Cyclization of Hydroxy Enol Ethers: A Stereocontrolled Approach to 3-Deoxy-D-*manno*-2-octulosonic Acid Containing Disaccharides

Arnaud Haudrechy and Pierre Sinaÿ*

Laboratoire de Chimie, U.R.A. 1110, Ecole Normale Supérieure, 24 Rue Lhomond, 75231 Paris Cédex 05, France

Received December 10, 1990 (Revised Manuscript Received October 4, 1991)

A method for the preparation of the carboxylic acids **14** and **15** has been developed, starting from known 2,3,5,6-di-*O*-isopropylidene-D-mannofuranose. Esterification of **14** and **15** with methanol, methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside, and 1,2,5,6-di-*O*-isopropylidene-α-D-glucofuranose, followed by reaction with Tebbe reagent and selective deprotection gave, respectively, the key complex hydroxy enol ethers **20**, **26**, and **35**. Stereoselective iodocyclization, followed by transformation of the CH_2I appendage into a methyloxycarbonyl group, gave the corresponding protected KDO-containing disaccharides.

Introduction

3-Deoxy-D-*manno*-2-octulosonic acid (KDO) occurs as a characteristic component of enterobacterial lipopolysaccharides (LPS) and has also been found in several acidic exopolysaccharides (K antigens), both located at the cell surface of Gram-negative bacteria.[1] The incorporation of KDO appears to be a vital step in growth of the bacteria, and the design of successful inhibitors of lipopolysaccharide biosynthesis of bacteria based on KDO analogues has been achieved.[2] Therefore, the synthetic chemistry involving KDO has become of increasing interest.

KDO-containing oligosaccharides have largely been synthesized so far by conventional glycosylation procedures involving either methyl 3-deoxy-4,5,7,8-tetra-*O*-acetyl-α-D-*manno*-octulopyranosonate chloride,[3] bromide,[4] or fluoride.[5] Selective O-alkylation at the anomeric center,[6] together with the use of a furan ring as a surrogate for the carboxylic acid residue of KDO,[7] have also been reported. As a result of the specific structure of KDO, where position 3 is deoxygenated, synthetic approaches to 2-deoxy α- or β-glycosides[8,9] should formally be transposable to KDO glycosides. Electrophilic activation of the retron A with phenylselenenyl triflate followed by intermolecular addition of an alcohol (the "endo-glycal approach", retrosynthetic pathway a, Scheme I) was recently developed.[10] The intramolecular oximercuration–demercuration of the enol ether retron B has also been achieved[11] (the "endo-enol ether approach", retrosynthetic pathway b, Scheme I). This lastly mentioned stratagem corresponds to the atypical retrosynthetic disconnection b, as opposed to the familiar disconnection a. Due to the presence of the alkyloxycarbonyl appendage in KDO derivatives, additional retrons (the "exo-glycal" C and the "exo-enol ether" D) can be envisaged (retrosynthetic pathways c and d, Scheme I). We would like to present in this paper some aspects of our current explorations of the exo approaches.

Results and Discussion

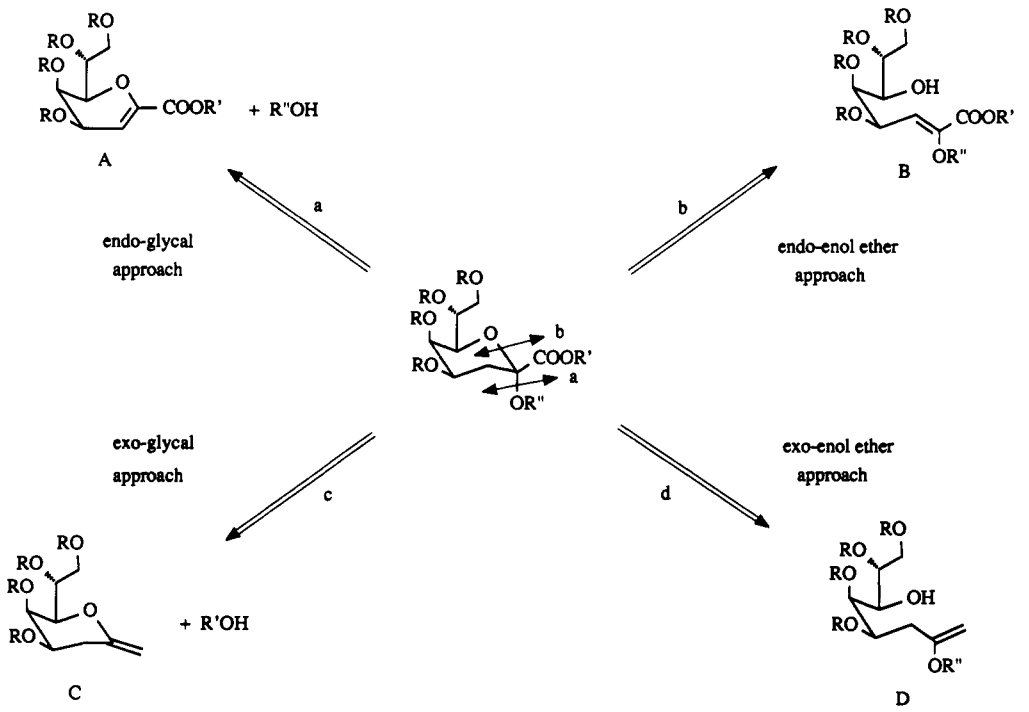
The Exo-Glycal Approach. We first decided to synthesize compound **6**, an easily available retron of type C (Scheme II). Wittig reaction converted known 2,3,5,6-di-*O*-isopropylidene-D-mannose (**1**)[12] into compound **2**. Reasonable yield (71%) was obtained when a solution of both methyltriphenylphosphonium bromide and **1** in oxolane–hexamethylphosphoramide (4:1) was treated with *n*-BuLi (hexane solution). In analogy with a similar reaction we carried out on 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose,[13] it appears that lithiation of the hemiacetal group prior to olefination is of importance.[14] Hydroboration of **2** with 9-BBN was sluggish and incomplete. A satisfactory reaction occured when **2** was first quantitatively converted into acetate **3**, subsequent hydroboration resulting into 70% of diol **4**. The one-step transformation of **4** into the lactone **5** was achieved in essentially quantitative yield using pyridinium chlorochromate (PCC) in dichloromethane, indicating that oxidation of the primary alcohol function occured selectively as the first step.[15] Lactone **5** has recently been synthesized from **1**, using another route.[16] Finally, **5** was easily converted into the expected exo-glycal **6** in 82% yield using a freshly prepared solution of Tebbe reagent[17] in toluene.[18]

1-Methylene sugars have recently been used as C-[19] and

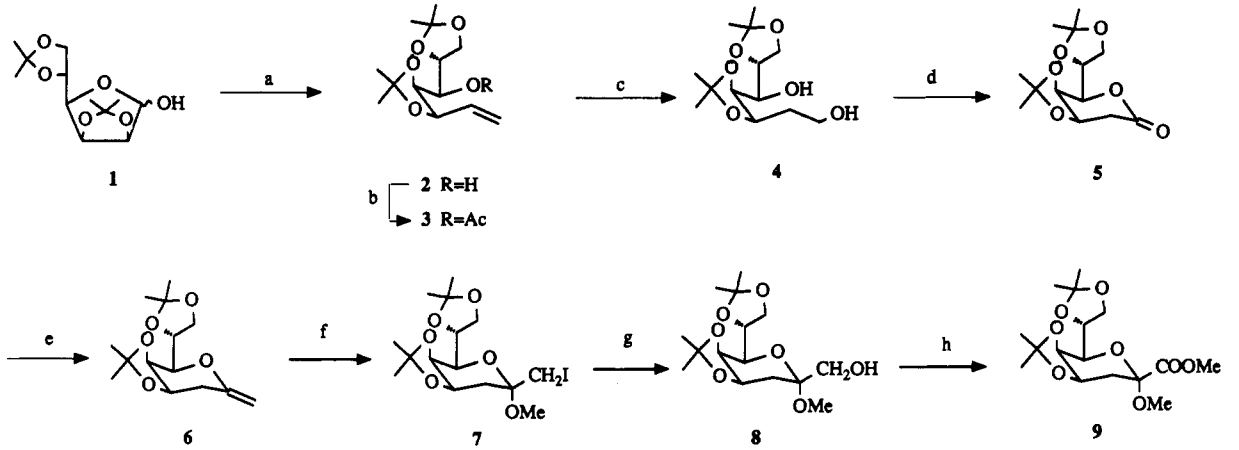
(1) Unger, F. M. *Adv. Carbohydr. Chem. Biochem.* **1981**, *38*, 323.
(2) Norbeck, D. W.; Rosenbrook, W.; Kramer, J. B.; Grampovnik, D. J.; Lartey, P. A. *J. Med. Chem.* **1989**, *32*, 625.
(3) Waldstätten, P.; Christian, R.; Kosma, P.; Kratky, C.; Schulz, G.; Paulsen, H.; Unger, F. M. *ACS Symp. Ser.* **1983**, *231*, 121.
(4) Paulsen, H.; Hayaushi, Y.; Unger, F. M. *Carbohydr. Res.* **1983**, *111*, c5. Paulsen, H.; Hayaushi, Y.; Unger, F. M. *Liebigs Ann. Chem.* **1984**, 1270 and 1288. Kosma, P.; Christian, R.; Schulz, G.; Unger, F. M. *Carbohydr. Res.* **1985**, *141*, 239. Paulsen, H.; Stiem, M.; Unger, F. M. *Tetrahedron Lett.* **1986**, 1135. Paulsen, H.; Schüller, M. *Liebigs Ann. Chem.* **1987**, 249. Paulsen, H.; Stiem, M.; Unger, F. M. *Ibid.* **1987**, 273. Kiso, M.; Fujita, M.; Hayashi, E.; Hasegawa, A.; Unger, F. M. *J. Carbohydr. Chem.* **1987**, *6*, 691. Kiso, M.; Tanahashi, M.; Hasegawa, A.; Unger, F. M. *Carbohydr. Res.* **1987**, *163*, 279. Kosma, P.; Gass, J.; Schulz, G.; Christian, R.; Unger, F. M. *Ibid.* **1987**, *167*, 39. Kiso, M.; Fujita, M.; Tanahashi, M.; Fujishima, Y.; Ogawa, Y.; Hasegawa, A.; Unger, F. M. *Ibid.* **1988**, *177*, 51. Kosma, P.; Schulz, G.; Unger, F. M.; Brade, H. *Ibid.* **1989**, *190*, 191. Kiso, M.; Fujita, M.; Ogawa, Y.; Ishida, H.; Hasegawa, A. *Ibid.* **1990**, *196*, 59.
(5) Imoto, M.; Kusunose, N.; Matsuura, Y.; Kusumoto, S.; Shiba, T. *Tetrahedron Lett.* **1987**, 6277. Kiso, M.; Kusumoto, S.; Kusunose, N.; Kamikawa, T.; Shiba, T. *Tetrahedron Lett.* **1988**, 6325.
(6) Schmidt, R. R.; Esswein, A. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1178. Esswein, A.; Rembold, H.; Schmidt, R. R. *Carbohydr. Res.* **1990**, *200*, 287.
(7) Danishefsky, S. J.; DeNinno, M. P.; Chen, S. *J. Am. Chem. Soc.* **1988**, *110*, 3929.
(8) Thiem, J.; Klaffke, W. *Top. Curr. Chem.* **1990**, *154*, 285 and references cited therein.
(9) Suzuki, K.; Mukaiyama, T. *Chem. Lett.* **1982**, 683. Suzuki, K.; Mukaiyama, T. *Ibid.* **1982**, 1525.
(10) Ikeda, K.; Akamatsu, S.; Achiwa, K. *Carbohydr. Res.* **1989**, *189*, C1.
(11) Paquet, F.; Sinaÿ, P. *J. Am. Chem. Soc.* **1984**, *106*, 8313.
(12) Schmidt, O. T. *Methods Carbohydr. Chem.* **1963**, *2*, 318.
(13) Pougny, J. R.; Nassr, M. A. M.; Sinaÿ, P. *J. Chem. Soc., Chem. Commun.* **1981**, 375.
(14) Lancelin, J. M.; Pougny, J. R.; Sinaÿ, P. *Carbohydr. Res.* **1985**, *136*, 369.
(15) Corey, E. J.; Ishiguro, M. *Tetrahedron Lett.* **1979**, 2745.
(16) Elliot, R. P.; Fleet, G. W. J.; Gyoung, Y. S.; Ramsden, N. G.; Smith, C. *Tetrahedron Lett.* **1990**, 3785.
(17) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611.
(18) (a) Chou, T.-S.; Huang, S.-B.; Hsu, W.-H. *J. Chin. Chem. Soc. (Taipei)* **1983**, *30*, 277; *Chem. Abstr.* **1984**, *100*, 85865p. (b) Kinney, W. K.; Coghlan, M. J.; Paquette, L. A. *J. Am. Chem. Soc.* **1985**, *107*, 7352.
(19) RajanBabu, T. V.; Reddy, G. S. *J. Org. Chem.* **1986**, *51*, 5458.

0022-3263/92/1957-4142$03.00/0

Scheme I. Retrosynthetic Analysis of KDO Glycosylation



Scheme II[a]



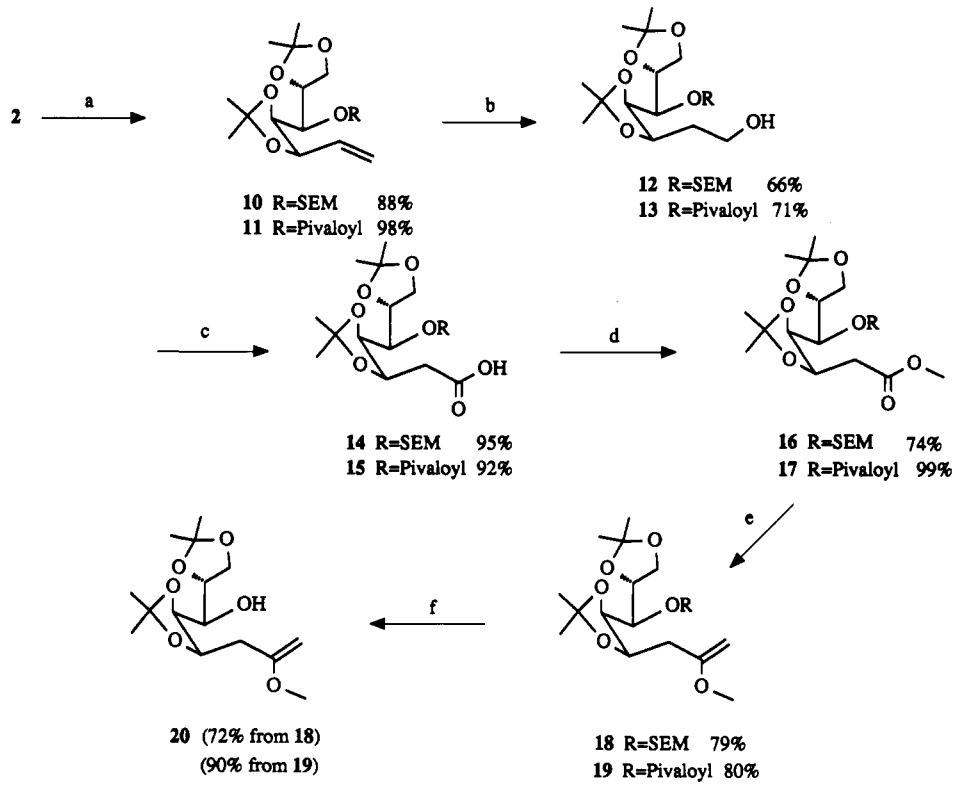
[a] Reagents: (a) $Ph_3P{=}CH_2$, THF, HMPA, rt, 15 h, 71%; (b) Ac_2O, pyridine, 3 h, 100%; (c) 9-BBN in THF, 3 h, then NaOH, H_2O_2, 90 min, 70%; (d) PCC, CH_2Cl_2, 1 h, 96%; (e) Tebbe reagent 0.2 M in toluene, −78 °C → rt, 15 min, 82%; (f) *t*-BuOK, I_2, THF, MeOH; (g) CsOAc, HMPA, 140 °C, 12 h then MeONa 1 M/MeOH, rt, 1 h, 71%; (h) $(COCl)_2$/DMSO then Et_3N; $NaClO_2$, H_2O_2, CH_3CN, rt, 5 h; CH_2N_2, ether 72%.

O-glycoside[20] precursors. We found that reaction of freshly prepared **6** with methanol in the presence of potassium *tert*-butoxide and iodine[21] selectively gave the α-methyl glycoside **7** in 70% yield (Scheme II). Attempts to condense various sugar alcohols in the same manner led to frustration. This led us to abandon this method and to study the exo-enol ether cyclization.

But, having in hand the glycoside **7**, we used it to address the problem of the chemical conversion of the CH_2I appendage into COOMe (Scheme II). Treatment of **7** with cesium acetate in hexamethylphosphoramide at 140 °C for 12 h, followed by conventional O-deacetylation, gave the crystalline alcohol **8** (71% yield) that was oxidized in two steps with Me_2SO–$(COCl)_2$–Et_3N,[22] then with $NaClO_2$.[23] Esterification with diazomethane gave (72% yield from **8**) crystalline **9** (mp 120 °C from ether and hexane), identical with a compound obtained by another route.[24] This comparison unambiguously established the anomery previously assigned to compound **7**. The ^1H NMR spectrum of **9** shows a shift of H-4 at δ 4.52 (ddd, $J_{3a/4}$ = 3 Hz, $J_{3b/4}$ = 4 Hz, $J_{4/5}$ = 7.5 Hz) which is considered as diagnostic of the α anomery when H-4 and -OR groups are in proximity.[25] The observed coupling constants indicate a deviation from the $^5C_2$(D) chair conformation (depicted in Scheme II) toward a boat or skew-boat form. Previously, such a distortion was constantly observed in a series of KDO derivatives where positions 4 and 5 were protected

(20) Noort, D.; Veeneman, G. H.; Boons, G. J. P. H.; van der Marel, G. A.; Mulder, G. J.; van Boom, J. H. *Synlett* **1990**, *4*, 205. Thiem, J.; Kleeberg, M. *Carbohydr. Res.* **1990**, *205*, 333.
(21) Barrett, A. G. M.; Bezuidenhout, B. C. B.; Gasiecki, A. F.; Howell, A. R.; Russell, M. A. *J. Am. Chem. Soc.* **1989**, *111*, 1392.
(22) Mancuso, A. J.; Brownfain, D. S.; Swern, D. *J. Org. Chem.* **1979**, *44*, 4148. Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165.
(23) Dalcanale, E.; Montanari, F. *J. Org. Chem.* **1986**, *51*, 567.
(24) Auzanneau, F. I.; Charon, D.; Szabó, L.; Mérienne, C. *Carbohydr. Res.* **1988**, *179*, 125.
(25) Unger, F. M.; Stix, O.; Schultz, G. *Carbohydr. Res.* **1980**, *80*, 191.

Scheme III[a]



[a] Reagents: (a) R = SEM, SEMCl, *i*-Pr_2NEt, CH_2Cl_2, 40 °C, 3 h; R = Piv, PivCl, pyridine, DMAP, rt, 32 h; (b) R = SEM, BH_3/THF, 30 min then H_2O_2, NaOH, rt; R = Piv, 9-BBN, THF, 2 h then H_2O_2, NaOH, rt; (c) $RuCl_3/NaIO_4$, CCl_4, CH_3CN, H_2O, rt, 90 min; (d) CH_2N_2, ether, 15 min; (e) Tebbe reagent 0.2 M in toluene, pyridine, −45 °C, 1 h; (f) removal of the SEM group, $F^-NBu_4^+$, THF, HMPA, ethylenediamine, 60 °C, 18 h; removal of the pivaloyl group, $LiAlH_4$, THF, 0 °C, 10 min.

by an isopropylidene group.[24] Having secured the $CH_2I \rightarrow$ COOMe transformation, we concentrated on iodocyclization.

The Exo-Enol Ether Approach. The successful "exo-enol ether" approach we would now like to describe relies on an easy access to the key retron D (Scheme I). The starting compound of the synthesis was the alcohol **2**, which was protected either with a SEM or a pivaloyl group to give, respectively, **10** (88%) and **11** (98%) (Scheme III). Hydroborations of **10** with borane–oxolane complex and **11** with 9-BBN gave the desired alcohols **12** and **13** in about 70% yield. Oxidation of the primary alcohol with $RuCl_3$–$NaIO_4$ in the solvent system CCl_4–CH_3CN–H_2O[26] for 90 min at room temperature gave the corresponding acids **14** and **15** in over 90% yield (Scheme III). In order to establish the feasability of the attempted strategy on a simple derivative, esterification of these acids with diazomethane was achieved to give, respectively, esters **16** (74%) and **17** (99%). The reaction with a toluene solution of Tebbe reagent proceeded smoothly to give the enol ethers **18** and **19**, respectively, in about 80% yield. Removal of the SEM group with tetrabutylammonium fluoride in oxolane–hexamethylphosphotriamide–ethylenediamine at 60 °C for 18 h gave the key secondary alcohol **20** in 72% yield. Removal of the pivaloyl group proceeded smoothly in the presence of lithium aluminum hydride in oxolane (10 min at 0 °C) to give the same alcohol **20** in 90% yield. A comparison of the two parallel routes shows the superiority of the pivaloyl protecting group which met all the requirements both in terms of chemical compatibility and simplicity–efficiency. Noticeable is the selective transformation **17** → **19** *which demonstrates that Tebbe reagent does not react with the bulky pivaloyl ester function.* Cyclization of **20** was easily achieved with *t*-BuOK and iodine at −78 °C to give previously reported α-methyl ketoside **7** as the single product of the reaction. The outstanding kinetic α-stereoselectivity of this cyclization is remarkable. The intrinsically high "Wittig-like" reactivity level for converting esters into vinyl ethers of type **19** was thus a key feature in our strategy,[27] providing an easy access to a retron of type D.

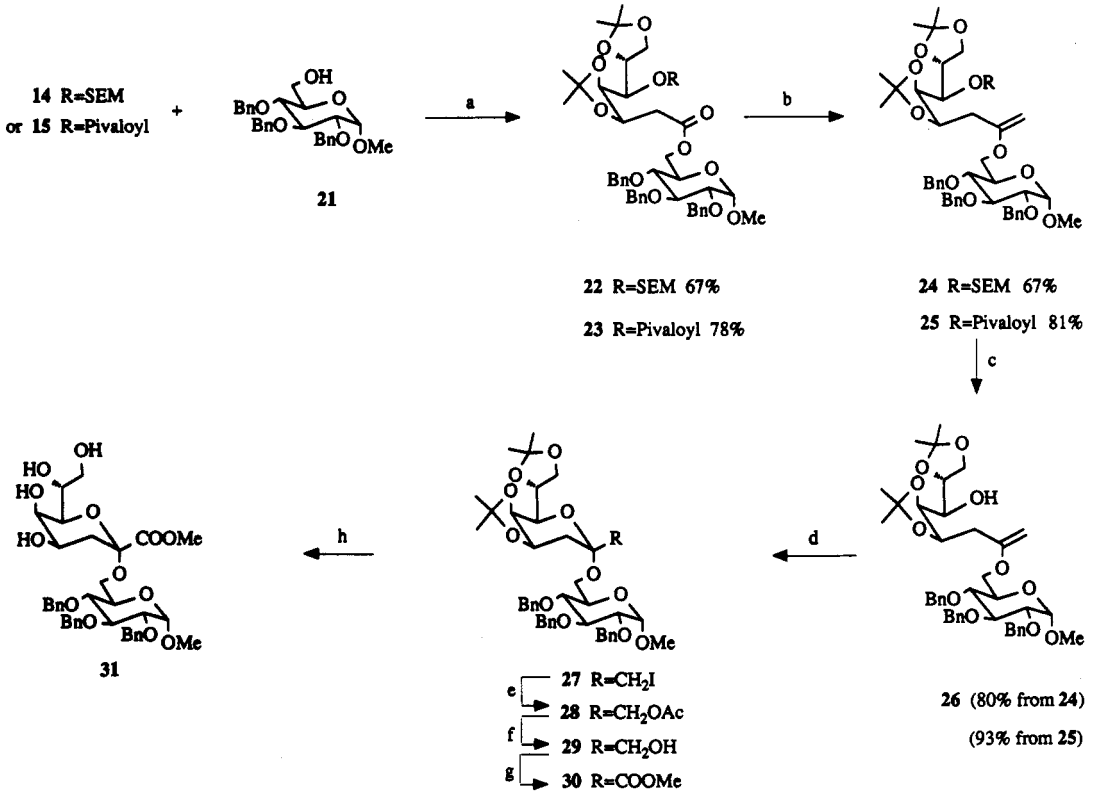
With these auspicious results now available, the synthesis of two protected KDO-containing disaccharides was easily materialized. Scheme IV shows the use of methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside[28] (**21**), finally resulting into disaccharide **30**. The esters **22** and **23** were prepared by reaction of **21** with **14** and **15**, respectively, in the presence of dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridine (DMAP). The key enol ether **26** was then obtained as previously described for the preparation of **20**. Again, the pivaloyl protecting group gave better yields. Cyclization of **26** with *t*-BuOK and iodine went very smoothly and gave **27** as the single product of the reaction. The transformation of **27** into **30** was achieved as described for the synthesis of **9**. The chemical shifts of H-4 in derivatives **27**, **28**, **29** and **30** (see Experimental Section) were close to the values observed in the previously described model derivatives and considered as diagnostic of the α-anomery. The selective removal of the isopropylidene groups in **30** was easily achieved using trifluoroacetic acid in a mixture of methanol–water to give the KDO derivative **31**. The same

(26) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

(27) A preliminary communication has been published: Haudrechy, A.; Sinaÿ, P. *Tetrahedron Lett.* **1990**, 5765.

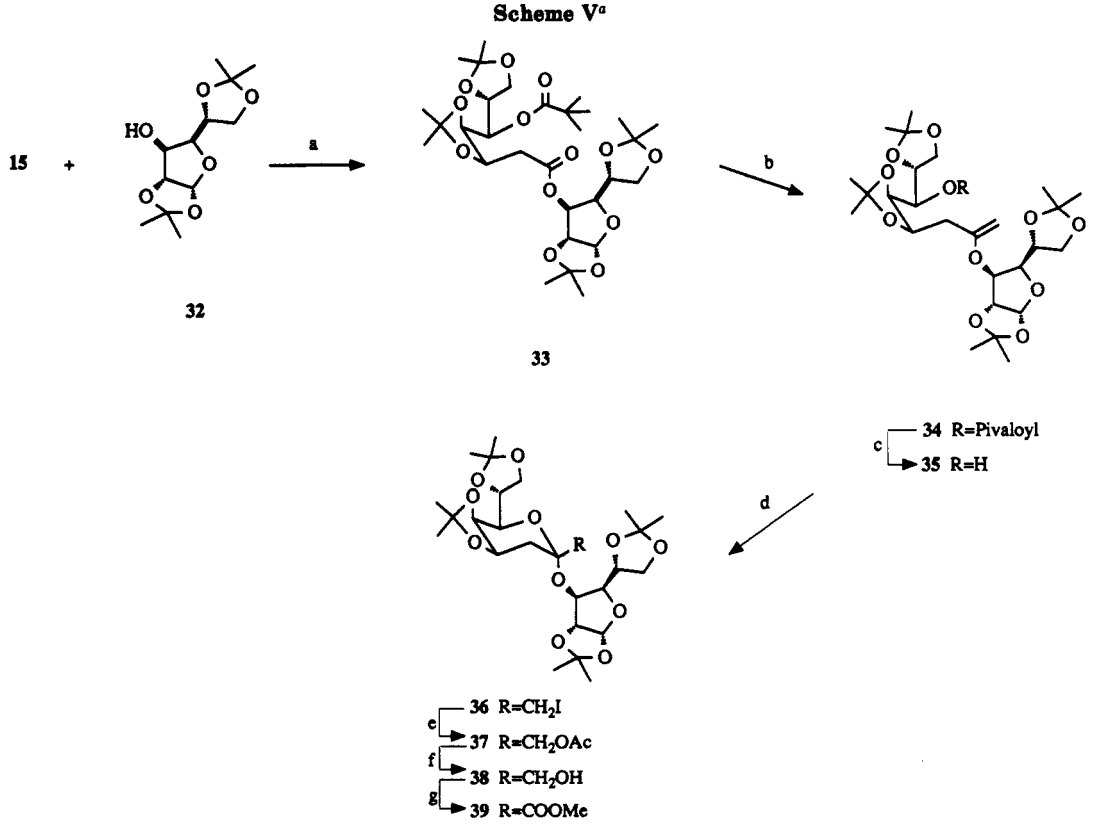
(28) Kováč, P.; Alföldi, J.; Kosik, M. *Chem. Zvesti* **1974**, *28*, 820; *Chem. Abstr.* **1975**, *82*, 112214x.

Scheme IV[a]



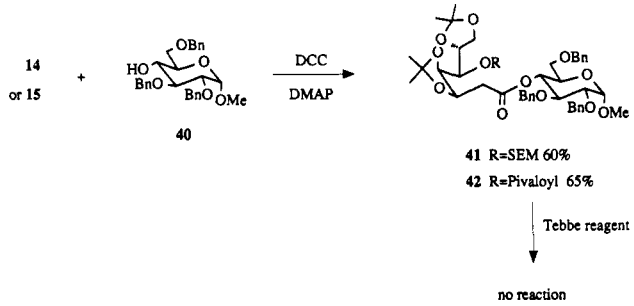
[a] Reagents: (a) DCC, DMAP, rt, 30 min; (b) Tebbe reagent 0.2 M in toluene, pyridine, −45 °C, 1 h; (c) removal of the SEM group, $F^-NBu_4^+$, THF, HMPA, ethylenediamine, 60 °C, 18 h; removal of the pivaloyl group, $LiAlH_4$, THF, 0 °C, 10 min; (d) *t*-BuOK, THF, rt, 10 min then I_2, −78 °C → rt, 4 h, 92%; (e) CsOAc, HMPA, 130 °C, 24 h, 68% (30% of recovered starting material); (f) MeONa 1 M/MeOH, rt, 1 h, 98%; (g) $(COCl_2)$/DMSO then Et_3N; $NaClO_2$, H_2O_2, CH_3CN, rt, 3 h; CH_2N_2, ether, 68%; (h) CF_3COOH, H_2O, MeOH, rt, 48 h, 90%.

Scheme V[a]



[a] Reagents: (a) DCC, DMAP, rt, 30 min, 80%; (b) Tebbe reagent 0.2 M in toluene, pyridine, −45 °C, 1 h, 87%; (c) $LiAlH_4$, THF, 0 °C, 10 min, 90%; (d) *t*-BuOK, THF, rt, 10 min then I_2, −78 °C → rt, 2 h, 90%; (e) CsOAc, HMPA, 130 °C, 36 h, 84%; (f) MeONa 1 M/MeOH, rt, 1 h, 97%; (g) $(COCl)_2$/DMSO then Et_3N; $NaClO_2$, H_2O_2, CH_3CN, rt, 3 h; CH_2N_2, ether, 63%.

Scheme VI



sequence was also achieved starting from commercially available 1,2,5,6-di-*O*-isopropylidene-α-D-glucofuranose (**32**), as shown in Scheme V. ^{1}H NMR spectra are again in agreement with the assigned structures.

A limitation to the generalization of this methodology may result from the lack of reactivity of some sterically hindered esters with Tebbe reagent.[29] For example, esters **41** and **42**, prepared in the manner previously reported from methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside,[30] did not react with Tebbe reagent (Scheme VI). A similar feature was recently observed by Barret et al.,[31] however, methylenylation using the Nozaki–Takai protocol[32] readily solved the problem.[31] The application of this procedure to make exo-enol ethers from esters may thus extend the scope of this work.

Experimental Section

General Procedures and Materials. All reactions were performed under an argon atmosphere. Oxolane was distilled from sodium/benzophenone ketyl. Melting points were determined on a Büchi 510 capillary melting point apparatus and are uncorrected. Flash chromatography was performed as described by Still et al. (Merck silica gel (230–400 mesh)). TLC analyses were performed on Merck aluminum-backed F_{254} silica gel plates and detected by charring with sulfuric acid. ^{1}H NMR spectra were recorded on a Cameca 250 (250 MHz) or a Bruker AM 400 (400 MHz). Chemical shifts are reported in ppm (δ) downfield from Me_4Si (δ = 0ppm) as an internal standard. Data were reported as follows: chemical shift (multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (hertz), integration). ^{13}C NMR spectrum were recorded on a Cameca 250. Optical rotations were measured at 20 ± 2° with a Perkin-Elmer Model 241 polarimeter. CI (ammonia) mass spectra were obtained with a Nermag R10-10 spectrometer. Elemental analyses were performed at the University Pierre et Marie Curie (Paris VI) or at the "Service Central d'Analyse du Centre National de la Recherche Scientifique" in Vernaison (France).

1,2-Dideoxy-3,4:6,7-di-*O*-isopropylidene-D-*manno*-hept-1-enitol (2). To a stirred suspension of 2,3,5,6-di-*O*-isopropylidene-D-mannose[12] (2 g, 7.7 mmol) and methyltriphenylphosphonium bromide (5.6 g, 15.7 mmol) in dry oxolane (80 mL) at −20 °C was added dropwise *n*-BuLi (15 mL, 1.6 M in hexane, 24 mmol). Stirring was continued for 15 h at 20 °C. Saturated aqueous NH_4Cl (120 mL) was then added. The mixture was repeatedly extracted with dichloromethane. The combined extracts were washed with saturated aqueous $NaHCO_3$ (100 mL), dried ($MgSO_4$), and evaporated to leave the residue, which was purified by chromatography (hexane–ethyl acetate (4:1)) to afford **2** (1.41 g, 71%) as a colorless syrup: $[\alpha]_D$ −33° (*c* 0.7, chloroform); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 6.16 (ddd, $J_{1a/2trans}$ = 17.5 Hz, $J_{1b/2cis}$ = 10.5 Hz, $J_{2/3}$ = 8 Hz, 1 H, H-2), 5.51, 5.36 (m, $J_{1a/1b}$ = 1.5 Hz, 2 H, H-1a,1b), 4.75 (dd, $J_{3/4}$ = 8 Hz, 1 H, H-3), 4.43 (dd, $J_{4/5}$ = 1.5 Hz, 1 H, H-4), 4.17–3.98 (m, 3 H, H-6,7a,7b), 3.48 (dd, $J_{5/6}$ = 8 Hz, 1 H, H-5), 1.54, 1.41, 1.40, 1.36 (4s, 12 H, 4×Me); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 134.1 (C-2), 119.6 (C-1), 109.2, 108.5 (2×*C*-$(Me)_2$), 79.0, 76.5, 75.9, 70.4 (C-3,4,5,6), 67.0 (C-7), 26.7, 26.5, 25.2, 24.4 (4×Me); MS (CI) *m*/*z* 259 (MH^+). Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.30; H, 8.71.

5-*O*-Acetyl-1,2-dideoxy-3,4:6,7-di-*O*-isopropylidene-D-*manno*-hept-1-enitol (3). To a solution of **2** (200 mg, 0.77 mmol) in dry pyridine (0.3 mL) at room temperature was added acetic anhydride (0.15 mL). After 3 h at room temperature, the reaction mixture was filtered through a Celite pad and concentrated under reduced pressure. The residue was chromatographed (hexane–ethyl acetate (4:1)) to afford **3** (231 mg, 100%) as a colorless syrup: $[\alpha]_D$ −26° (*c* 1.5, chloroform); ^{1}H NMR ($CDCl_3$, 250MHz) δ 5.79 (ddd unsolved, $J_{1b/2}$ = 10.5 Hz, $J_{2/3}$ = 6.5 Hz, 1 H, H-2), 5.41 (dd unsolved, 1 H, H-1a), 5.31 (dd unsolved, 1 H, H-1b), 5.06 (dd, $J_{4/5}$ = 1.5 Hz, $J_{5/6}$ = 6 Hz, 1 H, H-5), 4.74 (m, $J_{3/4}$ = 6 Hz, 1 H, H-3), 4.39 (dd, 1 H, H-4), 4.22 (ddd, $J_{6/7a}$ = 6 Hz, $J_{6/7b}$ = 5.5 Hz, 1 H, H-6), 4.02 (dd, $J_{7a/7b}$ = 8.5 Hz, 1 H, H-7a), 3.94 (dd, 1 H, H-7b), 2.10 (s, 3 H, $COCH_3$), 1.59, 1.41, 1.40, 1.39 (4s, 12 H, 4×Me); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 169.7 (CO), 132.4 (C-2), 118.8 (C-1), 109.1, 108.9 (2×*C*$(Me)_2$), 78.1, 76.9, 75.2, 70.5 (C-3,4,5,6), 65.9 (C-7), 26.5, 26.4, 25.5, 25.4 (4×Me), 21.2 ($COCH_3$); MS (CI) *m*/*z* 301 (MH^+). Anal. Calcd for $C_{15}H_{24}O_6$: C, 59.99; H, 8.05. Found: C, 59.92; H, 8.02.

2-Deoxy-3,4:6,7-di-*O*-isopropylidene-D-*manno*-heptitol (4). To a solution of **3** (180 mg, 0.6 mmol) in dry oxolane (3.5 mL) was dropwise added 9-BBN (3.5 mL, 0.5 M in oxolane, 1.75 mmol) at 0 °C. The reaction mixture was stirred at 0 °C and warmed to room temperature over a period of 3 h, then diluted with oxolane (7 mL); 30% H_2O_2 was added (4.4 mL) at 0 °C, followed by aqueous NaOH 4% (5 mL). The reaction mixture was stirred for 90 min then diluted with chloroform (25 mL), washed with water, and dried ($MgSO_4$). Removal of solvent under reduced pressure and chromatography of the residue (hexane–ethyl acetate (1:2)) afforded **4** (116 mg, 70%) as a colorless syrup: $[\alpha]_D$ −4° (*c* 1, chloroform); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 4.45 (ddd, $J_{2b/3}$ = 10 Hz, $J_{2a/3}$ = 3 Hz, $J_{3/4}$ = 7 Hz, 1 H, H-3), 4.33 (dd, $J_{4/5}$ = 1.5 Hz, 1 H, H-4), 4.12 (d unsolved, 1 H, H-7a), 4.02 (m, 2 H, H-6,7b), 3.84 (2ddd unsolved, $J_{1b/2}$ = 2 Hz, $J_{1a/2}$ = 5 Hz, 2 H, H-1a,1b), 3.50 (dd, $J_{5/6}$ = 7 Hz, 1 H, H-5), 2.12 (m, 1 H, H-2a), 1.87 (m, 1 H, H-2b), 1.52, 1.41, 1.41, 1.35 (4s, 12 H, 4×Me); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 109.2, 107.9 (2×*C*$(Me)_2$), 76.0, 75.2, 70.4 (C-3,4,5,6), 66.9, 60.3 (C-1,7), 32.4 (C-2), 26.7, 26.6, 25.1, 24.6 (4×Me); MS (CI) *m*/*z* 294 ($M + NH_4^+$), 277 (MH^+). Anal. Calcd for $C_{13}H_{24}O_6$: C, 56.51; H, 8.75. Found: C, 56.76; H, 8.81.

2-Deoxy-3,4:6,7-di-*O*-isopropylidene-D-*manno*-heptonic Acid 1,5-Lactone (5). To a solution of **4** (50 mg, 0.18 mmol) in dry dichloromethane (1 mL) was added pyridinium chlorochromate (120 mg, 0.56 mmol). The reaction mixture was stirred for 1 h, diluted with ether (1 mL), and filtered on silica gel. Removal of solvent under reduced pressure afforded **5** (47 mg, 96%) as a colorless syrup: $[\alpha]_D$ +64° (*c* 0.9, chloroform); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 4.77 (ddd, $J_{3/4}$ = 8.5 Hz, $J_{2a/3}$ = 2 Hz, $J_{2b/3}$ = 3.5 Hz, 1 H, H-3), 4.61 (dd, $J_{4/5}$ = 2 Hz), 4.43 (ddd, $J_{6/7a}$ = 4 Hz, $J_{6/7b}$ = 4 Hz, $J_{5/6}$ = 8.5 Hz, 1 H, H-6), 4.17 (dd, $J_{7a/7b}$ = 9 Hz, 1 H, H-7a), 4.09 (dd, 1 H, H-7b), 3.93 (dd, 1 H, H-5), 2.90 (dd, $J_{2a/2b}$ = 16 Hz, 1 H, H-2a), 2.53 (dd, 1 H, H-2b), 1.46, 1.46, 1.40, 1.37 (4s, 12 H, 4×Me); ^{13}C NMR ($CDCl_3$, 250MHz) δ 168.8 (C-1), 109.7, 109.6 (2×*C*$(Me)_2$), 77.7, 72.7, 71.3, 71.1 (C-3,4,5,6), 66.5 (C-7), 34.6 (C-2), 26.9, 25.8, 24.9, 24.1 (4×Me); MS (CI) *m*/*z* 290 ($M + NH_4^+$), 273 (MH^+). Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.35; H, 7.40. Found: C, 57.16; H, 7.54.

2,6-Anhydro-1,3-dideoxy-4,5:7,8-di-*O*-isopropylidene-D-*manno*-oct-1-enitol (6). To a solution of **5** (365 mg, 1.34 mmol) in dry pyridine (3 mL) was added a 0.5 M solution of Tebbe reagent[17] in dry toluene[18] (7 mL, 3.5 mmol) at −78 °C under argon. The mixture was stirred at room temperature for 15 min. It was then cooled to −40 °C, and a 15% sodium hydroxide solution (20 mL) was added. The cold bath was removed, and the reaction mixture was diluted with ether (50 mL). Stirring was continued for 10 min, and the residue was removed by filtration through

(29) For some examples of lack of reactivity of hindered ketones or esters with Tebbe reagent, see: Clawson, L.; Buchwald, S. L.; Grubbs, R. H. *Tetrahedron Lett.* **1984**, 5733. Pine, S. H.; Pettit, R. J.; Geib, G. D.; Cruz, S. G.; Gallego, C. H.; Tijerina, T.; Pine, R. D. *J. Org. Chem.* **1985**, *50*, 1212. Peterson, P. E.; Stepanian, M. J. *J. Org. Chem.* **1988**, *53*, 1903. Jasperse, C. P.; Curran, D. P. *J. Am. Chem. Soc.* **1990**, *112*, 5601.

(30) Küster, J. M.; Dyong, I. *Liebigs Ann. Chem.* **1975**, *12*, 2179.

(31) Barrett, A. G. M.; Bezuidenhout, B. C. B.; Melcher, L. M. *J. Org. Chem.* **1990**, *55*, 5196.

(32) Okazoe, T.; Takai, K.; Oshima, K.; Utimoto, K. *J. Org. Chem.* **1987**, *52*, 4410 and references cited therein.

a Celite pad. The filter cake was washed with ether, and the product was purified by chromatography [hexane–ethyl acetate (5:1) (+0.1% Et_3N)] to afford **6** (82%) as a syrup: ^1H NMR (C_6D_6, 250 MHz) δ 4.79 (s, 2 H, H-1a,1b), 4.37–4.18 (m, 2 H, H-4,5), 4.13–3.99 (m, 3 H, H-7,8a,8b), 3.52 (dd, $J_{5/6}$ = 7 Hz, $J_{6/7}$ = 7.5 Hz, 1 H, H-6), 2.58 (dd, $J_{3a/4}$ = 9.5 Hz, $J_{3a/3b}$ = 15.5 Hz, 1 H, H-3a), 2.30 (dd, $J_{3b/4}$ = 5 Hz, 1 H, H-3b), 1.38, 1.34, 1.26, 1.17 (4s, 12 H, 4×Me); MS (CI) m/z 271 (MH^+). **6** was rather unstable and should be used promptly.

Methyl 1,3-Dideoxy-1-iodo-4,5:7,8-di-*O*-isopropylidene-α-D-*manno*-octulopyranoside (7). From **6**: To a stirred solution of **6** (5 mg, 18.5 μmol) in dry oxolane (320 μL) at room temperature was added dry methanol (10 μL) and *t*-BuOK (10 mg, 44 μmol), the mixture was stirred for 10 min and cooled to −78 °C, and iodine (10 mg, 39 μmol) was added. The mixture was stirred for 10 min, then the temperature was raised to 0 °C. The reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ solution (0.5 mL) then extracted with dichloromethane. After drying ($MgSO_4$) and evaporation, column chromatography (hexane–ethyl acetate (3:1)) afforded **7** (70%) as a colorless syrup: $[\alpha]_D$ +13.7° (*c* 0.25, chloroform); ^1H NMR ($CDCl_3$, 250 MHz) δ 4.52 (ddd, $J_{4/5}$ = 7.5 Hz, $J_{3a/4}$ = 3.5 Hz, $J_{3b/4}$ = 3.5 Hz, 1 H, H-4), 4.27 (ddd, $J_{7/8a}$ = 6 Hz, $J_{7/8b}$ = 5 Hz, $J_{6/7}$ = 9 Hz, 1 H, H-7), 4.23 (dd, $J_{5/6}$ = 2 Hz, 1 H, H-5), 4.11 (dd, $J_{8a/8b}$ = 8.5 Hz, 1 H, H-8a), 3.96 (dd, 1 H, H-8b), 3.56 (d, $J_{1a/1b}$ = 11 Hz, H-1a + dd, 1 H, H-6), 3.41 (d, 1 H, H-1b), 3.23 (s, 3 H, OMe), 2.55 (dd, $J_{3a/3b}$ = 15.5 Hz, 1 H, H-3a), 1.65 (dd, 1 H, H-3b), 1.44, 1.42, 1.37, 1.33 (4s, 12 H, 4×Me); MS (CI) m/z 446 ($M + NH_4^+$). Anal. Calcd for $C_{15}H_{25}O_6I$: C, 42.07; H, 5.88. Found: C, 42.01; H, 5.99.

From **20**: To a stirred solution of **20** (140 mg, 0.46 mmol) in dry oxolane (8 mL) at room temperature was added *t*-BuOK (140 mg, 1.25 mmol), the mixture was stirred for 10 min and cooled to −78 °C, and iodine (220 mg, 867 μmol) was added. The mixture was stirred for 1 h, then the temperature was raised to 0 °C. The reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ solution (0.5 mL) then was extracted with dichloromethane. After drying ($MgSO_4$) and evaporation, column chromatography gave **7** (84%) as a colorless syrup, identical with the compound prepared from **6**.

Methyl 3-Deoxy-4,5:7,8-di-*O*-isopropylidene-α-D-*manno*-octulopyranoside (8). To a solution of **7** (80 mg, 0.187 mmol) in hexamethylphosphoramide (1 mL) was added cesium acetate (180 mg, 0.93 mmol). The reaction mixture was heated at 140 °C for 12 h, cooled to room temperature, washed with water, and extracted with ethyl acetate. After removal of solvent, the crude residue (61 mg, 133 μmol) was dissolved at room temperature in a 1 M solution of sodium methoxide in methanol (10 mL). The reaction mixture was stirred for 1 h. Removal of solvent under reduced pressure was followed by addition of ether and filtration through a Celite pad. The filter cake was washed with ether, the solvents were evaporated, and the residue was chromatographed (hexane–ethyl acetate (1:1)) to afford crystalline **8** (overall yield 71% from **7**): mp 70–71 °C (hexane); $[\alpha]_D$ +27° (*c* 0.7, chloroform); ^1H NMR ($CDCl_3$, 250 MHz) δ 4.54 (ddd unsolved, $J_{3a/4}$ = 3.5 Hz, $J_{3b/4}$ = 3.5 Hz, 1 H, H-4), 4.35–4.25 (m, 2 H, H-5,7), 4.13 (dd, $J_{8a/8b}$ = 8.5 Hz, $J_{7/8a}$ = 6 Hz, 1 H, H-8a), 3.98 (dd, $J_{7/8b}$ = 5 Hz, 1 H, H-8b), 3.72 (d unsolved, 1 H, H-1a), 3.66 (d unsolved, 1 H, H-1b), 3.62 (dd, $J_{6/5}$ = 2 Hz, $J_{6/7}$ = 7.5 Hz, 1 H, H-6), 3.27 (s, 3 H, OMe), 2.47 (dd, $J_{3a/3b}$ = 15.5 Hz, $J_{3a/4}$ = 3.5 Hz, 1 H, H-3a), 2.39 (s, 1 H, OH), 1.68 (dd, $J_{3b/4}$ = 3.5 Hz, 1 H, H-3b), 1.55, 1.43, 1.38, 1.35 (4s, 12 H, 4×Me); MS (CI) m/z 336 ($M + NH_4^+$). Anal. Calcd for $C_{15}H_{26}O_7$: C, 56.60; H, 8.23. Found: C, 56.90; H, 8.15.

Methyl (Methyl 3-deoxy-4,5:7,8-di-*O*-isopropylidene-α-D-*manno*-2-octulopyranosid)onate (9). To a stirred solution of oxalyl chloride (15 μL, 172 μmol) in dichloromethane (4.5 mL) at −78 °C was added dimethyl sulfoxide (15 μL, 211 μmol). After 10 min, a solution of **8** (22 mg, 69 μmol) in dichloromethane (1.5 mL) was added. After 15 min, the reaction mixture was treated with triethylamine (1.5 mL), then allowed to warm to 0 °C. The reaction mixture was filtered through a Celite pad. Removal of solvent under reduced pressure was followed by addition of ether and filtration through a Celite pad. Solvent was removed, and the residue was dissolved in acetonitrile (150 μL). To this stirred mixture was dropwise added in 2 h NaH_2PO_4 (10 mg) in water (70 μL), 35% H_2O_2 (15 μL), and a solution of $NaClO_2$ (4 mg) in water (210 μL). The reaction mixture was filtered through a Celite pad. The filter cake was washed with ethyl acetate. After removal of solvent under reduced pressure, ether was added and another filtration gave the desired carboxylic acid. Treatment with a diazomethane solution in ether followed by removal of solvent and chromatography (hexane–ethyl acetate (1:1)) afforded known crystalline **9** (72%), mp 120 °C (ether/hexane) (lit.[26] mp 120–123 °C (ether/hexane)).

1,2-Dideoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-[[(trimethylsilyl)ethoxy]methyl]-D-*manno*-hept-1-enitol (10). To a stirred solution of **2** (110 mg, 0.426 mmol) in dry dichloromethane (0.215 mL) at room temperature was dropwise added *N,N*-diisopropylethylamine (0.380 mL, 2.18 mmol) and (trimethylsilyl)ethoxymethyl chloride (0.250 mL, 1.4 mmol). The reaction mixture was heated for 3 h at 40 °C and filtered through a Celite pad. Removal of solvent under reduced pressure and chromatography of the residue (hexane–ethyl acetate (5:1)) afforded **10** (145 mg, 88%) as a colorless syrup: $[\alpha]_D$ +32° (*c* 1, chloroform); ^1H NMR ($CDCl_3$, 250 MHz) δ 6.09 (ddd unsolved, 1 H, H-2), 5.36 (2dd unsolved, 2 H, H-1a,1b), 4.88 (2d, J_{gem} = 11 Hz, 2 H, OCH_2O), 4.58 (dd, $J_{2/3}$ = 7.5 Hz, $J_{3/4}$ = 6 Hz, 1 H, H-3), 4.20–4.00 (m, 4 H, H-4,6,7a,7b), 3.86 (dd, $J_{4/5}$ = 4.5 Hz, $J_{5/6}$ = 6.5 Hz, 1 H, H-5), 3.70 (2dd, J_{gem} = 13 Hz, 2 H, $OCH_2CH_2SiMe_3$), 1.51, 1.40, 1.38, 1.35 (4s, 12 H, 4×Me), 0.95 (dd, J_{OCH-CH_2} = 7 Hz, $J_{OCH'-CH_2}$ = 10 Hz, 2 H, CH_2SiMe_3), 0 (s, 9 H, $SiMe_3$); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 134.3 (C-2), 119.0 (C-1), 108.7, 108.6 (2×$C(Me)_2$), 95.6 (OCH_2O), 79.0, 78.9, 76.3, 74.9 (C-3,4,5,6), 66.0, 65.5 (C-7,$OCH_2CH_2SiMe_3$), 27.4, 26.1, 25.6, 25.2 (4×Me), 17.8 (CH_2SiMe_3), −1.5 ($SiMe_3$); MS (CI) m/z 406 ($M + NH_4^+$). Anal. Calcd for $C_{19}H_{36}O_6Si$: C, 58.73; H, 9.34. Found: C, 58.59; H, 9.46.

1,2-Dideoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-pivaloyl-D-*manno*-hept-1-enitol (11). To a solution of **2** (50 mg, 0.194 mmol) in dry pyridine (1.5 mL) was added at room temperature pivaloyl chloride (0.05 mL, 0.406 mmol) and a catalytic amount of 4-(dimethylamino)pyridine. After 32 h at room temperature, the reaction mixture was filtered through a Celite pad and concentrated under reduced pressure. The residue was chromatographed (hexane–ethyl acetate (5:1)) to afford **11** (65 mg, 98%) as a colorless syrup: $[\alpha]_D$ −22° (*c* 0.4, chloroform); ^1H NMR ($CDCl_3$, 250 MHz) δ 5.63 (ddd, $J_{1b/2}$ = 17 Hz, $J_{1a/2}$ = 10 Hz, $J_{2/3}$ = 7 Hz, 1 H, H-2), 5.33 (dd, $J_{1a/1b}$ = 1.5 Hz, 1 H, H-1a), 5.23 (dd, 1 H, H-1a), 5.02 (dd, $J_{4/5}$ = 2 Hz, $J_{5/6}$ = 6 Hz, 1 H, H-5), 4.62 (dd, $J_{3/4}$ = 7 Hz, 1 H, H-3), 4.31 (dd, 1 H, H-4), 4.13 (ddd, $J_{6/7a}$ = 6 Hz, $J_{6/7b}$ = 7 Hz, 1 H, H-6), 3.88 (dd, $J_{7a/7b}$ = 8 Hz, 1 H, H-7a), 3.77 (dd, 1 H, H-7b), 1.48, 1.30, 1.30, 1.27 (4s, 12 H, 4×Me), 1.14 (s, 9 H, tBu); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 177 (CO), 132.4 (C-2), 119.6 (C-1), 108.9, 108.8 (2×$C(Me)_2$), 78.3, 77.2, 75.4, 70.3 (C-3,4,5,6), 65.9 (C-7), 38.8 ($C(Me)_3$), 27.1 ($C(Me)_3$), 26.7, 26.4, 25.3, 25.2 (4×Me); MS (CI) m/z 285 (M − *t*-Bu). Anal. Calcd for $C_{18}H_{30}O_6$: C, 63.14; H, 8.83. Found: C, 63.12; H, 8.79.

2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-[[(trimethylsilyl)ethoxy]methyl]-D-*manno*-heptitol (12). To a solution of **10** (145 mg, 0.374 mmol) in dry oxolane (4.2 mL) was added dropwise borane–oxolane complex (1 mL, 1 M in oxolane, 1 mmol) at 0 °C. The reaction mixture was stirred at 0 °C and warmed to room temperature over a period of 30 min, diluted with oxolane (5 mL) and 25% H_2O_2 was added (0.6 mL) followed by aqueous NaOH (3 M, 0.9 mL). The reaction mixture was diluted with dichloromethane (50 mL), washed with HCl (5%, 60 mL), water, and saturated aqueous $NaHCO_3$, and dried ($MgSO_4$). Removal of solvent under reduced pressure and chromatography of the residue (hexane–ethyl acetate (1:1)) afforded **12** (102 mg, 66%) as a colorless syrup: $[\alpha]_D$ +72.5° (*c* 0.2, chloroform); ^1H NMR ($CDCl_3$, 250 MHz) δ 4.75 (2d, 2 H, OCH_2O), 4.32 (ddd unsolved, 1 H, H-3), 4.10–3.52 (m, 7 H, H-1a,1b,4,5,6,7a,7b), 3.44 (2d, 2 H, $OCH_2CH_2SiMe_3$), 2.27 (s, 1 H, OH), 1.79 (m, 2 H, H-2a,2b), 1.44, 1.35, 1.30, 1.29 (4s, 12 H, 4×Me), 0.90 (m, 2 H, CH_2SiMe_3), 0 (s, 9 H, $SiMe_3$); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 108.9, 108.2 (2×$C(Me)_2$), 95.4 (OCH_2O), 78.9, 76.6, 76.3, 75.1 (C-3,4,5,6), 66.7, 65.5, 60.5 (C-1,7,$OCH_2CH_2SiMe_3$), 32.4 (C-2), 27.6, 26.0, 25.9, 25.0 (4×Me), 17.8 (CH_2SiMe_3), −1.5 ($SiMe_3$); MS (CI) m/z 424 ($M + NH_4^+$), 407 (MH^+). Anal. Calcd for $C_{19}H_{38}O_7Si$: C, 56.13; H, 9.42. Found: C, 56.07; H, 9.57.

2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-pivaloyl-D-*manno*-heptitol (13). To a solution of **11** (5.34 g, 15.6 mmol) in dry oxolane (60 mL) was dropwise added 9-BBN (60 mL, 0.5M in oxolane, 30 mmol) at 0 °C. The reaction mixture was stirred

at 0 °C, warmed to room temperature over a period of 2 h, and diluted with oxolane (60 mL), and 25% H_2O_2 was added (75 mL) at 0 °C, followed by aqueous NaOH 4% (60 mL). The reaction mixture was diluted with chloroform (100 mL), washed with HCl 5% (60 mL), water, and saturated aqueous $NaHCO_3$, and dried ($MgSO_4$). Removal of solvent under reduced pressure and chromatography of the residue (hexane–ethyl acetate (1:1)) afforded **13** (4 g, 71%) as a colorless syrup: $[\alpha]_D$ −5° (*c* 0.4, chloroform); ^1H NMR ($CDCl_3$, 250 MHz) δ 5.14 (dd unsolved, $J_{5/6}$ = 6 Hz, 1 H, H-5), 4.42–4.28 (m, 2 H, H-3,4), 4.20 (ddd, $J_{6/7a}$ = 6 Hz, $J_{6/7b}$ = 7 Hz, 1 H, H-6), 4.09 (dd, $J_{7a/7b}$ = 8.5 Hz, 1 H, H-7a), 3.95 (dd, 1 H, H-7b), 3.86–3.71 (m, 3 H, OH-1,H-1a,1b), 1.67 (m, 2 H, H-2a,2b), 1.50, 1.34, 1.32, 1.30 (4s, 12 H, 4×Me), 1.19 (s, 9 H, *t*-Bu); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 177.5 (CO), 108.9, 108.5 (2×*C*(Me)$_2$), 76.6, 75.8, 75.5, 70.4 (C-3,4,5,6), 65.9, 61.0 (C-1,7), 38.3 (*C*(Me)$_3$), 32.4 (C-2), 27.1 (C(*Me*)$_3$), 26.7, 26.4, 25.3, 25.2 (4×Me); MS (CI) *m*/*z* 378 (M + NH_4^+), 361 (MH^+). Anal. Calcd for $C_{18}H_{32}O_7$: C, 59.99; H, 8.95. Found: C, 59.68; H, 8.94.

2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-[[(trimethylsilyl)ethoxy]methyl]-D-*manno*-heptonic Acid (14). To a biphasic solution of **12** (200 mg, 0.494 mmol) in carbon tetrachloride (0.38 mL), acetonitrile (0.38 mL) and water (0.57 mL) were added ruthenium trichloride hydrate (11 mg) and sodium metaperiodate (529 mg). The mixture was stirred vigorously for 90 min at room temperature, then filtered through a Celite pad, dried ($MgSO_4$), and concentrated. The crude residue **14** (197 mg, 95%) was used for the next reaction without further purification.

2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-pivaloyl-D-*manno*-heptonic Acid (15). To a biphasic solution of **13** (400 mg, 1.11 mmol) in carbon tetrachloride (0.88 mL), acetonitrile (0.88 mL), and water (1.32 mL) were added ruthenium trichloride hydrate (6 mg) and sodium metaperiodate (1.19 g). The mixture was stirred vigorously for 1 h at room temperature, then filtered through a Celite pad, dried ($MgSO_4$), and concentrated. The crude residue **15** (382 mg, 92%) was used for the next reaction without further purification.

Methyl 2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-[[(trimethylsilyl)ethoxy]methyl]-D-*manno*-heptonate (16). To a solution of crude **14** (197 mg, 0.468 mmol) in dichloromethane (1 mL) at 0 °C was added an etheral diazomethane solution until complete disappearance of the starting material (TLC). Removal of solvent under reduced pressure and chromatography of the residue (hexane–ethyl acetate (9:2)) afforded **16** (147 mg, 70%) as a colorless syrup: $[\alpha]_D$ +55° (*c* 0.4, chloroform); ^1H NMR ($CDCl_3$, 400 MHz) δ 4.93 (d, J_{gem} = 7 Hz, 1 H, OCH_2O), 4.84 (d, 1 H, OCH_2O), 4.65 (ddd, $J_{3/4}$ = 6.5 Hz, $J_{2a/3}$ = 4.5 Hz, $J_{2b/3}$ = 10 Hz, 1 H, H-3), 4.20 (dd, $J_{4/5}$ = 6.5 Hz, 1 H, H-5), 4.16 (dd, $J_{7a/7b}$ = 13 Hz, $J_{6/7a}$ = 7.5 Hz, 1 H, H-7a), 4.08 (ddd, $J_{6/7b}$ = 6.5 Hz, 1 H, H-6), 3.97 (dd, 1 H, H-7b), 3.76 (dd, 1 H, H-4), 3.75 (s, 3 H, COO*Me*), 3.67 (2dd, 2 H, O$CH_2$$CH_2$SiMe$_3$), 2.83 (dd, $J_{2a/2b}$ = 15 Hz, 1 H, H-2a), 2.70 (dd, 1 H, H-2b), 1.51, 1.42, 1.38, 1.37 (4s, 12 H, 4×Me), 0.99 (2ddd, J_{gem} = 13 Hz, J_{OCH} = 9 Hz, J_{OCH} = 1.5 Hz, 2 H, CH_2SiMe$_3$), 0.06 (s, 9 H, Si*Me*$_3$); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 171.5 (C-1), 109.1, 108.4 (2×*C*(Me)$_2$), 95.5 (OCH_2O), 78.8, 76.6, 75.5, 74.0 (C-3,4,5,6), 67.1, 65.7 (C-7,O$CH_2$$CH_2$SiMe$_3$), 51.5 (OMe), 35.8 (C-2), 27.6, 26.1, 25.9, 25.0 (4×Me), 17.9 (CH_2SiMe$_3$), −1.5 (Si*Me*$_3$); MS (CI) *m*/*z* 452 (M + NH_4^+). Anal. Calcd for $C_{20}H_{38}O_8Si$: C, 55.27; H, 8.81. Found: C, 55.46; H, 8.94.

Methyl 2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-pivaloyl-D-*manno*-heptonate (17). To a solution of crude **15** (382 mg, 1.02 mmol) in dichloromethane (1 mL) at 0 °C was added an etheral diazomethane solution until complete disappearance of the starting material (TLC). Removal of solvent under reduced pressure and chromatography of the residue (hexane–ethyl acetate (1:1)) afforded **17** (393 mg, 91%) as a colorless syrup: $[\alpha]_D$ −8° (*c* 0.2, chloroform); ^1H NMR ($CDCl_3$, 400 MHz) δ 5.16 (dd, $J_{4/5}$ = 2.5 Hz, $J_{5/6}$ = 6 Hz, 1 H, H-5), 4.70 (ddd, $J_{3/4}$ = 7.5 Hz, $J_{2b/3}$ = 6.5 Hz, $J_{2a/3}$ = 7.5 Hz, 1 H, H-3), 4.47 (dd, 1 H, H-4), 4.26 (ddd, $J_{6/7a}$ = 6 Hz, $J_{6/7b}$ = 6 Hz, 1 H, H-6), 4.04 (dd, $J_{7a/7b}$ = 8.5 Hz, 1 H, H-7a), 3.87 (dd, 1 H, H-7b), 3.75 (s, 3 H, OMe), 2.62 (dd, $J_{2a/2b}$ = 15 Hz, 1 H, H-2a), 2.54 (dd, 1 H, H-2b), 1.56, 1.42, 1.41, 1.37 (4s, 12 H, 4×Me), 1.28 (s, 9 H, *t*-Bu); MS (CI) *m*/*z* 406 (M + NH_4^+), 389 (MH^+). Anal. Calcd for $C_{19}H_{32}O_8$: C, 58.75; H, 8.30. Found: C, 58.70; H, 8.35.

1,3-Dideoxy-4,5:7,8-di-*O*-isopropylidene-2-*O*-methyl-6-*O*-[[(trimethylsilyl)ethoxy]methyl]-D-*manno*-oct-1-enitol (18). To a solution of **16** (280 mg, 0.64 mmol) in dry pyridine (2 mL) was added a 0.2 M solution of Tebbe reagent[17] in dry toluene[18] (4 mL, 0.8 mmol) at −45 °C under argon. The mixture was stirred at −45 °C for 1 h and then at 0 °C for 30 min. It was cooled to −10 to −15 °C, and 15% sodium hydroxide was added (7 mL). The cold bath was removed, and the reaction mixture was diluted with ethyl acetate (50 mL). Stirring was continued for 30 min, and the residue was removed by filtration through a Celite pad. The filter cake was washed with ethyl acetate, and the product was purified by chromatography [hexane–ethyl acetate (3:1) (+0.1% Et_3N)] to afford **18** (79%) as a syrup: ^1H NMR ($CDCl_3$, 250 MHz) δ 4.88 (2d, 2 H, OCH_2O), 4.41 (ddd unsolved, 1 H, H-1a), 4.15–3.88 (m, 7 H, H-1b,4,5,6,7,8a,8b), 3.68 (ddd, J_{gem} = 14 Hz, 2 H, O$CH_2$$CH_2$SiMe$_3$), 3.56 (s, 3 H, OMe), 2.54 (dd, $J_{3a/4}$ = 5 Hz, $J_{3a/3b}$ = 13.5 Hz, 1 H, H-3a), 2.41 (dd, $J_{3b/4}$ = 9 Hz, 1 H, H-3b), 1.48, 1.40, 1.34, 1.34 (4s, 12 H, 4×Me), 0.94 (dd, J_{OCH} = 10 Hz, J_{OCH} = 6.5 Hz, 2 H, CH_2SiMe$_3$), 0 (s, 9 H, Si*Me*$_3$); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 160.6 (C-2), 108.9, 108.1 (2×*C*(Me)$_2$), 95.5 (OCH_2O), 82.6 (C-1), 78.7, 76.9, 75.2, 75.0 (C-4,5,6,7), 66.6, 65.6 (C-8,O$CH_2$$CH_2$SiMe$_3$), 54.7 (OMe), 35.6 (C-3), 27.5, 26.2, 26.0, 25.2 (4×Me), 17.9 (CH_2SiMe$_3$), −1.5 (Si*Me*$_3$); MS (CI) *m*/*z* 450 (M + NH_4^+).

1,3-Dideoxy-4,5:7,8-di-*O*-isopropylidene-2-*O*-methyl-6-*O*-pivaloyl-D-*manno*-oct-1-enitol (19). It was prepared from ester **17**, as previously described for the synthesis of **18**. Column chromatography [hexane–ethyl acetate (5:1) (+0.1% Et_3N)] afforded **19** (80%) as a syrup, $[\alpha]_D$ −13° (*c* 0.5, chloroform); ^1H NMR (C_6D_6N, 400MHz) δ 5.02 (dd, $J_{5/6}$ = 2 Hz, $J_{6/7}$ = 5.5 Hz, 1 H, H-6), 4.90–4.71 (m, 2 H, H-1a,1b), 4.67 (ddd, $J_{4/5}$ = 6.5 Hz, $J_{3b/4}$ = 7.5 Hz, $J_{3a/4}$ = 6.5 Hz, 1 H, H-4), 4.49 (dd, 1 H, H-5), 4.25 (ddd, $J_{7/8a}$ = 6.5 Hz, $J_{7/8b}$ = 6.5 Hz, 1 H, H-7), 4.01 (dd, $J_{8a/8b}$ = 8.5 Hz, 1 H, H-8a), 3.86 (dd, 1 H, H-8b), 3.53 (s, 3 H, OMe), 2.87 (dd, $J_{3a/3b}$ = 10.5 Hz, 1 H, H-3a), 2.59 (dd, 1 H, H-3b), 1.55, 1.41, 1.38, 1.36 (4s, 12 H, 4×Me), 1.29 (s, 9 H, *t*-Bu); MS (CI) *m*/*z* 404 (M + NH_4^+), 387 (MH^+). Anal. Calcd for $C_{20}H_{34}O_7$: C, 62.16; H, 8.87. Found: C, 62.01; H, 8.71.

1,3-Dideoxy-4,5:7,8-di-*O*-isopropylidene-2-*O*-methyl-D-*manno*-oct-1-enitol (20). From **18**: To a solution of **18** (10 mg, 23 μmol) in dry oxolane (10 μL) were added tetrabutylammonium fluoride (19 mg, 60 μmol), hexamethylphosphoramide (20 μL), and ethylenediamine (30 μL, 23 μmol). The reaction mixture was stirred for 18 h at 60 °C. Removal of solvent under reduced pressure and chromatography of the residue [hexane–ethyl acetate (3:1) (+0.1% Et_3N)] gave **20** (72%) as a colorless syrup: $[\alpha]_D$ −17° (*c* 0.33, chloroform); ^1H NMR ($CDCl_3$, 250 MHz) δ 4.56 (ddd, $J_{4/5}$ = 7 Hz, $J_{3/4}$ = 7 Hz, $J_{3b/4}$ = 6 Hz, 1 H, H-4), 4.36 (dd, $J_{5/6}$ = 1 Hz, 1 H, H-5), 4.20–3.97 (m, 5 H, H-1a,1b,7,8a,8b), 3.65 (ddd, $J_{6/OH}$ = 8 Hz, $J_{6/7}$ = 7.5 Hz, 1 H, H-6), 3.59 (s, 3 H, OMe), 2.64 (m, 2 H, H-3a,3b), 2.19 (d, 1 H, OH-6), 1.52, 1.40, 1.40, 1.36 (4s, 12 H, 4×Me); MS (CI) *m*/*z* 271 (M − OMe), 285 (M − Me). Anal. Calcd for $C_{15}H_{26}O_6$: C, 59.59; H, 8.67. Found: C, 59.49; H, 8.73.

From **19**: To a solution of **19** (90 mg, 0.233 mmol) in dry oxolane (1 mL) was slowly added lithium aluminum hydride (56 mg, 1.47 mmol) at 0 °C, and the reaction mixture was stirred for 30 min. Water was slowly added at 0 °C, and the residue was removed by filtration through a Celite pad. The filter cake was washed with ethyl acetate, and the product was chromatographed [hexane–ethyl acetate (3:1) (+0.1% Et_3N)] to give **20** (90%) as a colorless syrup. It was identical with the compound prepared from **18**.

(Methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranosid-6-yl) 2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-[[(trimethylsilyl)ethoxy]methyl]-D-*manno*-heptonate (22). Crude **14** (197 mg, 0.469 mmol) was dissolved in dry dichloromethane (0.5 mL), to which were added 1,3-dicyclohexylcarbodiimide (110 mg, 0.533 mmol), **21** (268 mg, 0.577 mmol), and 4-(dimethylamino)pyridine (64 mg, 0.524 mmol). The solution was stirred vigorously at room temperature for 30 min and filtered through a Celite pad. Removal of solvent under reduced pressure and chromatography of the residue (hexane–ethyl acetate (3:1)) afforded **22** (67%) as a colorless syrup, $[\alpha]_D$ +43° (*c* 0.75, chloroform); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.41–7.28 (m, 15 H, 3Ph), 5.03 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.91 (d, J_{gem} = 7 Hz, 1 H, OCH_2O), 4.89 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.87 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.83 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.81 (d, 1 H, OCH_2O), 4.70 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.63 (m, 1 H, H-3), 4.62 (d, $J_{1'/2'}$ = 3.5 Hz,

1 H, H-1′), 4.60 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.38 (d, $J_{5'/6'}$ = 3.5 Hz, 2 H, H-6′a,6′b), 4.19 (dd, $J_{3/4}$ = 5.5 Hz $J_{4/5}$ = 6.5 Hz, 1 H, H-4), 4.15 (dd, $J_{7a/7b}$ = 7 Hz, $J_{6/7a}$ = 7 Hz, 1 H, H-7a), 4.06 (ddd, $J_{6/7b}$ = 7.5 Hz, $J_{5/6}$ = 7 Hz, 1 H, H-6), 4.04 (dd, $J_{2'/3'}$ = 9 Hz, $J_{3'/4'}$ = 8.5 Hz, 1 H, H-3′), 3.95 (dd, 1 H, H-7b), 3.85 (dd, $J_{5'/6'}$ = 3.5 Hz, $J_{4'/5'}$ = 10 Hz, 1 H, H-5′), 3.73 (dd, 1 H, H-5), 3.66 (m, 2 H, $OCH_2CH_2SiMe_3$), 3.55 (dd, 1 H, H-2′), 3.52 (dd, 1 H, H-4′), 3.40 (s, 3 H, OMe), 2.81 (dd, $J_{2a/3}$ = 4 Hz, $J_{2a/2b}$ = 15 Hz, 1 H, H-2a), 2.67 (dd, $J_{2b/3}$ = 10 Hz, 1 H, H-2b), 1.47, 1.40, 1.35, 1.34 (4s, 12 H, 4×Me), 0.98 (2dd, 2 H, CH_2SiMe_3), 0.06 (s, 9 H, $SiMe_3$); MS (CI) m/z 884 (M + NH_4^+). Anal. Calcd for $C_{47}H_{66}O_{13}Si$: C, 65.10; H, 7.67. Found: C, 64.91; H, 7.88.

(Methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranosid-6-yl) 2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-pivaloyl-D-*manno*-heptonate (23). It was prepared from **15**, as previously described for the synthesis of **22**. Column chromatography (hexane–ethyl acetate (3:1)) afforded **23** (78%) as a colorless syrup: $[\alpha]_D$ +11° (*c* 0.7, chloroform); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.45–7.27 (m, 15 H, 3Ph), 5.11 (dd, $J_{5/6}$ = 5.5 Hz, $J_{4/5}$ = 2.5 Hz, 1 H, H-5), 5.05 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.89 (2d, J_{gem} = 11 Hz, J_{gem} = 11 Hz, 2 H, $2CH_2Ph$), 4.82 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.71 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.67 (m, 1 H, H-3), 4.64 (d, $J_{1'/2'}$ = 3.5 Hz, 1 H, H-1′), 4.57 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.44 (dd, $J_{3/4}$ = 6.5 Hz, 1 H, H-4), 4.36 (m, 2 H, H-6′a,6′b), 4.24 (ddd, $J_{6/7a}$ = 5.5 Hz, $J_{6/7b}$ = 7 Hz, 1 H, H-6), 4.04 (dd, $J_{2'/3'}$ = 9.5 Hz, $J_{3'/4'}$ = 9 Hz, 1 H, H-3′), 4.00 (dd, $J_{7a/7b}$ = 8 Hz, 1 H, H-7a), 3.85 (dd, 1 H, H-7b), 3.84 (m, 1 H, H-5′), 3.57 (dd, 1 H, H-2′), 3.51 (dd, $J_{4'/5'}$ = 9.5 Hz, 1 H, H-4′), 3.40 (s, 3 H, OMe), 2.56 and 2.55 (2d, 2 H, H-2a,2b), 1.50, 1.41, 1.36, 1.32 (4s, 12 H, 4×Me), 1.25 (s, 9 H, *t*-Bu); MS (CI) m/z 839 (M + NH_4^+). Anal. Calcd for $C_{46}H_{60}O_{13}$: C, 67.30; H, 7.37. Found: C, 67.00; H, 7.42.

1,3-Dideoxy-4,5:7,8-di-*O*-isopropylidene-2-*O*-(methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranosid-6-yl)-6-*O*-[[(trimethylsilyl)ethoxy]methyl]-D-*manno*-oct-1-enitol (24). It was prepared from **22**, as previously described for the synthesis of **18**. Column chromatography [hexane–ethyl acetate (5:1) (+0.1% Et_3N)] afforded **24** (67%) as a syrup: $[\alpha]_D$ +34° (*c* 1, chloroform); ^1H NMR (C_6D_6, 250 MHz) δ 7.38–7.04 (m, 15 H, 3Ph), 5.06 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 5.04 (s, 2 H, CH_2Ph), 4.99 (d, 1 H, OCH_2O), 4.86 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.64 (m, 3 H, OCH_2O, H-1′,4), 4.59 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.51 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.33–4.00 (m, 8 H, H-1a,1b,5,6,7,8a,8b,3′), 3.95–3.70 (m, 6 H, H-4′,5′,6′a,6′b, $OCH_2CH_2SiMe_3$), 3.64 (dd, $J_{1'/2'}$ = 3.5 Hz, $J_{2'/3'}$ = 9.5 Hz, 1 H, H-2′), 3.22 (s, 3 H, OMe), 2.87 (dd, $J_{3a/4}$ = 5.5 Hz, $J_{3a/3b}$ = 14 Hz, 1 H, H-3a), 2.68 (dd, $J_{3b/4}$ = 8 Hz, 1 H, H-3b), 1.57, 1.44, 1.33, 1.28 (4s, 12 H, 4×Me), 1.00 (2d, J_{CH_2O} = 8.5 Hz, 2 H, CH_2SiMe_3), 0 (s, 9 H, $SiMe_3$); MS (CI) m/z 882 (M + NH_4^+).

1,3-Dideoxy-4,5:7,8-di-*O*-isopropylidene-2-*O*-(methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranosid-6-yl)-6-*O*-pivaloyl-D-*manno*-oct-1-enitol (25). It was prepared from **23**, as previously described for the synthesis of **18**. Column chromatography [hexane–ethyl acetate (3:1) (+0.1% Et_3N)] afforded **25** (81%) as a colorless syrup: $[\alpha]_D$ +5.5° (*c* 0.55, chloroform); ^1H NMR (C_6D_5N, 400 MHz) δ 7.60–7.17 (m, 15 H, 3Ph), 5.70 (dd, $J_{6/5}$ = 2 Hz, $J_{6/7}$ = 5.5 Hz, 1 H, H-6), 5.15 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 5.09 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 5.04 (d, $J_{1'/2'}$ = 3.5 Hz, 1 H, H-1′), 4.99 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.93 (s, 2 H, CH_2Ph), 4.81 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.72 (ddd, $J_{4/5}$ = 6.5 Hz, $J_{3a/4}$ = 6.5 Hz, $J_{3b/4}$ = 7 Hz, 1 H, H-4), 4.52 (dd, 1 H, H-5), 4.44 (ddd, $J_{7/8a}$ = 6.5 Hz, $J_{7/8b}$ = 12 Hz, 1 H, H-7), 4.28 (dd, $J_{3'/2'}$ = 9.5 Hz, $J_{3'/4'}$ = 9.5 Hz, 1 H, H-3′), 4.24 (d, $J_{1a/1b}$ = 2 Hz, 1 H, H-1a), 4.17–3.99 (m, 6 H, H-1b,8a,8b,5′,6′a,6′b), 3.94 (dd, $J_{4'/5'}$ = 9.5 Hz, 1 H, H-4′), 3.83 (dd, 1 H, H-2′), 3.42 (s, 3 H, OMe), 2.63–2.61 (2d, 2 H, H-3a,3b), 1.60, 1.43, 1.36, 1.33 (4s, 12 H, 4×Me), 1.30 (s, 9 H, *t*-Bu); MS (CI) m/z 820 (MH^+), 837 (M + NH_4^+). Anal. Calcd for $C_{47}H_{62}O_{12}$: C, 68.93; H, 7.63. Found: C, 68.53; H, 7.67.

1,3-Dideoxy-4,5:7,8-di-*O*-isopropylidene-2-*O*-(methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranosid-6-yl)-D-*manno*-oct-1-enitol (26). It was prepared either from **24** or **25**, as previously described for the synthesis of **20**. From **24**: Column chromatography [hexane–ethyl acetate (2:1) (+0.1% Et_3N)] afforded **26** (80%) as a colorless syrup: $[\alpha]_D$ +44° (*c* 0.9, pyridine); ^1H NMR (C_6D_5N, 400 MHz) δ 7.57–7.18 (m, 15 H, 3Ph), 5.13 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 5.02 (d, $J_{1'/2'}$ = 3.5 Hz, 1 H, H-1′), 5.00 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.95 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.91 (s, 1 H, OH), 4.81 (ddd, $J_{4/5}$ = 7 Hz, $J_{3a/4}$ = 8.5 Hz, $J_{3b/4}$ = 5 Hz, 1 H, H-4), 4.80 (s, 2 H, CH_2Ph), 4.73 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.56 (dd, $J_{5/6}$ = 1 Hz, 1 H, H-5), 4.44 (ddd, $J_{7/8a}$ = 6.5 Hz, $J_{7/8b}$ = 6.5 Hz, $J_{6/7}$ = 7 Hz, 1 H, H-7), 4.33 (dd, $J_{8a/8b}$ = 7 Hz, 1 H, H-8a), 4.27 (dd, 1 H, H-8b), 4.25 (dd, $J_{3'/4'}$ = 9 Hz, $J_{2'/3'}$ = 9.5 Hz, 1 H, H-3′), 4.20 (d, $J_{1a/1b}$ = 1 Hz, 1 H, H-1a), 4.16 (d, 1 H, H-1b), 4.11–4.01 (m, 4 H, H-6,5′,6′a,6′b), 3.89 (dd, $J_{4'/5'}$ = 9 Hz, 1 H, H-4′), 3.78 (dd, 1 H, H-2′), 3.40 (s, 3 H, OMe), 3.10 (dd, $J_{3a/3b}$ = 15 Hz, 1 H, H-3a), 2.98 (dd, 1 H, H-3b), 1.62, 1.48, 1.39, 1.38 (4s, 12 H, 4×Me); MS (CI) m/z 753 (M + NH_4^+). Anal. Calcd for $C_{42}H_{54}O_{11}$: C, 68.65; H, 7.41. Found: C, 68.68; H, 7.35.

From **25**: The same compound was obtained in 93% yield.

Methyl (1,3-Dideoxy-1-iodo-4,5:7,8-di-*O*-isopropylidene-α-D-*manno*-octulopyranosyl)-(2→6)-(2,3,4-tri-*O*-benzyl-α-D-glucopyranoside) (27). It was prepared from **26**, as previously described for the synthesis of **7**. Column chromatography (hexane–ethyl acetate (3:1)) afforded **27** (92%) as a colorless syrup: $[\alpha]_D$ +12° (*c* 0.5, chloroform); ^1H NMR ($CDCl_3$, 250 MHz) δ 7.40–7.21 (m, 15 H, 3Ph), 4.99 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.87 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.80 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.77 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.66 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.61 (d, $J_{1'/2'}$ = 4 Hz, 1 H, H-1′), 4.59 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.45 (ddd, $J_{4/5}$ = 7 Hz, $J_{3a/4}$ = 4.5 Hz, $J_{3b/4}$ = 3.5 Hz, 1 H, H-4), 4.23 (ddd, $J_{7/8a}$ = 0.5 Hz, $J_{7/8b}$ = 4 Hz, $J_{6/7}$ = 8 Hz, 1 H, H-7), 4.18 (dd, $J_{5/6}$ = 2 Hz, 1 H, H-5), 4.12 (dd, $J_{8a/8b}$ = 8 Hz, 1 H, H-8a), 4.06 (dd, 1 H, H-8b), 3.96 (dd, $J_{3'/4'}$ = 6.5 Hz, $J_{2'/3'}$ = 9.5 Hz, 1 H, H-3′), 3.81 (ddd, $J_{4'/5'}$ = 8.5 Hz, $J_{5'/6'b}$ = 1 Hz, $J_{5'/6'a}$ = 2 Hz, 1 H, H-5′), 3.67 (dd, $J_{6'a/6'b}$ = 10 Hz, 1 H, H-6′a), 3.60 (dd, 1 H, H-6), 3.51 (dd, 1 H, H-2′), 3.46 (d, $J_{1a/1b}$ = 11 Hz, 1 H, H-1a), 3.36 (s, 3 H, OMe), 3.34 (dd, 1 H, H-6′b), 3.24 (dd, 1 H, H-4′), 3.20 (d, 1 H, H-1b), 2.45 (dd, $J_{3a/3b}$ = 15 Hz, 1 H, H-3a), 1.70 (dd, 1 H, H-3b), 1.42, 1.34, 1.32, 1.32 (4s, 12 H, 4×Me); MS (CI) m/z 878 (M + NH_4^+). Anal. Calcd for $C_{42}H_{53}O_{11}I$: C, 57.41; H, 6.31. Found: C, 57.35; H, 6.29.

Methyl (1-*O*-Acetyl-3-deoxy-4,5:7,8-di-*O*-isopropylidene-α-D-*manno*-octulopyranosyl)-(2→6)-(2,3,4-tri-*O*-benzyl-α-D-glucopyranoside) (28). It was prepared from **27**, as previously described for the synthesis of **8**. Column chromatography (hexane–ethyl acetate (2:1)) afforded **28** (68%) as a colorless syrup (with 30% of starting material recovered): $[\alpha]_D$ +26° (*c* 0.7, chloroform); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.41–7.28 (m, 15 H, 3Ph), 5.01 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.88 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.84 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.81 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.70 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.62 (d, $J_{1'/2'}$ = 4 Hz, 1 H, H-1′), 4.60 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.52 (ddd, $J_{4/5}$ = 7.5 Hz, $J_{3a/4}$ = 4 Hz, $J_{3b/4}$ = 3.5 Hz, 1 H, H-4), 4.30–4.23 (m, 2 H, H-5,7), 4.17 (d, $J_{1a/1b}$ = 7 Hz, 1 H, H-1a), 4.14 (d, 1 H, H-1b), 4.09 (dd, $J_{8a/8b}$ = 9 Hz, $J_{7/8a}$ = 4.5 Hz, 1 H, H-8a), 4.03 (d, $J_{3'/4'}$ = 10 Hz, 1 H, H-3′), 4.01 (dd, $J_{7/8b}$ = 0.5 Hz, 1 H, H-8b), 3.77 (ddd, $J_{4'/5'}$ = 9 Hz, $J_{5'/6'b}$ = 7 Hz, $J_{5'/6'a}$ = 1.5 Hz, 1 H, H-5′), 3.67 (dd, $J_{5/6}$ = 2 Hz, $J_{6/7}$ = 8 Hz, 1 H, H-6), 3.63 (dd, $J_{6'a/6'b}$ = 10 Hz, 1 H, H-6′a), 3.55 (d, 1 H, H-2′), 3.52 (dd, 1 H, H-6′b), 3.39 (s, 3 H, OMe), 3.33 (dd, 1 H, H-4′), 2.42 (dd, $J_{3a/3b}$ = 15.5 Hz, 1 H, H-3a), 2.00 (s, 3 H, $COCH_3$), 1.70 (dd, 1 H, H-3b), 1.47, 1.38, 1.36, 1.35 (4s, 12 H, 4×Me); MS (CI) m/z 810 (M + NH_4^+). Anal. Calcd for $C_{44}H_{56}O_{13},H_2O$: C, 65.17; H, 7.21. Found: C, 65.28; H, 7.28.

Methyl (3-Deoxy-4,5:7,8-di-*O*-isopropylidene-α-D-*manno*-octulopyranosyl)-(2→6)-(2,3,4-tri-*O*-benzyl-α-D-glucopyranoside) (29). It was prepared from **28**, as previously described for the synthesis of **8**. Column chromatography (hexane–ethyl acetate (1:1)) afforded **29** (98%) as a colorless syrup: $[\alpha]_D$ +7° (*c* 0.15, chloroform); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.42–7.30 (m, 15 H, 3Ph), 5.01 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.88 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.86 (d, J_{gem} = 10.5 Hz, 1 H, CH_2Ph), 4.82 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.70 (d, J_{gem} = 10.5 Hz, 1 H, CH_2Ph), 4.69 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph + d, $J_{1'/2'}$ = 3.5 Hz, 1 H, H-1′), 4.55 (ddd, $J_{4/5}$ = 7 Hz, $J_{3a/4}$ = 3.5 Hz, $J_{3b/4}$ = 4 Hz, 1 H, H-4), 4.34–4.25 (m, 2 H, H-5,7), 4.10 (dd, $J_{8a/8b}$ = 8.5 Hz, $J_{7/8a}$ = 6 Hz, 1 H, H-8a), 3.99 (d, 1 H, H-8b), 3.97 (dd unsolved, $J_{2'/3'}$ = 9.5 Hz, 1 H, H-3′), 3.82–3.67 (m, 5 H, H-1a,1b,4′,5′,6′a), 3.62 (dd, $J_{5/6}$ = 2 Hz, $J_{6/7}$ = 6 Hz, 1 H, H-6), 3.56 (d, 1 H, H-2′), 3.53 (dd unsolved, 1 H, H-6′b), 3.39 (s, 3 H, OMe), 2.61 (dd, $J_{3a/3b}$ = 15.5 Hz, 1 H, H-3a), 1.54 (dd, 1 H, H-3b), 1.46, 1.41, 1.41, 1.36 (4s, 12 H, 4×Me); MS (CI) m/z 768 (M + NH_4^+).

Anal. Calcd for $C_{42}H_{54}O_{12},H_2O$: C, 65.61; H, 7.34. Found: C, 65.77; H, 7.36.

Methyl (Methyl 3-deoxy-4,5:7,8-di-*O*-isopropylidene-α-D-*manno*-octulosonate)-(2→6)-(2,3,4-tri-*O*-benzyl-α-D-glucopyranoside) (30). It was prepared from **29**, as previously described for the synthesis of **9**. Column chromatography (hexane–ethyl acetate (2:1)) afforded crystalline **30** (68%): mp 101 °C (hexane); $[\alpha]_D$ +51° (*c* 0.2, chloroform); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.41–7.25 (m, 15 H, 3Ph), 5.00 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.87 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.81 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.80 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.69 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.63 (d, $J_{1'/2'}$ = 3.5 Hz, 1 H, H-1'), 4.58 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.51 (ddd, $J_{4/5}$ = 7.5 Hz, $J_{3a/4}$ = 4 Hz, $J_{3b/4}$ = 3 Hz, 1 H, H-4), 4.39 (ddd, $J_{6/7}$ = 6 Hz, $J_{7/8a}$ = 1.5 Hz, $J_{7/8b}$ = 3 Hz, 1 H, H-7), 4.30 (dd, $J_{5/6}$ = 2 Hz, 1 H, H-5), 4.12 (dd, $J_{8a/8b}$ = 8.5 Hz, 1 H, H-8a), 4.10 (dd, 1 H, H-8b), 4.00 (dd, $J_{2'/3'}$ = 9.5 Hz, $J_{3'/4'}$ = 9.5 Hz, 1 H, H-3'), 3.81–3.60 (m, 4 H, H-6,5',6'a,6'b), 3.69 (s, 3 H, COO*Me*), 3.54 (dd, 1 H, H-2'), 3.40 (s, 3 H, OMe), 3.32 (dd, $J_{4'/5'}$ = 9.5 Hz, 1 H, H-4'), 2.81 (dd, $J_{3a/3b}$ = 15.5 Hz, 1 H, H-3a), 1.89 (dd, 1 H, H-3b), 1.43, 1.39, 1.38, 1.35 (4s, 12 H, 4×Me); MS (CI) *m/z* 796 ($M + NH_4^+$). Anal. Calcd for $C_{43}H_{54}O_{13}$: C, 66.30; H, 6.99. Found: C, 66.13; H, 7.41.

Methyl (Methyl 3-deoxy-α-D-*manno*-octulosonate)-(2→6)-(2,3,4-tri-*O*-benzyl-α-D-glucopyranoside) (31). To a mixture of 1:3 methanol–water (0.25 ml) were added trifluoroacetic acid (0.01 mL) and a solution of **30** (20 mg, 0.026 mmol) in methanol (1.5 mL). The reaction mixture was stirred for 48 h, and Na_2CO_3 was added. After filtration through a Celite pad, removal of solvent under reduced pressure and thin-layer chromatography with 14:3:3 ethyl–acetate–benzene–methanol gave crystalline **31** (90%): mp 100 °C (hexane); $[\alpha]_D$ +38° (*c* 0.1, chloroform); ^1H NMR (C_6D_5N, 400 MHz) δ 7.48–7.22 (m, 15 H, 3Ph), 5.09 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 5.00 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.96 (d, $J_{1'/2'}$ = 3.5 Hz, 1 H, H-1'), 4.93 (ddd, $J_{4/5}$ = 0.5 Hz, $J_{5/6}$ = 3.5 Hz, 1 H, H-5), 4.90 (m, 1 H, H-8a), 4.88 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.74 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.72 (s, 2 H, CH_2Ph), 4.54 (m, $J_{7/8a}$ = 7 Hz, $J_{6/7}$ = 7.5 Hz, $J_{7/8b}$ = 6 Hz, 2 H, H-6,7), 4.36 (dd, $J_{8a/8b}$ = 11 Hz, 1 H, H-8b), 4.22 (m, 4 H, H-3',6'a,6'b,4), 4.11 (ddd, $J_{4'/5'}$ = 8.5 Hz, $J_{5'/6'a}$ = 3 Hz, $J_{5'/6'b}$ = 6 Hz, 1 H, H-5'), 3.72 (dd, $J_{2'/3'}$ = 10 Hz, 1 H, H-2'), 3.62 (dd, $J_{3'/4'}$ = 9.5 Hz, 1 H, H-4'), 3.60 (s, 3 H, COO*Me*), 3.33 (s, 3 H, OMe), 2.78 (dd, $J_{3a/3b}$ = 12 Hz, $J_{3a/4}$ = 12 Hz, 1 H, H-3a), 2.72 (dd, $J_{3b/4}$ = 5 Hz, 1 H, H-3b); MS (CI) *m/z* 698 (M). Anal. Calcd for $C_{37}H_{46}O_{13}$: C, 63.60; H, 6.64. Found: C, 63.59; H, 6.20.

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-yl 2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-pivaloyl-D-*manno*-heptonate (33). It was prepared from **15** and **32**, as previously described for the synthesis of **22**. Column chromatography (hexane–ethyl acetate (3:1)) afforded **33** (80%) as a colorless syrup: $[\alpha]_D$ −14° (*c* 0.3, chloroform); ^1H NMR ($CDCl_3$, 400 MHz) δ 5.87 (d, $J_{1'/2'}$ = 4 Hz, 1 H, H-1'), 5.32 (d, $J_{3'/4'}$ = 2.5 Hz, 1 H, H-3'), 5.10 (dd, $J_{5/6}$ = 6.5 Hz, $J_{4/5}$ = 3 Hz, 1 H, H-5), 4.68 (dd, $J_{3/4}$ = 6.5 Hz, $J_{2/3}$ = 7 Hz, 1 H, H-3), 4.53 (d, 1 H, H-2'), 4.43 (dd, 1 H, H-4), 4.30–4.21 (m, 2 H, H-6,4'), 4.17–4.04 (m, 4 H, H-5',6'a,6'b,7a), 3.84 (dd, $J_{7a/7b}$ = 8.5 Hz, $J_{6/7b}$ = 6.5 Hz, 1 H, H-7b), 2.59 (d, 2 H, H-2a,2b), 1.55, 1.54, 1.44, 1.42, 1.39, 1.37, 1.36, 1.34 (8s, 24 H, 8×Me), 1.27 (s, 9 H, *t*-Bu); MS (CI) *m/z* 634 ($M + NH_4^+$). Anal. Calcd for $C_{30}H_{48}O_{13}$: C, 58.44; H, 7.85. Found: C, 58.55; H, 7.88.

1,3-Dideoxy-2-*O*-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)-4,5:7,8-di-*O*-isopropylidene-6-*O*-pivaloyl-D-*manno*-oct-1-enitol (34). It was prepared from **33**, as previously described for the synthesis of **18**. Column chromatography [hexane–ethyl acetate (3:1) (+0.1% Et_3N)] afforded **34** (87%) as a colorless syrup: $[\alpha]_D$ −23 ° (*c* 1, chloroform); ^1H NMR (C_6D_6, 400 MHz) δ 5.96 (d, $J_{1'/2'}$ = 4 Hz, 1 H, H-1'), 5.55 (dd, $J_{5/6}$ = 2 Hz, $J_{6/7}$ = 6.5 Hz, 1 H, H-6), 4.70 (d, 1 H, H-2'), 4.67–4.59 (m, 4 H, H-1a,4,3',4'), 4.43 (dd, $J_{4/5}$ = 0.5 Hz, 1 H, H-5), 4.40 (ddd, $J_{7/8b}$ = 6.5 Hz, $J_{7/8a}$ = 6.5 Hz, 1 H, H-7), 4.37 (d, $J_{1a/1b}$ = 3 Hz, 1 H, H-1b), 4.33 (dd, $J_{5'/6'a}$ = 5 Hz, $J_{5'/6'b}$ = 6 Hz, 1 H, H-5'), 4.30 (dd, $J_{6'a/6'b}$ = 8.5 Hz, 1 H, H-6'a), 4.25 (dd, 1 H, H-6'b), 4.16 (dd, $J_{8a/8b}$ = 8.5 Hz, 1 H, H-8a), 4.10 (dd, 1 H, H-8b), 2.60 (dd, $J_{3a/3b}$ = 14.5 Hz, $J_{3a/4}$ = 8 Hz, 1 H, H-3a), 2.50 (dd, $J_{3b/4}$ = 5 Hz, 1 H, H-3b), 1.65, 1.53, 1.52, 1.50, 1.44, 1.43, 1.40, 1.20 (8s, 24 H, 8×Me), 1.35 (s, 9 H, *t*-Bu); MS (CI) *m/z* 615 (MH^+), 632 ($M + NH_4^+$). Anal. Calcd for $C_{31}H_{50}O_{12}$: C, 60.58; H, 8.20. Found: C, 60.43; H, 8.25.

1,3-Dideoxy-2-*O*-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)-4,5:7,8-di-*O*-isopropylidene-D-*manno*-oct-1-enitol (35). It was prepared from **34**, as previously described for the synthesis of **20**. Column chromatography [hexane–ethyl acetate (2:1) (+0.1% Et_3N)] afforded crystalline **35** (90%): mp 87 °C (hexane); $[\alpha]_D$ −13° (*c* 0.2, chloroform); ^1H NMR (C_6D_6, 400 MHz) δ 5.91 (d, $J_{1'/2'}$ = 4 Hz, 1 H, H-1'), 4.72 (d, $J_{3'/4'}$ = 3 Hz, 1 H, H-4'), 4.68–4.60 (m, 4 H, H-2',3',5',4), 4.52 (dd, $J_{4/5}$ = 7 Hz, $J_{5/6}$ = 1.5 Hz, 1 H, H-5), 4.39 (d, $J_{1a/1b}$ = 2.5 Hz, 1 H, H-1a), 4.33 (dd, $J_{5'/6'a}$ = 4.5 Hz, $J_{6'a/6'b}$ = 9 Hz, 1 H, H-6'a), 4.30 (d, 1 H, H-1b), 4.27–4.16 (m, 4 H, H-7,8a,8b,6'b), 3.71 (ddd, $J_{6/OH}$ = 8.5 Hz, $J_{6/7}$ = 8 Hz, 1 H, H-6), 2.94 (dd, $J_{3a/3b}$ = 15 Hz, $J_{3a/4}$ = 8.5 Hz, 1 H, H-3a), 2.68 (dd, $J_{3b/4}$ = 4.5 Hz, 1 H, H-3b), 2.25 (d, 1 H, OH-6), 1.54, 1.53, 1.51, 1.50, 1.42, 1.41, 1.35, 1.20 (8s, 24 H, 8×Me); MS (CI) *m/z* 531 (MH^+), 548 ($M + NH_4^+$). Anal. Calcd for $C_{26}H_{42}O_{11}$: C, 58.86; H, 7.98. Found: C, 58.97; H, 8.20.

(1,3-Dideoxy-1-iodo-4,5:7,8-di-*O*-isopropylidene-α-D-*manno*-octulopyranosyl)-(2→3)-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) (36). It was prepared from **35**, as previously described for the synthesis of **7**. Column chromatography (hexane–ethyl acetate (2:1)) afforded crystalline **36** (90%): mp 58 °C (hexane); $[\alpha]_D$ +5° (*c* 1.5, chloroform); ^1H NMR ($CDCl_3$, 400 MHz) δ 5.84 (d, $J_{1'/2'}$ = 3.5 Hz, 1 H, H-1'), 4.80 (d, 1 H, H-2'), 4.49 (ddd, $J_{4/5}$ = 7.5 Hz, $J_{3b/4}$ = 3 Hz, $J_{3a/4}$ = 4 Hz, 1 H, H-4), 4.45 (d, $J_{3'/4'}$ = 3 Hz, 1 H, H-3'), 4.38 (dd, $J_{5'/6'a}$ = 6 Hz, $J_{6'a/6'b}$ = 12.5 Hz, 1 H, H-6'a), 4.28–4.12 (m, 3 H, H-5,7,4'), 4.12–3.93 (m, 4 H, H-8a,8b,5',6'b), 3.78 (dd, $J_{5/6}$ = 2 Hz, $J_{6/7}$ = 5 Hz, 1 H, H-6), 3.64 (s, 2 H, CH_2I), 2.57 (dd, $J_{3a/3b}$ = 15.5 Hz, 1 H, H-3a), 1.81 (dd, 1 H, H-3b), 1.47, 1.43, 1.43, 1.42, 1.34, 1.33, 1.29, 1.29 (8s, 24 H, 8×Me); MS (CI) *m/z* 657 (MH^+), 674 ($M + NH_4^+$). Anal. Calcd for $C_{26}H_{41}O_{11}I$: C, 47.57; H, 6.29. Found: C, 47.52; H, 6.33.

(1-*O*-Acetyl-3-deoxy-4,5:7,8-di-*O*-isopropylidene-α-D-*manno*-octulopyranosyl)-(2→3)-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) (37). It was prepared from **36**, as previously described for the synthesis of **8**. Column chromatography (hexane–ethyl acetate (2:1)) afforded crystalline **37** (84%): mp 125 °C (hexane); $[\alpha]_D$ −2° (*c* 0.25, chloroform); ^1H NMR (C_6D_6, 250 MHz) δ 6.00 (d, $J_{1'/2'}$ = 3 Hz, 1 H, H-1'), 4.77 (d, 1 H, H-2'), 4.54 (s, 2 H, H-1a,1b), 4.51–4.36 (m, 3 H, H-4,8a,3'), 4.31 (dd, $J_{5/4}$ = 7.5 Hz, $J_{5/6}$ = 2 Hz, 1 H, H-5), 4.28–4.19 (m, 2 H, H-7,6'a), 4.08 (dd, $J_{3'/4'}$ = 2 Hz, $J_{4'/5'}$ = 7.5 Hz, 1 H, H-4'), 4.01–3.92 (m, 2 H, H-8b,5'), 3.77 (dd, $J_{5'/6'b}$ = 2 Hz, $J_{6'a/6'b}$ = 7.5 Hz, 1 H, H-6'b), 3.58 (dd, $J_{6/7}$ = 4 Hz, 1 H, H-6), 2.43 (dd, $J_{3a/3b}$ = 15.5 Hz, $J_{3a/4}$ = 2.5 Hz, 1 H, H-3a), 2.05 (s, 3 H, $COCH_3$), 1.52, 1.44, 1.40, 1.37, 1.29, 1.28, 1.26, 1.05 (8s, 24 H, 8×Me), 1.29 (dd unsolved, 1 H, H-3b); MS (CI) *m/z* 606 ($M + NH_4^+$). Anal. Calcd for $C_{28}H_{44}O_{13}$: C, 57.14; H, 7.53. Found: C, 57.37; H, 7.67.

(3-Deoxy-4,5:7,8-di-*O*-isopropylidene-α-D-*manno*-octulopyranosyl)-(2→3)-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) (38). It was prepared from **37**, as previously described for the synthesis of **8**. Column chromatography (hexane–ethyl acetate (2:1)) afforded **38** (97%) as a colorless syrup: $[\alpha]_D$ −19° (*c* 1.7, chloroform); ^1H NMR ($CDCl_3$, 400 MHz) δ 5.78 (d, $J_{1'/2'}$ = 3 Hz, 1 H, H-1'), 4.70 (d, 1 H, H-2'), 4.51 (ddd, $J_{3b/4}$ = 0.5 Hz, $J_{3a/4}$ = 2.5 Hz, $J_{4/5}$ = 6 Hz, 1 H, H-4), 4.33–4.21 (m, 3 H, H-8a,5',6'a), 4.17 (dd, $J_{5/6}$ = 2 Hz, 1 H, H-5), 4.13–3.91 (m, 5 H, H-1a,1b,3',4',6'b), 3.80 (dd, $J_{6/7}$ = 5 Hz, H-6), 3.73 (ddd, $J_{7/8a}$ = 5 Hz, $J_{7/8b}$ = 0.5 Hz, 1 H, H-7), 3.52 (dd, $J_{8a/8b}$ = 12.5 Hz, 1 H, H-8b), 2.81 (dd, $J_{3a/3b}$ = 15.5 Hz, 1 H, H-3a), 1.46, 1.40, 1.40, 1.36, 1.32, 1.31, 1.27, 1.24 (8s, 24 H, 8×Me), 1.42 (dd, 1 H, H-3b); MS (CI) *m/z* 564 ($M + NH_4^+$). Anal. Calcd for $C_{26}H_{42}O_{12}$: C, 57.14; H, 7.74. Found: C, 57.02; H, 7.90.

(Methyl 3-deoxy-4,5:7,8-di-*O*-isopropylidene-α-D-*manno*-octulosonate)-(2→3)-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) (39). It was prepared from **38**, as previously described for the synthesis of **9**. Column chromatography (hexane–ethyl acetate (2:1)) afforded crystalline **39** (63%): mp 132 °C (hexane); $[\alpha]_D$ +1° (*c* 0.5, chloroform); ^1H NMR ($CDCl_3$, 250 MHz) δ 5.76 (d, $J_{1'/2'}$ = 3 Hz, 1 H, H-1'), 4.54 (d, 1 H, H-2'), 4.46 (ddd unsolved, $J_{3b/4}$ = 2 Hz, $J_{3a/4}$ = 3 Hz, 1 H, H-4), 4.28 (m, 2 H, H-3',5'), 4.20 (dd unsolved, 1 H, H-5), 4.16 (m, 1 H, H-6), 4.08–4.01 (m, 3 H, H-6'a,6'b,7), 3.96 (dd unsolved, $J_{8a/8b}$ = 8.5 Hz, 1 H, H-8a), 3.91 (dd unsolved, 1 H, H-8b), 3.72 (dd unsolved, 1 H, H-4'), 3.69 (s, 3 H, COO*Me*), 3.02 (dd, $J_{3a/3b}$ = 15.5 Hz, 1 H, H-3a), 1.70 (dd, 1 H, H-3b), 1.41, 1.40, 1.32, 1.30, 1.27, 1.26, 1.23, 1.21 (8s, 24 H,

8×Me); MS (CI) m/z 592 ($M + NH_4^+$). Anal. Calcd for $C_{27}H_{42}O_{13}$: C, 56.44; H, 7.37. Found: C, 56.67; H, 7.48.

(Methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranosid-4-yl) 2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-[(trimethylsilyl)-ethoxymethyl]-D-*manno*-heptonate (41). It was prepared from **14** and **40**, as previously described for the synthesis of **22**. Column chromatography (hexane–ethyl acetate (5:1)) afforded **41** (60%) as a colorless syrup: $[\alpha]_D$ +16.5° (c 0.9, chloroform); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39–7.26 (m, 15 H, 3Ph), 5.15 (dd, $J_{4'/3'}$ = 9.5 Hz, $J_{4'/5'}$ = 10 Hz, 1 H, H-4'), 4.91 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.89 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.82 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.77 (2s, 2 H, OCH_2O), 4.74 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.66 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.64 (d, $J_{1'/2'}$ = 4 Hz, 1 H, H-1'), 4.59 (ddd, $J_{3/4}$ = 5.5 Hz, $J_{2a/3}$ = 3.5 Hz, $J_{2b/3}$ = 10.5 Hz, 1 H, H-3), 4.58 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.48 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.15 (dd, $J_{7a/7b}$ = 8 Hz, $J_{6/7a}$ = 6.5 Hz, 1 H, H-7a), 4.13 (dd, $J_{4/5}$ = 8 Hz, 1 H, H-4), 4.01 (ddd, $J_{6/7b}$ = 8 Hz, $J_{5/6}$ = 6.5 Hz, 1 H, H-6), 3.98 (dd, $J_{2'/3'}$ = 9.5 Hz, 1 H, H-3'), 3.93 (dd, 1 H, H-7b), 3.82 (ddd, $J_{5'/6'a}$ = 7.5 Hz, $J_{5'/6'b}$ = 5.5 Hz, 1 H, H-5'), 3.72–3.59 (m, 5 H, $OCH_2CH_2SiMe_3$, H-5,2',6'a), 3.51 (dd, $J_{6'a/6'b}$ = 11 Hz, 1 H, H-6'b), 3.44 (s, 3 H, OMe), 2.53 (dd, $J_{2a/2b}$ = 14 Hz, 1 H, H-2a), 2.45 (dd, 1 H, H-2b), 1.40, 1.36, 1.35, 1.28 (4s, 12 H, 4×Me), 1.07–0.86 (m, J_{OCH} = 10 Hz, $J_{OCH'}$ = 6.5 Hz, J_{gem} = 13 Hz, 2 H, CH_2SiMe_3), 0.06 (s, 9 H, $SiMe_3$); MS (CI) m/z 884 ($M + NH_4^+$). Anal. Calcd for $C_{47}H_{66}O_{13}Si$: C, 65.10; H, 7.67. Found: C, 65.21; H, 7.60.

(Methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranosid-4-yl) 2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-pivaloyl-D-*manno*-heptonate (42). It was prepared from **15** and **40**, as previously described for the synthesis of **22**. Column chromatography (hexane–ethyl acetate (3:1)) afforded **42** (65%) as a colorless syrup: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40–7.30 (m, 15 H, 3Ph), 5.16 (dd, $J_{3'/4'}$ = 9.5 Hz, $J_{4'/5'}$ = 10 Hz, 1 H, H-4'), 5.04 (dd, $J_{5/6}$ = 6.5 Hz, $J_{4/5}$ = 3 Hz, 1 H, H-5), 4.93 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.84 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.74 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.68 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.66 (d, $J_{1'/2'}$ = 4 Hz, 1 H, H-1'), 4.58 (m, 1 H, H-3), 4.55 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.50 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.31 (dd, $J_{3/4}$ = 6.5 Hz, 1 H, H-4), 4.17 (ddd, $J_{6/7b}$ = 7 Hz, $J_{6/7a}$ = 6 Hz, 1 H, H-6), 4.00 (dd, $J_{7a/7b}$ = 8.5 Hz, 1 H, H-7a), 3.95 (dd, $J_{2'/3'}$ = 9.5 Hz, 1 H, H-3'), 3.86 (m, 2 H, H-7b,5'), 3.64 (dd, 1 H, H-2'), 3.59 (dd, $J_{5'/6'a}$ = 2.5 Hz, $J_{6'a/6'b}$ = 11 Hz, 1 H, H-6'a), 3.51 (dd, $J_{5'/6'b}$ = 5 Hz, 1 H, H-6'b), 3.45 (s, 3 H, OMe), 2.32 (m, 2 H, H-2a,2b), 1.48, 1.40, 1.38, 1.30 (4s, 12 H, 4×Me), 1.23 (s, 9 H, *t*-Bu); MS (CI) m/z 839 ($M + NH_4^+$).

Registry No. **1**, 40036-82-6; **2**, 137945-76-7; **3**, 131444-81-0; **4**, 131444-82-1; **5**, 130481-65-1; **6**, 131444-80-9; **7**, 137945-77-8; **8**, 114729-42-9; **9**, 111833-99-9; **10**, 137945-78-9; **11**, 131444-70-7; **12**, 137945-79-0; **13**, 137945-80-3; **14**, 137945-81-4; **15**, 131444-71-8; **16**, 137945-82-5; **17**, 137945-83-6; **18**, 137945-84-7; **19**, 137945-85-8; **20**, 137945-86-9; **21**, 53008-65-4; **22**, 137945-87-0; **23**, 131456-52-5; **24**, 137964-64-8; **25**, 131444-84-3; **26**, 131465-47-9; **27**, 131444-86-5; **28**, 131444-88-7; **29**, 137945-88-1; **30**, 131444-89-8; **31**, 131444-90-1; **32**, 582-52-5; **33**, 131444-83-2; **34**, 131444-85-4; **35**, 131465-48-0; **36**, 131444-87-6; **37**, 131465-49-1; **38**, 137945-89-2; **39**, 131465-50-4; **40**, 19488-48-3; **41**, 137945-90-5; **42**, 137945-91-6.

Reaction of *N*-Vinylpyrazolium and *N*-Vinylindazolium Salts with Cyanide Ion: Formation of 1,2-Dihydropyrimidines, 3,4-Dihydroquinazolines, and Quinolines

José Elguero,† Marta García-Rodríguez,‡ Enrique Gutiérrez-Puebla,§ Antonio de la Hoz,⊥ María Angeles Monge,§ Carmen Pardo,*,‡ and María del Mar Ramos‡

Instituto de Química Médica, CSIC, Juan de la Cierva, 3, 28006 Madrid, Spain, Departamento de Química Orgánica, Facultad de Química, Universidad Complutense, 28040 Madrid, Spain, Instituto de Ciencia de Materiales Sede D, CSIC, Laboratorio de Difracción de Rayos X, Facultad de Química, Universidad Complutense, 28040 Madrid, Spain, and Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad de Castilla-La Mancha, 13071 Ciudad Real, Spain

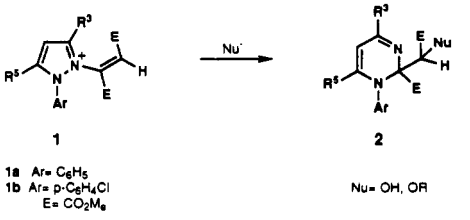
Received January 16, 1992

The reaction of 1-aryl-2-vinylpyrazolium tetrafluoroborates with potassium cyanide affords 2-hydroxy-1,2-dihydropyrimidines **3**, which exist as open-chain tautomers **4**, both in the solid state and in solution. The X-ray structure of the *p*-chlorophenyl derivative **4b** has been determined ($ClC_{14}N_2O_3H_{15}$, $P2_1/c$, a = 11.433 (3) Å, b = 16.086 (4) Å, c = 7.813 (4) Å, β = 94.22 (5)°, V = 1433.0 (9), Z = 4, R = 0.06 for 1334 observed reflections). Protonation of these vinylogous amidines **4** results in their cyclization and dehydration to pyrimidinium salts **6**. In the case of 1-vinyl-2-methylindazolium tetrafluoroborate **8**, the reaction with cyanide ion leads to a mixture of 3,4-dihydroquinazoline **12** and 2-(methoxycarbonyl)-3-cyanoquinoline (**13**). The mechanism proposed for this rearrangement is supported by the isolation of the open-chain intermediate in the case of 1-vinyl-2-phenylindazolium salt.

Introduction

Rearrangement of pyrazoles to pyrimidines is rather infrequent and usually takes place under strong conditions: use of sodium amide and high temperatures,[1] insertion of chlorocarbenes,[2] and flash vacuum pyrolysis.[3] We have reported such a rearrangement under very mild conditions, pH ca. 9 and room temperature.[4] The reaction takes place

Scheme I



when *N*-vinylpyrazolium salts **1** are treated with aqueous sodium carbonate or an alcohol. It proceeds through a

† Instituto de Química Médica.
‡ Departamento de Química Orgánica, Universidad Complutense.
§ Instituto de Ciencia de Materiales Sede D.
⊥ Universidad de Castilla-La Mancha.

0022-3263/92/1957-4151$03.00/0