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A Convenient Entry to C2- and C3-Substituted Gulono-γ-lactone Derivatives from L-Ascorbic Acid

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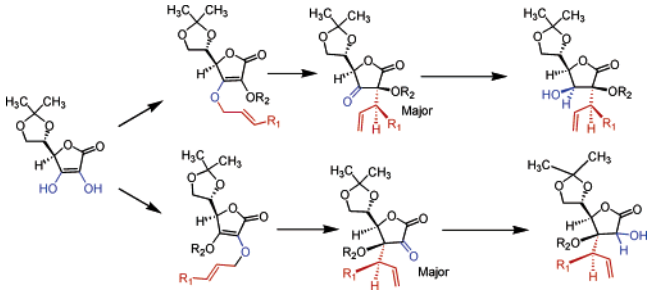

A convenient method to obtain unknown chiral C2- and C3-functionalized aldono-1,4-lactone derivatives starting from L-ascorbic acid, which would be valuable in the synthesis of derivatives of various pharmacologically active agents for structure−activity studies, is described. The practicality of this approach is demonstrated by the synthesis of a series of 5,6-*O*-isopropylidene-2-allyl-3-keto-L-galactono-γ-lactone and 5,6-*O*-isopropylidene-3-allyl-2-keto-L-galactono-γ-lactone derivatives using the thermal Claisen rearrangement of the corresponding 3-*O*- and 2-*O*-allyl derivatives of 5,6-*O*-isopropylidene-L-ascorbic acid, respectively, followed by stereospecific reduction to the corresponding alcohols. The synthetic steps are shown to be efficient, and enantiospecific, and they proceed with high yields.

Introduction

In addition to the well-known physiological and pharmacological properties of L-ascorbic acid,[1] it has also been commonly used as an inexpensive chiral synthon for the synthesis of a variety of natural products and pharmacologically active agents.[2] In addition to the common usage of the oxidatively cleaved C6−C3 fragment of ascorbic acid as a chiral synthon,[2a−m] the selective alteration or modification of its C2- and/or C3-OH functional groups provides a unique route to different classes of aldono-1,4-lactone derivatives which are important precursors for the synthesis of modified sugars and non-carbohydrate natural compounds.[3] One of the widely used aldonolactones in the synthesis of natural products is D-gulono-γ-lactone, also known as D-gulono-1,4-lactone, which is easily obtained from L-gulono-γ-lactone by intramolecular Walden inversion.[4] Although many aldonolactones are commercially available, they can also be readily obtained by oxidation of the respective monosaccharides. However, the corresponding C2- or C3-substituted aldonolactone derivatives are largely unknown.

Gulono-1,4-lactone is a very versatile precursor for a large number of pharmacologically active agents and natural products. For example, it is used as a precursor in the synthesis of (a) rare sugars such as L-ribofuranose, which are common starting materials for the synthesis of new nucleoside antibiotics such as novobiocin and antibacterial agents against Gram-positive bacteria,[6] (b) pharmacological agents for the suppression of abnormal T-cell responses,[7] (c) α-hydroxy-β-amino acid natural products that are known to display a broad range of biological activities, which include antibiotic, antifungal, antitumor and potent aminopeptidase protease inhibitors,[8] and (d) non-carbohydrate natural alkaloids with antitumor activity.[9] Furthermore, gulono-1,4-lactone also has applications in polymer chemistry for the synthesis of potentially renewable, biomedical polymeric materials that are biodegradable.[10] In addition to the usefulness of aldono-1,4-lactones as synthetic chemical precursors,[11] both L-galactono-γ-lactone and L-gulono-γ-lactone are also

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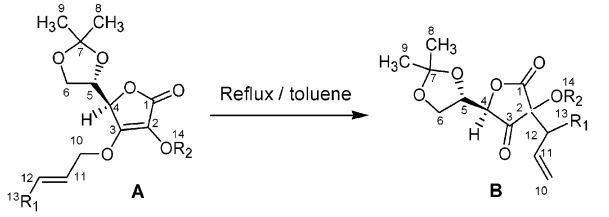
the key intermediate precursors of vitamin C biosynthesis in plants and animals, respectively.[12] Therefore, a direct and practical route to the synthesis of unknown C2- and C3-substituted gulono-1,4-lactone derivatives will be very valuable in the structure−activity studies of the above pharmacological agents to improve their pharamacokinetics and, thus, their therapeutic values.

Our previous studies have shown that C2-*O*- and C3-*O*-allyl derivatives of 5,6-*O*-isopropylidene-L-ascorbic acid,

SCHEME 1. Products of the Claisen Rearrangement of C3-*O*-Allyl Derivatives of 5,6-*O*-Isopropylidene-L-ascorbic Acid[a]



Reactant	R_1	R_2	Product [b]
1A	H	H	**1B**
2A	H	Ac	**2B**
3A	H	allyl	**3B**
4A	CH_3	H	**4B**
5A	CH_3	Ac	**5B**
6A	C_6H_5	Ac	**6B**
7A	C_6H_5	H	**7B**

[a] 100% conversion of **A** to **B** was obtained in 6 h. [b] ^{1}H-NMR analysis of crude reaction mixtures indicated that the product is a mixture of two diastereomers with >90% of the major.

which are cyclic enol ethers, undergo facile thermal Claisen rearrangement, providing excellent and convenient access to nonaccessible C2- and C3-substituted L-galactono-γ-lactones.[5] In the present study, we further extend our previous findings that thermal Claisen rearrangement of C2-*O*- and C3-*O*-allyl-L-ascorbic acid derivatives easily provides a convenient stereocontrolled entry to nonaccessible C2- and C3-substituted L-galactono-γ-lactones.[5] More importantly, we show that the Claisen-rearranged products can be stereoselectively reduced to produce a new series of C2-substituted L-gulono-γ-lactone derivatives, which are synthetically more demanding and could be used as chiral intermediates in the synthesis of a range of important natural products and pharmacologically active materials.[3,4,6−12]

Results and Discussion

We have previously reported the characterization of a series of thermal Claisen-rearranged products of 5,6-*O*-isopropylidene-3-*O*-allyl-L-ascorbic acid (**A**, Scheme 1) and 5,6-*O*-isopropylidene-2-*O*-allyl-L-ascorbic acid (**C**, Scheme 2) as the corresponding 5,6-*O*-isopropylidene-2-allyl-3-keto-L-galactono-γ-lactone (**B**, Scheme 1) and 5,6-*O*-isopropylidene-3-allyl-2-keto-L-galactono-γ-lactone (**D**, Scheme 2), respectively.[5] Although all the starting materials and rearranged products reported in this study[5] were carefully characterized based on the literature procedures available at the time, structural assignments of three 3-*O*-acetyl-2-*O*-allyl (**9C**, **11C**, and **13C** out of 28 reported) ascorbate derivatives and their rearranged products (Scheme 2; e.g., derivatives **9D** and **11D**) were incorrect. This was mainly due to the unexpected facile migration of the C3-*O*-acetyl group from the C3-*O* to C2-*O* position under the C2-*O*-alkylation conditions, as we and others have reported recently.[13] In the present study, we synthesized C3-*O*-acetyl derivatives listed in

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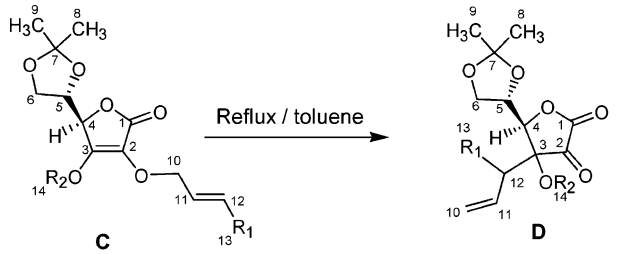
SCHEME 2. Products of the Claisen Rearrangement of C2-*O*-Allyl Derivatives of 5,6-*O*-Isopropylidene-L-ascorbic Acid[a]



Reactant (**C**)	R_1	R_2	Product (**D**)[b]
8C	H	H	**8D**
9C	H	Ac	**9D**
10C	CH_3	H	**10D**
11C	CH_3	Ac	**11D**
12C	C_6H_5	Me	**N/R**[c]
13C	C_6H_5	Ac	**N/R**[c]

[a] 100% conversion of **C** to **D** was obtained in 12 h. [b] ^{1}H-NMR analysis of the crude reaction mixtures indicated that only a single diastereomer was detectable. [c] **12C** & **13C** were not susceptible to rearrangement even under vigorous conditions (refluxing in xylene or styrene for over 72 h).

Scheme 2 by our newly developed direct C2-*O*-alkylation method[13] to resolve the ambiguity in the structural assignments of the starting materials and the rearranged products and confirmed that the previously reported 3-*O*-acetyl-2-*O*-allyl ascorbate derivatives were not the C3-*O*-acetyl-substituted derivatives as once reported,[5] but are the corresponding C2-*O*-acetyl-substituted derivatives **2A**, **5A**, and **6A**.[13] Therefore, their Claisen-rearranged products were also identical to the corresponding C3-*O* to C2-allyl migrated products[5] **2B**, **5B**, and **6B** (Scheme 1). To determine the nature of the Claisen-rearranged products of C3-*O*-acetyl-substituted derivatives, for the first time, the rearranged products of a series of C3-*O*-acetyl- and C2-*O*-allyl-substituted derivatives (Scheme 2) were fully characterized and compared with the rearranged products of the comparable C2-*O*-acetyl- and C3-*O*-allyl-substituted derivatives (Scheme 1).

In our recent study,[13] the detailed synthesis and unequivocal spectroscopic characterization of the starting materials, **1A**−**7A** and **8C**−**13C**, listed in Schemes 1 and 2, were reported. As previously reported,[5] the Claisen rearrangement of C3-*O*-allyl ascorbate derivatives listed in Scheme 1 quantitatively produced the C2-allylated products in about 6 h in boiling toluene. The ^{1}H NMR analysis of the crude reaction mixtures revealed that both possible diastereomers were produced with more than 73% diastereomeric excess (>90% of the major isomer formed by the approach of allyl fragment from the bottom face opposite to the bulky C4-substituent; Scheme 1).

In contrast to the smooth rearrangement of C3-*O*-allyl ascorbate derivatives under relatively mild conditions (Scheme 1), the rearrangement of their C2-*O*-allyl counterparts (Scheme 2) was found to be much slower and required much more drastic reaction conditions. For example, C2-*O*-allyl ascorbate derivatives such as **8C**−**11C** (Scheme 2) typically require about 12 h of refluxing in toluene for the complete conversion, in comparison to 6 h for corresponding C3-*O*-allyl ascorbate derivatives (Scheme 1). In addition, only a single diastereomer was detected by ^{1}H NMR analysis of the crude rearranged reaction mixtures of C2-*O*-allyl derivatives (Scheme 2). Sterically more hindered C2-*O*-allyl ascorbate derivatives such as **12C** and **13C** do not undergo any significant rearrangement, even in boiling xylene or styrene for 72 h. The relative unfavorability for the rearrangement of C2-*O*-allyl in comparison to C3-*O*-allyl derivatives could be due to a combination of steric and electronic effects. First, the steric constraints on the transition state for the C2-*O* to C3 allyl migration (Scheme 2) are more pronounced relative to that of the C3-*O* to C2 migration (Scheme 1), due to the presence of a bulky 1,2-*O*-isopropylidene-1,2-ethanediol moiety at the C4 of the molecule. Second, the relatively high lability of C3-*O*-allylic ether linkage compared to that of the C2-*O*-allylic ether linkage due to the direct interaction of the C3-*O* with the conjugated enone moiety could also facilitate the rearrangement to produce the thermodynamically more stable C2-allylated products.[13] Therefore, the facile rearrangement of the C3-*O*-allyl derivatives in comparison to the noncatalyzed conventional Claisen rearrangement, which requires high temperatures (150−240 °C), suggests that the thermodynamic lability of C3-*O*-allylic ether bond facilitates their efficient rearrangement to the C2-allylated products. This notion is further supported by the observation that the diallyl ascorbate derivative, **3A**, exclusively rearranged to produce the C2-allylated product, **3B**, and not the potential corresponding C3-allylated product.

The ^{13}C NMR spectra of C3-*O* to C2 and C2-*O* to C3 (Table 1) rearranged products show some interesting and characteristic features that could be used in their unequivocal identification. For example, the C3 and C2 carbonyl signals of two series of rearranged products, **B** and **D**, appear in the ranges of 205.7−200.9 and 186.3−195.3 ppm, respectively. The significant upfield shift of the ^{13}C NMR signals of C2 carbonyls of **D** series must be due to the electronic effects of the adjacent C1 lactone carbonyl in comparison to that of the isolated C3 carbonyl group of **B** series.[14] Similarly, the C1 ^{13}C NMR carbonyl signals of the two series were also quite distinguishable and appear in the ranges of 170.3−172.8 ppm for **B** and 158−159.4 ppm for **D**, again due to the electronic effects of the C2 carbonyl of **D** in comparison to that of the C3 carbonyl of **B**. Interestingly, C4 ^{13}C NMR signals of the two series of rearranged products were not significantly different. However, C4 ^{13}C NMR signals of both **B** and **D** series show a significant downfield shift ($\Delta\delta$ in the range of 5.3−9.5 ppm) in comparison to the corresponding starting materials (**A** and **C**). This most likely reflects the deshielding effects of the disappearance of the conjugated enone moiety of the starting materials due to the rearrangement. Therefore, the comparative analysis of the ^{13}C NMR characteristics of the starting materials and their products could conveniently be used to

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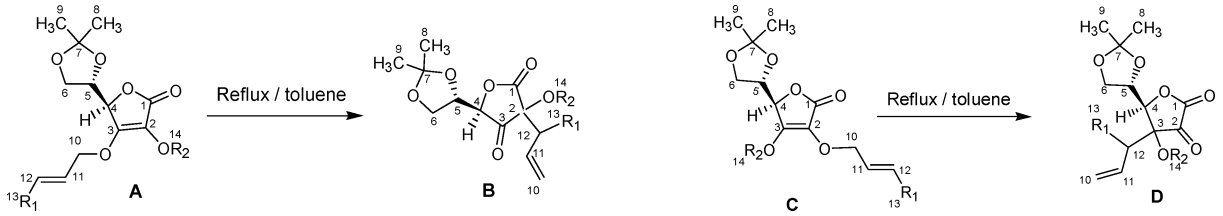
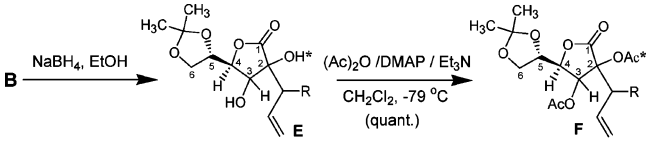
TABLE 1. ^{13}C NMR Chemical Shifts (δ) of Claisen Rearranged Products (B and D Series)



	$R_1 = H; R_2 = H$				$R_1 = H; R_2 = Ac$			
carbon #	**1A**	**1B**	**8C**	**8D**	**2A**	**2B**	**9C**	**9D**
δ (1-C)	171.0	172.6	168.8	159.4	167.6	170.9	166.4	158.2
δ (2-C)	119.2	74.5	121.4	193.9	114.6	73.8	130.1	186.3
δ (3-C)	148.2	205.5	156.4	77.2	159.5	201.0	143.8	78.4
δ (4-C)	75.6	81.5	73.9	80.8	75.3	82.1	74.5	81.1
	$R_1 = CH_3; R_2 = H$				$R_1 = CH_3; R_2 = Ac$			
carbon #	**4A**	**4B**	**10C**	**10D**	**5A**	**5B**	**11C**	**11D**
δ (1-C)	171.8	172.8	170.1	159.5	167.6	170.3	166.5	158.0
δ (2-C)	119.1	74.4	120.8	195.3	114.4	77.3	132.2	187.5
δ (3-C)	148.6	205.7	157.9	78.9	159.7	200.9	143.8	77.3
δ (4-C)	75.7	81.8	74.6	80.0	75.3	84.8	74.4	79.7

SCHEME 3. Reduction Products of 5,6-*O*-Isopropylidene-2-allyl-3-keto-L-galactono-γ-lactone (B)



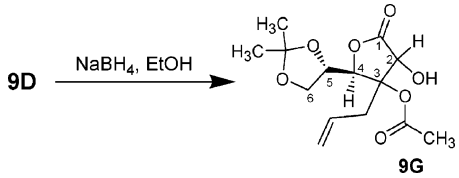
(B)	(E)	(F)	R
1B	**1E**	**1F**	H
3B	**3E**	**3F**	H
	*H = $CH_2CH{=}CH_2$	*Ac = $CH_2CH{=}CH_2$	
4B	**4E**	**4F**	CH_3
7B	**7E**	**7F**	C_6H_5

distinguish between the two series of Claisen-rearranged products (**B** and **D**).

To further explore the chemistry and synthetic utility of the Claisen-rearranged products **B** and **D**, we have attempted the selective reduction of their C3- and C2-keto groups by conventional methods. The reduction of the major isomers of the rearranged products of the **B** series (Scheme 3) with sodium borohydride in ethanol proceeds with high regio- and stereoselectivity in producing a ~7:1 diastereomeric mixture of alcohol products, **E** series, in almost quantitative yield. The diastereomeric mixture could easily be separated by normal phase silica gel column chromatography using ethyl acetate/hexane. Subsequent acetylation of **E** under the conditions of Scheme 3 gave the corresponding acetates (**F** series) in quantitative yield. In contrast to the **B** series, the attempts to reduce the rearranged C2-keto products (**D** series) gave uncharacterizable complex reaction mixtures under the above conditions. However, under carefully controlled conditions, we were able to obtain a clean reduced product **9G** from **9D** in 60% yield (Scheme 4) after careful silica gel chromatography with ethyl acetate/hexane solvent system.

The structures of the major isomers of sodium borohydride reduced products (**E**) and their acetates (**F**) were

SCHEME 4. Reduction Product of 5,6-*O*-Isopropylidene-3-allyl-2-keto-L-galactono-γ-lactone 9D

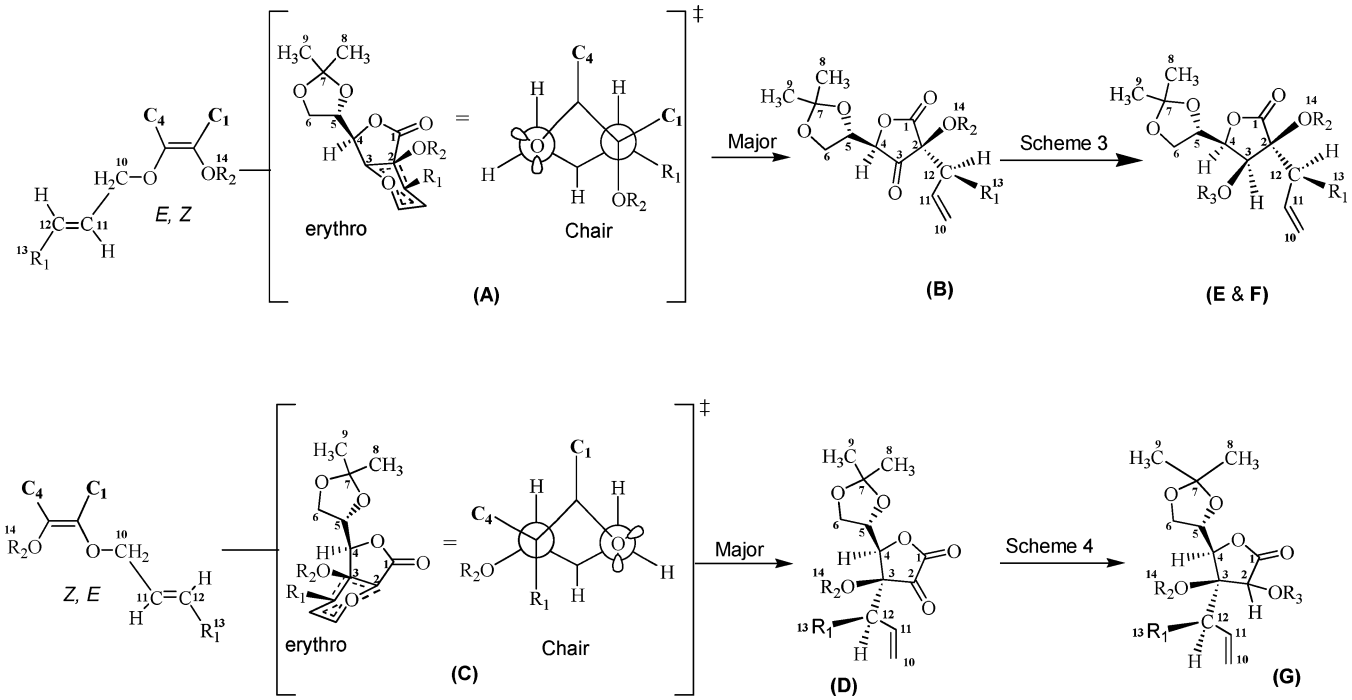


unequivocally identified by their ^1H and ^{13}C NMR characteristics. For example, upon reduction, the ^1H NMR C4−H doublets at 4.54−4.66 ppm in the starting materials (**B**, Scheme 3) were shifted to doublet of doublets at 4.44−4.48 ppm for hydroxyl derivatives (**E**, Scheme 3) and 4.08−4.43 ppm for the corresponding acetates (**F**, Scheme 3) as expected. In addition, a new ^1H NMR signal appeared in the range of 4.15−4.25 ppm for hydroxyl derivatives, and at 5.51−6.11 ppm for acetates, due to the newly generated C3−H of the reduced product. Furthermore, the characteristic ^{13}C NMR signals of the β-carbonyl carbon singlets in the range of 200.9−206.1 ppm disappeared upon reduction, and a new C3 ^{13}C NMR signal (doublet) appeared in the range of 71.9−74.7 ppm for alcohols (**E**, Scheme 3) and 72.2−73.0 ppm for acetates (**F**, Scheme 3). Similarly, the reduction of the C2 carbonyl of C2-*O* to C3-rearranged product, **9D**, resulted in a new ^1H NMR singlet at 4.09 ppm, which corresponds to the newly generated C2−H. The C2-carbonyl carbon ^{13}C NMR singlet of the starting material at 186.3 ppm is converted to a doublet at 71.8 ppm, confirming the reduction of the C2-carbonyl of **9D** to produce **9G**.[14]

Stereochemistry. The intrinsic stereochemistry at the C4 and C5 positions of all the starting materials, rearranged products, and their derivatives is fixed, since L-ascorbic acid is used in all cases.[1,15] The stereochemistry

(15) A collection of spectra and some X-ray crystallography data are included in Mahindaratne, M. P. D. Ph.D. Thesis, Wichita State University, Wichita, KS, May 2000.

SCHEME 5. Stereochemical Course of the Claisen Rearrangement of A and C



of the C2 of the Claisen-rearranged products (**B**) was previously assigned by their NMR spectroscopic characteristics and confirmed by X-ray crystallographic studies.[5,15] These studies unequivocally established that the least-bulky C3-*O*-allyl Claisen substrates (**1A**) yield a major diastereomer (~90%), which is C2-allylated from the bottom face of the lactone ring.[5,15] As reasoned above, we believe the preferential migration of the allylic functionality from the bottom face of the lactone ring must be primarily due to the steric constraints imposed by the bulky C4 substituent (1,2-*O*-isopropylidene-1,2-ethanediol moiety) on the top face of the molecule.[5,15] On the basis of these arguments, we conclude that C2-*O*-allyl Claisen rearrangements must also exclusively occur from the bottom face of the molecule, since the steric constraints of the C4 bulky substituent must be even more pronounced for the C2-*O* to C3 migrations (Scheme 2) in comparison to C3-*O* to C2 migration (Scheme 1).

The factors affecting the stereochemical outcome of the products of thermal Claisen rearrangement have been extensively studied and clearly defined based on the orbital symmetry rules on the concerted and highly ordered cyclic transition states.[16−20] The Claisen rearrangement is shown to preferentially progress through a chairlike transition state to minimize the steric interactions of various substituents, as illustrated in Scheme 5. Thus, the relative stereochemistry (*erythro*/*threo*) at the newly generated allylic stereocenters is controlled by the relative geometry of the allylic double bond of the Claisen substrate.[19] Therefore, as shown in Scheme 5, (*Z*,*Z*) and (*E*,*E*) Claisen substrates produce *threo* products, while (*E*,*Z*) and (*Z*,*E*) produce *erythro* as the major products.[19] Since the allylic functionality migrates from the bottom face of the lactone ring during the C3-*O* to C2 rearrangement as argued above, the C12 stereochemistry of the major isomer must be *erythro* with respect to $-OR_2$ functionality as shown in Scheme 5. On the basis of these arguments, we conclude that the major isomer of the Claisen-rearranged products of crotyl (**4B**, **5B**, **10D**, and **11D**) and cinnamyl (**7B**) derivatives must have *R* stereochemistry at the C12 as shown in Scheme 5.

The ^{1}H and ^{13}C NMR spectra of **E**, obtained from the sodium borohydride reduction of **B**, as well as their acetylated products, **F** (Scheme 3), were in good agreement with all reported spectra of similar compounds.[21] The stereochemistry of these compounds was confirmed by qualitative NOESY correlation studies. For instance, the strong NOESY correlation between the newly generated C3−H and the C4−H of all the products listed in Scheme 3 (**E** and **F** series) strongly suggests that the configuration of these protons are cis to each other and identical to the overall configuration of L-gulono-γ-lactones. However, since the C2-*O*-allyl to C3-allyl-rearranged product, **9D**, and its reduced product, **9G**, showed no strong NOESY correlation between the C4−H, C2−H, or C12−H_2, the C2 stereochemistry of the product **9G** could not be assigned with certainty. However, synthesis and complete structural characterization of a full series of C2-*O*-allyl to C3 Claisen-rearranged

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derivatives (D) and their reduced products (G) are currently in progress in our laboratory.

Experimental Section

Synthetic procedures for starting materials **1A**−**7A** and **8C**−**13C** have been reported previously.[13]

5,6-*O*-Isopropylidene-3-*O*-allyl-L-ascorbic Acid (1A). This was synthesized in 80% yield (light transparent oil) as previously described:[13] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 (3H, s), 1.39 (3H, s), 4.02 (1H, dd, J = 8.6, 6.6 Hz), 4.13 (1H, dd, J = 8.6, 6.6 Hz), 4.27 (1H, dt, J = 6.6, 3.8 Hz), 4.56 (1H, d, J = 3.8 Hz), 4.92−5.20 (2H, m), 5.30 (1H, dq, J = 10.3, 1.5 Hz), 5.40 (1H, dq, J = 17.3, 1.5 Hz), 6.01 (1H, ddt, J = 17.3, 10.3, 5.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.6, 25.9, 65.3, 72.3, 74.3, 75.7, 110.4, 119.1, 119.4, 132.2, 148.5, 171.2.

5,6-*O*-Isopropylidene-2-*O*-acetyl-3-*O*-allyl-L-ascorbic Acid (2A). This was synthesized in 70% yield (colorless semisolid) as previously described:[13] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.36 (3H, s), 1.40 (3H, s), 2.28 (3H, s), 4.07 (1H, dd, J = 8.6, 6.6 Hz), 4.17 (1H, dd, J = 8.6, 6.6 Hz), 4.37 (1H, dt, J = 6.6, 3.0 Hz), 4.68 (1H, d, J = 3.0 Hz), 4.81 (2H, m), 5.36 (1H, dq, J = 10.6, 1.2 Hz), 5.39 (1H, dq, J = 17.7, 1.6 Hz), 5.96 (1H, ddt, J = 17.7, 10.6, 5.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3, 25.5, 25.8, 65.2, 72.6, 73.7, 75.3, 110.5, 114.6, 119.5, 131.0, 159.5, 166.8, 167.6.

5,6-*O*-Isopropylidene-2,3-*O*-diallyl-L-ascorbic Acid (3A). This was synthesized in 61% yield (light yellow oil) as previously described:[5] ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (3H, s), 1.39 (3H, s), 4.04 (1H, dd, J = 8.5, 6.6 Hz), 4.14 (1H, dd, J = 8.5, 6.7 Hz), 4.30 (1H, dt, J = 6.7, 3.2 Hz), 4.55 (1H, d, J = 3.2 Hz), 4.62 (2H, m), 4.94 (2H, dt, J = 5.6, 1.5 Hz), 5.27 (1H, dq, J = 10.8, 1.4 Hz), 5.31 (1H, dq, J = 10.5, 1.4 Hz), 5.35 (1H, dq, J = 17.2, 1.6 Hz), 5.39 (1H, dq, J = 17.3, 1.6 Hz), 5.98 (1H, ddt, J = 17.3, 10.5, 5.6 Hz), 5.99 (1H, ddt, J = 17.2, 10.3, 6.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.6, 25.9, 65.3, 72.3, 72.5, 74.0, 74.7, 110.3, 118.9, 119.2, 121.5, 131.9, 132.9, 155.7, 168.9.

5,6-*O*-Isopropylidene-3-*O*-*trans*-crotyl-L-ascorbic Acid (4A). This was synthesized in 72% yield (light yellow oil) as previously described:[13] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.38 (3H, s), 1.39 (3H, s), 1.76 (3H, dq, J = 6.6, 1.6 Hz), 4.03 (1H, dd, J = 8.6, 6.7 Hz), 4.12 (1H, dd, J = 8.6, 6.7 Hz), 4.27 (1H, dt, J = 6.7, 3.9 Hz), 4.56 (1H, d, J = 3.9 Hz), 4.88 (2H, m), 5.68 (1H, dtq, J = 15.3, 6.6, 1.6 Hz), 5.91 (1H, dtq, J = 15.3, 6.6, 1.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.8, 25.6, 25.9, 65.3, 72.4, 74.4, 75.7, 110.4, 119.2, 125.2, 132.6, 148.6, 171.8.

5,6-*O*-Isopropylidene-2-*O*-acetyl-3-*O*-*trans*-crotyl-L-ascorbic Acid (5A). This was synthesized in 78% (light yellow semisolid) as previously described:[13] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37 (3H, s), 1.41 (3H, s), 1.75 (3H, dq, J = 6.6, 1.7 Hz), 2.27 (3H, s), 4.08 (1H, dd, J = 8.6, 6.5 Hz), 4.16 (1H, dd, J = 8.6, 6.5 Hz), 4.35 (1H, dt, J = 6.5, 3.1 Hz), 4.67 (1H, d, J = 3.1 Hz), 4.73 (2H, m), 5.63 (1H, dtq, J = 15.4, 6.6, 1.6 Hz), 5.88 (1H, dtq, J = 15.4, 6.6, 1.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.7, 20.2, 25.6, 25.8, 65.2, 72.6, 73.7, 75.3, 110.4, 114.4, 124.0, 133.2, 159.7, 167.0, 167.6.

5,6-*O*-Isopropylidene-2-*O*-acetyl-3-*O*-*trans*-cinnamyl-L-ascorbic Acid (6A). This was synthesized in 76% yield (colorless crystals) as previously described:[13] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37 (3H, s), 1.41 (3H, s), 2.29 (3H, s), 4.10 (1H, dd, J = 8.6, 6.5 Hz), 4.16 (1H, dd, J = 8.6, 6.6 Hz), 4.41 (1H, dt, J = 6.5, 3.0 Hz), 4.72 (1H, d, J = 3.0 Hz), 4.90−5.03 (m, 2H), 6.30 (1H, dt, J = 16.0, 6.3 Hz), 6.72 (1H, d, J = 16.0 Hz), 7.22−7.37 (3H, m), 7.36−7.41 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.2, 25.6, 25.7, 65.2, 72.6, 73.6, 75.3, 110.5, 114.7, 121.6, 126.7, 128.6, 128.7, 129.3, 135.5, 159.7, 166.9, 167.6.

5,6-*O*-Isopropylidene-2-*O*-allyl-L-ascorbic Acid (8C). This was synthesized in 80% yield (white semisolid) as previously described:[13] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.39 (3H, s), 1.44 (3H, s), 4.03 (1H, dd, J = 9.0, 6.7 Hz), 4.15 (1H, dd, J = 9.0, 6.7 Hz), 4.43 (1H, dt, J = 6.7, 3.5 Hz), 4.63 (2H, dt, J = 6.2, 1.2 Hz), 4.71 (1H, d, J = 3.5 Hz), 5.29 (1H, dq, J = 10.1, 2.1 Hz), 5.37 (1H, dq, J = 17.2, 2.1 Hz), 5.99 (1H, ddt, J = 17.3, 10.1, 6.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.3, 25.7, 64.9, 72.1, 73.8, 73.9, 110.6, 119.6, 121.4, 133.0, 156.4, 168.8.

5,6-*O*-Isopropylidene-3-*O*-acetyl-2-*O*-allyl-L-ascorbic Acid (9C). This was synthesized in 70% yield (light yellow oil) as previously described:[13] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 (3H, s), 1.39 (3H, s), 2.32 (3H, s), 4.01 (1H, dd, J = 8.3, 6.7 Hz), 4.16 (1H, dd, J = 8.3, 6.7 Hz), 4.30 (1H, dt, J = 6.7, 2.7 Hz), 4.77 (2H, m), 5.19 (1H, d, J = 2.7 Hz), 5.29 (1H, dq, J = 10.5, 2.2 Hz), 5.38 (1H, dq, J = 17.3, 2.2 Hz), 5.98 (1H, ddt, J = 17.3, 10.5, 5.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.6, 25.3, 25.6, 65.1, 71.3, 72.8, 74.5, 110.5, 118.9, 130.1, 132.4, 143.8, 166.3, 166.4.

5,6-*O*-Isopropylidene-2-*O*-*trans*-crotyl-L-ascorbic Acid (10C). This was synthesized in 72% yield (light yellow oil) as previously described:[13] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37 (3H, s), 1.40 (3H, s), 1.72 (3H, dq, J = 7.0, 1.7 Hz), 4.06 (1H, dd, J = 8.5, 6.7 Hz), 4.16 (1H, dd, J = 8.5, 6.7 Hz), 4.38 (1H, dt, J = 6.7, 3.6 Hz), 4.50 (2H, dt, J = 6.6, 1.7 Hz), 4.70 (1H, d, J = 3.6 Hz), 5.65 (1H, dtq, J = 15.8, 7.0, 1.7 Hz), 5.79 (1H, dtq, J = 15.8, 7.0, 1.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.8, 25.3, 25.7, 64.5, 72.3, 73.9, 74.6, 110.4, 120.8, 125.8, 132.6, 157.9, 170.1.

5,6-*O*-Isopropylidene-3-*O*-acetyl-2-*O*-*trans*-crotyl-L-ascorbic Acid (11C). This was synthesized in 84% yield (light yellow oil) as previously described:[13] ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.37 (3H, s), 1.39 (3H, s), 1.73 (3H, dq, J = 6.5, 1.7 Hz), 2.30 (3H, s), 4.02 (1H, dd, J = 8.4, 6.7 Hz), 4.13 (1H, dd, J = 8.4, 6.7 Hz), 4.27 (1H, dt, J = 6.7, 2.5 Hz), 4.69 (2H, dt, J = 6.5, 1.7 Hz), 5.17 (1H, d, J = 2.5 Hz), 5.65 (1H, dtq, J = 16.7, 6.5, 1.7 Hz), 5.84 (1H, dtq, J = 16.7, 6.5, 1.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$); δ 17.7, 20.5, 25.3, 25.6, 65.0, 71.4, 72.9, 74.4, 110.5, 125.4, 130.1, 132.2, 143.8, 166.3, 166.5.

5,6-*O*-Isopropylidene-2-*O*-*trans*-cinnamyl-3-*O*-methyl-L-ascorbic Acid (12C). This was synthesized in 71% yield (colorless crystals) as previously described:[5] mp 114−115 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (3H, s), 1.37 (3H, s), 4.02 (1H, dd, J = 8.5, 6.7 Hz), 4.13 (1H, dd, J = 8.5, 6.7 Hz), 4.16 (3H, s), 4.28 (1H, dt, J = 6.7, 3.0 Hz), 4.52 (1H, d, J = 3.0 Hz), 4.73 (1H, ddd, J = 12.1, 6.8, 1.2 Hz), 4.82 (1H, ddd, J = 12.1, 6.6, 1.2 Hz), 6.37 (1H, dt, J = 15.9, 6.7 Hz), 6.67 (1H, d, J = 15.9 Hz), 7.22−7.36 (3H, m), 7.37−7.43 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$); δ 25.5, 25.8, 59.6, 65.2, 72.4, 73.8, 74.5, 110.3, 121.1, 123.8, 126.7, 128.1, 128.6, 135.1, 136.2, 157.4, 169.0.

5,6-*O*-Isopropylidene-3-*O*-acetyl-2-*O*-*trans*-cinnamyl-L-ascorbic Acid (13C). This was synthesized in 76% yield (viscous oil) as previously described:[13] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.31 (3H, s), 1.33 (3H, s), 2.29 (3H, s), 4.03 (1H, dd, J = 8.4, 6.7 Hz), 4.13 (1H, dd, J = 8.4, 6.7 Hz), 4.30 (1H, dt, J = 6.7, 2.5 Hz), 4.88−5.00 (2H, m), 5.18 (1H, d, J = 2.5 Hz), 6.32 (1H, dt, J = 13.7, 6.5 Hz), 6.09 (1H, d, J = 13.7 Hz), 7.20−7.43 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.3, 25.4, 25.6, 65.1, 71.3, 72.9, 74.5, 110.6, 123.4, 126.7, 128.3, 128.6, 128.8, 134.8, 136.0, 144.6, 166.3, 166.6.

5,6-*O*-Isopropylidene-3-keto-2-(1-prop-2-enyl)-L-galactono-γ-lactone (1B). This was obtained as a major diastereomer with a small amount of a minor diastereomer[5] from the Claisen rearrangement of pure **1A** in refluxing toluene for 6 h (Scheme 1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (3H, s), 1.40 (3H, s), 2.65 (2H, d, J = 7.4 Hz), 4.09 (1H, dd, J = 8.7, 6.8 Hz), 4.20 (1H, dd, J = 8.7, 6.8 Hz), 4.55 (1H, dt, J = 6.8, 2.0 Hz), 4.67 (1H, d, J = 2.0 Hz), 5.26 (1H, dq, J = 16.7, 1.4 Hz), 5.29 (1H, dq, J = 10.5, 1.0 Hz), 5.70 (1H, ddt, J = 16.7, 10.5, 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.3, 25.5, 39.7, 64.8, 72.0, 74.5, 81.5, 111.4, 122.9, 127.6, 172.6, 205.5.

5,6-*O*-Isopropylidene-3-keto-2-*O*-acetyl-2-(1-prop-2-enyl)-L-galactono-γ-lactone (2B). This was obtained as a major diastereomer with a small amount of a minor diastereomer[5] from the Claisen rearrangement of pure **2A** in refluxing toluene for 6 h (Scheme 1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (3H, s), 1.42 (3H, s), 2.16 (3H, s), 2.80 (2H, m),

4.10 (1H, dd, J = 8.5, 7.1 Hz), 4.20 (1H, dd, J = 8.5, 7.1 Hz), 4.53 (1H, dt, J = 7.1, 1.6 Hz), 4.87 (1H, d, J = 1.7 Hz), 5.19 (1H, dq, J = 17.0, 1.5 Hz), 5.26 (1H, dq, J = 10.2, 1.5 Hz), 5.90 (1H, ddt, J = 17.2, 10.1, 7.0 Hz); ^{13}C NMR (75 MHz $CDCl_3$) δ 19.2, 25.5, 25.8, 34.5, 65.2, 73.7, 73.8, 82.1, 110.8, 120.8, 128.3, 169.7, 170.9, 201.0.

5,6-*O*-Isopropylidene-3-keto-2-*O*-(1-prop-2-enyl)-2-(1-prop-2-enyl)-L-galactono-γ-lactone (3B). This was obtained as a major diastereomer with small amount of a minor diastereomer[5] from the Claisen rearrangement of pure **3A** in refluxing toluene for 6 h (Scheme 1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (3H, s), 1.40 (3H, s), 2.67 (2H, m), 4.00 (2H, m), 4.07 (1H, dd, J = 8.7, 6.9 Hz), 4.16 (1H, dd, J = 8.7, 6.9 Hz), 4.55 (1H, d, J = 1.9 Hz), 4.65 (1H, dt, J = 6.9, 1.9 Hz), 5.20 (1H, dq, J = 10.5, 1.2 Hz), 5.22 (1H, dq, J = 17.0, 1.2 Hz), 5.26 (1H, dq, J = 10.4, 1.2 Hz), 5.31 (1H, dq, J = 17.3, 1.6 Hz), 5.75 (1H, dddd, J = 17.0, 10.4, 7.9, 6.9 Hz), 5.90 (1H, ddt, J = 17.3, 10.4, 5.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.4, 25.7, 41.2, 64.9, 69.2, 74.2, 79.9, 81.5, 110.9, 118.0, 122.2, 127.8, 133.2, 171.4, 206.1. Anal. Calcd for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 60.66; H, 6.70.

5,6-*O*-Isopropylidene-3-keto-2-(1-methyl-1-prop-2-enyl)-L-galactono-γ-lactone (4B). This was obtained as a major diastereomer with a small amount of a minor diastereomer[5] from the Claisen rearrangement of pure **4A** in refluxing toluene for 6 h (Scheme 1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (3H, d, J = 7.0 Hz), 1.35 (3H, s), 1.41 (3H, s), 2.69−2.81 (1H, m), 4.08 (1H, dd, J = 8.7, 6.8 Hz), 4.17 (1H, dd, J = 8.7, 6.8 Hz), 4.52 (1H, dt, J = 6.8, 2.1 Hz), 4.61 (1H, d, J = 2.2 Hz), 5.25 (1H, dt, J = 17.9, 1.0 Hz), 5.29 (1H, dt, J = 9.8, 1.0 Hz), 5.76 (1H, ddd, J = 17.9, 9.8, 8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.5, 25.4, 25.5, 44.3, 64.8, 74.3, 74.4, 81.8, 111.1, 120.0, 134.3, 172.8, 205.7.

5,6-*O*-Isopropylidene-3-keto-2-*O*-acetyl-2-(1-methyl-1-prop-2-enyl)-L-galactono-γ-lactone (5B). This was obtained as a major diastereomer with a small amount of a minor diastereomer[5] from the Claisen rearrangement of pure **5A** in refluxing toluene for 6 h (Scheme 1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23 (3H, d, J = 6.8 Hz), 1.39 (3H, s), 1.48 (3H, s), 2.16 (3H, s), 2.95 (1H, dq, J = 7.8, 6.8 Hz), 4.08−4.18 (2H, m), 4.46−4.55 (2H, m), 5.28 (1H, dt, J = 17.0, 1.1 Hz), 5.31 (1H, dt, J = 10.4, 1.1 Hz), 5.71 (1H, ddd, J = 17.0, 10.4, 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.4, 19.3, 25.3, 26.7, 41.4, 65.2, 75.1, 77.3, 84.8, 110.0, 120.6, 132.9, 169.3, 170.3, 200.9.

5,6-*O*-Isopropylidene-3-keto-2-*O*-acetyl-2-(1-phenyl-1-prop-2-enyl)-L-galactono-γ-lactone (6B). This was obtained as a major diastereomer with a small amount of a minor diastereomer[5] from the Claisen rearrangement of pure **6A** in refluxing toluene for 6 h (Scheme 1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (3H, s), 1.46 (3H, s), 2.13 (3H, s), 2.99 (1H, dt, J = 6.8, 6.1 Hz), 3.83 (1H, dd, J = 8.8, 6.9 Hz), 3.97 (1H, dd, J = 8.8, 6.9 Hz), 4.06 (1H, d, J = 8.6 Hz), 4.76 (1H, d, J = 6.8 Hz), 5.18 (1H, dt, J = 17.0, 1.1 Hz), 5.31 (1H, dt, J = 10.3, 1.1 Hz), 6.44 (1H, ddd, J = 17.0, 10.3, 8.6 Hz), 7.21−7.27 (2H, m), 7.32−7.40 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.3, 25.4, 26.4, 51.3, 64.9, 72.7, 76.0, 83.9, 110.2, 119.9, 128.5, 129.3, 129.8, 132.5, 134.9, 169.3, 170.6, 201.5.

5,6-*O*-Isopropylidene-3-keto-2-(1-phenyl-1-prop-2-enyl)-L-galactono-γ-lactone (7B). This was obtained as a major diastereomer with a small amount of a minor diastereomer[5] from the Claisen rearrangement of pure **7A** in refluxing toluene for 6 h (Scheme 1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (3H, s), 1.32 (3H, s), 3.55 (1H, d, J = 1.9 Hz), 3.88 (1H, dd, J = 8.6, 7.0 Hz), 3.91 (1H, dd, J = 8.6, 7.0 Hz), 3.94 (1H, d, J = 2.0 Hz), 4.45 (1H, dt, J = 7.0, 2.0 Hz), 5.39−5.49 (2H, m), 6.35−6.50 (1H, m), 7.19−7.36 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.3, 25.5, 56.7, 64.7, 74.0, 74.2, 81.9, 111.0, 122.3, 128.5, 128.7, 129.1, 131.1, 134.2, 172.0, 206.1.

5,6-*O*-Isopropylidene-2-keto-3-(1-prop-2-enyl)-L-galactono-γ-lactone (8D). This was obtained as a major diastereomer with an insignificant amount of a minor diastereomer from the Claisen rearrangement of pure **8C** in refluxing toluene for 12 h (Scheme 2): ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (3H, s), 1.32 (3H, s), 2.54 (2H, dt, J = 7.2, 1.2 Hz), 3.13 (1H, br), 4.10 (1H, dd, J = 8.8, 6.8 Hz), 4.17 (1H, dd, J = 15.2, 8.8 Hz), 4.52 (1H, dt, J = 13.2, 6.8 Hz), 4.70 (1H, d, J = 1.2 Hz), 5.25 (1H, dq, J = 17.2, 3.2 Hz), 5.35 (1H, dq, J = 10.4, 1.6 Hz), 5.81 (1H, ddd, J = 10.4, 7.2, 3.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 24.8, 39.6, 64.4, 73.1, 77.2, 80.8, 111.3, 121.9, 129.0, 159.4, 193.9.

5,6-*O*-Isopropylidene-2-keto-3-*O*-acetyl-3-(1-prop-2-enyl)-L-galactono-γ-lactone (9D). This was obtained as a major diastereomer with an insignificant amount of a minor diastereomer from the Claisen rearrangement of pure **9C** in refluxing toluene for 12 h (Scheme 2): ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32 (3H, s), 1.34 (3H, s), 2.16 (3H, s), 2.76 (1H, m), 2.97 (1H, m), 4.04 (1H, dd, J = 8.6, 7.2 Hz), 4.14 (1H, dd, J = 8.6, 7.2 Hz), 4.28 (1H, dt, J = 7.2, 1.6 Hz), 4.94 (1H, d, J = 1.6 Hz), 5.23 (2H, m), 5.62−5.73 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 25.0, 25.2, 36.9, 65.1, 72.6, 78.4, 81.1, 111.1, 121.9, 128.1, 158.2, 170.6, 186.3.

5,6-*O*-Isopropylidene-2-keto-3-(1-methyl-1-prop-2-enyl)-L-galactono-γ-lactone (10D). This was obtained as a major diastereomer with an insignificant amount of a minor diastereomer from the Claisen rearrangement of pure **10C** in refluxing toluene for 12 h (Scheme 2): ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15 (3H, d, J = 6.9 Hz), 1.29 (3H, s), 1.32 (3H, s), 2.71 (1H, m), 3.23 (1H, br), 4.08 (1H, dd, J = 8.7, 7.1 Hz), 4.18 (1H, dd, J = 8.4, 7.1 Hz), 4.52 (1H, dt, J = 7.1, 1.5 Hz), 4.75 (1H, d, J = 1.5 Hz), 5.18 (2H, m), 5.72−5.85 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.2, 24.8, 24.9, 43.8, 64.4, 73.4, 78.9, 80.0, 111.2, 118.6, 135.3, 159.5, 195.3.

5,6-*O*-Isopropylidene-2-keto-3-*O*-acetyl-3-(1-methyl-1-prop-2-enyl)-L-galactono-γ-lactone (11D). This was obtained as a major diastereomer with an insignificant amount of a minor diastereomer from the Claisen rearrangement of pure **11C** in refluxing toluene for 12 h (Scheme 2): ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.10 (3H, d, J = 7.0 Hz), 1.33 (3H, s), 1.35 (3H, s), 2.16 (3H, s), 3.17 (1H, m), 4.04 (1H, dd, J = 8.8, 7.1 Hz), 4.13 (1H, dd, J = 8.8, 7.1 Hz), 4.30 (1H, dt, J = 7.2, 2.4 Hz), 4.83 (1H, d, J = 2.4 Hz), 5.15−5.28 (2H, m), 5.64−5.81 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.8, 19.9, 25.2, 25.5, 42.1, 65.5, 73.4, 77.3, 79.7, 111.0, 119.7, 134.7, 158.0, 170.9, 187.5.

5,6-*O*-Isopropylidene-2-(1-prop-2-enyl)-L-gulono-γ-lactone (1E). To a stirred solution of diastereomerically pure **1B** (1.50 g, 5.85 mmol) in absolute EtOH (80 mL) at −79 °C was added $NaBH_4$ (244 mg, 6.44 mmol). The reaction mixture was kept at −79 °C for 5 min and then allowed to rise to room temperature for a period of no more than 30 min. The reaction mixture was concentrated under reduced pressure to about 25 mL and diluted with a mixture of 1:1 cold water and ethyl acetate (250 mL) and stirred for 30 min. The ethyl acetate layer was separated, and the aqueous layer was extracted twice with ethyl acetate. The combined ethyl acetate extracts were dried with anhydrous Na_2SO_4, and the solvents were removed under reduced pressure. The residue was chromatographed on silica gel using 3:1 *n*-hexane/ethyl acetate to give 1.39 g (92%) of pure **1E** as a white semisolid and ∼200 mg of its diastereomer (Scheme 3): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (3H, s), 1.43 (3H, s), 2.56 (1H, dd, J = 14.5, 8.8 Hz), 2.62 (1H, dd, J = 14.5, 6.2 Hz), 2.77 (1H, d, J = 4.5 Hz), 3.65 (1H, br), 4.03 (1H, dd, J = 8.4, 7.0 Hz), 4.15 (1H, t, J = 6.4 Hz), 4.17 (1H, m), 4.37 (1H, dt, J = 7.0, 4.5 Hz), 4.44 (1H, dd, J = 6.4, 4.5 Hz), 5.30 (1H, d, J = 12.0 Hz), 5.31 (1H, d, J = 16.4 Hz), 5.90−6.00 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.5, 25.9, 36.4, 65.2, 74.3, 75.9, 77.2, 79.8, 110.7, 121.1, 130.9, 175.4. Anal. Calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02. Found: C, 55.73; H, 7.04.

5,6-*O*-Isopropylidene-2-*O*-(1-prop-2-enyl)-2-(1-prop-2-enyl)-L-gulono-γ-lactone (3E). This was synthesized from diastereomerically pure **3B** in 90% yield as a semisolid using the same procedure as for **1E**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (3H, s), 1.46 (3H, s), 2.47 (1H, m), 2.77 (1H, m), 3.01 (1H,

d, J = 4.6 Hz), 3.83 (1H, dd, J = 8.4, 6.8 Hz), 4.21 (1H, dd, J = 8.8, 6.8 Hz), 4.25 (1H, t, J = 7.0 Hz), 4.28−4.31 (1H, m), 4.39 (1H, dt, J = 8.0, 4.6 Hz), 4.48 (1H, dd, J = 7.0, 4.6 Hz), 4.55−4.60 (1H, m), 5.19−5.24 (2H, m), 5.25−5.26 (2H, m), 5.72−5.82 (1H, m), 5.86−5.96 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.2, 26.6, 35.7, 65.5, 65.7, 71.9, 74.9, 78.2, 81.5, 110.1, 117.5, 120.8, 129.9, 133.7, 173.2. Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.52; H, 7.63.

5,6-*O*-Isopropylidene-2-(1-methyl-1-prop-2-enyl)-L-gulono-γ-lactone (4E). This was synthesized from diastereomerically pure **4B** in 91% yield as a semisolid using the same procedure as for **1E**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (3H, d, J = 7.2 Hz), 1.40 (3H, s), 1.43 (3H, s), 2.64 (1H, d, J = 4.5), 2.75 (1H, m), 4.03 (1H, dd, J = 8.8, 7.0 Hz), 4.15 (1H, dd, J = 8.8, 7.0 Hz), 4.23 (1H, t, J = 6.2 Hz), 4.35 (1H, dt, J = 7.0, 4.5 Hz), 4.45 (1H, dd, J = 6.2, 4.5 Hz), 5.26 (1H, d, J = 10.4 Hz), 5.29 (1H, d, J = 9.8 Hz), 5.99 (1H, ddd, J = 17.6, 10.4, 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 25.6, 25.9, 41.9, 65.3, 74.7, 76.9, 77.7, 80.5, 110.7, 118.5, 138.4, 175.2. Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.40; H, 7.22.

5,6-*O*-Isopropylidene-2-(1-phenyl-1-prop-2-enyl)-L-gulono-γ-lactone (7E). This was synthesized from diastereomerically pure **7B** in 90% yield (crude) as a semisolid using the same procedure as for **1E**: Since analytically pure **7E** could not be obtained by traditional chromatographic techniques, it was characterized as acetate (**7F**), which was easily obtained in its pure form (see below).

The Product of $NaBH_4$ Reduction of 5,6-*O*-Isopropylidene-2-keto-3-*O*-acetyl-3-(1-prop-2-enyl)-L-galactono-γ-lactone (9G). This was synthesized from diastereomerically pure **9D** in 60% yield as a white semisolid using the same procedure as for **1E** (Scheme 4): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (3H, s), 1.46 (3H, s), 2.25 (3H, s), 2.48 (1H, dd, J = 14.2, 8.0 Hz), 2.54 (1H, dd, J = 14.0, 7.5 Hz), 4.05 (1H, dd, J = 8.4, 6.8 Hz), 4.09 (1H, s), 4.20 (1H, dd, J = 8.4, 6.8 Hz), 4.30 (1H, d, J = 3.0 Hz), 4.53 (1H, dt, J = 6.8, 3.0 Hz), 5.24 (2H, dd, J = 15.2, 7.2 Hz), 5.52 (1H, br), 5.82−5.93 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 25.7, 40.9, 65.7, 71.8, 73.5, 77.7, 79.9, 111.1, 120.8, 130.8, 169.4, 170.1.

5,6-*O*-Isopropylidene-2,3-*O*-diacetyl-2-(1-prop-2-enyl)-L-gulono-γ-lactone (1F). To a stirred solution of a mixture of diastereomerically pure **1E** (1.20 g, 4.65 mmol), 4-DMAP (284 mg, 2.32 mmol), and triethylamine (3.3 mL, 23 mmol) in dichloromethane (30 mL) at −79 °C was added acetic anhydride (1.76 mL, 18.6 mmol). The reaction mixture was stirred for 3 h at −79 °C and then quenched with saturated aqueous sodium bicarbonate. The mixture was extracted with ethyl acetate, and the organic layer was washed with water and brine and then dried over anhydrous Na_2SO_4. The solvents were removed under reduced pressure, and the residue was chromatographed on silica gel using 10:1 n-hexane/ethyl acetate to give pure **1F** (1.59 g, quant.) as a white semisolid (Scheme 3): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (3H, s), 1.43 (3H, s), 2.15 (3H, s), 2.16 (3H, s), 2.58 (1H, m), 2.60 (1H, m), 3.98 (1H, dd, J = dd, J = 9.0, 6.0 Hz), 4.06 (1H, dd, J = 9.0, 7.0 Hz), 4.30 (1H, dd, J = 8.0, 6.0 Hz), 4.43 (1H, dt, J = 11.6, 6.0 Hz), 5.27 (1H, m), 5.83 (1H, m), 5.94 (1H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 20.5, 25.0, 26.1, 36.2, 64.6, 72.5, 74.6, 78.1, 81.3, 110.5, 121.4, 128.8, 169.3, 169.8, 169.9. Anal. Calcd for $C_{16}H_{22}O_8$: C, 56.13; H, 6.48. Found: C, 56.35; H, 6.38.

5,6-*O*-Isopropylidene-3-*O*-acetyl-2-*O*-(1-prop-2-enyl)-2-(1-prop-2-enyl)-L-gulono-γ-lactone (3F). This was synthesized from diastereomerically pure **3E** in quantitative yield (white semisolid) using the same procedure as for **1F**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (3H, s), 1.46 (3H, s), 2.11 (3H, s), 2.58 (1H, dt, J = 14.8, 7.6 Hz), 2.71 (1H, dt, J = 14.8, 7.6 Hz), 3.69 (1H, dd, J = 8.8, 6.8 Hz), 4.01 (1H, dd, J = 8.8, 6.8 Hz), 4.19 (1H, m), 4.22 (1H, m), 4.33 (1H, m), 4.43 (1H, dd, J = 8.0, 4.2 Hz), 5.12−5.16 (2H, m), 5.26−5.30 (2H, m), 5.51 (1H, d, J = 4.2 Hz), 5.78−5.90 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.6, 25.1, 26.5, 37.4, 65.2, 66.7, 72.4, 74.5, 79.2, 79.4, 110.3, 116.2, 120.8, 129.8, 134.0, 169.2, 172.4. Anal. Calcd for $C_{17}H_{24}O_7$: C, 59.99; H, 7.11. Found: C, 60.23; H, 7.39.

5,6-*O*-Isopropylidene-2,3-*O*-diacetyl-2-(1-methyl-1-prop-2-enyl)-L-gulono-γ-lactone (4F). This was synthesized from diastereomerically pure **4E** in quantitative yield (white semisolid) using the same procedure as for **1F**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (3H, d, J = 7.2 Hz), 1.37 (3H, s), 1.43 (3H, s), 2.14 (3H, s), 2.15 (3H, s), 2.75−2.84 (1H, m), 3.90 (1H, dd, J = 8.8, 6.4 Hz), 4.04 (1H, dd, J = 8.8, 6.4 Hz), 4.31 (1H, dd, J = 8.0, 6.0 Hz), 4.42 (1H, dt, J = 12.8, 6.4 Hz), 5.16 (1H, d, J = 14.8 Hz), 5.17 (1H, d, J = 12.8 Hz), 5.89−5.94 (1H, m), 5.96 (1H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.9, 20.5, 20.6, 25.0, 26.1, 41.6, 64.5, 73.0, 74.9, 78.7, 82.9, 110.4, 118.2, 135.8, 169.4, 169.8, 170. Anal. Calcd for $C_{17}H_{24}O_8$: C, 57.30; H, 6.79. Found: C, 57.48; H, 6.50.

5,6-*O*-Isopropylidene-2,3-*O*-diacetyl-2-(1-phenyl-1-prop-2-enyl)-L-gulono-γ-lactone (7F). This was synthesized from diastereomerically pure **7E** in quantitative yield (white semisolid) using the same procedure as for **1F**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (3H, s), 1.39 (3H, s), 1.94 (3H, s), 2.11 (3H, s), 3.91 (1H, dd, J = 9.0, 6.4 Hz), 4.00 (1H, dd, J = 9.0, 6.4 Hz), 4.08 (1H, dd, J = 8.0, 6.2 Hz), 4.31 (1H, dt, J = 11.9, 6.4 Hz), 5.20 (1H, d, J = 16.9 Hz), 5.26 (1H, d, J = 10.4 Hz), 6.11 (1H, d, J = 8.0 Hz), 6.22 (1H, ddd, J = 16.9, 10.4, 9.0 Hz), 7.26−7.35 (2H, m), 7.39−7.41 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.3, 20.6, 24.9, 26.0, 52.4, 64.5, 72.2, 74.4, 77.6, 83.1, 110.4, 119.3, 127.7, 128.5, 130.2, 134.2, 136.4, 169.1, 169.4, 169.7. Anal. Calcd for $C_{22}H_{26}O_8$: C, 63.15; H, 6.26. Found: C, 63.46; H, 6.04.

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Supporting Information Available: ^{1}H, ^{13}C, ^{1}H COSY, and NOESY spectra of new and selected compounds: **2B** and **5B**−**7B**, **8D**−**11D**, **1E**, **3E**, **4E**, **9G**, and all **F** series. This material is available free of charge via the Internet at http://pubs.acs.org.

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