JOC*Article*

β-Fragmentation of Primary Alkoxyl Radicals versus Hydrogen Abstraction: Synthesis of Polyols and α,*ω*-Differently Substituted Cyclic Ethers from Carbohydrates

Alicia Boto, Dácil Hernández, Rosendo Hernández,* and Ernesto Suárez*

Instituto de Productos Naturales y Agrobiología del C.S.I.C., Carretera de La Esperanza 3, 38206 La Laguna, Tenerife, Spain

rhernandez@ipna.csic.es

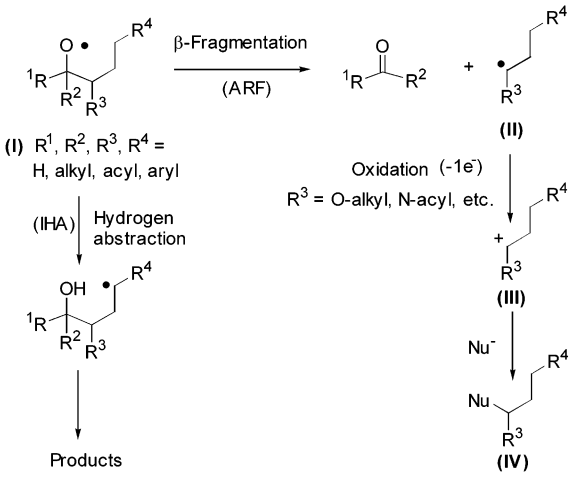
Received April 7, 2003

The *β*-fragmentation of primary alkoxyl radicals, described in many cases as low-yielding and plagued by side reactions, can proceed in satisfactory yields using carbohydrate substrates. The only reaction that can compete significantly with the *β*-scission is the intramolecular hydrogen abstraction. The ratio of *β*-fragmentation to hydrogen abstraction can be varied according to the reaction conditions, the stereochemistry of the substituents (e.g., α- or *β*-anomeric substituents), and the protecting groups chosen. The carbohydrate substrates are easily prepared, and the mild reaction conditions are compatible with most functional groups. The *β*-scission reaction provides an expedient way toward shorter and less common sugar series and also toward α,*ω*-differently substituted cyclic ethers. These units are useful building blocks and are present in many natural products with interesting biological activity.

Introduction

The *β*-fragmentation of alkoxyl radicals (ARF) (Scheme 1) is a useful synthetic methodology for the synthesis of a wide range of compounds, including medium- and large-sized rings, heterocycles, halogenated compounds, etc.[1] For instance, the syntheses of natural products[2,3] such as deoxyvernolepin,[2b,3f] cyclophellitol,[2i,o] rapamycin,[3k] and muscone[3q] used a *β*-scission as the key step. This fragmentation takes place easily when a tertiary alkoxyl radical is generated from the corresponding alcohol. However, with secondary or primary alkoxyl radicals the fragmentation usually competes with other reactions, such as intramolecular hydrogen abstraction (IHA),[4,5] addition to double bonds,[6] or oxidation.[1j] In the case of primary alkoxyl radicals (I, $R^1 = R^2 = H$) the scission is usually a very minor process, unless the resultant radical (II) is stabilized in some way, and hence has been seldom used in synthesis.

SCHEME 1. *β*-Fragmentation of Primary Alkoxyl Radicals ($R^1 = R^2 = H$) versus Hydrogen Abstraction



To provide stabilization to the C-radical (II), some functional groups R^3 such as aromatic rings, carbonyl groups, and heteroatoms could be used. When the C-radical is stabilized by heteroatoms,[7] it can evolve under oxidative conditions to a carbenium ion (III),[8] thus

(1) (a) Zhdankin, V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523−2584. (b) Hartung, J.; Gottwald, T.; Spehar, K. *Synthesis* **2002**, 1469−1498. (c) Togo, H.; Katohgi, M. *Synlett* **2001**, 565−581. (d) Suárez, E.; Rodríguez, M. S. In *Radicals in Organic Synthesis;* Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 2, pp 440−454. (e) Zhang, W. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 2, pp 234−245. (f) McCarroll, A. J.; Walton, J. C. *Angew. Chem., Int. Ed.* **2001**, *40*, 2224−2248. (g) Wirth, T.; Hirt, U. H. *Synthesis* **1999**, 1271−1287. (h) Yet, L. *Tetrahedron* **1999**, *55*, 9349−9403. (i) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic: New York, 1997. (j) Brun, P.; Waegell, B. In *Reactive Intermediates*; Abramovitch, R. A., Ed.; Plenum Press: New York, 1983; Vol. 3, pp 367−426. (k) See also: Wilsey, S.; Dowd, P.; Houk, K. N. *J. Org. Chem.* **1999**, *64*, 8801−8811 and references therein.

(2) For recent examples, see: (a) Deng, Y.; Snyder, J. K. *J. Org. Chem.* **2002**, *67*, 2864−2873. (b) Barrero, A. F.; Oltra, J. E.; Alvarez, M.; Rosales, A. *J. Org. Chem.* **2002**, *67*, 5461−5469. (c) Weavers, R. T. *J. Org. Chem.* **2001**, *66*, 6453−6461. (d) Wang, X.; Porco, J. A., Jr. *J. Org. Chem.* **2001**, *66*, 8215−8221. (e) Yoshimitsu, T.; Yanagisawa, S.; Nagaoka, H. *Org. Lett.* **2000**, *2*, 3751−3754. (f) Boto, A.; Hernández, R.; Suárez, A. *Tetrahedron Lett.* **2000**, *41*, 2899−2902. (g) Barrero, A. F.; Oltra, J. E.; Alvarez, M. *Tetrahedron Lett.* **2000**, *41*, 7639−7643. (h) Wipf, P.; Li, W. *J. Org. Chem.* **1999**, *64*, 4576−4577. (i) Mehta, G.; Mohal, N. *Tetrahedron Lett.* **1999**, *40*, 5791−5794. (j) Rigby, J. H.; Meyer, J. H. *Synlett* **1999**, 860−862. (k) Wipf, P.; Li, W. *J. Org. Chem.* **1999**, *64*, 4576−4577. (l) Armas, P.; García-Tellado, F.; Marrero-Tellado, J. J.; Robles, J. *Tetrahedron Lett.* **1998**, *39*, 131−134. (m) Lautens, M.; Blackwell, J. *Synthesis* **1998**, 537−546. (n) Crimmins, M. T.; Wang, Z.; McKerlie, L. A. *J. Am. Chem. Soc.* **1998**, *120*, 1747−1756. (o) Ziegler, F. E.; Wang, Y. *J. Org. Chem.* **1998**, *63*, 7920−7930.

10.1021/jo034442f CCC: $25.00
Published on Web 05/28/2003

making the fragmentation process irreversible. We reasoned that by carrying out the scission of primary alkoxyl radicals in carbohydrate chains (Figure 1, eq 1), the resultant radical would be stabilized by the adjacent oxygen functions and under oxidative conditions would evolve to an oxycarbenium ion, which could be trapped by nucleophiles. If this strategy worked, it would be a direct way to reduce by one carbon the chain length of polyols (eq 1) and to transform carbohydrates into shorter, less common series.[8,9] Other compounds that would be easily achieved are α,ω-differently substituted tetrahydrofuran or tetrahydropyran rings (Figure 1, eq 2). These heterocycles are present in a variety of natural products[10] such as marine polyethers,[10a,k,l,q,r] alkaloids,[10i,j]

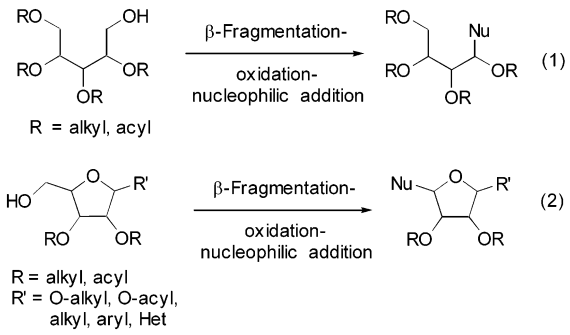


FIGURE 1. Synthetic use of the β-scission of primary alkoxyl radicals in polyols and carbohydrates.

terpenoids,[10c−h] acetogenins,[10u] and pheromones,[10x] many of which have potent biological activities.

In our research group we have developed the system diacetoxyiodobenzene (DIB) and iodine, or iodosylbenzene (PhIO) and iodine, to generate alkoxyl radicals from alcohols.[1d,8] The reaction conditions are mild, compatible with many functional groups, and hence very suitable to generate alkoxyl radicals from carbohydrate substrates. If the β-fragmentation takes place, the initial C-radical can be easily oxidized by excess reagent into an oxycarbenium ion. The feasibility of this approach and the synthesis of polyol derivatives and cyclic ethers with different substituents at the α,ω-positions is reported herein.

Results and Discussion

Synthesis of Precursors for the Fragmentation-Oxidation Reaction. To study the ARF reaction of primary alkoxyl radicals, substrates **1**−**7** were synthesized (Figure 2). In compound **1** the alkoxyl radical would be formed in a chain with more rotational freedom than in the rest of the substrates. Compounds **2** and **3** allow us to compare the fragmentation of anomeric alkoxyl radicals versus primary alkoxyl radicals. Substrates **4**−**7** are relatively rigid bicyclic systems, with different protecting groups in the anomeric position. Compounds **6** and **7** have a different C_1 stereochemistry, to study the competition between C_1-H abstraction and β-fragmentation.

(3) (a) For other interesting examples, see: Boto, A.; Freire, R.; Hernández, R.; Suárez, E.; Rodríguez, M. S. *J. Org. Chem.* **1997**, *62*, 2975−2981. (b) Oh, J. *Tetrahedron Lett.* **1997**, *38*, 3249−3250. (c) Banwell, M. G.; Cameron, J. M. *Tetrahedron Lett.* **1996**, *37*, 525−526. (d) Suginome, H.; Kondoh, T.; Gogonea, C.; Singh, V.; Goto, H.; Osawa, E. *J. Chem. Soc., Perkin Trans. 1* **1995**, 69−81. (e) Kim, H.; Ziani-Cherif, C.; Oh, J.; Cha, J. K. *J. Org. Chem.* **1995**, *60*, 729−793. (f) Hernández, R.; Rodríguez, M. S.; Velázquez, S. M.; Suárez, E. *J. Org. Chem.* **1994**, *59*, 6395−6403. (g) Suginome, H.; Nakayama, Y. *Tetrahedron* **1994**, *50*, 7771−7782. (h) Lee, J.; Oh, J.; Jin, S.-j.; Choi, J.-R.; Atwood, J. L.; Cha, J. K. *J. Org. Chem.* **1994**, *59*, 6955−6964. (i) Kobayashi, K.; Kanno, Y.; Seko, S.; Suginome, H. *J. Chem. Soc., Perkin Trans. 1* **1993**, 825−829. (j) Mowbray, C. E.; Pattenden, G. *Tetrahedron Lett.* **1993**, *34*, 127−130. (k) Hayward, C. M.; Fisher, M. J.; Yohannes, D.; Danishefsky, S. J. *Tetrahedron Lett.* **1993**, *34*, 3989−3992. (l) Chu-Moyer, M. Y.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1992**, *114*, 8333−8334. (m) Orito, K.; Yorita, K.; Suginome, H. *Tetrahedron Lett.* **1991**, *32*, 5999−6002. (n) Mehta, G.; Krishnamurthy, N.; Karra, S. R. *J. Am. Chem. Soc.* **1991**, *113*, 5765−5775. (o) Stork, G.; Mah, R. *Tetrahedron Lett.* **1989**, *30*, 3609−3612. (p) Suginome, H.; Yamada, S. *Chem. Lett.* **1988**, 245−248. (q) Suginome, H.; Yamada, S. *Tetrahedron Lett.* **1987**, *28*, 3963−3966. (r) Schreiber, S. L. *J. Am. Chem. Soc.* **1980**, *102*, 6163−6165. (s) Oh, J.; Lee, J.; Jin, S.-j.; Cha, J. K. *Tetrahedron Lett.* **1994**, *35*, 3449−3452. (t) Snider, B. B.; Kwon, T. *J. Org. Chem.* **1992**, *57*, 2399−2410.

(4) (a) Feray, L.; Kuznetsov, N.; Renaud, P. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 2, pp 246−278. (b) Robertson, J.; Pillai, J.; Lush, R. K. *Chem. Soc. Rev.* **2001**, *30*, 94−103. (c) Majetich, G.; Wheless, K. *Tetrahedron* **1995**, *51*, 7095−7129 and references therein.

(5) (a) Aubele, D. L.; Floreancig, P. E. *Org. Lett.* **2002**, *4*, 3443−3446. (b) Crich, D.; Huang, X.; Newcomb, M. *J. Org. Chem.* **2000**, *65*, 523−529. (c) Chatgilialoglu, C.; Gimisis, T.; Spada, G. P. *Chem.−Eur. J.* **1999**, 2866−2876. (d) Allen, P. A.; Brimble, M. A.; Prabaharan, H. *Synlett* **1999**, 295−298. (e) Petrovic, G.; Saicic, R. N.; Cekovic, Z. *Synlett* **1999**, 635−637. (f) Frey, B.; Wells, A. P.; Rogers, D. H.; Mander, L. N. *J. Am. Chem. Soc.* **1998**, *120*, 1914−1915. (g) Tsunoi, S.; Ryu, I.; Okuda, T.; Tanaka, M.; Komatsu, M.; Sonoda, N. *J. Am. Chem. Soc.* **1998**, *120*, 8692−8701. (h) Dorta, R. L.; Martín, A.; Salazar, J. A.; Suárez, E.; Prangé, T. *J. Org. Chem.* **1998**, *63*, 2251−2261. (i) Paquette, L. A.; Sun, L.-Q.; Friedrich, D.; Savage, P. B. *J. Am. Chem. Soc.* **1997**, *119*, 8438−8450. (j) Burke, S. D.; Kort, M. E.; Strickland, S. M. S.; Organ, H. M.; Silks, L. A. *Tetrahedron Lett.* **1994**, *35*, 1503−1506. (k) Danishefsky, S. J.; Armistead, D. M.; Wincott, F. E.; Selnick, H. G.; Hungate, R. *J. Am. Chem. Soc.* **1989**, *111*, 2967−2980. (l) Titouani, S. L.; Lavergne, J.-P.; Viallefont, P.; Jacquier, R. *Tetrahedron* **1980**, *36*, 2961−2965.

(6) (a) Hartung, J. *Eur. J. Org. Chem.* **2001**, 619−632. (b) Hartung, J. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 2, pp 427−439. (c) For recent examples, see: Hartung, J.; Kneuer, R. *Eur. J. Org. Chem.* **2000**, 1677−1683. (d) Hartung, J.; Kneuer, R.; Spehar, K. *Chem. Commun.* **2001**, 799−800.

(7) (a) Buckmelter, A. J.; Rychnovsky, S. D. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 2, pp 334−349. (b) Pearce, A. J.; Mallet, J.-M.; Sinaÿ, P. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 2, pp 538−577.

(8) (a) Boto, A.; Hernández, R.; Suárez, E. *Tetrahedron Lett.* **2001**, *42*, 9167−9170. (b) Adinolfi, M.; Barone, G.; Iadonisi, A. *Synlett* **1999**, 65−66. (c) de Armas, P.; Francisco, C. G.; Suárez, E. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 772−774. (d) Inanaga, J.; Sigimoto, Y.; Yokoyama, Y.; Hanamoto, T. *Tetrahedron Lett.* **1992**, *33*, 8109−8112.

(9) (a) Hartung, J.; Gottwald, T.; Kneuer, R. *Synlett* **2001**, 749−752. (b) Francisco, C. G.; León, E. I.; Martín, A.; Moreno, P.; Rodríguez, M. S.; Suárez, E. *J. Org. Chem.* **2001**, *66*, 6967−6976.

(10) (a) Blunt, J. W.; Copp, B. R.; Munro, M. H. G.; Northcote, P. T.; Prinsep, M. R. *Nat. Prod. Rep.* **2003**, *20*, 1−48. (b) Brenna, E.; Fuganti, C.; Serra, S. *Tetrahedron: Asymmetry* **2003**, *14*, 1−42. (c) Hanson, J. R. *Nat. Prod. Rep.* **2003**, *20*, 70−78. (d) Spivey, A. C.; Weston, M.; Woodhead, S. *Chem. Soc. Rev.* **2002**, *31*, 43−59. (e) Fraga, B. M. *Nat. Prod. Rep.* **2002**, *19*, 650−672. (f) Bruno, M.; Piozzi, F.; Rosselli, S. *Nat. Prod. Rep.* **2002**, *19*, 357−378. (g) Hanson, J. R. *Nat. Prod. Rep.* **2002**, *19*, 125−132. (h) Connolly, J. D.; Hill, R. A. *Nat. Prod. Rep.* **2002**, *19*, 494−513. (i) Lewis, J. R. *Nat. Prod. Rep.* **2002**, *19*, 223−258. (j) Jin, Z.; Li, Z.; Huang, R. *Nat. Prod. Rep.* **2002**, *19*, 454−476. (k) Yeung, K. S.; Paterson, I. *Angew. Chem., Int. Ed.* **2002**, *41*, 4632−4653. (l) Faulkner, D. J. *Nat. Prod. Rep.* **2002**, *19*, 1−48. (m) Hale, K. J.; Hummersone, M. G.; Manaviazar, S.; Frigerio, M. *Nat. Prod. Rep.* **2002**, *19*, 413−453. (n) Kalesse, M.; Christmann, M. *Synthesis* **2002**, 981−1003. (o) Paquette, L. A. *ChemTracts* **2002**, *15*, 345−366. (p) Mann, J. *Nat. Prod. Rep.* **2001**, *18*, 417−430. (q) Fernández, J. J.; Souto, M. L.; Norte, M. *Nat. Prod. Rep.* **2000**, *17*, 235−246. (r) Murata, M.; Yasumoto, T. *Nat. Prod. Rep.* **2000**, *17*, 293−314. (s) Brimble, M. A.; Nairn, M. R.; Prabaharan, H. *Tetrahedron* **2000**, *56*, 1937−1992. (t) Vogel, P.; Cossy, J.; Plumet, J.; Arjona, O. *Tetrahedron* **1999**, *55*, 13521−13642. (u) Figadère, B. *Acc. Chem. Res.* **1995**, *28*, 359−365. (v) Dutton, C. J.; Banks, B. J.; Cooper, C. B. *Nat. Prod. Rep.* **1995**, 165−181. (x) Mori, K. *Tetrahedron* **1989**, *45*, 3233−3298.

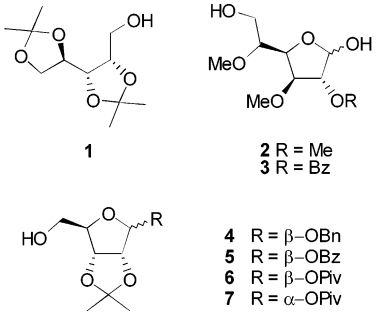
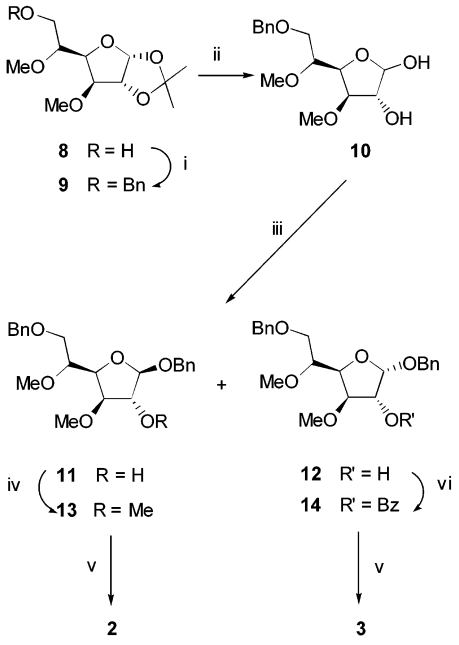


FIGURE 2. Precursors of the fragmentation-oxidation reaction.

SCHEME 2. Synthesis of Substrates 2 and 3[a]

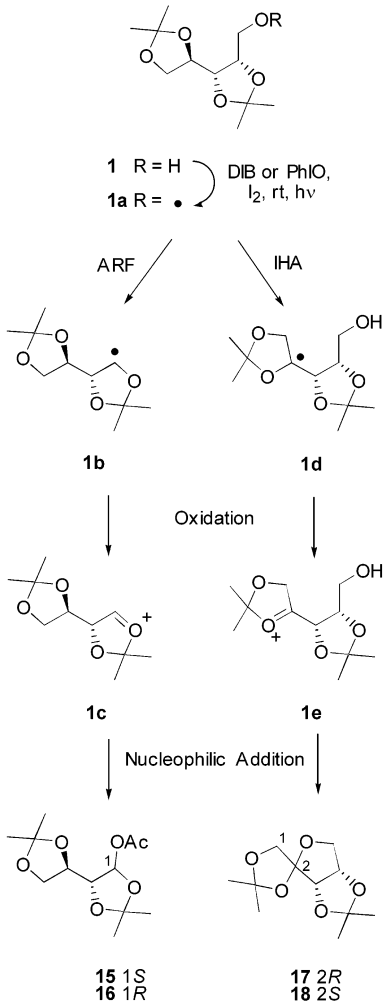


[a] Conditions: (i) NaH, $PhCH_2Br$, THF, 0 °C, 85%; (ii) TFA−H_2O 1:1, 98%; (iii) BnOH, camphorsulfonic acid, rt, yielded **11** (33%) and **12** (45%); (iv) NaH, MeI, THF, 0 °C, 94%; (v) H_2, 10% $Pd(OH)_2$/C, EtOAc, rt, yielded **2**, 88% or **3**, 94%; (vi) BzCl, Py, 93%.

Substrates **1**−**7** were prepared from commercial sugars. Compound **1** was synthesized from ribonolactone by treatment with 2,2-dimethoxypropane and *p*-TsOH.[11a] The resultant methyl 2,3:4,5-diisopropylidene-D-ribonic ester was reduced with lithium aluminum hydride[11b] to the polyol **1**, in excellent yield.

Compounds **2** and **3** were obtained from D-glucofuranose derivative **8**[12] (Scheme 2). After protection of the primary hydroxy group as its benzyl ether **9**, the isopropylidene acetal was cleaved, and the resultant diol **10** was selectively benzylated at the anomeric position, yielding the benzyl-*β*-D-glucofuranoside **11** and its α anomer **12** in good yield. Compound **11** was methylated to compound **13**, and then the benzyl groups were removed by hydrogenolysis to afford product **2**.

SCHEME 3. ARF versus IHA for Compound 1



To obtain substrate **3**, the benzyl-α-D-glucofuranoside **12** was treated with benzoyl chloride, affording compound **14**, which underwent hydrogenolysis, giving the diol **3**.

Compound **4** was formed from D-ribose according to reported procedures.[13] Compounds **5**−**7** were obtained from 5-*O*-*tert*-(butyldimethylsilyl)-2,3-*O*-isopropylidene-D-ribose following existing methodology.[14,15]

Study of the ARF−Oxidation Reaction of Primary Alkoxyl Radicals versus IHA. To study the possible competition between ARF and IHA, the polyol **1** was chosen as a substrate (Scheme 3), because the corresponding alkoxyl radical **1a** would be generated in an acyclic chain with considerable rotational freedom.

When the product **1** was treated with DIB and iodine, *β*-fragmentation took place, generating C-radical **1b**. This radical was oxidized to an oxycarbenium ion **1c**, which reacted with acetate ions coming from DIB, yielding compounds **15** and **16** (37%, 3:1).[16] However, the hydrogen abstraction was also an important pathway, generating C-radical **1d** that was oxidized to intermediate **1e**.

(11) (a) Barton, D. H. R.; Liu, W. *Tetrahedron* **1997**, *53*, 12067−12088. (b) Aslani-Shotorbani, G.; Buchanan, J. G.; Edgar, A. R.; Shahidi, P. K. *Carbohydr. Res.* **1985**, *136*, 37−52.

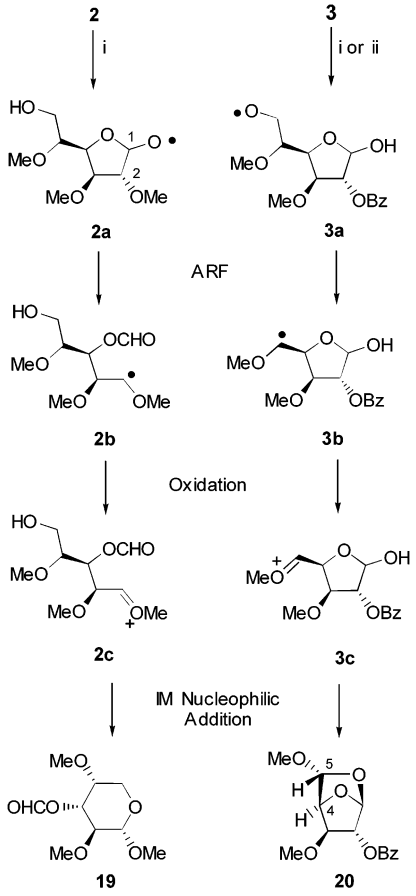
(12) Mariño-Albernas, J. R.; Verez-Bencomo, V.; Gonzalez, L.; Perez, C. S. *Carbohydr. Res.* **1987**, *165*, 197−206.

(13) Duvold, T.; Francis, G. W.; Papaioannou, D. *Tetrahedron Lett.* **1995**, *36*, 3153−3156.

(14) (a) Kaskar, B.; Heise, G. L.; Michalak, R. S.; Vishnuvajjala, B. R. *Synthesis* **1990**, 1031−1032. (b) Francisco, C. G.; González, C. C.; Suárez, E. *J. Org. Chem.* **1998**, *63*, 2099−2109.

(15) Francisco, C. G.; Freire, R.; González, C. G.; León E. I.; Riesco-Fagundo, C.; Suárez, E. *J. Org. Chem.* **2001**, *66*, 1861−1866.

SCHEME 4. Fragmentation of Anomeric Alkoxyl Radicals versus Primary Alkoxyl Radicals[a]



[a] Conditions: (i) PhIO (2 equiv), I_2 (2 equiv), CH_2Cl_2, rt, yielded **19** (45%) or **20** (33%); (ii) DIB (2 equiv), I_2 (2 equiv), CH_2Cl_2, 23%.

Subsequent intramolecular nucleophilic addition afforded the cyclic acetals **17** and **18**[17] in 40% yield (3:1). These cyclic acetals are interesting examples of the transformation of common aldoses from the D-series to unusual ketoses from the L-series.

In the substrates **2** and **3** (Scheme 4) the primary alkoxyl radical would be generated in a chain with less rotational freedom than in the previous case. In addition, in these substrates anomeric alkoxyl radicals could also be generated. The fragmentation of anomeric alkoxyl radicals is reported to be faster than the fragmentation of primary alkoxyl radicals,[18] but the influence of the substituents on their relative rates has still been scarcely studied.[19]

As expected, when the photolysis of substrate **2** was carried out, the fragmentation of the anomeric alkoxyl radical **2a** was the major pathway. The C_1-C_2 scission generated C-radical **2b**, which was oxidized in situ to an oxycarbenium ion. Intramolecular trapping of the latter by the primary hydroxy group[18] afforded pyranoside **19**. The reaction proceeded in 45% yield when the photolysis was carried out with iodosylbenzene and iodine.

The photolysis of substrate **3** gave an unexpected result. In this case, no products from the anomeric alkoxyl radical fragmentation were isolated. The main product was the bicyclic acetal **20**,[20] resulting from fragmentation of the primary alkoxyl radical **3a**. To our knowledge, this is the first reported case in which the *β*-fragmentation of primary alkoxyl radicals predominates over the scission of anomeric radicals and highlights the importance of the substituents in determining the preferred reaction pathway. In effect, the *β*-fragmentation can be a reversible process, and hence the stabilitiy of the resulting radicals influences the reaction outcome. The oxidation step is also determinant because it renders the entire process irreversible. When the 2-alkoxy group was replaced by an acyloxy group, the C-radical resulting from the C_1-C_2 fragmentation was less stabilized; the oxidation of this radical to an oxycarbenium ion was also hindered, because the acyloxy group is less electron-donating than the alkoxy group. This gave time for the fragmentation of the primary alkoxyl radical **3a** to take place. The resultant C-radical **3b** was adjacent to an alkoxyl group, which was easily oxidized to an oxycarbenium ion **3c**, shifting the whole process to the formation of the unusual diacetal **20**.

The competition between ARF and IHA was then studied with substrates **4** and **5**, which are relatively rigid bicyclic systems (Scheme 5). In these substrates, the anomeric α-hydrogen (C_1-H) would be out of reach from the primary alkoxyl radical; however, the distance between the alkoxyl radical and the C_2-H (about 2.7−2.9 Å)[21] is appropriate for abstraction.

When the benzyl *β*-D-ribofuranoside derivative **4** was reacted, an unexpected result was obtained. The major product was the seven-membered benzylic acetal **21**[22] (Table 1, entry 1). Although the IHA required an eight-membered transition state, the intermediate benzylic radical was stabilized by the adjacent oxygen and the phenyl group. However, no C_2-H abstraction was observed, probably because the resulting planar C-radical would generate a strained bicyclic system.[23]

The *β*-fragmentation also took place as the minor pathway, yielding the acetate **22** as a single isomer.[24] Compound **22** was formed when the intermediate oxycarbenium ion was trapped by acetate ions released from DIB.

(16) The stereochemistry of acetates **15** and **16** was determined in base to their coupling constants $J_{2,3}$. Thus, for acetate **15** (1*S*) $J_{2,3}$ = 3.5 Hz (cis), while for compound **16** (1*R*) $J_{2,3}$ = 1.8 Hz (trans). For similar examples, see ref 8a. Besides, a NOESY experiment for compound **16** showed a net spatial interaction between C_1-H (δ_H 6.26) and C_3-H (δ_H 4.03).

(17) The enantiomers of products **17** and **18** have been previously described: Collins, P. M.; Gupta, P.; Travis, A. S. *J. Chem. Soc., Perkin Trans. 1* **1980**, 277−281.

(18) de Armas, P.; Francisco, C. G.; Suárez, E. *J. Am. Chem. Soc.* **1993**, *115*, 8865−8866.

(19) (a) An example of the influence of the substituents on the relative rate of hydrogen abstraction versus *β*-fragmentation has been reported: Allen, P. R.; Brimble, M. A.; Farès, F. A. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2403−2411. (b) See also: Francisco, C. G.; González, C.; Suárez, E. *J. Org. Chem.* **1998**, *63*, 8092−8093.

(20) In the minimum energy conformation for compound 5*R*, (calculated with ChemBats3D ultra 6.0, CambridgeSoft.com) the dihedral angle $H_5-C_5-C_4-H_4$ was 86°, which would give a coupling constant of J = 0 Hz. This result agrees with the observed signal for C_5-H (δ = 5.19), which appears as a singlet. In the case of the 5*S* isomer, the dihedral angle $H_5-C_5-C_4-H_4$ was calculated to be −35°; the resulting J (about 5 Hz) would not match the experimental one.

(21) Calculations using a MM2 force field model implanted in ChemBats3D ultra 6.0, CambridgeSoft.com.

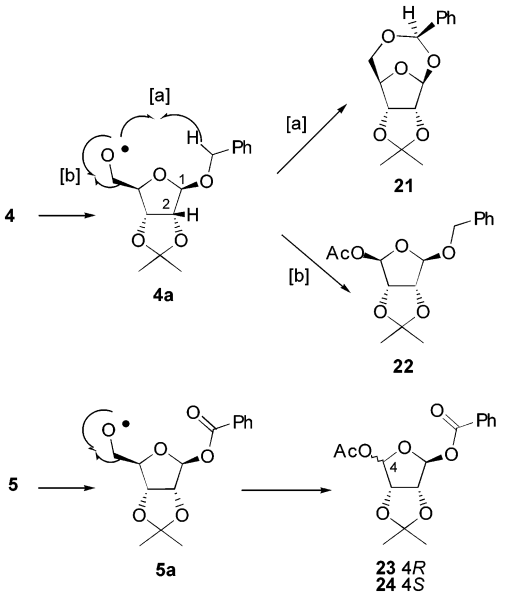
(22) The stereochemistry of compound **21** was determined in base to the ^{1}H and NOESY experiments. Thus, the benzylic proton had a strong spatial interaction with one of the C_5-H (C_5-H_a). C_5-H_a was coupled with C_4-H (J = 2.2 Hz); on the other hand, C_5-H_b showed no coupling with C_4-H.

TABLE 1. Fragmentation versus Hydrogen Abstraction for Substrates 4−7[a]

entry	substrate	reagents	solvent	products (%)[b]	β-scission yield (%)	H-abstraction yield (%)	overall yield (%)
1	**4**	DIB, I_2	CH_2Cl_2	**21** (42), **22** (28)	28	42	70
2	**5**	DIB, I_2	CH_2Cl_2	**23** (33), **24** (15)	48		48
3	**6**	DIB, I_2	CH_2Cl_2	**25** (10), **26** (32)	42		42
4	**6**	DIB, I_2	MeCN	**25** (2), **26** (6), **27** (10), **28** (50)	68		68
5	**6**	PhIO, I_2	MeCN	**27** (15), **28** (66)	81		81
6	**7**	DIB, I_2	CH_2Cl_2	**29** (26), **30** (35)	35	26	61
7	**7**	DIB, I_2	MeCN	**29** (53), **30** (7), **31** (17)	24	53	77
8	**7**	PhIO, I_2	MeCN	**29** (54), **31** (30)	30	54	84

[a] All reactions were performed with DIB or PhIO (2 equiv) and iodine (1 equiv) in dry solvents (10 mL per mmol of substrate) under nitrogen at room temperature, using irradiation with two 80-W tungsten-filament lamps for 1 h. [b] Yields are given for products purified by chromatography on silica gel.

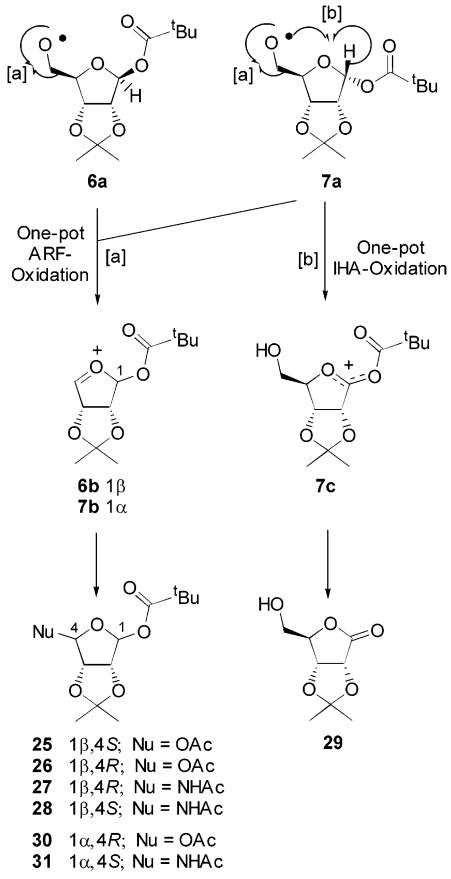
SCHEME 5. Influence of Substituents on ARF:IHA Ratio



It was clear that if the β-fragmentation was to predominate, the anomeric protecting group should be changed. With this objective in mind, the 1β-benzoyloxy derivative **5** was used as a substrate (Scheme 5). The reaction was carried out with DIB and iodine in dichloromethane (Table 1, entry 2), yielding the fragmentation products **23** and **24** (48% total yield; **23**:**24**, 2:1). To our satisfaction, no products from IHA were formed.

The next step was to determine the importance of C_1-H abstraction in the reaction outcome. The 1-pivaloyloxy epimers **6** and **7** were synthesized and reacted as shown in Scheme 6. The alkoxyl radical **6a**, derived from the 1β-pivaloyloxyribose **6**, reacted exclusively by β-fragmentation. On treatment with DIB−iodine in dichloromethane

SCHEME 6. Influence of Stereochemistry of Substituents on ARF:IHA Ratio



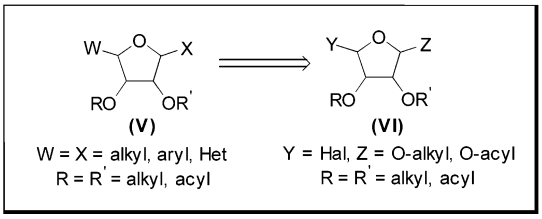
(Table 1, entry 3) the diacyloxy derivatives **25** and **26** were obtained as a separable mixture (42%; **25**: **26**, 1:3). When the reaction was run with DIB−iodine in acetonitrile (entry 4), two new fragmentation products, the 4-amido-1-pivaloyloxy derivatives **27** and **28**, were the major ones (60%; **27**:**28** 1:5). Rewardingly, when the fragmentation was carried out with PhIO−iodine in acetonitrile (entry 5), the yield of the amidoderivatives was increased (81%; **27**:**28**, 1:4). Compounds **27** and **28** were generated by a Ritter reaction between the oxycarbenium ion **6b** and acetonitrile, followed by addition of water to the intermediate during the workup.[25]

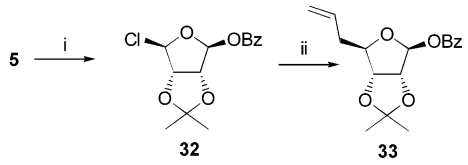
(23) No products arising from the geometrically possible abstraction of the C_2-H have been isolated, since this abstraction was disfavored by steric and stereoelectronic factors. See also: (a) Francisco, C. G.; Herrera, A. J.; Suárez, E. *J. Org. Chem.* **2002**, *67*, 7439−7445. (b) Francisco, C. G.; Freire, R.; Herrera, A. J.; Pérez-Martín, I.; Suárez, E. *Org. Lett.* **2002**, *4*, 1959−1961. (c) Francisco, C. G.; Herrera, A. J.; Suárez, E. *Tetrahedron Lett.* **2000**, *41*, 7869−7873. (d) For studies on stereoelectronic effects in IHA reactions, see: Malatesta, V.; Ingold, K. U. *J. Am. Chem. Soc.* **1981**, *103*, 609−614. (e) Beckwith, A. L. J.; Easton, C. J. *J. Am. Chem. Soc.* **1981**, *103*, 615−619.

(24) (a) For a preliminary communication of this work, see: Boto, A.; Hernández, R.; Suárez, E. *Tetrahedron Lett.* **2002**, *43*, 1821−1824. (b) For a related work from our group where acyloxyaldoses were formed from uronic acids, see: Francisco, C. G.; González, C. C.; Suárez, E. *Tetrahedron Lett.* **1997**, *38*, 4141−4144.

(25) (a) Bishop, R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 6, pp 261−300. (b) Kita, Y.; Shibata, N.; Kawano, N.; Yoshida, N.; Matsumoto, K.; Takebe, Y. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2321−2329.

SCHEME 7. Synthesis of α,ω-Differently Substituted Cyclic Ethers[a]





[a] Conditions: (i) DIB (2.0 equiv), ICl (1.0 equiv), CH_2Cl_2, *hν*, rt, **23** (10%), **24** (11%), **32** (53%); (ii) $Bu_3SnCH_2CH{=}CH_2$, AIBN, PhH, reflux, 82%.

In the case of the alkoxyl radical **7a**, derived from the 1α-pivaloyloxy derivative **7**, the distance $C_5{-}O\cdots H{-}C_1$ (about 2.6−2.8 Å) was appropriate for abstraction.[21] If this abstraction took place, the resulting C-radical would be stabilized by two oxygen functions and its oxidation to an oxycarbenium ion **7c** would probably be very fast.

According to these considerations, the photolysis of substrate **7** (entries 6−8) gave lactone **29**[26] as the major product. The best yields of **29** (53−54%) were obtained when the photolysis was run in acetonitrile (entries 7 and 8). Two minor products, resulting from *β*-fragmentation, were the diacyloxy derivative **30** and the 4-amido-1-pivaloyloxyfuranose **31**.

These results show that the fragmentation of primary alkoxyl radicals in carbohydrates proceeds in good yields when the hydrogen abstraction reaction is hindered. This encouraged us to study the synthesis of cyclic ethers (V) with different substituents at the α,ω-positions (Scheme 7). As commented before, this unit is present in many products[10] with biological activity; accordingly, different strategies have been developed to synthesize these systems.[27] A direct way to achieve this objective could start from the cyclic aldoses (VI). For instance, using Y = halogen and Z = alkoxy or acyloxy group, it would be possible to introduce a W substituent by a radical reaction[28] and an X substituent by an ionic one.[29]

Syntheses of the asymmetrical α-acyloxy (or alkoxy)-ω-haloaldoses (VI) are scarce.[30] Our methodology could be an expedient way to obtain this kind of compound, as shown in Scheme 7. The easily obtained 1*β*-benzoyloxy derivative **5** was used to test this strategy and was treated under the conditions listed in Table 2. In all cases, the reaction was carried out in dichloromethane to avoid the Ritter reaction. The best conditions were obtained when substrate **5** was treated with DIB and iodine monochloride (ICl) at room temperature (entry 4). A small amount of the two isomeric acetates **23** and **24** was isolated (21%), but the major product was the desired chloroderivative **32** (53%). The regioselective introduction of a lateral chain at the C_4 position by a radical reaction was tried next. To our pleasure, when compound **32** was treated with allyltributyltin and catalytic AIBN in benzene, the allyl derivative **33** was obtained in 82% yield, supporting the feasibility of this synthetic strategy.

TABLE 2. Synthesis of 1-Benzoyloxy-4-chlorofuranose 32[a]

entry	reagents (equiv)	products (%)[b]	scission yield (%)
1	DIB (2.0), I_2 (1.0)	**23** (15), **24** (33)	48
2	DIB (2.0), I_2 (1.0), *n*-Bu_4NCl (5.0)	**23** (16), **24** (20), **32** (7)	43
3	$PhICl_2$ (2.0), I_2 (1.0)	complex mixture	
4	DIB (2.0), ICl (1.0)	**23** (10), **24** (11), **32** (53)	74
5	PhIO (2.0), ICl (1.0)	complex mixture[c]	
6	$PhICl_2$ (2.0), ICl (1.0)	complex mixture	

[a] All reactions were run in dichloromethane, under irradiation of two 80-W tungsten-filament lamps for 1 h, at room temperature. [b] Yields are given for products purified by chromatography on silica gel. [c] The reaction with PhIO was very slow because of the low solubility of the reagent in CH_2Cl_2, and gave a complex mixture.

In summary, the *β*-fragmentation of primary alkoxyl radicals in carbohydrates proceeds in satisfactory yields when the hydrogen abstraction is disfavored. The ratio of *β*-fragmentation to hydrogen abstraction can be varied according to the reaction conditions, the stereochemistry of the substituents (e.g., α- or *β*-anomeric substituents), and the protecting groups chosen. The *β*-scission reaction provides an expedient way toward shorter and less common sugar series and also toward α,ω-differently substituted cyclic ethers. These units are useful building blocks and are present in many natural products with interesting biological activity.

Experimental Section

General Methods. Melting points were determined with a hot-stage apparatus and are uncorrected. Optical rotations were measured at the sodium line at ambient temperature in $CHCl_3$ solutions. IR spectra were recorded in $CHCl_3$ solutions. NMR spectra were determined at 500 MHz for ^1H and 125.7 MHz for ^{13}C in $CDCl_3$ unless otherwise stated in the presence of TMS as internal standard. Mass spectra were determined at 70 eV unless otherwise specified. Merck silica gel 60 PF_{254} and 60 (0.063−0.2 mm) were used for preparative thin-layer chromatography and column chromatography, respectively. Commercial reagents and solvents were of analytical grade or were purified by standard procedures prior to use.[31] All reactions involving air- or moisture-sensitive materials were carried out under a nitrogen atmosphere. The spray reagents for TLC analysis were 0.5% vanillin in H_2SO_4−EtOH (4:1) or 0.25% ninhydrin in EtOH, and the TLC was heated until development of color.

(26) Csuk, R.; Kühn, M.; Schöhl, D. *Tetrahedron* **1997**, *53*, 1311−1322.

(27) (a) Krause, N.; Hoffmann-Röder, A.; Canisius, J. *Synthesis* **2002**, 1759−1774. (b) Nicolaou, K. C.; Mitchell, H. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1576−1624. (c) Lee, E. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 2, pp 303−333. (d) Brimble, M. A.; Farès, F. A. *Tetrahedron* **1999**, *55*, 7661−7706. (e) Hoberg, J. O. *Tetrahedron* **1998**, *54*, 12631−12670. (f) Hoppe, R.; Scharf, H. D. *Synthesis* **1995**, 1447−1464. (g) Harmange, J. C.; Figadère, B. *Tetrahedron: Asymmetry* **1993**, *4*, 1711−1754.

(28) Keck, G. E.; Yates, J. B. *J. Am. Chem. Soc.* **1982**, *104*, 5831−5833.

(29) (a) For a review, see: Schmidt, R. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 6, pp 33−64. (b) For a recent work, see: Pilli, R. A.; Riatto, V. B. *Tetrahedron: Asymmetry* **2000**, *11*, 3675−3686 and references therein.

(30) (a) Giese, B.; Linker, T. *Synthesis* **1992**, 46−48. (b) Ferrier, R. J.; Tyler, P. C. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2767−2773.

(31) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: New York, 1988.

2,3:4,5-Di-*O*-isopropylideneribitol (1). Compound **1** was prepared by $LiAlH_4$ reduction[11b] of the methyl 2,3:4,5-di-*O*-isopropylidene-D-ribonate obtained by a one-pot procedure from D-ribo-1,4-lactone[11a] as a syrup; $[\alpha]_D$ +26 (c = 0.2) {lit. $[\alpha]_D$ +24, (c = 1.8)}.[11b] Compound **1** was poorly described in the literature:[11b] IR 3505 cm^{-1}; ^1H NMR δ 1.34 (3H, s), 1.36 (3H, s), 1.40 (3H, s), 1.41 (3H, s), 3.80 (1H, dd, J = 11.9, 5.4 Hz), 3.86 (1H, dd, J = 11.9, 5.4 Hz), 3.94 (1H, dd, J = 7.3, 3.1 Hz), 4.05 (1H, dd, J = 9.4, 5.8 Hz), 4.13−4.18 (2H, m), 4.35 (1H, ddd, J = 7.3, 5.7, 5.7 Hz); ^{13}C NMR δ 25.2 (CH_3), 25.4 (CH_3), 26.7 (CH_3), 27.8 (CH_3), 60.6 (CH_2), 68.1 (CH_2), 73.3 (CH), 77.4 (CH), 78.1 (CH), 108.8 (C), 110.1 (C); MS m/z (rel intensity) 217 (M^+ − Me, 26), 143 (27), 131 (19), 101 (63), 85 (13), 72 (12), 59 (100); HRMS calcd for $C_{10}H_{17}O_5$ 217.1076, found 217.1041. Anal. Calcd for $C_{11}H_{20}O_5$: C, 56.88; H, 8.68. Found: C, 56.97; H, 8.50.

6-*O*-Benzyl-1,2-isopropylidene-3,5-di-*O*-methyl-α-D-glucofuranose (9). To a solution of 1,2-isopropylidene-3,5-di-*O*-methyl-α-D-glucofuranose (**8**)[12] (630 mg, 2.42 mmol) in THF (20 mL) was added 60% NaH (150 mg, 3.75 mmol) portionwise, at 0 °C and under N_2. When hydrogen evolution ceased, benzyl bromide (0.4 mL, 3.36 mmol) was added at 0 °C. The temperature was allowed to reach room temperature, and the reaction mixture was stirred for 5 h. Then MeOH (1 mL) was added, and the resulting mixture was poured into water and extracted with CH_2Cl_2. The combined extracts were dried (Na_2SO_4) and concentrated at reduced pressure. The residue was then purified by column chromatography on silica gel (hexanes−EtOAc, 4:1) to yield product **9** (695 mg, 85%) as a crystalline solid: mp 78−80 °C (from *n*-hexane); $[\alpha]_D$ −40 (c = 0.4); {lit. mp 80.8−81.3 °C (from ligroin), $[\alpha]_D$ −41.65 (c = 10)}.[12] Compound **9** was poorly described in the literature:[12] IR 3080, 3065 cm^{-1}; ^1H NMR δ 1.33 (3H, s), 1.49 (3H, s), 3.44 (3H, s), 3.48 (3H, s), 3.60 (1H, dd, J = 10.6, 5.3 Hz), 3.67 (1H, ddd, J = 9.3, 5.4, 2.0 Hz), 3.80 (1H, d, J = 3.6 Hz), 3.87 (1H, dd, J = 10.6, 2.0 Hz), 4.20 (1H, dd, J = 9.3, 3.1 Hz), 4.56 (1H, d, J = 3.8 Hz), 4.60 (2H, s), 5.87 (1H, d, J = 3.8 Hz), 7.24−7.37 (5H, m); ^{13}C NMR δ 26.3 (CH_3), 26.7 (CH_3), 57.6 (CH_3), 58.2 (CH_3), 70.1 (CH_2), 73.3 (CH_2), 76.8 (CH), 78.6 (CH), 81.4 (CH), 83.6 (CH), 105.0 (CH), 111.6 (C), 127.2 (CH), 127.4 (2 × CH), 128.2 (2 × CH), 138.5 (C); MS m/z (rel intensity) 338 (M^+, 21), 323 (M^+ − Me, 4), 101 (62), 91 (100); HRMS calcd for $C_{18}H_{26}O_6$ 338.1729, found 338.1725. Anal. Calcd for $C_{18}H_{26}O_6$: C, 63.89; H, 7.74. Found: C, 63.74; H, 7.62.

6-*O*-Benzyl-3,5-di-*O*-methyl-D-glucofuranose (10). Compound **9** (695 mg, 2.06 mmol) was dissolved in 50% aqueous trifluoroacetic acid (10 mL) and stirred at room temperature for 8 h, and then the reaction mixture was poured into water and extracted with EtOAc. Column chromatography on silica gel (hexanes−EtOAc, 1:4) gave **10** (601 mg, 98%) as an inseparable anomeric mixture (α:β, 1.6:1): syrup; $[\alpha]_D$ −7 (c = 0.3); IR 3603, 3416, 3089 cm^{-1}; ^1H NMR δ anomer α 3.42 (3H, s), 3.46 (3H, s), 3.60 (1H, dd, J = 12.5, 3.8 Hz), 3.68 (1H, m), 3.77 (1H, d, J = 4.1 Hz), 3.82 (1H, dd, J = 12.5, 3.7 Hz), 4.07 (1H, d, J = 4.0 Hz), 4.26 (1H, dd, J = 8.5, 4.1 Hz), 4.59 (2H, s), 5.40 (1H, d, J = 4.0 Hz), 7.25−7.35 (5H, m); δ anomer β 3.45 (3H, s), 3.46 (3H, s), 3.60 (1H, dd, J = 12.5, 3.8 Hz), 3.68 (1H, m), 3.77 (1H, d, J = 4.0 Hz), 3.91 (1H, dd, J = 12.5, 4.0 Hz), 4.18 (1H, s), 4.29 (1H, dd, J = 9.5, 4.0 Hz), 4.58 (1H, d, J = 11.3 Hz), 4.60 (1H, d, J = 11.1 Hz), 5.40 (1H, s), 7.25−7.35 (5H, m); ^{13}C NMR (50.3 MHz) δ anomer α 58.1 (CH_3), 58.5 (CH_3), 70.2 (CH_2), 73.7 (CH_2), 74.1 (CH), 77.7 (CH), 77.8 (CH), 85.7 (CH), 97.1 (CH), 127.2 (CH), 127.3 (2 × CH), 128.0 (2 × CH), 138.3 (C); δ anomer β 58.2 (CH_3), 58.7 (CH_3), 66.8 (CH_2), 73.8 (CH_2), 74.1 (CH), 77.0 (CH), 78.0 (CH), 84.7 (CH), 103.7 (CH), 127.2 (CH), 127.3 (2 × CH), 128.0 (2 × CH), 138.0 (C); MS m/z (rel intensity) 280 (M^+ − H_2O, 1), 91 (100); HRMS calcd for $C_{15}H_{20}O_5$ 280.1311, found 280.1314. Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.72; H, 7.42.

Benzyl 6-*O*-Benzyl-3,5-di-*O*-methyl-β-D-glucofuranoside (11) and Benzyl 6-*O*-Benzyl-3,5-di-*O*-methyl-α-D-glucofuranoside (12). To a solution of product **10** (600 mg, 2.01 mmol) in benzyl alcohol (3.8 mL) was added camphorsulfonic acid (60 mg, 0.26 mmol), and the reaction mixture was stirred for 6 h at room temperature. The reaction was concentrated under high vacuum, and the residue was purified by column chromatography on silica gel (hexanes−EtOAc, 7:3) to yield compounds **11** (260 mg, 33%) and **12** (352 mg, 45%). Compound **11**: syrup; $[\alpha]_D$ −78 (c = 0.2); IR 3607, 3089, 3066 cm^{-1}; ^1H NMR δ 3.46 (3H, s), 3.47 (3H, s), 3.62 (1H, dd, J = 10.7, 4.9 Hz), 3.73 (1H, ddd, J = 9.0, 4.9, 2.1 Hz), 3.75 (1H, dd, J = 5.2, 1.6 Hz), 3.85 (1H, dd, J = 10.7, 2.1 Hz), 4.24 (1H, d, J = 1.6 Hz), 4.33 (1H, dd, J = 9.0, 5.1 Hz), 4.68 (1H, d, J = 12.3 Hz), 4.61 (2H, s), 4.71 (1H, d, J = 12.3 Hz), 4.93 (1H, s), 7.27−7.39 (10H, m); ^{13}C NMR (50.3 MHz) δ 57.9 (CH_3), 58.4 (CH_3), 69.6 (CH_2), 69.7 (CH_2), 73.3 (CH_2), 78.0 (CH), 78.5 (CH), 79.8 (CH), 85.3 (CH), 107.4 (CH), 127.4 (CH), 127.6 (2 × CH), 127.7 (CH), 128.0 (2 × CH), 128.2 (2 × CH), 128.3 (2 × CH), 137.6 (C), 138.5 (C); MS m/z (rel intensity) 282 (M^+ + H − C_7H_7O, 2), 280 (M^+ − C_7H_7OH, 2), 91 (100); HRMS calcd for $C_{15}H_{22}O_5$ 282.1467, found 282.1463. Anal. Calcd for $C_{22}H_{28}O_6$: C, 68.02; H, 7.26. Found: C, 68.00; H, 7.36. Compound **12**: syrup; $[\alpha]_D$ +50 (c = 0.3); IR 3544, 3089, 3066 cm^{-1}; ^1H NMR δ 3.46 (3H, s), 3.49 (3H, s), 3.61 (1H, dd, J = 10.5, 5.3 Hz), 3.66 (1H, ddd, J = 7.5, 5.3, 2.1 Hz), 3.79 (1H, dd, J = 4.4, 2.0 Hz), 3.82 (1H, dd, J = 10.6, 2.1 Hz), 4.18 (1H, dd, J = 4.8, 2.0 Hz), 4.28 (1H, dd, J = 8.3, 4.4 Hz), 4.58 (1H, d, J = 12.3 Hz), 4.60 (1H, d, J = 12.1 Hz), 4.62 (1H, d, J = 12.3 Hz), 4.82 (1H, d, J = 11.7 Hz), 5.19 (1H, d, J = 4.6 Hz), 7.27−7.39 (10H, m); ^{13}C NMR (50.3 MHz) δ 57.6 (CH_3), 58.3 (CH_3), 70.1 (2 × CH_2), 73.4 (CH_2), 75.9 (CH), 77.4 (CH), 77.6 (CH), 85.9 (CH), 100.1 (CH), 127.4 (CH), 127.5 (2 × CH), 128.0 (CH), 128.1 (2 × CH), 128.3 (2 × CH), 128.5 (2 × CH), 132.0 (C), 138.6 (C); MS m/z (rel intensity) 388 (M^+, <1), 91 (100); HRMS calcd for $C_{22}H_{28}O_6$ 388.1886, found 388.1884. Anal. Calcd for $C_{22}H_{28}O_6$: C, 68.02; H, 7.26. Found: C, 68.03; H, 7.23.

Benzyl 6-*O*-Benzyl-2,3,5-tri-*O*-methyl-β-D-glucofuranoside (13). A solution of alcohol **11** (152 mg, 0.392 mmol) in THF (5 mL) was treated with 60% NaH (26 mg, 0.65 mmol), under N_2 at 0 °C. When the hydrogen evolution ceased, methyl iodide (0.05 mL, 0.8 mmol) was added at 0 °C, and the reaction was stirred at room temperature for 5 h. Then MeOH (0.1 mL) was added, and the reaction mixture was poured into water and extracted with CH_2Cl_2. The combined extracts were dried (Na_2SO_4) and concentrated at reduced pressure. The residue was purified by column chromatography on silica gel (hexanes−EtOAc, 4:1) to yield the tri-*O*-methyl derivative **13** (148 mg, 94%) as a syrup: $[\alpha]_D$ −80 (c = 0.2); IR 3089, 3066, cm^{-1}; ^1H NMR δ 3.37 (3H, s), 3.46 (3H, s), 3.48 (3H, s), 3.61 (1H, dd, J = 10.6, 5.0 Hz), 3.74 (1H, ddd, J = 9.1, 5.0, 2.1 Hz), 3.78 (1H, s), 3.79 (1H, d, J = 4.6 Hz), 3.85 (1H, dd, J = 10.6, 2.1 Hz), 4.21 (1H, dd, J = 9.1, 4.5 Hz), 4.49 (1H, d, J = 12.3 Hz), 4.61 (2H, s), 4.71 (1H, d, J = 12.3 Hz), 4.99 (1H, s), 7.27−7.39 (10H, m); ^{13}C NMR δ 57.5 (CH_3), 58.0 (CH_3), 58.1 (CH_3), 69.8 (CH_2), 69.9 (CH_2), 73.3 (CH_2), 78.0 (CH), 79.7 (CH), 82.8 (CH), 87.7 (CH), 105.8 (CH), 127.4 (CH), 127.5 (2 × CH), 127.6 (CH), 127.9 (2 × CH), 128.2 (2 × CH), 128.3 (2 × CH), 137.6 (C), 138.6 (C); MS m/z (rel intensity) 296 (M^+ − C_7H_7 − CH_3, 1), 91 (100); HRMS calcd for $C_{15}H_{20}O_6$ 296.1260, found 296.1294. Anal. Calcd for $C_{23}H_{30}O_6$: C, 68.63; H, 7.51. Found: C, 68.74; H, 7.57.

2,3,5-Tri-*O*-methyl-D-glucofuranose (2). To a solution of compound **13** (177 mg, 0.44 mmol) in EtOAc (15 mL) was added 10% $Pd(OH)_2$/C (75 mg), and the mixture was hydrogenated at room temperature for 16 h. The suspension was filtered through silica gel−Celite, 1:1, and the organic layers were concentrated. Column chromatography on silica gel (hexanes−EtOAc, 1:1) gave **2** (86 mg, 88%) as an inseparable anomeric mixture (β: α, 1.2:1): syrup; $[\alpha]_D$ −39 (c = 0.2); IR 3538 cm^{-1}; ^1H NMR δ anomer β 3.44 (3H, s), 3.45 (3H, s), 3.49 (3H, s), 3.60 (1H, m), 3.78 (1H, dd, J = 11.8, 3.4 Hz), 3.78 (1H, s), 3.83 (1H, d, J = 3.9 Hz), 3.91 (1H, dd, J = 11.8, 4.4 Hz), 4.15 (1H, dd, J = 9.1, 3.9 Hz), 4.77 (1H, s, OH), 5.21 (1H, s); δ anomer α 3.44 (3H, s), 3.46 (3H, s), 3.50 (3H, s), 3.53 (1H,

m), 3.70 (1H, dd, J = 4.0, 1.1 Hz), 3.72 (1H, dd, J = 12.0, 3.5 Hz), 3.82 (1H, dd, J = 3.7, 1.1 H), 3.87 (1H, dd, J = 12.0, 4.3 Hz), 4.13 (1H, dd, J = 8.7, 3.7 Hz), 4.75 (1H, s, OH), 5.45 (1H, d, J = 4.0 Hz); ^{13}C NMR δ anomer β 57.6 (2 × CH_3), 58.2 (CH_3), 61.33 (CH_2), 78.19 (CH), 81.2 (CH), 82.1 (CH), 85.3 (CH), 100.6 (CH); δ anomer α 57.5 (CH_3), 57.7 (CH_3), 58.7 (CH_3), 61.27 (CH_2), 78.26 (CH), 82.1 (CH), 82.4 (CH), 85.3 (CH), 96.7 (CH); MS m/z (rel intensity) 223 (M^+ + H, 1), 205 (49), 173 (80), 141 (49), 115 (33), 101 (100), 87 (80) 75 (80); HRMS calcd for $C_9H_{19}O_6$ 223.1182, found 223.1100. Anal. Calcd for $C_9H_{18}O_6$: C, 48.64; H, 8.17. Found: C, 48.43; H, 8.46.

Benzyl 6-*O*-Benzyl-2-benzoyl-3,5-di-*O*-methyl-α-D-glucofuranoside (14). To a solution of product **12** (150 mg, 0.386 mmol) in dry pyridine (2.5 mL), at 0 °C and under N_2, was slowly added benzoyl chloride (0.2 mL, 1.72 mmol), and the mixture was stirred at room temperature for 16 h. The reaction mixture was poured into iced water and extracted with CH_2Cl_2. The combined extracts were washed with 10% aqueous HCl, aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated under vacuum. Chromatography on silica gel of the residue (hexanes−EtOAc, 85:15) gave the product **14** (176 mg, 93%) as a syrup: $[\alpha]_D$ +68 (c = 0.2); IR 3090, 3066, 1720, 1602 cm^{-1}; ^{1}H NMR δ 3.49 (3H, s), 3.51 (3H, s), 3.64 (1H, dd, J = 10.5, 5.3 Hz), 3.73 (1H, ddd, J = 7.2, 5.3, 2.1 Hz), 3.84 (1H, dd, J = 10.5, 2.2 Hz), 4.20 (1H, dd, J = 5.1, 3.0 Hz), 4.38 (1H, dd, J = 8.0, 5.2 Hz), 4.50 (1H, d, J = 12.1 Hz), 4.62 (2H, s), 4.73 (1H, d, J = 12.1 Hz), 5.26 (1H, dd, J = 4.4, 3.0 Hz), 5.45 (1H, d, J = 4.5 Hz) 7.14−7.19 (5H, m), 7.27 (1H, dd, J = 7.2, 7.1 Hz), 7.33 (2H, dd, J = 7.6, 7.1 Hz), 7.38 (2H, d, J = 7.1 Hz), 7.46 (2H, dd, J = 7.8, 7.7 Hz), 7.59 (1H, dd, J = 7.5, 7.5 Hz), 8.07 (2H, d, J = 7.2 Hz); ^{13}C NMR δ 58.0 (CH_3), 58.3 (CH_3), 69.9 (CH_2), 70.0 (CH_2), 73.4 (CH_2), 76.7 (CH), 77.7 (CH), 77.9 (CH), 83.3 (CH), 99.8 (CH), 127.3 (2 × CH), 127.36 (CH), 127.40 (CH), 127.5 (2 × CH), 128.1 (2 × CH), 128.3 (2 × CH), 128.4 (2 × CH), 129.7 (C), 129.8 (2 × CH), 133.2 (CH), 137.6 (C), 138.5 (C), 165.9 (C); MS m/z (rel intensity) 401 ($M^+ - C_7H_7$, 1), 105 (51), 91 (100); HRMS calcd for $C_{22}H_{25}O_7$ 401.1600, found 401.1556. Anal. Calcd for $C_{29}H_{32}O_7$: C, 70.71; H, 6.55. Found: C, 70.81; H, 6.65.

2-*O*-Benzoyl-3,5-di-*O*-methyl-D-glucofuranose (3). To a solution of compound **14** (176 mg, 0.358 mmol) in EtOAc (16 mL) was added 10% $Pd(OH)_2$/C (77 mg), and the mixture was hydrogenated at room temperature for 4 h. The suspension was filtered through silica gel−Celite (1:1), and the organic layers were concentrated under vacuum. Column chromatography on silica gel (hexanes−EtOAc, 3:7) gave the benzoyl derivative **3** (105 mg, 94%) as an inseparable anomeric mixture (α:β, 4:1): syrup; $[\alpha]_D$ +21 (c = 0.4); IR 3532, 3090, 3065, 1728, 1602 cm^{-1}; ^{1}H NMR δ anomer β 3.46 (3H, s), 3.63 (3H, s), 3.68 (1H, ddd, J = 9.3, 3.6, 3.5 Hz), 3.81 (1H, dd, J = 11.8, 3.1 Hz), 3.97 (1H, dd, J = 11.9, 4.0 Hz), 4.00 (1H, d, J = 3.8 Hz), 4.26 (1H, dd, J = 9.2, 3.9 Hz), 5.36 (1H, s), 5.37 (1H, s), 7.46 (2H, dd, J = 7.8, 7.7 Hz), 7.60 (1H, dd, J = 7.5, 7.4 Hz), 8.01 (2H, d, J = 7.3 Hz); δ anomer α 3.45 (3H, s), 3.52 (3H, s), 3.53 (1H, ddd, J = 9.1, 3.5, 3.4 Hz), 3.74 (1H, dd, J = 12.2, 3.3 Hz), 3.90 (1H, dd, J = 12.1, 3.4 Hz), 4.05 (1H, dd, J = 3.8, 1.3 Hz), 4.38 (1H, dd, J = 8.6, 4.3 Hz), 5.29 (1H, d, J = 4.3, 2.0 Hz), 5.69 (1H, d, J = 4.1 Hz), 7.49 (2H, dd, J = 7.6, 7.5 Hz), 7.61(1H, dd, J = 7.5, 7.4 Hz), 8.06 (2H, d, J = 7.3 Hz); ^{13}C NMR δ anomer α 57.7 (CH_3), 58.3 (CH_3), 61.1 (CH_2), 78.1 (CH), 78.3 (CH), 80.8 (CH), 82.1 (CH), 101.1 (CH), 128.4 (2 × CH), 128.9 (C), 129.7 (2 × CH), 133.6 (CH), 163.3 (C); δ anomer β 57.6 (CH_3), 57.9 (CH_3), 60.8 (CH_2), 76.2 (CH), 77.3 (CH), 77.5 (CH), 83.2 (CH), 96.1 (CH), 128.4 (2 × CH), 129.0 (C), 129.7 (2 × CH), 133.6 (CH), 165.5 (C); MS m/z (rel intensity) 281 (M^+ − OMe, 1), 105 (100), 77 (17); HRMS calcd for $C_{14}H_{17}O_6$ 281.1600, found 281.1556. Anal. Calcd for $C_{15}H_{20}O_7$: C, 57.68; H, 6.45. Found: C, 57.41; H, 6.51.

Benzyl 2,3-*O*-Isopropylidene-β-D-ribofuranoside (4). Mp 109−110 °C (from acetone−n-hexane); $[\alpha]_D$ −114 (c = 0.2) {lit.[13] mp 108−110 °C (from EtOAc−n-hexane); $[\alpha]_D$ −113 (c = 1)}.

Compounds **5**−**7** were prepared from 5-*O*-*tert*-(butyldimethylsilyl)-2,3-*O*-isopropylidene-D-ribose[14a] as previously described.[14b,15] **1-*O*-Benzoyl 2,3-*O*-isopropylidene-β-D-ribofuranose (5):** mp 102−104 °C (from EtOAc−n-pentane); $[\alpha]_D$ −42 (c = 0.2) {lit.[14b] mp 101−103 °C (from n-hexane−EtOAc); $[\alpha]_D$ −39.5 (c = 0.2)}. **2,3-*O*-Isopropylidene-1-*O*-pivaloyl-β-D-ribofuranose (6):** mp 95−96 °C (from EtOAc−n-hexane); $[\alpha]_D$ −62 (c = 0.2) {lit.[15] mp 93−94 °C (from n-hexane); $[\alpha]_D$ −61.6 (c = 0.268)}. **2,3-*O*-Isopropylidene-1-*O*-pivaloyl-α-D-ribofuranose (7):** {$[\alpha]_D$ +28 (c = 0.2) {lit.[15] $[\alpha]_D$ +27 (c = 0.24)}.

Generation of Primary Alkoxyl Radicals and Subsequent ARF or IHA. General Procedures. Method A. A solution of the substrate (0.2 mmol) in dry dichloromethane (2 mL) was treated with (diacetoxyiodo)benzene (DIB) (129 mg, 4 mmol) and iodine (51 mg, 0.2 mmol) under nitrogen. The reaction mixture was irradiated with two tungsten-filament lamps for 1 h at 22−25 °C, poured into aqueous 10% sodium thiosulfate, and extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4) and evaporated under vacuum, and the resulting residue was purified by column chromatography on silica gel.

Method B. Similar to Method A, but replacing DIB by iodosylbenzene (PhIO) (2 equiv). Longer reaction times were generally required (2−6 h).

Method C. Similar to Method A, but using MeCN as solvent.

Radical Reaction of 2,3:4,5-Di-*O*-isopropylideneribitol (1). Method A. The products were 1-acetoxy-1,2:3,4-di-*O*-isopropylidene-α-D-erythritol (**15**) (27%), 1-acetoxy-1,2:3,4-di-*O*-isopropylidene-β-D-erythritol (**16**) (10%), 1,2:3,4-di-*O*-isopropylidene-β-L-ribulofuranose (**17**) (30%), and 1,2:3,4-di-*O*-isopropylidene-α-L-ribulofuranose (**18**) (10%). Compound **15**: syrup; $[\alpha]_D$ −90 (c = 0.1); IR 1747 cm^{-1}; ^{1}H NMR δ 1.33 (3H, s), 1.38 (3H, s), 1.41 (3H, s), 1.48 (3H, s), 2.09 (3H, s), 4.02 (1H, dd, J = 8.8, 4.8 Hz), 4.08−4.12 (2H, m), 4.29 (1H, ddd, J = 7.7, 5.8, 5.0 Hz), 6.30 (1H, d, J = 3.5 Hz); ^{13}C NMR δ 21.2 (CH_3), 25.2 (CH_3), 26.0 (CH_3), 26.8 (CH_3), 28.1 (CH_3), 67.0 (CH_2), 73.1 (CH), 79.5 (CH), 93.7 (CH), 109.4 (C), 112.2 (C) 170.0 (C); MS m/z (rel intensity) 259 (M^+ − H, <1), 245 (M^+ − Me, 25), 101 (100), 85 (80), 59 (60); HRMS calcd for $C_{12}H_{19}O_6$ 259.1182, found 259.1209. Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.74. Found: C, 55.54; H, 7.55. Compound **16**: mp 38−40 °C (from n-pentane); $[\alpha]_D$ +56 (c = 0.2); IR 1748 cm^{-1}; ^{1}H NMR δ 1.34 (3H, s), 1.41 (3H, s), 1.45 (3H, s), 1.48 (3H, s), 2.09 (3H, s), 3.92 (1H, dd, J = 8.5, 4.7 Hz), 4.03 (1H, ddd, J = 8.2, 5.8, 4.9 Hz), 4.10 (1H, dd, J = 8.4, 6.1 Hz), 4.12 (1H, dd, J = 8.3, 1.9 Hz), 6.26 (1H, d, J = 1.8 Hz); ^{13}C NMR δ 21.2 (CH_3), 25.2 (CH_3), 26.7 (CH_3), 27.0 (CH_3), 27.6 (CH_3), 66.8 (CH_2), 75.2 (CH), 82.4 (CH), 96.9 (CH), 110.0 (C), 112.9 (C) 170.1 (C); MS m/z (rel intensity) 245 (M^+ − Me, 34), 101 (100); HRMS calcd for $C_{11}H_{17}O_6$ 245.1025, found 245.1030. Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.75. Found: C, 55.18; H, 7.69. Compound **17**: syrup; $[\alpha]_D$ +130 (c = 0.3); IR 1202, 1067, 856 cm^{-1}; ^{1}H NMR δ 1.31 (3H, s), 1.39 (3H, s), 1.42 (3H, s), 1.45 (3H, s), 3.87 (1H, dd, J = 10.4, 3.7 Hz), 3.94 (1H, d, J = 10.4 Hz), 4.05 (1H, d, J = 9.7 Hz), 4.27 (1H, d, J = 9.7 Hz), 4.55 (1H, d, J = 5.8 Hz), 4.84 (1H, dd, J = 5.8, 3.7 Hz); ^{13}C NMR δ 24.9 (CH_3), 26.2 (CH_3), 26.3 (CH_3), 26.5 (CH_3), 69.2 (CH_2), 71.2 (CH_2), 80.1 (CH), 84.7 (CH), 111.5 (C), 112.5 (C) 112.7 (C); MS m/z (rel intensity) 215 (M^+ − Me, 60), 155 (7), 117 (44), 114 (29), 97 (85), 85 (59), 59 (100); HRMS calcd for $C_{10}H_{15}O_5$ 215.0919, found 215.0949. Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.28; H, 8.04. Compound **18**: mp 89−91 °C (from n-pentane); $[\alpha]_D$ +9 (c = 0.2); IR 1232 cm^{-1}; ^{1}H NMR δ 1.36 (3H, s), 1.44 (3H, s), 1.52 (3H, s), 1.60 (3H, s), 3.95 (1H, dd, J = 10.4, 5.4 Hz), 3.97 (1H, d, J = 9.1 Hz), 3.99 (1H, dd, J = 10.4, 2.7 Hz), 4.02 (1H, d, J = 9.0 Hz), 4.45 (1H, d, J = 6.6 Hz), 4.78 (1H, ddd, J = 6.6, 5.5, 2.7 Hz); ^{13}C NMR δ 25.8 (CH_3), 26.0 (2 × CH_3), 26.7 (CH_3), 69.8 (CH_2), 71.4 (CH_2), 78.7 (CH), 81.0 (CH), 108.8 (C), 111.9 (C) 115.3 (C); MS m/z (rel intensity) 231 (M^+ + 1, <1), 215 (M^+ − Me, 43), 201 (33), 157 (16), 143 (94), 117 (24),

114 (17), 101 (100), 97 (27), 85 (36), 59 (69); HRMS calcd for $C_{11}H_{19}O_5$ 231.1232, found 231.1280. Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.16; H, 8.12.

Methyl 3-*O*-Formyl-2,4-di-*O*-methyl-α-D-arabinopyranoside (19). Compound **2** was treated according to Method B yielding product **19** in 45% yield: syrup; $[\alpha]_D$ −155 (c = 0.1); IR 1725 cm^{-1}; ^{1}H NMR δ 3.45 (3H, s), 3.46 (3H, s), 3.49 (3H, s), 3.71 (1H, dd, J = 12.8, 1.3 Hz), 3.72 (1H, m), 3.76 (1H, dd, J = 10.2, 3.5 Hz), 3.79 (1H, dd, J = 12.9, 3.2 Hz), 4.92 (1H, d, J = 3.5 Hz), 5.26 (1H, dd, J = 10.2, 3.2 Hz), 8.18 (1H, s); ^{13}C NMR δ 55.6 (CH_3), 57.6 (CH_3), 58.3 (CH_2), 59.0 (CH_3), 71.3 (CH), 75.7 (CH), 76.7 (CH), 98.6 (CH), 160.5 (CH); MS m/z (rel intensity) 219 (M^+ − H, <1), 205 (M^+ − Me, <1), 115 (64), 101 (100); HRMS calcd for $C_9H_{15}O_6$ 219.0869, found 219.0835. Anal. Calcd for $C_9H_{16}O_6$: C, 49.09; H, 7.32. Found: C, 48.87; H, 7.20.

(5*S*)-1,5-Anhydro-2-benzoyl-3,5-di-*O*-methyl-β-D-xylopentadialdo-1,4-furanose (20). Compound **3** was treated under Method A or B conditions, giving product **20** in 23% and 33% yield, respectively. Compound **20**: syrup; $[\alpha]_D$ −42 (c = 0.1); IR 3094, 3065, 1721, 1602 cm^{-1}; ^{1}H NMR δ 3.45 (3H, s), 3.48 (3H, s), 3.87 (1H, d, J = 5.1 Hz), 4.76 (1H, d, J = 5.1 Hz), 4.89 (1H, s), 5.19 (1H, s), 5.71 (1H, s), 7.46 (2H, dd, J = 7.8, 7.7 Hz), 7.59 (1H, dd, J = 7.4, 7.4 Hz), 8.06 (2H, d, J = 7.2 Hz); ^{13}C NMR δ 55.4 (CH_3), 59.0 (CH_3), 78.0 (CH), 78.9 (CH), 83.2 (CH), 98.2 (CH), 102.7 (CH), 128.5 (2 × CH), 129.3 (C), 129.8 (2 × CH), 133.5 (CH), 165.5 (C); MS m/z (rel intensity) 280 (M^+, <1), 249 (M^+ − OMe, 2), 105 (100); HRMS calcd for $C_{14}H_{16}O_6$ 280.0947, found 280.0939. Anal. Calcd for $C_{14}H_{16}O_6$: C, 60.00; H, 5.75. Found: C, 59.92; H, 6.04.

Radical Reaction of Benzyl 2,3-*O*-Isopropylidene-β-D-ribofuranoside (4). Method A. The reaction afforded 1,5-benzylidene-2,3-isopropylidene-β-D-ribofuranose (**21**) and 1-*O*-benzyl (4*R*)-4-*O*-acetyl-2,3-isopropylidene-β-D-*erythro*-tetradialdo-1,4-furanose (**22**) in 70% overall yield (**21**:**22**, 4:3). Compound **21**: mp 94−95 °C (from *n*-pentane); $[\alpha]_D$ + 34 (c = 0.2); IR 3094, 3068 cm^{-1}; ^{1}H NMR δ 1.34 (3H, s), 1.52 (3H, s), 3.79 (1H, dd, J = 12.6, 2.2 Hz), 4.05 (1H, d, J = 12.6 Hz), 4.65 (1H, d, J = 2.1 Hz), 4.75 (1H, d, J = 6.2 Hz), 4.76 (1H, d, J = 6.0 Hz), 5.63 (1H, s), 5.77 (1H, s), 7.36 (3H, m), 7.47 (2H, m); ^{13}C NMR δ 24.7 (CH_3), 26.3 (CH_3), 72.0 (CH_2), 81.9 (CH), 87.8 (CH), 88.3 (CH), 100.7 (CH), 105.7 (CH), 112.3 (C), 125.9 (2 × CH), 128.3 (2 × CH), 128.8 (CH), 138.5 (C); MS m/z (rel intensity) 278 (M^+, 27), 263 (4), 105 (100), 77 (85); HRMS calcd for $C_{15}H_{18}O_5$ 278.11542, found 278.11494. Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.61; H, 6.74. Compound **22**: mp 94−96 °C (from acetone−*n*-pentane); $[\alpha]_D$ −36 (c = 0.2) {lit.[24b] 93−94.5 °C (from *n*-hexane−EtOAc); $[\alpha]_D$ −34.4}.

Radical Reaction of 1-*O*-Benzoyl-2,3-*O*-isopropylidene-β-D-ribofuranose (5). Method A. Compounds (4*R*)-4-*O*-acetyl-1-*O*-benzoyl-2,3-*O*-isopropylidene-β-D-*erythro*-tetradialdo-1,4-furanose (**23**) and (4*S*)-4-*O*-acetyl-1-*O*-benzoyl-2,3-isopropylidene-α-D-*erythro*-tetradialdo-1,4-furanose (**24**) were obtained in 48% overall yield (**23**:**24**, 2:1). Compound **23**: syrup; $[\alpha]_D$ +53 (c = 0.6); IR 1735, 1602 cm^{-1}; ^{1}H NMR δ 1.36 (3H, s), 1.53 (3H, s), 1.98 (3H, s), 4.87 (1H, d, J = 5.7 Hz), 4.94 (1H, d, J = 5.7 Hz), 6.37 (1H, s), 6.56 (1H, s), 7.46 (2H, dd, J = 7.9, 7.8 Hz), 7.60 (1H, dd, J = 7.5, 7.4 Hz), 8.04 (2H, d, J = 8.4 Hz); ^{13}C NMR δ 20.9 (CH_3), 25.0 (CH_3), 26.3 (CH_3), 83.8 (CH), 83.9 (CH), 102.6 (CH), 103.0 (CH), 113.7 (C), 128.4 (2 × CH), 129.4 (C), 129.7 (2 × CH), 133.6 (CH), 164.5 (C), 168.9 (C); MS m/z (rel intensity) 307 (M^+ − Me, 42), 263 (16), 217 (22), 163 (46), 143 (32), 129 (55), 105 (100), 77 (72); HRMS calcd for $C_{15}H_{15}O_7$ 307.0818, found 307.0762. Anal. Calcd for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found: C, 59.76; H, 5.44. Compound **24**: syrup; $[\alpha]_D$ −7 (c = 0.2); IR 1733, 1602 cm^{-1}; ^{1}H NMR δ 1.40 (3H, s), 1.57 (3H, s), 2.17 (3H, s), 4.86 (1H, d, J = 5.8 Hz), 5.04 (1H, dd, J = 5.4, 4.5 Hz), 6.26 (1H, d, J = 4.0 Hz), 6.49 (1H, s), 7.45 (2H, dd, J = 7.9, 7.6 Hz), 7.60 (1H, dd, J = 7.6, 7.3 Hz), 8.01 (2H, d, J = 8.0 Hz); ^{13}C NMR δ 20.8 (CH_3), 25.6 (CH_3), 25.9 (CH_3), 70.9 (CH), 83.1 (CH), 98.2 (CH), 98.8 (CH), 114.7 (C), 128.5 (2 × CH), 129.1 (C), 129.9 (2 × CH), 133.7 (CH), 164.7 (C), 169.0 (C); MS m/z (rel intensity) 307 (M^+ − Me, 5), 217 (3), 105 (100), 77 (13); HRMS calcd for $C_{15}H_{15}O_7$ 307.0818, found 307.0810. Anal. Calcd for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found: C, 59.54; H, 5.42.

Radical Reaction of 2,3-*O*-Isopropylidene-1-*O*-pivaloyl-β-D-ribofuranose (6). Method C. The reaction afforded (4*S*)-4-*O*-acetyl-2,3-isopropylidene-1-*O*-pivaloyl-β-D-*erythro*-tetradialdo-1,4-furanose (**25**) (2%), (4*R*)-4-*O*-acetyl-2,3-isopropylidene-1-*O*-pivaloyl-β-D-*erythro*-tetradialdo-1,4-furanose (**26**) (6%), (4*R*)-4-*O*-acetylamino-2,3-isopropylidene-1-*O*-pivaloyl-β-D-*erythro*-tetradialdo-1,4-furanose (**27**) (10%), and (4*S*)-4-*O*-acetylamino-2,3-isopropylidene-1-*O*-pivaloyl-β-D-*erythro*-tetradialdo-1,4-furanose (**28**) (50%). Compound **25**: syrup; $[\alpha]_D$ −54 (c = 0.3); IR 1732 cm^{-1}; ^{1}H NMR δ 1.20 (9H, s), 1.38 (3H, s), 1.54 (3H, s), 2.16 (3H, s), 4.67 (1H, d, J = 5.9 Hz), 4.95 (1H, dd, J = 5.9, 4.1 Hz), 6.14 (1H, d, J = 4.1 Hz), 6.24 (1H, s); ^{13}C NMR δ 20.8 (CH_3), 25.6 (CH_3), 25.9 (CH_3), 26.9 (3 × CH_3), 38.8 (C), 77.9 (CH), 82.9 (CH), 98.0 (2 × CH), 114.6 (C), 169.0 (C), 176.6 (C); MS m/z (rel intensity) 287 (M^+ − Me, 35), 217 (17), 201 (93), 143 (60), 57 (100); HRMS calcd for $C_{13}H_{19}O_7$ 287.1131, found 287.1177. Anal. Calcd for $C_{14}H_{22}O_7$: C, 55.62; H, 7.33. Found: C, 55.89; H, 7.12. Compound **26**: mp 57−59 °C (from *n*-pentane); $[\alpha]_D$ −9 (c = 0.2); IR 1748 cm^{-1}; ^{1}H NMR δ 1.21 (9H, s), 1.34 (3H, s), 1.50 (3H, s), 2.06 (3H, s), 4.75 (1H, d, J = 5.7 Hz), 4.78 (1H, d, J = 5.8 Hz), 6.30 (1H, s), 6.31 (1H, s); ^{13}C NMR δ 20.9 (CH_3), 25.0 (CH_3), 26.3 (CH_3), 26.8 (3 × CH_3), 38.6 (C), 83.8 (CH), 83.9 (CH), 102.6 (CH), 102.8 (CH), 113.6 (C), 168.9 (C), 176.3 (C); MS m/z (rel intensity) 287 (M^+ − Me, 11), 243 (8), 201 (44), 159 (11), 143 (61), 129 (24), 101 (8), 85 (38), 57 (100); HRMS calcd for $C_{13}H_{19}O_7$ 287.1131, found 287.1121. Anal. Calcd for $C_{14}H_{22}O_7$: C, 55.62; H, 7.33. Found: C, 55.57; H, 7.28. Compound **27**: mp 140−142 °C (from acetone−*n*-pentane); $[\alpha]_D$ −47 (c = 0.2); IR 3436, 1740, 1694 cm^{-1}; ^{1}H NMR δ 1.21 (9H, s), 1.37 (3H, s), 1.54 (3H, s), 2.07 (3H, s), 4.69 (1H, d, J = 5.8 Hz), 4.70 (1H, dd, J = 5.9, 3.4 Hz), 5.93 (1H, dd, J = 10.0, 3.3 Hz), 6.10 (1H, s), 6.39 (1H, d, J = 9.8 Hz); ^{1}H NMR (C_6D_6) δ 1.15 (3H, s), 1.18 (9H, s), 1.46 (3H, s), 1.47 (3H, s), 4.13 (1H, dd, J = 5.8, 3.4 Hz), 4.47 (1H, d, J = 5.8 Hz), 6.18 (1H, d, J = 9.9 Hz), 6.25 (1H, dd, J = 10.1, 3.4 Hz), 6.56 (1H, s); ^{13}C NMR δ 23.4 (CH_3), 24.8 (CH_3), 26.1 (CH_3), 27.9 (3 × CH_3), 38.9 (C), 77.8 (CH), 81.1 (CH), 87.9 (CH), 98.0 (CH), 113.5 (C), 169.7 (C), 176.8 (C); MS m/z (rel intensity) 302 (M^+ + H, <1), 286 (2), 200 (83), 57 (100); HRMS calcd for $C_{14}H_{24}NO_6$ 302.1604, found 302.1591. Anal. Calcd for $C_{14}H_{23}NO_6$: C, 55.80; H, 7.69; N, 4.69. Found: C, 55.57; H, 7.99; N, 4.64. Compound **28**: mp 128−131 °C (from acetone−*n*-pentane); $[\alpha]_D$ −4 (c = 0.2); IR 3445, 1744, 1693 cm^{-1}; ^{1}H NMR δ 1.22 (9H, s), 1.32 (3H, s), 1.49 (3H, s), 1.97 (3H, s), 4.76 (1H, d, J = 5.9 Hz), 4.77 (1H, d, J = 5.9 Hz), 5.90 (1H, d, J = 8.4 Hz), 6.09 (1H, d, J = 7.8 Hz), 6.19 (1H, s); ^{13}C NMR δ 23.3 (CH_3), 25.0 (CH_3), 26.3 (CH_3), 26.9 (3 × CH_3), 38.6 (C), 84.3 (CH), 84.4 (CH), 89.1 (CH), 103.2 (CH), 113.4 (C), 169.0 (C), 176.3 (C); MS m/z (rel intensity) 302 (M^+ + H, <1), 200 (100); HRMS calcd for $C_{14}H_{24}NO_6$ 302.16036, found 302.16039. Anal. Calcd for $C_{14}H_{23}NO_6$: C, 55.80; H, 7.69; N, 4.65. Found: C, 55.57; H, 7.99; N, 4.64.

Radical Reaction of 2,3-*O*-Isopropylidene-1-*O*-pivaloyl-α-D-ribofuranose (7). Method C. The reaction afforded 2,3-*O*-isopropylidene-D-ribono-1,4-lactone (**29**) (53%), (4*R*)-4-*O*-acetyl-2,3-isopropylidene-1-*O*-pivaloyl-α-D-*erythro*-tetradialdo-1,4-furanose (**30**) (7%), and (4*S*)-4-*O*-acetylamino-2,3-isopropylidene-1-*O*-pivaloyl-α-D-*erythro*-tetradialdo-1,4-furanose (**31**) (17%). Lactone **29**: mp 135−137 °C (from acetone−*n*-pentane); $[\alpha]_D$ −78 (c = 0.2) {lit.[25] 138−139 °C; $[\alpha]_D$ −84.17 (c = 0.9)}. Acetate **30**: mp 53−56 °C (dryness from *n*-pentane); $[\alpha]_D$ −25 (c = 0.2); IR 1748, 1737 cm^{-1}; ^{1}H NMR δ 1.26 (9H, s), 1.36 (3H, s), 1.50 (3H, s), 2.09 (3H, s), 4.69 (1H, d, J = 6.0 Hz), 4.95 (1H, dd, J = 5.7, 4.2 Hz), 6.06 (1H, d, J = 4.0 Hz), 6.25 (1H, s); ^{13}C NMR δ 20.9 (CH_3), 25.7 (CH_3), 26.2 (CH_3), 27.0 (3 × CH_3), 38.8 (C), 77.8 (CH), 83.1 (CH), 97.8 (CH), 98.7 (CH), 114.5 (C), 169.2 (C), 176.6 (C); MS m/z (rel intensity) 287 (M^+ − Me, 12), 243 (9), 129 (75), 101 (25), 85 (79), 57 (100); HRMS

calcd for $C_{13}H_{19}O_7$ 287.1131, found 287.1130. Anal. Calcd for $C_{14}H_{22}O_7$: C, 55.62; H, 7.33. Found: C, 55.64; H, 7.30. Acetylamide **31**: mp 56−58 °C (from *n*-pentane); $[\alpha]_D$ −23 (*c* = 0.2); IR 3446, 3368, 1728, 1691 cm^{-1}; ^1H NMR δ 1.26 (9H, s), 1.36 (3H, s), 1.55 (3H, s), 2.01 (3H, s), 4.87 (1H, dd, *J* = 6.7, 2.0 Hz), 5.10 (1H, dd, *J* = 6.7, 4.5 Hz), 5.33 (1H, dd, *J* = 6.9, 1.9 Hz), 6.20 (1H, d, *J* = 4.5 Hz), 6.30 (1H, d, *J* = 6.5 Hz); ^{13}C NMR δ 23.3 (CH_3), 25.4 (CH_3), 26.3 (CH_3), 27.1 (3 × CH_3), 38.8 (C), 79.9 (CH), 84.0 (CH), 85.9 (CH), 98.0 (CH), 114.9 (C), 170.6 (C), 177.2 (C); MS *m*/*z* (rel intensity) 286 (M^+ − Me, 5), 200 (43), 100 (15), 85 (27), 71 (26), 57 (100); HRMS calcd for $C_{13}H_{20}NO_6$ 286.1291, found 286.1278. Anal. Calcd for $C_{14}H_{23}NO_6$: C, 55.80; H, 7.69; N 4.65. Found: C, 55.56; H, 7.73; N, 4.37.

(4*R*)-4-Chloro-4-deoxy-2,3-isopropylidene-1-*O*-benzoyl-*β*-D-*erythro*-tetradialdo-1,4-furanose (32). The photolysis of compound **5** (59 mg, 0.2 mmol) was performed with DIB (129 mg, 0.4 mmol) and ICl (36 mg, 0.22 mmol) in dichloromethane at room temperature for 1 h. Usual workup and chromatography afforded the acetates **23** (6 mg, 10%) and **24** (7 mg 11%), as well as (4*R*)-4-chloro-4-deoxy-2,3-isopropylidene-1-*O*-benzoyl-*β*-D-*erythro*-tetradialdo-1,4-furanose (**32**) (30 mg, 53%): mp 82−84 °C (dryness from CH_2Cl_2); $[\alpha]_D$ −7 (*c* = 0.2); IR 1732, 1602 cm^{-1}; ^1H NMR δ 1.37 (3H, s), 1.51 (3H, s), 5.04 (1H, d, *J* = 5.6 Hz), 5.14 (1H, d, *J* = 5.6 Hz), 6.15 (1H, s), 6.60 (1H, s), 7.46 (2H, dd, *J* = 7.9, 7.7 Hz), 7.60 (1H, dd, *J* = 7.5, 7.3 Hz), 8.08 (2H, d, *J* = 7.3 Hz); ^{13}C NMR δ 25.2 (CH_3), 25.3 (CH_3), 83.8 (CH), 88.2 (CH), 96.8 (CH), 104.1 (CH), 104.1 (C), 128.5 (2 × CH), 130.1 (C), 130.1 (2 × CH), 133.6 (CH), 164.6 (C); MS *m*/*z* (rel intensity) 285/283 (M^+ − Me, 3/10), 195/193 (3/9), 105 (100), 77 (18); HRMS calcd for $C_{13}H_{12}{}^{37}ClO_5$/$C_{13}H_{12}{}^{35}ClO_5$ 285.0345/283.0373, found 285.0311/283.0342. Anal. Calcd for $C_{14}H_{15}ClO_5$: C, 56.29; H, 5.06. Found: C, 56.35; H, 5.12.

1-*O*-Benzoyl-5,6,7-trideoxy-2,3-isopropylidene-*β*-D-*ribo*-hept-6-enofuranose (33). To a solution of the chloro derivative **32** (30 mg, 0.1 mmol) in dry C_6H_6 (3 mL) was added allyltributyl tin (90 μL, 0.4 mmol) and AIBN (6 mg) under N_2, and the mixture was heated to reflux for 4 h. After being cooled to room temperature, the solution was treated with KF (10 mg) in CH_3CN-H_2O (4 mL, 3:1) for 1 h, poured into water, and extracted with CH_2Cl_2. The organic layers were dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography on silica gel (hexanes−EtOAc, 95:5), giving the allyl derivative **33** (26 mg, 85%) as a crystalline solid: mp 55−56 °C (from *n*-pentane); $[\alpha]_D$ −49 (*c* = 0.3); IR 3066, 1725, 1643, 1602 cm^{-1}; ^1H NMR δ 1.35 (3H, s), 1.53 (3H, s), 2.34 (1H, ddd, *J* = 15.4, 8.0, 7.7 Hz), 2.48 (1H, ddd, *J* = 14.1, 7.2, 6.4 Hz), 4.41 (1H, dd, *J* = 7.8, 7.8 Hz), 4.70 (1H, d, *J* = 5.8 Hz), 4.90 (1H, d, *J* = 5.9 Hz), 5.07 (1H, dd, *J* = 17.0, 1.5 Hz), 5.09 (1H, dd, *J* = 9.1, 1.4 Hz), 5.79 (1H, dddd, *J* = 17.1, 10.4, 7.0, 6.6 Hz), 6.45 (1H, s), 7.45 (2H, dd, *J* = 7.9, 7.7 Hz), 7.58 (1H, dd, *J* = 7.4, 7.4 Hz), 8.01 (2H, d, *J* = 7.1 Hz); ^{13}C NMR δ 25.1 (CH_3), 26.5 (CH_3), 39.1 (CH_2), 83.3 (CH), 85.5 (CH), 87.5 (CH), 103.3 (CH), 112.9 (C), 118.1 (CH_2), 128.5 (2 × CH), 129.6 (2 × CH + C), 133.4 (2 × CH), 165.0 (C); MS *m*/*z* (rel intensity) 289 (M^+ − Me, 5), 105 (100), 77 (17); HRMS calcd for $C_{16}H_{17}O_5$ 289.1076, found 289.1098. Anal. Calcd for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62. Found: C, 66.89; H, 6.80.

Acknowledgment. This work was supported by the Investigation Programmes PB96-1461 and PPQ2000-0728 of the Plan Nacional de Investigación Científica, Desarrollo e Innovación Tecnológica, Dirección General de Investigación, Ministerio de Ciencia y Tecnología, Spain. We also thank the financial support from FEDER funds. D.H. thanks C.S.I.C.-Comunidad de Canarias for a fellowship.

JO034442F