Serial Radical Cyclization of Branched Carbohydrates. 2.[1,2] Claisen Rearrangement Routes to Multiply Substituted Pyranoside Diquinanes

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Pyranosidic diquinanes, which may be prepared by serial radical cyclization of suitably functionalized alkyl residues at C2 and C3, are potential precursors for polyquinane synthesis. The residues at C3 are installed via a Claisen rearrangement, and it is therefore possible to obtain more highly substituted diquinane synthons by incorporating methyl residues at the appropriate sites in the precursors. The consequences of these substituents on the stereoselectivity of the Claisen rearrangement have been examined.

Introduction

In the accompanying paper,[2] we outlined a general strategy for obtaining some bis-annulated sugars, which may be classified as pyranosidic diquinanes, from the 2-deoxy-3-keto sugar **1** (Scheme I). Three key steps are involved in this strategy: (1) alkylation of the C2 activated methylene group of **1**; (2) geminal dialkylation at C3 via a Claisen rearrangement protocol to give **2**; and (3) serial radical coupling of the functionalized C2 and C3 appendages to give **3**. Our interest in structure **3** comes from the realization that further manipulations should lead to the differently configured triquinane skeleta[3] **4–6**, in which all carbons of the original sugar have been retained.

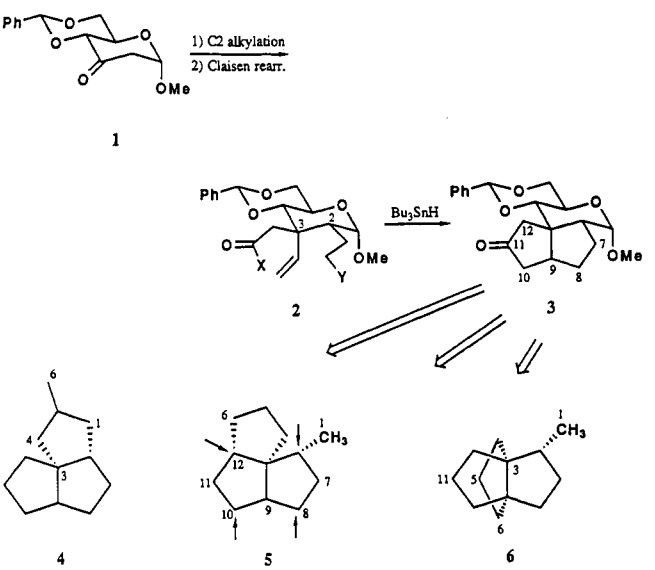
An additional advantage of this approach is that the stereochemical features of the triquinanes could be established unequivocally at the level of precursor **3**. In this connection, skeleton **5**, which occurs in several natural products,[3] carries methyl groups at (some of) the sites indicated by arrows. Therefore, it would be advantageous to incorporate the substituents at the stage of the precursor **3**, in order to take advantage of the stereodirecting properties of the pyranoside ring, as well as of the ease of making structure assignments in sugars via NMR analyses.

In the accompanying paper,[2] it was found that introduction of methyl groups at C10 and C12 by alkylative procedures, though stereocontrollable, was not regiocontrollable. (For the sake of consistency, carbohydrate numbering is used throughout.) A successful alternative to the C10 precursor was therefore developed that involved a conjugate radical addition strategy.[2] However, yet another alternative for installing these as well as other substituents could conceivably take advantage of the early key steps of C2 alkylation and/or C3 Claisen rearrangement.[4] Therefore, both of these avenues have been investigated and are discussed in this paper.

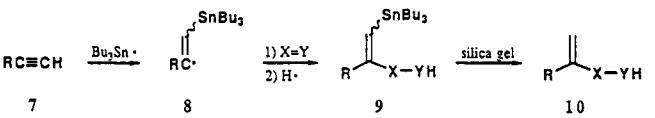
C2 Alkylations for C2 and C8 Substitution

(a) Terminal alkynes are excellent sources of vinyl radicals,[5] through the addition of tri-*n*-butyltin at the terminal carbon (**7**→**8**), and the product of radical capture, **9** (Scheme II), readily undergoes protiodestannylation to give **10** by simple stirring with silica gel.[6] Use of such a vinyl radical for the serial cyclization **2**→**3** would lead to a C8 exocyclic methylene group, which is a synthon, not only for CH_3 by reduction but also for a variety of functional groups by oxidative transformations.

Scheme I



Scheme II



The propargylated C3 ketone **12** (Scheme III) was therefore prepared by fragmentation of **11** with in situ alkylation.[2,7,8] Olefination under Horner–Emmons conditions afforded three isomers, **13E**, **13Z**, and **14**, in a 6:1:3.3 ratio, whereas Peterson olefination of **12** afforded **13E** as the only isomer.

Reduction of **13(E,Z)** with DIBAL afforded the allylic alcohol **15(E,Z)**. The Johnson–Faulkner version of the Claisen rearrangement[9] proved most effective for geminal alkylation at C3, and the product, **16a**, was transformed to the aldehyde **16b**, and thence to nitrile **16c** by standard procedures.[2] Reaction with tri-*n*-butyltin hydride, followed by protiodestannylation, afforded the C8-methylene diquinane **17**.

(1) This work is supported by a grant from NIH (GM 37380).

(2) Part 1: Dickson, J. K., Jr.; Tsang, R.; Llera, J. M.; Fraser-Reid, B. *J. Org. Chem.*, preceding paper in this issue.

(3) For a recent review, see: Paquette, L. A.; Doherty, A. M. *Polyquinane Chemistry: Reactivity and Structure*; Concepts in Organic Chemistry; Vol. 26; Springer-Verlag: New York, 1987.

(4) Tulshian, D. B.; Tsang, R.; Fraser-Reid, B. *J. Org. Chem.* **1984**, *49*, 2347. Fraser-Reid, B.; Tulshian, D. B.; Tsang, R.; Lowe, D.; Box, V. G. S. *Tetrahedron Lett.* **1984**, *25*, 4579.

(5) Stork, G.; Mook, R., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 2829. Nozaki, K.; Oshima, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 2547. Ardisson, J.; Ferezou, J. P.; Julia, M.; Pancrazi, A. *Tetrahedron Lett.* **1987**, *28*, 2001.

(6) Stork, G.; Mook, R., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 2829.

(7) Tsang, R.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1984**, 60.

(8) Chapleur, Y. *J. Chem. Soc., Chem. Commun.* **1983**, 141.

(9) Johnson, W. S.; Wertheman, L.; Bartlett, W. R.; Brockson, T. J.; Li, T.-T.; Faulkner, D. J.; Peterson, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741.

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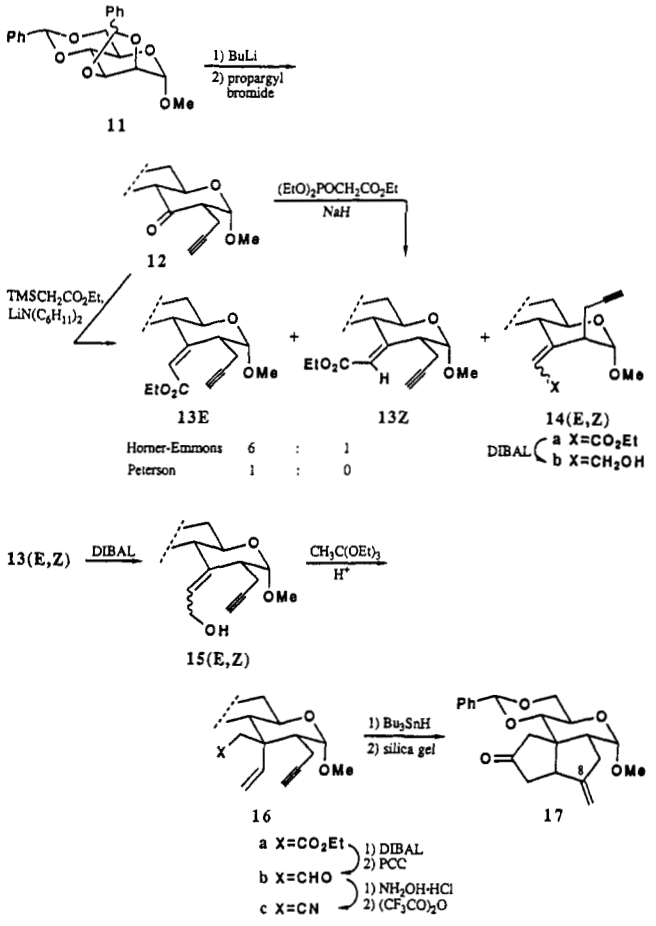
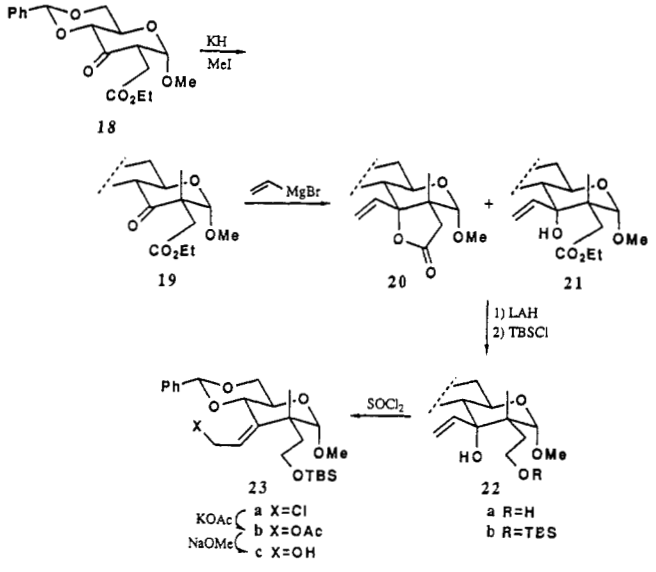
Scheme III



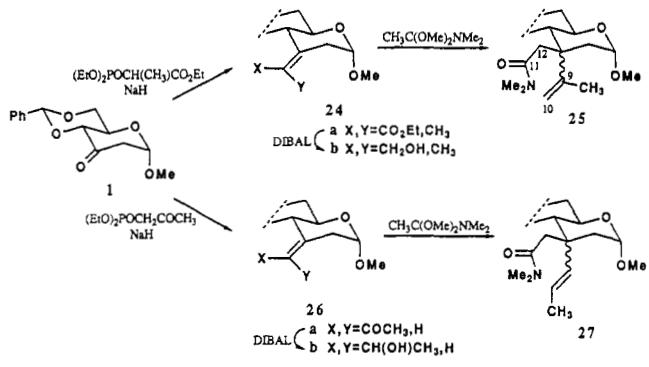
Scheme IV



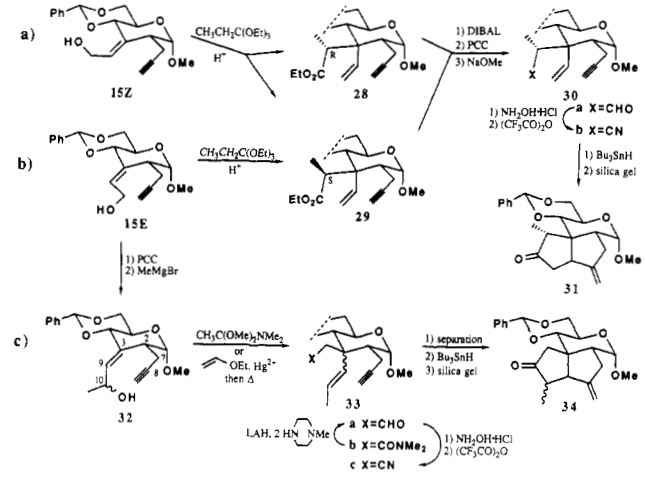
(b) The additional alkylation required at C2 of **5** could be furnished readily by dialkylation of the keto sugar **1**. Accordingly, methylation of the previously prepared[2] keto ester **18** gave **19** as the only di-C-alkylated stereoisomer (Scheme IV). Notably, the second alkyl group came in axially, suggesting that, in the case of monoalkylation, as in **12** and **18**, kinetic alkylation of the intermediate enolate ion is from the less hindered side, followed by in situ isomerization.

The hindered carbonyl group of **19** failed to react with Wittig, Horner–Emmons, or Peterson olefination reagents.

Scheme V



Scheme VI



Therefore, an alternative strategy was required to obtain the desired allylic alcohol **23c**. Addition of vinylmagnesium bromide to **19** gave a mixture of lactone **20** and ester **21**, both of which were reduced to the diol **22a**. The protected form, **22b**, was smoothly rearranged to the *Z* primary allylic chloride **23a** as the only geometric isomer by treatment with thionyl chloride. Acetolysis then gave the acetate **23b**, and hydrolysis gave the alcohol **23c**.

Claisen Rearrangement for C9, C10, or C12 Methyl Substituents

Provisions for alkylation at C9, C10, and/or C12 could conceivably be implemented by use of the appropriately substituted precursors for the Claisen rearrangements. These possibilities were first explored with the readily available[10] 2-deoxy ketone **1** (Scheme V). Horner–Emmons reaction with the phosphopropionate ester gave one geometric isomer (stereochemistry undetermined) of alkene **24a**, which was reduced to the alcohol **24b**.

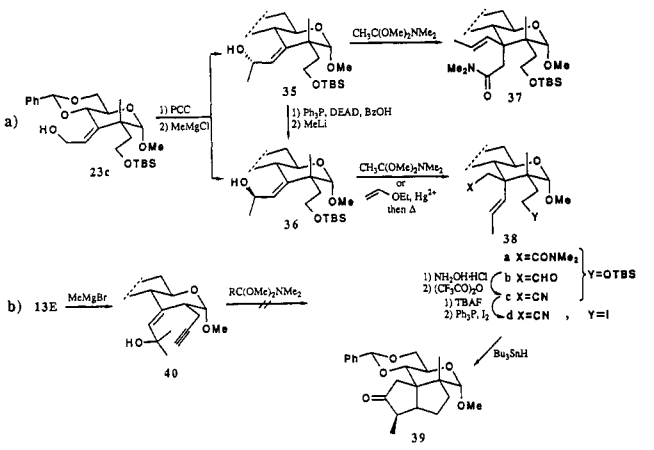
Eschenmoser–Claisen rearrangement with *N,N*-dimethylacetamide dimethyl acetal proved to be nonstereoselective, giving a mixture of the C3 epimers **25**.

Reaction of ketone **1** with the keto phosphonate reagent gave one geometric isomer (stereochemistry undetermined) of enone **26a**. However, again the Claisen rearrangement of the corresponding alcohol **26b** was nonstereoselective, giving a mixture of the C3 epimers **27**.

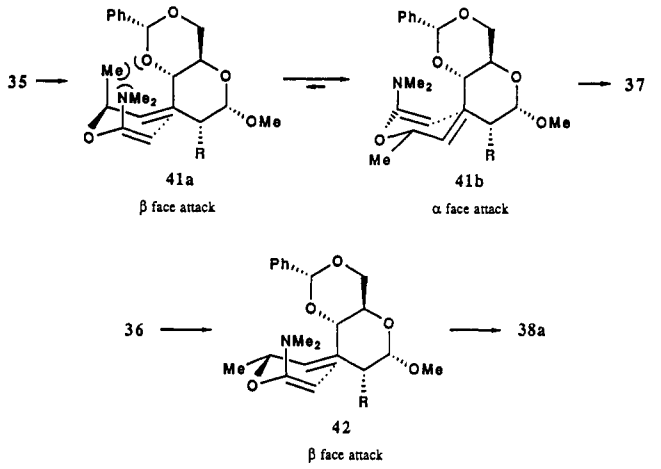
With these exploratory studies completed, we returned to the C2-propargylated derivative **15** (Scheme III) to see whether a more highly substituted diquinane could be prepared therefrom. The geometric isomers were sepa-

(10) Horton, D.; Weckerle, W. *Carbohydr. Res.* **1975**, *44*, 227. Kelmer, A.; Rodemeyer, G. *Chem. Ber.* **1974**, *107*, 2612.

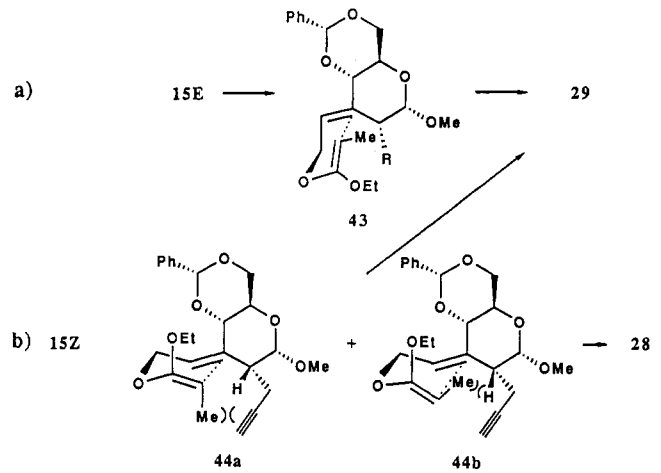
Scheme VII



Scheme VIII



Scheme IX



rated, and Claisen rearrangements involving trimethyl orthopropionate were examined. Isomer **15Z** gave a 2.2:1 mixture of **28** and **29**, respectively (Scheme VI, part a). The configurations were assigned by conversion of the major isomer into diquinane **31** (via **30a** and **30b**) on the assumption that the C12 orientation was not altered during the cyclization. The C12 configuration of **31** was determined by NOE enhancement of H4 upon irradiation of the CH_3 group.

The minor isomer, **29**, could be converted completely into the major, **28**, by treatment with sodium methoxide in methanol.

Geometric isomer **15E** gave **29** as the sole product of Claisen rearrangement (Scheme VI, part b). It therefore follows that both C12 epimers **28** and **29** can be obtained in pure forms by the processes indicated in Scheme VI, parts a and b.

The secondary allylic alcohol **32** was prepared as a 2:1 mixture from **15E** and transformed into aldehyde **33a** directly by the classical Claisen rearrangement, or indirectly by the Eschenmoser version, followed by a modified Mukaiyama reduction[11] (Scheme VI, part c).

As in the case of **26** (Scheme V), the additional CH_3 group at C10 of **32** caused a loss of C3 stereoselectivity in the rearrangement. However, only the isomer with the axial propenyl group can undergo the desired serial cyclization (**2** → **3**, Scheme I), since the other would involve formation of a five-membered ring trans-fused to the pyranoside ring. Thus, the appropriate isomer of **33a** was converted into the nitrile **33c**, and the latter was treated directly with tri-*n*-butyltin hydride. The diquinane **34** was thereby obtained in 92% yield.

The primary allylic alcohol **23c** (Scheme VII, part a) was also processed to give secondary alcohols, but unlike **32**, the component isomers, **35** and **36**, were readily separated by column chromatography, the structure of the former being established by X-ray crystallography. It was therefore possible to establish that each isomer gave a different rearrangement product, **37** and **38a**, respectively. Since only the latter can lead to a diquinane, its precursor, alcohol **36**, was accumulated by Mitsunobu inversion[12] of the unwanted epimer **35**.

Attempts to obtain aldehyde **38b** by hydride reduction of amide **38a** led only to the corresponding *N,N*-dimethylamine. The aldehyde **38b** was therefore prepared by the classical Claisen rearrangement and transformed into the nitrile **38c**, from which the iodide **38d** was then obtained. Radical cyclization then afforded diquinane **39**, notably as a single isomer whose configuration at C10 was established to be *R* by X-ray crystallography.

The tertiary allylic alcohol **40** (Scheme VII, part b) was a plausible precursor for the targets with the *gem*-dimethyl groups at C10. However, it did not prove possible to effect Claisen rearrangement on this material.

It is interesting to speculate, with the aid of hindsight, about the stereochemical factors that influence the outcome of the Claisen rearrangements. Earlier experiments in our laboratory had shown that (a) the geometry of the precursor (obtained via Wittig reaction) is usually *Z* and (b) the rearrangement usually occurs by folding from the β face.[4] The presence of the axial glycosidic OCH_3 is undoubtedly a controlling element. It may be noted that both geometric isomers **15E** and **15Z** experienced β-face attack exclusively (Scheme VI, parts a and b).

On the basis of these precedents, we can examine the results with the secondary alcohols **35** and **36**. An assumption that the transition state **42** (from isomer **36**) is chair-like, as shown in Scheme VIII, seems to provide a rationalization for (a) β-face attack and (b) *E*-olefinic geometry, as was indeed found in the product **38a**. In the case of **41a** (from isomer **35**), the transition state for β-face attack is seen to be destabilized by 1,3-interactions of the pseudoaxial CH_3 and NMe_2 groups. On the other hand, α-face attack (**41b**) does not experience any such 1,3-interactions across the chair-like transition state, and thus the C3 epimer **37** is favored.

The stereochemical differences observed in these Claisen rearrangements for substituents bearing a C10-CH_3 (**26**,

(11) Muraki, M.; Mukaiyama, T. *Chem. Lett.* **1975**, 875.

32, 35, and 36) are therefore rationalizable.

Examination of the examples in Scheme VI, parts a and b, with respect to the C12-CH_3, is shown in Scheme IX. It is assumed that precursors 43 and 44 will exist in the chair-like transition states with the C12-CH_3 in pseudoequatorial arrangement. The corollary of this is that the intermediate enolate esters must be of cis geometry, as shown. For 43, this accounts for the observed *S* configuration at C12 in the sole product 29.

In the case of the *Z* isomer, the 2.2:1 ratio of the mixture indicates that neither transition state **44a** nor **44b** (Scheme IX, part b) is overwhelmingly preferred. This indeed seems to be supported by the fact that both ketene acetals **44a** and **44b** are destabilized by interactions either with the C2-H or with the C2-propargyl group.

The strategies reported in these papers are being utilized for polyquinane syntheses, and further developments will be described in due course.

Experimental Section

For general and standard procedures, see accompanying paper.[2]

Methyl 4,6-*O*-Benzylidene-2-deoxy-2-*C*-propynyl-α-D-*ribo*-hexopyranosid-3-ulose (12). Compound 11 (50 g, 0.135 mol) was fragmented[11] and then alkylated in situ with propargyl bromide, according to the standard procedure, to give **12** (14.3 g, 35%) as a white solid: R_f 0.51 (20% EtOAc/petroleum ether); IR ($CDCl_3$) 1740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50–7.33 (m, 5 H, C_6H_5), 5.56 (s, 1 H, PhC*H*), 5.26 (d, 1 H, H1), 4.37 (dd, 1 H, $J_{6(ax),6(eq)}$ = 4.6 Hz, $J_{5,6(eq)}$ = 10.2 Hz, H6(eq)), 4.29 (dd, 1 H, $J_{2,4}$ = 1.3 Hz, $J_{4,5}$ = 9.7 Hz, H4), 4.10 (m, 1 H, H5), 3.92 (t, 1 H, *J* = 10.2 Hz, H6(ax)), 3.40 (s, 3 H, OCH_3), 2.97 (m, 1 H, H2), 2.66–2.57 (ddd, 1 H, $J_{2,7}$ = 4.9 Hz, $J_{7,C\equiv CH}$ = 2.9 Hz, $J_{7,7'}$ = 17.5 Hz, H7), 2.51–2.41 (ddd, $J_{2,7'}$ = 10.4 Hz, $J_{7',C\equiv CH}$ = 2.7 Hz, $J_{7',7}$ = 17.3 Hz, H7′), 1.97 (t, 1 H, $J_{7,C\equiv CH}$ = 2.7 Hz, C≡C*H*). Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.40; H, 5.99.

Horner–Emmons Reaction of 12. The ketone **12** (10 g, 0.03 mol) was treated under standard Horner–Emmons conditions to afford a mixture of **13E**, **13Z**, and **14a(E,Z)** (10.5 g, 85%) in a ratio of 6:1:3.3 as a syrupy solid. The mixture was reduced by using standard DIBAL reduction conditions to give a mixture of **15E**, **15Z**, and **14b(E,Z)** (8.6 g, 92%). **14bE**: syrup; R_f 0.12 (25% EtOAc/petroleum ether); $[\alpha]^{20}_D$ + 65.8° (*c* 0.88, $CHCl_3$); IR (neat) 3450 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.52–7.34 (m, 5 H, C_6H_5), 6.06 (dt, $J_{4,9}$ = 1.9 Hz, $J_{9,10}$ = 7.3 Hz, H9), 5.63 (s, 1 H, PhC*H*), 4.68 (s, 1 H, H1), 4.24–3.77 (m, 6 H, H10, H10′, H4, H5, H6(ax), H6(eq)), 3.35 (s, 3 H, OCH_3), 3.16 (t, 1 H, $J_{2,7}$ = 8.3 Hz, H2), 2.62–2.41 (m, 2 H, H7, H7′), 2.06 (t, 1 H, $J_{C\equiv CH,7}$ = 2.7 Hz, C≡C*H*), 1.54 (br s, 1 H, O*H*). Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.08; H, 6.71. Found: C, 69.03; H, 6.93. **14bZ**: syrup; R_f 0.19 (25% EtOAc/petroleum ether); $[\alpha]^{20}_D$ +63.7° (*c* 0.61, $CHCl_3$); IR (neat) 3425 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.35 (m, 5 H, C_6H_5), 5.68 (t, 1 H, $J_{9,10}$ = 6.2 Hz, H9), 5.58 (s, 1 H, PhC*H*), 4.71 (s, 1 H, H1), 4.35–4.24 (m, 4 H, H10, H10′, H6(eq), H4), 3.95–3.88 (m, 1 H, H5), 3.79 (t, 1 H, *J* = 10.3 Hz, H6(ax), 3.39 (s, 3 H, OCH_3), 2.63–2.39 (m, 3 H, H2, H7, H7′), 2.07 (t, 1 H, $J_{C\equiv CH,7}$ = 2.5 Hz, C≡C*H*), 1.96 (br s, 1 H, O*H*). Anal. Calcd for $C_{19}H_{22}O_5$: C 69.08; H, 6.71. Found: C, 69.31; H, 6.90. **15E**: white solid; mp 135–136 °C; R_f 0.30 (25% EtOAc/petroleum ether); $[\alpha]^{20}_D$ +119.2° (*c* 1.43, $CHCl_3$); IR (CH_2Cl_2) 3500 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.52–7.33 (m, 5 H, C_6H_5), 6.00 (t, 1 H, $J_{9,10}$ = 7.5 Hz, H9), 5.61 (s, 1 H, PhC*H*), 4.87 (d, 1 H, $J_{1,2}$ = 2.2 Hz, H1), 4.29–4.22 (m, 3 H, H10, H10′, H6), 3.93 (d, 1 H, $J_{4,5}$ = 8.5 Hz, H4), 3.81–3.70 (m, 2 H, H5, H6′), 3.39 (s, 3 H, OCH_3), 2.81–2.62 (m, 3 H, H2, H7, H7′), 2.04 (t, 1 H, $J_{7,C\equiv CH}$ = 2.5 Hz, C≡C*H*), 1.83 (s, 1 H, O*H*). Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.08; H, 6.71. Found: C, 69.16; H, 6.63. **15Z**: white solid; mp 166–167 °C; R_f 0.22 (25% EtOAc/petroleum ether); $[\alpha]^{20}_D$ +76.7° (*c* 0.24, $CHCl_3$); IR (CH_2Cl_2) 3300 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.35 (m, 5 H, C_6H_5), 5.55 (s, 1 H, PhC*H*), 5.40 (t, 1 H, $J_{9,10}$ = 6.3 Hz, H9), 4.90 (d, 1 H, $J_{1,2}$ = 3.2 Hz, H1), 4.36 (d, 2 H, $J_{9,10}$ = 6.4 Hz, H10, H10′), 4.27 (dd, 1 H, $J_{5,6(eq)}$ = 4.4 Hz, $J_{6(ax),6(eq)}$ = 10.0 Hz, H6(eq)), 4.22 (d, 1 H, $J_{4,6}$ = 9.3 Hz, H4), 3.88 (m, 1 H, H5), 3.77 (t, 1 H, *J* = 10.2 Hz, H6(ax)), 3.37 (s, 3 H, OCH_3), 2.60 (br s, 1 H, H2), 2.41 (m, 2 H, H7, H7′), 2.00 (t, 1 H, $J_{C\equiv CH,2}$ = 2.5 Hz, C≡C*H*), 1.81 (br s, 1 H, O*H*); LRMS (CI/NH_3) 348.25 $(M + NH_4)^+$, calcd for $C_{19}H_{22}O_5$ 348.18.

Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-((ethoxycarbonyl)methyl)-2-*C*-propynyl-3-*C*-vinyl-α-D-allopyranoside (16a). Compounds **15E** and **15Z** (257 mg, 0.78 mmol) were treated to the standard Johnson–Faulkner variation of the Claisen rearrangement[9] using triethyl orthoacetate to yield **16a** (275 mg, 88%) as a syrup: R_f 0.87 (20% EtOAc/petroleum ether); $[\alpha]^{20}_D$ +49.8° (*c* 3.14, $CHCl_3$); IR (CH_2Cl_2) 1700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.32 (m, 5 H, C_6H_5), 6.44 (dd, 1 H, $J_{9,10(cis)}$ = 11.1 Hz, $J_{9,10(trans)}$ = 17.6 Hz, H9), 5.54 (s, 1 H, PhC*H*), 5.25 (d, 1 H, $J_{9,10(cis)}$ = 11.2 Hz, H10(cis)), 5.03 (d, 1 H, $J_{9,10(trans)}$ = 17.3 Hz, H10(trans)), 4.92 (d, 1 H, $J_{1,2}$ = 2.6 Hz, H1), 4.30 (dd, 1 H, $J_{5,6(eq)}$ = 4.6 Hz, $J_{6(ax),6(eq)}$ = 10.2 Hz, H6(eq)), 4.21–3.95 (m, 4 H, OCH_2CH_3, H5, H4), 3.71 (t, 1 H, *J* = 9.9 Hz, H6(ax)), 3.41 (s, 3 H, OCH_3), 2.87 (d, 1 H, $J_{12,12'}$ = 13.9 Hz, H12), 2.51 (d, 1 H, $J_{12,12'}$ = 14.1 Hz, H12′), 2.30 (m, 3 H, H2, H7, H7′), 1.96 (br s, 1 H, C≡C*H*), 1.28 (t, 3 H, *J* = 7.1 Hz, OCH_2CH_3). Anal. Calcd for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 69.12; H, 7.14.

Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-(formylmethyl)-2-*C*-propynyl-3-*C*-vinyl-α-D-allopyranoside (16b). Compound **16a** (320 mg, 0.80 mmol) was reduced by the standard reduction procedure using DIBAL, and the corresponding alcohol was oxidized to the aldehyde by using PCC (same procedure as described for **32**) in CH_2Cl_2 to give **16b** (243 mg, 86%) over two steps as a syrupy solid: R_f 0.38 (20% EtOAc/petroleum ether); $[\alpha]^{20}_D$ +28.5° (*c* 2.8, $CHCl_3$); IR (CH_2Cl_2) 1715 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.79 (d, 1 H, $J_{12,CHO}$ = 3.1 Hz, C*H*O), 7.35 (m, 5 H, C_6H_5), 6.32 (dd, 1 H, $J_{9,10(cis)}$ = 11.2 Hz, $J_{9,10(trans)}$ = 17.8 Hz, H9), 5.47 (s, 1 H, PhC*H*), 5.36 (d, 1 H, $J_{9,10(cis)}$ = 11.4 Hz, H10(cis)), 5.13 (d, 1 H, $J_{9,10(trans)}$ = 17.8 Hz, H10(trans)), 4.83 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H1), 4.31 (dd, 1 H, $J_{5,6(eq)}$ = 5.0 Hz, $J_{6(ax),6(eq)}$ = 10.4 Hz, H6(eq)), 4.08 (m, 1 H, H5), 3.69 (t, 2 H, *J* = 9.9 Hz, H4, H6′), 3.38 (s, 3 H, OCH_3), 3.06 (d, 1 H, $J_{12,12'}$ = 15.6 Hz, H12), 2.35–1.98 (m, 5 H, H2, H8′, H8′, H12′, C≡C*H*). Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79. Found: C, 70.53; H, 6.94.

Methyl 4,6-*O*-Benzylidene-3-*C*-(cyanomethyl)-2,3-dideoxy-2-*C*-propynyl-3-*C*-vinyl-α-D-allopyranoside (16c). Compound **16b** (271 mg, 0.76 mmol) was converted by using the standard procedure to afford nitrile **16c** (173 mg, 64%) as a white solid: mp 125–126 °C; R_f 0.26 (15% Et_2O/petroleum ether); $[\alpha]^{20}_D$ +13.7° (*c* 0.60, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.40 (m, 5 H, C_6H_5), 6.41 (dd, 1 H, $J_{9,10(cis)}$ = 11.2 Hz, $J_{9,10(trans)}$ = 17.6 Hz, H9), 5.58 (s, 1 H, PhC*H*), 5.33 (d, 1 H, $J_{9,10(cis)}$ = 11.2 Hz, H10(cis)), 4.98 (d, 1 H, $J_{9,10(trans)}$ = 17.6 Hz, H10(trans)), 4.88 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H1), 4.31 (dd, 1 H, $J_{5,6(eq)}$ = 5.1 Hz, $J_{6(ax),6(eq)}$ = 10.5 Hz, H6(eq)), 4.02 (m, 1 H, H5), 3.75 (t, 2 H, *J* = 10.1 Hz, H4, H6(ax)), 3.41 (s, 3 H, OCH_3), 2.97 (d, 1 H, $J_{12,12'}$ = 16.9 Hz, H12), 2.78 (d, 1 H, $J_{12,12'}$ = 16.9 Hz, H12′), 2.45–2.15 (m, 3 H, H2, H7, H7′), 2.05 (t, 1 H, $J_{7,C\equiv CH}$ = 2.6 Hz, C≡C*H*). Anal. Calcd for $C_{21}H_{24}NO_4$: C, 71.17; H, 6.83. Found: C, 70.84; H, 6.76.

Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-α-D-allopyranosido[3,2-*c*]-8-methylenebicyclo[3.3.0]octan-11-one (17).[13] Compound **16c** (67 mg, 0.19 mmol) was treated to standard cyclization conditions to give **17** (58 mg, 85%), after protiodestannylation, as a syrupy solid: R_f 0.30 (20% EtOAc/petroleum ether); $[\alpha]^{20}_D$ +73.8° (*c* 2.92, $CHCl_3$); IR (neat) 1745 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 5 H, C_6H_5), 5.52 (s, 1 H, PhC*H*), 5.05 (d, 1 H, $J_{7,C=CH}$ = 2.4 Hz, C=C*H*), 4.88 (d, 1 H, $J_{7,C=CH'}$ = 2.4 Hz, C=C*H*′), 4.62 (d, 1 H, $J_{1,2}$ = 5.13 Hz, H1), 4.30 (dd, 1 H, $J_{5,6(eq)}$ = 4.9 Hz, $J_{6(ax),6(eq)}$ = 10.18 Hz, H6(eq)), 4.02 (m, 1 H, H5), 3.74 (m, 2 H, H6(ax), H4), 3.45 (d, 1 H, *J* = 9.6 Hz, H7), 3.32 (s, 3 H, OCH_3), 2.80–2.16 (m, 7 H, H7′, H2, H9, H10, H10′, H12, H12′). Anal. Calcd for $C_{21}O_5H_{24}$: C, 70.77; H, 6.79. Found: C, 70.78; H, 6.84.

Methyl 4,6-*O*-Benzylidene-2-deoxy-2-*C*-((ethoxycarbonyl)methyl)-2-*C*-methyl-α-D-*ribo*-hexopyranosid-3-ulose (19). Potassium hydride (3.60 g, 35% dispersion in mineral oil, 31.5 mmol) was washed with petroleum ether several times, followed by addition of tetrahydrofuran (50 mL). The suspension was cooled to 0 °C under argon, and a mixture of keto ester **18** (10.0 g, 28.6 mmol) and methyl iodide (8.9 mL, 140 mmol) in tetrahydrofuran (250 mL) was added dropwise over 1 h. The

(12) Mitsunobu, O. *Synthesis* **1981**, 1.

(13) The numbering in this compound is the same as in compound 3, Scheme I.

reaction mixture was stirred at 0 °C for 3 h and then quenched with saturated aqueous ammonium chloride solution (50 mL). The solvent was removed in vacuo, and the resultant mixture was extracted with ethyl acetae (3 × 200 mL). The organic extracts were combined, washed with brine (3 × 50 mL), and dried (Na_2SO_4). Evaporation of the solvent followed by flash chromatography (15–30% EtOAc/petroleum ether) gave **19** (6.78 g, 65%) as a colorless oil, which crystallized on standing, and recovered **18** (1.66 g, 17%). Yield based on recovered starting material: 78%. **19**: mp 88–94 °C; R_f 0.43 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D$ +60.3° (*c* 0.771, $CHCl_3$); IR (neat) 1725 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.52–7.30 (m, 5 H, aromatic), 5.56 (s, 1 H, PhC*H*), 5.11 (s, 1 H, H1), 4.56 (d, 1 H, $J_{4,5}$ = 9.9 Hz, H4), 4.34 (dd, 1 H, $J_{5,6(eq)}$ = 4.6 Hz, $J_{6(eq),6(ax)}$ = 10.2 Hz, H6(eq)), 4.15–4.05 (m, 3 H, H5, CH_2CH_3), 3.92 (dd, 1 H, $J_{5,6(ax)}$ = 10.2 Hz, $J_{6(eq),6(ax)}$ = 10.2 Hz, H6(ax)), 3.33 (s, 3 H, O*Me*), 2.83 (d, 1 H, $J_{7,7'}$ = 17.0 Hz, H7), 2.61 (d, 1 H, $J_{7,7'}$ = 17.0 Hz, H7'), 1.52 (s, 3 H, CH_3), 1.24 (t, 3 H, *J* = 7.1 Hz, CH_2CH_3). Anal. Calcd for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64. Found: C, 62.43; H, 6.86.

Methyl 4,6-*O*-Benzylidene-2-*C*-(2-(*tert*-butyldimethylsiloxy)ethyl)-2-deoxy-2-*C*-methyl-3-*C*-vinyl-α-D-allopyranoside (22b). To a solution of keto ester **19** (5.37 g, 14.8 mmol) in tetrahydrofuran (100 mL) at 0 °C under argon was added vinylmagnesium bromide (16.3 mL, 1.0 M in tetrahydrofuran, 16.3 mmol) over 20 min. The reaction mixture was stirred for 15 min and then quenched by the addition of saturated aqueous ammonium chloride solution (10 mL). The solvent was removed in vacuo, and the resultant mixture was extracted with ethyl acetate (100 mL). The organic layer was washed with saturated aqueous ammonium chloride solution (2 × 50 mL) and brine (50 mL) and dried (Na_2SO_4). Evaporation of the solvent gave the crude lactone as a colorless oil. A solution of the crude lactone in tetrahydrofuran (75 mL) was added dropwise over 20 min to a suspension of lithium aluminum hydride (562 mg, 14.8 mmol) in tetrahydrofuran (50 mL) at 0 °C under argon. The reaction mixture was stirred at 0 °C for 45 min and then quenched by slow dropwise addition of methanol until gas evolution ceased. Ethyl acetate (200 mL) and saturated aqueous sodium potassium tartrate solution (300 mL) were added, and the resultant mixture was stirred vigorously at room temperature overnight. The aqueous layer was extracted with ethyl acetate (2 × 100 mL). The organic extracts were combined, washed with saturated aqueous sodium potassium tartrate solution (50 mL) and brine (50 mL), and dried (Na_2SO_4). Evaporation of the solvent gave the crude diol **22a** as a colorless oil. A mixture of the crude diol, *tert*-butyldimethylsilyl chloride (2.68 g, 17.8 mmol), and imidazole (2.01 g, 29.6 mmol) in tetrahydrofuran (100 mL) was stirred at room temperature for 30 min. The solvent was removed in vacuo, and ethyl acetate (200 mL) was added. The organic layer was washed with water (50 mL), saturated aqueous sodium bicarbonate solution (50 mL), and brine (50 mL) and dried (Na_2SO_4). Evaporation of the solvent followed by flash chromatography (10% EtOAc/petroleum ether) gave **22b** (5.04 g, 73%) as a colorless oil: R_f 0.17 (10% EtOAc/petroleum ether) gave **22b** (5.04 g, 73%) as a colorless oil: R_f 0.17 (10% EtOAc/petroleum ether); $[\alpha]^{22}_D$ +4.80° (*c* 2.12, $CHCl_3$); IR (neat) 3500 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.27 (m, 5 H, aromatic), 5.75 (ddd, 1 H, $J_{9,10(cis)}$ = 10.7 Hz, $J_{9,10(trans)}$ = 17.1 Hz, $J_{9,OH}$ = 1.0 Hz, H9), 5.56 (s, 1 H, PhC*H*), 5.49 (dd, 1 H, $J_{9,10(trans)}$ = 17.1 Hz, $J_{10(cis),10(trans)}$ = 2.0 Hz, H10(trans)), 5.32 (dd, 1 H, $J_{9,10(cis)}$ = 10.7 Hz, $J_{10(cis),10(trans)}$ = 2.0 Hz, H10(cis)), 4.50 (s, 1 H, H1), 4.32 (dd, 1 H, $J_{5,6(eq)}$ = 4.9 Hz, $J_{6(eq),6(ax)}$ = 10.0 Hz, H6(eq)), 4.11 (ddd, 1 H, $J_{4,5}$ = 9.7 Hz, $J_{5,6(eq)}$ = 4.9 Hz, $J_{5,6(ax)}$ = 10.0 Hz, H5), 3.90 (d, 1 H, $J_{4,5}$ = 9.7 Hz, H4), 3.81 (dd, 1 H, $J_{5,6(ax)}$ = 10.0 Hz, $J_{6(eq),6(ax)}$ = 10.0 Hz, H6(ax)), 3.73–3.62 (m, 2 H, H8, H8'), 3.58 (d, 1 H, $J_{9,OH}$ = 1.0 Hz, O*H*), 3.41 (s, 3 H, O*Me*), 2.22–2.11 (m, 1 H, H7), 1.54–1.43 (m, 1 H, H7'), 1.17 (s, 3 H, CH_3), 0.87 (s, 9 H, Si*t*-*Bu*), 0.03 (s, 6 H, Si*Me*$_2$). Anal. Calcd for $C_{25}H_{40}O_6Si$: C, 64.62; H, 8.68. Found: C, 64.51; H, 8.73.

Methyl 4,6-*O*-Benzylidene-2-*C*-(2-(*tert*-butyldimethylsiloxy)ethyl)-3-*C*-((*Z*)-2-chloroethylidene)-2,3-dideoxy-2-*C*-methyl-α-D-*ribo*-hexopyranoside (23a). To a mixture of alcohol **22b** (3.25 g, 7.00 mmol) and pyridine (1.7 mL, 21 mmol) in tetrahydrofuran (50 mL) at 0 °C under argon was added thionyl chloride (0.77 mL, 11 mmol) dropwise. The reaction mixture was stirred at 0 °C for 1 h. Water (10 mL) was added, and the solvent was removed in vacuo. Ethyl acetate (50 mL) was added, and the organic layer was washed with saturated aqueous sodium bicarbonate solution (2 × 20 mL) and brine (10 mL) and dried (Na_2SO_4). Evaporation of the solvent followed by flash chromatography (5–10% EtOAc/petroleum ether) gave **23a** (2.33 g, 69%) as a colorless oil: R_f 0.30 (10% EtOAc/petroleum ether); $[\alpha]^{24}_D$ +10.9° (*c* 0.569, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.53–7.33 (m, 5 H, aromatic), 5.56 (s, 1 H, PhC*H*), 5.57–5.50 (m, 1 H, H9), 4.70 (dd, 1 H, $J_{9,10}$ = 8.3 Hz, $J_{10,10'}$ = 11.8 Hz, H10), 4.58 (d, 1 H, $J_{4,5}$ = 8.6 Hz, H4), 4.40 (dd, 1 H, $J_{9,10'}$ = 6.0 Hz, $J_{10,10'}$ = 11.8 Hz, H10'), 4.27 (s, 1 H, H1), 4.25 (dd, 1 H, $J_{5,6(eq)}$ = 4.3 Hz, $J_{6(eq),6(ax)}$ = 10.0 Hz, H6(eq)), 3.90 (ddd, 1 H, $J_{4,5}$ = 8.6 Hz, $J_{5,6(eq)}$ = 4.3 Hz, $J_{5,6(ax)}$ = 9.8 Hz, H5), 3.83–3.64 (m, 3 H, H6(ax), H8, H8'), 3.33 (s, 3 H, O*Me*), 1.95–1.84 (m, 1 H, H7), 1.79–1.68 (m, 1 H, H7'), 1.29 (s, 3 H, CH_3), 0.91 (s, 9 H, Si*t*-*Bu*), 0.07 (s, 6 H, Si*Me*$_2$). Anal. Calcd for $C_{25}H_{39}ClO_5Si$: C, 62.15; H, 8.14. Found: C, 62.24; H, 8.20.

Methyl 4,6-*O*-Benzylidene-2-*C*-(2-(*tert*-butyldimethylsiloxy)ethyl)-2,3-dideoxy-3-*C*-((*Z*)-2-hydroxyethylidene)-2-*C*-methyl-α-D-*ribo*-hexopyranoside (23c). A mixture of chloride **23a** (2.33 g, 4.83 mmol) and anhydrous potassium acetate (711 mg, 7.25 mmol) in *N*,*N*-dimethylformamide (50 mL) was maintained at 100 °C for 2 h. The reaction mixture was cooled to room temperature, and water (50 mL) and ethyl acetate (200 mL) were added. The aqueous layer was extracted with ethyl acetate (2 × 50 mL). The organic layers were combined, washed with water (50 mL) and brine (2 × 50 mL), and dried (Na_2SO_4). Evaporation of the solvent gave the crude acetate as a colorless oil. To a solution of the crude acetate in methanol (50 mL) was added a sodium methoxide/methanol solution (0.25 mL, 2.0 M, 0.48 mmol). The reaction mixture was stirred at room temperature overnight, followed by addition of saturated aqueous ammonium chloride solution (2 mL). The solvent was removed in vacuo, and ethyl acetate (50 mL) was added. The mixture was washed with brine (2 × 10 mL) and dried (Na_2SO_4). Evaporation of the solvent followed by flash chromatography (20% EtOAc/petroleum ether) gave **23c** (1.78 g, 79%) as a colorless oil: R_f 0.24 (20% EtOAc/petroleum ether); $[\alpha]^{21}_D$ +53.1° (*c* 3.58, $CHCl_3$); IR (neat) 3420 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49–7.32 (m, 5 H, aromatic), 5.61–5.55 (m, 1 H, H9), 5.56 (s, 1 H, PhC*H*), 4.54 (dd, 1 H, $J_{4,5}$ = 9.2 Hz, $J_{4,9}$ = 1.3 Hz, H4), 4.43–4.20 (m, 4 H, H10, H10', H1, H6(eq)), 3.93–3.63 (m, 4 H, H5, H6(ax), H8, H8'), 3.32 (s, 3 H, O*Me*), 2.15 (br s, 1 H, O*H*), 1.96–1.85 (m, 1 H, H7), 1.77–1.66 (m, 1 H, H7'), 1.27 (s, 3 H, CH_3), 0.89 (s, 9 H, Si*t*-*Bu*), 0.06 (s, 6 H, Si*Me*$_2$). Anal. Calcd for $C_{25}H_{40}O_6Si$: C, 64.62; H, 8.68. Found: C, 64.60; H, 8.71.

Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-((*N*,*N*-dimethylcarbamoyl)methyl)-3-*C*-(2-propenyl)-α-D-*ribo*- and -*arabino*-hexopyranoside (25). Compound **1** (50 mg, 0.19 mmol) was subjected to the standard Horner–Emmons procedure followed by standard DIBAL reduction conditions to afford **24b** (27 mg, 71%) over two steps. Compound **24b** (27 mg, 0.09 mmol) was treated to standard Eschenmoser Claisen conditions to yield a 2:1 mixture of **25** (15 mg, 44%) as a yellow syrup: R_f 0.16 and 0.26 (50% EtOAc/petroleum ether; IR (CH_2Cl_2) 1650 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47–7.33 (m, 10 H, 2(C_6H_5)), 5.73 (br s, 1 H, H10(major)), 5.56 (s, 1 H, PhC*H*(minor)), 5.45 (s, 1 H, PhC*H*(major)), 4.98 (br s, 1 H, H10'(major)), 4.93 (s, 1 H, H10-(minor)), 4.88 (s, 1 H, H10'(minor)), 4.76 (d, 1 H, $J_{1,2}$ = 3.4 Hz, H1(minor)), 4.64 (d, 1 H, $J_{1,2}$ = 2.1 Hz, H1(major)), 4.32–3.54 (m, 8 H, 2(H4), 2(H5), 2(H6(ax)), 2(H6(eq))), 3.34 (s, 3 H, OCH_3-(minor)), 3.28 (s, 3 H, OCH_3(major)), 3.25–1.95 (m, 20 H, 2(H2), 2(H2'), 2(H12), 2(H12'), 2(CONC*H'*$_3$), 2(CONCH_3), 1.88 (s, 6 H, 2(C=CCH_3)); HRMS (CI/NH_3) 376.2124 (M + H)$^+$, calcd for $C_{21}H_{29}NO_5$ 376.2116.

Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-((*N*,*N*-dimethylcarbamoyl)methyl)-3-*C*-((*E*)-1-propenyl)-α-D-*ribo*- and -*arabino*-hexopyranoside (27). Compound **1** (90 mg, 0.34 mmol) was subjected to the standard Horner–Emmons procedure followed by standard DIBAL reduction conditions to afford **26b** (75 mg, 83%) over two steps. Compound **26b** (75 mg, 0.25 mmol) was treated to standard Eschenmoser Claisen conditions to yield a 3:1 mixture of **27** (56 mg, 60%) as a yellow syrup: R_f 0.13 and 0.26 (35% EtOAc/petroleum ether) (3:1 mixture); IR (neat) 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48–7.33 (m, 10 H, 2(C_6H_5)), 5.95–5.47 (m, 6 H, 2(H9), 2(H10), 2(PhC*H*)), 4.72–3.51 (m, 10 H, 2(H1), 2(H5), 2(H6(ax)), 2(H6(eq))), 3.32 (s, 3 H, OCH_3(major)),

3.27 (s, 3 H, OCH_3(minor)), 3.12–2.29 (m, 20 H, 2(H2), 2(H2′), 2(H12), 2(H12′), 2($CONCH_3$), 2($CONCH_3$′)), 1.7 (dd, 3 H, $J_{10,C=CCH_3}$ = 1.6 Hz, 6.3 Hz, C=CCH_3(minor)), 1.64 (dd, 3 H, $J_{10,C=CCH_3}$ = 1.5 Hz, J = 6.6 Hz, C=CCH_3(major)). Anal. Calcd for $C_{21}H_{29}NO_5$: C, 67.18; H, 7.79. Found: C, 67.08; H, 7.82.

Orthoester Claisen Reaction of (*E*)- and (*Z*)-Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-(2-hydroxyethylidene)-2-*C*-propynyl-α-D-*ribo*-hexopyranosides. Compounds **15E** and **15Z** (100 mg, 0.30 mmol) were treated to the Johnson–Faulkner Claisen procedure[9] using triethyl orthopropionate to give **28** and its epimer **29** (106 mg, 85%) upon purification by flash chromatography. **28**: syrup; R_f 0.53 (10% EtOAc/petroleum ether); $[\alpha]^{20}_D$ +46.7° (*c* 1.37, $CHCl_3$); IR (CH_2Cl_2) 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44–7.31 (m, 5 H, C_6H_5), 6.17 (dd, 1 H, $J_{9,10(cis)}$ = 11.7, $J_{9,10(trans)}$ = 17.9 Hz, H9), 5.43–5.33 (m, 3 H, PhC*H*, H10(cis), H10(trans)), 4.91 (d, 1 H, J = 3.7 Hz, H1), 4.27 (dd, 1 H, $J_{5,6(eq)}$ = 5.0, $J_{6(ax),6(eq)}$ = 10.3 Hz, H6(eq)), 4.05 (m, 1 H, H5), 3.82 (q, 1 H, $J_{OCHH'CH_3,OCHH'CH_3}$ = 7.1 Hz, OC*H*H′CH_3), 3.82 (q, 1 H, $J_{OCH'CH_3,OCHH'CH_3}$ = 7.1 Hz, OCH*H*′CH_3), 3.66 (m, 2 H, H4, H6(ax)), 3.38 (s, 3 H, OCH_3), 3.17 (q, 1 H, J_{12,CH_3} = 7.4 Hz, H12), 2.47–2.23 (m, 3 H, H2, H7, H7′), 1.98 (t, 1 H, $J_{7,C\equiv CH}$ = 3.6 Hz, C≡C*H*), 1.22 (d, 3 H, J_{12,CH_3} = 7.4 Hz, CH_3), 1.07 (t, 3 H, J = 7.1 Hz, OCH_2CH_3). Anal. Calcd for $C_{24}H_{30}O_6$: C, 69.55; H, 7.30. Found: C, 69.64; H, 7.25. **29**: syrup; R_f 0.74 (10% EtOAc/petroleum ether); $[\alpha]^{20}_D$ +77.4° (*c* 1.53, $CHCl_3$); IR (neat) 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47–7.32 (m, 5 H, C_6H_5), 6.12 (dd, 1 H, $J_{9,10(cis)}$ = 11.6, $J_{9,10(trans)}$ = 17.9 Hz, H9), 5.64 (s, 1 H, PhC*H*), 5.31 (d, 1 H, $J_{9,10(cis)}$ = 11.7 Hz, H10(cis)), 5.07 (d, 1 H, $J_{9,10(trans)}$ = 17.9 Hz, H10(trans)), 4.86 (d, 1 H, $J_{1,2}$ = 3.4 Hz, H1), 4.33–4.06 (m, 5 H, H5, H6(eq), OCH_2CH_3), 3.78 (t, 1 H, $J_{5,6(ax)}$ = 10.1 Hz, $J_{6(eq),6(ax)}$ = 10.1 Hz, H6(ax)), 3.36 (s, 3 H, OCH_3), 3.06 (q, 1 H, J_{12,CH_3} = 7.3 Hz, H12), 2.53–2.24 (m, 2 H, H7, H7′), 1.94 (t, 1 H, $J_{7,C\equiv CH}$ = 2.7 Hz, C≡C*H*), 1.89–1.83 (dt, 1 H, $J_{1,2}$ = 3.6 Hz, $J_{2,7}$ = 11.8 Hz, H2), 1.32 (m, 6 H, CH_3, OCH_2CH_3). Anal. Calcd for $C_{24}H_{30}O_6$: C, 69.55; H, 7.30. Found: C, 69.46; H, 7.36.

Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-(1-formylethyl)-2-*C*-propynyl-3-*C*-vinyl-α-D-glucopyranoside (30a). Compound **28** and its epimer **29** (106 mg, 0.26 mmol) were reduced by the standard procedure using DIBAL, and the corresponding alcohol was oxidized to the aldehyde by using PCC (same procedure as described for **32**) in CH_2Cl_2 to give a mixture of aldehydes, which was then treated without purification to epimerization conditions using NaOMe/MeOH to give **30a** (82 mg, 85%) over three steps as a white solid: mp 171–172 °C; R_f 0.35 (10% EtOAc/petroleum ether); $[\alpha]^{20}_D$ +15.2° (*c* 1.54, $CHCl_3$); IR (CH_2Cl_2) 1710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.80 (s, 1 H, C*H*O), 7.42 (m, 5 H, C_6H_5), 6.22 (dd, 1 H, $J_{9,10(cis)}$ = 11.7 Hz, $J_{9,10(trans)}$ = 18.1 Hz, H9), 5.49 (s, 1 H, PhC*H*), 5.52 (d, 1 H, $J_{9,10(cis)}$ = 11.7 Hz, H10(cis)), 5.33 (d, 1 H, $J_{9,10(trans)}$ = 18.1 Hz, H10(trans)), 4.84 (d, 1 H, $J_{1,2}$ = 3.4 Hz, H1), 4.31 (dd, 1 H, $J_{5,6(eq)}$ = 5.1, $J_{6(ax),6(eq)}$ = 10.4 Hz, H6(eq)), 4.04 (m, 1 H, H5), 3.70 (t, 1 H, J = 10.3 Hz, H6(ax)), 3.61 (d, 1 H, $J_{4,5}$ = 9.5 Hz, H4), 3.36 (s, 3 H, OCH_3), 2.88 (q, 1 H, J_{12,CH_3} = 7.0 Hz, H12), 2.40–2.12 (m, 3 H, H2, H7, H7′), 2.01 (t, 1 H, $J_{7,C\equiv CH}$ = 2.6 Hz, C≡C*H*), 1.44 (d, 3 H, J_{12,CH_3} = 7.3 Hz, CH_3). Anal. Calcd for $C_{22}H_{25}O_5$: C, 71.53; H, 6.82. Found: C, 71.43; H, 7.05.

Methyl 4,6-*O*-Benzylidene-3-*C*-(1-cyanoethyl)-2,3-dideoxy-2-*C*-propynyl-3-*C*-vinyl-α-D-glucopyranoside (30b). Compound **30a** (82 mg, 0.22 mmol) was converted by using the standard procedure to give **30b** (53 mg, 65%) as a white solid: mp 139–139.5 °C; R_f 0.17 (10% EtOAc/petroleum ether); $[\alpha]^{20}_D$ +34.4° (*c* 1.36, $CHCl_3$); IR (CH_2Cl_2) 2250 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53–7.31 (m, 5 H, C_6H_5), 6.22 (dd, 1 H, $J_{9,10(cis)}$ = 11.7 Hz, $J_{9,10(trans)}$ = 18.1 Hz, H9), 5.58 (s, 1 H, PhC*H*), 5.17 (d, 1 H, $J_{9,10(cis)}$ = 11.5 Hz, H10(cis)), 5.33 (d, 1 H, $J_{9,10(trans)}$ = 18.0 Hz, H10(trans)), 4.84 (d, 1 H, $J_{1,2}$ = 3.4 Hz, H1), 4.30 (dd, 1 H, $J_{5,6(eq)}$ = 5.1, $J_{(6ax),6(eq)}$ = 10.4 Hz, H6(eq)), 4.05 (m, 1 H, H5), 3.72 (m, 2H, H4, H6(ax)), 3.41 (q, 1 H, J_{12,CH_3} = 7.3, H12), 3.36 (s, 3 H, OCH_3), 2.40–2.20 (m, 3 H, H2, H7, H7′), 2.01 (t, 1 H, $J_{7,C\equiv CH}$ = 2.6 Hz, C≡C*H*), 1.44 (d, 3 H, J_{12,CH_3} = 7.3, CH_3). Anal. Calcd for $C_{22}H_{25}NO_4$: C, 71.91; H, 6.86. Found: C, 71.86; H, 6.81.

(12*R*)-Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-α-D-glucopyranosido[3,2-*c*]-12-methyl-8-methylenebicyclo[3.3.0]octan-11-one (31).[13] Compound **30b** (970 mg, 2.64 mmol) was treated to standard cyclization conditions to give **31** (636 mg, 65%), after protiodestannylation, as a syrupy solid: R_f 0.24 (10% EtOAc/petroleum ether; $[\alpha]^{20}_D$ +39.9° (*c* 1.08, $CHCl_3$); IR (CH_2Cl_2) 1740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.40 (m, 1 H, C_6H_5), 5.48 (s, 1 H, PhC*H*), 5.07 (d, 1 H, $J_{7,C=CH}$ = 2.0 Hz, 4.7 Hz, C=C*H*), 4.94 (d, 1 H, $J_{7,C=CH'}$ = 2.3 Hz, 4.7 Hz, C=C*H*′), 4.66 (d, 1 H, $J_{1,2}$ = 5.2 Hz, H1), 4.34 (dd, 1 H, $J_{5,6(eq)}$ = 5.05 Hz, $J_{6(ax),6(eq)}$ = 10.2 Hz, H6(eq)), 4.06 (m, 1 H, H5), 3.78 (d, 1 H, $J_{4,5}$ = 9.7 Hz, H4), 3.78 (t, 1 H, J = 10.2 Hz, H6(ax)), 3.49 (br d, 1 H, $J_{7,7'}$ = 8.1 Hz, H7), 3.35 (s, 3 H, OCH_3), 2.74–2.30 (m, 5 H, H7′, H10, H10′, H2, H9), 2.04 (q, 1 H, J_{12,CH_3} = 6.8 Hz, H12), 1.12 (d, 3 H, J_{12,CH_3} = 7.02 Hz, CH_3). Anal. Calcd for $C_{22}H_{26}O_5$: C, 71.33; H, 7.07. Found: C, 71.54; H, 7.20.

Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-((*E*)-2-hydroxypropylidene)-2-*C*-propynyl-α-D-*ribo*-hexopyranoside (32) (2:1 Mixture). Compound **15E** (120 mg, 0.36 mmol) was dissolved in dry CH_2Cl_2 (10 mL). PCC (388 mg, 1.8 mmol), Celite (388 mg) anhydrous sodium acetate (148 mg, 1.8 mmol), and Florisil (39 mg) were added to the solution and stirred at room temperature. Upon completion, the reaction mixture was diluted with ether and filtered through a short column of Florisil. The column was eluted with additional ether and the filtrate concentrated in vacuo. The residue was purified by flash chromatography and dried under vacuum (1–5 mmHg) to afford the corresponding aldehyde (133 mg, 0.41 mmol, 90%), which was dissolved in anhydrous THF (5 mL) at 5 °C. A 1.5 M solution of MeMgBr in toluene/tetrahydrofuran (75:25) (0.41 mL, 0.62 mmol) was added slowly. Upon completion, the reaction mixture was quenched with saturated aqueous NH_4Cl (0.5 mL) and extracted with ether (2 × 2 mL). The combined solvents were dried (Na_2SO_4), filtered, and evaporated in vacuo. Purification by flash chromatography on silica gel gave a 2:1 mixture of **32** (130 mg, 93%) as a syrup: R_f 0.22 (25% EtOAc/petroleum ether); IR (neat) 3450 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.52–7.36 (m, 10 H, 2(C_6H_5)), 5.83 (d, 1 H, $J_{9,10}$ = 8.6 Hz, H9(major)), 5.73 (d, 1 H, $J_{9,10}$ = 8.6 Hz, H9(minor)), 5.60 (s, 2 H, 2(PhC*H*)), 4.90 (d, 1 H, $J_{1,2}$ = 2.0 Hz, H1(major)), 4.82 (d, 1 H, $J_{1,2}$ = 2.0 Hz, H1(minor)), 4.75 (m, 1 H, H10(minor)), 4.64 (m, 1 H, H10(major)), 4.25–3.63 (m, 8 H, 2(H4), 2(H5), 2(H6), 2(H6′)), 3.40 (s, 3 H, OCH_3(major)), 3.45 (s, 3 H, OCH_3(minor)), 3.92–1.77 (m, 10 H, 2(H2), 2(H7), 2(H7′), 2(C≡CH), 2(O*H*); LRMS (CI/NH_3) 362.25 (M + NH_4)$^+$, calcd for $C_{20}H_{24}O_5$ 362.20.

Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-((*N*,*N*-dimethylcarbamoyl)methyl)-3-*C*-((*E*)-1-propenyl)-2-*C*-propynyl-α-D-allopyranoside (33b). Compound **32** (480 mg, 1.39 mmol) was treated to standard Eschenmoser Claisen conditions to yield an approximate 1:1 mixture of **33b** and its C3 isomer (493 mg, 86%) as a yellow syrup: R_f 0.29 (25% EtOAc/petroleum ether); $[\alpha]^{20}_D$ −4.3° (*c* 1.23, $CHCl_3$); IR (CH_2Cl_2) 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45–7.30 (m, 5 H, C_6H_5), 5.92 (dd, 1 H, $J_{9,10}$ = 15.9 Hz, $J_{9,C=CCH_3}$ = 1.6 Hz, H9), 5.57 (dq, 1 H, $J_{10,C=CCH_3}$ = 6.35 Hz, $J_{9,10}$ = 15.9 Hz, H10), 5.55 (s, 1 H, PhC*H*), 4.97 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H1), 4.31 (dd, 1 H, $J_{5,6(eq)}$ = 4.9 Hz, $J_{6(ax),6(eq)}$ = 10.3 Hz, H6(eq)), 3.95 (m, 1 H, H5), 3.72 (t, 1 H, J = 10.2 Hz, H6(ax)), 3.61 (d, 1 H, $J_{4,5}$ = 9.6 Hz, H4), 3.42 (s, 3 H, OCH_3), 2.97 (s, 3 H, $CONCH_3$), 2.98 (d, 1 H, $J_{12,12'}$ = 16.2 Hz, H12), 2.95 (s, 3 H, $CONCH_3$), 2.90 (d, 1 H, $J_{12,12'}$ = 14.7 Hz, H12′), 2.79 (s, 3 H, $CONCH_3$′), 2.69–2.44 (m, 2 H, H7, H7′), 2.11 (dt, 1 H, $J_{1,2}$ = 3.6 Hz, $J_{2,7}$ = 11.9 Hz, H2), 1.95 (t, 1 H, $J_{7,C\equiv CH}$ = 2.6 Hz, C≡C*H*), 1.73 (dd, 3 H, J_{9,CH_3} = 1.5 Hz, J_{10,CH_3} = 6.3 Hz, CH_3). Anal. Calcd for $C_{24}H_{31}NO_5$: C, 69.71; H, 7.56. Found: C, 69.61; H, 7.59.

Methyl 4,6-*O*-Benzylidene-3-*C*-(cyanomethyl)-2,3-dideoxy-3-*C*-((*E*)-1-propenyl)-2-*C*-propynyl-α-D-allopyranoside (33c). Compounds **33b**, a 1:1 mixture at C3, were separated, and the desired isomer (methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-((*N*,*N*-dimethylcarbamoyl)methyl)-3-*C*-((*E*)-1-propenyl)-2-*C*-propynyl-α-D-allopyranoside) (230 mg, 0.55 mmol) was converted by using standard procedures to yield **33c** (250 mg, 80%) as a white solid: R_f 0.28 (10% EtOAc/petroleum ether); $[\alpha]^{20}_D$ +31.4° (*c* 0.47, $CHCl_3$); IR (CH_2Cl_2) 2250 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.47 (m, 5 H, C_6H_5), 5.99 (dd, 1 H, $J_{9,10}$ = 15.9 Hz, J_{9,CH_3} = 1.4 Hz, H9), 5.55 (s, 1 H, PhC*H*), 5.39–5.32 (dq, J_{10,CH_3} = 6.4 Hz, $J_{9,10}$ = 15.9 Hz, H10), 4.85 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H1), 4.28 (dd, 1 H, $J_{5,6(eq)}$ = 5.1 Hz, $J_{6(ax),6(eq)}$ = 10.3 Hz, H6(eq)), 3.99 (m, 1 H, H5), 3.72 (t, 1 H, J = 10.3 Hz, H6(ax)), 3.69 (d, 1 H, $J_{4,5}$ = 9.5 Hz, H4), 3.39 (s, 3 H, OCH_3), 2.93 (d, 1 H, $J_{12,12'}$ = 17.0 Hz,

H12), 2.70 (d, 1 H, $J_{12',12}$ = 16.9 Hz, H12'), 2.37–2.13 (m, 3 H, H2, H7, H7'), 2.02 (t, 1 H, $J_{7,C\equiv CH}$ = 2.7 Hz, C≡C*H*), 1.73 (dd, J_{10,CH_3} = 6.3 Hz, J_{9,CH_3} = 1.6 Hz, C*H*$_3$); HRMS (EI) 367.1785, M^+ calcd for $C_{22}H_{25}NO_4$ 367.1783.

(10*R*)- and (10*S*)-Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-α-D-allopyranosido[3,2-*c*]-10-methyl-8-methylenebicyclo-[3.3.0]octan-11-one (34).[13] Compound **33c** (30 mg, 0.08 mmol) was cyclized by using the standard procedure to yield a 1:1 mixture of **34** (28 mg, 92%) as a syrup after protiodestannylation: R_f 0.06 (10% EtOAc/petroleum ether); IR (neat) 1745 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (m, 10 H, 2(C$_6$*H*$_5$)), 5.54 (d, 2 H, 2(PhC*H*)), 5.04–4.79 (4 s, 4 H, 2(C=CH), 2(C=CH')), 4.61 (t, 2 H, 2(H1)), 4.31–3.65 (m, 8 H, 2(H6(ax)), 2(H6(eq)), 2(H5), 2(H4)), 3.44 (d, 2 H, $J_{9,10}$ = 8.5 Hz, 2(H9)), 3.31–3.30 (2 s, 6 H, 2(OC*H*$_3$)), 2.94 (m, 2 H, 2(H10)), 2.71–2.12 (m, 10 H, 2(H2), 2(H7), 2(H7'), 2(H12), 2(H12')), 1.10 (t, 6 H, 2(C*H*$_3$)). Anal. Calcd for $C_{22}H_{26}O_5$: C, 71.33; H, 7.07. Found: C, 71.23; H, 7.09.

(10*S*)-Methyl 4,6-*O*-Benzylidene-2-*C*-(2-(*tert*-butyldimethylsiloxy)ethyl)-2,3-dideoxy-3-*C*-((*Z*)-2-hydroxypropylidene)-2-*C*-methyl-α-D-*ribo*-hexopyranoside (35) and (10*R*)-Methyl 4,6-*O*-Benzylidene-2-*C*-(2-(*tert*-butyldimethylsiloxy)ethyl)-2,3-dideoxy-3-*C*-((*Z*)-2-hydroxypropylidene)-2-*C*-methyl-α-D-*ribo*-hexopyranoside (36). To a mixture of alcohol **23c** (1.10 g, 2.37 mmol), Celite (1.5 g), and anhydrous sodium acetate (583 mg, 7.11 mmol) in dichloromethane (25 mL) was added pyridinium chlorochromate (1.53 g, 7.11 mmol). The reaction mixture was stirred at room temperature for 20 min, followed by addition of diethyl ether (25 mL). The resultant slurry was stirred for 5 min and then fitlered through a short pad of Florisil with the aid of diethyl ether. Concentration of the filtrate in vacuo gave the crude enal as a colorless oil. A solution of the crude enal in tetrahydrofuran (25 mL) was cooled to 0 °C under argon. Methylmagnesium chloride (0.95 mL, 3.0 M in tetrahydrofuran, 2.84 mmol) was added dropwise. The reaction mixture was stirred for 10 min and then quenched by slow addition of saturated aqueous ammonium chloride solution (5 mL). The solvent was removed in vacuo, and ethyl acetate (30 mL) was added. The organic layer was washed with saturated aqueous ammonium chloride solution (2 × 10 mL) and brine (2 × 10 mL) and dried (Na_2SO_4). Evaporation of the solvent followed by flash chromatography (15% EtOAc/petroleum ether) gave a separable mixture of **35** (696 mg, 61%) and **36** (249 mg, 22%). **35**: colorless oil, which crystallized on standing; mp 85–88 °C; R_f 0.32 (20% EtOAc/petroleum ether); $[\alpha]^{24}_D$ +50.7° (*c* 1.24, $CHCl_3$); IR (Nujol) 3500 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.33 (m, 5 H, aromatic), 5.60 (s, 1 H, PhC*H*), 5.42 (dd, 1 H, $J_{9,10}$ = 7.3 Hz, $J_{4,9}$ = 1.6 Hz, H9), 5.06–4.94 (m, 1 H, H10), 4.57 (dd, 1 H, $J_{4,5}$ = 9.2 Hz, $J_{4,9}$ = 1.6 Hz, H4), 4.29–4.22 (m, 1 H, H6(eq)), 4.26 (s, 1 H, H1), 3.94–3.62 (m, 4 H, H5, H6(ax), H8, H8'), 3.31 (s, 3 H, O*Me*), 2.40 (br s, 1 H, O*H*), 1.97–1.85 (m, 1 H, H7), 1.76–1.65 (m, 1 H, H7'), 1.26 (s, 3 H, H14's), 1.17 (d, 3 H, $J_{10,13}$ = 6.4 Hz, H13's), 0.90 (s, 9 H, Si*t*-*Bu*), 0.06 (s, 6 H, Si*Me*$_2$). Anal. Calcd for $C_{26}H_{42}O_6Si$: C, 65.24; H, 8.84. Found: C, 65.26; H, 8.75. **36**: colorless oil; R_f 0.24 (20% EtOAc/petroleum ether); $[\alpha]^{24}_D$ +22.9° (*c* 1.20, $CHCl_3$); IR (neat) 3450 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49–7.34 (m, 5 H, aromatic), 5.57 (s, 1 H, PhC*H*), 5.39 (dd, 1 H, $J_{9,10}$ = 6.8 Hz, $J_{4,9}$ = 1.7 Hz, H9), 5.06–4.94 (m, 1 H, H10), 4.55 (br d, 1 H, $J_{4,5}$ = 9.3 Hz, H4), 4.27–4.20 (m, 1 H, H6(eq)), 4.25 (s, 1 H, H1), 3.93–3.62 (m, 4 H, H5, H6(ax), H8, H8'), 3.32 (s, 3 H, O*Me*), 1.93–1.81 (m, 1 H, H7), 1.75–1.64 (m, 1 H, H7'), 1.27 (s, 3 H, H14's), 1.24 (d, 3 H, $J_{10,13}$ = 6.5 Hz, H13's), 0.89 (s, 9 H, Si*t*-*Bu*), 0.06 (s, 6 H, Si*Me*$_2$). Anal. Calcd for $C_{26}H_{42}O_6Si$: C, 65.24; H, 8.84. Found: C, 65.50; H, 8.61.

Mitsunobu Inversion of 35 into 36. To a mixture of alcohol **35** (594 mg, 1.24 mmol), triphenylphosphine (487 mg, 1.86 mmol), and benzoic acid (227 mg, 1.86 mmol) in tetrahydrofuran (10 mL) under argon was added diethyl azodicarboxylate (0.29 mL, 1.86 mmol) dropwise. The orange reaction solution was stirred at room temperature for 5 min, at which time the solvent was removed in vacuo. Flash chromatography (10% EtOAc/petroleum ether) gave the benzoate contaminated with a byproduct. A solution of the benzoate in tetrahydrofuran (10 mL) was cooled to 0 °C under argon. Methyllithium (1.9 mL, 1.4 M in diethyl ether, 2.73 mmol) was added slowly. The reaction mixture was stirred for 10 min and then quenched by addition of saturated aqueous ammonium chloride solution (2 mL). The solvent was removed in vacuo, and ethyl acetate (20 mL) was added. The organic layer was washed with saturated aqueous ammonium chloride solution (2 × 5 mL) and brine (5 mL) and dried (Na_2SO_4). Evaporation of the solvent followed by flash chromatography (15–20% EtOAc/petroleum ether) gave previously described **36** (462 mg, 78%).

Methyl 4,6-*O*-Benzylidene-2-*C*-(2-(*tert*-butyldimethylsiloxy)ethyl)-2,3-dideoxy-3-*C*-((*N*,*N*-dimethylcarbamoyl)methyl)-2-*C*-methyl-3-*C*-((*E*)-1-propenyl)-α-D-glucopyranoside (37). Claisen rearrangement of compound **35** (30 mg, 0.063 mmol) by the Eschenmoser variation over 3 h gave **37** (27 mg, 79%) as a colorless oil: R_f 0.18 (20% EtOAc/petroleum ether); $[\alpha]^{22}_D$ −8.01° (*c* 1.51, $CHCl_3$); IR (neat) 1640 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.29 (m, 5 H, aromatic), 5.66–5.45 (m, 3 H, H9, PhC*H*, H10), 4.44 (s, 1 H, H1), 4.30 (dd, 1 H, $J_{5,6(eq)}$ = 4.7 Hz, $J_{6(eq),6(ax)}$ = 10.2 Hz, H6(eq)), 4.17 (d, 1 H, $J_{4,5}$ = 9.8 Hz, H4), 3.97 (ddd, 1 H, $J_{4,5}$ = 9.8 Hz, $J_{5,6(eq)}$ = 4.7 Hz, $J_{5,6(ax)}$ = 9.8 Hz, H5), 3.80–3.61 (m, 3 H, H6(ax), H8, H8'), 3.33 (s, 3 H, O*Me*), 3.18 (d, 1 H, $J_{12,12'}$ = 14.3 Hz, H12), 3.01 (d, 1 H $J_{12,12'}$ = 14.3 Hz, H12'), 2.84 (s, 3 H, N*Me*), 2.69 (s, 3 H, N*Me'*), 2.43–2.32 (m, 1 H, H7), 1.72–1.58 (m, 4 H, H13's, H7'), 1.04 (s, 3 H, H14's), 0.87 (s, 9 H, Si*t*-*Bu*), 0.03 (s, 6 H, Si*Me*$_2$). Anal. Calcd for $C_{30}H_{49}NO_6Si$: C, 65.78; H, 9.02. Found: C, 65.51; H, 8.92.

Methyl 4,6-*O*-Benzylidene-2-*C*-(2-(*tert*-butyldimethylsiloxy)ethyl)-2,3-dideoxy-3-*C*-((*N*,*N*-dimethylcarbamoyl)methyl)-2-*C*-methyl-3-*C*-((*E*)-1-propenyl)-α-D-allopyranoside (38a). Claisen rearrangement of compound **36** (63 mg, 0.13 mmol) by the Eschenmoser variation overnight gave **38a** (50 mg, 70%) as a yellow oil: R_f 0.13 (20% EtOAc/petroleum ether); $[\alpha]^{24}_D$ +42.9° (*c* 1.39, $CHCl_3$); IR (neat) 1635 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.28 (m, 5 H, aromatic), 6.25 (dd, 1 H, $J_{9,10}$ = 15.8 Hz, $J_{9,13}$ = 1.7 Hz, H9), 5.56 (s, 1 H, PhC*H*), 5.49 (dq, 1 H, $J_{9,10}$ = 15.8 Hz, $J_{10,13}$ = 6.3 Hz, H10), 4.72 (d, 1 H, $J_{4,5}$ = 10.0 Hz, H4), 4.29 (s, 1 H, H1), 4.21 (dd, 1 H, $J_{5,6(eq)}$ = 4.9 Hz, $J_{6(eq),6(ax)}$ = 10.0 Hz, H6(eq)), 4.06 (ddd, 1 H, $J_{4,5}$ = 10.0 Hz, $J_{5,6(eq)}$ = 4.9 Hz, $J_{5,6(ax)}$ = 10.0 Hz, H5), 3.75 (dd, 1 H, $J_{5,6(ax)}$ = 10.0 Hz, $J_{6(eq),6(ax)}$ = 10.0 Hz, H6(ax)), 3.70–3.56 (m, 2 H, H8, H8'), 3.31 (s, 3 H, O*Me*), 2.92 (s, 3 H, N*Me*), 2.74 (s, 3 H, N*Me'*), 2.58 (2 s, 2 H, H12, H12'), 2.12–2.00 (m, 1 H, H7), 1.75 (dd, 3 H, $J_{9,13}$ = 1.7 Hz, $J_{10,13}$ = 6.3 Hz, H13's), 1.38–1.27 (m, 1 H, H7'), 1.20 (s, 3 H, H14's), 0.88 (s, 9 H, Si*t*-*Bu*), 0.04 (s, 6 H, Si*Me*$_2$). Anal. Calcd for $C_{30}H_{49}NO_6Si$: C, 65.78; H, 9.02. Found: C, 65.93; H, 8.82.

Methyl 4,6-*O*-Benzylidene-2-*C*-(2-(*tert*-butyldimethylsiloxy)ethyl)-2,3-dideoxy-3-*C*-(formylmethyl)-2-*C*-methyl-3-*C*-((*E*)-1-propenyl)-α-D-allopyranoside (38b). The allyl vinyl ether of **36** (1.15 g, 2.41 mmol) was prepared and rearranged by the classical Claisen rearrangement procedure over 24 h to give **38b** (942 mg, 78%) as a colorless oil: R_f 0.28 (15% EtOAc/petroleum ether); $[\alpha]^{24}_D$ +15.6° (*c* 2.05, $CHCl_3$); IR (neat) 1715 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.79 (dd, 1 H, $J_{12,CHO}$ = 2.2 Hz, $J_{12',CHO}$ = 3.2 Hz, C*H*O), 7.38–7.29 (m, 5 H, aromatic), 6.05 (br d, 1 H, $J_{9,10}$ = 16.2 Hz, H9), 5.49 (s, 1 H, PhC*H*), 5.42 (dq, 1 H, $J_{9,10}$ = 16.2 Hz, $J_{10,13}$ = 6.4 Hz, H10), 4.33 (s, 1 H, H1), 4.29 (dd, 1 H, $J_{5,6(eq)}$ = 4.9 Hz, $J_{6(eq),6(ax)}$ = 10.1 Hz, H6(eq)), 4.12 (ddd, 1 H, $J_{4,5}$ = 9.8 Hz, $J_{5,6(eq)}$ = 4.9 Hz, $J_{5,6(ax)}$ = 10.0 Hz, H5), 3.85 (d, 1 H, $J_{4,5}$ = 9.8 Hz, H4), 3.72 (dd, 1 H, $J_{5,6(ax)}$ = 10.0 Hz, $J_{6(eq),6(ax)}$ = 10.1 Hz, H6(ax)), 3.68–3.54 (m, 2 H, H8, H8'), 3.33 (s, 3 H, O*Me*), 2.71 (dd, 1 H, $J_{12,CHO}$ = 2.2 Hz, $J_{12,12'}$ = 16.0 Hz, H12), 2.45 (dd, 1 H, $J_{12',CHO}$ = 3.2 Hz, $J_{12,12'}$ = 16.0 Hz, H12'), 2.06–1.94 (m, 1 H, H7), 1.76 (dd, 3 H, $J_{9,13}$ = 1.6 Hz, $J_{10,13}$ = 6.4 Hz, H13's), 1.28–1.17 (m, 1 H, H7'), 1.14 (s, 3 H, H14's), 0.87 (s, 9 H, Si*t*-*Bu*), 0.03 (s, 6 H, Si*Me*$_2$). Anal. Calcd for $C_{28}H_{44}O_6Si$: C, 66.63; H, 8.79. Found: C, 66.56; H, 8.54.

Methyl 4,6-*O*-Benzylidene-2-*C*-(2-(*tert*-butyldimethylsiloxy)ethyl)-3-*C*-(cyanomethyl)-2,3-dideoxy-2-*C*-methyl-3-*C*-((*E*)-1-propenyl)-α-D-allopyranoside (38c). The aldehyde **38b** (91 mg, 0.18 mmol) was converted into the nitrile **38c** (63 mg, 70%) by the standard procedure. Compound **38c** was a clear glass: R_f 0.46 (20% EtOAc/petroleum ether); $[\alpha]^{19}_D$ +21.3° (*c* 2.80, $CHCl_3$); IR (neat) 2240 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44–7.30 (m, 5 H, aromatic), 6.17 (dd, 1 H, $J_{9,10}$ = 15.9 Hz, $J_{9,13}$ = 1.5 Hz, H9), 5.55 (s, 1 H, PhC*H*), 5.46 (dq, 1 H, $J_{9,10}$ = 15.9 Hz, $J_{10,13}$ = 6.4 Hz, H10), 4.37 (s, 1 H, H1), 4.27 (dd, 1 H, $J_{5,6(eq)}$ = 4.9 Hz, $J_{6(eq),6(ax)}$ = 10.3 Hz, H6(eq)), 4.02 (ddd, 1 H, $J_{4,5}$ = 9.8 Hz, $J_{5,6(eq)}$ = 4.9 Hz, $J_{5,6(ax)}$ = 10.0 Hz, H5), 3.85 (d, 1 H, $J_{4,5}$ = 9.8 Hz, H4), 3.72 (dd, 1 H, $J_{5,6(ax)}$ = 10.0 Hz, $J_{6(eq),6(ax)}$ = 10.3 Hz,

H6(ax)), 3.72-3.58 (m, 2 H, H8, H8'), 3.35 (s, 3 H, O*Me*), 2.76 (d, 1 H, $J_{12,12'}$ = 17.3 Hz, H12), 2.61 (d, 1 H, $J_{12,12'}$ = 17.3 Hz, H12'), 2.09-1.97 (m, 1 H, H7), 1.77 (dd, 3 H, $J_{9,13}$ = 1.5 Hz, $J_{10,13}$ = 6.4 Hz, H13's), 1.59-1.48 (m, 1 H, H7'), 1.31 (s, 3 H, H14's), 0.88 (s, 9 H, Si^t*Bu*), 0.04 (s, 6 H, SiMe_2). Anal. Calcd for $C_{28}H_{43}NO_5Si$: C, 67.03; H, 8.64. Found: C, 66.87; H, 8.57.

Methyl 4,6-*O*-Benzylidene-3-*C*-(cyanomethyl)-2,3-dideoxy-2-*C*-(2-iodoethyl)-2-*C*-methyl-3-*C*-((*E*)-1-propenyl)-α-D-allopyranoside (38d). A mixture of nitrile **38c** (110 mg, 0.220 mmol) and tetrabutylammonium fluoride (0.24 mL, 1.0 M in THF, 0.242 mmol) in tetrahydrofuran (2 mL) was stirred at room temperature for 2 h, concentrated in vacuo, and passed through a short column of silica gel (60% EtOAc/petroleum ether) to give the alcohol as a colorless oil. To a mixture of the alcohol, triphenylphosphine (173 mg, 0.660 mmol), and imidazole (90 mg, 1.32 mmol) in benzene (2 mL) under argon was added iodine (168 mg, 0.660 mmol) in three portions. The reaction mixture was stirred at room temperature for 5 min, followed by addition of saturated aqueous sodium bisulfite (1 mL). After all solids had dissolved, ethyl acetate (10 mL) was added, and the organic layer was washed with saturated aqueous sodium bicarbonate solution (2 × 2 mL) and brine and then dried (Na_2SO_4). Evaporation of the solvent followed by flash chromatography (20% EtOAc/petroleum ether) gave **38d** (81 mg, 74%) as a clear glass: R_f 0.45 (1:1 CH_2Cl_2/10% EtOAc/petroleum ether); $[\alpha]^{19}_D$ +20.4° (*c* 1.95, $CHCl_3$); IR (neat) 2250 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.29 (m, 5 H, aromatic), 6.13 (d, 1 H, $J_{9,10}$ = 16.0 Hz, H9), 5.57-5.42 (m, 2 H, PhC*H*, H10), 4.33-4.23 (m, 2 H, H1, H6(eq)), 4.00 (ddd, 1 H, $J_{4,5}$ = 9.6 Hz, $J_{5,6(eq)}$ = 4.8 Hz, $J_{5,6(ax)}$ = 10.1 Hz, H5), 3.83 (d, 1 H, $J_{4,5}$ = 9.6 Hz, H4), 3.71 (dd, 1 H, $J_{5,6(ax)}$ = 10.1 Hz, $J_{6(eq),6(ax)}$ = 10.1 Hz, H6(ax)), 3.37 (s, 3 H, O*Me*), 3.21-3.10 (m, 1 H, H8), 3.05-2.94 (m, 1 H, H8'), 2.73 (d, 1 H, $J_{12,12'}$ = 17.2 Hz, H12), 2.62 (d, 1 H, $J_{12,12'}$ = 17.2 Hz, H12'), 2.44 (ddd, 1 H, $J_{7,7'}$ = 13.4 Hz, $J_{7,8}$ = 13.4 Hz, $J_{7,8'}$ = 4.9 Hz, H7), 1.96 (ddd, 1 H, $J_{7,7'}$ = 13.4 Hz, $J_{7',8}$ = 4.9 Hz, $J_{7',8'}$ = 13.4 Hz, H7), 1.80 (d, 3 H, $J_{10,13}$ = 6.4 Hz, H13's), 1.29 (s, 3 H, H14's); HRMS (CI/NH_3) 515.1407 (M + NH_4)$^+$, calcd for $C_{22}H_{32}N_2O_4I$ 515.1412.

(10*R*)-Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-2-*C*-methyl-α-D-glucopyranosido[3,2-*c*]-10-methylbicyclo-[3.3.0]octan-11-one (39).[13] Compound **38d** (55 mg, 0.11 mmol) was cyclized by the standard free-radical procedure over 1 h to give **39** (30 mg, 73%) as a white solid: mp 138-155 °C; R_f 0.35 (1:1 CH_2Cl_2/10% EtOAc/petroleum ether); $[\alpha]^{22}_D$ -5.2° (*c* 0.77, $CHCl_3$); IR (neat) 1740 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (br s, 5 H, aromatic), 5.49 (s, 1 H, PhC*H*), 4.30 (dd, 1 H, $J_{5,6(eq)}$ = 5.0 Hz, $J_{6(eq),6(ax)}$ = 10.2 Hz, H6(eq)), 4.22 (s, 1 H, H1), 4.08 (ddd, 1 H, $J_{4,5}$ = 10.2 Hz, $J_{5,6(eq)}$ = 5.0 Hz, $J_{5,6(ax)}$ = 9.5 Hz, H5), 3.77 (d, 1 H, $J_{4,5}$ = 10.2 Hz, H4), 3.72 (dd, 1 H, $J_{5,6(ax)}$ = 9.5 Hz, $J_{6(eq),6(ax)}$ = 10.2 Hz, H6(ax)), 3.35 (s, 3 H, O*Me*), 3.29-3.18 (m, 1 H, H9), 2.95-2.84 (m, 1 H, H10), 2.29 (d, 1 H, $J_{12,12'}$ = 19.2 Hz, H12), 2.18 (d, 1 H, $J_{12,12'}$ = 19.2 Hz, H12'), 1.98-1.83 (m, 1 H, H8), 1.81-1.71 (m, 1 H, H7), 1.51-1.20 (m, 2 H, H7', H8'), 1.10 (s, 3 H, H14's), 0.97 (d, 3 H, $J_{10,13}$ = 7.1 Hz, H13's). Anal. Calcd for $C_{22}H_{28}O_5$: C, 70.94; H, 7.58. Found: C, 70.78; H, 7.82.

Registry No. **1**, 63598-31-2; **11**, 114129-69-0; **12**, 122674-58-2; (*E*)-**13**, 122592-03-4; (*Z*)-**13**, 122592-04-5; (*E*)-**14a**, 122592-05-6; (*Z*)-**14a**, 122592-06-7; (*E*)-**14b**, 122592-09-0; (*Z*)-**14b**, 122592-10-3; (*E*)-**15**, 122592-07-8; (*E*)-**15** aldehyde, 122592-26-1; (*Z*)-**15**, 122592-08-9; **16a**, 122592-11-4; **16b**, 122592-12-5; **16c**, 122592-13-6; **17**, 122592-14-7; **18**, 122672-65-5; **19**, 122672-66-6; **20**, 122592-15-8; **21**, 122592-16-9; **22a**, 122622-39-3; **22b**, 122592-17-0; **23a**, 122622-40-6; **23b**, 122622-17-7; **23c**, 122592-18-1; **24a**, 122592-19-2; **24b**, 122592-20-5; **25** isomer 1, 122592-21-6; **25** isomer 2, 122592-22-7; **26a**, 122592-23-8; **26b**, 122592-24-9; **27** isomer 1, 122622-18-8; **27** isomer 2, 122672-67-7; **28**, 122622-19-9; **29**, 122672-68-8; **30a**, 122622-20-2; **30b**, 122622-21-3; **31**, 122592-25-0; **32** isomer 1, 122622-22-4; **32** isomer 2, 122672-69-9; **33b** isomer 1, 122622-23-5; **33b** isomer 2, 122672-70-2; **33c**, 122622-24-6; **34**, 122592-27-2; **35**, 122622-25-7; **36**, 122672-71-3; **37**, 122622-26-8; **38a**, 122672-72-4; **38b**, 122622-27-9; **38c**, 122622-28-0; **38d**, 122622-29-1; **39**, 122592-28-3; $(EtO)_2POCH_2CO_2Et$, 867-88-9; $TMSCH_2CO_2Et$, 4071-88-9; $(EtO)_2POCH(CH_3)CO_2Et$, 3699-66-9; $CH_3C(OMe)_2NMe_2$, 18871-66-4; $(EtO)_2POCH_2COH_3$, 1067-71-6; propargyl bromide, 106-96-7; triethyl orthoacetate, 78-39-7; triethyl orthopropionate, 115-80-0.

Spiro-Fused 2,5-Cyclohexadienones from the Thermal 1,3-Alkyl Migrations of Quinol Vinyl Ethers. A Strategy for Conversion of a Carbonyl Carbon to a Quaternary Carbon

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Reaction of *p*-benzoquinone monoketals with 2-lithio derivatives of acetophenone and propiophenone dimethyl ketals results in organolithium addition to the carbonyl group of the quinone monoketal to afford the ketals of 4-aryl-4-hydroxy-2,5-cyclohexadienones. Reaction of these products with aqueous acid results in hydrolysis of the 2,5-cyclohexadienone ketal and intramolecular mixed ketal formation between the 4-hydroxyl group and the 2-substituted acetyl or propionyl side chain of the aromatic ring. Conversion of this cyclic ketal to the vinyl ether by loss of methanol affords the quinol ether derivatives for thermolysis. Variants of this chemistry were used to prepare a number of spiro-fused vinyl ethers of the *p*-quinols. At 130-170 °C these molecules undergo high-yield conversion of the vinyl ether moiety to a ketone, affording spiro-fused 4,4-disubstituted 2,5-cyclohexadienones. Rates have been measured for several of these formal [1,3]-shifts, and a ρ value of -0.87 was calculated for rearrangement of compounds having aryl substituents on the vinyl ether double bond. This chemistry establishes a high-yield strategy for conversion of *p*-benzoquinone monoketals, 4,4-dialkoxy-2,5-cyclohexadienones, to spiro-fused 2,5-cyclohexadienones.

Introduction

Thermally induced alkyl shifts from carbon to oxygen as represented by the Claisen rearrangement have been widely studied from both the mechanistic and synthetic viewpoints.[1] The importance of this reaction in synthesis is undoubtedly associated with the stereochemical control of, and moderate temperatures required for, this symmetry-allowed [3,3]-sigmatropic shift. Claisen[2,3] in 1896 also reported that the thermal rearrangement of 1-alkoxy-

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