JOC Article

Intramolecular Hydrogen Abstraction Reaction Promoted by *N*-Radicals in Carbohydrates. Synthesis of Chiral 7-Oxa-2-azabicyclo[2.2.1]heptane and 8-Oxa-6-azabicyclo[3.2.1]octane Ring Systems

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The reaction of phenyl and benzyl amidophosphates and alkyl and benzyl carbamate derivatives of aminoalditols with (diacetoxyiodo)benzene or iodosylbenzene and iodine is a mild and selective procedure for the synthesis of chiral 7-oxa-2-azabicyclo[2.2.1]heptane and 8-oxa-6-azabicyclo[3.2.1]-octane ring systems under neutral conditions. This reaction can be considered to be an intramolecular *N*-glycosidation that goes through an intramolecular 1,5-hydrogen abstraction promoted by an *N*-amido radical followed by oxidation of the transient *C*-radical intermediate to an oxycarbenium ion. This methodology proved to be useful not only as a suitable strategy for the preparation of these bicyclic arrays but also for the selective oxidation of specific carbons of the carbohydrate skeleton, constituting a good procedure for the synthesis of protected *N*,*O*-uloses.

The 8-oxa-6-azabicyclo[3.2.1]octane ring system forms the characteristic framework of several physiologically active alkaloids of the samandarine, ribasine, and zoanthamine types.[1] On the other hand, only a few examples of carbohydrates containing this oxa-azabicyclo ring system in their skeleton have been described. They have been synthesized through intramolecular nucleophilic displacement of good leaving groups at C-6 by nitrogen nucleophiles at the anomeric center.[2] Several 7-amino-2,7-anhydro-1,7-dideoxy-D-*gulo*-hept-2-ulopyranose derivatives that mimic α-L-fucose and are potent inhibitors of fucosidases have been prepared by cyclization of the corresponding acyclic hydroxy amino ketones.[3]

The most general approach to the 7-oxa-2-azabicyclo-[2.2.1]heptane heterocyclic ring system implies an intermolecular 1,3-dipolar cycloaddition reaction.[4] The only carbohydrate possessing this heterocyclic ring system in its skeleton is, as far as we know, a byproduct formed during the TMSOTf-catalyzed reaction of methyl 1,2,3-tri-*O*-acetyl-5-(acetylamino)-5-deoxy-β-D-allofuranuronate with bis-siylated thymine under the conditions of a Vorbrüggen coupling.[5]

In previous papers from this laboratory, we have reported that *N*-nitroamides, *N*-cyanamides, and *N*-phosphoramidates react with hypervalent iodine reagents in the presence of iodine to generate *N*-radicals through homolytic fragmentation of a hypothetical iodoamide intermediate.[6] The mechanism is purported to be similar to the radical fragmentation of the hypoiodite reaction.[7] Nitrogen radicals generated in this way may participate in an intramolecular 1,5-hydrogen abstraction reaction (IHA) from unactivated carbons, the result being the formation of pyrrolidines. The reaction, which resembles the Hofmann−Löffler−Freytag[8] (HLF) synthesis of pyrrolidines, proceeds under very mild neutral conditions compatible with the stability of the protective groups most frequently used in synthetic organic chemistry. Although a few examples of the HLF reaction under mild conditions are known,[9] the procedure traditionally re-

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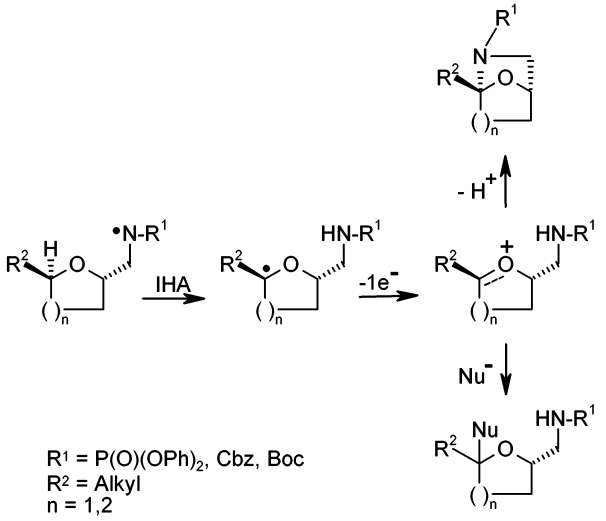
SCHEME 1



quires strong acid concentrations, which severely limits its use for the synthesis of complex or sensitive molecules.

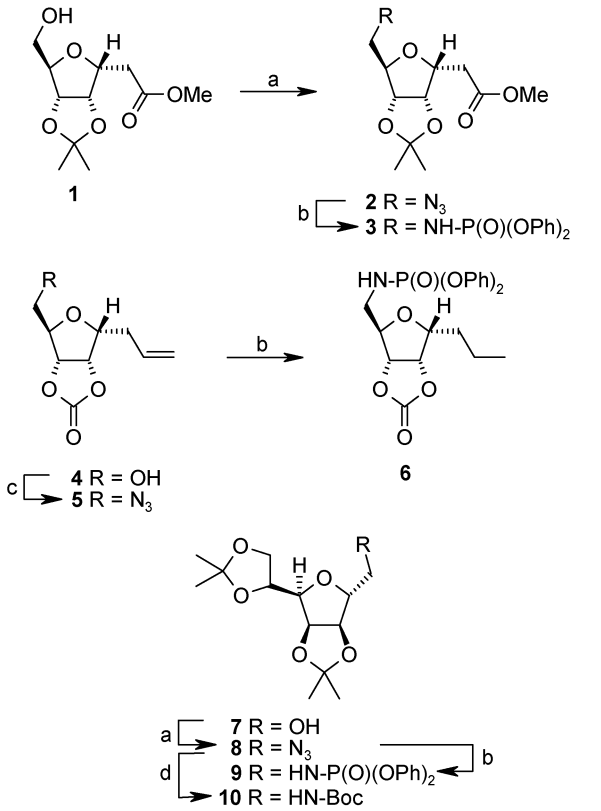
To our knowledge, the only precedent of the IHA reaction triggered by amidyl radicals, generated from the photolysis of *N*-iodocarboxamides, is described as giving γ-butyrolactones.[10] A study of the radical amidation onto aromatic rings using sulfonamides and hypervalent iodine reagents has recently been published.[11]

With these results in mind, we decided to study the *N*-radical-promoted IHA from carbons where the radical abstraction could be favored by electron-donor groups. In these systems the *C*-radical initially formed could be subsequently oxidized by an excess of reagent to an oxycarbenium ion, as described in Scheme 1. Intramolecular nucleophilic cyclization of the amide group to this oxycarbenium ion intermediate could give rise to an oxa-azabicyclic system. As shown in the scheme, nucleophilic species present in the medium can also be competitively trapped by the oxycarbenium ion.

In this paper we describe a convenient synthesis of carbohydrate derivatives of chiral 7-oxa-2-azabicyclo-[2.2.1]heptane and 8-oxa-6-azabicyclo[3.2.1]octane ring systems using this protocol.[12]

Preparation of Substrates and Discussion. The synthesis of the starting amine derivatives proceeded

SCHEME 2. Substrates for the 7-Oxa-2-azabicyclo[2.2.1]heptane Series[a]



[a] Reagents: (a) $ZnN_6 \cdot 2Py$, Ph_3P, DIAD, MePh, rt; (b) (i) H_2, Pd/C (5%), EtOAc, rt, ap; (ii) $(PhO)_2P(O)Cl$, TEA, CH_2Cl_2, rt; (c) (i) MsCl, Py, rt, 20 min; (ii) NaN_3, DMF, 80 °C, 30 min, 99%; (d) H_2, Pd/C (5%), di-*tert*-butyl dicarbonate, EtOAc, rt, ap, 5 h, 90%.

according to the following: The furanose amides **3**, **6**, **9**, and **10** were synthesized from the corresponding alcohols **1**,[13] **4**,[14] and **7**[15] by Mitsunobu azidation[16] and subsequent reduction, followed by treatment of the resulting amine with the corresponding protective group reagent (Scheme 2). On the other hand, the pyranose amides were prepared from the corresponding heptonitriles **11**,[17] **13**,[17c,18] **15**,[19] and **20**[20] obtained, in turn, by cyanoglycosidation.[21] LAH reduction of the nitriles and appropriate protection of the resulting amines afforded the desired amide

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(17) Obtained as a byproduct during the hydrogenolysis of 5,7-di-*O*-acetyl-2,6-anhydro-3,4-dideoxy-D-*arabino*-hept-3-enonitrile. (a) De las Heras, F. G.; San-Felix, A. S.; Fernández-Resa, P. *Tetrahedron* **1983**, *39*, 1617−1620. (b) Grikiewicz, G.; BeMiller, J. N.; *Carbohydr. Res.* **1982**, *108*, 229−236. (c) Overkleeft, H. S.; Verhelst, S. H. L.; Pieterman, E.; Meeuwenoord, N. J.; Overhand, M.; Cohen, L. H.; Marel, G. A.; Boom, J. H. *Tetrahedron Lett.* **1999**, *40*, 4103−4106.

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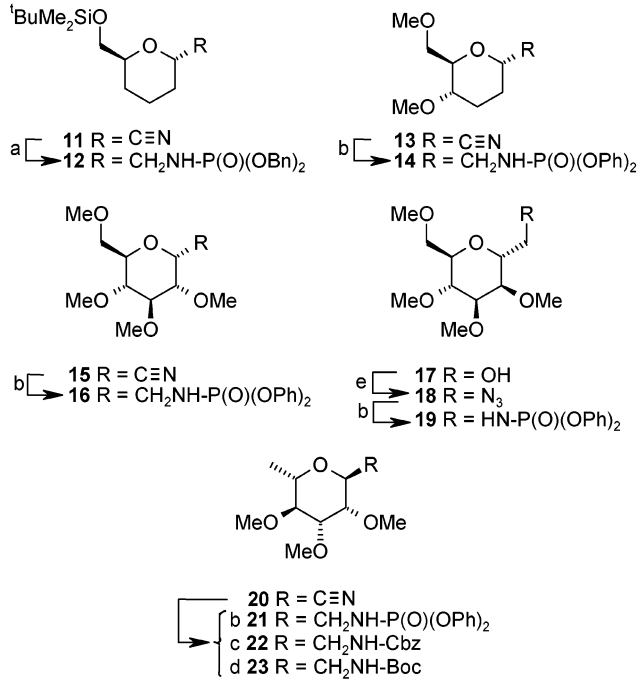
SCHEME 3. Substrates for the 8-Oxa-6-azabicyclo[3.2.1]octane Series[a]



[a] Reagents: (a) (i) LAH, THF, reflux, 30 min; (ii) $(BnO)_2P(O)Cl$, TEA, $CHCl_3$, rt, 1.5 h, 54%; (b) (i) LAH, THF, rt, (ii) $(PhO)_2P(O)Cl$, TEA, $CHCl_3$, rt; (c) (i) LAH, THF, reflux, 1 h, (ii) dibenzyl dicarbonate, TEA, THF, 57%; (d) (i) LAH, THF, rt, 1 h, (ii) di-*tert*-butyl dicarbonate, DMF, rt, 1.5 h, 49%; (e) $ZnN_6{\cdot}2Py$, Ph_3P, DIAD, MePh, rt, 30 h, 65%.

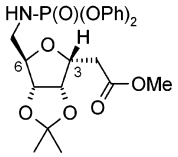
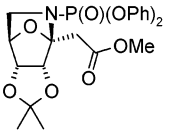
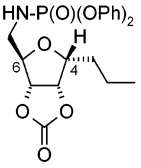
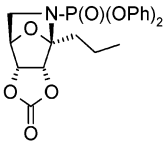
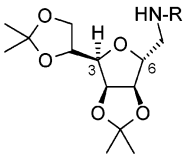
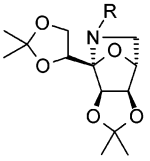
derivatives **12**, **14**, **16**, and **21**−**23** (Scheme 3). The phosphoramidate **19** was prepared accordingly by azidation−reduction of the known alcohol **17**.[13] These polyfunctionalized amides were synthesized to delineate the influence of the substituents in the IHA reaction.

We elected phenyl and benzyl amidophosphates and alkyl and benzyl carbamates derivatives not only to avoid the oxidation of the amine groups during the formation of the iodoamide, but also because they will exert a control on the stability of the *N*-radical during the IHA reaction. Furthermore, the regeneration of the disubstituted amine at the end of the process should be possible, since they are suitable amino-protecting groups.

The synthesis of homochiral 7-oxa-2-azabicyclo[2.2.1]-heptane systems from *C*-glycoside derivatives of carbohydrates in furanose form are shown in Table 1. The reactions were accomplished in two ways: from a phosphoramidate group at the side chain of a D-*ribo*, substrates **3** and **6** (Table 1, entries 1 and 2), or by placing the amide group on a tether attached to the C-1 of D-mannofuranose derivatives **9** and **10** (Table 1, entries 3 and 4). In both cases, we avoided the interaction with the neighboring protective ring, and the IHA reaction with iodosylbenzene and iodine proceeded smoothly to give azabicycles **24**−**27** in good to excellent yields (Table 1, entries 1−4). The structures were confirmed by ^1H and ^{13}C NMR spectra (DEPT, COSY, and HMBC experiments), revealing in all cases a selective abstraction of the shown proton.

The use of a carbonate to protect the *cis*-diol did not change the cyclization yield and this should be convenient

TABLE 1. Synthesis of Homochiral 7-Oxa-2-azabicyclo[2.2.1]heptane System[a]

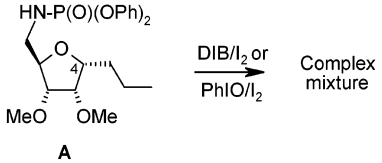
entry	substrate	iodine (mmol)	time (h)	product	yield (%)
1	 **3**	1.2	1.3	 **24**	75
2	 **6**	1	1.75	 **25**	74
3[b]	 **9** R = P(O)(OPh)$_2$	1.2	1	 **26** R = P(O)(OPh)$_2$	96
4[b,c]	**10** R = Boc	1	10	**27** R = Boc	84

[a] All reactions were performed at room temperature under nitrogen containing iodosylbenzene (2 mmol) and iodine per mmol of substrate in the solvent specified in the Experimental Section and under irradiation with two 80 W tungsten-filament lamps. [b] Solid $NaHCO_3$ was added. [c] At reflux temperature, irradiation was omitted.

when further modification of the molecule is required (entry 2). In preliminary experiments some hydrolysis of the acid-sensitive 1,2-isopropylidene group of the di-*O*-isopropylidene-D-mannofuranoses **9** and **10** was observed, probably autocatalyzed by the acidity of the amide groups. This could be avoided by adding an equimolecular amount of solid $NaHCO_3$ to the reaction mixture (Table 1, entries 3 and 4). The conformational rigidity that the [3.3.1]bicycle confers to the starting materials seems to play a critical role in the IHA reaction. Attempts to perform the reaction on a more flexible structure such as 4,7-anhydro-1,2,3,8-tetradeoxy-8-[(diphenoxyphosphoryl)amino]-5,6-di-*O*-methyl-D-*altro*-octitol (**A**) were unsuccessful.[22]

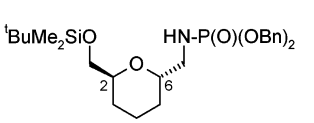
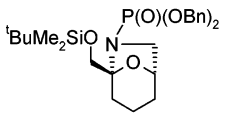
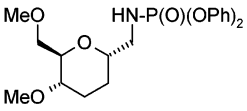
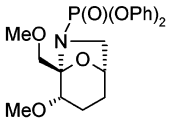
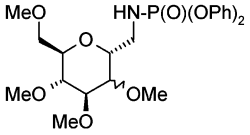
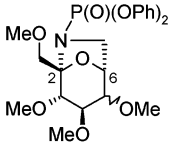
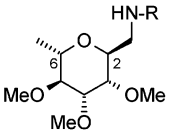
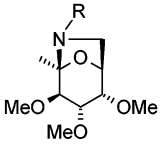
The results obtained during the synthesis of the 8-oxa-6-azabicyclo[3.2.1]octane ring system are summarized in

(22) The reaction of **A** with DIB/I_2 or $PhIO/I_2$ under different conditions gave a complex mixture. Hydrogen abstraction from other positions (e.g. 5) and radical β-fragmentation reactions could possibly compete.



A

TABLE 2. Synthesis of Homochiral 8-Oxa-6-azabicyclo[3.2.1]octane System[a]

entry	substrate	method	product	yield (%)
1[b]	 **12**	A	 **28**	66
2	 **14**	B	 **29**	68
3	 **16** D-*gluco*	A	 **30** D-*gluco*	44
4	**19** D-*manno*	A	**31** D-*manno*	80
5	 **21** R = P(O)(OPh)$_2$	B	 **32** R = P(O)(OPh)$_2$	69
6	**22** R = Cbz	B	**33** R = Cbz	82
7	**23** R = Boc	B	**34** R = Boc	87

[a] All reactions were performed at room temperature under nitrogen containing iodine in CH_2Cl_2 and under irradiation with two 80 W tungsten-filament lamps. Method A, PhIO was used. Method B, DIB was used. [b] At reflux temperature, irradiation was omitted.

Table 2. The reactions of the first four examples proceed on the α-side of the molecule with the carbohydrate ring in its more stable $^4C_1$ chair conformation, which allows a 1,3-diaxial relationship between the phosphoramidate tether at C-6 and the hydrogen atom at C-2 (Table 2, entries 1−4). In preliminary studies, observations were made that the use of (diacetoxyiodo)benzene (DIB) reduced the oxa-azabicyclo yield as a consequence of the external nucleophilic competition of the acetyl group. In the reaction of compound **14** with DIB (method B), under the conditions shown in entry 2, after 1.75 h of reaction, the desired anhydro **29** (68%) was accompanied by minor amounts (5%) of 2-*O*-acetyl-4,5,7-trideoxy-7-[(diphenoxyphosphoryl)amino]-1,3-di-*O*-methyl-D-*threo*-hept-2-ulopyranose. Notwithstanding, when the reaction was stopped at earlier stages (45 min), the above-mentioned 2-acetate, coming from external nucleophilic attack, was the principal product of the reaction (65%). Without a doubt, the tertiary acetate formed initially is transformed over time into the bicycle by acid-catalyzed cyclization under the reaction conditions.

The much lower yield obtained for the D-*gluco* anhydro derivative **30** (Table 2, entry 3) when compared with the D-*manno* analogue **31** (entry 4) was somewhat surprising. Although it is presumably due to the difference of the stereochemistry at C-5, we could not find a plausible explanation other than steric interference between the bulky diphenyl phosphoramidate group and the vicinal syn α-methyl ether.

The 8-oxa-6-azabicyclo[3.2.1]octane ring system can also be obtained from the *C*-glycoxyl derivatives of L-rhamnose **21**−**23** (Table 2, entries 5−7). The IHA reaction proceeded this time on the *β*-side of the molecule through a chairlike six-membered transition state to give the L-*altro*-hept-2-ulopyranose derivatives **32**−**34**. The carbohydrate ring was in a more stable $^1C_4$ chair conformation. This allowed the required approach between the *N*-radical and the hydrogen at C-6 for the IHA reaction to take place.

It is clear from the above examples and previous work of this group[23] that this reagent system is very tolerant of the common carbohydrate protective groups and that this modified HLF reaction provides a suitable strategy for the synthesis of these sensitive *N*,*O*-protected ulose derivatives. Other notable features of this one-step methodology in comparison with the traditional HLF reaction are the following: (a) The unstable iodoamide intermediates are generated in situ. (b) The iodoamide homolysis proceeds thermally at low temperature (20−40 °C) or by irradiation with visible light, ultraviolet light being unnecessary.

Experimental Section

General Methods. Melting points were determined with a hot-stage apparatus. Optical rotations were measured at the sodium line at ambient temperature in $CHCl_3$ solutions unless otherwise stated. IR spectra were obtained as a thin film smeared onto NaCl plates. NMR spectra were determined at 500 MHz for ^{1}H and 125.7 MHz for ^{13}C in $CDCl_3$, unless otherwise stated, in the presence of TMS as internal standard. Mass spectra were determined at 70 eV. Merck silica gel 60 PF (0.063−0.2 mm) was 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. "Usual workup" means aqueous treatment, extraction with CH_2Cl_2, washing with 10% aqueous sodium thiosulfate, drying with Na_2SO_4, filtration, and evaporation in vacuo. All reactions involving air- or moisture-sensitive materials were carried out under a nitrogen atmosphere. The spray reagent for TLC analysis was 0.5% vanillin in H_2SO_4−EtOH (4:1) and further heating until development of color.

Methyl 3,7-Anhydro-2,7-dideoxy-7-[(diphenoxyphosphoryl)amino]-4,5-*O*-isopropylidene-D-*ribo*-hept-3-ulofuranosonate (24). A solution of the amide **3** (25.5 mg, 0.053 mmol) in a mixture of CH_2Cl_2−cyclohexane (1:1) (3 mL) containing iodosylbenzene (22 mg, 0.106 mmol) and iodine (15 mg, 0.064 mmol) was irradiated with two 80 W tungsten-filament lamps at room temperature under nitrogen for 80 min. The usual workup followed by column chromatography (hexanes−EtOAc, 85:15) afforded the anhydrosugar **24** (19 mg, 0.04 mmol, 75%) as a colorless oil: $[\alpha]_D$ −46.5 (c = 0.97); IR 2988, 2950, 1747, 1591, 1488, 1191 cm^{-1}; ^{1}H NMR 1.19 (3H, s), 1.40 (3H, s), 3.06 (1H, dd, J = 3.0, 8.1 Hz), 3.20 (1H, d, J = 16.1 Hz), 3.33 (1H, dddd, J = 3.7, 3.7, 3.7, 4.0 Hz), 3.44 (1H, d, J = 16.5 Hz), 3.56 (3H, s), 4.23 (1H, d, J = 5.2 Hz), 4.37

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(1H, d, J = 5.5 Hz), 4.61 (1H, d, J = 5.2 Hz), 7.1−7.34 (10H, m); ^{13}C NMR 25.3 (CH_3), 25.8 (CH_3), 33.1 (CH_2), 47.2 (CH_2), 51.6 (CH_3), 78.7 (CH, $^3J_{CP}$ = 6.1 Hz), 81.1 (CH), 83.8 (CH), 95.9 (C, $^2J_{CP}$ = 8.8 Hz), 112.4 (C), 120.1 (4 × CH), 125.7 (2 × CH), 129.7 (4 × CH), 150.7 (2 × C), 168.7 (C); MS (EI) *m*/*z* (rel intensity) 475 (M^+, 24), 460 (3), 417 (98), 324 (100); HRMS calcd for $C_{23}H_{26}NO_8P$ 475.1395896, found 475.13797. Anal. Calcd for $C_{23}H_{26}NO_8P$: C, 58.10; H, 5.51; N, 2.95. Found: C, 58.04; H, 5.62; N, 3.01.

1,2,3,8-Tetradeoxy-8-[(diphenoxyphosphoryl)amino]-5,6-*O*-oxomethylene-D-*ribo*-oct-4-ulofuranose (25). A solution of the amide **6** (165 mg, 0.38 mmol) in dry CH_2Cl_2 (7 mL) containing iodosylbenzene (168 mg, 0.76 mmol) and iodine (97 mg, 0.38 mmol) was irradiated with two 80 W tungsten-filament lamps at room temperature under nitrogen for 1.75 h. The usual workup followed by Chromatotron chromatography (hexanes−EtOAc, 80:20→70:30) afforded the anhydrosugar **25** (120 mg, 0.28 mmol, 74%) as a colorless oil: $[\alpha]_D$ +10 (c = 0.58); IR 3055, 2966, 1814, 1487, 1160 cm^{-1}; ^{1}H NMR 0.90 (3H, t, J = 7.3 Hz), 1.46 (2H, m), 2.09 (1H, ddd, J = 5.3, 10.7, 15.5 Hz), 2.39 (1H, ddd, J = 4.8, 10.7, 15.3 Hz), 3.31 (1H, dd, J = 3.4, 9.0 Hz), 3.41 (1H, dd, J = 4.3, 9.0 Hz), 4.62 (1H, d, J = 6.0 Hz), 4.69 (1H, d, J = 6.0 Hz), 4.79 (1H, d, J = 4.4 Hz), 7.22 (6H, m), 7.35 (4H, m); ^{13}C NMR 13.3 (CH_3), 15.2 (CH_2), 27.8 (CH_2), 47.1 (CH_2), 78.0 (CH, $^3J_{CP}$ = 6.1 Hz), 79.3 (CH), 80.8 (CH), 98.1 (C, $^2J_{CP}$ = 9.2 Hz), 119.1 (2 × CH), 119.3 (2 × CH), 124.8 (2 × CH), 129.1 (2 × CH), 129.2 (2 × CH), 149.4 (C), 149.5 (C), 153.0 (C); MS (EI) *m*/*z* (rel intensity) 431 (M^+, 41), 387 (53), 345 (39); HRMS calcd for $C_{21}H_{22}NO_7P$ 431.1133771, found 431.113914. Anal. Calcd for $C_{21}H_{22}NO_7P$: C, 58.47; H, 5.14; N, 3.25. Found: C, 58.66; H, 5.22; N, 3.33.

3,7-Anhydro-7-deoxy-7-[(diphenoxyphosphoryl)amino]-1,2:4,5-di-*O*-isopropylidene-D-*allo*-hept-3-ulofuranose (26) A solution of the amide **9** (15 mg, 0.03 mmol) in a mixture of CH_2Cl_2−cyclohexane (1:1) (3 mL) containing iodosylbenzene (13 mg, 0.06 mmol), iodine (9 mg, 0.036 mmol), and solid $NaHCO_3$ (15 mg) was irradiated with two 80 W tungsten-filament lamps at room temperature under nitrogen for 1 h. The usual workup followed by column chromatography (hexanes−EtOAc, 70:30) afforded the anhydrosugar **26** (14.5 mg, 0.029 mmol, 96%) as a crystalline solid: mp 136−137 °C (from *n*-pentane−EtOAc); $[\alpha]_D$ −37.5 (c = 0.31); IR 2986, 1593, 1489, 1198 cm^{-1}; ^{1}H NMR 1.16 (3H, s), 1.28 (3H, s), 1.33 (3H, s), 1.39 (3H, s), 3.10 (1H, dd, J = 3.0, 8.2 Hz), 3.20 (1H, ddd, J = 4.0, 8.3, 11.8 Hz), 4.12 (2H, d, J = 6.9 Hz), 4.20 (1H, d, J = 5.2 Hz), 4.32 (1H, d, J = 5.6 Hz), 4.63 (1H, d, J = 3.9 Hz), 5.03 (1H, dd, J = 7.1, 7.1 Hz), 7.10−7.35 (10H, m); ^{13}C NMR 24.8 (CH_3), 25.5 (CH_3), 25.5 (CH_3), 26.0 (CH_3), 47.1 (CH_2), 66.1 (CH_2), 71.7 (CH), 78.8 (CH, $^3J_{CP}$ = 7.6 Hz), 81.2 (CH), 83.1 (CH), 97.6 (C, $^2J_{CP}$ = 11.4 Hz), 108.3 (C), 112.3 (C), 120.1 (2 × CH), 120.3 (2 × CH), 124.8 (CH), 125.1 (CH), 129.3 (2 × CH), 129.6 (2 × CH), 150.7 (2 × C); MS (EI) *m*/*z* (rel intensity) 503 (M^+, 38), 488 (22), 445 (9); HRMS calcd for $C_{25}H_{30}NO_8P$ 503.170888, found 503.173279. Anal. Calcd for $C_{25}H_{30}NO_8P$: C, 59.64; H, 6.01; N, 2.78. Found: C, 59.98; H, 6.23; N, 2.46.

3,7-Anhydro-7-deoxy-7-[(*tert*-butoxycarbonyl)amino]-1,2:4,5-di-*O*-isopropylidene-D-*allo*-hept-3-ulofuranose (27). A solution of the amide **10** (30 mg, 0.08 mmol) in dry CH_2Cl_2 (3 mL) containing iodosylbenzene (35 mg, 0.16 mmol), iodine (20 mg, 0.08 mmol), and solid $NaHCO_3$ (30 mg) was heated at reflux temperature under nitrogen for 10 h. The usual workup followed by column chromatography (hexanes−EtOAc, 75:25) afforded the anhydrosugar **27** (25 mg, 0.067 mmol, 84%) as a crystalline solid: mp 90−91.5 °C (from *n*-hexanes−EtOAc); $[\alpha]_D$ −59.5 (c = 0.36, CCl_4); IR 2981, 2937, 1694, 1403, 1255, 1210, 1165, 1088 cm^{-1}; ^{1}H NMR 1.26 (3H, s), 1.39 (3H, s), 1.41 (3H, s), 1.43 (3H, s), 1.48 (9H, s), 3.09 (1H, br d, J = 8.2 Hz), 3.36 (1H, dd, J = 4.2, 9.6 Hz), 4.13 (2H, d, J = 6.8 Hz), 4.31 (1H, br s), 4.41 (1H, br s), 4.56 (1H, d, J = 4.2 Hz), 4.90 (1H, br s); ^{13}C NMR 25.1 (CH_3), 25.6 (CH_3), 25.9 (CH_3), 26.0 (CH_3), 28.3 (3 × CH_3), 46.8 (CH_2), 66.4 (CH_2), 72.1 (CH), 78.0 (CH), 81.5 (2 × CH), 81.7 (C), 95.8 (C), 108.5 (C), 112.6 (C), 155.8 (C); MS (EI) *m*/*z* (rel intensity) 371 (M^+, 6), 356 (1), 300 (12); HRMS calcd for $C_{18}H_{29}NO_7$ 371.1943853, found 371.190636. Anal. Calcd for $C_{18}H_{29}NO_7$: C, 58.20; H, 7.87; N, 3.77. Found: C, 58.35; H, 7.81; N, 3.72.

2,7-Anhydro-7-{[bis(benzyloxy)phosphoryl]amino}-1-*O*-(*tert*-butyldimethyl)silyl-3,4,5,7-tetradeoxy-β-D-*glycero*-hep-2-ulopyranose (28). A solution of the amide **12** (20 mg, 0.038 mmol) in dry CH_2Cl_2 (3 mL) containing iodosylbenzene (17.5 mg, 0.076 mmol), iodine (10 mg, 0.038 mmol), and solid $NaHCO_3$ (20 mg) was heated at reflux temperature under nitrogen for 100 min. The usual workup followed by column chromatography (hexanes−EtOAc, 70:30) afforded the anhydrosugar **28** (13 mg, 0.025 mmol, 66%) as a colorless oil: $[\alpha]_D$ −17 (c = 1.1); IR 2927, 1462, 1017 cm^{-1}; ^{1}H NMR (200 MHz) 0.04 (6H, s), 0.87 (9H, s), 1.38−1.92 (6H, m), 3.30 (2H, m), 3.84 (1H, d, J = 11.1 Hz), 4.08 (1H, d, J = 11.1 Hz), 4.98−5.08 (4H, m), 7.32 (10H, br s); ^{13}C NMR (50.3 MHz) −5.1 (CH_3), −5.4 (CH_3), 16.3 (CH_2), 18.5 (C), 26.0 (3 × CH_3), 28.6 (CH_2), 30.7 (CH_2), 50.7 (CH_2, $^2J_{CP}$ = 4.3 Hz), 66.4 (CH_2), 67.7 (CH_2, $^2J_{CP}$ = 5.5 Hz), 68.0 (CH_2, $^2J_{CP}$ = 5.5 Hz), 74.2 (CH, $^3J_{CP}$ = 8.8 Hz), 96.7 (C, $^2J_{CP}$ = 10.1 Hz), 127.6 (4 × CH), 128.2 (2 × CH), 128.5 (4 × CH), 136.5 (2 × C); MS (EI) *m*/*z* (rel intensity) 517 (M^+, <1), 502 (<1), 484 (1), 460 (17), 91 (100); HRMS calcd for $C_{27}H_{40}NO_5PSi$ 517.2413207, found 517.241501. Anal. Calcd for $C_{27}H_{40}NO_5PSi$: C, 62.64; H, 7.79; N, 2.71. Found: C, 62.45; H, 7.81; N, 2.75.

2,7-Anhydro-4,5,7-trideoxy-7-[(diphenoxyphosphoryl)-amino]-1,3-di-*O*-methyl-β-D-*threo*-hept-2-ulopyranose (29). A solution of the amide **14** (80 mg, 0.19 mmol) in dry CH_2Cl_2 (5 mL) containing (diacetoxyiodo)benzene (DIB) (92 mg, 0.285 mmol) and iodine (48 mg, 0.19 mmol) was irradiated with two 80 W tungsten-filament lamps at room temperature under nitrogen for 110 min. The usual workup followed by column chromatography (hexanes−EtOAc, 60:40) afforded the anhydrosugar **29** (54 mg, 0.13 mmol, 68%) and 2-*O*-acetyl-4,5,7-trideoxy-7-[(diphenoxyphosphoryl)amino]-1,3-di-*O*-methyl-D-*threo*-hept-2-ulopyranose (4 mg, 0.01 mmol, 5%). Compound **29**: colorless oil; $[\alpha]_D$ −27.6 (c = 0.21); IR 3066, 2945, 1591, 1488 cm^{-1}; ^{1}H NMR (200 MHz) 1.58 (1H, m), 1.61 (1H, m), 1.89 (1H, m), 2.02 (1H, m), 3.29 (3H, s), 3.37 (3H, s), 3.37 (1H, d, J = 6.7 Hz), 3.51 (1H, dd, J = 5.6, 9.6 Hz), 3.58 (1H, dd, J = 7.0, 7.0 Hz), 3.74 (1H, d, J = 10.3 Hz), 4.5 (1H, s), 4.19 (1H, d, J = 10.3 Hz), 7.1−7.32 (10H, m); ^{13}C NMR 22.3 (CH_2), 28.9 (CH_2), 50.7 (CH_2), 56.4 (CH_3), 59.1 (CH_3), 71.6 (CH_2), 73.5 (CH, $^3J_{CP}$ = 8.5 Hz), 77.3 (CH), 96.9 (C, $^2J_{CP}$ = 10.5 Hz), 120.3 (4 × CH), 124.4 (2 × CH), 129.3 (4 × CH), 137.7 (2 × C); MS (EI) *m*/*z* (rel intensity) 419 (M^+, 83), 404 (70); HRMS calcd for $C_{21}H_{26}NO_6P$ 419.1497614, found 419.147217. Anal. Calcd for $C_{21}H_{26}NO_6P$: C, 60,14; H, 6,25; N, 3,34. Found: C, 60.11; H, 6.42; N, 3.53. Acetylated compound: colorless oil; ^{1}H NMR (200 MHz) 1.31 (1H, m), 1.55−2.0 (3H, m), 1.99 (3H, s), 3.05 (1H, m), 3.16 (1H, m), 3.33 (3H, s), 3.33 (3H, s), 3.41 (1H, m), 3.68 (1H, m), 3.76 (1H, d, J = 9.9 Hz), 3.99 (1H, d, J = 9.9 Hz); ^{13}C NMR (50.3 MHz) 20.9 (CH_2), 21.3 (CH_2), 21.9 (CH_3), 45.8 (CH_2), 57.3 (CH_3), 59.3 (CH_3), 70.2 (CH_2), 71.6 (CH, $^3J_{CP}$ = 6.1 Hz), 72.4 (CH), 103.2 (C), 120.3 (4 × CH), 124.8 (2 × CH), 129.6 (4 × CH), 135.3 (2 × C), 168.6 (C); MS (EI) *m*/*z* (rel intensity) 420 ($M^+ - C_3H_7O$, 8), 406 (6); HRMS calcd for $C_{20}H_{23}NO_7P$ 420.1212017, found 420.127136. Anal. Calcd for $C_{23}H_{30}NO_8P$: C, 57.62; H, 6.31; N, 2.92. Found: C, 57.83; H, 6.42; N, 3.01. When, under the same conditions, the reaction was interrupted after 50 min, the acetyl derivative was the major product (65%) with only 11% of the anhydrosugar **29**.

2,7-Anhydro-7-deoxy-7-[(diphenoxyphosphoryl)amino]-1,3,4,5-tetra-*O*-methyl-β-D-*ido*-hept-2-ulopyranose (30). A solution of the amide **16** (57 mg, 0.118 mmol) in dry CH_2Cl_2 (6 mL) containing iodosylbenzene (116 mg, 0.53 mmol) and iodine (30 mg, 0.118 mmol) was irradiated with two 80 W tungsten-filament lamps at room temperature under nitrogen for 7 h. The usual workup followed by Chromatotron chromatography (hexanes−EtOAc, 60:40) afforded the anhydrosugar **30** (25 mg, 0.052 mmol, 44%) as a colorless oil: $[\alpha]_D$ −14 (c =

0.34); IR 3069, 2933, 1592, 1488, 1106 cm^{-1}; ^1H NMR 3.29 (1H, dd, J = 8.0, 8.0 Hz), 3.37 (1H, dd, J = 4.4, 8.3 Hz), 3.38 (3H, s), 3.39 (1H, d, J = 7.8 Hz), 3.44 (3H, s), 3.45 (1H, m), 3.49 (3H, s), 3.50 (3H, s), 3.60 (1H, dd, J = 1.9, 10.8 Hz), 3.62 (1H, d, J = 10.4 Hz), 4.24 (1H, d, J = 10.4 Hz), 4.49 (1H, dd, J = 5.1, 5.1 Hz), 7.13−7.34 (10H, m); ^{13}C NMR 46.3 (CH_2), 57.8 (CH_3), 58.4 (CH_3), 59.2 (CH_3), 59.8 (CH_3), 70.6 (CH_2), 72.3 (CH, $^3J_{CP}$ = 8.6 Hz), 80.4 (CH), 82.9 (CH), 83.2 (CH), 95.4 (C, $^2J_{CP}$ = 11.2 Hz), 119.1 (2 × CH), 119.6 (2 × CH), 123.8 (CH), 123.9 (CH), 128.6 (2 × CH), 128.8 (2 × CH), 150.0 (C), 150.4 (C); MS (EI) *m*/*z* (rel intensity) 479 (M^+, 4), 464 (4), 448 (29); HRMS calcd for $C_{23}H_{30}NO_8P$ 479.170888, found 479.164001. Anal. Calcd for $C_{23}H_{30}NO_8P$: C, 57.62; H, 6.31; N, 2.92. Found: C, 57.72; H, 6.29; N, 3.00.

2,7-Anhydro-7-deoxy-7-[(diphenoxyphosphoryl)amino]-1,3,4,5-tetra-*O*-methyl-*β*-D-*altro*-hept-2-ulopyranose (31). A solution of the amide **19** (25 mg, 0.052 mmol) in dry CH_2Cl_2 (5 mL) containing iodosylbenzene (22 mg, 0.104 mmol) and iodine (13 mg, 0.052 mmol) was irradiated with two 80 W tungsten-filament lamps at room temperature under nitrogen for 40 min. The usual workup followed by column chromatography (hexanes−EtOAc, 25:75) afforded the anhydrosugar **31** (20 mg, 0.04 mmol, 80%) as a colorless oil: $[\alpha]_D$ −66.5 (c = 1.71); IR 3075, 2979, 2932, 2891, 2824, 1592, 1455, 1287, 1195, 1126 cm^{-1}; ^1H NMR 3.16 (1H, br d, J = 9.1 Hz), 3.34 (1H, dd, J = 4.1, 8.6 Hz), 3.37 (6H, s), 3.48 (3H, s), 3.49 (1H, dd, J = 2.5, 4.1 Hz), 3.53 (3H, s), 3.57 (1H, d, J = 8.6 Hz), 3.61 (1H, ddd, J = 2.0, 6.6, 9.1 Hz), 3.85 (1H, d, J = 10.2 Hz), 4.13 (1H, d, J = 10.2 Hz), 4.71 (1H, br d, J = 6.6 Hz); ^{13}C NMR 47.2 (CH_2), 56.9 (CH_3), 57.4 (CH_3), 58.3 (CH_3), 59.7 (CH_3), 69.8 (CH_2), 72.1 (CH, $^3J_{CP}$ = 9.1 Hz), 76.7 (CH), 79.0 (CH), 80.9 (CH), 96.1 (C, $^2J_{CP}$ = 9.1 Hz), 119.3 (2 × CH), 119.5 (2 × CH), 123.9 (2 × CH), 128.7 (2 × CH), 128.8 (2 × CH), 150.1 (C), 150.3 (C); MS (EI) *m*/*z* (rel intensity) 479 (M^+, 5), 464 (7), 448 (60), 416 (4); HRMS calcd for $C_{23}H_{30}NO_8P$ 479.170888, found 479.168571. Anal. Calcd for $C_{23}H_{30}NO_8P$: C, 57.62; H, 6.31; N, 2.92. Found: C, 57.72; H, 6.42; N, 2.94.

2,7-Anhydro-1,7-dideoxy-7-[(diphenoxyphosphoryl)-amino]-3,4,5-tri-*O*-methyl-*β*-L-*altro*-hept-2-ulopyranose (32). A solution of the amide **21** (52 mg, 0.115 mmol) in dry CH_2Cl_2 (2.5 mL) containing DIB (50 mg, 0.15 mmol) and iodine (30 mg, 0.115 mmol) was irradiated with two 80 W tungsten-filament lamps at room temperature under nitrogen for 75 min. The usual workup followed by column chromatography (*n*-hexanes−EtOAc, 50:50) afforded the anhydrosugar **32** (34 mg, 0.08 mmol, 69%) as a crystalline solid: mp 101−102 °C (from *n*-hexane−CH_2Cl_2); $[\alpha]_D$ +87.5 (c = 0.64); IR 2935, 2829, 1592, 1489, 1195 cm^{-1}; ^1H NMR 1.77 (3H, s), 3.11 (1H, d, J = 9.1 Hz), 3.24 (1H, dd, J = 4.0, 8.8 Hz), 3.28 (1H, d, J = 8.8 Hz), 3.34 (3H, s), 3.45 (1H, dd, J = 2.6, 4.0 Hz), 3.48 (3H, s), 3.52 (3H, s), 3.58 (1H, ddd, J = 2.7, 6.4, 9.0 Hz), 4.59 (1H, d, J = 6.6 Hz), 7.1−7.3 (10H, m); ^{13}C NMR 21.1 (CH_3), 48.2 (CH_2), 58.1 (CH_3), 58.2 (CH_3), 60.9 (CH_3), 72.6 (CH, $^3J_{CP}$ = 8.4 Hz), 77.7 (CH), 79.8 (CH), 85.6 (CH), 96.1 (C, $^2J_{CP}$ = 9.4 Hz), 119.9 (CH), 120.1 (CH), 124.6 (2 × CH), 124.7 (2 × CH), 129.4 (2 × CH), 129.5 (2 × CH), 150.8 (C), 151.0 (C); MS (EI) *m*/*z* (rel intensity) 449 (M^+, 2), 434 (15), 418 (99); HRMS calcd for $C_{22}H_{28}NO_7P$ 449.1603247, found 449.160004. Anal. Calcd for $C_{22}H_{28}NO_7P$: C, 58.79; H, 6.28; N, 3.12. Found: C, 58.99; H, 6.22; N, 2.95.

2,7-Anhydro-7-{[(benzyloxy)carbonyl]amino}-1,7-dideoxy-3,4,5-tri-*O*-methyl-*β*-L-*altro*-hept-2-ulopyranose (33). A solution of the amide **22** (190 mg, 0.538 mmol) in dry CH_2Cl_2 (10 mL) containing DIB (313 mg, 0.97 mmol) and iodine (137 mg, 0.54 mmol) was irradiated with two 80 W tungsten-filament lamps at room temperature under nitrogen for 8 h. The usual workup followed by Chromatotron chromatography (hexanes−EtOAc, 70:30 → 60:40) afforded the anhydrosugar **33** (155 mg, 0.441 mmol, 82%) as a colorless oil: $[\alpha]_D$ +94 (c = 1.38); IR 2923, 2952, 1723, 1112 cm^{-1}; ^1H NMR (60 °C) 1.79 (3H, br s), 3.23 (1H, d, J = 10.4 Hz), 3.28 (1H, dd, J = 4.2, 8.8 Hz), 3.33 (1H, d, J = 8.8 Hz), 3.47 (3H, s), 3.52 (3H, s), 3.54 (1H, m), 3.56 (3H, s), 3.67 (1H, dd, J = 6.9, 10.4 Hz), 4.52 (1H, dd, J = 2.1, 6.9 Hz), 5.10 (1H, d, J = 12.5 Hz), 5.18 (1H, d, J = 12.5 Hz), 7.29−7.38 (5H, m); ^{13}C NMR (60 °C) 20.4 (CH_3), 47.8 (CH_2), 57.9 (CH_3), 58.0 (CH_3), 61.1 (CH_3), 66.9 (CH_2), 71.8 (CH), 77.8 (CH), 80.4 (CH), 86.0 (CH), 93.9 (C), 127.7 (2 × CH), 127.7 (CH), 128.3 (2 × CH), 136.7 (C), 156.5 (C); MS (EI) *m*/*z* (rel intensity) 351 (M^+, 2), 336 (2), 320 (72), 91 (100); HRMS calcd for $C_{18}H_{25}NO_6$ 351.1681728, found 351.168671. Anal. Calcd for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; N, 3.99. Found: C, 61.40; H, 7.37; N, 4.01.

2,7-Anhydro-7-[(*tert*-butoxycarbonyl)amino]-1,7-dideoxy-3,4,5-tri-*O*-methyl-*β*-L-*altro*-hept-2-ulopyranose (34). A solution of the amide **23** (244 mg, 0.76 mmol) in dry CH_2Cl_2 (2 mL) containing DIB (492 mg, 1.53 mmol) and iodine (145 mg, 0.57 mmol) was irradiated with two 80 W tungsten-filament lamps at room temperature under nitrogen for 85 min. The usual workup followed by column chromatography (hexanes−EtOAc, 25:75) afforded the anhydrosugar **34** (210 mg, 0.66 mmol, 87%) as a colorless oil: $[\alpha]_D$ +100 (c = 0.8); IR 2977, 1714, 1682, 1402, 1114 cm^{-1}; ^1H NMR 1.45 (9H, s), 1.73 (3H, s), 3.16 (1H, m), 3.24 (1H, m), 3.28 (1H, d, J = 8.6 Hz), 3.44 (3H, s), 3.50 (3H, s), 3.51 (1H, m), 3.54 (3H, s), 3.60 (1H, dd, J = 7.2, 10.4 Hz), 4.51 (1H, br d, J = 7.0 Hz); ^{13}C NMR 21.1 (CH_3), 28.3 (3 × CH_3), 47.5 (CH_2), 57.8 (2 × CH_3), 58.0 (CH_3), 61.1 (CH), 71.2 (CH), 77.7 (CH), 80.0 (CH), 81.1 (C), 85.9 (CH), 93.4 (C), 150.7 (C); MS (EI) *m*/*z* (rel intensity) 317 (M^+, 1), 286 (15); HRMS calcd for $C_{15}H_{27}NO_6$ 317.183822, found 317.183006. Anal. Calcd for $C_{15}H_{27}NO_6$: C, 56.76; H, 8.57; N, 4.41. Found: C, 56.38; H, 8.93; N, 4.42.

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Supporting Information Available: A complete description of experimental details and characterization data for compounds **2**, **3**, **5**, **6**, **8**−**10**, **12**−**14**, **16**, and **18**−**23**. This material is available free of charge via the Internet at http://pubs.acs.org.

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