Fragmentation of Carbohydrate Anomeric Alkoxy Radicals. Synthesis of Polyhydroxy Piperidines and Pyrrolidines Related to Carbohydrates

Cosme G. Francisco, Raimundo Freire, Concepción C. González, Elisa I. León, Concepción Riesco-Fagundo, and Ernesto Suárez*

Instituto de Productos Naturales y Agrobiología del CSIC, Carretera de La Esperanza 3, 38206-La Laguna, Tenerife, Spain

esuarez@ipna.csic.es

Received November 27, 2000

Imino sugars of the piperidine and pyrrolidine types can be specifically obtained when protected 5-amino-5-deoxyfuranopentoses, 5-amino-5-deoxyfuranohexoses, 6-amino-6-deoxyfuranohexoses, and 6-amino-6-deoxypyranohexoses undergo a tandem alkoxy radical β-fragmentation−intramolecular cyclization reaction. The reaction is promoted by the system: iodosylbenzene−iodine under mild conditions. The *tert*-butoxycarbonyl, benzyloxycarbonyl, and diphenylphosphinoyl radicals have been studied as amino-protecting groups. Using this methodology, polyhydroxylated pyrrolidines of the D-erythrofuranoses **34** and **35**, D-threofuranose **36**, L-xylofuranose **42**, and D-arabinofuranose **43** series and polyhydroxylated piperidines of the D-arabinopyranose type **37** and **38** were obtained.

The synthesis of sugar-mimic glycosidase inhibitors has recently received considerable attention from organic chemists.[1] These polyhydroxylated piperidines and pyrrolidines, structurally related to cyclic carbohydrates, the so-called *azasugars*,[2] in which the ring oxygen has been replaced by a basic nitrogen atom, bind specifically to the active sites of the enzyme by mimicking the corresponding carbohydrate. Since glycosidases are involved in many types of important biological processes, some of these substances have a promising therapeutic potential as antiviral and anticancer agents and in the treatment of diabetes.[3] The study of the β-fragmentation reaction of anomeric alkoxy radicals of carbohydrates using hypervalent iodine reagents has engaged the attention of our laboratory for several years.[4] The application of this protocol allows us to obtain carbohydrates with one carbon less and it is therefore useful for descending the aldose series and for the preparation of chiral synthons.[4a] The synthesis of cyclic aldoses[4b] and ketoses[4c] in furanose and pyranose form as well as alduronic acid lactones[4d,f] and aldonitriles[4e] can also be accomplished using this methodology.

In Scheme 1 we depict the basic features of our strategy directed toward the synthesis of imino-sugars within the context of a research program devoted to the study of the alkoxy radical β-fragmentation reaction (ARF). This methodology relies on the initial formation of an alkoxy anomeric radical (I) originated by the action of the hypervalent iodine reagent in the presence of iodine, presumably through an alkyl hypoiodite intermediate.[5] Subsequently, the alkoxy radical undergoes a fragmentation of the C1−C2 bond and gives rise to a C2 radical (II) that is afterward oxidized by an excess of reagent to the oxycarbenium ion (III). The intramolecular nucleophilic cyclization of the amine derivative affords the required sugar derivative. A similar protocol using alcohols as nucleophiles has previously been reported by

(1) For reviews see, inter alia: (a) Driguez, H.; Thiem, J. *Topics in Current Chemistry*; Springer: Berlin, Germany, 1997; Vol. 187, pp 157−186. (b) Depezay, J.-C. In *Carbohydrate mimics: Concepts and Methods*; Chapleur, Y., Ed.; Wiley-VCH Publishers: Weinheim, 1998; pp 307−326. (c) Ganem, B. *Acc. Chem. Res.* **1996**, *29*, 340−347. (d) Sears, P.; Wong, C.-H. *Angew. Chem., Int. Ed.* **1999**, *38*, 2300−2324. (e) Heightman, T. D.; Vasella, A. T. *Angew. Chem., Int. Ed.* **1999**, *38*, 750−770. (f) Bols, M. *Acc. Chem. Res.* **1998**, *31*, 1−8. For recent references, see, inter alia: (g) Hansen, A.; Tagmose, T. M.; Bols, M. *Tetrahedron* **1997**, *53*, 697−706. (h) Cipolla, L.; Lay, L.; Nicostra, F.; Pangrazio, C.; Panza, L. *Tetrahedron* **1995**, *51*, 4679−4690. (i) Poitout, L.; Lemerrer, Y.; Depezay, J. C. *Tetrahedron Lett.* **1996**, *37*, 1609−1612. (j) Henderson, I.; Laslo, K.; Wong, C.-H. *Tetrahedron Lett.* **1994**, *35*, 359−362. (k) Takaoka, Y.; Kajimoto, T.; Wong, C.-H. *J. Org. Chem.* **1993**, *58*, 4809−4812. (l) Dondoni, A.; Merino, P.; Perrone, D. *Tetrahedron* **1993**, *49*, 2939−2958. (m) Furneaux, R. H.; Tyler, P. C.; Whitehouse, L. A. *Tetrahedron Lett.* **1993**, *34*, 3613−3616. (n) Fairbanks, A. J.; Carpenter, N. C.; Fleet, G. W. J.; Ramsden, N. G.; Cenci de Bello, I.; Winchester, B. G.; Al-Daher, S. S.; Nagahashi, G. *Tetrahedron*. **1992**, *48*, 3365−3376. (o) Straub, A.; Effenberger, F.; Fischer, P. *J. Org. Chem.* **1990**, *55*, 3926−3932. (p) Fleet, G. W. J.; Ramsden, N. G.; Witty, D. R. *Tetrahedron Lett.* **1988**, *29*, 2871−2874.

(2) Although frequently used, the term *azasugar* is not recommended for this type of compounds (Nomenclature of Carbohydrates, IUPAC, Rule 2-Carb-34.1).

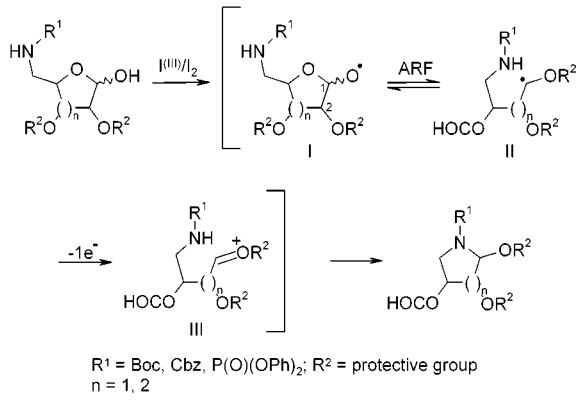
(3) (a) Asano, N.; Nash, R. J.; Molyneux, R. J.; Fleet, G. W. J. *Tetrahedron*: *Asymmetry* **2000**, *11*, 1645−1680. (b) Hughes, A. B.; Rudge, A. J. *Nat. Prod. Rep.* **1994**, *11*, 135−162. (c) Look, G. C.; Fotsch, C. H.; Wong, C.-H. *Acc. Chem. Res.* **1993**, *26*, 182−190. (d) Winchester, B.; Fleet, G. W. J. *Glycobiology* **1992**, *2*, 199−210. (e) van den Broek, L. A. G. M.; Vermaas, D. L.; Heskamp, B. M.; van Boeckel, C. A. A.; Tan, M. C. A. A.; Bolscher, J. G. M.; Ploegh, H. L.; van Kemenade, F. J.; de Goede, R. E. Y.; Miedema, F. *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 82−94. (f) Fleet, G. W. J.; Karpas, A.; Dwek, R. A.; Fellows, L. E.; Tyms, A. S.; Petursson, S.; Namgoong, S. K.; Ramsden, N. G.; Smith, P. W.; Son, J. C.; Wilson, F.; Witty, D. R.; Jacob, G. S.; Rademacher, T. M. *FEBS Lett.* **1988**, *237*, 128−132.

(4) (a) Armas, P.; Francisco, C. G.; Suárez, E. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 772−774. (b) Armas, P.; Francisco, C. G.; Suárez, E. *J. Am. Chem. Soc.* **1993**, *115*, 8865−8866. (c) Armas, P.; Francisco, C. G.; Suárez, E. *Tetrahedron Lett.* **1993**, *34*, 7331−7334. (d) Francisco, C. G.; González, C. C.; Suárez, E. *Tetrahedron Lett.* **1996**, *37*, 1687−1690. (e) Hernández, R.; León, E. I.; Moreno, P.; Suárez, E. *J. Org. Chem.* **1997**, *62*, 8974−8975. (f) Francisco, C. G.; González, C. C.; Suárez, E. *J. Org. Chem.* **1998**, *63*, 2099−2109. (g) Francisco, C. G.; León, E. I.; Moreno, P.; Suárez, E. *Tetrahedron: Asymmetry* **1998**, *9*, 2975−2978. (h) Francisco, C. G.; González, C. C.; Suárez, E. *J. Org. Chem.* **1998**, *63*, 8092−8093. (i) Martín. A.; Rodríguez, M. S.; Suárez, E. *Tetrahedron Lett.* **1999**, *40*, 7525−7528.

(5) Courtneidge, J. L.; Lusztyk, J.; Pagé, D. *Tetrahedron Lett.* **1994**, *35*, 1003−1006.

10.1021/jo0057452 CCC: $20.00
Published on Web 01/31/2001

Scheme 1



this research group for the specific synthesis of furanose or pyranose forms of cyclic aldoses and ketoses.[4b,c] This methodology has also been applied to an approach to the synthesis of (+)-preussin.[6]

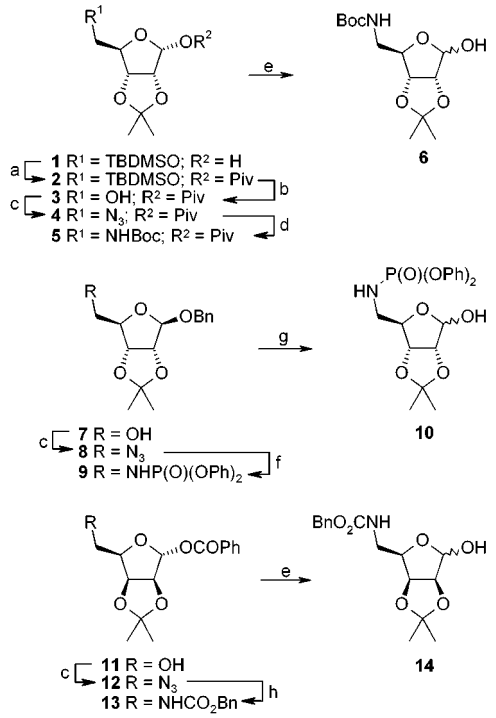
Results and Discussion

Herein, we report on an extension of the ARF methodology that is particularly effective for the synthesis of five- and six-membered imino-sugars under mild conditions that are compatible in many cases with the stability of the protective groups most widely used in carbohydrate chemistry. In a previous communication, we described the preliminary results obtained,[7] and we now report full details of these experiments and their extension to a number of new models. To test the scope of the reaction, we have prepared substrates from both the pentose and hexose series of carbohydrates as depicted in Schemes 2 and 3.

Substrates from Pentose Series. The 5-amino-5-deoxy-D-*ribo* derivatives **6** and **10** were synthesized starting from 2,3-*O*-isopropylidene-D-ribofuranose[8] using well-established methods (Scheme 2). The azides **4** and **8** were prepared directly from the respective primary alcohols using zinc azide−pyridine complex under Mitsunobu substitution conditions.[9] Reduction of the azides and protection of the resulting amines with di-*tert*-butyl dicarbonate[10] and diphenyl chlorophosphate[11] gave after deprotection of the anomeric alcohols the required substrates **6** and **10**, respectively. The D-lyxose derivative **14** was prepared from benzoyl 5-azido-5-deoxy-2,3-*O*-isopropylidene-D-lyxofuranoside (**12**),[12] after reduction of the azide, reaction of the obtained amine with benzyl chloroformate, and deprotection of the anomeric alcohol (Scheme 2).

Substrates from Hexose Series. The reduction of the azide **16**, obtained from the known benzyl 2,3,4-tri-*O*-methyl-*β*-D-glucopyranoside (**15**),[4f] with Bu_3SnH and

Scheme 2. Synthesis of Substrates from Pentose Series[a]



[a] Key: (a) PivCl, Py, 0 °C to room temperature, 52 h, 89%; (b) TBAF, THF, rt, 1 h, 92%; (c) ZnN_6·2Py, PPh_3, DIAD, toluene, rt, 24−63 h, 65−93%; (d) H_2, Pd/C, Boc_2O, EtOAc, rt, 20 h, 83%; (e) NaOMe, MeOH, 0−40 °C, 1−4 h, 52−84%; (f) Bu_3SnH, AIBN, PhH, reflux, 1.5 h, then diphenyl chlorophosphate, TEA, rt, 21 h, 91%; (g) H_2, $Pd(OH)_2$/C, EtOAc, rt, 20 h, 90%; (h) H_2, Pd/C, EtOAc, rt, 20 h, then benzyl chloroformate, $NaHCO_3$, 0 °C to rt, 1 h, 62%.

subsequent treatment with di-*tert*-butyl dicarbonate gave the *N*-Boc-D-gluco derivative **17**. The anomeric benzyl ether was then hydrogenolyzed with $Pd(OH)_2$/C to give the intended substrate **18** (Scheme 3).

The 6-amino-6-deoxy-D-manno derivative **25** was obtained starting from benzoyl 2,3-*O*-isopropylidene-α-D-mannofuranoside (**19**) which was selectively silylated at the more reactive 6-hydroxyl with *t*-$BuMe_2SiCl$ in the presence of imidazole. The secondary hydroxyl was protected as its methyl ether, and the *tert*-butyldimethylsilyl ether at C6 hydrolyzed to give alcohol **22**. This time, azide grouping was introduced by mesylation of the primary alcohol to provide the crude mesylate, which was then treated with NaN_3 in DMF to give azide **23**. Subsequent in situ hydrogenation−protection of the azide afforded, after removal of the anomeric benzoyl ester with NaOMe, *N*-Boc-D-manno derivative **25** (Scheme 3). The preparation of 5-amino-5-deoxy-L-gulo model **28** was also started with compound **20**. The 5-azide grouping was introduced by triflation of the secondary alcohol and S_N2 displacement with sodium azide. One-pot hydrogenation−protection of the azide with a *tert*-butoxycarbonyl group afforded, after hydrolysis of the anomeric ester, the required *N*-Boc-L-gulo substrate **28**. The *N*-Boc-D-manno analogue **33** was also synthesized starting from compound **20** by a double inversion of configuration at C5. The stereochemistry of the 5-hydroxyl was first inverted using Mitsunobu[13] conditions to give after

(6) Armas, P.; Garcia-Tellado, F.; Marrero-Tellado, J. J.; Robles, J. *Tetrahedron Lett.* **1998**, *39*, 131−134.

(7) Francisco, C. G.; Freire, R.; González, C. C.; Suárez, E. *Tetrahedron*: *Asymmetry* **1997**, *8*, 1971−1974.

(8) Kaskar, B.; Heise, G. L.; Michalak, R. S.; Vishnuvajjala, B. R. *Synthesis* **1990**, 1031−1032. Duvoid, T.; Francis, G. W.; Papaioannou, D. *Tetrahedron Lett.* **1995**, *36*, 3153−3156.

(9) Viand, M. C.; Rollin, P. *Synthesis* **1990**, 130−132.

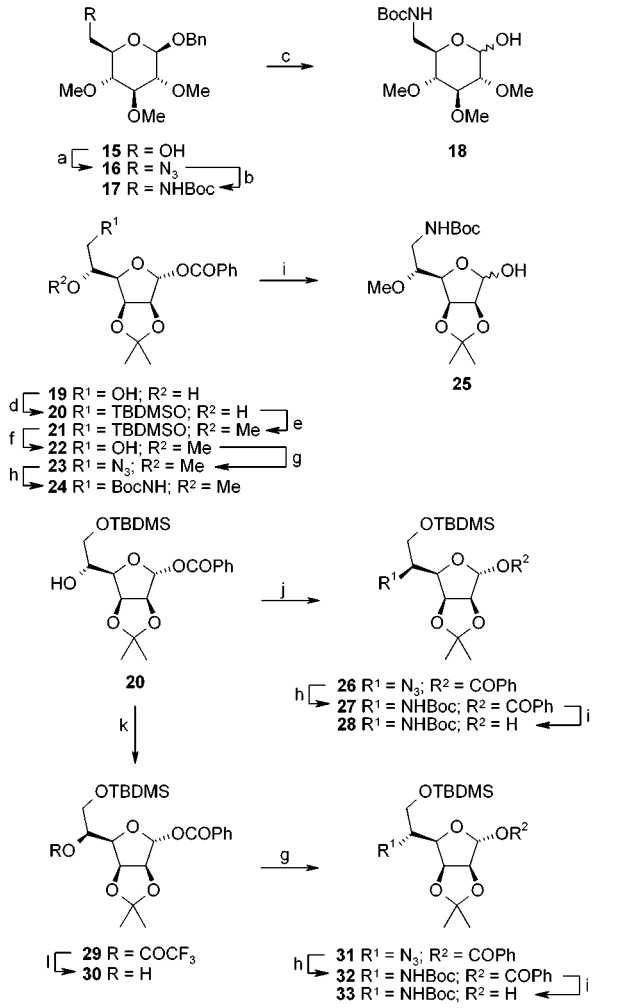
(10) Saito, S.; Nakajima, H.; Inaba, M.; Moriwake, T. *Tetrahedron Lett.* **1989**, *30*, 837−838.

(11) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley & Sons: New York, 1991; p 376.

(12) Ichikawa, Y.; Igarashi, Y. *Tetrahedron Lett.* **1995**, *36*, 4585−4586.

(13) (a) Mitsunobu, O. *Synthesis* **1981**, 1−28. (b) Hughes, D. L. *Org. React.* **1992**, *42*, 335−656.

Scheme 3. Synthesis of Substrates from Hexose Series[a]



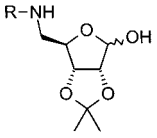
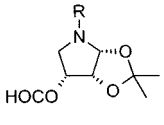
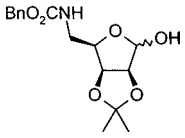
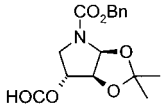
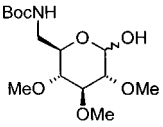
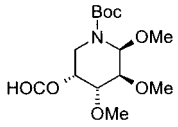
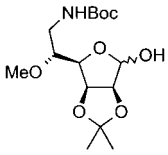
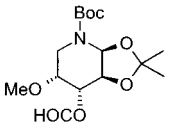
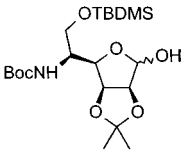
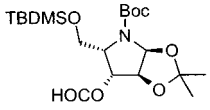
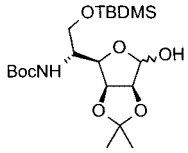
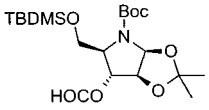
[a] Key: (a) $ZnN_6 \cdot 2Py$, PPh_3, DIAD, toluene, rt, 48 h, 75%; (b) Bu_3SnH, AIBN, PhH, reflux, 1.5 h, then $(Boc)_2O$, TEA, DMF, 40 °C to rt, 2 h, 97%; (c) H_2, $Pd(OH)_2/C$, EtOH, rt, 4 h, 92%; (d) TBDMSCl, imidazole, DMF, rt, 30 min, 91%; (e) MeI, Ag_2O, acetone, rt, 24 h, 93%; (f) PPTS, MeOH, rt, 20 h, 99%; (g) mesyl chloride, Py, 0 °C, 30 min, 99% then NaN_3, DMF, rt, 3−6 h, 85%; (h) H_2, Pd/C, Boc_2O, EtOAc, rt, 1−20 h, 79−99%; (i) NaOMe, MeOH, rt, 0.5−2 h, 89−98%; (j) (i) triflic anhydride, Py, CH_2Cl_2, 0 °C, 30 min, 90%; (ii) NaN_3, DMF, rt, 2 h, 87%; (k) DIAD, PPh_3, CF_3CO_2H, THF, 0 °C → rt, 16 h, 61%; (l) MeOH, $NaHCO_3$, rt, 30 min, 85%.

hydrolysis of the trifluoroacetate ester intermediate the alcohol **30**, which was then mesylated and treated with NaN_3 with overall retention of configuration. The 5-azide-5-deoxy-D-manno **31** obtained was transformed into the *N*-Boc-protected amine **33** using the protocol described above for the preparation of compound **28**.

As can be observed in Table 1, our procedure was applied to carbohydrates of the pentose and hexose series in pyranose or furanose form with the object of obtaining polyhydroxylated substances with pyrrolidine or piperidine skeletons. We therefore undertook a systematic investigation of this reaction, focusing on the scope and stereochemical course of the process.

When the reaction was performed with the *N*-Boc-protected 5-amino-5-deoxy-D-ribo derivative **6** using iodosylbenzene and iodine as oxidizing system under the conditions shown in Table 1 (entry 1), the 4-amino-4-deoxy-D-erythrofuranose derivative **34** was obtained in

Table 1. Synthesis of Imino Sugars Using an Alkoxy Radical Fragmentation Reaction[a]

entry	substrate	$PhIO/I_2$[b] (mmol)	time (h)	product	yield (%)
1	 **6** R = Boc	2.5/1	21	 **34** R = Boc	76
2	**10** R = P(O)(OPh)$_2$	2.5/1.2	2	**35** R = P(O)(OPh)$_2$	72
3	 **14**	2.2/1.2	2	 **36**	70
4	 **18**	2.2/1.2	1	 **37**	68
5	 **25**	3/1.2	2.3	 **38**	15[c]
6	 **28**	3/1.2	2	 **42**	78
7	 **33**	1.6/0.2[e]	1	 **43**	28[d]

[a] The reactions were performed in dry CH_2Cl_2 at rt. [b] mmol of iodosylbenzene and iodine per mmol of substrate. [c] Compound **40** (42%) is also obtained. [d] Compound **44** (33%) is also obtained. [e] CCl_4 was used as solvent.

good yield. The ^1H and ^{13}C NMR spectra of this *N*-Boc derivative appear at room temperature as a mixture of two conformers due to the restricted rotation of the nitrogen−carbon bond of the carbamate group. To overcome this situation, NMR spectra were run at 75 °C. At this temperature, the spectra are consistent with the proposed structure. The phosphoramidate **10** was synthesized starting with the same ribofuranoside to investigate the influence of the amine protecting group in the cyclization reaction. In this case, the reaction behaved analogously and compound **35** was obtained in similar yield (entry 2). The NMR spectra of this substance showed a complex pattern because of the presence of long-range coupling between the phosphorus atom and certain carbons and hydrogens of the molecule.

The reaction does not seem to be dependent on the stereochemistry at C2 or C3 since the *N*-Cbz-protected 5-amino-5-deoxy-D-lyxofuranose derivative **14**, which required a sterically more crowded transition state for the

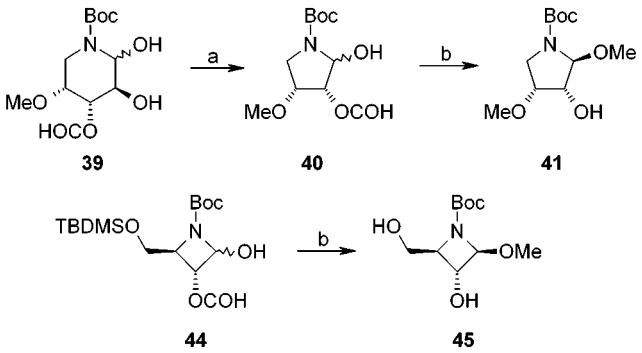
cyclization step, gave rise to the D-threofuranose derivative **36** also in a similar yield (entry 3).

For the sake of completeness, this methodology was also extended to the synthesis of imino-sugars of the pentose series in pyranose form, through a 1,6-coupling cyclization reaction. The *N*-Boc-protected 6-amino-6-deoxy-D-glucopyranose derivative **18** was transformed into the 5-amino-5-deoxy-D-arabinopyranose derivative **37** under the conditions shown in Table 1 (entry 4). The proposed stereochemistry at C1 was based on the small coupling constant observed between the H1 and H2 protons (3.5 Hz) in the ^{1}H NMR spectrum, which preclude a trans-diaxial relationship between them and is clearly indicative of the β-orientation of the C1-substituent. The observed correlation of the anomeric methoxyl group with the β-proton at C5 in a ROESY experiment in combination with COSY, DEPT and HMQC spectra, to assign carbons and protons, not only confirms the proposed stereochemistry at the anomeric carbon but also suggests a $^1C_4$ conformation for the piperidine ring. Furthermore, the observed coupling constants are in accord with those calculated over a $^1C_4$-minimized structure using the MMX force field.[14]

To test the possibility of exploiting this procedure to prepare imino-pentoses in pyranose form starting from conveniently functionalized furanohexoses, we synthesized 6-amino-6-deoxy-D-mannofuranose derivative **25**. In this case, however, results were only partially satisfactory from the synthetic point of view. In fact, the expected piperidine derivative **38** was formed only as a minor product (15%), the principal compound being the pyrrolidine derivative **40** obtained in 42% yield (entry 5). The structure of compound **40** was further confirmed by converting it into the methyl erythrofuranoside derivative **41**, using MeOH/HCl. The ^{1}H and ^{13}C NMR spectra of this compound at room temperature correspond to a clearly defined mixture of two rotamers in a ratio of 1:1. The observed null value for the coupling constant between H1 and H2 is in complete accord with a β-configuration for the methoxyl group at C1. We first expected the tandem fragmentation−cyclization reaction to proceed in good yield to give **38**, but the sensitive 1,2-isopropylidene was hydrolyzed by the iodine[15] present in the reaction medium to afford 1,2-diol **39** (Scheme 4). This compound could not be isolated because was oxidized in situ with an excess of iodosylbenzene and subsequently transformed into **40**. This assumption turned out to be partially incorrect. Inasmuch as the pure compound **38** seems to be stable under the reaction conditions (iodosylbenzene/iodine at room temperature for 5 h) and the hydrolysis of the isopropylidene has had to occur at an earlier stage before the cyclization step.

The diastereoisomeric 5-amino-5-deoxy-L-gulofuranose **28** and 5-amino-5-deoxy-D-mannofuranose **33** were prepared in order to check the validity of this method in the synthesis of imino-sugars with a pentofuranoses structure. This type of compounds are directly related with the polyhydroxylated pyrrolidines: nectrisine, 4-*epi*-nectrisine, DAB-1, and LAB-1,[16] which are powerful

Scheme 4[a]



[a] Key: (a) PhIO, I_2, CH_2Cl_2, rt, 1 h; (b) MeOH, HCl, rt, 1 h.

inhibitors of a range of α-glucosidases and α-mannosidases.[17] In the first case, the reaction proceeded smoothly and the 4-amino-4-deoxy-L-xylofuranose **42** was formed in good yield (entry 6). No products were detected that derived from deprotection of the 1,2-isopropylidene group. However, during the reaction of compound **33**, partial cleavage of the 1,2-isopropylidene group took place and the expected 4-amino-4-deoxy-D-arabinofuranose **43** was only obtained in 28% yield (entry 7), the principal compound being the interesting azetidine derivative **44** (33%) (Scheme 4). On the basis of spectroscopic evidence, the 2-hydroxyazetidine **44** would exist predominantly in the thermodynamically stable cyclic form as a hemiacetal.[18] The reaction of **44** with MeOH/HCl simultaneously removed the *tert*-butyldimethylsilyl ether and the formyl group and introduced the methyl group at the anomeric center to afford methyl 3-amino-3-deoxy-β-D-erythrooxetoside **45**. The assignment of the stereochemistry of the methoxyl group at C1 was made on the basis of the coupling constant between H1 and H2 (found ∼0 Hz, calcd 1.5 Hz).[14] The lability of the 1,2-isopropylidene in the D-arabino derivative **43** compared to its L-xylo **42** counterpart may be due to steric hindrance between one of the methyls of the protecting group and the tether at C4 in the transition state of the cyclization step.

Derivatives of 4-amino-4-deoxy-L-xylofuranose and 4-amino-4-deoxy-D-arabinofuranose have recently been synthesized by Kitahara et al.[16a] starting from D-(−)-diethyl tartrate, as intermediates in their synthesis of nectrisine and 4-*epi*-nectrisine.

In conclusion, this two-step tandem procedure allows, under mild conditions, the synthesis of polyhydroxy pyrrolidines and piperidines corresponding to carbohydrates of the tetroses and pentoses series. In this latter series, the preparation of the five- or six-membered heterocycles can be specifically achieved only by changing the relative position of the amine group.

(14) MMX force field as implemented in PCMODEL (v. 4.0), Serena Software, Bloomington, IN, 47402-3076.

(15) Although deprotection of isopropylidene derivatives has never been observed under the reaction conditions, iodine is a mild Lewis acid that has been used for the formation and cleavage of acetals. (a) Kartha, K. P. R. *Tetrahedron Lett.* **1986**, *27*, 3415−3416. (b) Szarek, W. A.; Zamojski, A.; Tiwari, K. N.; Ison, E. R. *Tetrahedron Lett.* **1986**, *27*, 3827−3830.

(16) (a) Kim, Y. J.; Takatsuki, A.; Kogoshi, N.; Kitahara, T. *Tetrahedron* **1999**, *55*, 8353−8364. (b) Kim, Y. J.; Kido, M.; Bando, M.; Kitahara, T. *Tetrahedron* **1997**, *53*, 7501−7508. (c) Chen, S. H.; Danishefsky, S. J. *Tetrahedron Lett.* **1990**, *31*, 2229−2232. (d) Kayakiri, H.; Nakamura, K.; Takase, S.; Setoi, H.; Uchida, I.; Terano, H.; Hashimoto, M.; Tada, T.; Koda, S. *Chem. Pharm. Bull.* **1991**, *39*, 2807.

(17) (a) Furukawa, J.; Okuda, S.; Saito, K.; Hatanaka, S. I. *Phytochemistry* **1985**, *24*, 593−594. (b) Nash, R. J.; Bell, E. A.; Williams, J. M. *Phytochemistry* **1985**, *24*, 1620−1622. (c) Fleet, G. W. J.; Nicholas, S. I.; Smith, P. W.; Evans, S. V.; Fellows, L. E.; Nash, R. J. *Tetrahedron Lett.* **1985**, *26*, 3127−3130. (d) Shibata, T.; Nakayama, O.; Tsurumi, Y.; Okuhara, M.; Terano, H.; Kohsaka, M. *J. Antibiot.* **1988**, *41*, 296.

(18) Chelucci, G.; Saba, A. *Tetrahedron*: *Asymmetry* **1997**, *8*, 699−702.

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 CCl_4 solutions unless otherwise stated. NMR spectra were determined at 500 MHz for ^1H and 125.7 MHz for ^{13}C in $CDCl_3$ at 26 °C unless otherwise stated, in the presence of TMS as internal standard. Mass spectra were determined at 70 eV. Merck silica gel 60 PF (0.063−0.2 mm) were used for column chromatography. Circular layers of 1 mm of Merck silica gel 60 PF_{254} were used on a Chromatotron for centrifugally assisted chromatography. Commercially available reagents and solvents were analytical grade or were purified by standard procedures prior to use.[19] All reactions involving air- or moisture-sensitive materials were carried out under a nitrogen atmosphere. The spray reagents for TLC analysis were conducted with 0.5% vanillin in H_2SO_4−EtOH (4:1) and further heating until development of color.

General Procedure for the Alkoxy Radical Fragmentation Reaction. To a solution of the amine derivative (1 mmol) in CH_2Cl_2 (35 mL) were added freshly prepared iodosylbenzene[20] (1.6−3 mmol) and I_2 (0.2−1.2 mmol), and the reaction was stirred at room temperature for 1−21 h. The reaction mixture was then poured into aqueous 10% $Na_2S_2O_3$ and extracted with CH_2Cl_2. The organic layer was then washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The obtained residue was purified by chromatography under the conditions specified in each case.

4-(*tert*-Butoxycarbonyl)amino-4-deoxy-3-*O*-formyl-1,2-*O*-isopropylidene-α-D-erythrofuranose (34). Following the general procedure, compound **6** (50 mg, 0.17 mmol) in CH_2Cl_2 (6 mL) containing iodosylbenzene (93.5 mg, 0.43 mmol) and I_2 (43 mg, 0.17 mmol) was stirred at room temperature for 21 h. Chromatotron chromatography (hexanes−EtOAc, 80:20) of the reaction residue afforded compound **34** (36 mg, 0.13 mmol, 76%) as a crystalline solid (two rotamers in a ratio of 2:3): mp 71−73 °C (from CH_2Cl_2); $[\alpha]_D$ −73.3 (c = 0.514); IR 1736, 1714 cm^{-1}; ^1H NMR (75 °C) 1.35 (3H, s), 1.48 (9H, s), 1.50 (3H, s), 3.38 (1H, dd, J = 9.4, 10.4 Hz), 3.96 (1H, dd, J = 7.6, 10.4 Hz), 4.75 (1H, dd, J = 4.7, 4.6 Hz), 4.95 (1H, ddd, J = 4.7, 9.4, 7.6 Hz), 5.85 (1H, s), 8.04 (1H, s); ^{13}C NMR (75 °C, one quaternary carbon missing) 26.1 (CH_3), 26.6 (CH_3), 28.2 (3 × CH_3), 45.8 (CH_2), 69.7 (CH), 80.8 (CH), 88.3 (CH), 112.7 (C), 153.3 (C), 159.4 (CH); MS (rel intensity) 288 (M^+ + 1, 2), 272 (3), 241 (8), 230 (4), 214 (7), 185 (19), 172 (11), 170 (4), 156 (16), 128 (11), 112 (19). Anal. Calcd for $C_{13}H_{21}NO_6$: C, 54.35; H, 7.37; N, 4.88. Found: C, 54.25; H, 7.37; N, 4.89.

4-Deoxy-4-(*N*-diphenylphosphinoyl)amino-3-*O*-formyl-1,2-*O*-isopropylidene-α-D-erythrofuranose (35). Following the general procedure, compound **10** (33 mg, 0.078 mmol) in dry CH_2Cl_2 (3 mL) containing iodosylbenzene (38 mg, 0.17 mmol) and I_2 (24 mg, 0.09 mmol) was stirred at room temperature for 2 h. Chromatotron chromatography (hexanes−EtOAc, 70:30) of the residue afforded compound **35** (23.5 mg, 0.057 mmol, 72%): syrup; $[\alpha]_D$ −25.9 (c = 0.328); IR 1737 cm^{-1}; ^1H NMR 1.33 (3H, s), 1.38 (3H, s), 3.35 (1H, ddd, J = 9.7, 9.3 Hz, J_P = 2.5 Hz), 3.82−3.86 (1H, m), 4.72−4.77 (2H, m), 5.86 (1H, dd, J = 4.3 Hz, J_P = 2.8 Hz), 7.17−7.21 (2H, m), 7.27−7.37 (8H, m), 8.06 (1H s); ^1H NMR (75 °C) 1.31 (3H, s), 1.38 (3H, s), 3.34 (1H, ddd, J = 9.4, 9.4 Hz, J_P = 2.9 Hz), 3.80−3.84 (1H, m), 4.70−4.75 (2H, m), 5.85 (1H, dd, J = 4.3 Hz, J_P = 2.1 Hz), 7.13−7.16 (2H, m), 7.25−7.32 (8H, m), 8.01 (1H, s); ^{13}C NMR (75 °C) 25.8 (CH_3), 26.1 (CH_3), 46.4 (CH_2, J_P = 3.8 Hz), 71.0 (CH, J_P = 11.4 Hz), 76.8 (CH, J_P = 9.5 Hz), 90.5 (CH, J_P = 3.8 Hz), 112.1 (C), 120.0 (2 × CH, J_P = 3.8 Hz), 120.1 (2 × CH, J_P = 5.7 Hz), 124.9 (2 × CH, J_P = 5.7 Hz), 129.5 (4 × CH, J_P = 7.6 Hz), 150.6 (2 × C, J_P = 5.7 Hz), 159.3 (CH); MS (rel intensity) 419 (M^+, <1), 404 (9), 373 (37), 344 (19), 316 (100), 315 (47), 251 (15), 233 (7); HRMS calcd for $C_{20}H_{22}NO_7P$ 419.1134, found 419.1145. Anal. Calcd for $C_{20}H_{22}NO_7P$: C, 57.28; H, 5.29; N, 3.34. Found: C, 57.44; H, 5.46; N, 3.25.

4-(*N*-Benzyloxycarbonyl)amino-4-deoxy-3-*O*-formyl-1,2-*O*-isopropylidene-β-D-threofuranose (36). Following the general procedure, compound **14** (42 mg, 0.13 mmol) in dry CH_2Cl_2 (7 mL) containing iodosylbenzene (75 mg, 0.34 mmol) and I_2 (41 mg, 0.16 mmol) was stirred at room temperature for 2 h. Chromatotron chromatography (hexanes−EtOAc, 80:20 → 70:30) of the residue afforded compound **36** (30 mg, 0.09 mmol, 70%) as a crystalline solid (two rotamers in a ratio of 1:1): mp 72−74 °C (from ether−*n*-hexane); $[\alpha]_D$ +68 (c = 0.540); IR 1736, 1723 cm^{-1}; ^1H NMR (75 °C) 1.34 (3H, s), 1.45 (3H, s), 3.75 (1H, dd, J = 3.9, 13.0 Hz), 3.82 (1H, d, J = 13.0 Hz), 4.56 (1H, d, J = 4.5 Hz), 5.17 (1H, d, J = 12.7 Hz), 5.21 (1H, d, J = 12.7 Hz), 5.24 (1H, d, J = 3.9 Hz), 6.03 (1H, brs), 7.27−7.39 (5H, m), 7.98 (1H, s); ^{13}C NMR (75 °C) 25.8 (CH_3), 26.8 (CH_3), 49.6 (CH_2), 67.2 (CH_2), 74.3 (CH), 82.3 (CH), 88.8 (CH), 112.3 (C), 127.7 (2 × CH), 127.8 (CH), 128.3 (2 × CH), 136.0 (C), 154.2 (C), 159.0 (CH); MS (rel intensity) 321 (M^+, 13), 306 (6), 263 (9), 219 (11), 214 (8), 174 (13), 156 (10); HRMS calcd for $C_{16}H_{19}NO_6$ 321.1212, found 321.1216. Anal. Calcd for $C_{16}H_{19}NO_6$: C, 59.81; H, 5.96; N, 4.36. Found: C, 59.74; H, 6.05; N, 4.30.

Methyl 5-(*N*-*tert*-Butoxycarbonyl)amino-5-deoxy-4-*O*-formyl-2,3-di-*O*-methyl-β-D-arabinopyranoside (37). Following the general procedure, compound **18** (34 mg, 0.106 mmol) in dry CH_2Cl_2 (5 mL) containing iodosylbenzene (73 mg, 0.33 mmol) and I_2 (32 mg, 0.13 mmol) was stirred at room temperature for 1 h. Chromatotron chromatography (hexanes−EtOAc, 95:5) of the residue afforded compound **37** (23 mg, 0.072 mmol, 68%) as a syrup (two rotamers in a ratio of 3:2): $[\alpha]_D$ −92.1 (c = 0.34); IR 1732, 1703 cm^{-1}; ^1H NMR 1.45 (9H, s), 1.47 (9H, s), 3.03 (1H, d, J = 14.7 Hz), 3.09 (1H, d, J = 14.3 Hz), 3.30 (3H, s), 3.32 (3H, s), 3.44 (3H, s), 3.45 (3H, s), 3.48 (1H, dd, J = 6.7, 3.5 Hz), 3.50 (1H, dd, J = 6.6, 3.5 Hz), 3.54 (3H, s), 3.56 (3H, s), 3.61 (1H, dd, J = 10.0, 3.4 Hz), 3.64 (1H, dd, J = 9.9, 3.3 Hz), 4.10 (1H, dd, J = 2.6, 14.7 Hz), 4.20 (1H, dd, J = 1.9, 14.7 Hz), 5.32 (1H, brs), 5.43 (1H, d, J = 3.5 Hz), 5.47 (1H, brs), 5.61 (1H, d, J = 3.5 Hz), 8.09 (1H, s), 8.11 (1H, s); ^1H NMR (75 °C) 1.46 (9H, s), 3.06 (1H, d, J = 14.8 Hz), 3.32 (3H, s), 3.43 (3H, s), 3.46 (1H, dd, J = 9.9, 3.7 Hz), 3.53 (3H, s), 3.60 (1H, dd, J = 9.9, 3.4 Hz), 4.11 (1H, brs), 5.33 (1H, brs), 5.53 (1H, brs), 8.06 (1H, s); ^{13}C NMR (75 °C) 28.5 (3 × CH_3), 40.8 (CH_2), 55.5 (CH_3), 58.3 (CH_3), 58.7 (CH_3), 78.1 (2 × CH), 78.5 (2 × CH), 81.0 (C), 154.8 (C), 160.0 (CH); MS (rel intensity) 319 (M^+, <1), 287 (3), 246 (2), 231 (3), 218 (5), 204 (29), 190 (2), 186 (1), 158 (11), 142 (100); HRMS calcd for $C_{14}H_{25}NO_7$ 319.1631, found 319.1635. Anal. Calcd for $C_{14}H_{25}NO_7$: C, 52.65; H, 7.89; N, 4.39. Found: C, 52.56; H, 7.84; N, 4.01.

5-(*tert*-Butoxycarbonyl)amino-5-deoxy-3-*O*-formyl-1,2-*O*-isopropylidene-4-*O*-methyl-β-D-arabinopyranose (38). Following the general procedure, compound **25** (46 mg, 0.14 mmol) in CH_2Cl_2 (5 mL) containing iodosylbenzene (92 mg, 0.42 mmol) and I_2 (42 mg, 0.17 mmol) was stirred at room temperature for 2.3 h. Silica gel flash chromatography (hexanes−EtOAc, 85:15 → 70:30) of the residue afforded compound **38** (7 mg, 0.021 mmol, 15%) and compound **40** (15 mg, 0.051 mmol, 42%). Compound **38** (two rotamers in a ratio of 2:1): oil; $[\alpha]_D$ −51 (c = 0.47); IR 1714 cm^{-1}; ^1H NMR (70 °C) 1.40 (3H, s), 1.49 (3H, s), 1.49 (9H, s), 3.19 (1H, brd, J = 13 Hz), 3.37 (3H, s), 3.71 (1H, ddd, J = 2.9, 2.9, 4.9 Hz), 4.15 (1H, brd, J = 10 Hz), 4.23 (1H, dd, J = 6.2, 6.7 Hz), 5.10 (1H, dd, J = 6.7, 2.8 Hz), 6.10 (1H, brd, J = 5.8 Hz), 8.14 (1H, s); ^{13}C NMR (70 °C) 26.4 (CH_3), 27.8 (CH_3), 28.3 (3 × CH_3), 40.4 (CH_2), 57.0 (CH_3), 71.5 (CH), 72.8 (CH), 73.82 (CH), 81.4 (C), 81.8 (CH), 107.7 (C), 154.7 (C), 160.2 (CH); MS (rel intensity) 331 (M^+, <1), 316 (3), 260 (6), 258 (3), 217 (6); HRMS calcd for $C_{15}H_{25}NO_7$ 331.163102, found 331.164749. Anal. Calcd for $C_{15}H_{25}NO_7$: C, 54.35; H, 7.61; N, 4.23. Found: C, 54.38; H, 7.50; N, 4.33. Compound **40** (two rotamers in a ratio of 4:1): oil; $[\alpha]_D$ +8.0 (c = 0.91); IR (neat) 3420, 1731, 1699 cm^{-1}; ^1H NMR (C_6D_6) (major rotamer) 1.36 (9H, s), 2.93 (3H, s), 3.35

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

(20) Saltzman, H.; Sharefkin, J. G. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. V, pp 658−659.

(1H, dd, J = 8.1, 10.5 Hz), 3.54 (1H, dd, J = 7.1, 10.0 Hz), 3.95 (1H, ddd, J = 3.9, 7.7, 7.7 Hz), 5.38 (1H, d, J = 3.8 Hz), 5.55 (1H, s), 7.47 (1H, s); ^{13}C NMR (C_6D_6) (major rotamer) 28.3 (3 × CH_3) 47.8 (CH_2), 57.8 (CH_3), 73.9 (CH), 77.6 (CH), 80.5 (C) 83.9 (CH), 155.1 (C), 159.4 (CH); MS (rel intensity) 260 (M^+ − H, <1), 244 (<1), 202 (1), 188 (4), 173 (5); HRMS calcd for $C_{11}H_{18}NO_6$ 260.113413, found 260.121101. Anal. Calcd. for $C_{11}H_{19}NO_6$: C, 50.56; H, 7.33; N, 5.36. Found: C, 50.21; H, 6.98; N, 5.43.

Methyl 4-(*tert*-Butoxycarbonyl)amino-4-deoxy-3-*O*-methyl-*β*-D-erythrofuranoside (41). A solution of compound **40** (15.9 mg, 0.061 mmol) in MeOH (0.5 mL) was treated with an undetermined catalytic amount of HCl (some gas taken with a Pasteur pipet from the headspace of a concd HCl bottle) and stirred at room temperature for 1 h. The reaction mixture was then poured into aqueous saturated $NaHCO_3$ and extracted with EtOAc. Chromatotron chromatography (hexanes−EtOAc, 80:20) of the residue afforded compound **41** (13.4 mg, 0.054 mmol, 76%) as an oil (two rotamers in a ratio of 1:1): $[\alpha]_D$ −12.3 (c = 0.65); IR (neat) 3450, 1705 cm^{-1}; ^{1}H NMR (C_6D_6) 1.38 (9H, s), 1.40 (9H, s), 2.23 (1H, brs, OH), 2.41 (1H, brs, OH), 2.72 (3H, s), 2.77 (3H, s), 3.20 (3H, s), 3.39 (3H, s), 3.40 (1H, dd, J = 8.1, 10.5 Hz), 3.53 (1H, dd, J = 7.9, 10.3 Hz), 3.59 (1H, dd, J = 7.6, 11.0 Hz), 3.63 (1H, dd, J = 7.6, 10.5 Hz), 3.77 (1H, ddd, J = 4.3, 7.2, 7.2 Hz), 3.84 (1H, ddd, J = 3.8, 7.6, 7.6 Hz), 4.03 (1H, d, J = 3.8 Hz), 4.05 (1H, d, J = 3.8 Hz), 4.41 (1H, s), 5.09 (1H, s); ^{13}C NMR (C_6D_6) 28.3 (3 × CH_3), 48.0 (CH_2), 48.1 (CH_2), 55.8 (CH_3), 56.4 (CH_3), 57.1 (CH_3), 57.1 (CH_3), 72.2 (CH), 73.4 (CH), 78.6 (CH), 79.4 (CH), 79.6 (C), 79.8 (C), 92.9 (CH), 93.2 (CH), 154.6 (C), 155.6 (C); MS (rel intensity) 247 (M^+, 1), 215 (4), 183 (1), 160 (3), 159 (3); HRMS calcd for $C_{11}H_{21}NO_5$ 247.141973, found 247.138393. Anal. Calcd for $C_{11}H_{21}NO_5$: C, 53.42; H, 8.56; N, 5.67. Found: C, 53.35; H, 8.65; N, 5.42.

4-(*tert*-Butoxycarbonyl)amino-5-*O*-(*tert*-butyldimethylsilyl)-4-deoxy-3-*O*-formyl-1,2-*O*-isopropylidene-α-L-xylofuranose (42). Following the general procedure, compound **28** (105 mg, 0.24 mmol) in CH_2Cl_2 (9 mL) containing iodosylbenzene (158 mg, 0.72 mmol) and I_2 (73 mg, 0.287 mmol) was stirred at room temperature for 2 h. Chromatotron chromatography (hexanes−EtOAc, 95:5) of the residue afforded compound **42** (80 mg, 0.18 mmol, 78%) as an oil (two rotamers in a ratio of 3:1): $[\alpha]_D$ +30 (c = 0.742); IR 1736, 1711 cm^{-1}; ^{1}H NMR (75 °C) 0.056 (3H, s), 0.063 (3H, s), 0.91 (9H, s), 1.37 (3H, s), 1.50 (9H, s), 1.51 (3H, s), 3.76 (1H, brd, J = 9.8 Hz), 3.84 (1H, dd, J = 10.3, 4.9 Hz), 4.29 (1H, ddd, J = 4.9, 2.4, 6.5 Hz), 4.68 (1H, dd, J = 5.2, 4.8 Hz), 5.37 (1H, dd, J = 4.8, 6.5 Hz), 5.79 (1H, d, J = 5.2 Hz), 8.08 (1H, s); ^{13}C NMR (75 °C) −5.5 (2 × CH_3), 18.2 (C), 25.9 (3 × CH_3), 27.0 (CH_3), 27.8 (CH_3), 28.5 (3 × CH_3), 59.1 (CH_2), 60.8 (CH), 76.7 (CH), 80.9 (C), 81.6 (CH), 88.7 (CH), 113.1 (C), 153.8 (C), 159.7 (CH); MS (rel intensity) 416 (M^+ - CH_3, <1), 374 (1), 358 (11), 318 (59), 274 (76); HRMS calcd for $C_{19}H_{34}NO_7Si$ 416.2104, found 416.2091. Anal. Calcd for $C_{20}H_{37}NO_7Si$: C, 55.65; H, 8.64; N, 3.25. Found: C, 55.72; H, 8.71; N, 3.04.

4-(*tert*-Butoxycarbonyl)amino-5-*O*-(*tert*-butyldimethylsilyl)-4-deoxy-3-*O*-formyl-1,2-*O*-isopropylidene-*β*-D-arabinofuranose (43). Following the general procedure, compound **33** (83 mg, 0.191 mmol) in CCl_4 (7 mL) containing iodosylbenzene (68 mg, 0.31 mmol) and I_2 (9.7 mg, 0.038 mmol) was stirred at room temperature for 1 h. Chromatotron chromatography (hexanes−EtOAc, 95:5 → 80:20) of the residue afforded compound **43** (23.3 mg, 0.054 mmol, 28%) and compound **44** (22.6 mg, 0.063 mmol, 33%). Compound **43** (two rotamers in a ratio of 2:3): oil; $[\alpha]_D$ −44.5 (c = 1.13); IR ($CHCl_3$) 1724, 1703 cm^{-1}; ^{1}H NMR (70 °C) 0.05 (6H, s), 0.87 (9H, s), 1.39 (3H, s), 1.48 (12H, s), 3.20 (1H, d, J = 13.4 Hz), 3.97 (1H, m), 4.13 (1H, ddd, J = 2.4, 1.6, 4.7 Hz), 4.20 (1H, dd, J = 7.3, 5.9 Hz), 4.95 (1H, dd, J = 7.3, 2.4 Hz), 6.11 (1H, brs), 8.11 (1H, s); ^{13}C NMR (70 °C) −5.0 (CH_3), −4.96 (CH_3), 18.1 (C), 25.6 (3 × CH_3), 26.6 (CH_3), 27.9 (CH_3), 28.3 (3 × CH_3), 44.8 (CH_2), 66.2 (CH), 71.5 (CH), 74.7 (CH), 81.3 (C), 81.9 (CH), 107.5 (C), 154.8 (C), 160.3 (C); MS (rel intensity) 416 (M^+ − CH_3, <1), 358 (2), 318 (48), 316 (3), 312 (2), 300 (1); HRMS calcd for $C_{19}H_{34}NO_7Si$ 416.210456, found 416.207977. Anal. Calcd for $C_{20}H_{37}NO_7Si$: C, 55.65; H, 8.64; N, 3.25 Found: C, 56.05; H, 8.26; N, 3.40. Compound **44**: (two rotamers in a ratio of 7:3): oil; $[\alpha]_D$ −13.6 (c = 0.36); IR (neat) 3420, 1735, 1703 cm^{-1}; ^{1}H NMR (major rotamer) 0.07 (3H, s), 0.08 (3H, s), 0.87 (9H, s), 1.44 (9H, s), 3.22 (1H, dd, J = 7.1, 10.7 Hz), 3.64 (1H, dd, J = 6.6, 10.7 Hz), 4.56 (1H, ddd, J = 4.1, 6.6, 6.6 Hz), 5.10 (1H, brs), 5.34 (1H, brs), 8.11 (1H, s); ^{13}C NMR (C_6D_6, major rotamer) −5.4 (CH_3), −5.2 (CH_3), 25.7 (3 × CH_3), 28.3 (3 × CH_3), 50.5 (CH_2), 69.3 (CH), 76.6 (CH), 84.0 (CH), 159.3 (CH) (three quaternary carbons missing); MS (rel intensity) 304 (M^+ − C_4H_9, 1), 186 (31), 158 (12), 129 (17), 103 (100); HRMS calcd for $C_{12}H_{22}NO_6Si$ 304.121641, found 304.121078. Anal. Calcd for $C_{16}H_{31}NO_6Si$: C, 53.16; H, 8.64; N, 3.87. Found: C, 53.14; H, 8.57; N, 3.62. Treatment of **44** with MeOH/HCl under the same conditions used for the preparation of **41** afforded methyl 3-(*tert*-butoxycarbonyl)amino-3-deoxy-D-erythrooxetoside (**45**) (50%): oil (two rotamers in a ratio of 6:4); ^{1}H NMR (C_6D_6) 1.44 (9H, s), 1.46 (9H, s), 3.25 (3H, s), 3.40 (1H, dd, J = 7.7, 9.7 Hz), 3.44 (3H, s), 3.59 (1H, m), 3.61 (1H, dd, J = 7.8, 9.7 Hz), 3.70 (1H, dd, J = 10.7, 7.7 Hz), 3.84 (1H, brd, J = 3.4 Hz), 3.94 (1H, brs), 5.05 (1H, s), 5.30 (1H, s); MS (rel intensity) 233 (M^+, 14), 177 (7), 160 (26), 146 (19), 132 (25), 115 (100); HRMS calcd for $C_{10}H_{19}NO_5$ 233.126323, found 233.130611.

Acknowledgment. This work was supported by the Investigation Program No. PB96-1461 of the Dirección General de Investigación Científica y Técnica, Spain and Program Nos. 93/030 and 93/014 of the Dirección General de Universidades e Investigación del Gobierno de Canarias. C.C.G. and C.R.-F. thank the Ministerio de Educación y Ciencia, Spain, and the Dirección General de Universidades e Investigación del Gobierno de Canarias, respectively, for fellowships.

Supporting Information Available: Experimental procedures, physical properties, and spectroscopic data for compounds **2**−**33**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0057452