Fragmentation of Carbohydrate Anomeric Alkoxy Radicals. A New General Method for the Synthesis of Alduronic Acid Lactones

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Alduronic acid 4,1-, 5,1-, and 5,2-lactones can be specifically obtained when hexuronic and penturonic acids belonging to the erythrose and threose carbohydrate series undergo a tandem β-fragmentation−intramolecular cyclization reaction. In this way, γ-lactones such as 3-*O*-formyl-1,2-*O*-isopropylidene-D-threurono-4,1-lactone (**38**), 3-*O*-formyl-1,2-di-*O*-methyl-D-threurono-4,1-lactones (**39**), or 3-*O*-formyl-1,2-*O*-isopropylidene-D-erythrurono-4,1-lactone (**41**), and δ-lactones such as 1-*O*-(*tert*-butyldimethylsilyl)-4-*O*-formyl-2,3-*O*-isopropylidene-D-lyxurono-5,1-lactones (**40**), or 4-*O*-formyl-1,2,3-tri-*O*-methyl-D-arabinurono-5,1-lactones (**42**), or 3-*O*-benzyl-4-*O*-formyl-1,2-*O*-isopropylidene-D-arabinurono-5,1-lactone (**43**), were obtained. Alternatively, an intermolecular reaction took place when the carboxyl group was lactonized. Thus, 1,4-di-*O*-acetyl-3-formyl-1-iodo-D-arabinurono-5,2-lactone (**45**) was prepared from 2,5-di-*O*-acetyl-D-glucurono-6,3-lactone (**37**). The reaction is promoted by two different systems: (diacetoxyiodo)benzene (DIB)−iodine, under mild conditions, or diphenylhydroxyselenium acetate (DHSA)−iodine under visible light irradiation. With this new strategy, nor-aldopyranosuronic and aldofuranosuronic acid lactones are formed via 1,5 and 1,6 intramolecular cyclization.

Introduction

Intramolecular radical cyclizations leading to the formation of carbocycles or heterocycles have been extensively used in a large number of synthetic applications.[1] The combination of consecutive reactions in a single synthetic step (tandem process) which allows the regio- and stereocontrolled formation of ring systems is an area of growing interest in synthetic methodology.[2] Since the biological activity of the molecules is dependent on their absolute configuration, it is important to have access to a procedure able to furnish enantiomerically pure products. Carbohydrates have attracted the attention of synthetic organic chemists because of their potential usefulness as easily available chiral substrates. Their well-defined stereochemistry and a highly functionalized nature make them suitable starting materials to translate their structural and stereochemical features into intermediates for the synthesis of bioactive compounds.[3] As part of our ongoing research directed to the development of new methodology leading to functionalized heterocycles as precursors of natural products and biologically active substances, we have reported on the application of the β-fragmentation reaction of hemiacetals[4] to the anomeric alcohols of carbohydrates in order to obtain chiral furanose and pyranose derivatives.[5] The reaction is mostly based on the use of iodine hypervalent compounds that have become very common reagents.[6]

In the context of a program directed to synthesize alduronic acid lactones,[7] also called pseudolactones, we conceived a tandem strategy starting with cyclic alduronic acids. The methodology relies upon the formation, in a first step, of an alkoxy anomeric radical that is originated through the action of the system formed by oxidizing reagent−iodine that favors, under mild conditions, a β-fragmentation reaction of the C1−C2 bond. In a second step, the intermediate C2 radical can be oxidized by an excess of reagent to give an oxonium ion that reacts intramolecularly with the nucleophilic carboxyl group to give the lactone (Scheme 1).

Erythruronic and threuronic acid 4,1-lactones are interesting starting materials for the synthesis of carbocycles from carbohydrates.[8] The application of the Fujimoto−Belleau reaction[9] or its Wadsworth−Emmons modification to these pseudolactones gave enantiomerically pure dihydroxycyclopentenones,[10] which are important synthons for the preparation of carbocyclic nucleosides and prostaglandins.[11] Starting from 4,1- or 1,4-pseudolactones of the same sugar, enantiodivergent synthesis of these cyclopentenones may be possible.

(1) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon−Carbon Bonds*; Pergamon Press: New York, 1986. (b) Surzur, J.-M.; Bertrand, M. P. *Pure Appl. Chem.* **1988**, *60*, 1659. (c) Clive, D. L. *Pure Appl. Chem.* **1988**, *60*, 1645. (d) Neumann, W. P. *Synthesis* **1987**, 665. (e) Stork, G.; Reynolds, M. E. *J. Am. Chem. Soc.* **1988**, *110*, 6911.

(2) Ho, T.-L. *Tandem Organic Reactions*; Wiley-Interscience: New York, 1992. (b) Bunce, R. A. *Tetrahedron* **1995**, *51*, 13103.

(3) Hanessian, S. *Total Synthesis of Natural Products. The Chiron Approach*; Pergamon Press: Oxford, 1983. Inch, T. D. *Tetrahedron* **1984**, *40*, 3161.

(4) Freire, R.; Marrero, J. J.; Rodríguez, M. S.; Suárez, E. *Tetrahedron Lett.* **1986**, *27*, 383. (b) Arencibia, M. T.; Freire, R.; Perales, A.; Rodríguez, M. S.; Suárez, E. *J. Chem. Soc., Perkin Trans. 1* **1991**, 3349.

(5) (a) Armas, P.; Francisco, C. G.; Suárez, E. *J. Am. Chem. Soc.* **1993**, *115*, 8865. (b) Armas, P.; Francisco, C. G.; Suárez, E. *Tetrahedron Lett.* **1993**, *34*, 7331.

(6) For late reviews on iodine hypervalent reagents see: (a) Prakash, O.; Saini, N.; Sharma, P. K. *Heterocycles* **1994**, *38*, 409. (b) Varvoglis, A. *Tetrahedron* **1997**, *53*, 1179. (c) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: San Diego, 1997 and references therein.

(7) For preliminary report see: Francisco, C. G.; González, C. C.; Suárez, E. *Tetrahedron Lett.* **1996**, *37*, 1687.

(8) (a) Agrofoglio, L.; Suhas, E.; Farese, A.; Condom, R.; Challand, S. R.; Earl, R. A.; Guedj, R. *Tetrahedron* **1994**, *50*, 10611. (b) Jenkins, G. N.; Turner, N. J. *Chem. Soc. Rev.* **1995**, *24*, 169. (c) Huryn, D. M.; Okabe, M. *Chem. Rev.* **1992**, *92*, 1745.

(9) (a) Belleau, B. *J. Am. Chem. Soc.* **1951**, *73*, 5441. (b) Fujimoto, G. I. *J. Am. Chem. Soc.* **1951**, *73*, 1856.

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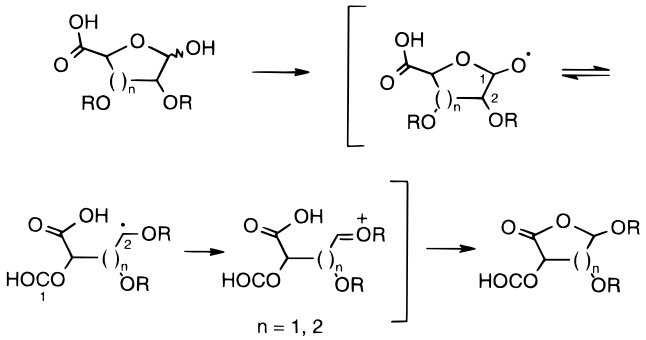
Scheme 1

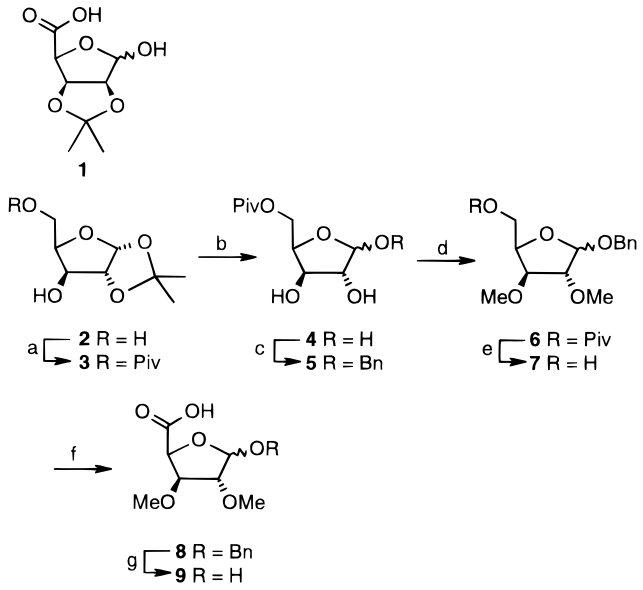


Analogously, alduronic acid 5,1-lactones are also interesting intermediates in the synthesis of polyhydroxycyclohexanes following the above-mentioned methodology,[12] as an alternative to the classical Ferrier carbocyclization.[13] In fact, this method has been applied to the synthesis of inositols and some glyoxalase inhibitors which have been studied as cytotoxic and potentially cancerostatic agents.[12] The synthesis of 4,1- and 5,1-alduronic acid lactones has been traditionally accomplished using degradative approaches or by ozonolysis of the hex-5-enopyranoside intermediate of the Ferrier reaction, but no general methodology has been described.[14]

Results and Discussion

Herein we describe the cleavage, with simultaneous one-carbon degradation and cyclization, of aldopyranosuronic and aldofuranosuronic acid lactones under conditions compatible with the stability of the protective groups most frequently used in carbohydrate chemistry. In a recent paper[7] we described the preliminary results obtained with DIB/I_2, and we now report full details of these experiments, their extension to a number of substrates, and the use of another oxidizing system based on a selenium(IV) reagent, as a possible alternative to DIB. We have investigated the use of new oxidizing agents based on selenium(IV) such as diphenylselenium diacetate, diphenylselenium bis(trifluoroacetate), and diphenylhydroxyselenium acetate as possible alternatives to those of hypervalent iodine, and we found[15] that this latter reagent is a nonhygroscopic, crystalline, and readily available solid able to promote the generation of alkoxy radicals. To test the scope of these reactions, we prepared substrates from both threose and erythrose carbohydrate series, as depicted in Schemes 2−7.

Scheme 2[a]



[a] Key: (a) pivaloyl chloride, py, 0 °C, 10 min, 83%. (b) 60% aqueous TFA, rt, 2 h, 94%. (c) benzyl alcohol, CSA, 40 °C, 3 h, 62%. (d) F_4BH, CH_2Cl_2, rt, 85%. (e) NaOMe, MeOH, 40 °C, 5 h, 92%. (f) PDC, DMF, rt, 24 h, 73%. (g) $Pd(OH)_2$/C, H_2, EtOH, rt, 20 h, 98%.

Substrates from Threose Series. The lyxuronic acid derivative **1** was prepared starting from 2,3-*O*-isopropylidene-D-mannose following the procedure described by Schmidt et al.[16] Xyluronic acid derivative **9** was obtained from the commercially available 1,2-*O*-isopropylidene-D-xylose (**2**) that was selectively monoprotected with pivaloyl chloride to give the ester **3**. Then, after cleavage of the acetal, the resulting triol **4** was benzylated at the anomeric position to give **5** that was methylated[17] to yield **6**. Deprotection of the pivaloate[18] group and oxidation of the primary alcohol gave acid **8** from which the desired substrate **9** was obtained by hydrogenolysis (Scheme 2). The galacturonic acid derivative **13** was prepared from the commercial acid that was treated with benzyl alcohol and dimethoxypropane to give the isopropylidene derivative **11** which after silylation and hydrogenolysis yielded **13** (Scheme 3).

Substrates from Erythrose Series. 5-*O*-*tert*-(Butyldimethylsilyl)-2,3-*O*-isopropylidene-D-ribose[19] (**14**) was

(10) (a) Borcherding, D. R.; Scholtz, S. A.; Borchardt, R. T. *J. Org. Chem.* **1987**, *52*, 5457. (b) Wolfe, M. S.; Borcherding, D. R.; Borchardt, R. T. *Tetrahedron Lett.* **1989**, *30*, 1453. (c) Ali, S. M.; Ramesh, K.; Borchardt, R. T. *Tetrahedron Lett.* **1990**, *31*, 1509. For other methods of synthesis of 2,3-dihydroxy-4-cyclopentenones see: (d) Armstrong, A.; Hayter, B. R. *Tetrahedron: Asymmetry* **1997**, *8*, 1677. (e) Sundermann, B.; Scharf, H.-D. *Tetrahedron: Asymmetry* **1996**, *7*, 1995. (f) Johnson, C. R.; Esker, J. L.; Van Zandt, M. C. *J. Org. Chem.* **1994**, *59*, 5854. (g) Beer, D.; Meuwly, R.; Vasella, A. *Helv. Chim. Acta* **1982**, *65*, 2570. (h) Bélanger, P.; Prasit, P. *Tetrahedron Lett.* **1988**, *29*, 5521. (i) Bestmann, H. J.; Moenius, T. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 994. (j) Deardorft, D. R.; Shambayati, S.; Myles, D. C.; Heerding, D. *J. Org. Chem.* **1988**, *53*, 3614. (k) Hudlicky, T.; Luna, H. Barbieri, G.; Kwart, L. D. *J. Am. Chem. Soc.* **1988**, *110*, 4735.

(11) (a) Johnson, C. R. *Pure Appl. Chem.* **1987**, *59*, 969. (b) Johnson, C. R.; Penning, T. D. *J. Am. Chem. Soc.* **1986**, *108*, 5655. (c) Johnson, C. R.; Chen, Y.-F. *J. Org. Chem.* **1991**, *56*, 3344. (d) Lim, M.-I.; Marquez, V. E. *Tetrahedron Lett.* **1983**, *24*, 5559. (e) Medich, J. R.; Kunnen, K. B.; Johnson, C. R. *Tetrahedron Lett.* **1987**, *28*, 4131. (f) Nokami, J.; Matsuura, H.; Takahashi, H.; Yamashita, M. *Synlett* **1994**, 491. (g) Hill, J. M.; Hutchinson, E. J.; Le Grand, D. M.; Roberts, S. M.; Thorpe, A. J.; Turner, N. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1483. (h) Wolfe, M. S.; Anderson, B. L.; Borcherding, D. R.; Borchardt, R. T. *J. Org. Chem.* **1990**, *55*, 4712. (i) Bestmann, H. J.; Roth, D. *Synlett* **1990**, 751. (j) Wang, P.; Agrofoglio, L. A.; Newton, M. G.; Chu, C. K. *Tetrahedron Lett.* **1997**, *38*, 4207. (k) Roth, G. J.; Kirschbaum, S.; Bestmann, H. J. *Synlett* **1997**, 618.

(12) Aloui, M.; Lygo, B.; Trabsa, H. *Synlett* **1994**, 115. (b) Mirza, S.; Molleyres, L. P.; Vasella, A. *Helv. Chim. Acta* **1985**, *68*, 988.

(13) (a) Ferrier, R. J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1455. For examples see: (b) Semeria, D.; Philippe, M.; Delaumeny, J. M.; Sepulchre, A. M.; Gero, S. D. *Synthesis* **1983**, 710. (c) Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1979**, *64*, 1990. (d) Jaramillo, C.; Chiara, J. L.; Martín-Lomas, M. *J. Org. Chem.* **1994**, *59*, 3135.

(14) Timoshchuk, V. A. *Russ. Chem. Rev.* **1995**, *64*, 675.

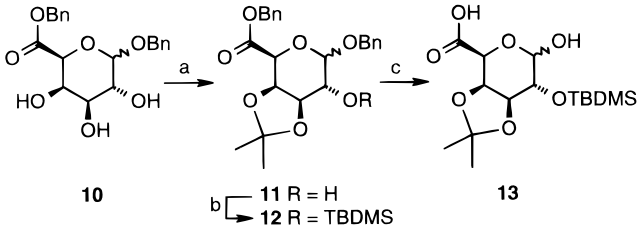
(15) (a) Dorta, R. L.; Francisco, C. G.; Freire, R.; Suárez, E. *Tetrahedron Lett.* **1988**, *29*, 5429. (b) Dorta, R. L.; Francisco, C. G.; Suárez, E. *Tetrahedron Lett.* **1994**, *35*, 1083. (c) Dorta, R. L.; Francisco, C. G.; Suárez, E. *Tetrahedron Lett.* **1994**, *35*, 2049.

(16) Schmidt, R. R.; Hermetin, P. *Chem. Ber.* **1979**, *112*, 3616.

(17) Neeman, M.; Johnson, W. S. *Organic Syntheses*; Wiley: New York, 1973; Coll. Vol. V, p 245.

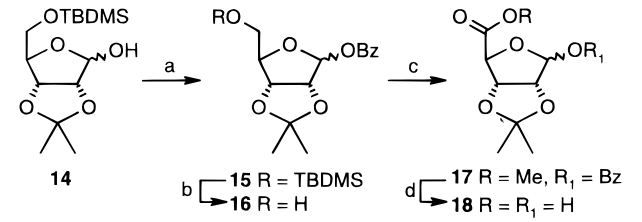
(18) Nakatani, K.; Arai, K.; Hirayama, N.; Matsuda, F.; Terashima, S. *Tetrahedron* **1992**, *48*, 633.

Scheme 3[a]



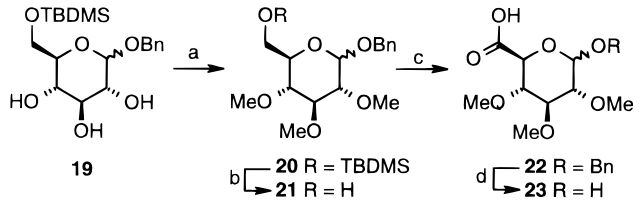
[a] Key: (a) dimethoxypropane (DMP), CSA, rt, 12 h, 81%. (b) TBDMSCl, imidazole, DMF, rt, 18 h, 82%. (c) $Pd(OH)_2/C$, H_2, EtOH, rt, 20 h, 83%.

Scheme 4[a]



[a] Key: (a) benzoyl chloride, DMAP, py, rt, 4.5 h, 91%. (b) TBAF, THF, rt, 4 h, 98%. (c) (i) PDC, DMF, rt, 10 h; (ii) CH_2N_2, diethyl ether, 0 °C, 15 min, 70%. (d) NaOH, H_2O, rt, 15 h, 87%.

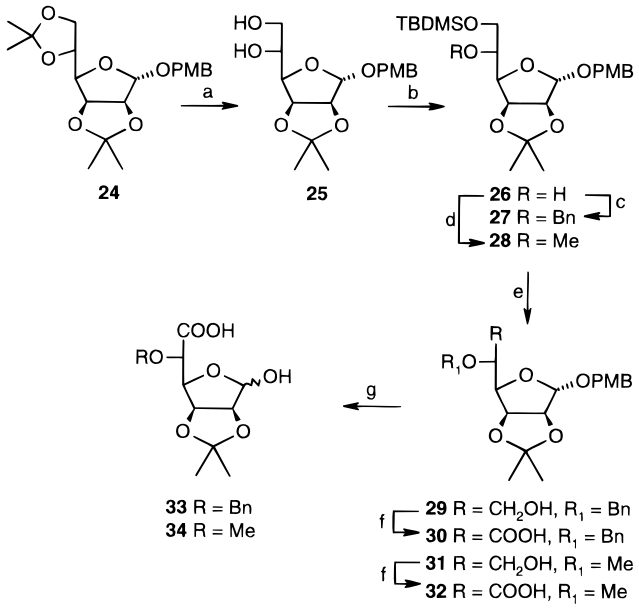
Scheme 5[a]



[a] Key: (a) NaH, CH_3I, DMF, 0 °C, 2 h, 98%. (b) TBAF, THF, rt, 2 h, 89%. (c) PDC, DMF, rt, 20 h, 89%. (d) $Pd(OH)_2/C$, H_2, MeOH, rt, 8 h, 83%.

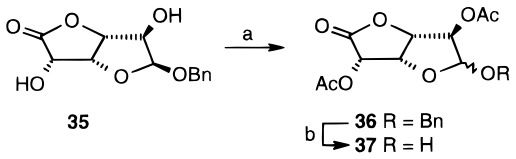
benzoylated, and the resulting ester **15** was desilylated and oxidized[20] to give the acid that was methylated and then hydrolyzed to the riburonic acid derivative **18**[21] (Scheme 4). Glucuronic acid derivative **23** was prepared starting with D-glucose that was selectively protected at C1, with benzyl alcohol/camphorsulfonic acid, and at C6, with *tert*-butyldimethylsilyl chloride/imidazole to give triol **19**; this triol was methylated with MeI and desilylated to yield the alcohol **21** that was oxidized to acid **22** which after debenzylation with $H_2/Pd(OH)_2/C$ gave substrate **23** (Scheme 5). Mannofuranosuronic acid derivatives **33** and **34** were prepared from the silyl ether **26**, obtained from the commercially available 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose that was *p*-methoxybenzylated, had the 5,6 acetal cleaved and was selectively silylated at C6. The alcohol **26** was successively benzylated, desilylated,[22] and oxidized to give acid **30** that after removal[23] of the *p*-methoxybenzyl group with CAN afforded substrate **33**. Alternatively, methylation of alcohol **26** following the same procedure gave substrate **34**

Scheme 6[a]



[a] Key: (a) 70% aqueous AcOH, rt, 18 h, 93%. (b) TBDMSCl, imidazole, DMF, rt, 6 h, 86%. (c) NaH, benzyl bromide, DMF, rt, 10 h, 79%. (d) NaH, CH_3I, DMF, rt, 5 h, 90%. (e) NH_4F, MeOH, rt, 20 h, 91%. (f) PDC, DMF, rt, 20 h, 70%. (g) CAN, acetonitrile/H_2O, 0 °C, 90 min, 74%.

Scheme 7[a]



[a] Key: (a) Ac_2O, py, rt, 1 h, 72%. (b) $Pd(OH)_2/C$, H_2, EtOAc, rt, 38 h, 92%.

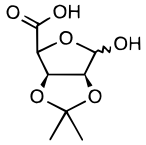
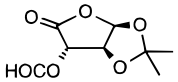
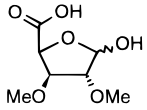
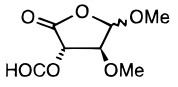
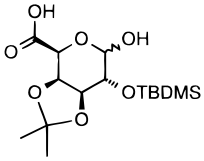
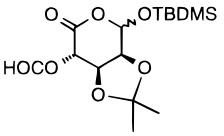
(Scheme 6). As a last model we prepared 2,5-di-*O*-acetyl-D-glucurono-6,3-lactone (**37**) starting from D-glucurono-6,3-lactone by formation of the benzyl glycoside **35**, acetylation, and subsequent deprotection of the anomeric alcohol (Scheme 7).

As can be seen in Tables 1 and 2, our procedure was applied to pentoses and hexoses of the two series of carbohydrates with the aim to obtain alduronic acid 4,1- and 5,1-lactones. When the reaction was performed with the lyxuronic acid derivative **1** using DIB/iodine as oxidizing system (method A, Table 1, entry 1) in dry CH_2Cl_2, at room temperature, the butyrolactone **38** was obtained in moderate yield. A singlet appears at 8.09 ppm in its ^1H NMR spectrum assignable to the proton of the OCOH group, originated by C1 after the scission of the C1−C2 bond, the corresponding carbon at 159.1 ppm being observed in the ^{13}C NMR spectrum. The β-fragmentation of the xyluronic acid derivative **9** using the same reagent gave a differently protected threuronic acid lactone **39** as a separable anomeric mixture (α:β, 1:1.75) (entry 3). A ROESY interaction between H1 and H2 in the β-anomer, not observed in the α-anomer, confirmed the stereochemistry assigned.

The use of the system diphenylhydroxyselenium acetate/iodine as oxidizing agent (method B) was also shown to be able to produce the β-fragmentation−cyclization reaction of these uronic acid derivatives, as seen in Table 1 (entries 2 and 4) with a somewhat lower yield; in this

(19) Kaskar, B.; Heise, G. L.; Michalak, R. S.; Vishnuvajjala, B. R. *Synthesis* **1990**, 1031.
(20) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, *5*, 399.
(21) Schmidt, R. R.; Jung, K.-H.; Hermetin, P. *Chem. Ber.* **1978**, 3311.
(22) Zhang, W.; Robins, M. J.; *Tetrahedron Lett.* **1992**, *33*, 1177.
(23) Johansson, R.; Samuelsson, B. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2371.

Table 1. Synthesis of Alduronic Acid Lactones of the Threose Series

entry	substrate	method[a]	time(h)	product	yield (%)
1	 **1**	A	1	 **38**	51
2	**1**	B	3	**38**	40
3	 **9**	A	1.5	 **39**α,β	62 (1:1.75)
4	**9**	B	3	**39**α,β	51 (1:1)
5	 **13**	A	1	 **40**α,β	70 (2.7:1)
6	**13**	B	1	**40**α,β	70 (2.7:1)

[a] Method A: (Diacetoxyiodo)benzene (DIB) (2 mmol) and I_2 (1.2 mmol) in CH_2Cl_2 (0.05 mmol/mL) at room temperature. Method B: diphenylhydroxyselenium acetate (DHSA) [$Ph_2Se(OH)(OAc)$] (2.5 mmol) and I_2 (1.2 mmol) in CCl_4 (0.05 mmol/mL) at reflux temperature under irradiation with two 80 W tungsten filament lamps.

case the reaction was performed in CCl_4, heated to 80 °C, and favored by visible light irradiation.

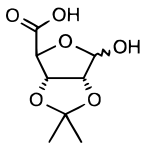
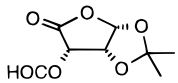
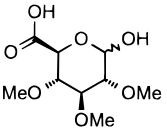
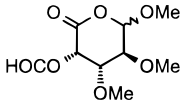
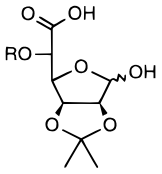
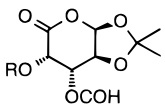
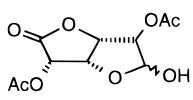
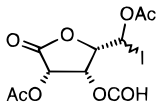
This reaction can also be used with the hexopyranose derivative of the galacturonic acid **13** to give an anomeric mixture (α:*β*, 2.7:1) of 5,1-lyxuronic acid lactone **40** (entry 5), easily separable by chromatography. In the ^1H NMR in C_6D_6 as solvent the doublet corresponding to H1 is displayed at 5.35 ppm (J = 6.8 Hz), for the α-anomer, and at 5.37 ppm (J = 3.4 Hz) for the *β*-anomer. The C1 stereochemistry was confirmed by ROESY experiments; the α-anomer shows transannular interaction between H1 and H4 at the *β*-side of the molecule. Both oxidizing agents gave similar yields (70%) (entries 5 and 6).

The results obtained in the reaction with different uronic acids belonging to the erythrose series of carbohydrates are collected in Table 2. Riburonic acid (**18**) led to 4,1-erythruronic acid lactone **41** as the only reaction product with the expected 1,2 *cis*-stereochemistry.

The reaction of the glucuronic acid derivative **23** yielded a chromatographically separable anomeric mixture (1:1) of arabinopyranuronic acid lactones **42**. The coupling constants between H1 and H2 in both α- and *β*-anomers are very similar (4.5 and 3.2 Hz, respectively) and the stereochemistry at C1 was established on the basis of the ROESY spectrum, interactions of H1 with H3 and H4 being observed in the α-anomer, while they are not observable in the *β*-anomer.

A furanose fragmentation followed by a six-membered ring cyclization transformed mannofuranuronic acid **33** into another 5,1-arabinopyranuronic acid lactone **43**, in which the formate ester protected the hydroxyl group at C3. Only the 1,2-*cis*-isopropylidene isomer was obtained, but it is remarkable to note the influence of the protective group at C5 because when the reaction was performed

Table 2. Synthesis of Alduronic Acid Lactones of the Erythrose Series

entry	substrate	method[a]	time(h)	product	yield (%)
1	 **18**	A	1	 **41**	43
2	**18**	B	3	**41**	37
3	 **23**	A	1	 **42**α,β	57 (1:1)
4	**23**	B	3	**42**α,β	51 (1:1)
5	 **33** R = Bn	A	3	 **43** R = Bn	52
6	**33** R = Bn	B	3	**43** R = Bn	44
7	**34** R = Me	A	3	**44** R = Me	25
8	 **37**	A	1.5	 **45**	67

[a] Method A: (Diacetoxyiodo)benzene (DIB) (2 mmol) and I_2 (1.2 mmol) in CH_2Cl_2 (0.05 mmol/mL) at room temperature. Method B: diphenylhydroxyselenium acetate (DHSA) [$Ph_2Se(OH)(OAc)$] (2.5 mmol) and I_2 (1.2 mmol) in CCl_4 (0.05 mmol/mL) at reflux temperature under irradiation with two 80 W tungsten filament lamps.

with the methyl ether **34** only a small amount of lactone **44** was obtained, although an explanation for this fact is not clear at present.

In the second step of this tandem process competition may exist between an intramolecular cyclization with the carboxyl group or an intermolecular trapping of the radical or cation at C2, respectively, by atoms of iodine or acetate anions coming from the reagents in the medium (Scheme 1). Although side products from these intermolecular reactions were not detected in the above-mentioned models, we prepared the *γ*-lactone **37** from glucuronic acid in order to check this possibility. As shown in Table 2 (entry 8) the fragmentation of **37** using method A led to a 5,2-arabinuronic acid lactone derivative **45** in which the radical intermediate reacted with an atom of iodine, before the oxidation to the oxonium ion could take place.

As can be observed from Table 2 (entries 3−8) a number of arabinuronic lactones possessing very different patterns of protection have been synthesized in order to explore the utility of this metodology for the synthesis of chiral synthons.

We observed that the *β*-fragmentation reaction behavior does not depend on the C2 stereochemistry of the substrates or the protective groups in that position, nor

even on ring size since it takes place with furanose or pyranose substrates, as can be deduced from the tables.

In summary, this procedure provides a new, simple methodology to transform alduronic acids into the corresponding 1-noralduronic acid 4,1- and 5,1-lactones. This one-pot two-step protocol begins with the anomeric alkoxy radical formation, by the action of DIB or the DHSA−iodine system, promoting a β-fragmentation reaction that converts the C1 in the formate carbon of the protective group of the alcohol function α or β to the carboxyl group of the final lactone. In a second step the C2 oxonium ion formed is intramolecularly trapped by a carboxyl group to yield the lactone, with one carbon less than the starting uronic acid, so this can also be considered to be a procedure to descend the uronic acid series step by step. This is a simple general method to obtain these pseudolactones, which have been previously synthesized by degradative pathways of the C5 and/or C6 of the carbohydrate skeleton.[14] The different substitution pattern in the final products seems convenient if selective transformations of these chiral synthons are needed.

DHSA can be used as an alternative to DIB since the behavior of the reaction is similar, and the minor yields mostly observed in these experiments we believe are closely related with the low solubility of the reagent in the solvent.

Experimental Section

General. Melting points were determined with a hot-stage apparatus and are uncorrected. Optical rotation measurements were recorded at room temperature in $CHCl_3$. IR spectra were recorded in CCl_4 solutions, unless otherwise stated. NMR spectra were determined at 200, 400, or 500 MHz for ^1H and 50.3 MHz for ^{13}C for $CDCl_3$ solutions in the presence of TMS as internal standard, unless otherwise stated. Mass spectra were determined by EI at 70 eV, unless otherwise stated. Merck silica gel 60 PF_{254} and 60 (0.063−0.2 mm) were used for preparative thin-layer chromatography (TLC) and column chromatography, respectively. Circular layers of 1 mm of Merck silica gel 60 PF_{254} were used on a Chromatotron for centrifugally assisted chromatography. Commercial reagents and solvents were analytical grade or were purified by standard procedures prior to use. All reactions involving air- or moisture-sensitive materials were carried out under an argon atmosphere. The spray reagent for TLC was vanillin (1 g) in H_2SO_4−EtOH (4:1; 200 mL). (Diacetoxyiodo)benzene (DIB) 98% was purchased from Aldrich. Diphenylhydroxyselenium acetate (DHSA) [$Ph_2Se(OH)(OAc)$] has been previously prepared in this laboratory.

1,2-*O*-Isopropylidene-5-*O*-pivaloyl-α-D-xylofuranose (3). To a solution of commercially available 1,2-*O*-isopropylidene-α-D-xylofuranose (**2**)[24] (4.44 g, 23.4 mmol) in dry pyridine (15 mL) was slowly added at 0 °C pivaloyl chloride (3.5 mL, 28.04 mmol) and stirred for 10 min. The reaction was poured into water and extracted with diethyl ether. The combined extracts were washed with aqueous HCl, $NaHCO_3$, and water and dried over Na_2SO_4. Silica gel flash chromatography of the residue (hexanes−EtOAc, 8:2) gave compound **3** (5.26 g, 83%) as a syrup: $[\alpha]_D$ +34° (c = 0.176); IR 3498, 1716 cm^{-1}; ^1H NMR 1.22 (9H, s), 1.32 (3H, s), 1.51 (3H, s), 4.03 (1H, d, J = 2.4 Hz), 4.14 (1H, dd, J = 4.4, 10.4 Hz), 4.22 (1H, ddd, J = 4.4, 7.5, 2.4 Hz), 4.56 (1H, dd, J = 7.5, 10.4 Hz), 4.57 (1H, d, J = 3.5 Hz), 5.92 (1H, d, J = 3.5 Hz); ^{13}C NMR 26.0 (q), 26.6 (q), 26.9 (3 × q), 38.7 (s), 61.0 (t), 74.2 (d), 78.4 (d), 84.8 (d), 104.6 (d), 111.6 (s), 179.4 (s); MS m/z (rel intensity) 275 (M^+ + 1, 3), 260 (18), 259 (96), 217 (5), 199 (3), 159 (30), 172 (16), 115 (15). Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.90; H, 8.09. Found: C, 56.73; H, 8.17.

(24) *Carbohydrates*; Collins, P. M., Ed.; Chapman and Hall: London, 1987; p 301.

5-*O*-Pivaloyl-D-xylofuranose (4). Compound **3** (5.1 g, 18.6 mmol) was dissolved in TFA 60% (40 mL), stirred at room temperature for 2 h, concentrated, and purified by silica gel flash chromatography (hexanes−EtOAc, 1:1 → EtOAc) to give **4** (4.1 g, 17.5 mmol, 94%) as a syrup: IR 3604, 3450, 1717 cm^{-1}; ^1H NMR 1.20 (9H, s), 1.21 (9H, s), 4.09−4.39 (5H, m), 5.22 (1H, s), 5.49 (1H, d, J = 3.8 Hz); ^{13}C NMR 27.1 (6 × q), 38.8 (s), 38.8 (s), 63.0 (t), 63.7 (t), 75.5 (d), 75.7 (d), 76.6 (2 × d), 80.1 (2 × d), 96.1 (d), 102.8 (d), 179.5 (s), 179.7 (s); MS (CI, CH_4) m/z (rel intensity) 235 (M^+ + 1, 5), 217 (100), 199 (11), 159 (1), 133 (14), 115 (45), 97 (23). Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.27; H, 7.75. Found: C, 51.20; H, 7.81.

Benzyl 5-*O*-Pivaloyl-D-xylofuranoside (5). To a solution of compound **4** (1.63 g, 7 mmol) in benzyl alcohol (10 mL) was added camphorsulfonic acid (170 mg) and stirred at 40 °C for 3 h. The reaction was concentrated under high vacuum and purified by flash chromatography (hexanes−EtOAc, 1:1) to give **5** (1.39 g, 62%) as an inseparable anomeric mixture: syrup, IR 3524, 1724 cm^{-1}; ^1H NMR 1.23 (9H, s), 1.24 (9H, s), 4.13−4.50 (5H, m), 4.57 (1H, d, J = 11.6 Hz), 4.62 (1H, d, J = 11.6 Hz), 4.80 (1H, d, J = 11.6 Hz), 4.88 (1H, d, J = 11.6 Hz), 5.05 (1H, s), 5.24 (1H, d, J = 3.8 Hz), 7.31−7.37 (5H, m); ^{13}C NMR 27.1 (6 × q), 38.7 (2 × s), 62.3 (t), 63.7 (t), 69.3 (t), 70.0 (t), 76.2 (d), 76.4 (d), 76.7 (d), 78.1 (d), 79.6 (d), 80.7 (d), 99.8 (d), 106.3 (d), 128.0 (4 × d), 128.2 (2 × d), 128.4 (4 × d), 133.7 (s), 136.9 (s), 178.6 (s), 178.9 (s); MS m/z (rel intensity) 325 (M^+ + 1, 2), 307 (6), 217 (36), 199 (3), 131 (21), 116 (9), 142 (6). Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46. Found: C, 63.12; H, 7.53.

Benzyl 2,3-di-*O*-Methyl-5-*O*-pivaloyl-D-xylofuranoside (6). To a solution of compound **5** (500 mg, 1.54 mmol) in CH_2Cl_2 (5 mL) were added F_4BH (0.14 g, 19.6 mmol) dissolved in diethyl ether (6 mL) and CH_2Cl_2 (2 mL). This mixture was treated dropwise at room temperature with CH_2N_2 in CH_2Cl_2 until the reaction turned yellow; then it was poured into water and extracted with CH_2Cl_2. The organic extract was concentrated and purified by flash chromatography (hexanes−EtOAc, 8:2 → 1:1) to give **6** (462 mg, 85%), as an anomeric mixture, which was partially resolved under these conditions. β-Anomer **6**β: syrup; $[\alpha]_D$ −38.3° (c = 0.316); IR 1731 cm^{-1}; ^1H NMR 1.23 (9H, s), 3.38 (3H, s), 3.42 (3H, s), 3.84−3.87 (2H, m), 4.23 (1H, dd, J = 7.7, 11.1 Hz), 4.40 (1H, dd, J = 4.1, 11.1 Hz), 4.46−4.53 (1H, m), 4.49 (1H, d, J = 11.9 Hz), 4.83 (1H, d, J = 11.9 Hz), 5.03 (1H, s), 7.31−7.37 (5H, m); ^{13}C NMR 27.0 (3 × q), 38.6 (s), 57.5 (q), 58.3 (q), 63.9 (t), 69.2 (t), 78.4 (d), 84.3 (d), 88.5 (d), 105.1 (d), 127.6 (d), 127.9 (2 × d), 128.2 (2 × d), 137.3 (s), 178.1 (s); MS m/z (rel intensity) 353 (M^+ + 1, 1), 261 (1), 245 (99), 229 (3), 213 (2), 214 (1). Anal. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01. Found: C, 64.55; H, 7.90. α-Anomer **6**α: syrup; $[\alpha]_D$ +138.6° (c = 0.22); IR 1732 cm^{-1}; ^1H NMR 1.23 (9H, s), 3.41 (3H, s), 3.43 (3H, s), 3.82 (1H, dd, J = 4.3, 6.0 Hz), 4.05 (1H, dd, J = 6.0, 6.8 Hz), 4.16 (1H, dd, J = 6.5, 11.9 Hz), 4.30 (1H, dd, J = 3.8, 11.9 Hz), 4.41 (1H, ddd, J = 6.8, 3.8, 6.5 Hz), 4.61 (1H, d, J = 12.2 Hz), 4.83 (1H, d, J = 12.2 Hz), 5.04 (1H, d, J = 4.3 Hz), 7.31−7.40 (5H, m); ^{13}C NMR 27.0 (3 × q), 38.6 (s), 58.1 (q), 58.5 (q), 62.9 (t), 68.9 (t), 74.9 (d), 83.2 (d), 85.8 (d), 97.7 (d), 127.7 (d), 128.1 (2 × d), 128.3 (2 × d), 137.4 (s), 178.1 (s); MS m/z (rel intensity) 245 (M^+ − OBn, 24), 229 (1), 213 (1), 177 (22), 145 (10), 129 (20). Anal. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01. Found: C, 64.74; H, 7.97.

Benzyl 2,3-di-*O*-Methyl-D-xylofuranoside (7). To a solution of compound **6** (385 mg, 1.09 mmol) in MeOH (10 mL) was added NaOMe (40 mg, 0.74 mmol). The reaction was stirred at 40 °C for 5 h, poured into water, and extracted with ethyl acetate, and after concentration the residue was purified by silica gel flash chromatography (hexanes−EtOAc, 80:20 → 1:1) to yield **7** (270 mg, 92%). This anomeric mixture (ratio 1:1) could be separated under these conditions. β-Anomer **7**β: syrup; $[\alpha]_D$ −94° (c = 0.132); IR 3573 cm^{-1}; ^1H NMR 3.38 (3H, s), 3.44 (3H, s), 3.75−3.81 (2H, m), 3.90 (1H, d, J = 1.6 Hz), 3.95 (1H, d, J = 3.8 Hz), 4.37 (1H, m), 4.56 (1H, d, J = 11.9 Hz), 4.82 (1H, d, J = 11.9 Hz), 5.04 (1H, d, J = 1.6 Hz), 7.31−7.34 (5H, m); ^{13}C NMR 57.4 (q), 58.1 (q), 61.9 (t), 69.5 (t), 80.5 (d), 84.9 (d), 88.6 (d), 105.2 (d), 127.6 (d), 127.9 (2 ×

d), 128.1 (2 × d), 137.1 (s); MS *m/z* (rel intensity) 269 (M^+ + 1, 4), 251 (11), 219 (8), 177 (26), 162 (2), 161 (5), 145 (7), 143 (2), 129 (20). Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.91; H, 7.33. α-Anomer **7**α: syrup; $[\alpha]_D$ +156.5° (*c* = 0.122); IR 3568 cm^{-1}; ^1H NMR 3.38 (3H, s), 3.49 (3H, s), 3.74−3.85 (3H, m), 4.19 (1H, dd, *J* = 4.7, 6.2 Hz), 4.28 (1H, dd, *J* = 4.0, 7.7 Hz), 4.62 (1H, d, *J* = 12.2 Hz), 4.81 (1H, d, *J* = 12.2 Hz), 5.13 (1H, d, *J* = 4.0 Hz), 7.32−7.34 (5H, m); ^{13}C NMR 57.4 (q), 58.15 (q), 61.4 (t), 68.4 (t), 76.4 (d), 83.6 (d), 86.0 (d), 96.9 (d), 127.4 (d), 127.6 (2 × d), 127.9 (2 × d), 137.0 (s); MS *m/z* (rel intensity) 251 (M^+ − OH, 2), 219 (2), 177 (25), 161 (5), 145 (4), 129 (5). Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.49; H, 7.35.

Benzyl 2,3-Di-*O*-methy-*β*-D-xylofuranosiduronic Acid (8). To a solution of compound **7***β* (216 mg, 0.81 mmol) in DMF (10 mL) was added PDC (2.1 g, 5.58 mmol). The reaction was stirred at room temperature for 24 h, poured into aqueous HCl, and extracted with diethyl ether. The combined extracts were washed with brine, dried, and concentrated. Silica gel flash chromatography (hexanes−EtOAc, 1:1) of the residue gave acid **8***β* (166 mg, 0.59 mmol, 73%) as a syrup: $[\alpha]_D$ −132.2° (*c* = 0.18); IR 3500−3300, 1732 cm^{-1}; ^1H NMR 3.37 (3H, s), 3.45 (3H, s), 3.87 (1H, d, *J* = 1.4 Hz), 4.04 (1H, dd, *J* = 1.4, 5.6 Hz), 4.70 (1H, d, *J* = 12.1 Hz), 4.88 (1H, d, *J* = 5.6 Hz), 4.92 (1H, d, *J* = 12.1 Hz), 5.18 (1H, s), 7.28−7.39 (5H, m); ^{13}C NMR 57.5 (q), 58.7 (q), 70.0 (t), 81.1 (d), 83.7 (d), 86.6 (d), 106.1 (d), 127.8 (d), 128.1 (2 × d), 128.4 (2 × d), 137.0 (s), 172.3 (s); MS *m/z* (rel intensity) 283 (M^+ + 1, 1), 265 (3), 237 (4), 159 (5), 145 (12), 143 (10), 113 (45), 115 (20). Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.56; H, 6.43. Found: C, 59.63; H, 6.35. Analogously, compound **7**α yielded the anomer **8**α (70%) as a syrup: $[\alpha]_D$ +86° (*c* = 0.092); IR 3400, 1731 cm^{-1}; ^1H NMR 3.43 (3H, s), 3.47 (3H, s), 3.88 (1H, dd, *J* = 4.3, 5.8 Hz), 4.26 (1H, dd, *J* = 5.8, 6.9 Hz), 4.64 (1H, d, *J* = 12.2 Hz), 4.83 (1H, d, *J* = 6.9 Hz), 4.84 (1H, d, *J* = 12.2 Hz) 5.29 (1H, d, *J* = 4.3 Hz), 7.32−7.38 (5H, m); ^{13}C NMR 58.1 (q), 58.7 (q), 69.3 (t), 77.0 (d), 83.7 (d), 84.4 (d), 98.9 (d), 127.6 (d), 127.9 (2 × d), 128.2 (2 × d), 137.0 (s), 173.3 (s); MS *m/z* (rel intensity) 283 (M^+ + 1, 1), 265 (7), 237 (13), 191 (4), 175 (3), 159 (16), 145 (51), 143 (11), 113 (100). Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.56; H, 6.43. Found: C, 59.68; H, 6.58.

2,3-Di-*O*-methyl-D-xylofuranuronic Acid (9). To a solution of compound **8** (207 mg, 0.73 mmol) in EtOH (15 mL) was added $Pd(OH)_2/C$ (40 mg), and the mixture was hydrogenated at room temperature for 20 h; then the suspension was filtered through Celite and concentrated to give acid **9** (138 mg, 0.72 mmol, 98%) as a syrup: IR 3689, 3426, 1727, 1602 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz) 3.29 (3H, s), 3.30 (3H, s), 3.32 (3H, s), 3.34 (3H, s), 3.59 (1H, dd, *J* = 1.8, 4.7 Hz), 3.64 (1H, dd, *J* = 4.7, 6.2 Hz), 3.82 (1H, dd, *J* = 2.7, 5.1 Hz), 4.00 (1H, dd, *J* = 5.1, 6.6 Hz), 4.43 (1H, d, *J* = 6.2 Hz), 4.52 (1H, d, *J* = 6.6 Hz), 5.00 (1H, d, *J* = 1.8 Hz), 5.31 (1H, d, *J* = 2.7 Hz); ^{13}C NMR (DMSO-d_6) 57.0 (q), 57.4 (2 × q), 58.0 (q), 76.0 (d), 79.8 (d), 82.9 (d), 83.2 (d), 84.3 (d), 88.7 (d), 95.3 (d), 101.6 (d), 170.6 (s), 170.9 (s); MS *m/z* (rel intensity) 193 (M^+ + 1, 6), 164 (3), 160 (5), 147 (16), 142 (23), 115 (10). Anal. Calcd for $C_7H_{12}O_6$: C, 43.75; H, 6.29. Found: C, 43.83; H, 6.15.

Benzyl (Benzyl D-Galactopyranosid)uronate (10). To a solution of D-galacturonic acid (500 mg, 2.36 mmol) in benzyl alcohol (20 mL) was added *p*-TsOH (90 mg, 0.47 mmol), and then it was stirred for 4 h at 80 °C. The solution was neutralized with Dowex 1-X8 and concentrated under high vacuum (1 mmHg). The residue was purified by column chromatography (CH_2Cl_2−MeOH, 90:10), yielding an inseparable anomeric mixture of ester **10** (825.2 mg, 94%): syrup, IR ($CHCl_3$) 3564, 3458, 1757, 1602 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz) 3.37, 3.8−5.57 (18H, m), 7.27−7.37 (10H, m); ^{13}C NMR (DMSO-d_6) 65.9 (t), 65.9 (t), 68.3 (t), 68.8 (t), 70.8 (d), 73.3 (d), 77.1 (d), 82.0 (d), 83.0 (d), 100.2 (d), 107.1 (d), 127.4−128.5 (10 × d), 136.1 (s), 137.9 (s), 172.2 (s); MS (CI, 15 eV, CH_4) *m/z* (rel intensity) 357 (M^+ − OH, 1), 283 (3), 267 (10), 265 (3), 249 (2), 221 (1), 148 (1), 131 (4); HRMS calcd for $C_{13}H_{15}O_7$ 283.08178, found 283.07684.

Benzyl (Benzyl 3,4-*O*-Isopropylidene-D-galactopyranosid)uronate (11). To a solution of ester **10** (200 mg, 0.53 mmol) in 2,2-dimethoxypropane (2 mL) was added camphorsulfonic acid (17.4 mg), and the reaction was stirred at room temperature for 12 h. After neutralization with basic resin (Dowex 1-X8), the reaction was concentrated and purified by column chromatography (hexanes−EtOAc, 1:1) to give the ester **11** (180 mg, 0.4 mmol, 81%), as a syrupy anomeric mixture: IR 3449, 1742 cm^{-1}; ^1H NMR (200 MHz) 1.33 (3H, s), 1.50 (3H, s), 3.97 (1H, dd, *J* = 4.0, 5.9 Hz), 4.38 (1H, dd, *J* = 5.9, 6.4 Hz), 4.57 (1H, dd, *J* = 6.4, 2.4 Hz), 4.65 (1H, d, *J* = 11.8 Hz), 4.72 (1H, d, *J* = 2.4 Hz), 4.86 (1H, d, *J* = 11.8 Hz), 5.13 (1H, d, *J* = 4.0 Hz), 5.24 (1H, d, *J* = 12.3 Hz), 5.35 (1H, d, *J* = 12.3 Hz), 7.33−7.41 (10H, m); ^{13}C NMR 25.6 (q), 26.1 (q), 27.1 (q), 27.8 (q), 66.7 (t), 66.9 (t), 68.1 (d), 68.7 (d), 70.2 (t), 70.8 (t), 72.1 (d), 72.8 (d), 73.4 (d), 73.6 (d), 75.2 (d), 78.3 (d), 96.6 (d), 100.7 (d), 110.0 (s), 110.5 (s), 127.8−128.6 (10 × d), 135.4 (s), 136.7 (s), 166.5 (s), 167.9 (s); MS *m/z* (rel intensity) 399 (M^+ − Me, 2), 323 (1), 305 (1), 290 (2), 249 (2). Anal. Calcd for $C_{23}H_{26}O_7$: C, 66.65; H, 6.32. Found: C, 66.54; H, 6.42.

Benzyl (Benzyl 2-*O*-(*tert*-Butyldimethylsilyl)-3,4-*O*-isopropylidene-D-galactopyranosid)uronate (12). To a solution of the ester **11** (242 mg, 0.63 mmol) in dry DMF (1 mL) at 0 °C, under Ar, were added imidazole (120 mg, 1.17 mmol) and TBDMSCl (104.6 mg, 0.70 mmol). The reaction was kept with stirring at room temperature for 18 h, poured into ice−water, and extracted with EtOAc. After concentration the residue was purified by silica gel flash chromatography (hexanes−EtOAc, 90:10) to give the silyl derivative **12** (231 mg, 82%) as a syrup: IR 1771, 1737 cm^{-1}; ^1H NMR −0.02 (6H, s), 0.88 (9H, s), 1.48 (3H, s), 1.51 (3H, s), 3.84 (1H, dd, *J* = 3.5, 7.2 Hz), 4.26 (1H, dd, *J* = 7.2, 6.1 Hz), 4.52 (1H, dd, *J* = 6.1, 3.0 Hz), 4.58 (1H, d, *J* = 12.3 Hz), 4.72 (1H, d, *J* = 3.0 Hz), 4.76 (1H, d, *J* = 12.3 Hz), 4.91 (1H, d, *J* = 3.5 Hz), 5.19 (1H, d, *J* = 12.4 Hz), 5.40 (1H, d, *J* = 12.4 Hz), 7.28−7.38 (sc); ^{13}C NMR −4.7 (2 × q), −4.6 (2 × q), 18.0 (2 × s), 25.7 (q), 26.2 (q), 26.3 (q), 27.7 (q), 28.0 (q), 66.8 (t), 68.1 (2 × d), 70.0 (t), 70.6 (t), 70.9 (t), 71.9 (d), 73.4 (d), 73.9 (d), 74.0 (d), 76.7 (d), 80.0 (d), 98.2 (d), 101.3 (d), 109.4 (s), 127.7−128.5 (10 × d), 135.5 (s), 136.9 (s), 168.2 (2 × s); MS (EI, 30 eV) *m/z* (rel intensity) 513 (M^+ − Me, 1), 471 (1), 413 (1), 363 (1), 305 (10). Anal. Calcd for $C_{29}H_{40}O_7Si$: C, 65.88; H, 7.63. Found: C, 65.91; H, 7.74.

2-*O*-(*tert*-Butyldimethylsilyl)-3,4-*O*-isopropylidene-D-galactopyranuronic Acid (13). Following the procedure described for **9**, TBDMS ether **12** (231 mg, 0.465 mmol) afforded, after purification by rotative chromatography on a Chromatotron (CH_2Cl_2−MeOH, 80:20), acid **13** (122.2 mg, 83%) as a syrup: IR ($CHCl_3$) 3521, 3430, 1775, 1602 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz) 0.05 (6H, s), 0.07 (6H, s), 0.85 (18H, s), 1.25 (6H, s), 1.39 (6H, s), 3.30 (1H, dd, *J* = 7.6, 6.9 Hz), 3.59 (1H, dd, *J* = 3.3, 7.0 Hz), 3.97 (1H, dd, *J* = 7.0, 6.7 Hz), 4.08 (1H, dd, *J* = 5.6, 6.9 Hz), 4.35 (1H, d, *J* = 7.6 Hz), 4.35 (1H, d, *J* = 5.6, 2.1 Hz), 4.45 (1H, dd, *J* = 6.7, 2.5 Hz), 4.46 (1H, d, *J* = 2.1 Hz), 4.62 (1H, d, *J* = 2.5 Hz), 4.94 (1H, d, *J* = 3.3 Hz); ^{13}C NMR (DMSO-d_6) −4.8 (q), −4.7 (q), −4.6 (q), −4.4 (q), 17.9 (2 × s), 25.8 (3 × q), 25.7 (3 × q), 26.1 (q), 26.4 (q), 27.86 (q), 27.94 (q), 66.3 (d), 70.7 (d), 71.4 (d), 73.7 (d), 74.4 (d), 75.6 (d), 76.2 (d), 80.0 (d), 91.8 (d), 95.7 (d), 108.3 (s), 108.8 (s), 168.8 (s), 169.4 (s); MS (EI, 30 eV) *m/z* (rel intensity) 348 (M^+, <1), 347 (1), 333 (3), 285 (1), 274 (1), 273 (7), 233 (5), 229 (10), 215 (11); HRMS calcd for $C_{14}H_{25}O_7Si$ 333.13696, found 333.13699.

Benzoyl 5-*O*-(*tert*-Butyldimethylsilyl)-2,3-*O*-isopropylidene-D-ribofuranose (15). To a solution of 5-*O*-(*tert*-butyldimethylsilyl)-2,3-*O*-isopropylidene-D-ribofuranose (**14**) (4.68 g, 15.4 mmol) in pyridine (10 mL) was added, under Ar, DMAP (187 mg); the reaction was cooled at 0 °C and benzoyl chloride (3.11 mL, 26.7 mmol) was added dropwise and then stirred at room temperature for 4.5 h, poured into aqueous HCl, and extracted with diethyl ether. Silica gel flash chromatography (hexanes−AcOEt, 95:5) of the concentrate yielded **15** (5.75, 14.1 mmol, 91%) as an anomeric mixture (*β*:α, 5:1), that could be separated under these conditions. *β*-Anomer **15***β* as a crystalline solid: mp 35−37 °C (from *n*-hexanes−EtOAc); $[\alpha]_D$ −49° (*c* = 0.546); IR 1736, 1696 cm^{-1}; ^1H NMR 0.02 (6H, s), 0.86 (9H, s), 1.36 (3H, s), 1.53 (3H, s), 3.61 (1H, dd, *J* = 10.3, 5.3 Hz), 3.71 (1H, dd, *J* = 10.3, 8.8 Hz), 4.36 (1H, dd, *J*

= 5.3, 8.8 Hz), 4.85 (2H, s), 6.42 (1H, s), 7.45−7.60 (3H, m), 7.98−8.02 (2H, m); ^{13}C NMR −5.5 (q), −5.4 (q), 18.2 (s), 25.0 (q), 25.8 (3 × q), 26.4 (q), 63.5 (t), 81.7 (d), 85.1 (d), 88.0 (d), 103.0 (d), 112.8 (s), 128.4 (2 × d), 129.6 (2 × d), 133.3 (d), 164.9 (s), one aromatic (s) could not be observed; MS *m*/*z* (rel intensity) 393 (M^+ − Me, 13), 351 (11), 303 (2), 292 (13), 287 (2), 257 (7), 229 (17). Anal. Calcd for $C_{21}H_{32}O_6Si$: C, 61.74; H, 7.89. Found: C, 62.05; H, 7.95. α-Anomer **15**α: syrup; $[\alpha]_D$ +3.7° (*c* = 0.74); IR 1728, 1603 cm^{-1}; ^{1}H NMR 0.09 (6H, s), 0.92 (9H, s), 1.35 (3H, s), 1.40 (3H, s), 3.78−3.81 (2H, m), 4.77 (1H, dd, *J* = 2.1 Hz), 4.79 (1H, dd, *J* = 2.1, 6.5 Hz), 4.89 (1H, dd, *J* = 6.5, 4.3 Hz), 6.41 (1H, d, *J* = 4.3 Hz), 7.39−7.56 (3H, m), 8.08−8.13 (2H, m); ^{13}C NMR −5.6 (q),-5.5 (q), 18.1 (s), 25.2 (q), 25.8 (3 × q), 25.9 (q), 63.8 (t), 80.6 (d), 83.7 (d), 98.4 (d), 114.4 (s), 128.2 (2 × d), 129.7 (s), 129.8 (2 × d), 133.0 (d), 165.0 (s), one aromatic (s) could not be observed; MS *m*/*z* (rel intensity) 393 (M^+ − Me, 6), 351 (5), 303 (2), 293 (10), 287 (32), 257 (6), 229 (21). Anal. Calcd for $C_{21}H_{32}O_6Si$: C, 61.74; H, 7.89. Found: C, 61.90; H, 7.85.

Benzoyl 2,3-*O*-Isopropylidene-D-ribofuranoside (16). To a solution of the mixture **15** (5.75 g, 14.1 mmol) in dry THF (50 mL) was added TBAF (16.9 mL, 16.9 mmol) 1 M in THF; the reaction was stirred at room temperature for 4 h, poured into aqueous $NaHCO_3$, and extracted with CH_2Cl_2. Silica gel flash chromatography (hexanes−EtOAc, 1:1) of the residue gave compound **16** (4.06 g, 98%). The anomeric mixture (*β*:α, 5:1) could be separated under these conditions. *β*-Anomer **16***β* as a crystalline solid: mp 101−103 °C (from *n*-hexanes−EtOAc); $[\alpha]_D$ −39.5° (*c* = 0.2); IR 3584, 1738 cm^{-1}; ^{1}H NMR 1.36 (3H, s), 1.54 (3H, s), 3.65−3.82 (2H, m), 4.49 (1H, t, *J* = 5.5 Hz), 4.84 (1H, d, *J* = 6.1 Hz), 4.88 (1H, d, *J* = 6.1 Hz), 6.49 (1H, s), 7.41−7.48 (2H, m), 7.55−7.60 (1H, m), 7.96−8.00 (2H, m); ^{13}C NMR 24.9 (q), 26.4 (q), 63.4 (t), 81.1 (d), 85.5 (d), 88.8 (d), 103.2 (d), 113.0 (s), 128.6 (2 × d), 129.2 (s), 129.6 (2 × d), 133.6 (d), 164.8 (s); MS *m*/*z* (rel intensity) 295 (M^+ + 1, 26), 279 (29), 277 (31), 237 (39), 189 (9), 173 (100). Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.20; H, 6.17. Found: C, 61.54; H, 6.30. α-Anomer **16**α: syrup; $[\alpha]_D$ +67.2° (*c* = 0.268); IR 3608, 3502, 1728, 1603 cm^{-1}; ^{1}H NMR 1.36 (3H, s), 1.42 (3H, s), 3.78 (1H, dd, *J* = 3.1, 12.2 Hz), 3.91 (1H, dd, *J* = 3.1, 12.2 Hz), 4.49 (1H, ddd, *J* = 3.0, 3.1, 3.1 Hz), 4.83 (1H, dd, *J* = 3.0, 7.1 Hz), 4.92 (1H, dd, *J* = 7.1, 4.3 Hz), 6.48 (1H, d, *J* = 4.3 Hz), 7.40−7.48 (2H, m), 7.53−7.58 (1H, m), 8.08−8.13 (2H, m); ^{13}C NMR 25.2 (q), 25.9 (q), 62.6 (t), 80.0 (d), 80.8 (d), 84.1 (d), 97.4 (d), 115.7 (s), 128.4 (2 × d), 129.8 (2 × d), 133.2 (d), 165.3 (s), one aromatic (s) could not be observed; MS *m*/*z* (rel intensity) 279 (M^+ − Me, 15), 189 (3), 173 (6), 131 (44), 115 (2), 114 (9). Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.20; H, 6.17. Found: C, 61.15; H, 6.24.

Methyl (Benzoyl 2,3-*O*-isopropylidene-*β*-D-ribofuranosid)uronate (17*β*). Following the procedure described for **8**, compound **16***β* (952 mg, 3.24 mmol) afforded, after methylation in diethyl ether at 0 °C with an excess of CH_2N_2 and purification by silica gel flash chromatography, product **17***β* (727 mg, 70%) as a crystalline solid: mp 56−58 °C (from *n*-hexanes−EtOAc); $[\alpha]_D$ −37.5° (*c* = 0.248); IR 1743 cm^{-1}; ^{1}H NMR 1.38 (3H, s), 1.54 (3H, s), 3.44 (3H, s), 4.77 (1H, s), 4.88 (1H, d, *J* = 5.8 Hz), 5.38 (1H, d, *J* = 5.8 Hz), 6.50 (1H, s), 7.40−7.58 (3H, m), 7.93−7.97 (2H, m); ^{13}C NMR 22.4 (q), 23.7 (q), 49.7 (q), 79.4 (d), 81.6 (d), 82.2 (d), 99.4 (d), 110.8 (s), 125.8 (2 × d), 126.6 (s), 127.1 (2 × d), 131.0 (d), 161.8 (s), 167.5 (s); MS *m*/*z* (rel intensity) 307 (M^+ − Me, 18), 264 (2), 263 (2), 217 (25), 173 (11), 159 (65). Anal. Calcd for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found: C, 59.78; H, 5.46.

2,3-*O*-Isopropylidene-D-ribofuranuronic Acid (18). The ester **17** (228.3 mg, 0.71 mmol) was dissolved in aqueous NaOH 0.25 N (8 mL) and stirred at room temperature for 15 h. Then it was acidified to pH 4 with HCl 10% and extracted with diethyl ether. The aqueous layer was acidified to pH < 1 and extracted with ethyl acetate, and this extract was concentrated to dryness and purified by chromatography (CH_2Cl_2−MeOH, 90:10) to give the acid **18** (144.6 mg, 0.71 mmol, 87%) as a hygroscopic solid: IR ($CHCl_3$) 3500, 1730, 1602 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz) 1.25 (3H, s), 1.37 (3H, s), 4.42 (1H, s), 4.43 (1H, d, *J* = 4 Hz), 5.07 (1H, d, *J* = 4 Hz), 5.26 (1H, s); ^{13}C NMR (DMSO-d_6) 24.8 (q), 26.3 (q), 81.8 (d), 82.5 (d), 84.7 (d), 101.7 (d), 111.5 (s), 172.1 (s); MS *m*/*z* (rel intensity) 189 (M^+ − Me, 44), 187 (7), 159 (5), 129 (32). Anal. Calcd for $C_8H_{12}O_6$: C, 47.06; H, 5.92. Found: C, 47.13; H, 6.14.

Benzyl 6-*O*-(*tert*-Butyldimethylsilyl)-D-glucopyranoside (19). To a solution of D-glucose (513 mg, 2.59 mmol) in benzyl alcohol (8 mL) was added CSA (52 mg, 0.22 mmol), and the reaction was stirred at 80 °C for 24 h, neutralized with basic ion-exchange resin (Dowex 1-X8), and concentrated at high vacuum. The residue was purified by silica gel flash chromatography (CH_2Cl_2−MeOH 90:10) to give the benzyl glucopyranoside that was carried on to the next step without characterization. The obtained product (770 mg, 2.85 mmol) and imidazole (714 mg, 10.5 mmol) were dissolved in anhydrous DMF (10 mL), and TBDMSCl (508 mg, 3.37 mmol) was added at 0 °C, under Ar. The mixture was stirred for 20 h at room temperature and then poured into water and extracted with ethyl acetate. The combined extracts were concentrated under vacuum and purified by silica gel flash chromatography (hexanes−EtOAc, 3:7) to give compound **19** (794 mg, 2.07 mmol, 73%) as an inseparable anomeric mixture: foam, IR ($CHCl_3$) 3402 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz) 0.02 (6H, s), 0.05 (6H, s), 0.84 (9H, s), 0.86 (9H, s), 3.01−3.85 (8H, m), 4.38−4.95 (10H, m), 7.29−7.35 (10H, m); ^{13}C NMR −5.2 (4 × q), 18.4 (2 × s), 26.0 (6 × q), 63.4 (t), 63.8 (t), 69.0 (t), 70.6 (t), 71.1 (d), 71.3 (d), 72.0 (2 × d), 73.4 (d), 74.4 (d), 75.7 (d), 76.5 (d), 97.1 (d), 101.2 (d), 127.8−128.4 (10 × d), 137.1 (2 × s); MS *m*/*z* (rel intensity) 385 (M^+ +1, <1), 349 (3), 309 (7), 277 (6), 259 (12), 251 (1), 220 (7), 202 (6). Anal. Calcd for $C_{19}H_{32}O_6Si$: C, 59.35; H, 8.39. Found: C, 59.56; H, 8.58.

Benzyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-tri-*O*-methyl-D-glucopyranoside (20). To a suspension of NaH (225 mg, 9.4 mmol) in DMF (7 mL) was slowly added, at 0 °C, under Ar, the silyl derivative **19** (0.5 g, 1.3 mmol) in DMF (3 mL). When the hydrogen evolution ceased, an excess of CH_3I (0.5 mL) was added and the mixture was stirred for 2 h. MeOH was then added to eliminate the excess of NaH, and the resulting mixture was poured into water and extracted with ethyl acetate. After concentration the crude was purified by silica gel flash chromatography (hexanes−EtOAc, 8:2) to give a partially separable anomeric mixture of the methylated compound **20** (544 mg, 98%). α-Anomer **20**α: syrup; $[\alpha]_D$ +129° (*c* = 0.3); ^{1}H NMR 0.035 (3H, s), 0.04 (3H, s), 0.87 (9H, s), 3.12 (1H, dd, *J* = 3.6, 9.3 Hz), 3.15 (1H, dd, *J* = 9.4, 9.3 Hz), 3.38 (3H, s), 3.48−3.63 (2H, m), 3.51 (3H, s), 3.60 (3H, s), 3.70 (1H, dd, *J* = 2.1, 11.2 Hz), 3.78 (1H, dd, *J* = 4.0, 11.2 Hz), 4.53 (1H, d, *J* = 12.2 Hz), 4.68 (1H, d, *J* = 12.2 Hz), 4.91 (1H, d, *J* = 3.6 Hz), 7.22−7.34 (5H, m); ^{13}C NMR −5.4 (q), −5.2 (q), 18.3 (s), 25.8 (3 × q), 58.4 (q), 60.3 (q), 60.8 (q), 61.9 (t), 68.7 (t), 71.6 (d), 79.2 (d), 81.7 (d), 83.4 (d), 94.6 (d), 127.7 (d), 128.2 (4 × d), 137.2 (s); MS *m*/*z* (rel intensity) 337 (M^+ − C_4H_9 − CH_3OH, 2), 319 (1), 287 (19), 247 (5), 231 (15), 199 (8). Anal. Calcd for $C_{22}H_{38}O_6Si$: C, 61.94; H, 8.98. Found: C, 62.06; H, 9.06. *β*-Anomer **20***β*: syrup; $[\alpha]_D$ −20° (*c* = 0.552); ^{1}H NMR 0.09 (3H, s), 0.10 (3H, s), 0.92 (9H, s), 2.96−3.18 (4H, m), 3.55 (3H, s), 3.60 (3H, s), 3.63 (3H, s), 3.80 (1H, dd, *J* = 3.1, 10.0 Hz), 3.87 (1H, dd, *J* = 1.1, 10.0 Hz), 4.34 (1H, d, *J* = 7.5 Hz), 4.63 (1H, d, *J* = 11.9 Hz), 4.90 (1H, d, *J* = 11.9 Hz), 7.35−7.38 (5H, m); ^{13}C NMR −5.4 (q), −5.1 (q), 18.3 (s), 25.8 (3 × q), 60.3 (q), 60. 4 (q), 60.8 (q), 62.3 (t), 70.5 (t), 75.7 (d), 79.1 (d), 83.8 (d), 86.4 (d), 101.9 (d), 127.6 (d), 127.8 (2 × d), 128.3 (2 × d), 137.5 (s); MS 337 (M^+ − C_4H_9 − CH_3OH, 1), 319 (1), 287 (17), 231 (9), 199 (5). Anal. Calcd for $C_{22}H_{38}O_6Si$: C, 61.94; H, 8.98. Found: C, 61.85; H, 9.01.

Benzyl 2,3,4-Tri-*O*-methyl-D-glucopyranoside (21). Following the procedure described for **16**, compound **20** (477 mg, 1.1 mmol) afforded compound **21** (309 mg, 0.99 mmol, 89%) as a separable anomeric mixture (α:*β*, 2:1) by silica gel flash chromatography (hexanes−EtOAc, 1:1). α-Anomer **21**α as a crystalline solid: mp 44−45 °C (from *n*-hexanes−EtOAc); $[\alpha]_D$ +158.7° (*c* = 0.08); IR 3610 cm^{-1}; ^{1}H NMR 3.15 (1H, dd, *J* = 1.6, 9.6 Hz), 3.19 (1H, dd, *J* = 3.8, 9.6 Hz), 3.43 (3H, s), 3.54−3.62 (2H, m), 3.57 (3H, s), 3.65 (3H, s), 3.69−3.75 (2H, m), 4.60 (1H, d, *J* = 12.2 Hz), 4.72 (1H, d, *J* = 12.2 Hz), 4.97 (1H, d, *J*

= 3.7 Hz), 7.31−7.37 (5H, m); ^{13}C NMR 58.4 (q), 60.4 (q), 60.7 (q), 61.5 (t), 69.1 (t), 70.8 (d), 79.3 (d), 81.6 (d), 83.0 (d), 94.9 (d), 127.7 (d), 128.0 (2 × d), 128.2 (2 × d), 136.9 (s); MS *m/z* (rel intensity) 313 (M^+ + 1, 2), 295 (11), 263 (22), 231 (8), 205 (50), 203 (5), 189 (13), 187 (5), 157 (84). Anal. Calcd for $C_{16}H_{24}O_6$: C, 61.51; H, 7.75. Found: C, 61.28; H, 7.80. *β*-Anomer **21***β*: syrup; $[\alpha]_D$ −35.5° (*c* = 0.166); IR3606, 3474 cm^{-1}; ^{1}H NMR (500 Hz) 3.06 (1H, dd, *J* = 7.8, 8.5 Hz), 3.17 (1H, dd, *J* = 8.5, 7.5 Hz), 3.21−3.23 (1H, m), 3.55 (3H, s), 3.61 (3H, s), 3.63 (3H, s), 3.70−3.74 (2H, m), 3.88 (1H, m), 4.41 (1H, d, *J* = 7.8 Hz), 4.69 (1H, d, *J* = 12.0 Hz), 4.88 (1H, d, *J* = 12.0 Hz), 7.31−7.37 (5H, m); ^{13}C NMR 60.2 (q), 60.3 (q), 60.6 (q), 61.5 (t), 71.0 (t), 74.9 (d), 79.1 (d), 83.6 (d), 86.1 (d), 102.3 (d), 127.4 (2 × d), 127.6 (d), 128.2 (2 × d), 137.2 (s); MS *m/z* (rel intensity) 313 (M^+ + 1, 2), 295 (21), 263 (63), 231 (10), 205 (83), 189 (29), 187 (8), 173 (100), 157 (91). Anal. Calcd for $C_{16}H_{24}O_6$: C, 61.51; H, 7.75. Found: C, 61.59; H, 7.85.

Benzyl 2,3,4-Tri-*O*-methyl-D-glucopyranosiduronic Acid (22). Following the procedure described for **8**, compound **21**α (375 mg, 1.2 mmol) afforded, after purification by silica gel flash chromatography (hexanes−EtOAc, 1:1), acid **22**α (348 mg, 89%) as a syrup: $[\alpha]_D$ +114.8° (*c* = 0.196); IR 3428, 1728, 1608 cm^{-1}; ^{1}H NMR 3.26 (1H, dd, *J* = 3.6, 9.3 Hz), 3.39 (1H, dd, *J* = 8.9, 10 Hz), 3.41 (3H, s), 3.57 (3H, s), 3.64 (3H, s), 3.62 (1H, dd, *J* = 9.3, 8.9 Hz), 4.16 (1H, d, *J* = 10 Hz), 4.62 (1H, d, *J* = 12.1 Hz), 4.78 (1H, d, *J* = 12.1 Hz), 5.05 (1H, d, *J* = 3.6 Hz), 7.32−7.40 (5H, m); ^{13}C NMR 58.6 (q), 60.5 (q), 60.9 (q), 69.5 (t), 69.7 (d), 81.0 (d), 81.0 (d), 82.7 (d), 95.2 (d), 128.0 (d), 128.3 (2 × d), 128.4 (2 × d), 136.4 (s), 173.4 (s); MS *m/z* (rel intensity) 327 (M^+ + 1, 1), 309 (1), 277 (4), 219 (1), 187 (6), 187 (5), 157 (17), 155 (5), 143 (10). Anal. Calcd for $C_{16}H_{22}O_7$: C, 58.88; H, 6.79. Found: C, 58.93; H, 6.67. Analogously, compound **21***β* yielded anomer **22***β* (93%) as a syrup: $[\alpha]_D$ −54.6° (*c* = 0.24); ^{1}H NMR 3.18 (1H, dd, *J* = 7.0, 7.5 Hz), 3.23 (1H, dd, *J* = 8.4, 9 Hz), 3.48 (1H, dd, *J* = 7.5, 9 Hz), 3.57 (3H, s), 3.59 (3H, s), 3.61 (3H, s), 3.86 (1H, d, *J* = 8.4 Hz), 4.49 (1H, d, *J* = 7.0 Hz), 4.65 (1H, d, *J* = 12.0 Hz), 4.94 (1H, d, *J* = 12.0 Hz), 7.31−7.37 (5H, m); ^{13}C NMR 60.3 (2 × q), 60.5 (q), 71.4 (t), 81.3 (d), 83.2 (d), 85.5 (2 × d), 102.4 (d), 127.7 (d), 128.3 (4 × d), 137.2 (s), 174.6 (s). Anal. Calcd for $C_{16}H_{22}O_7$: C, 58.88; H, 6.79. Found: C, 58.61; H, 6.92.

2,3,4-Tri-*O*-methyl-D-glucopyranuronic Acid (23). Following the procedure described for **9**, acid **22** (125 mg, 0.38 mmol) in MeOH (10 mL) afforded the title compound **23** (75 mg, 0.32 mmol, 83%) as a syrup: IR ($CHCl_3$) 3688, 3398, 1730 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 Hz) 2.78 (1H, dd, *J* = 7.7, 8.7 Hz), 3.07−3.23 (5H, m), 3.32 (3H, s), 3.36 (3H, s), 3.37 (3H, s), 3.43 (3H, s), 3.44 (3H, s), 3.48 (3H, s), 3.57 (1H, d, *J* = 9.0 Hz), 3.96 (1H, d, *J* = 7.7 Hz), 5.17 (1H, bs); ^{13}C NMR (DMSO-d_6) 57.0 (2 × q), 59.1 (q), 59.3 (2 × q), 59.6 (q), 69.1 (d), 73.3 (d), 80.5 (d), 80.6 (d), 80.7 (d), 81.6 (d), 83.9 (d), 84.4 (d), 89.6 (d), 96.4 (d), 170.1 (s), 170.9 (s); MS *m/z* (rel intensity) 218 ($M^+ - H_2O$), 186 (1), 161 (42), 159 (1), 145 (3), 129 (3), 113 (7). Anal. Calcd for $C_9H_{16}O_7$: C, 45.76; H, 6.83. Found: C, 45.83; H, 6.91.

***p*-Methoxybenzyl 2,3:5,6-Di-*O*-isopropylidene-α-D-mannofuranoside (24).** To a suspension of NaH (1.3 g, 27 mmol) in DMF (25 mL) was added, under Ar at 0 °C, 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (5 g, 19.2 mmol) dissolved in DMF (5 mL). When the hydrogen evolution ceased, *p*-methoxybenzyl chloride (3.9 mL, 28.8 mmol) was added at 0 °C, and the reaction was stirred at room temperature for 24 h. Then MeOH was added to eliminate the excess of NaH, and the resulting mixture was poured into water and extracted with ethyl acetate. The combined extracts were dried over Na_2SO_4, concentrated at reduced pressure, and the crude purified by silica gel flash chromatography (hexanes−EtOAc, 1:1) to yield compound **24** (6 g, 82%) as a syrup: $[\alpha]_D$ +74.3° (*c* = 0.23); ^{1}H NMR 1.32 (3H, s), 1.40 (3H, s), 1.47 (6H, s), 3.81 (3H, s), 3.98 (1H, dd, *J* = 3.5, 7.8 Hz), 4.03 (1H, dd, *J* = 4.5, 8.7 Hz), 4.14 (1H, dd, *J* = 6.1, 8.7 Hz), 4.39−4.47 (1H, m), 4.42 (1H, d, *J* = 11.2 Hz), 4.59 (1H, d, *J* = 11.2 Hz), 4.64 (1H, d, *J* = 5.6 Hz), 4.82 (1H, dd, *J* = 3.5, 5.8 Hz), 5.06 (1H, s), 6.89 (2H, m), 7.26 (2H, m); ^{13}C NMR 24.4 (q), 25.1 (q), 25.8 (q), 26.8 (q), 55.2 (q), 66.9 (t), 68.6 (t), 73.0 (d), 79.5 (d), 80.3 (d), 85.1 (d), 105.2 (d), 109.1 (s), 112.4 (s), 113.8 (2 × d), 129.2 (s), 129.6 (2 × d), 159.3 (s); MS (EI, 30 eV) *m/z* (rel intensity) 380 (M^+, 3), 365 (17), 322 (3), 259 (44), 243 (1), 201 (71), 185 (6), 143 (64), 127 (4). Anal. Calcd for $C_{20}H_{28}O_7$: C, 63.14; H, 7.42. Found: C, 63.02; H, 7.71.

***p*-Methoxybenzyl 2,3-*O*-Isopropylidene-α-D-mannofuranoside (25).** Compound **24** (5.5 g, 14.47 mmol) was dissolved in 70% AcOH (40 mL), and the mixture was stirred at room temperature for 18 h, poured into water, and extracted with diethyl ether. The organic layer was washed with $NaHCO_3$ until no acidic reaction was observed. It was then dried and concentrated, and the residue was purified by silica gel flash chromatography (hexanes−EtOAc, 1:1) to give **25** (4.57 g, 13.44 mmol, 93%) as a noncrystalline solid: $[\alpha]_D$ +81° (*c* = 0.406); IR 3601, 3475 cm^{-1}; ^{1}H NMR 1.32 (3H, s), 1.47 (3H, s), 3.70 (1H, dd, *J* = 5.4, 11.2 Hz), 3.80 (3H, s), 3.87 (1H, dd, *J* = 2.9, 11.2 Hz), 3.94−4.04 (2H, m), 4.42 (1H, d, *J* = 11.5 Hz), 4.57 (1H, d, *J* = 11.5 Hz), 4.63 (1H, d, *J* = 5.9 Hz), 4.85 (1H, dd, *J* = 3.4, 5.9 Hz), 5.09 (1H, s), 6.87 (2H, m), 7.24 (2H, m); ^{13}C NMR 24.5 (q), 25.8 (q), 55.2 (q), 64.3 (t), 68.6 (t), 70.1 (d), 79.1 (d), 80.0 (d), 84.7 (d), 105.0 (d), 112.5 (s), 113.8 (2 × d), 129.2 (s), 129.7 (2 × d), 159.2 (s); MS (EI, 30 eV) *m/z* (rel intensity) 340 (M^+, 11), 325 (6), 282 (2), 219 (1), 203 (1), 161 (100), 145 (10), 143 (34). Anal. Calcd for $C_{17}H_{24}O_7$: C, 59.97; H, 7.11. Found: C, 59.66; H, 7.40.

***p*-Methoxybenzyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3-*O*-isopropylidene-α-D-mannofuranoside (26).** Following the procedure described for **12**, compound **25** (3 g, 8.82 mmol) afforded **26** (3.44 g, 86%) as a syrup: $[\alpha]_D$ +70.8° (*c* = 0.212); IR 3567 cm^{-1}; ^{1}H NMR 0.00 (6H, s), 0.81 (9H, s), 1.21 (3H, s), 1.36 (3H, s), 3.60−3.75 (2H, m), 3.69 (3H, s), 3.87 (2H, m), 4.28 (1H, d, *J* = 11.3 Hz), 4.47 (1H, d, *J* = 11.3 Hz), 4.52 (1H, d, *J* = 5.8 Hz), 4.75 (1H, dd, *J* = 5.8, 3.1 Hz), 4.95 (1H, s), 6.76 (2H, m), 7.13 (2H, m); ^{13}C NMR −0.1 (q), 0.0 (q), 18.21 (s), 24.5 (q), 25.8 (3 × q), 25.9 (q), 55.1 (q), 64.4 (t), 68.5 (t), 69.5 (d), 78.8 (d), 80.1 (d), 84.9 (d), 105.2 (d), 112.3 (s), 113.7 (2 × d), 129.3 (s), 129.6 (2 × d), 159.2 (s); MS (EI, 30 eV) *m/z* (rel intensity) 439 (M^+ − Me, 15), 317 (4), 276 (4), 275 (18), 259 (1), 241 (22). Anal. Calcd for $C_{23}H_{38}O_7Si$: C, 60.76; H, 8.42. Found: C, 60.51; H, 8.52.

***p*-Methoxybenzyl 5-*O*-Benzyl-6-*O*-*tert*-(butyldimethylsilyl)-2,3-*O*-isopropylidene-α-D-mannofuranoside (27).** To a suspension of NaH (132 mg, 5.5 mmol) in DMF (10 mL) was added, at 0 °C under Ar, the product **26** (890 mg, 1.96 mmol) dissolved in DMF (2 mL). When the hydrogen evolution ceased, benzyl bromide (0.3 mL, 2.53 mmol) was added at 0 °C, and the mixture was stirred at room temperature for 10 h. Then MeOH was added to quench the excess of NaH, and the resulting mixture poured into water and extracted with diethyl ether. Silica gel flash chromatography of the residue (hexanes−EtOAc, 80:20) gave **27** (840 mg, 79%) as a syrup: $[\alpha]_D$ +46.3° (*c* = 0.356); ^{1}H NMR 0.13 (6H, s), 0.95 (9H, s), 1.34 (3, s), 1.47 (3H, s), 3.75 (1H, dd, *J* = 5.6, 10.6 Hz), 3.81 (3H, s), 3.85 (1H, ddd, *J* = 1.7, 5.6, 9.0 Hz), 3.97 (1H, dd, *J* = 1.7, 10.6 Hz), 4.05 (1H, dd, *J* = 9.0, 3.4 Hz), 4.40 (1H, d, *J* = 11.4 Hz), 4.59 (1H, d, *J* = 11.4 Hz), 4.62 (1H, d, *J* = 5.6 Hz), 4.70 (1H, d, *J* = 11.1 Hz), 4.84 (1H, d, *J* = 11.1 Hz), 4.85 (1H, dd, *J* = 5.6, 3.4 Hz), 5.06 (1H, s), 6.88 (2H, m), 7.22−7.39 (7H, m); ^{13}C NMR −5.4 (q), −5.3 (q), 18.3 (s), 24.9 (q), 25.9 (3 × q), 26.1 (q), 55.2 (q), 64.2 (t), 68.4 (t), 73.3 (t), 77.8 (d), 78.4 (d), 80.0 (d), 84.7 (d), 105.3 (d), 112.0 (s), 113.8 (2 × d), 127.3 (d), 128.0 (2 × d), 128.1 (2 × d), 129.5 (s), 129.6 (2 × d), 139.0 (s), 159.2 (s); MS (EI, 30 eV) *m/z* (rel intensity) 529 (M^+ − Me, 4), 423 (2), 365 (7), 381 (2), 259 (5). Anal. Calcd for $C_{30}H_{44}O_7Si$: C, 66.14; H, 8.14. Found: C, 66.10; H, 8.27.

***p*-Methoxybenzyl 5-*O*-Benzyl-2,3-*O*-isopropylidene-α-D-mannofuranoside (29).** To a solution of **27** (716 mg, 1.3 mmol) in MeOH (15 mL) was added at 0 °C NH_4F (400 mg, 10.8 mmol), and the reaction was stirred at room temperature for 20 h, poured into water, and extracted with EtOAc. Silica gel flash chromatography of the residue (gradient hexanes−EtOAc, 8:2 → 1:1) gave **29** (514 mg, 1.19 mmol, 91%) as a syrup: $[\alpha]_D$ +70.5° (*c* = 0.312); IR 3586 cm^{-1}; ^{1}H NMR 1.34 (3H, s), 1.47 (3H, s), 3.80 (3H, s), 3.77−3.94 (3H, m), 4.12 (1H, dd, *J* = 8.2, 3.4 Hz), 4.41 (1H, d, *J* = 11.4 Hz), 4.59 (1H, d, *J*

= 11.4 Hz), 4.64 (1H, d, J = 5.8 Hz), 4.68 (1H, d, J = 11.1 Hz), 4.75 (1H, d, J = 11.1 Hz), 4.84 (1H, dd, J = 5.8, 3.4 Hz), 5.07 (1H, s), 6.86−6.90 (2H, m), 7.23−7.40 (7H, m); ^{13}C NMR 24.8 (q), 26.1 (q), 55.2 (q), 62.5 (t), 68.6 (t), 72.8 (t), 76.5 (d), 79.1 (d), 79.8 (d), 84.8 (d), 105.1 (d), 112.2 (s), 113.8 (2 × d), 127.8 (d), 128.0 (2 × d), 128.3 (2 × d), 129.3 (s), 129.7 (2 × d), 138.3 (s), 159.3 (s); MS (EI, 30 eV) m/z (rel intensity) 430 (M^+, 2), 415 (5), 309 (12), 308 (5), 293 (3), 291 (4), 250 (71), 235 (10), 233 (47). Anal. Calcd for $C_{24}H_{30}O_7$: C, 66.96; H, 7.02. Found: C, 66.93, H, 7.09.

***p*-Methoxybenzyl 5-*O*-Benzyl-2,3-*O*-isopropylidene-α-D-mannofuranosiduronic Acid (30).** Following the procedure described for **8**, compound **29** (550 mg, 1.28 mmol) afforded, after purification by silica gel flash chromatography (hexanes−EtOAc, 1:1), acid **30** (398 mg, 0.90 mmol, 70%) as a syrup: $[\alpha]_D$ +58.2° (c = 0.11); IR 3514, 1724, 1614 cm^{-1}; ^{1}H NMR 1.31 (3H, s), 1.45 (3H, s), 3.79 (3H, s), 4.26 (1H, dd, J = 8.2, 3.2 Hz), 4.33 (1H, d, J = 8.2 Hz), 4.37 (1H, d, J = 11.2 Hz), 4.57 (1H, d, J = 11.2 Hz), 4.62 (1H, d, J = 5.8 Hz), 4.64 (1H, d, J = 11.3 Hz), 4.78 (1H, d, J = 11.3 Hz), 4.84 (1H, dd, J = 3.2, 5.8 Hz), 5.14 (1H, s), 6.83−6.88 (2H, m), 7.19−7.39 (7H, m); ^{13}C NMR 24.8 (q), 25.8 (q), 55.2 (q), 68.7 (t), 73.3 (t), 76.0 (d), 78.9 (d), 79.3 (d), 84.5 (d), 105.3 (d), 112.6 (s), 113.8 (2 × d), 128.0 (d), 128.2 (2 × d), 128.3 (2 × d), 129.0 (s), 129.8 (2 × d), 136.8 (s), 159.3 (s), 175.6 (s); MS (EI, 30 eV) m/z (rel intensity) 444 (M^+, 4), 429 (7), 265 (94), 250 (5), 219 (23), 201 (11), 173 (10). Anal. Calcd for $C_{24}H_{28}O_8$: C, 64.85; H, 6.35. Found: C, 65.02; H, 6.43.

5-*O*-Benzyl-2,3-*O*-isopropylidene-α-D-mannofuranuronic Acid (33). To a solution of acid **30** (200 mg. 0.45 mmol) in CH_3CN/H_2O, 9/1 (10 mL) was added at 0 °C CAN (497 mg, 0.9 mmol). The reaction was stirred at 0 °C for 90 min, and then the solvent was concentrated under reduced pressure. Silica gel flash chromatography (hexanes−EtOAc, 1:1; CH_2Cl_2−MeOH 90:10) of the residue yielded compound **33** (107.4 mg, 0.33 mmol, 74%) as a hygroscopic solid: IR ($CHCl_3$) 3406, 1720 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz) 1.26 (3H, s), 1.32 (3H, s), 3.98 (1H, d, J = 9.4 Hz), 4.09 (1H, dd, J = 9.4, 3.5 Hz), 4.42 (1H, d, J = 11.7 Hz), 4.45 (1H, d, J = 5.8 Hz), 4.55 (1H, d, J = 11.7 Hz), 4.66 (1H, dd, J = 5.8, 3.5 Hz), 5.12 (1H, s), 7.28−7.34 (5H, m); ^{13}C NMR (DMSO-d_6) 24.9 (q), 26.1 (q), 70.7 (t), 78.3 (d), 78.9 (d), 79.9 (d), 85.2 (d), 100.5 (d), 111.1 (s), 127.1 (d), 127.4 (2 × d), 127.9 (2 × d), 138.7 (s), 174.9 (s); MS m/z (rel intensity) 309 (M^+ − Me, 3), 291 (10), 279 (3), 266 (19), 265 (31), 251 (5), 247 (16), 233 (3), 217 (8), 215 (16), 175 (37), 173 (20), 155 (48). Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.12; H, 6.25.

***p*-Methoxybenzyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3-*O*-isopropylidene-5-*O*-methyl-α-D-mannofuranoside (28).** Following the procedure described for **20**, compound **26** (1.29 g, 2.85 mmol) afforded, after silica gel flash chromatography (hexanes−EtOAc, 9:1), compound **28** (1.20 g, 2.56 mmol, 90%) as a syrup: $[\alpha]_D$ +67.5° (c = 0.234); ^{1}H NMR 0.116 (3H, s), 0.12 (3H, s), 0.94 (9H, s), 1.33 (3H, s), 1.46 (3H, s), 3.51 (3H, s), 3.57 (1H, ddd, J = 5.1, 1.8, 9.2 Hz), 3.71 (1H, dd, J = 5.1, 11.2 Hz), 3.79 (3H, s), 3.99 (2H, m), 4.38 (1H, d, J = 11.6 Hz), 4.58 (1H, d, J = 11.6 Hz), 4.60 (1H, d, J = 5.8 Hz), 4.80 (1H, dd, J = 3.5, 5.8 Hz), 5.04 (1H, s), 6.87 (2H, m), 7.24 (2H, m); ^{13}C NMR −5.43 (q), −5.38 (q), 18.3 (s), 24.9 (q), 25.9 (3 × q), 26.1 (q), 55.1 (q), 58.3 (q), 63.0 (t), 68.3 (t), 78.1 (d), 78.8 (d), 79.9 (d), 84.7 (d), 105.0 (d), 112.0 (s), 113.7 (2 × d), 129.4 (s), 129.6 (2 × d), 159.2 (s); MS (EI, 30 eV) m/z (rel intensity) 469 (M^+ + 1, 1), 453 (10), 411 (23), 353 (1), 347 (2), 331 (29), 273 (2). Anal. Calcd for $C_{24}H_{40}O_7Si$: C, 61.51; H, 8.60. Found: C, 61.63; H, 8.81.

***p*-Methoxybenzyl 2,3-*O*-Isopropylidene-5-*O*-methyl-α-D-mannofuranoside (31).** To a solution of **28** (1.47 g, 3.14 mmol) in MeOH (25 mL) was added, at 0 °C, NH_4F (1 g, 27 mmol). The reaction was stirred at room temperature for 24 h and then poured into water and extracted with EtOAc. Silica gel flash chromatography of the crude (hexanes−EtOAc, 1:1) gave product **31** (978.5 mg, 88%) as a syrup: $[\alpha]_D$ +85.6° (c = 0.32); IR 3591 cm^{-1}; ^{1}H NMR 1.32 (3H, s), 1.45 (3H, s), 3.48 (3H, s), 3.70 (1H, dd, J = 5.4, 11.2 Hz), 3.79 (3H, s), 3.87 (1H, dd, J = 2.9, 11.2 Hz), 3.94−4.04 (2H, m), 4.03 (1H, dd, J = 3.5, 8.3 Hz), 4.40 (1H, d, J = 11.4 Hz), 4.57 (1H, d, J = 11.4 Hz), 4.61 (1H, d, J = 5.8 Hz), 4.78 (1H, dd, J = 3.5, 5.8 Hz), 5.04 (1H, s), 6.87 (2H, m), 7.24 (2H, m); ^{13}C NMR 24.7 (q), 25.9 (q), 55.1 (q), 58.0 (q), 61.5 (t), 68.5 (t), 77.9 (d), 78.7 (d), 79.7 (d), 84.7 (d), 104.9 (d), 112.2 (s), 113.7 (2 × d), 129.2 (s), 129.7 (2 × d), 159.2 (s); MS (EI, 30 eV) m/z (rel intensity) 354 (M^+, 13), 339 (8), 296 (1), 233 (53), 217 (5), 201 (19), 175 (100), 159 (17), 143 (4). Anal. Calcd for $C_{18}H_{26}O_7$: C, 61.00; H, 7.39; Found: C, 61.18; H, 7.51.

***p*-Methoxybenzyl 2,3-*O*-Isopropylidene-5-*O*-methyl-α-D-mannofuranosiduronic Acid (32).** Following the procedure described for **8**, compound **31** (500 mg, 1.41 mmol) afforded, after purification by silica gel flash chromatography (hexanes−EtOAc, 1:1), acid **32** (430 mg, 1.17 mmol, 83%) as a syrup: $[\alpha]_D$ +82.4° (c = 0.17); IR 2993, 2936, 1724 cm^{-1}; ^{1}H NMR 1.32 (3H, s), 1.49 (3H, s), 3.51 (3H, s), 3.79 (3H, s), 4.11 (1H, d, J = 8.0 Hz), 4.19 (1H, dd, J = 8.0, 3.5 Hz), 4.35 (1H, d, J = 11.5 Hz), 4.56 (1H, d, J = 11.5 Hz), 4.62 (1H, d, J = 5.7 Hz), 4.82 (1H, dd, J = 3.5, 5.7 Hz), 5.13 (1H, s), 6.86 (2H, m), 7.23 (2H, m); ^{13}C NMR 24.7 (q), 25.8 (q), 55.2 (q), 58.8 (q), 68.6 (t), 78.4 (d), 78.9 (d), 79.3 (d), 84.5 (d), 105.1 (d), 112.7 (s), 113.8 (2 × d), 129.0 (s), 129.8 (2 × d), 159.3 (s), 175.2 (s); MS (EI, 30 eV) m/z (rel intensity) 368 (M^+, 11), 353 (9), 247 (20), 231 (2), 189 (53), 173 (5), 145 (5), 129 (31). Anal. Calcd for $C_{18}H_{24}O_8$: C, 58.67; H, 6.57. Found: C, 58.58; H, 6.21.

2,3-*O*-Isopropylidene-5-*O*-methyl-α-D-mannofuranuronic Acid (34). Compound **32** (200 mg, 0.54 mmol) was hydrogenated at atmospheric pressure and room temperature in the presence of $Pd(OH)_2$/C (40 mg, 20% w) in EtOH (10 mL). The suspension was then filtered and the solvent evaporated to give substrate **34** (127 mg, 0.51 mmol, 94%) as a hygroscopic solid: ^{1}H NMR (DMSO-d_6, 200 MHz) 1.25 (3H, s), 1.37 (3H, s), 3.24 (3H, s), 3.76 (1H, d, J = 9.3 Hz), 4.00 (1H, dd, J = 9.3, 3.6 Hz), 4.43 (1H, d, J = 5.8 Hz), 4.72 (1H, dd, J = 5.8, 3.6 Hz), 5.10 (1H, s); ^{13}C NMR (DMSO-d_6) 24.6 (q), 25.9 (q), 57.4 (q), 78.1 (d), 78.2 (d), 79.1 (d), 85.0 (d), 100.3 (d), 111.5 (s), 172.0 (s); MS (EI, 30 eV) m/z (rel intensity) 249 (M^+ + 1, 1), 233 (4), 203 (1), 173 (2), 145 (2), 127 (4). Anal. Calcd for $C_{10}H_{16}O_7$: C, 48.38; H, 6.50. Found: C, 48.45; H, 6.38.

Benzyl α-D-Glucofuranosidurono-6,3-lactone (35). α-D-Glucurono-6,3-lactone (3 g, 17 mmol) was dissolved in benzyl alcohol/HCl 2% (70 mL) and stirred at 80 °C for 8 h, neutralized with basic ion-exchange resin (Dowex 1-X8), and concentrated under high vacuum to yield after silica gel flash chromatography (hexanes−EtOAc, 1:1) compound **35** (4.44 g, 98%) as a crystalline solid: mp 88−90 °C (from *n*-hexanes−EtOAc); $[\alpha]_D$ +96.7° (EtOH, c = 0.06); IR ($CHCl_3$) 3554, 1799 cm^{-1}; ^{1}H NMR 4.42 (1H, d, J = 4.6 Hz), 4.51 (1H, d, J = 4.9 Hz), 4.67 (1H, d, J = 11.5 Hz), 4.79 (1H, d, J = 3.3 Hz), 4.89 (1H, dd, J = 3.3, 4.9 Hz), 4.93 (1H, d, J = 11.5 Hz), 5.38 (1H, d, J = 4.5 Hz), 7.27−7.43 (5H, m); ^{13}C NMR 70.2 (d), 70.9 (t), 76.1 (d), 76.4 (d), 84.7 (d), 101.6 (d), 128.3 (2 × d), 128.5 (d), 128.7 (2 × d), 134.0 (s), 174.2 (s); MS (IE, 30 eV) m/z (rel intensity) 266 (M^+, <1), 249 (2), 191 (10), 175 (4), 166 (18), 159 (3), 148 (42), 131 (2); HRMS calcd for $C_{13}H_{14}O_6$ 266.07904, found 266.07850. Anal. Calcd for $C_{13}H_{14}O_6$: C, 58.64; H, 5.30. Found: C, 58.41; H, 5.18.

Benzyl 2,5-Di-*O*-acetyl-α-D-glucofuranosidurono-6,3-lactone (36). To a solution of **35** (1 g, 3.76 mmol) in dry pyridine (5 mL) was added acetic anhydride (1.4 mL) and stirred at room temperature for 1 h. The reaction was poured into HCl 10% and extracted with CH_2Cl_2. Silica gel flash chromatography (hexanes−EtOAc 8:2) of the extract yielded product **36** (940 mg, 72%) as a crystalline solid: mp 94−95 °C (from *n*-hexanes−EtOAc); $[\alpha]_D$ +205.6° (c = 0.198); IR ($CHCl_3$) 1808, 1750 cm^{-1}; ^{1}H NMR 2.08 (3H, s), 2.24 (3H, s), 4.50 (1H, d, J = 11.6 Hz), 4.75 (1H, d, J = 11.6 Hz), 4.95 (1H, dd, J = 4.1, 5.6 Hz), 5.04 (1H, dd, J = 1.6, 4.6 Hz), 5.07 (1H, dd, J = 4.1, 1.6 Hz), 5.47 (1H, d, J = 5.6 Hz), 5.53 (1H, d, J = 4.6 Hz), 7.23−7.35 (5H, m); ^{13}C NMR 20.1 (q), 20.1 (q), 68.5 (d), 70.6 (t), 73.2 (d), 78.3 (d), 83.0 (d), 101.5 (d), 127.6 (2 × d), 127.8 (d), 128.3 (2 × d), 136.7 (s), 169.6 (s), 169.6 (s), 169.9 (s); MS (CI, CH_4) m/z (rel intensity) 290 (M^+ − AcOH, 2) 259 (4), 243 (42), 201 (3), 184 (32). Anal. Calcd for $C_{17}H_{18}O_8$: C, 58.29; H, 5.18. Found: C, 58.31; H, 5.08.

2,5-Di-*O*-acetyl-D-glucofuranurono-6,3-lactone (37). Following the procedure described for **9**, compound **36** (272 mg, 0.78 mmol) in ethyl acetate afforded, after purification by silica gel flash chromatography (hexanes−EtOAc, 8:2), lactone **37** (185 mg, 0.71 mmol, 92%) as a syrupy anomeric mixture: IR ($CHCl_3$) 3595, 1810, 1748, 1711 cm^{-1}; ^1H NMR 2.13 (3H, s), 2.25 (3H, s), 5.03 (1H, d, J = 5.1 Hz), 5.17 (1H, dd, J = 5.1, 6.9 Hz), 5.29 (1H, d, J = 8.4 Hz), 5.31 (1H, dd, J = 8.4, 6.9 Hz), 5.51 (1H, s); ^{13}C NMR 20.3 (2 × q), 20.4 (q), 20.6 (q), 69.0 (2 × d), 73.7 (d), 75.9 (d), 77.0 (d), 77.8 (d), 78.7 (d), 81.9 (d), 82.8 (d), 97.1 (d), 101.3 (d), 169.5 (s), 169.8 (s), 170.0 (s); MS (CI, CH_4) *m/z* (rel intensity) 261 (M^+ + 1, 3), 243 (56), 218 (10), 201 (4), 200 (2), 183 (11). Anal. Calcd for $C_{10}H_{12}O_8$: C, 46.16; H, 4.65. Found: C, 46.32; H, 4.68.

Synthesis of Alduronic Acid Lactones. General Procedure. Method A with DIB/I_2. To a solution of the acid derivative in dry CH_2Cl_2 (0.05 mmol/mL) were added DIB (2 mmol) and I_2 (1.2 mmol), and the reaction was stirred at room temperature. The reaction that was monitored by TLC went to completion in 1 h to 3 h, and then it was poured into aqueous 10% $Na_2S_2O_3$ and extracted with diethyl ether. The combined extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified either by silica gel flash chromatography or by rotative chromatography using hexanes/EtOAc mixtures as solvent to yield the corresponding lactones. **Method B with DHSA/I_2.** To a solution of the acid derivative in dry CCl_4 (0.03 mmol/mL) were added, under Ar, DHSA (2.5 mmol) and I_2 (1.2 mmol). The reaction was stirred under reflux and irradiated with two 80 W tungsten filament lamps until TLC analysis showed the consumption of the starting material. Then the mixture was poured into 10% $Na_2S_2O_3$ and extracted with diethyl ether. The combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure to give a residue that was purified by rotative chromatography or flash chromatography with hexanes/EtOAc mixtures as solvent, to give the lactones.

3-*O*-Formyl-1,2-*O*-isopropylidene-threurono-1,4-lactone (38). Starting with acid **1** (50 mg, 0.245 mmol) and using method A for 1 h and purifying the crude by rotative chromatography (hexanes−diethyl ether, 6:4) the lactone **38** was obtained (25 mg, 0.124 mmol, 51%). The experiment performed by method B from **1** (38 mg, 0.19 mmol), after 3 h gave **38** (15 mg, 40%) as a crystalline solid: mp 70.8−72.6 °C (from *n*-hexane); $[\alpha]_D$ −11.4° (c = 0.14); IR 1805, 1736 cm^{-1}; ^1H NMR 1.46 (3H, s), 1.53 (3H, s), 4.75 (1H, d, J = 3.9 Hz), 5.15 (1H, s), 6.29 (1H, d, J = 3.9 Hz), 8.09 (1H, s); ^{13}C NMR 27.0 (q), 28.0 (q), 73.4 (d), 80.6 (d), 103.9 (d), 115.6 (s), 159.1 (s), the lactonic (s) could not be observed; MS *m/z* (rel intensity) 203 (M^+ + 1, 2), 187 (77), 159 (21), 145 (3), 129 (16). Anal. Calcd for $C_8H_{10}O_6$: C, 47.53; H, 4.99. Found: C, 47.34; H, 5.01.

3-*O*-Formyl-1,2-di-*O*-methyl-threurono-4,1-lactones (39). When the reaction was performed by method A from acid **9** (36 mg, 0.19 mmol) for 1.5 h, and after purifying the crude by rotative chromatography (gradient hexanes−EtOAc, 9:1 → 8:2), the anomeric mixture of the lactones **39** was resolved (22 mg, 0.115 mmol, 62%, α:β = 1:1.75). Irradiation of acid **9** (32 mg, 0.17 mmol) for 3 h under the conditions of method B gave the anomeric mixture of lactones **39** (16 mg, 0.08 mmol, 51%, α:β = 1:1). Anomer **39**α: syrup, $[\alpha]_D$ +68.1° (c = 0.53); IR 1809, 1747 cm^{-1}; ^1H NMR 3.48 (3H, s), 3.62 (3H, s), 3.98 (1H, dd, J = 4.0, 6.8 Hz), 5.28 (1H, d, J = 4.0 Hz), 5.58 (1H, d, J = 6.8 Hz), 8.17 (1H, s); ^{13}C NMR 58.0 (q), 58.6 (q), 71.8 (d), 84.1 (d), 105.9 (d), 158.8 (s), 167.8 (s); MS *m/z* (rel intensity) 191 (M^+ + 1, <1), 159 (2), 130 (2), 115 (2), 101 (45), 102 (37), 87 (13). Anal. Calcd for $C_7H_{10}O_6$: C, 44.21; H, 5.30. Found: C, 44.10; H, 5.37. Anomer **39**β: syrup, $[\alpha]_D$ −30.4° (c = 0.102); IR 1820, 1749 cm^{-1}; ^1H NMR 3.50 (3H, s), 3.62 (3H, s), 4.23 (1H, dd, J = 4.7, 9.2 Hz), 5.46 (1H, d, J = 4.7 Hz), 5.82 (1H, d, J = 9.2 Hz), 8.20 (1H, s); ^{13}C NMR 57.4 (q), 58.2 (q), 70.3 (d), 79.4 (d), 100.1 (d), 158.9 (s), 168.5 (s); MS *m/z* (rel intensity) 159 (M^+ − OMe, 2), 130 (2), 115 (2), 101 (45), 102 (37), 87 (13). Anal. Calcd for $C_7H_{10}O_6$: C, 44.21; H, 5.30. Found: C, 44.54; H, 5.59.

1-*O*-(*tert*-Butyldimethylsilyl)-4-*O*-formyl-2,3-*O*-isopropylidene-lyxopyranurono-5,1-lactone (40). Starting with acid **13** (54 mg, 0.16 mmol) and applying method A, for 1 h, after rotative chromatography (hexanes−EtOAc, 8:2) the lactone was obtained as an isomeric mixture **40** (37.5 mg, 70%, α:β = 2.7:1). When the reaction was performed using method B for 1 h, from **13** (28 mg, 0.08 mmol) the isomeric mixture of lactones **40** (19.6 mg, 70%) was also obtained in the same ratio. Anomer **40**α: syrup, $[\alpha]_D$ = −13.4° (c = 0.112); IR 1789, 1745 cm^{-1}; ^1H NMR 0.21 (3H, s), 0.23 (3H, s), 0.96 (9H, s), 1.39 (3H, s), 1.56 (3H, s), 4.44 (1H, dd, J = 3.4, 8.1 Hz), 4.60 (1H, dd, J = 7.4, 8.1 Hz), 5.67 (1H, d, J = 3.4 Hz), 6.02 (1H, d, J = 7.4 Hz), 8.22 (1H, s); ^1H NMR (C_6D_6, 500 MHz) 0.06 (3H, s), 0.12 (3H, s), 0.98 (9H, s), 1.00 (3H, s), 1.31 (3H, s), 3.82 (1H, dd, J = 6.8, 8.1 Hz), 4.00 (1H, dd, J = 7.9, 8.1 Hz), 5.35 (1H, d, J = 6.8 Hz), 5.65 (1H, d, J = 7.9 Hz), 7.63 (1H, s); ^{13}C NMR −5.2 (q), −5.1 (q), 17.8 (s), 24.9 (q), 25.4 (3 × q), 26.1 (q), 70.4 (d), 72.9 (d), 73.4 (d), 94.4 (d), 113.5 (s), 159.1 (s), 165.8 (s); MS (EI, 30 eV) *m/z* (rel intensity) 331 (M^+ − Me, 9), 289 (8), 231 (7), 215 (6), 203 (7), 187 (20). Anal. Calcd for $C_{15}H_{26}O_7Si$: C, 52.00; H, 7.57. Found: C, 52.10; H, 7.73. Anomer **40**β as a crystalline solid: mp 120−122 °C (from *n*-hexanes−EtOAc); $[\alpha]_D$ = +77.5° (c = 0.16); IR 1784, 1746 cm^{-1}; ^1H NMR 0.21 (6H, s), 0.95 (9H, s), 1.39 (3H, s), 1.52 (3H, s), 4.27 (1H, dd, J = 8.0, 6.8 Hz), 4.50 (1H, dd, J = 8.1, 7.9 Hz), 5.45 (1H, d, J = 6.8 Hz), 5.46 (1H, d, J = 7.9 Hz), 8.22 (1H, s); ^1H NMR (C_6D_6, 500 MHz) 0.08 (3H, s), 0.16 (3H), 0.99 (9H, s), 1.14 (3H, s), 1.50 (3H, s), 3.76 (1H, dd, J = 3.4, 8.1 Hz), 4.22 (1H, dd, J = 7.4, 8.1 Hz), 5.37 (1H, d, J = 3.4 Hz), 6.36 (1H, d, J = 7.4 Hz), 8.73 (1H, s); ^{13}C NMR −5.2 (q), −4.7 (q), 17.9 (s), 24.6 (q), 25.4 (3 × q), 26.7 (q), 70.5 (d), 73.1 (d), 77.3 (d), 96.9 (d), 112.4 (s), 159.1 (s), 163.8 (s); MS (EI, 30 eV) *m/z* (rel intensity) 331 (M^+ − Me, 8), 289 (18), 231 (7), 215 (9), 187 (5). Anal. Calcd for $C_{15}H_{26}O_7Si$: C, 52.00; H, 7.57. Found: C, 52.18; H, 7.65.

3-*O*-Formyl-1,2-*O*-isopropylidene-erythrurono-4,1-lactone (41). Starting with acid **18** (50 mg, 0.245 mmol) and using the method A, for 1 h, the crude was purified by rotative chromatography (hexanes−EtOAc, 7:3) to give the lactone **41** (21 mg, 0.1 mmol, 43%) as a volatile oil. By performing the experiment for 3 h under the conditions described in method B from **18** (45 mg, 0.22 mmol) lactone **41** was also obtained (14 mg, 37%): IR 1775, 1752 cm^{-1}; ^1H NMR 1.47 (3H, s), 1.56 (3H, s), 5.02 (1H, dd, J = 4.6, 3.1 Hz), 5.57 (1H, d, J = 4.6 Hz), 6.11 (1H, d, J = 3.1 Hz), 8.22 (1H, s); ^{13}C NMR 26.9 (q), 27.9 (q), 69.2 (d), 76.1 (d), 101.2 (d), 116.9 (s), 159.0 (s), 168.3 (s); MS *m/z* (rel intensity) 187 (M^+ − Me, 24), 173 (3), 159 (8), 145 (4), 129 (5). Anal. Calcd for $C_8H_{10}O_6$: C, 47.53; H, 4.99. Found: C, 47.62; H, 5.07.

4-*O*-Formyl-1,2,3-tri-*O*-methyl-D-arabinopyranurono-5,1-lactones (42). Under the conditions of method A for 1 h from acid **23** (30 mg, 0.148 mmol an anomeric mixture of lactones **42** (16.8 mg, 57%), in 1:1 ratio, was obtained, which was separated by rotative chromatography (hexanes−EtOAc, 85:15). Using the conditions of method B for 3 h from **23** (56 mg, 0.24 mmol), lactones **42** (25.5 mg, 0.11 mmol, 51%, ratio 1:1) were obtained. Anomer **42**α: syrup, $[\alpha]_D$ +103° (c = 0.35); IR 1741 cm^{-1}; ^1H NMR 3.52 (6H, s), 3.63 (3H, s), 3.61 (1H, dd, J = 4.5, 1.8 Hz), 3.79 (1H, dd, J = 1.8, 2.6 Hz), 5.14 (1H, d, J = 4.5 Hz), 5.56 (1H, dd, J = 2.6, 0.7 Hz), 8.24 (1H, d, J = 0.7 Hz); ^{13}C NMR 57.9 (q), 58.4 (2 × q), 68.6 (d), 78.0 (d), 80.0 (d), 104.7 (d), 159.3 (d), 164.5 (s); MS (EI, 30 eV) *m/z* (rel intensity) 175 (M^+ − CO_2Me, 1), 157 (29), 158 (3), 142 (16), 129 (10), 115 (55). Anal. Calcd for $C_9H_{14}O_7$: C, 46.15; H, 6.02. Found: C, 46.30; H, 6.25. Anomer **42**β: syrup, $[\alpha]_D$ −60° (c = 0.17); IR 1741 cm^{-1}; ^1H NMR 3.55 (3H, s), 3.58 (3H, s), 3.65 (3H, s), 3.77 (1H, dd, J = 3.2, 3.8 Hz), 3.95 (1H, dd, J = 3.8, 4.2 Hz), 5.36 (1H, d, J = 3.2 Hz), 5.96 (1H, dd, J = 4.2, 0.9 Hz), 8.23 (1H, d, J = 0.9 Hz); ^{13}C NMR 58.1 (q), 59.4 (q), 59.7 (q), 67.9 (d), 77.7 (d), 78.1 (d), 101.9 (d), 159.2 (d), 165.2 (s). MS (EI, 30 eV) *m/z* (rel intensity) 235 (M^+ + 1, 8), 203 (3), 175 (10). Anal. Calcd for $C_9H_{14}O_7$: C, 46.15; H, 6.02. Found: C, 46.20; H, 6.15.

3-*O*-Benzyl-4-*O*-formyl-1,2-*O*-isopropylidene-D-arabinopyranurono-5,1-lactone (43). Under the experimental conditions of method A from acid **33** (40 mg, 0.12 mmol), after 3 h and purification of the crude by rotative chromatography (hexanes−EtOAc, 8:2), the lactone **43** (20 mg, 0.06 mmol, 52%)

was obtained. Applying method B for 3 h from acid **33** (40 mg, 0.14 mmol), lactone **43** was obtained (17.3 mg, 0.05 mmol, 44%): syrup; $[\alpha]_D$ −31.5° (c = 0.46); IR 1742 cm^{-1}; ^1H NMR 1.37 (3H, s), 1.40 (3H, s), 4.34 (1H, d, J = 2.8 Hz), 4.44 (1H, dd, J = 4.3, 3.5 Hz), 4.72 (1H, d, J = 11.9 Hz), 4.93 (1H, d, J = 11.9 Hz), 5.58 (1H, ddd, J = 0.9, 3.5, 2.8 Hz), 5.97 (1H, d, J = 4.3 Hz), 7.30−7.37 (5H, m), 8.08 (1H, d, J = 0.9 Hz); ^{13}C NMR 25.6 (q), 26.9 (q), 69.8 (d), 70.9 (d), 73.1 (t), 74.4 (d), 99.5 (d), 112.6 (s), 128.4 (2 × d), 128.5 (d), 128.6 (2 × d), 136.1 (s), 159.1 (s), 166.3 (s); MS (EI, 30 eV) m/z (rel intensity) 322 (M^+, 2), 307 (4), 279 (7), 276 (5), 231 (28), 218 (12), 201 (97), 187 (97), 173 (53), 129 (64). Anal. Calcd for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found: C, 59.48; H, 5.71.

4-*O*-Formyl-1,2-*O*-isopropylidene-3-*O*-methyl-D-arabinopyranurono-5,1-lactone (44). Under the experimental conditions of method A from acid **34** (50 mg, 0.2 mmol), after 3 h and purification of the crude by rotative chromatography (hexanes−EtOAc, 8:2), the lactone **44** (12.5 mg, 0.05 mmol, 25%) was obtained: syrup; $[\alpha]_D$ −19° (c = 0.42); ^1H NMR 1.43 (3H, s), 1.58 (3H, s), 3.62 (3H, s), 4.19 (1H, d, J = 2.6 Hz), 4.48 (1H, dd, J = 4.0, 3.7 Hz), 5.68 (1H, dd, J = 3.7, 2.6 Hz), 5.99 (1H, d, J = 4.0 Hz), 8.11 (1H, s); ^{13}C NMR 25.7 (q), 27.1 (q), 58.8 (q), 68.9 (d), 74.2 (d), 74.6 (d), 99.6 (d), 113.9 (s), 159.1 (s), 166.0 (s); MS (EI, 30 eV) m/z (rel intensity) 218 (M^+ − CO, 7), 202 (2), 200 (6), 198 (13), 175 (11), 172 (5), 159 (16), 144 (2). Anal. Calcd for $C_{10}H_{14}O_7$: C, 48.78; H, 5.73. Found: C, 48.52; H, 5.77.

1,4-Di-*O*-acetyl-3-formyl-1-iodo-D-arabinofuranurono-5,2-lactone (45). Under the experimental conditions of method A from 2,5-di-*O*-acetyl-D-glucofuranosidurono-6,3-lactone (**37**) (50 mg, 0.19 mmol), after 1.5 h and purification of the crude by silica gel flash chromatography (hexanes−EtOAc, 80:20) the 1,4-di-*O*-acetyl-3-formyl-1-iodo-D-arabinofuranurono-5,2-lactone (**45**) (50 mg, 0.13 mmol, 67%) was obtained: syrup, IR ($CHCl_3$) 1824, 1773, 1747 cm^{-1}; ^1H NMR 2.14 (3H, s), 2.16 (3H, s), 5.06 (1H, dd, J = 9.6, 0.9 Hz), 5.80 (1H, d, J = 4.9 Hz), 6.02 (1H, dd, J = 4.9, 0.9 Hz), 6.86 (1H, d, J = 9.6 Hz), 8.09 (1H, s); ^{13}C NMR 20.0 (q), 20.9 (q), 47.8 (d), 68.0 (d), 69.9 (d), 78.8 (d), 158.8 (s), 167.9 (s), 168.8 (s), 169.1 (s); MS (CI, CH_4) m/z (rel intensity) 387 (M^+ + 1, 1), 327 (100), 299 (42), 285 (29), 281 (4), 259 (17), 239 (23), 217 (6), 157 (14). Anal. Calcd for $C_{10}H_{11}IO_8$: C, 31.11; H, 2.87. Found: C, 31.46; H, 3.01.

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