Allenyl Ethers as Precursors of α-Methylene-γ-butyrolactones and Botryodiplodin Derivatives†

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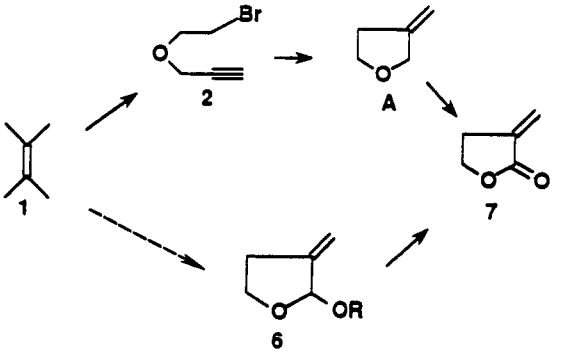
Received March 23, 1993•

β-Bromopropargyl ethers **2a–h**, **11**, and **12** or allyl propargyl ethers **8d–h** are easily isomerized with potassium *tert*-butoxide (KO-*t*-Bu) into the corresponding allenyl derivatives **3a–h**, **13**, **14**, and **9d–h**. These compounds afford α-methylene-γ-butyrolactones **7a–h**, **25**, and **26** by application of the sequence halogenation/dehydrohalogenation/homolytic carbocyclization. Starting from methyl vinyl ketone **1i**, similar transformations lead to botryodiplodin (**27**) or ethoxybotryodiplodin (**28**).

There has been considerable work on the synthesis of α-methylene γ-butyrolactones[1] due to the discovery of many naturally occurring cytotoxic or antitumor agents (e.g., vernolepin,[2] elephantopin,[3] europarotin,[4] or helenalin[5]). Little is known about the relationship between structure and activity of these compounds,[6] but their cytotoxicity may result from their chemical reactivity which involves a "Michael-type" addition of reactive nucleophilic thiol-rich enzymes;[7] the importance of the *cis* or *trans* junction in bicyclic compounds in cross reactivity in allergic contact has also been investigated.[8]

Among the large number of synthetic methods arising from a retrosynthetic approach,[1b] methylene tetrahydrofurans **A** (Scheme I) have recently received much attention, owing to their performed methylene moiety;[9] they can readily be synthesized by radical cyclization of β-bromoprop-2-ynyl ethers **2** and then oxidized into the corresponding α-methylene-γ-butyrolactones **7** by an excess of chromium trioxide–pyridine complex. The difficulty of the workup of the oxidation step, due to the formation of a large quantity of insoluble chromium species, notably decreases the yields and limits the usefulness of this synthetic approach. In order to enlarge the scope of this procedure, we prospected the possibility to synthesize 2-alkoxy-3-methylenetetrahydrofuran derivatives **6** since the acetal function should generate easily the lactone moiety.[9a,10] It is the aim of this paper to describe the full experimental details of our studies on a

Scheme I



new application of the tandem halogenation/dehydrohalogenation of alkenes **1** to generate either β-bromoprop-2-ynyl mixed acetal **5** or bromovinyl bis(allyl) mixed acetal **10**, precursors of α-methylene-γ-butyrolactones **7** by intramolecular radical cyclization and oxidation.[11] The regio- and stereoselectivity of the overall sequence halogenation/dehydrohalogenation/radical cyclization enhance the efficiency of this procedure.

By extention of this tandem sequence to α,β-unsaturated carbonyl compounds, we have developed a new stereoselective entry to the synthesis of antileukemic botryodiplodin (**27**) and related derivatives.[12]

Results

β-Bromopropargyl ethers **2a–h** are easily obtained by addition of *N*-bromosuccinimide (NBS) to olefins **1a–h** at −20 °C in propargyl alcohol (Scheme II). Catalytic isomerization of **2a–h** (KO-*t*-Bu, 0.3–0.5 equiv in pentane or benzene) affords bromo allenyl ethers **3a–h**. Addition of a solution of NBS in acetone to **3a–h** in methanol at −30 °C gives chemo- and regioselectively mixed acetals **4a–h**, which upon selective dehydrohalogenation (KO-*t*-Bu, 1.1 equiv, 0 °C) furnish β-bromoprop-2-ynyl mixed acetals **5a–h** in good yields. The next step is the intramolecular radical cyclization of **5a–h**, promoted by tributyltin hydride or cobaloxime(I)[9a,13] which gives rise to the

† Taken in part from the Ph.D. Thesis of M.N.M., University of Marseilles.

• Abstract published in *Advance ACS Abstracts,* September 1, 1993.

(1) (a) Grieco, P. A. *Synthesis* **1975**, 67. (b) Gammill, R. M.; Wilson, C. A.; Bryson, T. A. *Synth. Commun.* **1975**, 245. (c) Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94. (d) Petragnani, N.; Ferraz, H. M. C.; Silva, G. V. J. *Synthesis* **1986**, 157. (e) Sarma, J. C.; Sharma, R. P. *Heterocycles* **1986**, *24*, 441.

(2) (a) Sequeria, L.; Hemingway, R. J.; Kupchan, S. M. *Science* **1968**, *161*, 789. (b) Kupchan, S. M.; Hemingway, R. J.; Werner, D.; Karim, A. *J. Org. Chem.* **1969**, *34*, 3903. (c) Kato, M.; Kido, F.; Masuda, Y.; Watanabe, M. *J. Chem. Soc., Chem. Commun.* **1992**, 697.

(3) Kupchan, S. M.; Aynechchi, Y.; Cassady, J. M.; Schnoes, H. K.; Burlingame, L. *J. Org. Chem.* **1969**, *34*, 3867.

(4) Kupchan, S. M.; Kelsay, J. E.; Marvyama, M.; Cassady, J. M.; Hemingway, J. C.; Knox, J. R. *J. Org. Chem.* **1969**, *34*, 3876.

(5) Lee, K. H.; Huang, E. S.; Piantadosi, C.; Pagno, J. S.; Geissman, T. A. *Cancer Res.* **1971**, *31*, 1649; Ohfune, Y.; Grieco, P. A.; Wang, C. L. J.; Majetich, G. *J. Am. Chem. Soc.* **1978**, *100*, 5946.

(6) Kupchan, S. M.; Eakin, M. A.; Thomas, A. M. *J. Med. Chem.* **1971**, *14*, 1147.

(7) Kupchan, S. M.; Fessler, D. C.; Eakin, M. A.; Giacobbe, T. J. *Science* **1970**, *168*, 376.

(8) Schaeffer, M.; Talaga, P.; Stampf, J. L.; Benezra, C. *Contact Dermatitis* **1990**, *22*, 32.

(9) (a) Okabe, M.; Abe, M.; Tada, M. *J. Org. Chem.* **1982**, *47*, 1775. (b) Srikrishna, A. *J. Chem. Soc., Chem. Commun.* **1987**, 587.

(10) (a) Craig, J. C.; Horning, E. C. *J. Org. Chem.* **1960**, *25*, 2098. (b) Brown, H. C.; Garg, C. P.; Liu, K. T. *J. Org. Chem.* **1971**, *36*, 387.

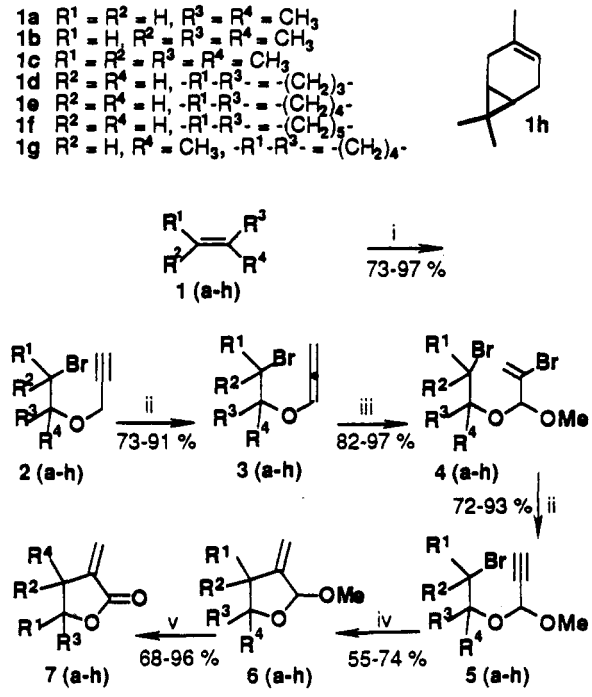
(11) Dulcère, J. P.; Mihoubi, M. N.; Rodriguez, J. *J. Chem. Soc., Chem. Commun.* **1988**, 237. Note that the structures in Scheme 3 of this article are incorrect owing to a transcription error.

(12) Dulcère, J. P.; Mihoubi, M. N.; Rodriguez, J. *Nat. Prod. Lett.* **1992**, *1*, 209.

(13) (a) Schrauzer, G. N. *Inorg. Synth.* **1968**, *11*, 61. (b) Begley, M. J.; Ladlow, M.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1095.

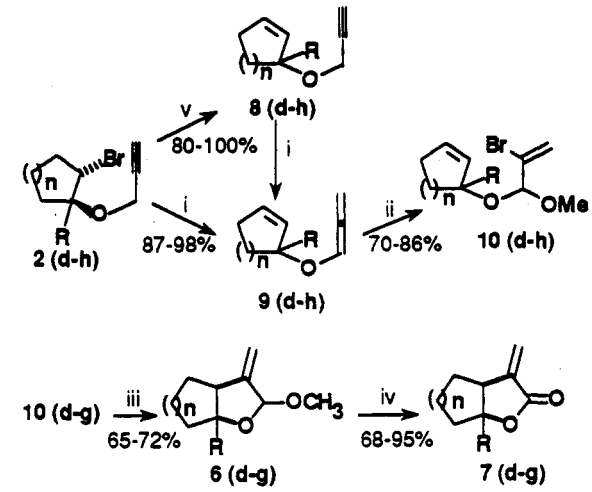
0022-3263/93/1958-5709$04.00/0

Scheme II[a]



[a] Key: (i) NBS/propargyl alcohol, −20 °C; (ii) KO-*t*-Bu/(0.5 equiv), pentane, 25 °C; (iii) NBS/acetone/methanol, −30 °C; (iv) $HSnBu_3$/AIBN, reflux 3 h, or cobaloxime(I); (v) Jones oxidation.

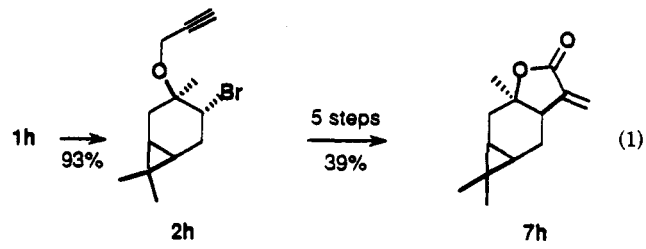
Scheme III[a]



[a] Key: (i) KO-*t*-Bu/benzene, 60 °C; (ii) NBS/acetone/methanol, −30 °C; (iii) $HSnBu_3$/AIBN/benzene, reflux, 3 h; (iv) Jones' oxidation; (v) DBU, 110 °C, 3 h.

expected 2-alkoxy-3-methylenetetrahydrofurans **6a–h**, precursors of the corresponding α-methylene-γ-butyrolactones **7a–h** by chromic oxidation. According to the previously reported selectivity of the intramolecular radical cyclization,[14] all bicyclic compounds **6d–h** are *cis*-ring fused. Specifically, starting from cycloalkenes **1d–g**, a more direct procedure can be used for the preparation of bicyclic acetals **6d–g** (Scheme III). Actually, treating **2d–h** with an excess of KO-*t*-Bu (1.5 equiv in benzene, 60 °C) results in the formation of allyl allenyl ethers **9d–h**, arising from isomerization of the propargyl unit together with dehydrohalogenation. This one-step preparation of **9d–h** proceeds in good yield, providing the reaction temperature does not exceed 60 °C. Overheating results in thermal rearrangements of allyl allenyl ethers **9d–h**.[15]

Selective halogenation of **9d–h** by addition of NBS in methanol cleanly leads to *bis*(allyl) mixed acetals **10d–h**. Intramolecular homolytic carbocyclization converts **10d–g** into the bicyclic methylene acetal **6d–g** precursors of the corresponding α-methylene-γ-butyrolactones **7d–g** by oxidation. **7h** was isolated as a single enantiomer in 36% overall yield from (+)-Δ^3-carene (eq 1);[11] indeed, the regio-



and stereoselectivity of the reaction of halogenation giving **2h**, together with the diastereoselectivity of the intramolecular radical cyclization of **5h**, allow the formation of the appropriate acetal **6h**, easily converted into **7h** by oxidation under mild conditions.[16]

Another procedure for the preparation of cyclic allyl allenyl ethers **9d–h** involves the isolation of allyl propargyl ethers **8d–h**, easily prepared by dehydrohalogenation of β-bromopropargyl ethers **2d–h** with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU, 3 equiv, 110 °C). Subsequent isomerization of **8d–h** was carried out with 0.3 equiv of KO-*t*-Bu at 50–60 °C in benzene to afford allyl allenyl ethers **9d–h**. Mixed acetals of type **10** constitute the key intermediates of the synthesis of bicyclic α-methylene γ-butyrolactones **7d–g** (Scheme III).

It is interesting to note that a recently reported[17] preparation of compounds **10** involves the addition of NBS to butoxyallene, in allylic alcohols which act as both reactant and solvent; the main drawback of this procedure is the 3-fold excess of allylic alcohol required, in order to prevent substantial competition between direct dibromination of butoxyallene and cohalogenation.

The efficiency of our procedure is enhanced by the general and easy incorporation of the allenyl moiety on simple alkenes and conversion into the bromovinyl acetals simply by using NBS and an excess of MeOH. This alternate mode for the preparation of compounds **10** is therefore more efficient to provide direct precursors of cyclic α-methylene-γ-butyrolactones from readily available starting materials. Interestingly, it has been shown that, in most biologically active sesquiterpenoids, both the α-methylene-γ-butyrolactone unit and the presence of an oxygenated function at the homoallylic position are responsible for the activity.[6,18] The synthesis of such functionalized heterocycles was investigated by application of the cohalogenation/isomerization/intramolecular radical cyclization to α,β-unsaturated carbonyl compounds

(14) (a) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925. (b) Stork, G.; Mook, R. *J. Am. Chem. Soc.* **1983**, *105*, 3720. (c) Stork, G.; Mook, R.; Biller, S. A.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **1983**, *105*, 3741. (d) Giese, B. In *Radicals in Organic Synthesis*; Pergamon Press: New York, 1986.

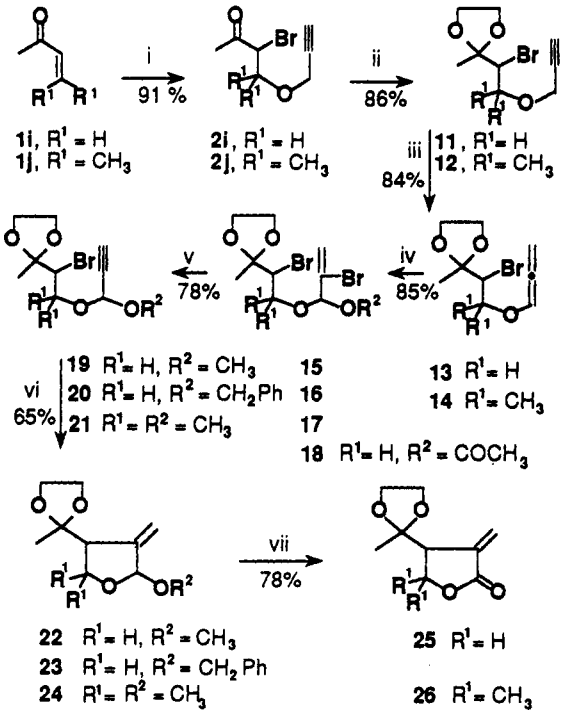
(15) Dulcère, J. P.; Crandall, J.; Faure, R.; Santelli, M.; Agati, V.; Mihoubi, M. N. *J. Org. Chem.* Preceding article in this issue.

(16) Grieco, P. A.; Oguri, T.; Yokoyama, Y. *Tetrahedron Lett.* **1978**, 419.

(17) Moriya, O.; Okawara, M.; Ueno, Y. *Chem. Lett.* **1984**, 1437.

(18) Hudrlik, P. F.; Chou, D. T. W.; Stephenson, M. A. *J. Org. Chem.* **1982**, *47*, 2987.

Scheme IV[a]

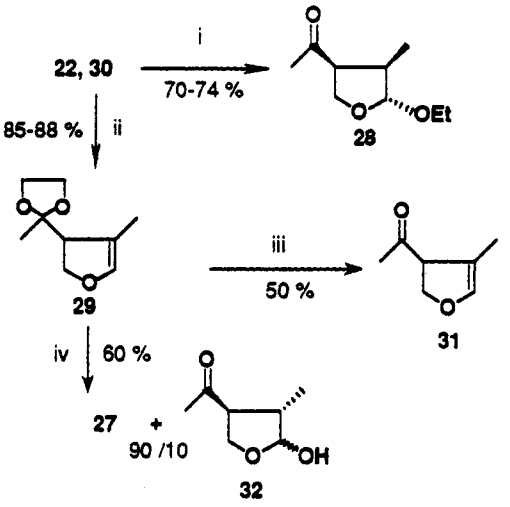


[a] Key: (i) NBS, propargyl alcohol, H^+, 0 °C; (ii) $ClSiMe_3$, ethylene glycol; (iii) KO-*t*-Bu (0.5 equiv), benzene, reflux; (iv) NBS, MeOH, BnOH, or AcOH, acetone, −30 °C; (v) KO-*t*-Bu (1.1 equiv), 0 °C; (vi) Bu_3SnH or cobaloxime(I); (vii) Jones oxidation.

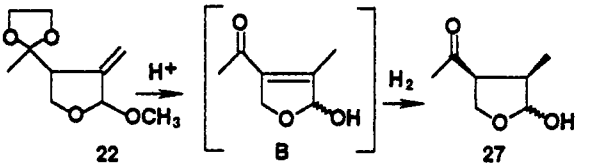
(Scheme IV). The efficiency of this strategy is based on the highly regioselective formation of α-bromo-β-alkoxy ketones,[19] when NBS reacts with α,β-unsaturated compounds **1i** and **1j** in propargyl alcohol, in the presence of a catalytic amount of H_2SO_4. Since α-bromo-β-alkoxy ketones polymerize in the presence of KO-*t*-Bu, or lead to acyl furans on reaction with softer bases such as DBU,[20] the KO-*t*-Bu-catalyzed isomerization of propargyl ethers **2i** and **2j** into allenyl ethers **13** and **14** first required the protection of the carbonyl group. The transformations of **2i** and **2j**, respectively, into **11** and **12** proceed in good yield, since the acetalization promoted by $ClSiMe_3$ in ethylene glycol is facilitated in the case of such activated α-bromocarbonyl compounds.[21] The selectivity of the intramolecular radical cyclization of **19–21**, according to the 5-exodigonal mode,[14] accounts for the formation of cyclic acetals **22–24**. Finally, Jones oxidation of acetals **22** and **24** provides α-methylene-γ-butyrolactones **25** and **26**. Interestingly, the remaining protective group during the oxidation step prevents the isomerization of **25** and **26** into butenolides.[19b]

The facile isolation of acetals **22** and **23** starting from methyl vinyl ketone **1i** prompted us to apply this methodology to a stereoselective synthesis of botryodiplodin derivatives.[12,22] Botryodiplodin (**27**) is a mycotoxin isolated from a strain of *Penicillium roqueforti*. This toxin shows antimicrobial and antileukemic activities.[23] Experimental data collected with botryodiplodin acetate indicate a *cis* relationship between the methyl and acetyl substituents;[23a] this relative stereochemistry should be provided by hydrogenation of 4-acyl-2-hydroxy-3,4-dihydrofuran (**B**), theoretically available by hydrolysis of **22** (eq 2). In fact, all attempts for deprotection of **22** met

Scheme V[a]



[a] Key: (i) Pd/C, H_2, H^+, ethanol; (ii) Pd/C, H_2, hexane or ethanol; (iii) SiO_2, H^+, 3 h; (iv) SiO_2, H^+, 16 h.



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with failure. Difficulties during chromatographic separations, related to the previously reported unusual sensitivity of **27**,[22b] account for this observation. On the other hand, an interesting result was observed by hydrogenation of **22** in ethanol, in the presence of palladium on charcoal, resulting in the selective formation of ethoxybotryodiplodin (**28**) (Scheme V). Reproducible experiments were obtained by catalytic addition of HCl to the reaction mixture. Further investigations have shown that, in the absence of acid, conversion of **22** into the enol ether **29** is cleanly accomplished in 85% yield by monitoring the reaction time (ca. 10 min) by TLC, in order to prevent subsequent reduction. These observations can be accommodated by involving the formation of "Pd–H" species, since the isomerization does not occur in the absence of H_2. The presence of hydrogen as traces in the Pd-catalyzed isomerization of allylic ethers into enol ethers has recently been reported by Nicolaou.[24] Interestingly, among the various syntheses described in the literature, McCurry[22f] reported an elaborate preparation of enol ether **29** as a direct precursor of botyrodiplodin acetate. According to the reactivity of enol ethers with respect to electrophilic

(19) (a) Heasley, V. L.; Wade, K. E.; Aucoin, T. G.; Gipe, D. E.; Shellhamer, D. F.; Heasley, G. E. *J. Org. Chem.* **1983**, *48*, 1377. (b) Dulcère, J. P.; Rodriguez, J.; Santelli, M.; Zahra, J. P. *Tetrahedron Lett.* **1987**, *28*, 2009.

(20) Dulcère, J. P.; Faure, R.; Rodriguez, J. *Synlett* **1992**, 737.

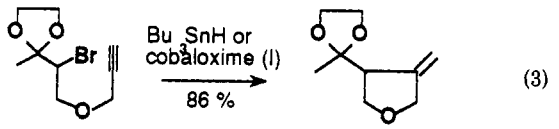
(21) Chan, T. H.; Brook, M. A.; Chaly, T. *Synthesis* **1983**, 203.

(22) (a) Wilson, S. R.; Myers, R. S. *J. Org. Chem.* **1975**, *40*, 3309. (b) Rehnberg, N.; Magnusson, G. *Acta Chem. Scand.* **1990**, *40*, 377. (c) Mukaiyama, T.; Wada, M.; Hanna, J. *Chem. Lett.* **1974**, 1181. (d) Sakai, K.; Amemiya, S.; Inove, K.; Kojima, K.; *Tetrahedron Lett.* **1979**, *25*, 2365. (e) Mc Curry, P. M., Jr.; Abe, K. *J. Am. Chem. Soc.* **1973**, *95*, 5824. (f) Mc Curry, P. M., Jr.; Abe, K. *Tetrahedron Lett.* **1973**, *42*, 4103.

(23) (a) Moreau, S.; Lablache-Combier, A.; Biguet, J.; Foulon, C.; Delfosse, M. *J. Org. Chem.* **1982**, *47*, 2358. (b) Renauld, F.; Moreau, S.; Lablache-Combier, A. *Tetrahedron* **1984**, *40*, 1823. (c) Moule, Y.; Darracq, N. *Carcinogenesis* **1984**, *5*, 1375. (d) Moule, Y.; Renauld, F.; Darraq, N. *Carcinogenesis* **1984**, *5*, 907. (e) Douce, C.; Moreau, S.; Decloitre, F.; Moule, Y. *Carcinogenesis* **1982**, *3*, 587.

(24) Nicolaou, K. C.; Duggan, M. E.; Hwong, C. K. *J. Am. Chem. Soc.* **1989**, *111*, 6666.

additions, the acetal moiety can indeed be introduced on **29** during the last step of the synthesis, making therefore unnecessary the synthesis of quite rather elaborated intermediates **19** and **20** (Scheme IV). This observation has prompted us to investigate a more direct access to **29** by isomerization of the readily available 3-methylenetetrahydrofuran **30**, prepared according to eq 3. This



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isomerization promoted by Pd/C and H_2 in hexane or ethanol proceeds in high yield, providing the reaction time does not exceed 10 min. On the other hand, when isomerization of **30** is performed in ethanol, Pd/C, H_2, in the presence of H^+, ethoxybotryodiplodin (**28**) is recovered in 70% yield, after filtration on silica gel (Scheme V). An examination of the reactivity of **29** showed that, using mild conditions, deprotection of the ethylene ketal results in the formation of **31** (30%) along with recovered starting material. Furthermore, a mixture of botryodiplodin (**27**) and epibotryodiplodin (**32**) (90/10) is obtained when **29** is allowed to stand in a mixture of SiO_2 and (15%) H_2SO_4 in methylene chloride. Unfortunately, these two isomers are unstable and rapidly decompose, making impossible the isolation of pure botryodiplodin (**27**).

The four-step synthesis of the key intermediate (**29**) to botryodiplodin derivatives looks very attractive since it appears to be more efficient than other procedures which have already been reported.[22]

In conclusion, the application of the sequence cohalogenation/isomerization/dehydrohalogenation of alkenes provides an efficient route to β-bromoprop-2-ynyl mixed acetals and bromovinyl bis(allyl) mixed acetals, precursors of α-methylene-γ-butyrolactones by subsequent radical carbocyclization and oxidation. According to this strategy, α,β-unsaturated carbonyl compounds are selectively converted into functionalized tetrahydrofurans. More particularly, this work enhances the usefulness of allenyl ethers as building blocks in organic synthesis.[25]

Experimental Section

General. Infrared (IR) spectra were determined on thin films between NaCl disks or on solutions in $CDCl_3$ on a Perkin-Elmer 298. Nuclear magnetic resonance (NMR) spectra were recorded on $CDCl_3$ solutions using Varian XL 200, EM 360 and Bruker AC 200 instruments. The multiplicities of ^{13}C signals were determined by APT or DEPT techniques. Mass spectra (MS) were obtained on a Varian MAT-311 spectrometer. Flash chromatography was performed using Merck silica gel 60 (250–400 mesh).

Preparation of β-Bromopropargyl Ethers 2a–h. To a mixture of olefin **1** (0.1 mol) and freshly distilled propargyl alcohol (18 mL, 3 equiv) in CH_2Cl_2 (10 mL) at −20 °C under argon was added NBS (20 g, 1.1 equiv) in small portions over 0.5 h. After the mixture was stirred for 2 h at −20 °C and 15 h at room temperature, water (30 mL) was added, and the mixture was extracted three times with 50-mL portions of CH_2Cl_2. The extracts were washed with saturated $NaHSO_3$ solution, aqueous K_2CO_3, and water, dried ($MgSO_4$), and concentrated. The crude products were purified by distillation or chromatographed to obtain pure materials for spectroscopic characterization, but they were usually pure enough to use directly in subsequent conversions. The following products were obtained in this manner. They all showed characteristic IR bands near 3300 and 2120 cm^{-1}.

1-Bromo-2-methyl-2-(2-propyn-1-yloxy)propane (2a): 80% yield; ^1H NMR δ 4.17 (d, 2, J = 2.4 Hz), 3.48 (s, 2), 2.48 (t, 1, J = 2.4 Hz), 1.43 (s, 6); ^{13}C NMR δ 81.0, 75.5, 73.7, 51.0, 40.8, 24.8 (2 CH_3). Anal. Calcd for $C_7H_{11}BrO$: C, 44.00; H, 5.80; Br, 41.82. Found: C, 44.20; H, 5.78; Br, 42.11.

2-Bromo-3-methyl-3-(2-propyn-1-yloxy)butane (2b): 73% yield; ^1H NMR δ 4.18 (q, 1, J = 6.8 Hz), 4.14 (d, 2, J = 2.1 Hz), 2.40 (t, 1, J = 2.1 Hz), 2.40 (t, 1, J = 2.1 Hz), 1.69 (d, 3, J = 6.8 Hz), 1.39 (s, 3), 1.34 (s, 3); ^{13}C NMR δ 81.1, 78.4, 73.4, 56.6, 50.8, 23.2, 21.5, 21.4. Anal. Calcd for $C_8H_{13}BrO$: C, 46.85; H, 6.39; Br, 38.96. Found: C, 47.03; H, 6.40; Br, 39.11.

2-Bromo-2,3-dimethyl-3-(2-propyn-1-yloxy)butane (2c): 80% yield; ^1H NMR δ 4.25 (d, 2, J = 2.3 Hz), 2.45 (t, 1, J = 2.3 Hz), 1.88 (s, 6), 1.50 (s, 6); ^{13}C NMR δ 81.8, 81.0, 74.1, 73.1, 51.7, 29.9, 21.7. Anal. Calcd for $C_9H_{15}BrO$: C, 49.33; H, 6.90; Br, 36.47. Found: C, 49.08; H, 6.92; Br, 36.65.

***trans*-1-Bromo-2-(2-propyn-1-yloxy)cyclopentane (2d):**[15] 76% yield. ***trans*-1-Bromo-2-(2-propyn-1-yloxy)cyclohexane (2e):**[15] 88% yield. ***trans*-1-Bromo-2-(2-propyn-1-yloxy)cycloheptane (2f):**[15] 84% yield. ***trans*-1-Bromo-2-methyl-2-(2-propyn-1-yloxy)cyclohexane (2g):**[15] 97% yield. **(1*R*,3*R*,4*R*,6*S*)-3-Bromo-4-(2-propyn-1-yloxy)-4,7,7-trimethylbicyclo[4.1.0]heptane (2h):**[15] 93% yield.

Preparation of α-Bromo-β-Propargyl Ketones 2i and 2j. NBS (40 g, 1 equiv) was added in one portion under a nitrogen atmosphere to a stirred solution of the olefin **1i** or **1j** (0.22 mol) in propargyl alcohol (60 mL, 1 mol, 4.7 equiv). Two or three drops of concentrated sulfuric acid were added immediately after the NBS. The resulting exothermic reaction was controlled by cooling the reaction flask at −20 °C. After being stirred for 2 h at room temperature, the reaction mixture was added to a sodium bisulfite solution and extracted with dichloromethane. The organic phase was washed with aqueous sodium bicarbonate and dried with $MgSO_4$, and the solvent was removed at reduced pressure. The crude products were purified by flash chromatography on silica gel to obtain pure materials for spectroscopic characterization, but they were pure enough for subsequent conversions.

3-Bromo-4-(2-propyn-1-yloxy)butan-2-one (2i): 94% yield; IR 3300, 2940, 2120, 1720, 1090 cm^{-1}; ^1H NMR δ 4.40 (dd, 1, J = 7.6, 6.0 Hz), 4.21 (d, 2, J = 2.3 Hz), 4.00 (dd, 1, J = 10.3, 7.6 Hz), 3.87 (dd, 1, J = 10.3, 6.0 Hz), 2.57 (t, 1, J = 2.3 Hz), 2.37 (s, 3); ^{13}C NMR δ 200.6, 78.7, 75.4, 69.7, 58.6, 48.6, 26.9; HRMS calcd for $C_7H_9O_2$ $(M-Br)^+$ 125.0603, found 125.0604. Anal. Calcd for $C_7H_9BrO_2$: C, 41.00; H, 4.42; Br, 38.97. Found: C, 41.09; H, 4.43; Br, 39.05.

3-Bromo-4-methyl-4-(2-propyn-1-yloxy)pentan-2-one (2j): 88% yield; IR 3300, 2950, 2110, 1720, 1100 cm^{-1}; ^1H NMR δ 4.31 (s, 1), 4.17 (d, 2, J = 2.4 Hz), 2.42 (t, 1, J = 2.4 Hz), 2.41 (s, 3), 1.44 (s, 6); ^{13}C NMR δ 191.4, 80.7, 77.3, 73.8, 61.3, 51.2, 29.1, 23.8, 22.8. Anal. Calcd for $C_9H_{13}BrO_2$: C, 46.37; H, 5.62; Br, 34.28. Found: C, 46.29; H, 5.63; Br, 34.30.

Preparation of Ethylene Ketals 11 and 12. To a solution of **2i** or **2j** (0.2 mol) in ethylene glycol (220 mL) under a nitrogen atmosphere was added chlorotrimethylsilane (40 mL, 0.31 mol). The reaction was stirred for 16 h at room temperature. Aqueous sodium hydrogen carbonate solution (5%) was added, the mixture was extracted with ether, and the extracts were washed with brine. The combined extracts were dried over $MgSO_4$, and the solvent was removed under reduced pressure. Crude products were used without purification.

3-Bromo-4-(2-propyn-1-yloxy)butan-2-one ethylene ketal (11): 87% yield; IR 3300, 2900, 2120, 1120 cm^{-1}; ^1H NMR δ 4.27 (d, 2, J = 2.3 Hz), 4.08–4.04 (m, 6), 3.80 (dd, 1, J = 9.5, 2.8 Hz), 2.50 (t, 1, J = 2.3 Hz), 1.52 (s, 3); ^{13}C NMR 108.6, 79.1, 75.1, 71.1, 65.3, 65.5, 56.3, 56.1, 21.7; HRMS calcd for $C_8H_{10}O_3{}^{79}Br$ $(M-CH_3)^+$ 232.9813, found 232.9814. Anal. Calcd for $C_9H_{13}BrO_3$: C, 43.40; H, 5.26; Br, 32.08. Found: 43.58; H, 5.25; Br, 32.19.

3-Bromo-4-methyl-4-(2-propyn-1-yloxy)pentan-2-one ethylene ketal (12): 85% yield; IR 3300, 2900, 2110, 1120 cm^{-1}; ^1H NMR δ 4.16 (d, 2, J = 2.3 Hz), 4.12 (s, 1), 4.02 (m, 4), 2.44 (t, 1, J = 2.3 Hz), 1.60 (s, 3), 1.50 (s, 3), 1.47 (s, 3) ^{13}C NMR 108.0, 83.8,

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77.3, 73.3, 65.3, 65.2, 61.4, 50.8, 23.5, 22.6, 22.1. Anal. Calcd for $C_{11}H_{17}BrO_3$: C, 47.67; H, 6.18; Br, 28.83. Found: C, 47.91; H, 6.19; Br, 28.71.

Preparation of β-Bromo Allenyl Ethers 3a–h, 13, and 14. A mixture of **2a–h**, 11, or 12 (50 mmol), KO-*t*-Bu (1.70–2.80 g, 0.3–0.5 equiv) and 18-crown-6 (10 mg) in pentane (100 mL) (**2a–h**) or benzene (**11,12**) was stirred for 20 h at reflux. The mixture was filtered through silica gel which was washed with 60 mL of 1/1 pentane–ether. Removal of the solvent gave **3a–h**, **13**, and **14** in adequate purity for further reaction. Pure samples for spectroscopic characterization were obtained by flash chromatography on silica gel. All these compounds showed characteristic IR bands near 1960, 1600, and 1100 cm^{-1}.

1-Bromo-2-methyl-2-(1,2-propadienyloxy)propane (3a): 73% yield; ^1H NMR δ 6.55 (t, 1, J = 5.9 Hz), 5.37 (d, 2, J = 5.9 Hz), 3.55 (s, 2), 1.50 (s, 6); ^{13}C NMR δ 203.5, 113.9, 87.3, 77.3, 40.4, 24.6. Anal. Calcd for $C_7H_{11}BrO$: C, 44.0; H, 5.80; Br, 41.82. Found: C, 44.12; H, 5.81; Br, 42.06.

2-Bromo-3-methyl-3-(1,2-propadienyloxy)butane (3b): 91% yield; ^1H NMR δ 6.49 (t, 1, J = 5.9 Hz), 5.31 (d, 2, J = 5.9 Hz), 4.27 (q, 1, J = 6.8 Hz), 1.71 (d, 3, J = 6.8 Hz), 1.46 (s, 3), 1.40 (s, 3); ^{13}C NMR δ 203.5, 113.8, 87.1, 80.3, 55.8, 24.1, 21.8, 20.8. Anal. Calcd for $C_8H_{13}BrO$: C, 46.85; H, 6.39; Br, 38.96. Found: C, 47.10; H, 6.40; Br, 39.04.

2-Bromo-2,3-dimethyl-3-(1,2-propadienyloxy)butane (3c): 75% yield; ^1H NMR δ 6.62 (t, 1, J = 6.0 Hz), 5.37 (d, 2, J = 6.0 Hz), 1.90 (s, 6), 1.55 (s, 6); ^{13}C NMR δ 203.0, 115.0, 86.7, 83.3, 73.0, 30.0, 22.4. Anal. Calcd for $C_9H_{15}BrO$: C, 49.33; H, 6.90; Br, 36.40. Found: C, 49.55; H, 6.93; Br, 36.41.

***trans*-1-Bromo-2-(1,2-propadienyloxy)cyclopentane (3d)**:[15] 71% yield. ***trans*-1-Bromo-2-(1,2-propadienyloxy)cyclohexane (3e)**:[15] 83% yield. ***trans*-1-Bromo-2-(1,2-propadienyloxy)cycloheptane (3f)**:[15] 69% yield. ***trans*-1-Bromo-2-methyl-2-(1,2-propadienyloxy)cyclohexane (3g)**:[15] 84% yield. **(1*R*,3*R*,4*R*,6*S*)-3-Bromo-4-(1,2-propadienyloxy)-4,7,7-trimethylbicyclo[4.1.0]heptane (3h)**:[15] 82% yield. **3-Bromo-4-(1,2-propadienyloxy)butan-2-one ethylene ketal (13)**: 87% yield: ^1H NMR δ 6.81 (t, 1, J = 6.0 Hz), 5.52 (d, 2, J = 6.0 Hz), 4.19 (dd, 1, J = 8.2, 3.6 Hz), 4.00 (m, 5), 3.87 (dd, 1, J = 11.2, 8.2 Hz), 1.52 (s, 3); ^{13}C NMR δ 200.1, 121.3, 108.6, 91.6, 69.7, 65.5, 65.4, 55.2, 21.8; HRMS calcd for $C_6H_{10}O_2{}^{79}Br$ (M – $OCH{=}C{=}CH_2$)$^+$ 192.9864, found 192.9860. Anal. Calcd for $C_9H_{13}BrO_3$: C, 43.40; H, 5.26; Br, 32.08. Found: C, 43.46; H, 5.26; Br, 32.11.

3-Bromo-4-methyl-4-(1,2-propadienyloxy)pentan-2-one ethylene ketal (14): 81% yield; ^1H NMR δ 6.51 (t, 1, J = 5.9 Hz), 5.30 (d, 2, J = 5.9 Hz), 4.25 (s, 1), 4.08 (m, 4), 1.52 (s, 3), 1.50 (s, 3), 1.47 (s, 3); ^{13}C NMR δ 203.6, 113.6, 109.9, 87.1, 80.1, 65.9, 65.2, 64.9, 26.8, 24.6, 23.3. Anal. Calcd for $C_{11}H_{17}BrO_3$: C, 47.67; H, 6.18; Br, 28.83. Found: C, 47.71; H, 6.19; Br, 28.91.

Preparation of β-Bromo Bromovinyl Bis(allyl) Mixed Acetals 4a–h and 15–18. NBS (5.4 g, 0.032 mol) in anhydrous acetone (50 mL) was slowly added (20 min) to a solution of allenyl ether **3a–h**, **13**, or **14** (0.03 mol) in anhydrous methanol (40 mL) at −40 °C. For the preparation of **16** and **17**, methanol was replaced by a solution of dichloromethane (20 mL), containing, respectively, benzyl alcohol (19 mL, 6 equiv) or glacial acetic acid (10 mL, 6 equiv). At the end of the addition, the solvents were removed under reduced pressure; the crude product was dissolved in a mixture of pentane–ether (3/7) which allowed the precipitation of succinimide; after filtration of succinimide on silica gel and evaporation of the solvent, flash chromatography afforded the bromovinyl bis(allyl) mixed acetals. These compounds showed characteristics IR bands near 1630 and 1100 cm^{-1}.

1-Bromo-2-methyl-2-[(2-bromo-1-methoxy-2-propen-1-yl)oxy]propane (4a): 92% yield; ^1H NMR δ 6.16 (s br, 1), 5.72 (s br, 1), 5.06 (s, 1), 3.42 (s, 2), 3.21 (s, 3), 1.39 (s, 3), 1.37 (s, 3); ^{13}C NMR δ 129.8, 120.1, 96.8, 76.2, 50.3, 42.1, 25.0, 24.8. Anal. Calcd for $C_8H_{14}Br_2O_2$: C, 31.82; H, 4.67; Br, 52.92. Found: C, 31.92; H, 4.66; Br, 53.03.

2-Bromo-3-methyl-3-[(2-bromo-1-methoxy-2-propen-1-yl)oxy]butane (4b): 91% yield; (mixture of diastereomers) ^1H NMR δ 6.19 (m, 1), 5.76 (s, 1), 5.10 (m, 1), 4.16 (m, 1), 3.24, 3.23 (2s, 3), 1.74, 1.71 (2d, s, J = 6.8 Hz), 1.45, 1.40 (2s, 3), 1.39, 1.36 (2s, 3); ^{13}C NMR δ 132.7, 120.0, 103.4, 79.3, 63.8, 53.3, 50.4, 32.7, 26.9, 24.8, 24.6, 23.3, 22.5. Anal. Calcd for $C_9H_{16}Br_2O_2$: C, 34.21; H, 5.10; Br, 50.57. Found: C, 34.31; H, 5.08; Br, 50.61.

2-Bromo-2,3-dimethyl-3-[(2-bromo-1-methoxy-2-propen-1-yl)oxy]butane (4c): 97% yield; ^1H NMR δ 6.29 (s br, 1), 5.83 (s br, 1), 5.24 (s, 1), 3.31 (s, 3), 1.91 (s, 6), 1.55 (s, 3), 1.51 (s, 3); ^{13}C NMR δ 130.2, 120.2, 96.9, 81.9, 74.0, 50.1, 30.1, 30.0, 23.2, 21.9. Anal. Calcd for $C_{10}H_{18}Br_2O_2$: C, 36.39; H, 5.50; Br, 48.42. Found: C, 36.29; H, 5.43; Br, 48.53.

***trans*-1-Bromo-2-[(2-bromo-1-methoxy-2-propen-1-yl)oxy]cyclopentane (4d)**: 82% yield; (mixture of diastereomers) ^1H NMR δ 6.13, 6.10 (2s br, 1), 5.77, 5.76 (2s, 1), 4.89, 4.84 (2s, 1), 4.33 (m, 1), 4.27 (m, 1), 3.36, 3.34 (2s, 3), 2.30–1.80 (m, 6); ^{13}C NMR δ 129.4, 120.0, 102.5, 85.4, 54.6, 54.1, 53.3, 53.2, 34.8, 30.5, 30.0, 21.9, 21.8; HRMS calcd for $C_5H_9O^{79}Br$ (M – C_4H_5OBr)$^+$ 163.9837, found 163.9840. Anal. Calcd for $C_9H_{14}Br_2O_2$: C, 34.42; H, 4.49; Br, 50.89. Found: C, 34.39; H, 4.47; Br, 50.98.

***trans*-1-Bromo-2-[(2-bromo-1-methoxy-2-propen-1-yl)oxy]cyclohexane (4e)**: 90% yield; (mixture of diastereomers) ^1H NMR δ 6.24, 6.18 (2m, 1), 5.80 (m, 1), 5.05, 4.97 (2s, 1), 4.06 (m, 1), 3.68 (m, 1), 3.44, 3.27 (2s, 3), 2.34 (m, 1), 2.16 (m, 1), 1.76 (m, 3), 1.40 (m, 3); ^{13}C NMR δ 130.1, 120.5, 103.2, 75.4, 61.8, 53.2, 36.3, 26.7, 24.2; HRMS calcd for $C_6H_{11}O^{81}Br$ (M – C_4H_5OBr)$^+$ 179.9973, found 179.9970; calcd for $C_6H_{10}{}^{79}Br$ 177.9993, found 178.0002. Anal. Calcd for $C_{10}H_{16}Br_2O_2$: C, 36.61; H, 4.92; Br, 48.72. Found: C, 36.65; H, 4.98; Br, 48.65.

***trans*-1-Bromo-2-[(2-bromo-1-methoxy-2-propen-1-yl)oxy]cycloheptane (4f)**: 93% yield; (mixture of diastereomers); ^1H NMR δ 6.24, 6.21 (2 s br, 1), 5.84 (s br, 1), 5.07, 4.97 (2s, 1), 4.37 (m, 1), 4.10 (dt, 1, J = 7.0, 3.4 Hz), 3.49, 3.36 (2s, 3), 2.36–1.48 (m, 10); ^{13}C NMR δ 129.9, 129.4, 120.4, 120.2, 103.3, 101.7, 84.6, 82.7, 58.9, 58.6, 53.1, 52.3, 34.8, 34.7, 31.6, 29.8, 28.1, 27.9, 24.6, 22.2; HRMS calcd for (M – $C_7H_{10}O^{81}Br$) 190.9894, found 190.9873. Anal. Calcd for $C_{11}H_{18}Br_2O_2$: C, 38.62; H, 5.30; Br, 46.72. Found: C, 38.68; H, 5.34; Br, 46.70.

***trans*-1-Bromo--2-methyl-2-[(2-bromo-1-methoxy-2-propen-1-yl)oxy]cyclohexane (4g)**: 95% yield; (mixture of diastereomers) ^1H NMR δ 6.35, 6.21 (2 s br, 1), 5.85 (s br, 1), 5.25, 5.18 (2s, 1), 4.31–4.24 (m, 1), 3.32, 3.31 (2s, 3), 2.30–1.65 (m, 8), 1.51, 1.46 (2s, 3); ^{13}C NMR δ 130.7, 120.2, 119.8, 96.7, 78.9, 60.8, 60.0, 50.6, 50.3, 34.9, 34.2, 33.2, 24.7, 23.3, 22.7, 22.3, 21.9, 20.6; HRMS calcd for $C_7H_{10}O^{79}Br$ (M – C_4H_5OBr)$^+$ 192.0150, found 192.0153. Anal. Calcd for $C_{11}H_{18}Br_2O_2$: C, 38.62; H, 5.30; Br, 46.72. Found: C, 38.72; H, 5.35; Br, 46.67.

(1*R*,3*R*,4*R*,6*S*)-3-Bromo-4-[(2-bromo-1-methoxy-2-propen-1-yl)oxy]-4,7,7-trimethylbicyclo[4.1.0]heptane (4h): 88% yield; (mixture of diastereomers) ^1H NMR (60 MHz) δ 6.25 (s br, 1), 5.86 (s br, 1), 4.85 (s br, 1), 4.10 (m, 1), 3.33 (s, 3), 2.50–2.20 (m, 4), 1.33 (s, 3), 1.03, 1.00 (2s, 6), 0.96–0.61 (m, 2); ^{13}C NMR δ 129.3, 120.8, 120.2, 96.4, 95.7, 78.1, 61.1, 59.8, 50.2, 49.9, 32.9, 32.0, 31.6, 28.5, 21.8, 19.7, 19.6, 17.2, 15.6. Anal. Calcd for $C_{14}H_{22}Br_2O_2$: C, 44.00; H, 5.80; Br, 41.82. Found: C, 43.70; H, 5.71; Br, 41.90.

3-Bromo-4-[(2-bromo-1-methoxy-2-propen-1-yl)oxy]butan-2-one ethylene ketal (15): 98% yield; (mixture of diastereomers) ^1H NMR δ 6.20 (d, 1, J = 1.5 Hz), 5.80 (d, 1, J = 1.5 Hz), 4.92, 4.90 (2s, 1), 4.22–3.92 (m, 6), 3.84–3.65 (m, 1), 3.41, 3.40 (2s, 3), 1.51, 1.50 (2s, 3); ^{13}C NMR δ 128.1, 128.0, 120.8, 120.7, 108.6, 108.5, 102.1, 102.0, 67.1, 67.0, 65.5, 65.3, 56.5, 56.2, 53.3, 53.1, 21.7, 21.6; HRMS calcd for $C_6H_{10}O_2{}^{81}Br$ (M – OCH(OMe)-$CBr{=}CH_2$) 194.9884, found 194.9842; calcd for $C_6H_{10}O_2{}^{79}Br$ 192.9864, found 192.9885. Anal. Calcd for $C_{10}H_{16}Br_2O_4$: C, 33.36; H, 4.48; Br, 44.39. Found: C, 33.40; H, 4.46; Br, 44.45.

3-Bromo-4-[[2-bromo-1-(benzyloxy)-2-propen-1-yl]oxy]butan-2-one ethylene ketal (16): 51% yield; (mixture of diastereomers) ^1H NMR δ 7.37–7.25 (m, 5), 6.27 (s br, 1), 5.82 (s br, 1), 5.08 (s br, 1), 4.75–4.58 (m, 2), 4.13–4.0 (m, 2), 3.99 (s, 4), 3.77–3.67 (dd, 1, J = 10.6, 8.5 Hz), 1.49 (s, 3); ^{13}C NMR δ 137.1, 128.7, 128.6, 128.4, 128.2, 128.0, 127.9, 127.8, 127.6, 120.8, 120.7, 108.6, 108.5, 100.9, 100.5, 67.8, 67.7, 66.9, 66.8, 65.4, 65.2, 56.6, 56.3, 21.7, 21.6. Anal. Calcd for $C_{16}H_{20}Br_2O_4$: C, 44.06; H, 4.62; Br, 36.64. Found: C, 44.31; H, 4.68; Br, 36.72.

3-Bromo-4-[(2-bromo-1-acetoxy-2-propen-1-yl)oxy]butan-2-one ethylene ketal (17): 96% yield; IR 3120, 1700, 1630, 1250 cm^{-1}; (mixture of diastereomers) ^1H NMR δ 6.35 (s br, 1), 6.15 (s br, 1), 5.82 (s br, 1), 4.05 (m, 7), 2.20 (s, 3), 1.46 (s, 3); ^{13}C NMR δ 176.2, 136.5, 121.1, 109.6, 109.4, 101.2, 67.1, 65.5, 65.3, 58.7, 56.3,

21.84, 21.80, 21.4. Anal. Calcd for $C_{11}H_{16}Br_2O_5$: C, 34.05; H, 4.16; Br, 41.18. Found: C, 34.23; H, 4.17; Br, 40.99.

3-Bromo-4-methyl-4-[(2-bromo-1-methoxy-2-propen-1-yl)oxy]pentan-2-one ethylene ketal (18): 98% yield; (mixture of diastereomers) ^{1}H NMR δ 6.28, 6.20 (2d, 1, J = 1.5 Hz), 5.77 (d, 1, J = 1.5 Hz), 5.13 (s, 1), 4.03 (m, 5), 3.27, 3.23 (2s, 3), 1.64, 1.60 (2s, 3), 1.59, 1.54 (2s, 3), 1.53, 1.49 (2s, 3); ^{13}C NMR δ 129.8, 129.6, 120.6, 120.1, 110.2, 110.0, 97.2, 96.8, 78.6, 67.7, 65.3, 65.2, 64.4, 50.5, 50.4, 27.1, 26.6, 26.1, 26.0, 22.8, 22.7. Anal. Calcd for $C_{12}H_{20}Br_2O_4$: C, 37.14; H, 5.19; Br, 41.18. Found: C, 37.28; H, 5.22; Br, 40.95.

Preparation of β-Bromo Propargyl Acetals 5a–h, 19–21. KO-*t*-Bu (3.4 g, 0.03 mol) and 18-crown-6 (50 mg) were added at 20 °C to a solution of **4a-h**, **15**, **16**, or **18** (0.025 mol) in benzene (50 mL). After the addition, the mixture was stirred for 2–18 h at room temperature (**4a–h**) or at reflux (**15**, **16**, **18**) for 4 h (the reaction time was monitored by TLC). After filtration on silica gel, the precipitate was washed with a mixture of ether–pentane (1/4); the solvents were removed under reduced pressure, and the products were purified by flash chromatography on silica gel. These compounds showed characteristic IR bands near 3300, 2120, and 1100 cm^{-1}. Compounds **5d–h** and **19–21** were obtained as mixtures of diastereomers.

1-Bromo-2-methyl-2-[(1-methoxy-2-propyn-1-yl)oxy]propane (5a): 89% yield; ^{1}H NMR δ 5.50 (d, 1, J = 1.8 Hz), 3.40 (s, 2), 3.39 (s, 3), 2.54 (d, 1, J = 1.8 Hz), 1.38 (s, 6); ^{13}C NMR δ 87.1, 79.0, 76.4, 73.8, 50.3, 41.7, 25.0, 24.9. Anal. Calcd for $C_8H_{13}BrO_2$: C, 43.46; H, 5.93; Br, 36.14. Found: C, 43.68; H, 5.94; Br, 36.06.

2-Bromo-3-methyl-3-[(1-methoxy-2-propyn-1-yl)oxy]butane (5b): 87% yield; (mixture of diastereomers) ^{1}H NMR δ 5.46 (m, 1), 4.08 (q, 1, J = 6.8 Hz), 3.35 (m, 3), 2.49 (d, 1, J = 1.7 Hz), 1.64 (d, 3, J = 6.8 Hz), 1.36 (s, 3), 1.31 (s, 3); ^{13}C NMR δ 87.5, 87.3, 79.6, 79.4, 73.5, 73.4, 57.8, 57.4, 50.8, 50.4, 25.1, 23.9, 23.0, 22.2, 22.1, 21.1. Anal. Calcd for $C_9H_{15}BrO_2$: C, 45.98; H, 6.43; Br, 33.98. Found: C, 46.18; H, 6.42; Br, 33.91.

2-Bromo-2,3-dimethyl-3-[(1-methoxy-2-propyn-1-yl)oxy]butane (5c): 72% yield; ^{1}H NMR δ 5.52 (d, 1, J = 1.7 Hz), 3.19 (s, 3), 2.48 (d, 1, J = 1.7 Hz), 1.81 (s, 6), 1.46 (s, 3), 1.45 (s, 3); ^{13}C NMR δ 87.5, 81.7, 79.4, 73.1, 73.0, 50.3, 29.9, 29.7, 23.6, 21.6. Anal. Calcd for $C_{10}H_{17}BrO_2$: C, 48.21; H, 6.88; Br, 32.07. Found: C, 48.37; H, 6.89; Br, 31.98.

***trans*-1-Bromo-2-[(1-methoxy-2-propyn-1-yl)oxy]cyclopentane (5d)**: 93% yield; ^{1}H NMR δ 5.39, 5.31 (2d, 1, J = 1.6 Hz), 4.52 (m, 1), 4.36 (m, 1), 3.48, 3.46 (2s, 3), 2.68, 2.67 (2d, 1, J = 1.6 Hz), 2.44–1.74 (m, 6); ^{13}C NMR δ 91.4, 84.4, 84.3, 81.8, 74.1, 54.4, 54.0, 52.2, 52.1, 34.4, 34.3, 30.3, 29.7, 21.5. Anal. Calcd for $C_9H_{13}BrO_2$: C, 46.37; H, 5.62; Br, 34.28. Found: C, 46.53; H, 5.62; Br, 34.53.

***trans*-1-Bromo-2-[(1-methoxy-2-propyn-1-yl)oxy]cyclohexane (5e)**: 92% yield; ^{1}H NMR δ 5.50, 5.35 (2d, 1, J = 1.5 Hz), 4.0 (m, 1), 3.80–3.66 (m, 1), 3.47, 3.40 (2s, 3), 2.57 (d, 1, J = 1.5 Hz), 2.46–1.30 (m, 8); ^{13}C NMR δ 93.0, 90.5, 80.7, 77.4, 74.2, 73.9, 55.4, 54.3, 52.8, 51.3, 35.6, 35.1, 32.7, 30.4, 25.2, 24.9, 23.4, 22.9. Anal. Calcd for $C_{10}H_{15}BrO_2$: C, 48.60; H, 6.12; Br, 32.33. Found: C, 48.81; H, 6.11; Br, 32.24.

***trans*-1-Bromo-2-[(1-methoxy-2-propyn-1-yl)oxy]cycloheptane (5f)**: 83% yield; ^{1}H NMR δ 5.50, 5.38 (2d, 1, J = 1.6 Hz), 4.37–4.09 (m, 2), 3.56, 3.49 (2s, 3), 2.67 (d, 1, J = 1.6 Hz), 2.63–1.38 (m, 10); ^{13}C NMR δ 91.0, 84.5, 82.3, 74.3, 58.6, 52.8, 52.0, 34.8, 30.0, 28.1, 24.6, 22.2. Anal. Calcd for $C_{11}H_{17}BrO_2$: C, 50.59; H, 6.56; Br, 30.60. Found: C, 50.63; H, 6.58; Br, 30.48.

***trans*-1-Bromo-2-methyl-2-[(1-methoxy-2-propyn-1-yl)oxy]cyclohexane (5g)**: 80% yield; ^{1}H NMR δ 5.61, 5.60 (2d, 1, J = 1.7 Hz), 4.29–4.16 (m, 1), 3.43, 3.41 (2s, 3), 2.56 (d, 1, J = 1.7 Hz), 2.40–1.57 (m, 8), 1.44, 1.42 (2s, 3); ^{13}C NMR δ 86.9, 86.3, 79.0, 78.9, 73.3, 60.3, 59.7, 50.5, 36.1, 34.3, 33.7, 33.0, 24.0, 23.4, 22.1, 21.9, 21.8, 20.9. Anal. Calcd for $C_{11}H_{17}BrO_2$: C, 50.59; H, 6.56; Br, 30.60. Found: C, 50.63; H, 6.57; Br, 30.57.

(1*R*,3*R*,4*R*,6*S*)-3-Bromo-4-[(1-methoxy-2-propyn-1-yl)oxy]-4,7,7-trimethylbicyclo[4.1.0]heptane (5h): 85% yield; ^{1}H NMR δ 5.74, 5.62 (2d, 1, J = 1.6 Hz), 4.1 (m, 1), 3.51, 3.46 (2s, 3), 2.61 (d, 1, J = 1.6 Hz), 2.52–2.23 (m, 4), 1.54, 1.50 (2s, 3), 1.06, 1.03 (2s, 6), 0.85–0.62 (m, 2); ^{13}C NMR δ 87.6, 86.1, 77.4, 76.8, 73.3, 61.1, 59.6, 50.8, 50.4, 33.5, 32.2, 31.9, 31.7, 28.6, 21.8, 21.7, 19.7, 18.9, 18.0, 17.0, 15.7. Anal. Calcd for $C_{14}H_{21}BrO_2$: C, 55.82; H, 7.03; Br, 26.53. Found: C, 55.78; H, 7.02; Br, 26.48.

3-Bromo-4-[(1-methoxy-2-propyn-1-yl)oxy]butan-2-one ethylene ketal (19): 76% yield; ^{1}H NMR δ 5.29 (d, 1, J = 1.5 Hz), 4.20–3.90 (m, 6), 3.74 (dd, 1, J = 10.7, 8.5 Hz), 3.45 (s, 3), 2.64 (m, 1), 1.51 (s, 3); ^{13}C NMR δ 108.7, 92.1, 91.9, 77.8, 74.6, 74.5, 66.7, 66.4, 65.5, 65.3, 56.5, 56.1, 53.6, 53.2, 21.7, 21.6; HRMS calcd for $C_6H_{10}O_2{}^{79}Br$ (M – OCH(OMe)CCH)$^+$ 192.9864, found 192.9870. Anal. Calcd for $C_{10}H_{15}BrO_4$: C, 43.03; H, 5.42; Br, 28.63. Found: C, 42.85; H, 5.41; Br, 28.71.

3-Bromo-4-[[1-(benzyloxy)-2-propyn-1-yl]oxy]butan-2-one ethylene ketal (20): 66% yield; ^{1}H NMR δ 7.40–7.26 (m, 5), 5.45 (d, 1, J = 1.7 Hz), 4.88–4.66 (m, 2), 4.28–4.21 (m, 1), 4.15–4.01 (m, 1), 4.03 (s, 4), 3.89–3.80 (dd, 1, J = 10.8, 8.8 Hz), 2.64 (d, 1, J = 1.7 Hz), 1.51 (s, 3); ^{13}C NMR δ 128.4, 128.2, 127.9, 127.6, 127.5, 108.64, 108.59, 90.7, 90.5, 78.0, 74.8, 74.6, 68.0, 67.9, 66.6, 66.4, 65.5, 65.3, 56.5, 56.2, 21.7, 21.6. Anal. Calcd for $C_{16}H_{19}BrO_4$: C, 54.10; H, 5.39; Br, 22.49. Found: C, 54.18; H, 5.40; Br, 22.56.

3-Bromo-4-methyl-4-[(1-methoxy-2-propyn-1-yl)oxy]pentan-2-one ethylene ketal (21): 93% yield; ^{1}H NMR δ 5.59, 5.55 (2d, 1 J = 1.7 Hz), 4.02 (m, 5), 3.45, 3.41 (2s, 3), 1.76 (d, 1, J = 1.7 Hz), 1.62 (s, 3), 1.56, 1.54 (2s, 3), 1.53, 1.51 (2s, 3); ^{13}C NMR δ 110.23, 110.16, 87.4, 86.8, 79.0, 78.6, 73.3, 67.7, 67.5, 65.2, 65.1, 64.8, 64.4, 50.7, 50.5, 27.8, 27.4, 25.0, 24.3, 23.2, 22.7. Anal. Calcd for $C_{12}H_{19}BrO_4$: C, 46.92; H, 6.23; Br, 26.01. Found: C, 47.01; H, 6.30; Br, 25.97.

Preparation of 2-Alkoxy-3-methylenetetrahydrofurans 6a–h, 22–24, and 30. (a) Radical-Mediated Cyclizations Using Tributylstannate. A solution of propargyl acetals **5a–h**, **19–21**, and **11** (4 mmol) in dry degassed benzene (200 mL) containing azoisobutyronitrile (AIBN, 65 mg) and Bu_3SnH (5 mmol, 1.25 equiv) under argon was heated at 80 °C for 3 h. The mixture was then cooled to room temperature and the solvent evaporated under reduced pressure. Chromatography on silica gel led to the 2-alkoxy-3-methylenetetrahydrofurans **6a–h**, **22–24**, and **30**. These compounds showed characteristic IR bands near 1670–1650 and 1100 cm^{-1}. Compounds **6b,d,f** were obtained as mixtures of diastereomers.

2,2-Dimethyl-4-methylene-5-methoxytetrahydrofuran (6a): 73% yield: ^{1}H NMR (60 MHz, CCl_4) δ 5.42 (m, 1), 4.98 (m, 2), 3.26 (s, 3), 2.47 (m, 2), 1.30 (s, 3), 1.27 (s, 3); ^{13}C NMR δ 140.0, 109.7, 105.1, 84.0, 54.4, 43.9, 29.9, 29.3. Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.60; H, 9.90.

2,2,3-Trimethyl-4-methylene-5-methoxytetrahydrofuran (6b): 68% yield: ^{1}H NMR δ 5.26 (d, 1, J = 2.7 Hz), 5.20 (s br, 1), 5.07 (m, 1), 3.44 (s, 3), 2.66 (m, 1), 1.44 (s, 3), 1.09 (s, 3), 1.07 (d, 3, J = 7 Hz); ^{13}C NMR δ 136.1, 108.4, 108.0, 104.1, 103.9, 83.7, 54.3, 47.3, 44.9, 28.5, 27.4, 23.3, 23.2, 12.1. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.33; H, 10.40.

2,2,3,3-Tetramethyl-4-methylene-5-methoxytetrahydrofuran (6c): 69% yield; ^{1}H NMR δ 5.24 (s br, 1), 5.14 (s br, 1), 5.01 (s, 1), 3.42 (s, 3), 1.12 (s, 6), 1.03 (s, 3), 1.01 (s, 3). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 71.01; H, 10.68.

***cis*-3-Methoxy-2-methylene-4-oxabicyclo[3.3.0]octane (6d)**: 71% yield; ^{1}H NMR δ 6.20, 6.18 (2s br, 1), 5.84, 5.83 (2s, 1), 4.96, 4.91 (2s, 1), 4.42, 4.22 (m, 2), 3.44, 3.42 (2s, 3), 2.47–1.85 (m, 6). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.43; H, 9.16.

***cis*-8-Methoxy-9-methylene-7-oxabicyclo[4.3.0]nonane (6e)**: 70% yield; ^{1}H NMR δ 5.24 (m, 1), 5.09 (m, 2), 5.18 (s, 1), 3.50 (s, 3), 2.52 (m, 1), 1.98 (m, 1), 1.70–1.20 (m, 7); ^{13}C NMR δ 153.8, 108.5, 104.0, 75.6, 54.9, 42.2, 28.5, 27.8, 23.5, 20.4. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.04; H, 9.57.

***cis*-9-Methoxy-10-methylene-8-oxabicyclo[5.3.0]decane (6f)**: 55% yield; ^{1}H NMR δ 5.31–5.04 (m, 3), 4.51 (m, 1), 3.46, 3.45 (2s, 3), 2.95 (m, 1), 2.27–0.95 (m, 10); ^{13}C NMR δ 153.6, 109.0, 108.7, 105.1, 105.0, 82.2, 54.6, 54.2, 46.3, 45.2, 31.9, 31.4, 30.6, 28.6, 27.9, 24.2. Anal. Calcd for $C_{11}H_{18}O_2$: C, 71.39; H, 9.59. Found: C, 71.24; H, 9.60.

***cis*-8-Methoxy-1-methyl-7-methylene-9-oxabicyclo[4.3.0]nonane (6g)**: 74% yield; ^{1}H NMR δ 5.36 (s br, 2), 5.12 (s br, 1), 3.54 (s, 3), 2.50 (m, 1), 2.07–1.61 (m, 8), 1.41 (s, 3); ^{13}C NMR δ 151.0, 108.2, 104.2, 82.2, 55.6, 47.8, 35.6, 24.8, 23.8, 20.4. Anal. Calcd for $C_{11}H_{18}O_2$: C, 71.39; H, 9.59. Found: C, 71.64; H, 9.58.

(1*R*,3*R*,5*S*,7*R*)-4,4-Dimethyl-9-methoxy-8-methylene-10-oxabicyclo[5.3.0.0^{3,5}]decane (6h): 70% yield; ^{1}H NMR (60 MHz, CCl_4) δ 5.80–5.10 (m, 3), 3.27 (s, 3), 2.96–1.70 (m, 5), 1.35 (s, 3), 1.00 (s, 6), 0.97–0.43 (m, 2). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.48; H, 9.95.

4-Acetyl-2-methoxy-3-methylenetetrahydrofuran ethylene ketal (22): 62% yield; ^{1}H NMR δ 5.50 (s br, 1), 5.37 (s br, 1), 5.23 (s, 1), 4.14–3.90 (m, 6), 3.41 (s, 3), 2.98 (m, 1), 1.29 (s, 3); ^{13}C NMR δ 147.2, 113.2, 110.8, 105.2, 68.5, 64.8, 64.7, 54.7, 49.3, 20.3; HRMS calcd for $C_6H_{13}O_3$ ($M - OCH_3$)$^+$ 169.0865, found 169.0868. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.69; H, 8.06.

4-Acetyl-2-(benzyloxy)-3-methylenetetrahydrofuran ethylene ketal (23): 50% yield; ^{1}H NMR δ 7.35–7.26 (m, 5), 5.5 (s br, 1), 5.39 (s br, 1), 4.72 (d, 1, J = 11.9 Hz), 4.70 (s, 1), 4.60 (d, 1, J = 11.9 Hz), 4.20–3.96 (m, 2), 3.95 (m, 4), 3.01 (m, 1), 1.27 (s, 3). Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.44; H, 7.29.

4-Acetyl-2-methoxy-5,5-dimethyl-3-methylenetetrahydrofuran ethylene ketal (24): 85% yield; ^{1}H NMR δ 5.25 (m, 1), 5.00 (m, 2), 3.83 (s, 4), 3.27 (s, 3), 2.50 (s, 1), 1.30 (s, 3), 1.23 (s, 6); ^{13}C NMR δ 149.2, 114.4, 110.0, 104.2, 82.9, 64.8, 63.6, 58.9, 55.1, 31.6, 24.7, 21.7. Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83. Found: C, 63.34; H, 8.84.

4-Acyl-3-methylenetetrahydrofuran ethylene ketal (30): 86% yield; ^{1}H NMR δ 5.26 (s, br, 1), 5.08 (s br, 1), 4.29 (d, 2, J = 8.2 Hz), 4.02–3.95 (m, 6), 2.93 (m, 1), 1.32 (s, 3); ^{13}C NMR δ 147.5, 110.9, 107.3, 72.2, 70.9, 64.9, 64.8, 51.2, 20.9. Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.24; H, 8.32. Using the same reaction conditions, tributyltinhydride-promoted radical cyclization of bromovinyl bis(allyl) mixed acetals **10d–g** afforded bicyclic acetals: **6d**, 65%; **6e**, 70%; **6f**, 72%; **6g**, 70%.

(b) Radical-Mediated Cyclizations Using Cobaloxime(I). Sodium borohydride (380 mg, 0.01 mol) was added to a stirred degassed mixture of aqueous sodium hydroxide (10 M, 1 mL) and ethanol (75 mL) through which argon was continuously bubbled. After addition of 0.01 mol of bromoacetals **5d–h**, **19**, or bromopropargyl ether **11**, the mixture was heated at 50–60 °C; bis(dimethylglyoximato)pyridiniumcobalt III chloride[13a] (400 mg) was added in small portions until a persistent black end point was observed. After 2.5 h, the mixture was allowed to cool to room temperature and the solvent was removed under reduced pressure. After addition of saturated aqueous sodium chloride, the product was extracted with ether and the ethereal extracts were dried. The solvent was evaporated under reduced pressure to leave the crude cyclic acetal as an oil; the products were purified by chromatography on silica gel to give the following: **6d**, 55%, **6e**, 72%; **6f**, 75%; **6g**, 80%; **6h**, 78%; **22**, 65%; **30**, 90%.

Preparation of α-Methylene-γ-butyrolactones 7a–g, 25, and 26. Jones reagent[10b] (1.6 M, 4 mL, 6.4 mmol) was added dropwise to a stirred solution of the acetal **6a–g**, **22**, and **24** (2.14 mmol) in acetone (5 mL) at 0 °C. After addition, the mixture was stirred for 2 h at room temperature. The chromium salts were separated by filtration and washed with a small amount of acetone, and the combinated filtrates were concentrated under reduced pressure. The residue was dissolved in ether and washed with saturated aqueous sodium hydrogen carbonate. The crude product obtained after evaporation of the dried organic solution ($MgSO_4$) was purified by chromatography on silica gel. All compounds **7** showed characteristic IR bands near 1760 and 1650 cm^{-1}.

4,5-Dihydro-5,5-dimethyl-3-methylene-(3*H*)-furan-2-one (7a): 89% yield; ^{1}H NMR (60 MHz, CCl_4) δ 6.10 (m, 1), 5.50 (m, 1), 2.70 (m, 2), 1.40 (s, 6); ^{13}C NMR δ 169.8, 136.1, 122.1, 81.6, 41.2, 28.4 (2 CH_3). Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 67.01; H, 8.00.

4,5-Dihydro-4,5,5-trimethyl-3-methylene-(3*H*)-furan-2-one (7b): 93% yield; ^{1}H NMR (60 MHz, CCl_4) δ 5.97 (d, 1, J = 3.0 Hz), 5.38 (d, 1, J = 3.0 Hz), 3.00–2.56 (m, 1), 1.46 (d, 3, J = 7.0 Hz), 1.20 (s, 3), 1.16 (s, 3); ^{13}C NMR δ 169.7, 141.8, 120.1, 85.0, 44.9, 27.1, 22.8, 12.7. Anal. Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.77; H, 8.64.

4,5-Dihydro-4,4,5,5-tetramethyl-3-methylene-(3*H*)-furan-2-one (7c): 68% yield; ^{1}H NMR δ 6.06 (s br, 1), 5.36 (s br, 1), 1.34 (s, 6), 1.22 (s, 6); ^{13}C NMR δ 169.9, 147.0, 118.7, 87.0, 45.2, 23.5, 23.3. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.24; H, 9.13.

***cis*-2-Methylene-4-oxabicyclo[3.3.0]octan-3-one (7d)**: 92% yield; ^{1}H NMR (60 MHz, CCl_4), δ 6.05 (d, 1, J = 3.0 Hz), 5.55 (d, 1, J = 3.0 Hz), 5.08–4.72 (m, 1), 3.67–3.13 (m, 1), 2.23–0.73 (m, 6); ^{13}C NMR δ 171.0, 140.6, 122.5, 83.2, 43.1, 35.6, 33.9, 23.0. Anal. Calcd for $C_8H_{10}O_2$: C, 69.55; H, 7.30. Found: C, 69.63; H, 7.31.

***cis*-9-Methylene-7-oxabicyclo[4.3.0]nonan-8-one (7e)**: 96% yield; ^{1}H NMR (60 MHz, CCl_4), δ 6.00 (d, 1, J = 4.0 Hz), 5.43 (d, 1, J = 4.0 Hz), 4.68–4.27 (m, 1), 3.20–2.78 (m, 1), 2.00–1.10 (m, 8); ^{13}C NMR δ 170.9, 140.1, 119.6, 76.9, 39.6, 28.9, 26.4, 21.2, 20.5. Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 70.84; H, 7.96.

***cis*-10-Methylene-8-oxabicyclo[5.3.0]decan-9-one (7f)**: 95% yield; ^{1}H NMR δ 6.24 (d, 1, J = 3.0 Hz), 5.51 (d, 1, J = 3.0 Hz), 4.74–4.62 (m, 1), 3.24–3.14 (m, 1), 2.08–1.22 (m, 10); ^{13}C NMR δ 170.3, 140.5, 121.8, 82.2, 43.1, 31.8, 31.3, 30.7, 27.4, 24.3. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.98; H, 8.50.

***cis*-1-Methyl-7-methylene-9-oxabicyclo[4.3.0]nonan-8-one (7g)**: 90% yield; ^{1}H NMR δ 6.24 (d, 1, J = 4.0 Hz), 5.48 (d, 1, J = 4.0 Hz), 2.84–2.71 (m, 1), 1.96–1.24 (m, 8), 1.52 (s, 3); ^{13}C NMR δ 170.3, 140.2, 119.2, 83.5, 45.8, 35.9, 25.1, 24.9, 21.9, 20.4. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.13; H, 8.50.

4,5-Dihydro-4-acetyl-3-methylenefuran-2-one 4-(ethylene ketal) (25): 76% yield; ^{1}H NMR δ 6.38 (d, 1, J = 2.1 Hz), 5.91 (d, 1, J = 2.1 Hz), 4.38 (m, 2), 4.02–3.97 (m, 4), 3.30 (m, 1), 1.30 (s, 3); ^{13}C NMR δ 170.5, 134.1, 125.5, 110.0, 67.2, 65.1, 65.0, 46.5, 20.6; HRMS calcd for $C_8H_9O_4$ ($M - CH_3$)$^+$ 169.0501, found 169.0497. Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.89; H, 6.50.

4-Hydro-4-acetyl-5,5-dimethyl-3-methylenefuran-2-one 4-(ethylene ketal) (26): 80% yield; ^{1}H NMR (60 MHz, CCl_4) δ 6.13 (m, 1), 5.73 (m, 1), 3.93 (s, 4), 2.93 (m, 1), 1.47 (s, 3), 1.40 (s, 3), 1.33 (s, 3); ^{13}C NMR δ 169.5, 137.0, 125.1, 109.5, 83.6, 64.8, 64.1, 56.9, 30.9, 24.2, 22.0. Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.15; H, 7.60.

Preparation of (1*R*,3*R*,5*S*,7*R*)-4,4-Dimethyl-10-methylene-8-oxabicyclo[5.3.0.0^{3,5}]decan-9-one (7h). *m*-Chloroperbenzoic acid (MCPBA, 446 mg, 2.2 mmol) was added at room temperature to a solution of **6h** (444 mg, 2.0 mmol) in dry methylene chloride (8 mL) containing boron trifluoride etherate (BF_3·Et_2O, 100 μL, 1 mmol). After 3 h, ether (50 mL) was added, and the reaction mixture was washed succesively with 10% aqueous sodium thiosulfate, saturated sodium bicarbonate, and brine. After drying ($MgSO_4$), the solvent was removed and the crude product was purified by flash chromatography on silica gel to afford (**7h**): 92% yield; $[\alpha]^{20}_{578}$ +68.5° (*c* 7.3, methanol); IR 2950, 1760, 1665, 1080 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ 6.18 (d, 1, J = 2.4 Hz), 5.50 (d, 1, J = 2.4 Hz), 3.0–1.73 (m, 5) 1.43 (s, 3), 1.07 (s, 6), 0.97–0.43 (m, 2); ^{13}C NMR δ 169.9, 140.3, 122.5, 84.5, 44.7, 30.6, 28.9, 28.2, 26.5, 20.6, 19.8, 19.2, 14.7. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.60; H, 8.81.

Preparation of Allyl Propargyl Ethers 8d–h. According to ref 15, the following compounds were obtained: **3-(2-propyn-1-yloxy)cyclopentene (8d)**, 80% yield; **3-(2-propyn-1-yloxy)-cyclohexene (8e)**, 100% yield; **3-(2-propyn-1-yloxy)cycloheptene (8f)**, 98% yield; **3-methyl-3-(2-propyn-1-yloxy)cyclohexene (8g)**, 100% yield; **(1*S*,4*R*,6*S*)-4-(2-propyn-1-yloxy)-4,7,7-trimethylbicyclo[4.1.0]hept-2-ene (8h)**, 95% yield.

Preparation of Allyl Allenyl Ethers 9d–h. According to ref 15, the following compounds were obtained: **3-(1,2-propadienyloxy)cyclopentene (9d)**, 87% yield; **3-(1,2-propadienyloxy)cyclohexene (9e)**, 95% yield; **3-(1,2-propadienyloxy)-cycloheptene (9f)**, 90% yield; **3-methyl-3-(1,2-propadienyloxy)cyclohexene (9g)**, 98% yield; **(1*S*,4*R*,6*S*)-4-(1,2-propadienyloxy)-4,7,7-trimethylbicyclo[4.1.0]hept-2-ene (9h)**, 87% yield.

Preparation of Bromovinyl Bis(allyl) Mixed Acetals 10d–h. NBS (5.4 g, 0.032 mol) in anhydrous acetone (50 mL) was slowly added (20 min) to a solution of allenyl ethers **9d–h** (0.03 mol) in anhydrous methanol (40 mL), at −40 °C. At the end of the addition, the solvents were removed under reduced pressure; the crude product was dissolved in a mixture of pentane and ether (3/7); after filtration of succinimide on silica gel and

evaporation of the solvent, chromatography on silica gel afforded compounds **10d–h**. All compounds **10** showed characteristic IR bands near 3940, 2830, 1630, and 1080 cm^{-1}.

3-[(2-Bromo-1-methoxy-2-propen-1-yl)oxy]cyclopentene (10d): 82% yield; (mixture of diastereomers) ^1H NMR δ 6.12 (s br, 1), 5.87 (m, 2), 5.70 (s br, 1), 4.87 (s, 1), 4.70 (m, 1), 3.28, 3.22 (2s, 3), 2.70–1.62 (m, 4); ^{13}C NMR δ 136.0, 135.9, 131.0, 130.6, 129.8, 119.7 ($2CH_2$), 101.8, 101.7, 82.7, 82.3, 52.8, 52.3, 31.0, 30.9, 30.6, 30.2. Anal. Calcd for $C_9H_{13}BrO_2$: C, 46.37; H, 5.62; Br, 34.28. Found: C, 46.41; H, 5.61; Br, 34.30.

3-[(2-Bromo-1-methoxy-2-propen-1-yl)oxy]cyclohexene (10e): 83% yield; (mixture of diastereomers) ^1H NMR δ 6.15 (s br, 1), 5.91–5.75 (m, 2), 5.75 (s br, 1), 4.92 (s, 1), 4.14 (m, 1), 3.33 and 3.32 (2s, 3), 2.00–1.50 (m, 6); ^{13}C NMR δ 131.5, 131.3, 129.9, 129.8, 127.6, 127.1, 119.7 ($2\ CH_2$), 101.4, 101.0, 70.6, 70.5, 52.4, 52.1, 29.4, 28.8, 25.1, 19.2, 19.1. Anal. Calcd for $C_{10}H_{15}BrO_2$: C, 48.60; H, 6.12; Br, 32.33. Found: C, 48.53; H, 6.12; Br, 32.31.

3-[(2-Bromo-1-methoxy-2-propen-1-yl)oxy]cycloheptene (10f): 70% yield; (mixture of diastereomers) ^1H NMR δ 6.11 (m, 1), 5.75 (m, 2), 5.72 (m, 1), 4.66, 4.84 (2s, 1), 4.37–4.11 (m, 1), 3.30, 3.27 (2s, 3), 2.26–1.20 (m, 8); ^{13}C NMR δ 135.5, 135.0, 131.0, 131.2, 130.0, 119.7, 101.5, 101.3, 75.8, 52.5, 52.3, 33.7, 33.1, 28.7, 27.2, 26.9, 26.7. Anal. Calcd for $C_{11}H_{17}BrO_2$: C, 50.59; H, 6.56; Br, 30.60. Found: C, 50.50; H, 6.57; Br, 30.58.

3-Methyl-3-[(2-Bromo-1-methoxy-2-propen-1-yl)oxy]cyclohexene (10g): 86% yield; (mixture of diastereomers) ^1H NMR δ 6.19 (s br, 1), 6.05–5.60 (m, 2), 5.78 (s br, 1), 5.11, 5.09 (2s, 1), 3.32, 3.30 (2s, 3), 2.17–1.47 (m, 6), 1.42, 1.39 (2s, 3); ^{13}C NMR δ 131.9, 131.4, 131.1, 130.6, 119.2, 97.9, 97.3, 75.9, 51.1, 50.8, 36.2, 35.5, 28.2, 27.6, 25.2, 25.1, 19.9, 19.4. Anal. Calcd for $C_{11}H_{17}BrO_2$: C, 50.59; H, 6.56; Br, 30.60. Found: C, 50.44; H, 6.55; Br, 30.89.

(1*S*,4*R*,6*S*)-4-[(2-Bromo-1-methoxy-2-propen-1-yl)oxy]-4,7,7-trimethylbicyclo[4.1.0]hept-2-ene (10h): 70% yield; (mixture of diastereomers) ^1H NMR δ 6.06 (s br, 1), 5.83–5.50 (m, 3), 4.90 (s br, 1), 3.10 (s, 3), 2.06–1.60 (m, 2), 1.33 (s, 3), 1.10 (s, 3), 0.98 (s, 3), 0.98–0.80 (m, 2); ^{13}C NMR δ 135.8, 136.0, 131.3, 127.1, 126.6, 119.4, 119.3, 97.8, 97.6, 78.1, 51.4, 50.8, 33.1, 32.6, 27.7, 27.6, 27.5, 27.3, 22.2, 20.5, 20.3, 15.41, 15.36. Anal. Calcd for $C_{14}H_{21}BrO_2$: C, 55.82; H, 7.03; Br, 26.53. Found: C, 55.91; H, 7.03; Br, 26.48.

Preparation of (2*R,3*R**,4*S**)-4-Acetyl-2-ethoxy-3-methyltetrahydrofuran (28) and 4-Acetyl-4,5-dihydro-3-methylfuran Ethylene Ketal (29).** A stirred solution of **22** (1 g, 5 mmol) in ethanol (8 mL) was treated with Pd/C (500 mg, 10 wt %), in the presence of 37 wt % HCl (50 μL); a hydrogen atmosphere was introduced by using a hydrogen-filled balloon, with repeated evacuation under reduced pressure. After 15 min of stirring, the hydrogen was replaced with argon; the reaction mixture was filtered through a Celite pad, and the filtrate was concentrated. Purification by flash chromatography on silica gel afforded **28** in 70% yield. When reduction of **22** was performed in hexane or ethanol, but in the absence of hydrochloric acid, **29** was obtained after purification on silica gel in 85% yield.

28: IR 1700, 1090 cm^{-1}; ^1H NMR δ 4.78 (s, 1), 4.29 (t, 1, J = 8.6 Hz), 3.93 (t, 1, J = 8.6 Hz), 3.70 (m, 2), 3.42 (m, 1), 2.59 (q, 1, J = 7.2 Hz), 2.19 (s, 3), 1.19 (t, 3, J = 7.2 Hz), 0.87 (d, 3, J = 7.2 Hz); ^{13}C NMR δ 206.5, 109.1, 65.9, 62.4, 53.4, 42.0, 30.3, 15.2, 12.6. Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.80; H, 9.34.

29: IR 2890, 1670, 1100 cm^{-1}; ^1H NMR δ 6.14 (d, 1, J = 1.5 Hz), 4.33 (m, 2), 4.02–3.87 (m, 4), 2.96 (t, 1, J = 8.0 Hz), 1.69 (s, 3), 1.28 (s, 3); ^{13}C NMR δ 142.9, 111.2, 110.2, 72.3, 64.9, 64.2, 53.7, 19.9, 10.7; HRMS calcd for M^+ $C_9H_{14}O_3$ 170.0943, found 170.0940. Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.81; H, 8.30. In the same reaction conditions, isomerization of **30** promoted by Pd/C, HCl, and catalytic H_2 led to **28** (74%) or to **29** (88%) in absence of HCl.

Preparation of 4,5-Dihydro-4-acetyl-3-methylfuran (31), (3*R,4*S**)-4-Acetyl-2-hydroxy-3-methyltetrahydrofuran (27) (*Botryodiplodin*), and (3*R**,4*R**)-4-Acetyl-3-hydroxy-3α-methyltetrahydrofuran (32) (*Epibotryodiplodin*).** H_2SO_4 (15%, 1.5 mL) was added with continuous magnetic stirring to a suspension of silica gel (3 g, silica gel 60 Merck, for column chromatography 70–230 mesh) in dichloromethane (7 mL). After disappearance of the water phase, the ketal **29** (1 g, 5.9 mmol) in dichloromethane (2 mL) was added, and stirring was continued at room temperature; the reaction was monitored by thin-layer chromatography. After 3 h, the solid phase was separated by suction filtration on a sintered glass funnel, and the solid was washed several times with dichloromethane. Evaporation of the solvent under reduced pressure gave starting material **29** (50%) and **31** (50%). When the reaction time was continued for 16 h, after filtration, the solid was washed with ether; the combined organic phases were stirred with $NaHCO_3$; evaporation of solvents and chromatography on silica gel gave a mixture of botryodiplodin (**27**)[23b] and epibotryodiplodin (**32**)[23b] (90/10 in 60% overall yield).

31: IR 1700, 1670 cm^{-1}; ^1H NMR δ 6.14 (m, 1), 4.42 (dd, 1, J = 9.8, 6.0 Hz), 4.31 (t, 1, J = 9.8 Hz), 3.86 (m, 1), 2.11 (s, 3), 1.57 (s, 3); ^{13}C NMR δ 206.0, 143.4, 111.0, 71.7, 59.8, 27.1, 10.0; HRMS calcd for $M^+C_7H_{10}O_2$ 126.0681, found 126.0678. Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.71; H, 7.98.