JOC Article

Efficient Conversion of Carbohydrates into 1-*C*-Alditols: Application to the Synthesis of Chiral γ-Substituted Butenolides and Bicyclic Alkaloid Analogues

Alicia Boto,* Dácil Hernández, and Rosendo Hernández*

Instituto de Productos Naturales y Agrobiología del CSIC, Avda. Astrofísico Francisco Sánchez 3, 38206-La Laguna, Tenerife, Spain

alicia@ipna.csic.es; rhernandez@ipna.csic.es

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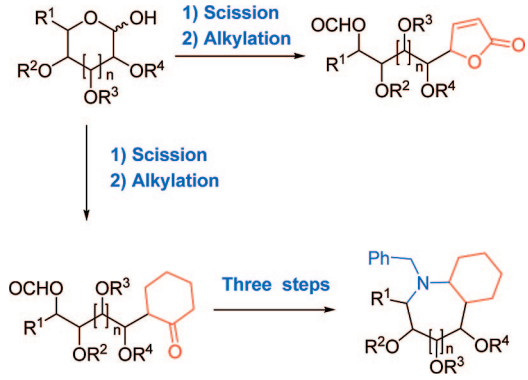
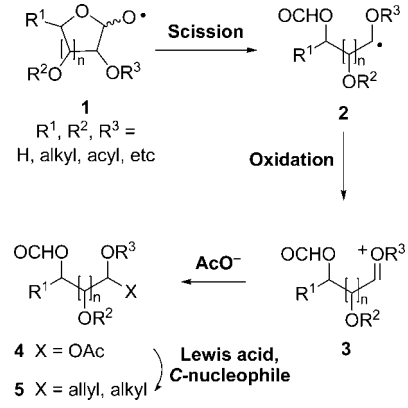


Readily available sugar derivatives were transformed in a few steps into valuable, more complex products. The tandem radical scission of carbohydrates−oxidation reaction gave acetoxy acetals, which were converted into a variety of chiral *C*-alditols in good global yields and excellent 1,2-*trans* stereoselectivity. The reaction was the key step in the synthesis of hydroxylated γ-substituted butenolides and bicyclic alkaloid analogues.

Introduction

Carbohydrates have proven very valuable to generate other chiral compounds with polyhydroxylated chains.[1] However, when the required stereochemistry corresponds to sugars of unusual series, expensive starting materials or considerable manipulation of common chains is required. In an effort to transform readily available, inexpensive sugars into those of less usual series, the β-fragmentation reaction of anomeric alkoxyl radicals **1** (Scheme 1) was studied. To generate the *O*-radicals, the carbohydrates were treated with (diacetoxy-)iodobenzene (DIB) and iodine.[2,3] A β-fragmentation reaction took place, producing a carbon radical **2**, which was oxidized in the reaction mixture to an oxycarbenium ion **3**.[2,3] This, in turn, was trapped by an acetate moiety from DIB (Scheme 1) to give the acetoxy derivatives **4**. In this way, a D-galactose chain could be transformed into a D-lyxose unit, a ribose derivative was transformed into a threose moiety, and so on, under very mild conditions.

SCHEME 1. Conversion of Carbohydrate Derivatives into Sugars of Less Common Series and 1-*C*-Alditols



(1) (a) Nakata, P. In *Glycoscience*; Fraser-Reid, B. O., Tatsuta, K., Thiem, J., Eds.; Springer: Berlin, Germany, 2001; Vol. 2, pp 1175−1214. (b) Hanessian, S. *Total Synthesis of Natural Products. The "Chiron" Approach*; Pergamon Press: Oxford, 1983.

(2) For the preliminary communications on this work, see: (a) Boto, A.; Hernández, D.; Hernández, R. *Org. Lett.* **2007**, *9*, 1721−1724. (b) Boto, A.; Hernández, R.; Suárez, E. *Tetrahedron Lett.* **2001**, *42*, 9176–9170.

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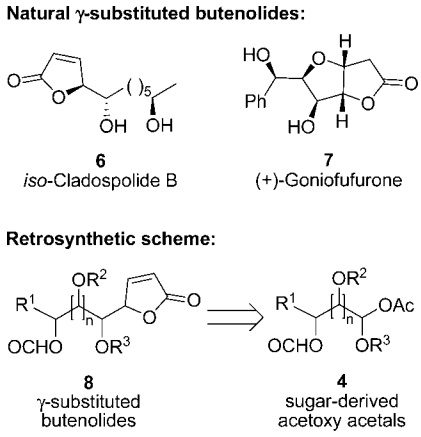
SCHEME 2. Butenolides with Hydroxylated γ-Substituents: Possible Targets for the Fragmentation/Alkylation Methodology



We reasoned that products **4** could be treated with different carbon nucleophiles (such as allylsilanes or enolsilyl ethers), in the presence of a Lewis acid, to give 1-*C*-alditols **5** (Scheme 1), which are useful precursors of many bioactive products. A possible modification of this methodology would couple the scission and the nucleophilic addition steps, avoiding the purification of the acetate intermediates **4**. In this article we study the feasibility of these approaches and the application of the scission-oxidation reaction to prepare valuable products such as chiral butenolides with hydroxylated γ-substituents and polyhydroxylated alkaloid analogues.

The butenolide moiety with hydroxylated chains at the γ-position (Scheme 2) is present in many natural products and bioactive compounds,[4] such as *iso*-cladospolide B (**6**)[5] and vitamin C analogues.[6] Besides, it is an important synthetic intermediate, as exemplified in the preparation of the cytotoxic goniofufurone (**7**),[7] hydroxylated carbocycles,[8] and higher-carbon sugars.[9] A variety of γ-substituted butenolide derivatives

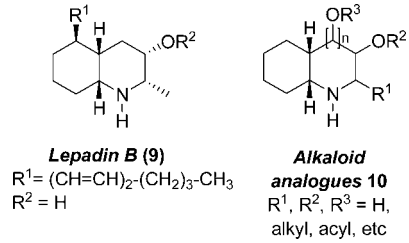


FIGURE 1. Decahydroquinoline alkaloids and their analogues.

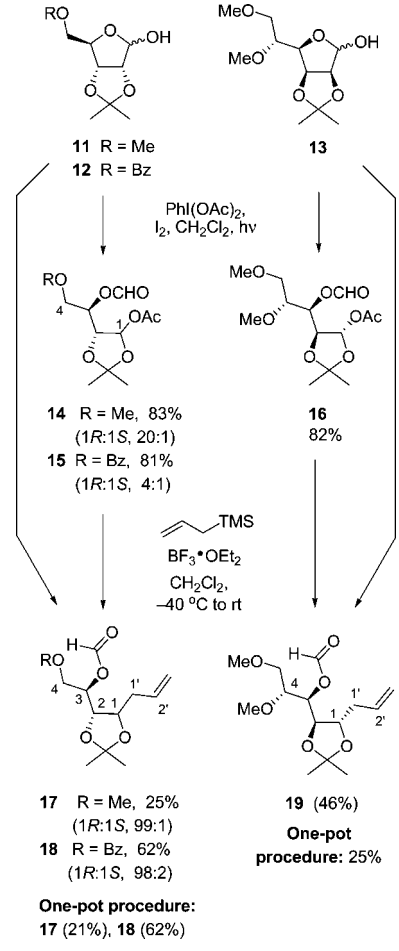
8 could be formed by addition of a furan-derived nucleophile such as (trimethylsilyloxy)furan (TMSOF)[10] to the acetoxy acetals **4**.

An even more challenging target would be the decahydroquinoline family of alkaloids[11] (Figure 1), such as Lepadin B (**9**),[12] which has displayed potent antitumoral activity. To study the structure−activity relationships, it would be useful to prepare bicyclic analogues **10** with different ring sizes and substituents. By introducing changes in the substituents, it would be possible to modulate the hydrophilicity of the analogues and their biological activity. The application of the scission/alkylation procedure to the preceding examples would allow determination of the scope and versatility of this methodology.

Results and Discussion

The starting materials for the fragmentation reaction were ribose and mannose derivatives **11**−**13** (Scheme 3), which were

SCHEME 3. Conversion of Carbohydrate Derivatives into Acetoxy Acetals and 1-Allyl Polyols[15]



(3) For related work on this subject, see: (a) Boto, A.; Hernández, D.; Hernández, R.; Álvarez, E. *J. Org. Chem.* **2007**, *72*, 9523–9532. (b) Francisco, C. G.; González, C.; Suárez, E. *J. Org. Chem.* **1998**, *63*, 8092–8093. (c) de Armas, P.; Francisco, C. G.; Suárez, E. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 772–774. (d) For a review on the modification of carbohydrates through radical chemistry, see: Hansen, S. G.; Skrydstrup, T. *Top. Curr. Chem.* **2006**, *264*, 135–162.

(4) (a) Koch, S. S. C.; Chamberlin, A. R. In *Enantiomerically Pure γ-Butirolactones in Natural Products Synthesis*; Atta-ur-Rahman, Ed.; Elsevier Science: Amsterdam, 1995; pp 687−725. (b) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701–712. (c) Rassu, G.; Zanardi, F.; Battistini, L.; Casiraghi, G. *Chem. Soc. Rev.* **2000**, 109–118. (d) For recent articles on the subject, see: Schuyler, A.; Caufield, C. E.; Hu, W.; Keeney, D.; Labthavikul, P.; Morris, K.; Naughton, S. M.; Petersen, P.; Rasmussen, B. A.; Singh, G.; Yang, Y. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 176–180. (e) Li, R. T.; Han, Q. B.; Zheng, Y. T.; Wang, R. R.; Yang, L. M.; Lu, Y.; Sang, S. Q.; Zheng, Q.-T.; Zhao, Q. S.; Sun, H. D. *Chem. Commun.* **2005**, *23*, 2936–2938. (f) Teijeira, M.; Suárez, P. L.; Gómez, G.; Terán, C.; Fall, Y. *Tetrahedron Lett.* **2005**, *46*, 5889–5892, and references therein.

(5) (a) Trost, B. M.; Aponick, A. *J. Am. Chem. Soc.* **2006**, *128*, 3931–3933. (b) Sharma, G. V. M.; Reddy, K. L.; Reddy, J. J. *Tetrahedron Lett.* **2006**, *47*, 6537–6540. (c) Pandey, S. K. *Tetrahedron Lett.* **2005**, *46*, 6625–6627. (d) Franck, X.; Araujo, M. E.; Jullian, J.-C.; Hocquemiller, R.; Figadere, B. *Tetrahedron Lett.* **2001**, *42*, 2801–2803.

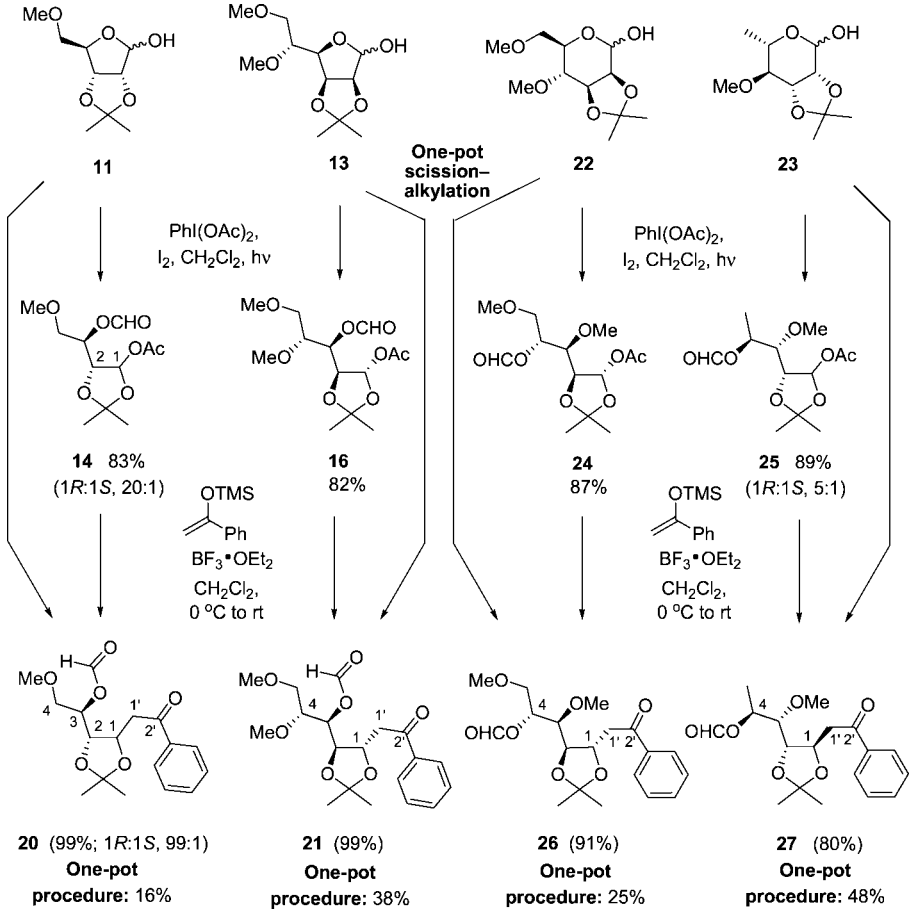
(6) (a) Ge, P.; Kira, K. L. *J. Org. Chem.* **1996**, *61*, 8671–8673.

(7) (a) Prasad, K. R.; Gholap, S. L. *J. Org. Chem.* **2008**, *73*, 2–11. (b) Yadav, V. K.; Agrawal, D. *Chem. Commun.* **2007**, 5232–5234, and references therein.

(8) (a) Rassu, G.; Auzzas, L.; Zambrano, V.; Burreddu, P.; Battistini, L.; Curti, C. *Tetrahedron: Asymmetry* **2003**, *14*, 1665–1670. (b) Rassu, G.; Auzzas, L.; Pinna, L.; Zambrano, V.; Battistini, L.; Zanardi, F.; Marzocchi, L.; Acquotti, D.; Casiraghi, G. *J. Org. Chem.* **2001**, *66*, 8070–8075. (c) Rassu, G.; Auzzas, L.; Pinna, L.; Battistini, L.; Zanardi, F.; Marzocchi, L.; Acquotti, D.; Casiraghi, G. *J. Org. Chem.* **2000**, *65*, 6307–6318. (d) Horneman, A. M.; Lundt, I. *Tetrahedron* **1997**, *53*, 6879–6892.

(9) Martin, S. F.; Zinke, P. W. *J. Am. Chem. Soc.* **1989**, *111*, 2311–2313.

SCHEME 4. Conversion of Carbohydrates into Acetoxy Acetals and Polyhydroxylated Ketones



prepared according to reported procedures.[2a,3a] When they were treated with DIB and iodine under irradiation with visible light (80-W tungsten-filament lamp), the scission took place affording the acetoxy acetals **14**−**16**[2a,3a] in good yields. The acetals **14**−**16** were then treated with $BF_3 \cdot OEt_2$ and allyltrimethylsilane, using different solvents (CH_2Cl_2 or MeCN) and temperatures; the best results were obtained with CH_2Cl_2 at −40 °C.

The yield for compound **17** was low (21%);[13] however, its 5-benzoate analogue **18** and the allyl derivative **19** were isolated in satisfactory yields (62% and 46%, respectively).[14]

The direct transformation of carbohydrate substrates **11**−**13** into the allyl derivatives **17**−**19** was studied next. The substrates were treated under the previous scission conditions for 1 h, and then the reaction mixture was cooled to −40 °C, followed by dropwise addition of allylTMS and $BF_3 \cdot OEt_2$. The solution was allowed to reach 0 °C and was stirred for 3 h. The one-pot procedure generated the allyl derivatives **17** and **18**, the yields being similar to those obtained in the two-step sequence (21% for **17**, 62% for **18**). In the case of product **19** (25%), the two-step method gave better results than the one-pot procedure.

The acetoxy acetals **14** and **16** were also reacted with silyl enol ethers. When 1-phenyl-(trimethylsilyloxy)ethene was used as the nucleophile, the phenyl ketones **20** and **21** (Scheme 4) were obtained quantitatively. In contrast, the one-pot scission−alkylation from sugar substrates **11** and **13** proceeded in low yields.

The scission/alkylation procedure was then studied with pyranose substrates **22** and **23**. Thus, the mannopyranose and rhamnopyranose derivatives **22**[16] and **23**[2a,3a] (Scheme 4) were transformed into their acetoxy acetals **24** and **25**,[2a,3a] respectively. These acetates were treated with $PhC(OTMS)=CH_2$ and $BF_3 \cdot OEt_2$, affording the phenyl ketones **26** and **27**[2a,3a] in good yields. However, the one-pot procedure gave low yields of the phenyl ketones. Therefore, the other examples (giving butenolides and bicyclic alkaloid precursors, see below) were carried out using the two-step sequence.

The phenyl ketones were obtained with high 1,2-*trans* stereoselectivity:[17,18] when the acetate precursors **14**−**16** and

(10) (a) For instance, the coupling of commercial 2-trimethylsilyloxyfuran (TMSOF) with aldehydes is a remarkable strategy for butenolide synthesis Maulide, N.; Marko, I. E. *Org. Lett.* **2006**, *8*, 3705–3707. (b) De Rosa, M.; Citro, L.; Soriente, A. *Tetrahedron Lett.* **2006**, *47*, 8507–8510.

(11) (a) Banner, E. J.; Stevens, E. D.; Trudell, M. L. *Tetrahedron Lett.* **2004**, *45*, 4411–4414. (b) Toyooka, N.; Okumura, M.; Nemoto, H. *J. Org. Chem.* **2002**, *67*, 6078–6081. (c) Daly, J. W.; Garraffo, H. M.; Spande, T. F. In *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W.; Ed.; Pergamon Press: New York, 1999; Vol. 13, pp 1−161. (d) Daly, J. W. In *The Alkaloids*; Cordell, G. A., Ed.; Academic Press: New York, 1988; Vol. 50, pp 141−169.

(12) Wu, Q.; Ma, D. *Nat. Prod. Rep.* **2006**, *23*, 772–788.

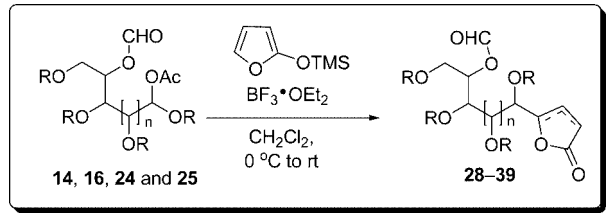
(13) Compound **17** was volatile, and loss of weight was observed under vacuum.

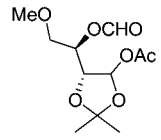
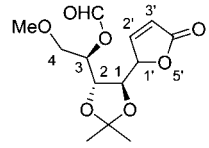
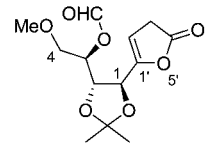
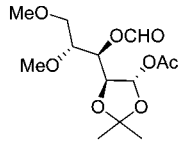
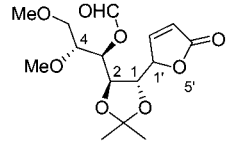
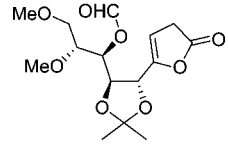
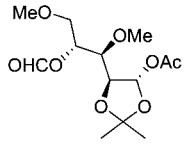
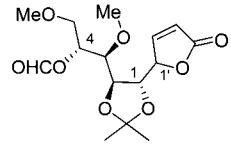
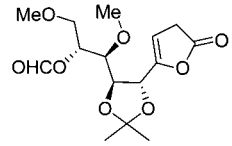
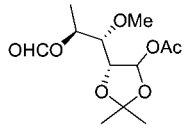
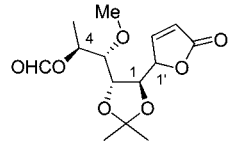
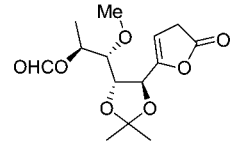
(14) For related allyl systems and their synthetic applications, see: (a) Lievens, S. C.; Molinski, T. F. *J. Am. Chem. Soc.* **2006**, *128*, 11764–11765. (b) Shing, T. K. M.; Wong, W. F.; Ikeno, T.; Yamada, T. *Org. Lett.* **2007**, *9*, 207–209. (c) Enders, D.; Lenzen, A.; Backes, M.; Janeck, C.; Catlin, K.; Lannon, M. I.; Runsink, J.; Raabe, G. *J. Org. Chem.* **2005**, *70*, 10538–10551.

(15) The numbering shown on the *C*-alditol figures does not always match the IUPAC rules. However, this numbering system allows an easier discussion of the results: the polyhydroxylated chain is numbered as the acetoxy acetal precursor, and the new allyl or alkyl chain is numbered starting from the position closer to the polyol unit.

(16) Substrate **22** was previously reported: Kapoor, V. P. *Indian J. Chem.* **1973**, *11*, 13–16. However, our synthetic strategy differs from the previous version, and therefore, it is described in Supporting Information.

TABLE 1. Addition of (TMS)Furan to Acetoxy Acetals



acetoxy acetals	products **28**–**39** (%)[a]		global yield (%)
			
14	**28** (1′*R*, 28%) **29** (1′*S*, 7%)	**30** (48%)	83%
			
16	**31** (1′*S*, 27%) **32** (1′*R*, 19%)	**33** (40%)	86%
			
24	**34** (1′*S*, 21%) **35** (1′*R*, 11%)	**36** (30%)	62%
			
25	**37** (1′*R*, 29%) **38** (1′*S*, 10%)	**39** (37%)	76%

[a] Yields for products purified by chromatography on silica gel.

24−**25** were treated with the Lewis acid, an oxycarbenium ion was formed. The adjacent stereogenic center controlled the addition of the nucleophile, which took place from the less hindered side of the cyclic oxycarbenium intermediate,[3a] affording the 1,2-*trans* products.

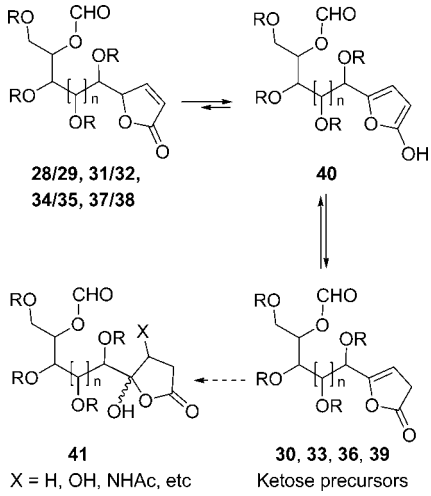
Application of the Fragmentation/Alkylation Procedure to the Synthesis of Chiral γ-Substituted Butenolides. An expedient way to prepare butenolides is shown in Table 1. The acetoxy acetals **14**, **16**, **24**, and **25** were reacted with (trimethylsilyloxy)furan, in the presence of $BF_3 \cdot OEt_2$, yielding the furanones **28**−**39** in good global yield. The nucleophilic addition was stereoselective, and in all cases, the 1,2-*trans* products were obtained exclusively.[18,19] As for the stereochemistry of C-1′ in the conjugated furanones **28/29**, **31/32**, **34/35**, and **37/38**, the major diastereomer presented an 1,1′-*anti* (1,1′-*erythro*) disposition. Their stereochemistry was unequivocally determined by comparison with related compounds,[19] which presented a $J_{1,1'} = 0-3$ Hz for the 1,1′-*threo* diastereomers and a $J_{1,1'} = 8-10$ Hz for the 1,1′-*erythro* isomers.

(17) NOESY experiments were carried out with compounds **21** and **26**. The spatial interactions observed for compound **21** were 1-H (δ_H 4.63)/3-H (δ_H 5.43), 2-H (δ_H 4.28)/1′-H_a (δ_H 2.86), 2-H/1′-H_b (δ_H 3.06). Compound **26** showed the following spatial interactions: 1-H (δ_H 4.69)/3-H (δ_H 3.65), 1-H/4-H (δ_H 5.18), 2-H (δ_H 3.91)/1′-H_a (δ_H 3.16), 2-H/1′-H_b (δ_H 3.49)

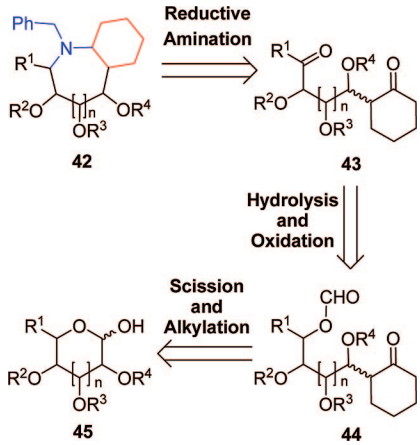
(18) The experimental coupling constants observed for compounds **21** ($J_{1,2}$ = 8.1 Hz) and **26** ($J_{1,2}$ = 7.8 Hz) and for the other scission−alkylation products ($J_{1,2}$ = 6.5−8.5 Hz) matched theoretical coupling constants for 1,2-*trans* derivatives. The theoretical $J_{1,2}$ for the 1,2-*trans* and the 1,2-*cis* products were calculated over minimized structures by using the Karplus−Altona equation implemented in the Macromodel 7.0 program. The calculations were performed with a MMFF force field, using high-quality parameters. Values of $J_{1,2} = 6.3-10.0$ Hz and $J_{1,2} = 4.0-6.0$ Hz were obtained for the 1,2-*trans* and the 1,2-*cis* compounds, respectively.

(19) (a) Hornemann, A. M.; Lundt, I. *Synthesis* **1999**, 317–325. (b) Hornemann, A. M.; Lundt, I. *Tetrahedron* **1997**, *53*, 6879–6892. (c) de March, P.; Figueredo, M.; Font, J.; Raya, J.; Alvarez-Larena, A.; Piniella, J. F. *J. Org. Chem.* **2003**, *68*, 2437–2447.

SCHEME 5. Conversion of Conjugated Lactones into Enol Esters and Higher Sugars



SCHEME 6. Retrosynthesis of Polyhydroxylated Bicyclic Alkaloids



Surprisingly, the unconjugated lactones **30**, **33**, **36**, and **39** were the major products, and in most cases their yield was similar to the combined yield of the conjugated isomers. Their formation can be explained as shown in Scheme 5. The nucleophilic addition would initially yield the conjugated lactones, which would undergo proton abstraction at C-1′, generating the 4′-hydroxyfuran intermediates **40**. These intermediates would be in tautomeric equilibrium with the unconjugated lactones, as suggested by the ^{1}H and ^{13}C NMR spectra, where the 3′-H_2 and the 3′-C are observed at very low fields ($\delta_H \approx 5.0$ and $\delta_C \approx 80.0$, respectively). The lactones **30**, **33**, **36**, and **39** are useful precursors of ketoses **41**.[19]

In a similar way, the conjugated furanones **28/29**, **31/32**, **34/35**, and **37/38** can be modified by reduction, alkylation, dihydroxylation, amino hydroxylation, etc.,[20] giving a variety of functionalized butenolides and higher-carbon sugars with different substituents and stereochemistries.

Application of the Fragmentation/Alkylation Procedure to the Synthesis of Bicyclic Alkaloid Analogues. The decahydroquinoline alkaloids have elicited many synthetic efforts[21,22] due to their interesting biological properties.[23] In order to study the influence of substituents on their hydrophilicity and their biological activity, a short process to obtain hydroxylated derivatives was developed (Scheme 6). Thus, the bicyclic core in **42** could be formed by reductive amination[24]of diketone **43**. The latter can be prepared from the cyclohexanone derivative **44**, by hydrolysis of the formate group and oxidation. Finally, **44** would be prepared from readily available sugars **45**, using the fragmentation/alkylation sequence.

Thus, the scission products **14**, **16**, **24**, and **25** were treated with (trimethylsilyloxy)cyclohexene and $BF_3 \cdot OEt_2$, yielding the cyclohexanones **46**−**49** (Table 2) in good global yields. The nucleophilic addition gave exclusively 1,2-*trans* products,[25] but inseparable mixtures of C-1′ epimers were formed. The diastereomers were separated at a later stage.

Thus, the cyclohexanones **46**, **47**, and **49** were transformed into the alkaloid analogues **56**−**61** (Scheme 7).

On treatment with methanolic $NaHCO_3$, the alcohols **50**−**52** were generated in excellent yields and then were oxidized to the diketones **53**−**55**. The following step required considerable experimentation, but finally the reductive amination[24] was achieved with the system benzylamine/AcOH/$NaBH_3CN$, in the presence of molecular sieves.

To our satisfaction, only two of the eight possible diastereomers were detected in each reaction. In all cases, a *cis* ring fusion was observed. The stereochemistry was based on NOESY experiments (Figure 2) and on the value of the H−H coupling constants in the ^{1}H NMR spectra.[26]

Thus, for compound **56** the ^{1}H NMR spectra gave a coupling constant $J_{4a,8a} = 4.7$ Hz, which suggested a *cis* relationship between 4a-H and 8a-H (the *trans* relationship would imply $J_{4a,8a} \approx 11$ Hz).[26] Similarly, $J_{4,4a} = 11.7$ Hz (4-H/4a-H *trans*) and $J_{2,3} = 9.6$ Hz (2-H/3-H *trans*). The NOESY experiment

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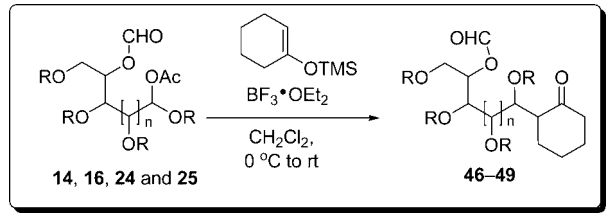
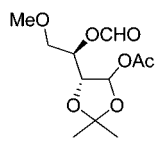
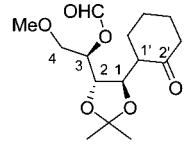
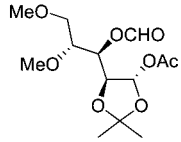
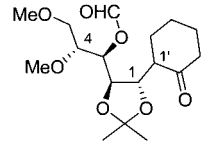
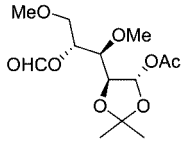
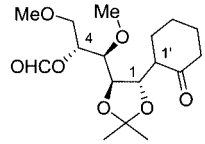
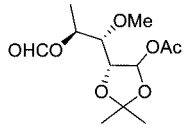
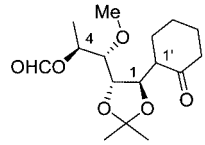
(24) (a) Gravier-Pelletier, C.; Maton, W.; Le Merrer, Y. *Synlett* **2003**, 333–336. (b) Manescalchi, F.; Nardi, A. R.; Savoia, D. *Tetrahedron Lett.* **1994**, *35*, 2775–2778.

(25) NOESY experiments were carried out for compound **49** and for products derived from the cyclohexanones **46**−**49**, such as the bicyclic systems **56**−**61** (commented later in the text), supporting the assigned 1,2-*trans* stereochemistry. For compound **49**, the following spatial interactions were observed: 1-H (δ_H 4.49/4.36)/3-H (δ_H 3.56/3.43), 2-H (δ_H 3.95)/1′-H (δ_H 2.75), 2-H (δ_H 3.95/3.86)/4-H (δ_H 5.15), 2-H/cyclohexanone protons (δ_H 1.5−2.5).

(26) (a) The experimental coupling constants matched theoretical ones, calculated as described in ref 18. (b) For information on the Karplus−Altona equation, see: Haasnoot, C. A. G.; de Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783–2792. (c) For more information on this software, see: Mohamadi, F.; Richard, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrikson, T.; Stille, W. C. *J. Comput. Chem.* **1990**, *11*, 440.

TABLE 2. Addition of (Trimethylsilyloxy)cyclohexene to Acetoxy Acetals



acetoxy acetals	products	yield[a]	dr[b]
			
14	**46**	79%	3:1
			
16	**47**	>99%	2.5:1
			
24	**48**	69%	2:1
			
25	**49**	64%	3:1

[a] Yields for products purified by chromatography. [b] The d.r. were determined by ^{1}H NMR.

showed the spatial correlations 2-H/8-Hα, 4-H/8-Hα, and 3-H/4a-H, which supported the assigned stereochemistry. The minor diastereomer **57** presented $J_{2,3}$ = 9.7 Hz (2-H/3-H *trans*) and the following NOESY spatial correlations: 2-H/8a-H, 2-H/4-H, and 4-H/8a-H.

The other quinoline derivatives, compounds **58** and **59**, were obtained in similar overall yield (51%) and diastereomeric ratio. Their configurations were determined using the $J_{H,H}$ coupling constants from the ^{1}H NMR spectra and the spatial correlations from the NOESY experiments, as shown in Figure 2.

The formation of the polyhydroxylated decahydrobenzoazepines **60** and **61** took place in moderate global yield (39%). However, this result is remarkable since the formation of medium-size rings is often difficult, and in addition, four steps are involved in the reductive amination−cyclization reaction. The azepine **60** presented a *cis* relationship between 2-H and 3-H ($J_{2,3}$ = 4.5 Hz), while its diastereomer **61** possessed a 2,3-*trans* relationship ($J_{2,3}$ = 8.0 Hz).[27] On the other side, the NOESY experiment for compound **60** showed a 4-H/5a-H spatial correlation, whereas for isomer **61** the following correlations were observed: 2-Me/9a-H, 2-Me/3-H, 2-Me/5-H, 3-H/5-H and 5-H/9a-H. The formation of the functionalized bicyclic products **56**−**61** shows the versatility of this methodology. In a similar way, other polycyclic systems could be prepared by using different sugar-derived acetoxy acetals and cyclic silyl enol ethers.

Conclusion

A mild, efficient strategy to prepare *C*-alditols, which are valuable as synthetic intermediates or as bioactive compounds, is reported herein. The method is based on a tandem radical scission−oxidation reaction and uses readily available carbohydrates as starting materials. The fragmentation of sugar derivatives afforded acetoxy acetals, which were transformed by allylation or alkylation into a variety of *C*-alditols in good

(27) The theoretical calculations gave $J_{2,3}$ = 3.0−4.5 Hz for the 2,3-*cis* relationship and $J_{2,3}$ = 8.5−10.1 Hz for the 2,3-*trans* relationship.

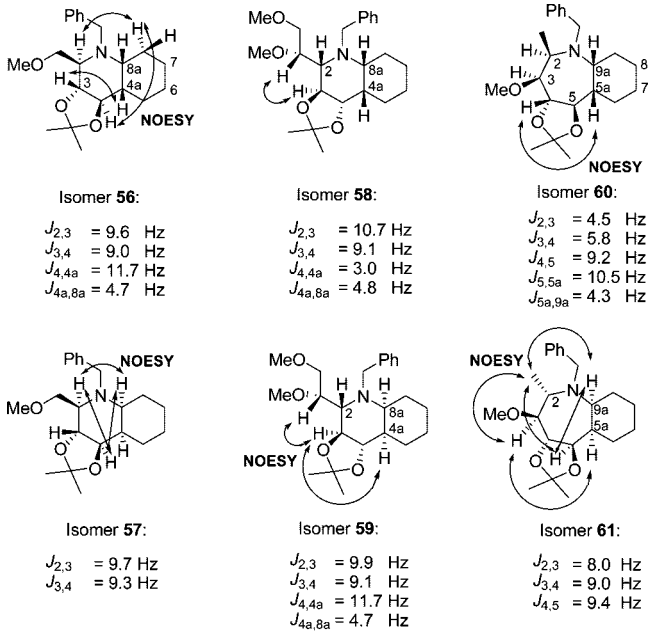
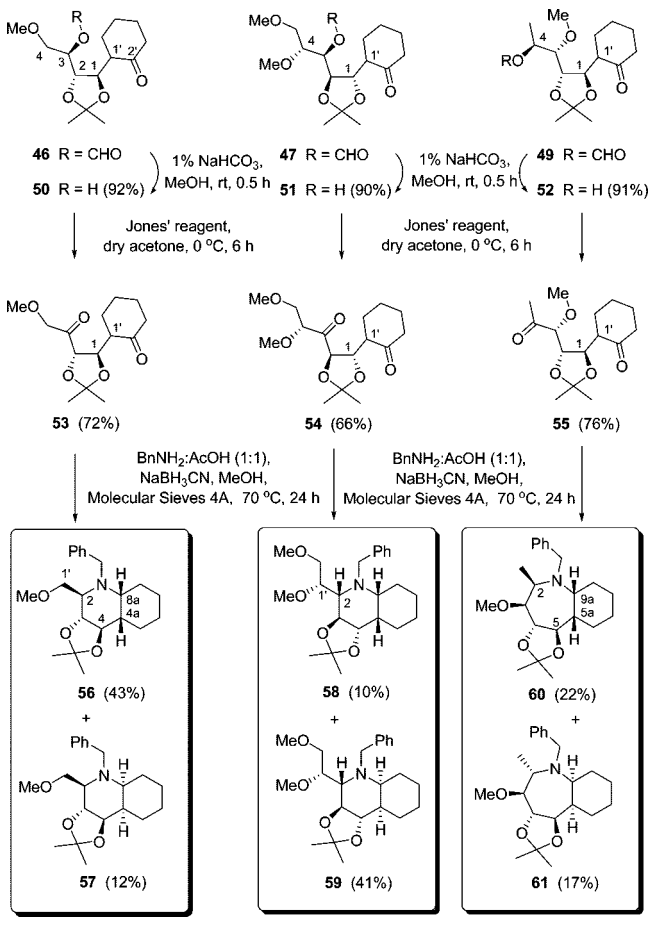


FIGURE 2. $J_{H,H}$ (from ^{1}H NMR) and NOESY spatial correlations for products **56**−**61**.

SCHEME 7. Synthesis of Polyhydroxylated Bicyclic Alkaloid Analogues 56−61



global yields and excellent 1,2-*trans* stereoselectivity. To highlight its versatility, the scission/alkylation process was applied to prepare chiral polyhydroxylated butenolides and highly functionalized bicyclic alkaloid analogues.

Experimental Section

General Procedure for *β*-Fragmentation of Carbohydrate Derivatives 11−13, 22, and 23. To a solution of the carbohydrate (1.0 mmol) in dry CH_2Cl_2 (10 mL) under nitrogen were added (diacetoxyiodo)benzene (DIB) (386 mg, 1.2 mmol) and iodine (254 mg, 1.0 mmol). The reaction mixture was stirred at room temperature (26 °C) under irradiation with visible light (80-W tungsten-filament lamp) for 1 h. Then it was poured into aqueous 10% sodium thiosulfate ($Na_2S_2O_3$) and extracted with dichloromethane. The organic layer was washed with brine, dried on Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by chromatography on silica gel (hexanes/EtOAc), yielding the purified acetoxy acetals **14**−**16**,[2] **24**, and **25**.[2]

(1*S*)-1-Acetoxy-4-*O*-formyl-1,2-*O*-isopropylidene-3,5-di-*O*-methyl-D-arabinitol (24). The acetate was obtained as the 1,2-*trans* isomer (87%). Colorless oil; $[\alpha]_D$ −53 (*c* 0.30, $CHCl_3$); IR ($CHCl_3$) 1728, 1083, 1084 cm^{-1}; ^{1}H NMR (500 MHz) δ_H 1.46 (3H, s), 1.48 (3H, s), 2.08 (3H, s), 3.37 (3H, s), 3.53 (3H, s), 3.64 (1H, dd, J = 4.8, 11.1 Hz), 3.67 (1H, dd, J = 3.7, 6.8 Hz), 3.68 (1H, dd, J = 2.8, 11.1 Hz), 4.28 (1H, dd, J = 3.1, 3.3 Hz), 5.12 (1H, ddd, J = 2.7, 4.6, 7.2 Hz), 6.21 (1H, d, J = 2.7 Hz), 8.08 (1H, s); ^{13}C NMR (125.7 MHz) δ_C 21.2 (CH_3), 26.4 (CH_3), 26.7 (CH_3), 59.0 (CH_3), 60.8 (CH_3), 70.2 (CH_2), 72.3 (CH), 77.8 (CH), 82.3 (CH), 96.7 (CH), 113.2 (C), 160.1 (CH), 170.4 (C); MS *m*/*z* (rel intensity) 291 (M^+ − Me, 14), 101 ([2,2-dimethyldioxolane − H]$^+$, 100); HRMS calcd for $C_{12}H_{19}O_8$, 291.1080; found, 291.1050; calcd for $C_5H_9O_2$, 101.0603; found, 101.0645. Anal. Calcd for $C_{13}H_{22}O_8$: C, 50.98; H, 7.24. Found: C, 51.00; H, 7.55.

Conversion of Acetoxy Acetals 14−16 into Allyl Derivatives 17−19. A solution of the acetoxy acetals (1 equiv) in dry CH_2Cl_2 (2 mL/mmol substrate) at −40 °C was treated with allyltrimethylsilane (3 equiv), and then $BF_3\cdot OEt_2$ (2 equiv) was added dropwise. The reaction mixture was allowed to reach 26 °C and then was stirred for 0.5−3.0 h. Then it was poured into saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was dried on Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by chromatography on silica gel (hexanes/EtOAc) affording the allyl derivatives **17**−**19**.

(1*R*/1*S*)-Allyl-3-*O*-formyl-1,2-*O*-isopropylidene-4-*O*-methyl-D-erythritol (17). The allyl derivative **17** was obtained as a volatile colorless oil (25%). Product **17** is an inseparable mixture of the 1*R* and 1*S* diastereomers (*trans*:*cis* 99:1), but only the major isomer is described. IR ($CHCl_3$) 1725, 1117, 1089 cm^{-1}; ^{1}H NMR (500 MHz) δ_H 1.39 (3H, s), 1.42 (3H, s), 2.35 (1H, ddd, J = 7.1, 7.1, 14.4 Hz), 2.44 (1H, ddd, J = 4.3, 6.3, 14.6 Hz), 3.38 (3H, s), 3.62 (1H, dd, J = 5.8, 11.0 Hz), 3.67 (1H, dd, J = 3.6, 11.0 Hz), 3.91 (1H, dd, J = 6.3, 7.0 Hz), 4.03 (1H, ddd, J = 4.3, 7.3, 7.4 Hz), 5.12 (1H, dd, J = 1.4, 18.5 Hz), 5.15 (1H, d, J = 10.3 Hz), 5.19 (1H, ddd, J = 3.6, 5.9, 5.9 Hz), 5.88 (1H, dddd, J = 6.8, 6.9, 10.3, 17.2 Hz), 8.31 (1H, s); ^{13}C NMR (125.7 MHz) δ_C 26.9 (CH_3), 27.3 (CH_3), 37.8 (CH_2), 59.2 (CH_3), 70.9 (CH_2), 72.5 (CH), 77.9 (CH), 78.2 (CH), 108.9 (C), 117.8 (CH_2), 133.6 (CH), 160.2 (CH); MS *m*/*z* (rel intensity) 229 (M^+ − Me, 100); HRMS calcd for $C_{11}H_{17}O_5$, 229.1076; found, 229.1042. Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 59.28; H, 8.01.

(1*R*/1*S*)-Allyl-4-*O*-benzoyl-3-*O*-formyl-1,2-*O*-isopropylidene-D-erythritol (18). The allyl derivative **18** was obtained as a mixture of the 1*R* and 1*S* diastereomers (67%, *trans*:*cis* 98:2). The minor isomer could not be purified from the major diastereomer. Colorless syrup; IR ($CHCl_3$) 3075, 1728, 1643, 1274, 1173 cm^{-1}; ^{1}H NMR (500 MHz) major isomer δ_H 1.43 (3H, s), 1.44 (3H, s), 2.39 (1H, ddd, J = 7.1, 7.1, 14.7 Hz), 2.47 (1H, ddd, J = 4.9, 7.1, 14.6 Hz), 3.97 (1H, dd, J = 7.1, 7.2 Hz), 4.09 (1H, ddd, J = 4.5, 7.2, 7.2 Hz), 4.46 (1H, dd, J = 7.0, 12.2 Hz), 4.72 (1H, dd, J = 2.9, 12.2 Hz), 5.15 (1H, dd, J = 1.4, 9.8 Hz), 5.16 (1H, dd, J = 1.2, 18.8 Hz), 5.44 (1H, ddd, J = 2.8, 6.6, 6.6 Hz), 5.87 (1H, dddd, J = 6.9, 6.9, 10.3, 17.1 Hz), 7.45 (2H, dd, J = 7.7, 7.9 Hz), 7.58 (1H, dd, J = 7.4, 7.5 Hz), 8.02 (2H, d, J = 7.4 Hz), 8.13 (1H, s); ^{13}C NMR

(125.7 MHz) δ_C 26.9 (CH_3), 27.3 (CH_3), 37.8 (CH_2), 63.3 (CH_2), 71.5 (CH), 78.1 (CH), 78.2 (CH), 109.9 (C), 118.1 (CH_2), 128.5 (2 × CH), 129.6 (C), 129.7 (2 × CH), 133.2 (2 × CH), 159.9 (CH), 166.1 (C); MS *m*/*z* (rel intensity) 319 (M^+ − Me, 43), 105 ($[PhCO]^+$, 100); HRMS calcd for $C_{17}H_{19}O_6$, 319.1182; found, 319.1171; calcd for C_7H_5O, 105.0340; found, 105.0345. Anal. Calcd for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63. Found: C, 64.65; H, 6.79.

(1S)-Allyl-3-*O*-formyl-1,2-*O*-isopropylidene-4,5-di-*O*-methyl-D-arabinitol (19). The allyl derivative **19** was obtained as the 1,2-*trans* isomer (45%). Colorless oil; $[\alpha]_D$ −12 (*c* 0.35, $CHCl_3$); IR ($CHCl_3$) 1728, 1173, 1098 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ_H 1.38 (3H, s), 1.41 (3H, s), 2.35 (1H, ddd, *J* = 6.9, 7.1, 14.3 Hz), 2.43 (1H, m), 3.34 (3H, s), 3.37 (1H, dd, *J* = 4.6, 10.6 Hz), 3.47 (3H, s), 3.57 (1H, ddd, *J* = 2.7, 4.5, 7.6 Hz), 3.63 (1H, dd, *J* = 2.7, 10.6 Hz), 3.77 (1H, ddd, *J* = 4.7, 7.1, 8.1 Hz), 4.02 (1H, dd, *J* = 2.3, 8.3 Hz), 5.10−5.16 (3H, m), 5.84 (1H, dddd, *J* = 6.8, 7.0, 10.2, 17.0 Hz), 8.14 (1H, s); ^{13}C NMR (125.7 MHz) δ_C 26.6 (CH_3), 27.3 (CH_3), 36.5 (CH_2), 58.4 (CH_3), 59.4 (CH_3), 68.7 (CH), 70.6 (CH_2), 75.7 (CH), 78.2 (CH), 78.7 (CH), 108.7 (C), 117.8 (CH_2), 133.4 (CH), 160.0 (CH); MS *m*/*z* (rel intensity) 273 (M^+ − Me, 69), 247 (M^+ − allyl, 14), 89 ($[MeOCH_2CHOMe]^+$, 100), 59 ($[Me_2C{=}OH]^+$, 69); HRMS calcd for $C_{13}H_{21}O_6$, 273.1338; found, 273.1352; calcd for $C_4H_9O_2$, 89.0602; found, 89.0626. Anal. Calcd for $C_{14}H_{24}O_6$: C, 58.32; H, 8.39. Found: C, 58.38; H, 8.12.

Conversion of Acetoxy Acetals 14, 16, 24, and 25 into Phenyl Ketone Derivatives 20, 21, 26, and 27. Similar to the allylation reaction, but using 1-phenyl-1-(trimethylsilyloxy)ethane as the nucleophile and carrying out the addition at 0 °C.

(1*S*)-1-(2-Oxo-2-phenylethyl)-4-*O*-formyl-1,2-*O*-isopropylidene-3,5-di-*O*-methyl-D-arabinitol (26). Obtained from acetoxy acetal **24** (91%) as a yellow oil; $[\alpha]_D$ −4 (*c* 0.2, $CHCl_3$); IR (film) 1726, 1685, 1111, 1082 cm^{-1}; ^1H NMR (500 MHz) δ_H 1.38 (3H, s), 1.42 (3H, s), 3.16 (1H, dd, *J* = 5.7, 16.9 Hz), 3.38 (3H, s), 3.49 (1H, dd, *J* = 6.3, 16.9 Hz), 3.57 (3H, s), 3.65 (1H, dd, *J* = 2.4, 6.9 Hz), 3.68 (1H, dd, *J* = 5.3, 11.0 Hz), 3.76 (1H, dd, *J* = 2.6, 11.0 Hz), 3.91 (1H, dd, *J* = 2.4, 7.8 Hz), 4.69 (1H, ddd, *J* = 6.0, 6.2, 7.8 Hz), 5.18 (1H, ddd, *J* = 2.5, 4.6, 7.1 Hz), 7.47 (2H, dd, *J* = 7.6, 7.8 Hz), 7.58 (1H, dd, *J* = 7.4, 7.4 Hz), 7.97 (2H, d, *J* = 7.4 Hz), 8.10 (1H, s); ^{13}C NMR (125.7 MHz) δ_C 26.6 (CH_3), 27.3 (CH_3), 42.7 (CH_2), 58.9 (CH_3), 60.9 (CH_3), 70.5 (CH_2), 72.5 (CH), 73.3 (CH), 77.3 (CH), 80.9 (CH), 109.2 (C), 128.2 (2 × CH), 128.7 (2 × CH), 133.4 (CH), 136.7 (C), 160.4 (CH), 197.4 (C); MS *m*/*z* (rel intensity) 351 (M^+ − Me, 4), 219 (M^+ − $MeOCH_2CH$-(OCHO)CHOMe, 42), 147 ($[MeOCH_2CH(OCHO)CHOMe]^+$, 12), 105 ($[PhCO]^+$, 100), 77 ($[Ph]^+$, 26); HRMS calcd for $C_{18}H_{23}O_7$, 351.1444; found, 351.1430; calcd for C_7H_5O, 105.0340; found, 105.0301. Anal. Calcd for $C_{19}H_{26}O_7$: C, 62.28; H, 7.15. Found: C, 62.36; H, 7.06.

Conversion of Acetoxy Acetals 14, 16, 24, and 25 into Butenolides 28−39. Similar to the allylation reaction, but using 2-(trimethylsilyloxy)furan as the nucleophile and carrying out the addition at 0 °C.

(1*S*)-4-*O*-Formyl-1,2-*O*-isopropylidene-3,5-di-*O*-methyl-1-(4′-oxo-(1′*S*)-(1′*H*)-furanyl)-D-arabinitol (34), (1*S*)-4-*O*-Formyl-1,2-*O*-isopropylidene-3,5-di-*O*-methyl-1-(4′-oxo-(1′*R*)-(1′*H*)-furanyl)-D-arabinitol (35), and (1*S*)-4-*O*-Formyl-1,2-*O*-isopropylidene-3,5-di-*O*-methyl-1-(4′-oxo-1′(3′*H*)-furanyl)-D-arabinitol (36). Obtained from the acetoxy acetal **24** (21% for product **34**, 11% for **35**, and 30% for **36**). Compound **34**: colorless oil; $[\alpha]_D$ −44 (*c* 0.3, $CHCl_3$); IR (film) 1790, 1759, 1727, 1112, 1086 cm^{-1}; ^1H NMR (500 MHz) δ_H 1.38 (3H, s), 1.40 (3H, s), 3.39 (3H, s), 3.45 (3H, s), 3.66 (1H, dd, *J* = 5.0, 11.1 Hz), 3.70 (1H, dd, *J* = 2.3, 7.3 Hz), 3.74 (1H, dd, *J* = 2.5, 11.1 Hz), 3.77 (1H, dd, *J* = 7.9, 8.1 Hz), 4.19 (1H, dd, *J* = 2.3, 7.6 Hz), 4.94 (1H, ddd, *J* = 1.7, 1.7, 8.4 Hz), 5.19 (1H, ddd, *J* = 2.4, 5.0, 7.3 Hz), 6.23 (1H, dd, *J* = 1.9, 5.7 Hz), 7.68 (1H, dd, *J* = 1.3, 5.7 Hz), 8.12 (1H, s); ^{13}C NMR (100.6 MHz) δ_C 26.6 (CH_3), 26.9 (CH_3), 59.0 (CH_3), 60.8 (CH_3), 70.4 (CH_2), 72.8 (CH), 76.6 (CH), 77.0 (CH), 80.0 (CH), 83.3 (CH), 110.4 (C), 122.2 (CH), 155.2 (CH), 160.2 (CH), 172.1 (C); MS *m*/*z* (rel intensity) 315 (M^+ − Me, 51), 183 (M^+ − $MeOCH_2CH$-(OCHO)CHOMe, 62), 147 ($[MeOCH_2CH(OCHO)CHOMe]^+$, 62), 101 ([2,2-dimethyl-1,3-dioxolane − H]$^+$, 100), 59 ($[Me_2C{=}OH]^+$, 26); HRMS calcd for $C_{14}H_{19}O_8$, 315.1080; found, 315.1055; calcd for $C_5H_9O_2$, 101.0603; found, 101.0577. Anal. Calcd for $C_{15}H_{22}O_8$: C, 54.54; H, 6.71. Found: C, 54.53; H, 6.75. Compound **35**: colorless oil; $[\alpha]_D$ +29 (*c* 0.1, $CHCl_3$); IR (film) 1785, 1761, 1727, 1163, 1086 cm^{-1}; ^1H NMR (500 MHz) δ_H 1.33 (3H, s), 1.39 (3H, s), 3.38 (3H, s), 3.53 (3H, s), 3.57 (1H, dd, *J* = 1.8, 5.1 Hz), 3.67 (1H, dd, *J* = 5.1, 10.9 Hz), 3.72 (1H, dd, *J* = 3.1, 10.9 Hz), 4.30 (2H, br s), 5.15 (1H, br s), 5.21 (1H, ddd, *J* = 3.1, 5.6, 5.6 Hz), 6.22 (1H, dd, *J* = 2.2, 5.8 Hz), 7.50 (1H, dd, *J* = 1.4, 5.8 Hz), 8.11 (1H, s); ^{13}C NMR (100.6 MHz) δ_C 26.2 (CH_3), 26.9 (CH_3), 59.0 (CH_3), 60.8 (CH_3), 70.3 (CH_2), 72.3 (CH), 75.0 (CH), 76.4 (CH), 77.9 (CH), 81.0 (CH), 110.5 (C), 122.9 (CH), 152.8 (CH), 160.2 (CH), 172.4 (C); MS *m*/*z* (rel intensity) 315 (M^+ − Me, 69), 183 (M^+ − $MeOCH_2CH(OCHO)CHOMe$, 68), 147 ($[MeOCH_2CH$-(OCHO)CHOMe]$^+$, 52), 101 ([2,2-dimethyl-1,3-dioxolane − H]$^+$, 100), 59 ($[Me_2C{=}OH]^+$, 28); HRMS calcd for $C_{14}H_{19}O_8$, 315.1080; found, 315.1139; calcd for $C_5H_9O_2$, 101.0603; found, 101.0625. Anal. Calcd for $C_{15}H_{22}O_8$: C, 54.54; H, 6.71. Found: C, 54.58; H, 6.66. Compound **36**: colorless oil; $[\alpha]_D$ −5 (*c* 0.17, $CHCl_3$); IR (film) 1758, 1727, 1113, 1079 cm^{-1}; ^1H NMR (500 MHz) δ_H 1.43 (3H, s), 1.47 (3H, s), 3.37 (3H, s), 3.63 (3H, s), 3.66 (1H, dd, *J* = 5.5, 11.1 Hz), 3.75 (1H, dd, *J* = 2.4, 11.1 Hz), 3.81 (1H, dd, *J* = 1.9, 6.8 Hz), 3.99 (1H, dd, *J* = 2.0, 8.2 Hz), 4.85 (1H, dd, *J* = 1.5, 8.3 Hz), 4.88 (2H, s), 5.15 (1H, ddd, *J* = 2.2, 5.5, 6.7 Hz), 7.53 (1H, d, *J* = 1.4 Hz), 8.09 (1H, s); ^{13}C NMR (125.7 MHz) δ_C 26.4 (CH_3), 26.6 (CH_3), 58.9 (CH_3), 60.8 (CH_3), 70.4 (CH_2), 70.7 (CH_2), 71.2 (CH), 73.2 (CH), 76.3 (CH), 80.7 (CH), 109.8 (C), 133.0 (C), 147.2 (CH), 160.3 (CH), 172.0 (C); MS *m*/*z* (rel intensity) 315 (M^+ − Me, 42), 183 (M^+ − $MeOCH_2CH(OCHO)CHOMe$, 32), 165 (M^+ − [2 × MeO + $Me_2C{=}O$ + OCHO, 100), 147 ($[MeOCH_2CH$-(OCHO)CHOMe]$^+$, 42), 101 ([2,2-dimethyl-1,3-dioxolane − H]$^+$, 75); HRMS calcd for $C_{14}H_{19}O_8$, 315.1080; found, 315.1040; calcd for $C_9H_9O_3$, 165.0552; found, 165.0611. Anal. Calcd for $C_{15}H_{22}O_8$: C, 54.54; H, 6.71. Found: C, 54.32; H, 6.95.

Conversion of Acetoxy Acetals 14, 16, 24, and 25 into Cyclohexanones 46−49. Similar to the allylation reaction, but using 1-(trimethylsiloxy)cyclohexene as the nucleophile and carrying out the addition at 0 °C.

(1*S*,1′*R*/*S*)-4-*O*-Formyl-1,2-*O*-isopropylidene-3,5-di-*O*-methyl-1-[2′-oxo-1′-cyclohexyl]-D-arabinitol (48). Obtained from acetoxy acetal **24** (90%) as an inseparable diastereomer mixture (2.5:1). Yellow oil; $[\alpha]_D$ −11 (*c* 0.3, $CHCl_3$); IR ($CHCl_3$) 1724, 1712, 1102, 1078 cm^{-1}; ^1H NMR (500 MHz) major diastereomer δ_H 1.32 (3H, s), 1.40 (3H, s), 1.66−1.68 (3H, m), 1.94 (1H, m), 2.08 (1H, m), 2.33−2.39 (3H, m), 2.48 (1H, ddd, *J* = 5.8, 6.6, 12.4 Hz), 3.37 (3H, s), 3.56 (3H, s), 3.65 (1H, dd, *J* = 5.6, 11.0 Hz), 3.749 (1H, dd, *J* = 2.5, 6.5 Hz), 3.754 (1H, dd, *J* = 2.3, 11.2 Hz), 3.87 (1H, dd, *J* = 2.5, 6.5 Hz), 4.39 (1H, dd, *J* = 6.9, 7.0 Hz), 5.13 (1H, ddd, *J* = 2.3, 5.8, 6.6 Hz), 8.09 (1H, s); minor diastereomer (the signals overlapped with those of the major isomer are not described): δ_H 1.32 (3H, s), 1.38 (3H, s), 1.64−1.68 (3H, m), 1.94 (1H, m), 2.08 (1H, m), 2.15 (1H, m), 2.33−2.39 (2H, m), 2.74 (1H, ddd, *J* = 5.2, 5.6, 11.5 Hz), 3.37 (3H, s), 3.57 (3H, s), 3.62 (1H, dd, *J* = 1.8, 8.4 Hz), 3.95 (1H, dd, *J* = 1.8, 7.8 Hz), 4.50 (1H, dd, *J* = 5.2, 7.9 Hz), 8.10 (1H, s); ^{13}C NMR (125.7 MHz) major isomer δ_C 24.8 (CH_2), 26.8 (CH_3), 27.6 (CH_3), 27.7 (CH_2), 30.3 (CH_2), 42.5 (CH_2), 54.9 (CH), 59.0 (CH_3), 60.8 (CH_3), 70.7 (CH_2), 73.7 (CH), 75.2 (CH), 78.1 (CH), 80.6 (CH), 109.2 (C), 160.5 (CH), 211.7 (C); minor diastereomer δ_C 24.5 (CH_2), 26.6 (CH_3), 27.2 (CH_3), 27.5 (CH_2), 28.9 (CH_2), 42.3 (CH_2), 53.3 (CH), 58.8 (CH_3), 60.7 (CH_3), 70.6 (CH_2), 73.8 (CH), 74.6 (CH), 77.5 (CH), 77.6 (CH), 108.8 (C), 160.5 (CH), 211.0 (C); MS *m*/*z* (rel intensity) 329 (M^+ − Me, 7), 246 (M^+ − cyclohexanone, 53), 139 (M^+ − [$MeOCH_2CH(OCHO)CHOMe$ + $Me_2C{=}O$], 100), 59 ($[Me_2C{=}OH]^+$, 77); HRMS calcd for $C_{16}H_{25}O_7$, 329.1600; found,

329.1609; calcd for $C_8H_{11}O_2$, 139.0759; found, 139.0791. Anal. Calcd for $C_{17}H_{28}O_7$: C, 59.29; H, 8.19. Found: C, 59.25; H, 8.49.

Hydrolysis of the Formate Group in Cyclohexanones 46, 47, and 49. The cyclohexanone (0.2 mmol) was treated with 1% methanolic $NaHCO_3$ (2 mL). The solution was stirred at room temperature for 30 min, poured into water, and extracted with CH_2Cl_2. The organic layer was dried with sodium sulfate, filtered, and evaporated under vacuum. The residue was purified by column chromatography on silica gel (hexanes/EtOAc) to give alcohols **50**, **51**, or **52**.

(1*R*,1′*R*/*S*)-1,2-*O*-Isopropylidene-4-*O*-methyl-1-[2′-oxo-1′-cyclohexyl]-D-erythritol (50). Isolated as an inseparable diastereomer mixture (2:1). Colorless oil; $[\alpha]_D$ +30 (*c* 0.83, $CHCl_3$); IR 3568, 3456, 1706, 1236, 1132, 1096 cm^{-1}; ^1H NMR (500 MHz) major diastereomer δ_H 1.37 (3H, s), 1.39 (3H, s), 1.62−1.76 (3H, m), 1.95 (1H, m), 2.04 (1H, m), 2.21 (1H, m), 2.31 (1H, m), 2.44 (1H, m), 2.63 (1H, ddd, J = 5.7, 5.7, 11.0 Hz), 2.91 (1H, br s), 3.40 (3H, s), 3.48 (1H, dd, J = 1.3, 9.7 Hz), 3.59 (1H, dd, J = 2.5, 10.0 Hz), 3.74−3.82 (2H, m), 4.55 (1H, dd, J = 5.5, 5.5 Hz); minor diastereomer δ_H 1.35 (3H, s), 1.38 (3H, s), 1.62−1.76 (3H, m), 1.93−1.96 (2H, m), 2.09 (1H, m), 2.31 (1H, m), 2.44 (1H, m), 2.76 (1H, ddd, J = 5.0, 5.0, 10.1 Hz), 3.07 (1H, d, J = 3.9 Hz), 3.40 (3H, s, OMe), 3.50 (1H, dd, J = 1.9, 9.7 Hz), 3.62 (1H, dd, J = 2.8, 9.7 Hz), 3.79 (1H, m), 3.90 (1H, dd, J = 6.5, 7.9 Hz), 4.40 (1H, dd, J = 4.9, 6.5 Hz); ^{13}C NMR (125.7 MHz) major diastereomer δ_C 24.4 (CH_2), 27.3 (CH_2), 27.6 (2 × CH_3), 28.0 (CH_2), 42.1 (CH_2), 53.1 (CH), 59.2 (CH_3), 72.4 (CH), 73.8 (CH_2), 77.4 (CH), 78.5 (CH), 109.5 (C), 211.9 (C); minor diastereomer δ_C 23.9 (CH_2), 27.5 (CH_2), 27.6 (2 × CH_3), 29.6 (CH_2), 42.2 (CH_2), 53.2 (CH), 59.2 (CH_3), 72.2 (CH), 73.7 (CH_2), 77.9 (CH), 78.9 (CH), 108.9 (C), 212.4 (C); MS *m*/*z* (rel intensity) 257 (M^+ − Me, 7), 197 (M^+ − [$MeOCH_2CH(OH)$], 25), 174 (M^+ − cyclohexanone, 21), 139 (M^+ − [$MeOCH_2CH(OH)$ + Me_2C=O], 100), 59 ([Me_2C=OH]$^+$, 47); HRMS calcd for $C_{13}H_{21}O_5$, 257.1389; found, 257.1385; calcd for $C_8H_{11}O_2$, 139.0759; found, 139.0755. Anal. Calcd for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.62; H, 8.89.

(1*S*,1′*R*/*S*)-1,2-*O*-Isopropylidene-4,5-di-*O*-methyl-1-[2′-oxo-1′-cyclohexyl]-D-arabinitol (51). Isolated as an inseparable diastereomer mixture (7:3). Yellow oil; $[\alpha]_D$ −22 (*c* 0.08, $CHCl_3$); IR 3559, 1709, 1236, 1382, 1232, 1098 cm^{-1}; ^1H NMR (500 MHz) major diastereomer δ_H 1.37 (3H, s), 1.43 (3H, s), 1.65−1.71 (3H, m), 1.93 (1H, m), 2.04 (1H, m), 2.27 (1H, m), 2.40 (1H, m), 2.47 (1H, ddd, J = 5.4, 5.4, 11.4 Hz), 2.58 (1H, d, J = 8.4 Hz), 3.29 (1H, ddd, J = 1.4, 4.3, 8.5 Hz), 3.38 (3H, s), 3.43 (3H, s), 3.59 (1H, dd, J = 1.4, 10.4 Hz), 3.68 (1H, dd, J = 1.6, 8.3 Hz), 3.70 (1H, dd, J = 4.0, 10.2 Hz), 3.96 (1H, dd, J = 1.7, 7.9 Hz), 4.46 (1H, dd, J = 6.0, 7.8 Hz); minor diastereomer δ_H 1.38 (3H, s), 1.42 (3H, s), 1.65−1.71 (3H, m), 1.93−2.02 (2H, m), 2.07 (1H, m), 2.33 (1H, m), 2.65 (1H, d, J = 8.8 Hz), 2.69 (1H, ddd, J = 5.7, 5.7, 11.0 Hz), 3.29 (1H, m), 3.43 (3H, s), 3.44 (3H, s), 3.56 (1H, dd, J = 1.6, 8.7 Hz), 3.60 (1H, dd, J = 1.4, 10.4 Hz), 3.70 (1H, dd, J = 4.0, 10.2 Hz), 4.10 (1H, dd, J = 1.2, 8.6 Hz), 4.41 (1H, dd, J = 6.1, 8.4 Hz); ^{13}C NMR (125.7 MHz) major diastereomer δ_C 24.5 (CH_2), 27.0 (CH_3), 27.3 (CH_3), 27.4 (CH_2), 29.0 (CH_2), 42.3 (CH_2), 52.8 (CH), 58.0 (CH_3), 59.3 (CH_3), 68.2 (CH), 71.6 (CH_2), 74.6 (CH), 78.5 (CH), 80.5 (CH), 108.7 (C), 211.0 (C); minor diastereomer δ_C 24.3 (CH_2), 27.0 (CH_3), 27.1 (CH_3), 27.6 (CH_2), 29.5 (CH_2), 42.1 (CH_2), 53.3 (CH), 58.1 (CH_3), 59.3 (CH_3), 68.0 (CH), 71.2 (CH_2), 74.9 (CH), 78.5 (CH), 80.6 (CH), 108.6 (C), 211.0 (C); MS *m*/*z* (rel intensity) 301 (M^+ − Me, 4), 139 (M^+ − [$MeOCH_2CH(OMe)CHOH$ + Me_2C=O], 100), 59 ([Me_2C=OH]$^+$, 32); HRMS calcd for $C_{15}H_{25}O_6$, 301.1651; found, 301.1645; calcd for $C_8H_{11}O_2$, 139.0759; found, 139.0765. Anal. Calcd for $C_{16}H_{28}O_6$: C, 60.74; H, 8.92. Found: C, 60.71; H, 8.95.

(1*R*,1′*R*/*S*)-5-Deoxy-1,2-*O*-Isopropylidene-3-*O*-methyl-1-[2′-oxo-1′-cyclohexyl]-L-arabinitol (52). Isolated as an inseparable diastereomer mixture (3:2). Colorless oil; $[\alpha]_D$ +24 (*c* 0.36, $CHCl_3$); IR 3469, 1708, 1215, 1099, 1045 cm^{-1}; ^1H NMR (500 MHz) major diastereomer δ_H 1.24 (3H, d, J = 6.4 Hz), 1.35 (3H, s), 1.43 (3H, s), 1.57−1.74 (4H, m), 1.92−1.94 (2H, m), 2.28−2.33 (2H, m), 2.49 (1H, ddd, J = 5.3, 6.5, 10.4 Hz), 2.83 (1H, br s), 3.26 (1H, dd, J = 2.7, 5.5 Hz), 3.51 (3H, s), 4.04−4.09 (2H, m), 4.46 (1H, dd, J = 6.7, 7.2 Hz); minor diastereomer δ_H 1.26 (3H, d, J = 6.5 Hz), 1.35 (3H, s), 1.43 (3H, s), 1.57−1.73 (3H, m), 1.93 (1H, m), 1.96 (1H, m), 2.04 (1H, m), 2.32 (1H, m), 2.37 (1H, m), 2.71 (1H, ddd, J = 5.2, 6.2, 10.3 Hz), 2.83 (1H, br s), 3.13 (1H, dd, J = 1.7, 7.3 Hz), 3.51 (3H, s), 4.06 (1H, m), 4.16 (1H, dd, J = 1.6, 8.0 Hz), 4.53 (1H, dd, J = 5.0, 7.9 Hz); ^{13}C NMR (125.7 MHz) major diastereomer δ_C 20.0 (CH_3), 24.1 (CH_2), 26.8 (CH_3), 27.4 (CH_2), 27.7 (CH_3), 30.0 (CH_2), 42.4 (CH_2), 54.8 (CH), 59.0 (CH_3), 67.1 (CH), 75.4 (CH), 80.4 (CH), 82.0 (CH), 108.9 (C), 211.8 (C); minor diastereomer δ_C 20.1 (CH_3), 24.5 (CH_2), 26.6 (CH_3), 27.2 (CH_3), 27.6 (CH_2), 29.3 (CH_2), 42.3 (CH_2), 53.0 (CH), 59.0 (CH_3), 67.1 (CH), 75.2 (CH), 77.5 (CH), 81.7 (CH), 109.1 (C), 211.1 (C); MS *m*/*z* (rel intensity) 271 (M^+ − Me, 3), 139 (M^+ − [$MeCH(OH)CHOMe$ + Me_2C=O], 48), 89 ([$MeCH(OH)CHOMe$]$^+$, 100), 59 (Me_2C=OH, 49); HRMS calcd for $C_{14}H_{23}O_5$, 271.1545; found, 271.1546; calcd for $C_4H_9O_2$, 89.0603; found, 89.0602. Anal. Calcd for $C_{15}H_{26}O_5$: C, 62.91; H, 9.15. Found: C, 62.63; H, 8.99.

Oxidation of Hydroxyketones 50−52 to Diketones 53−55. Jones' reagent was added dropwise to a solution of the hydroxyketone (0.2 mmol) in dry acetone (4 mL) at 0 °C, until total conversion of the starting material was observed by TLC analysis (3−6 h). The reaction mixture was poured into a saturated aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic layers were dried as before, and the solvent was removed under vacuum. The residue was purified by chromatography on silica gel (hexanes/EtOAc), affording the diketones **53**, **54**, or **55**.

(1*R*,1′*R*/*S*)-3-Deoxy-1,2-*O*-isopropylidene-4-*O*-methyl-1-[2′-oxo-1′-cyclohexyl]-D-erythritol-3-one (53). Isolated as an inseparable diastereomer mixture (3:2). Colorless oil; $[\alpha]_D$ +10 (*c* 0.29, $CHCl_3$); IR 1734, 1710, 1451, 1384, 1161, 1101 cm^{-1}; ^1H NMR (500 MHz) major diastereomer δ_H 1.40 (3H, s), 1.43 (3H, s), 1.52 (1H, m), 1.60−1.66 (3H, m), 1.95 (1H, m), 2.06 (1H, m), 2.28 (1H, m), 2.41 (1H, m), 2.59 (1H, ddd, J = 5.8, 6.1, 11.2 Hz), 3.45 (3H, s), 4.15 (1H, d, J = 7.7 Hz), 4.35 (1H, d, J = 18.2 Hz), 4.42 (1H, d, J = 18.2 Hz), 4.50 (1H, dd, J = 6.4, 7.6 Hz); minor diastereomer δ_H 1.42 (6H, s), 1.52 (1H, m), 1.60−1.66 (3H, m), 1.95 (1H, m), 2.06 (1H, m), 2.28 (1H, m), 2.43 (1H, m), 2.77 (1H, ddd, J = 5.4, 6.2, 10.7 Hz), 3.44 (3H, s), 4.33 (1H, d, J = 18.2 Hz), 4.34 (1H, d, J = 7.7 Hz), 4.42 (1H, d, J = 18.2 Hz), 4.48 (1H, dd, J = 5.1, 7.3 Hz); ^{13}C NMR (125.7 MHz) major diastereomer δ_C 24.3 (CH_2), 26.1 (CH_3), 27.0 (CH_3), 27.5 (CH_2), 28.9 (CH_2), 41.9 (CH_2), 52.6 (CH), 59.3 (CH_3), 75.4 (CH_2), 76.6 (CH), 80.4 (CH), 110.6 (C), 205.1 (C), 210.4 (C); minor diastereomer δ_C 24.3 (CH_2), 26.7 (2 × CH_3), 27.0 (CH_2), 29.3 (CH_2), 42.1 (CH_2), 52.9 (CH), 59.3 (CH_3), 75.6 (CH_2), 76.0 (CH), 79.9 (CH), 110.5 (C), 205.5 (C), 210.4 (C); MS *m*/*z* (rel intensity) 270 (M^+, 2), 238 (M^+ − MeOH, 1), 212 (M^+ − Me_2C=O, 4), 197 (M^+ − $MeOCH_2CO$, 39), 139 (M^+ − [$MeOCH_2CO$ + Me_2C=O], 100); HRMS calcd for $C_{14}H_{22}O_5$, 270.1467; found, 270.1471; calcd for $C_8H_{11}O_2$, 139.0759; found, 139.0757. Anal. Calcd for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20. Found: C, 62.03; H, 8.40.

(1*S*,1′*R*/*S*)-3-Deoxy-1,2-*O*-isopropylidene-4,5-di-*O*-methyl-1-[2′-oxo-1′-cyclohexyl]-D-arabinitol-3-one (54). Isolated as an inseparable diastereomer mixture (3:1). Colorless oil; $[\alpha]_D$ +11 (*c* 0.10, $CHCl_3$); IR 1709, 1382, 1232, 1098, 1048 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) major diastereomer δ_H 1.41 (3H, s), 1.43 (3H, s), 1.61−1.77 (4H, m), 2.06 (1H, m), 2.17 (1H, m), 2.33 (1H, m), 2.41 (1H, m), 2.64 (1H, ddd, J = 6.3, 6.3, 12.3 Hz), 3.37 (3H, s), 3.52 (3H, s), 3.67 (1H, dd, J = 6.0, 10.7 Hz), 3.78 (1H, dd, J = 3.1, 10.7 Hz), 4.22 (1H, dd, J = 3.1, 6.0 Hz), 4.36 (1H, d, J = 7.2 Hz), 4.51 (1H, dd, J = 6.9, 7.1 Hz); minor diastereomer δ_H 1.42 (3H, s), 1.43 (3H, s), 1.61−1.77 (4H, m), 2.17 (1H, m), 2.31−2.37 (2H, m), 2.48 (1H, m), 2.82 (1H, m), 3.37 (3H, s), 3.51 (3H, s), 3.69 (1H, dd, J = 5.5, 10.1 Hz), 3.77 (1H, dd, J = 3.9, 10.1 Hz), 4.20 (1H, dd, J = 3.2, 5.6 Hz), 4.53 (1H, s), 4.54 (1H, s); ^{13}C NMR (125.7 MHz, $CDCl_3$) major diastereomer δ_C 24.3 (CH_2), 26.2

(CH_3), 27.0 (CH_2), 27.3 (CH_3), 29.4 (CH_2), 41.9 (CH_2), 53.7 (CH), 58.7 (CH_3), 59.3 (CH_3), 72.0 (CH_2), 76.3 (CH), 79.7 (CH), 85.2 (CH), 110.6 (C), 205.8 (C), 210.7 (C); minor diastereomer δ_C 24.1 (CH_2), 26.2 (CH_3), 26.9 (CH_3), 27.7 (CH_2), 29.3 (CH_2), 42.2 (CH_2), 52.7 (CH), 58.8 (CH_3), 59.3 (CH_3), 72.0 (CH_2), 76.4 (CH), 78.9 (CH), 84.7 (CH), 110.6 (C), 206.0 (C), 210.8 (C); MS *m/z* (rel intensity) 299 (M^+ − Me, 1), 256 (M^+ − Me_2C═O, 1), 139 (M^+ − [MeOCH$_2$CH(OMe)CO + Me_2C═O], 100), 59 ([Me_2C═OH]$^+$, 22); HRMS calcd for $C_{15}H_{23}O_6$, 299.1495; found, 299.1483; calcd for $C_8H_{11}O_2$, 139.0759; found, 139.0754. Anal. Calcd for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34. Found: C, 61.31; H, 8.19.

(1*R*,1′*R*/*S*)-4,5-Dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-1-[2′-oxo-1′-cyclohexyl]-L-arabinitol-4-one (55). Isolated as an inseparable diastereomer mixture (2:1). Colorless oil; $[\alpha]_D$ +92 (*c* 0.20, $CHCl_3$); IR 1707, 1450, 1216, 1133, 1075, 1034 cm^{-1}; ^{1}H NMR (500 MHz) major diastereomer δ_H 1.32 (3H, s), 1.43 (3H, s), 1.53−1.60 (3H, m), 1.92 (1H, m), 2.08 (1H, m), 2.24 (3H, s), 2.34 (1H, m), 2.37−2.41 (2H, m), 2.50 (1H, m), 3.51 (3H, s), 3.88 (1H, d, *J* = 2.9 Hz), 4.01 (1H, dd, *J* = 2.9, 6.2 Hz), 4.39 (1H, dd, *J* = 6.2, 8.2 Hz); minor diastereomer δ_H 1.33 (3H, s), 1.43 (3H, s), 1.53−1.60 (3H, m), 1.97 (1H, m), 2.08 (1H, m), 2.16 (1H, m), 2.24 (3H, s), 2.37−2.41 (2H, m), 2.79 (1H, m), 3.52 (3H, s), 3.74 (1H, d, *J* = 2.6 Hz), 4.06 (1H, dd, *J* = 2.5, 7.7 Hz), 4.61 (1H, dd, *J* = 4.8, 7.7 Hz); ^{13}C NMR (125.7 MHz) major diastereomer δ_C 24.6 (CH_2), 26.7 (CH_3), 27.2 (CH_3), 27.4 (CH_3), 27.8 (CH_2), 30.8 (CH_2), 42.6 (CH_2), 55.3 (CH), 59.5 (CH_3), 75.5 (CH), 78.9 (CH), 86.4 (CH), 109.6 (C), 211.2 (C), 211.8 (C); minor diastereomer δ_C 24.4 (CH_2), 26.5 (CH_3), 27.1 (CH_3), 27.3 (CH_3), 27.4 (CH_2), 28.2 (CH_2), 42.2 (CH_2), 53.0 (CH), 59.4 (CH_3), 74.5 (CH), 78.5 (CH), 86.1 (CH), 109.0 (C), 211.0 (C), 211.5 (C); MS *m/z* (rel intensity) 269 (M^+ − Me, 2), 252 (M^+ − MeOH, 6), 241 (M^+ − MeCO, 13), 197 (M^+ − MeCOCHOMe, 57), 139 (M^+ − [MeCOCHOMe + Me_2C═O], 100), 87 ([MeCOCHOMe]$^+$, 50); HRMS calcd for $C_{14}H_{21}O_5$, 269.1389; found, 269.1379; calcd for $C_8H_{11}O_2$, 139.0759; found, 139.0762. Anal. Calcd for $C_{15}H_{24}O_5$: C, 63.36; H, 8.51. Found: C, 63.31; H, 8.39.

Reductive Amination of Diketones 53−55. Synthesis of Chiral Decahydroquinolines 56−59 and Benzodiazepines 60 and 61. To a solution of the diketone (0.1 mmol), dry benzylamine (11 μL, 0.1 mmol), and AcOH (6μL, 0.1 mmol) in dry MeOH (2 mL), at 60 °C, was added dropwise a solution of $NaBH_3CN$ (8 mg, 0.12 mmol) in dry MeOH (0.25 mL). The resulting mixture was stirred at 60 °C for 24 h, cooled to room temperature, poured into 10% aqueous NaOH, and extracted with CH_2Cl_2. The organic layer was dried, evaporated, and purified as usual to yield the decahydroquinolines **56**−**59** (from diketones **53** and **54**) and the benzodiazepines **60** and **61** (from diketone **55**).

***N*-Benzyl-(2*R*,3*R*,4*R*,4a*S*,8a*R*)-3,4-*O*-Isopropylidene-2-methoxymethyl-4a,8a-decahydroquinoline (56) and *N*-Benzyl-(2*R*,3*R*,4*R*,4a*R*,8a*S*)-3,4-*O*-Isopropylidene-2-methoxymethyl-4a,8a-decahydroquinoline (57).** Generated from diketone **53** (43% of product **56** and 12% of its isomer **57**). Compound **56**: colorless oil; $[\alpha]_D$ +20 (*c* 0.14, $CHCl_3$); IR 3084, 3063, 1452, 1372, 1231, 1106, 1092 cm^{-1}; ^{1}H NMR (500 MHz) δ_H 1.05 (1H, m), 1.34 (1H, m), 1.38−1.43 (2H, m), 1.45 (3H, s), 1.46 (3H, s), 1.52 (1H, m), 1.72−1.80 (2H, m), 1.94 (1H, m), 2.09 (1H, m), 2.75 (1H, ddd, *J* = 4.7, 4.7, 12.5 Hz), 3.13 (1H, ddd, *J* = 1.9, 6.5, 9.6 Hz), 3.26 (3H, s), 3.36 (1H, dd, *J* = 9.0, 9.7 Hz), 3.51 (1H, dd, *J* = 6.6, 10.5 Hz), 3.73 (1H, dd, *J* = 1.8, 10.5 Hz), 3.77 (1H, d, *J* = 14.7 Hz), 3.83 (1H, dd, *J* = 8.8, 11.7 Hz), 4.05 (1H, d, *J* = 14.8 Hz), 7.22 (1H, dd, *J* = 7.2, 7.3 Hz), 7.30 (2H, dd, *J* = 7.3, 7.7 Hz), 7.36 (2H, d, *J* = 7.2 Hz); ^{13}C NMR (125.7 MHz) δ_C 20.5 (CH_2), 20.6 (CH_2), 25.4 (CH_2), 26.4 (CH_2), 26.8 (CH_3), 27.2 (CH_3), 38.1 (CH), 51.8 (CH_2), 57.7 (CH), 58.5 (CH), 58.6 (CH_3), 72.4 (CH_2), 76.2 (CH), 78.4 (CH), 109.5 (C), 126.5 (CH), 127.9 (2 × CH), 128.1 (2 × CH), 141.4 (C); MS *m/z* (rel intensity) 345 (M^+, 2), 330 (M^+ − Me, 3), 300 (M^+ − $MeOCH_2$, 100), 242 (M^+ − [$MeOCH_2$ + Me_2C═O], 79), 91 ([$PhCH_2$]$^+$, 74); HRMS calcd for $C_{21}H_{31}NO_3$, 345.2304; found, 345.2308; calcd for $C_{19}H_{26}NO_2$, 300.1964; found, 300.1963. Anal. Calcd for $C_{21}H_{31}NO_3$: C, 73.01; H, 9.04; N, 4.05. Found: C, 72.97; H, 9.09; N, 4.16. Compound **57**: colorless oil; $[\alpha]_D$ +37 (*c* 0.10, $CHCl_3$); IR 3081, 3064, 1454, 1373, 1120 cm^{-1}; ^{1}H NMR (500 MHz) δ_H 1.10 (1H, m), 1.22−1.28 (2H, m), 1.48 (3H, s), 1.49 (3H, s), 1.60−1.80 (3H, m), 2.00 (1H, m), 2.10−2.13 (2H, m), 2.28 (1H, m), 2.92 (1H, dd, *J* = 3.4, 9.7 Hz), 3.18 (1H, m), 3.21 (3H, s), 3.50 (1H, dd, *J* = 9.3, 9.4 Hz), 3.55 (1H, dd, *J* = 4.7, 10.5 Hz), 3.73 (1H, d, *J* = 10.5 Hz), 3.90 (1H, d, *J* = 17.2 Hz), 4.14 (1H, d, *J* = 17.1 Hz), 7.24 (1H, dd, *J* = 7.1, 7.2 Hz), 7.32 (2H, dd, *J* = 7.4, 7.6 Hz), 7.42 (2H, d, *J* = 7.5 Hz); ^{13}C NMR (125.7 MHz) δ_C 24.8 (CH_2), 25.6 (CH_2), 26.9 (CH_3), 27.1 (CH_3), 28.9 (CH_2), 31.5 (CH_2), 44.5 (CH), 52.8 (CH_2), 58.8 (CH_3), 64.8 (CH), 66.1 (CH), 71.9 (CH_2), 76.8 (CH), 82.7 (CH), 110.0 (C), 126.1 (CH), 127.5 (2 × CH), 128.0 (2 × CH), 142.2 (C); MS *m/z* (rel intensity) 345 (M^+, 1), 330 (M^+ − Me, 4), 300 (M^+ − $MeOCH_2$, 99), 242 (M^+ − [$MeOCH_2$ + Me_2C═O], 80), 91 ([$PhCH_2$]$^+$, 100); HRMS calcd for $C_{21}H_{31}NO_3$, 345.2304; found, 345.2297; calcd for C_7H_7, 91.0548; found, 91.0551. Anal. Calcd for $C_{21}H_{31}NO_3$: C, 73.01; H, 9.04; N, 4.05. Found: C, 72.94; H, 9.25; N, 3.74.

***N*-Benzyl-(2*S*,3*S*,4*S*,4a*R*,8a*S*)-3,4-*O*-Isopropylidene-2-[(1′*S*)-2′-dimethoxyethyl)-4a,8a-decahydroquinoline (58) and *N*-Benzyl-(2*S*,3*S*,4*S*,4a*S*,8a*R*)-3,4-*O*-Isopropylidene-2-[(1′*S*)-2′-dimethoxyethyl)-4a,8a-decahydroquinoline (59).** Generated from diketone **54** (10% of product **58** and 41% of its isomer **59**). Compound **58**: colorless oil; $[\alpha]_D$ −48 (*c* 0.12, $CHCl_3$); IR 3084, 3064, 1493, 1373, 1232, 1120, 1074 cm^{-1}; ^{1}H NMR (500 MHz) δ_H 1.13 (1H, m), 1.25−1.42 (3H, m), 1.34 (3H, s), 1.35 (3H, s), 1.53 (1H, m), 1.65−1.75 (2H, m), 1.98 (1H, m), 2.35 (1H, m), 2.63 (1H, ddd, *J* = 4.8, 5.0, 12.4 Hz), 3.26 (1H, dd, *J* = 4.8, 10.7 Hz), 3.36 (3H, s), 3.47 (3H, s), 3.57 (1H, m), 3.60 (1H, dd, *J* = 9.1, 10.3 Hz), 3.66 (1H, dd, *J* = 4.3, 10.3 Hz), 3.74 (1H, ddd, *J* = 4.6, 4.7, 6.8 Hz), 3.77 (1H, d, *J* = 16.1 Hz), 3.79 (1H, dd, *J* = 3.0, 9.1 Hz), 4.42 (1H, d, *J* = 15.7 Hz), 7.20 (1H, dd, *J* = 7.1, 7.1 Hz), 7.30 (2H, dd, *J* = 7.4, 7.8 Hz), 7.34 (2H, d, *J* = 7.4 Hz); ^{13}C NMR (125.7 MHz) δ_C 20.3 (CH_2), 26.0 (CH_2), 26.2 (CH_2), 26.9 (CH_2), 27.0 (CH_3), 27.1 (CH_3), 34.9 (CH), 52.7 (CH_2), 58.4 (CH), 58.8 (CH), 59.0 (CH_3), 59.3 (CH_3), 73.5 (CH_2), 75.1 (CH), 77.8 (CH), 79.9 (CH), 108.5 (C), 126.3 (CH), 127.2 (2 × CH), 128.2 (2 × CH), 141.7 (C); MS *m/z* (rel intensity) 374 (M^+ − Me, 4), 300 (M^+ − $MeOCH_2CHOMe$, 98), 242 (M^+ − [$MeOCH_2CHOMe$ + Me_2C═O], 99), 91 ([$PhCH_2$]$^+$, 100); HRMS calcd for $C_{22}H_{32}NO_4$, 374.2331; found, 374.2338; calcd for $C_{16}H_{20}NO$, 242.1545; found, 242.1555; calcd for C_7H_7, 91.0548; found, 91.0552. Anal. Calcd for $C_{23}H_{35}NO_4$: C, 70.92; H, 9.06; N, 3.60. Found: C, 70.72; H, 9.12; N, 3.99. Compound **59**: colorless oil; $[\alpha]_D$ −25 (*c* 0.11, $CHCl_3$); IR 3064, 3035, 1452, 1382, 1232, 1164, 1101, 1079 cm^{-1}; ^{1}H NMR (500 MHz) δ_H 1.05 (1H, m), 1.25−1.45 (3H, m), 1.45 (6H, s), 1.60 (1H, m), 1.67 (1H, m), 1.76 (1H, m), 1.96 (1H, m), 2.13 (1H, m), 2.71 (1H, ddd, *J* = 4.7, 4.7, 12.5 Hz), 3.22 (1H, d, *J* = 9.9 Hz), 3.36 (3H, s), 3.37 (3H, s), 3.50 (1H, dd, *J* = 9.1, 9.8 Hz), 3.61 (1H, dd, *J* = 4.8, 8.9 Hz), 3.71 (1H, ddd, *J* = 1.5, 4.7, 5.2 Hz), 3.73 (1H, dd, *J* = 4.6, 9.2 Hz), 3.81 (1H, dd, *J* = 8.8, 11.7 Hz), 3.86 (1H, d, *J* = 15.5 Hz), 4.05 (1H, d, *J* = 15.5 Hz), 7.22 (1H, dd, *J* = 7.1, 7.2 Hz), 7.30 (2H, dd, *J* = 7.3, 7.7 Hz), 7.34 (2H, d, *J* = 7.2 Hz); ^{13}C NMR (125.7 MHz) δ_C 20.5 (CH_2), 21.9 (CH_2), 25.6 (CH_2), 26.5 (CH_2), 27.0 (CH_3), 27.2 (CH_3), 37.3 (CH), 52.1 (CH_2), 58.0 (CH), 58.2 (CH_3), 58.9 (CH_3), 59.0 (CH), 73.1 (CH_2), 76.6 (CH), 77.6 (CH), 80.9 (CH), 109.2 (C), 126.5 (CH), 127.5 (2 × CH), 128.3 (2 × CH), 141.1 (C); MS *m/z* (rel intensity) 389 (M^+, <1), 344 (M^+ − $MeOCH_2$, 1), 300 (M^+ − $MeCH_2CHOMe$, 88), 242 (M^+ − [$MeOCH_2CHOMe$ + Me_2C═O], 73), 91 ([$PhCH_2$]$^+$, 100); HRMS calcd for $C_{23}H_{35}NO_4$, 389.2566; found, 389.2550; calcd for C_7H_7, 91.0547; found, 91.0548. Anal. Calcd for $C_{23}H_{35}NO_4$: C, 70.92; H, 9.06; N, 3.60. Found: C, 70.94; H, 9.14; N, 3.58.

***N*-Benzyl-(2*R*,3*S*,4*S*,5*R*,5a*S*,9a*R*)-4,5-*O*-Isopropylidene-2-methyl-3-methoxy-5a,9a-decahydro-1*H*-benzo[*b*]azepine (60) and *N*-Benzyl-(2*S*,3*S*,4*S*,5*R*,5a*R*,9a*S*)-4,5-*O*-isopropylidene-2-methyl-3-meth-**

oxy-5a,9a-decahydro-1*H*-benzo[*b*]azepine (61). Generated from diketone **55** (22% of product **60** and 17% of its isomer **61**). Compound **60**: colorless oil; $[\alpha]_D$ +55 (*c* 0.12, $CHCl_3$); IR 3081, 3064, 1506, 1457, 1369 cm^{-1}; ^1H NMR (500 MHz) δ_H 1.10−1.65 (5H, m), 1.20 (3H, d, J = 6.9 Hz), 1.41 (3H, s), 1.43 (3H, s), 1.72−1.78 (2H, m), 2.12 (1H, m), 2.30 (1H, m), 2.60 (1H, ddd, J = 4.3, 4.5, 12.5 Hz), 3.31 (1H, dd, J = 4.6, 5.8 Hz), 3.39 (1H, dddd, J = 4.5, 6.8, 6.9, 6.9 Hz), 3.47 (3H, s), 3.64 (1H, d, J = 16.1 Hz), 3.87 (1H, dd, J = 5.9, 9.2 Hz), 3.94 (1H, dd, J = 9.4, 10.5 Hz), 4.28 (1H, d, J = 16.2 Hz), 7.20 (1H, m), 7.25−7.33 (4H, m); ^{13}C NMR (125.7 MHz) δ_C 17.7 (CH_3), 21.4 (CH_2), 26.6 (CH_2), 27.1 (CH_3), 27.2 (CH_3), 27.5 (CH_2), 28.2 (CH_2), 38.4 (CH), 50.4 (CH), 50.8 (CH_2), 57.1 (CH), 59.5 (CH_3), 74.0 (CH), 86.3 (CH), 87.6 (CH), 108.3 (C), 126.2 (CH), 127.4 (2 × CH), 128.1 (2 × CH), 142.5 (C); MS *m*/*z* (rel intensity) 359 (M^+, 4), 344 (M^+ − Me, 68), 328 (M^+ − MeO, 67), 270 (M^+ − [MeO + Me_2C═O], 30), 91 ($[PhCH_2]^+$, 100); HRMS calcd for $C_{22}H_{33}NO_3$, 359.2460; found, 359.2448; calcd for C_7H_7, 91.0548; found, 91.0545. Anal. Calcd for $C_{22}H_{33}NO_3$: C, 73.50; H, 9.25; N, 3.90. Found: C, 73.72; H, 9.12; N, 3.99. Compound **61**: colorless oil; $[\alpha]_D$ +14 (*c* 0.12, $CHCl_3$); IR 3084, 3062, 1456, 1371, 1235, 1152, 1090 cm^{-1}; ^1H NMR (500 MHz) δ_H 1.17 (3H, d, J = 6.6 Hz), 1.20−1.60 (5H, m), 1.45 (3H, s), 1.46 (3H, s), 1.80 (1H, m), 1.85−1.95 (3H, m), 2.82 (1H, m), 2.92 (1H, dddd, J = 6.9, 6.9, 7.0, 7.1 Hz), 3.10 (1H, dd, J = 8.8, 9.0 Hz), 3.54 (3H, s), 3.87−3.94 (3H, m), 4.09 (1H, dd, J = 9.1, 9.4 Hz), 7.21 (1H, m), 7.23−7.31 (4H, m); ^{13}C NMR (125.7 MHz) δ_C 19.0 (CH_3), 20.2 (CH_2), 26.5 (CH_2), 27.2 (CH_3), 27.3 (CH_3), 27.6 (CH_2), 29.3 (CH_2), 40.1 (CH), 59.8 (CH_2), 60.1 (CH_3), 61.1 (CH), 61.4 (CH), 77.8 (CH), 81.8 (CH), 86.4 (CH), 107.9 (C), 126.7 (CH), 127.9 (2 × CH), 128.2 (2 × CH), 141.7 (C); MS *m*/*z* (rel intensity) 359 (M^+, 5), 328 (M^+ − MeO, 66), 91 ($[PhCH_2]^+$, 100); HRMS calcd for $C_{22}H_{33}NO_3$, 359.2460; found, 359.2470; calcd for C_7H_7, 91.0548; found, 91.0552. Anal. Calcd for $C_{22}H_{33}NO_3$: C, 73.50; H, 9.25; N, 3.90. Found: C, 73.14; H, 9.32; N, 3.89.

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Supporting Information Available: Preparation of substrate **22**, including spectroscopic data of the synthetic intermediates and the final product. Procedures for the allylation and alkylation reactions, and spectroscopic data of phenyl ketones **20**, **21**, **27**, butenolides **28**−**33** and **37**−**39**, and cyclohexanones **46**, **47**, and **49**. ^1H and ^{13}C NMR spectra for acetoxy acetal **24**, allyl derivatives **18** and **19**, phenyl ketones **20**, **21**, **26**, and **27**, butenolides **28**−**39**, cyclohexanones **46**−**48** and **50**−**55**, alkaloid analogues **56**−**61**, and substrates **63**−**65** and **22**. This material is available free of charge via the Internet at http://pubs.acs.org.

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