 1H, H-5), 4.35 (ddd, $J = 4.5$, 11.2 Hz, 1H, H-1′), 4.26 (dd, $J = 2.3$, 5.2 Hz, 1H, H-2), 4.20−4.14 (m, 2H, H-5′, H-6′a), 4.11 (dd, $J = 1.7$, 7.9 Hz, 1H, H-4), 3.96 (dd, $J = 6.4$, 10.4 Hz, 1H, H-6′b), 2.81−2.74 (m, 1H, H-8a), 2.20−2.17 (m, 1H, H-8b), 2.09, 2.01, 1.99, 1.97 (4s, 12H, OAc), 1.61, 1.42, 1.33, 1.31 (4s, 12H, Me); ^{13}C ($CDCl_3$) δ 170.5, 170.1, 169.8 (CO), 130.5 (C-7), 127.1(C-6), 109.1, 108.3 (CMe_2), 96.6 (C-1), 72.7 (C-4), 71.9 (C-1), 70.9 (C-3), 70.0(C-2), 68.3 (C-4′), 68.2 (C-2′), 67.9 (C-3′,C-5′), 63.1 (C-5), 61.1 (C-6), 25.9, 25.8, 25.0 (C-8), 24.7, 24.2, 20.8, 20.7, 20.6, 20.6 (Me). HRMS (FAB): Calcd for $C_{28}H_{41}O_{14}$: 601.2496; Found: 601.2524 ($M + 1$).

E-Isomer: white solid, mp 65 °C; $[\alpha]^{20}_D = -1°$ (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.68−5.67 (m, 2H, H-6, H-7), 5.48 (d, $J = 5.0$ Hz, 1H, H-1), 5.38 (d, $J = 2.2$ Hz, 1H, H-4′), 5.21 (dd, $J = 5.1$, 9.4 Hz, 1H, H-2′), 5.15 (dd, $J = 3.3$, 9.4 Hz, 1H, H-3′), 4.55 (dd, $J = 2.4$, 7.8 Hz, 1H, H-3), 4.26−4.24 (m, 2H, H-1′, H-5), 4.20 (d, $J = 2.7$ Hz, 1H, H-2), 4.14−4.10 (m, 2H, H-4, H-6′a), 4.07−4.03 (m, 2H, H-5′, H-6′b), 2.47−2.42 (m, 1H, H-8a), 2.37−2.28 (m, 1H, H-8b), 2.08, 2.02, 2.00, 1.98 (4s, 12H, OAc), 1.48, 1.41, 1.29, 1.28 (4s, 12H, Me); ^{13}C ($CDCl_3$) 170.4, 170.0, 169.9, 169.8 (CO), 128.9, 128.7 (C-6, C-7), 109.1, 108.3 (CMe_2), 96.3 (C-1), 73.6 (C-4), 71.5 (C-1′), 70.8 (C-3), 70.3 (C-5), 68.7 (C-2), 68.2 (C-2′), 68.0 (C-3′), 67.9 (C-5′), 67.4 (C-4′), 61.1 (C-6′), 29.7 (C-8), 26.1, 25.9, 24.8, 24.3, 20.7, 20.6, 20.6, 20.6 (Me). Anal. Calcd for $C_{28}H_{40}O_{14}$: C, 55.99; H, 6.71. Found: C, 56.21; H, 6.52.

Dimerization of 27 (27a). Using the conditions described above (A, Table 1), dimerization of **27** gave **27a** as pure *E* and *Z* isomers (65%) which were separated by silica gel column chromatography (ethyl acetate:hexane 1:2) in 5:1 ratio.

Z-Isomer: thick syrup, $[\alpha]^{20}_D = -110°$ (*c* 1, $CHCl_3$);^{1}H NMR ($CDCl_3$) δ 5.71 (dd, $J = 1.4$, 4.4 Hz, 1H, H-6), 5.52 (d, $J = 5.0$ Hz, 1H, H-1), 4.64 (dd, $J = 1.9$, 4.4 Hz, 1H, H-5), 4.54 (dd, $J = 2.4$, 7.9 Hz, 1H, H-3), 4.29 (dd, $J = 1.9$, 7.9 Hz, 1H, H-4), 4.25 (dd, $J = 2.4$, 5.0 Hz, 1H, H-2), 1.51, 1.44, 1.31, 1.30 (4s, OAc, 12H); ^{13}C ($CDCl_3$) δ 128.4 (C-6), 109.1, 108.3 (CMe_2), 96.3 (C-1), 73.2 (C-4), 70.6 (C-3), 70.2 (C-2), 65.3 (C-5), 26.2, 25.9, 24.8, 24.2 (Me). MS (FAB) *m*/*z*: 485.2600 ($M + 1$).

E-Isomer: white solid, mp 127 °C; $[\alpha]^{20}_D = -166°$ (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.86 (dd, $J = 1.9$, 4.0 Hz, 1H, H-6), 5.50 (d, $J = 5.0$ Hz, 1H, H-1), 4.55 (dd, $J = 2.4$, 7.9 Hz,1H, H-3), 4.29 (ddd, $J = 1.9$, 4.0, 1H, H-5), 4.25 (dd, $J = 2.4$, 5.0 Hz, 1H, H-2), 4.19 (dd, $J = 1.9$, 7.9 Hz, 1H, H-4), 1.49, 1.43, 1.30, 1.29 (4s, 12H); ^{13}C ($CDCl_3$) δ 129.5 (C-6), 109.1, 108.4 (CMe_2), 96.3 (C-1), 73.5 (C-4), 70.8 (C-3), 70.4 (C-2), 68.7 (C-5), 26.1, 25.9, 24.9, 24.3 (Me). HRMS (FAB): Calcd for $C_{24}H_{37}O_{10}$: 485.2387; Found: 485.2333 ($M + 1$).

Cross-Metathesis of 22 with 4-Acetoxystyrene (9). Compound **23** was isolated as a syrup by silica gel column chromatography using ethyl acetate and hexane (1/1) as eluent; ^{1}H NMR ($CDCl_3$) δ 7.32,7.01 (2d, $J = 8.5$ Hz, aromatic), 6.41 (d, $J = 15.8$ Hz, 1H, H-3′), 6.05 (dt, $J = 7.3$, 15.8, 1H, H-2′), 5.41 (t, $J = 3.2$ Hz, 1H, H-4), 5.26 (dd, $J = 4.7$, 9.1 Hz, 1H, H-2), 5.18 (dd, $J = 3.2$, 9.1 Hz, 1H, H-3), 4.35 (ddd, $J = 4.7$, 10.2, 1H, H-1), 4.21 (dd, $J = 7.8$, 11.3 Hz, 1H, H-6a), 4.11 (m, 1H, H-5), 4.04 (dd, $J = 4.7$, 11.4, 1H, H-6b), 2.61−2.58 (m, 1H, H-1′a), 2.43−2.38 (m, 1H, H-1′b), 2.25, 2.09, 2.04, 2.01, 1.85 (5s, 15 H, OAc); ^{13}C ($CDCl_3$) δ 170.6, 170.0, 169.8, 169.8, 169.3 (CO), 149.8, 134.9, 131.6, 126.9, 125.1, 121.6 (aromatic and olefinic), 71.3 (C-1), 68.5 (C-2), 68.4 (C-5), 67.8 (C-3), 67.5 (C-4), 61.4 (C-6), 30.3 (C-1′), 21.0, 20.7, 20.7, 20.6, 20.5 (Me). MS (FAB) *m*/*z*: 545.21 ($M + K^+$).

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