[N-1 Me (*M*)], 6.45 [syn *N*-Me (*M*)], 6.75 [syn *N*-Me (*P*)], 8.57 [H-5 (*P*)], 8.66 [H-5 (*M*)], 9.36 [H-6 (*P*)], 9.44 [H-6 (*M*)]. $\Delta\epsilon$ (275 nm, MeOH): +2.4 [**13a**, (*M*)], −2.4 [**13b**, (*P*)].

(7*M*,9*S*)-*anti*-3-[[*N*-Methyl-*N*-(α-methylbenzyl)amino]carbonyl]-1,2,4-trimethylpyridinium Iodide (13c). Upon heating of pure **13b** in CD_3CN during several hours at reflux temperature, an equilibrium mixture is produced containing all four diastereoisomers. Compound **13c**, which could not be isolated as a pure substance, is the minor component (<10%). ^1H NMR (CD_3CN): δ 1.56 (d, *J* = 7 Hz, 3 H, α-Me), 2.25 (s, 3 H, C-4 Me), 2.57 (s, 3 H, C-2 Me), 3.09 (s, 3 H, syn *N*-Me), 4.05 (s, 3 H, N-1 Me), 4.61 (q, *J* = 7 Hz, 1 H, *N*-CH), 7.80 (d, *J* = 7.5 Hz, 1 H, H-5), 8.63 (d, *J* = 7.5 Hz, 1 H, H-6); [**13c** + 50 mg of (+)-Eu(hfc)$_3$] δ 3.94 (C-4 Me), 4.65 (N-1 Me), 5.46 (syn *N*-Me), 9.24 (H-6). Compare with the corresponding values for **13b**: δ 3.99 (C-4 Me), 4.78 (N-1 Me), 5.94 (syn *N*-Me), 9.19 (H-6).

(7*P*,9*S*)-*syn*-3-[[*N*-Methyl-*N*-(α-methylbenzyl)amino]carbonyl]-1,2,4-trimethylpyridinium Iodide (14b).[26] **X-ray Data**: $C_{18}H_{23}N_2O^+\cdot I^-$, M_r = 410.30, orthorhombic, $P2_12_12_1$, *a* = 7.0112 (9) Å, *b* = 14.385 (1) Å, *c* = 37.213 (2) Å, *V* = 3753.2 (6) Å^3, *Z* = 8, D_{calcd} = 1.452 g cm^{-3}, Mo Kα, λ = 0.71073 Å, μ = 16.9 cm^{-1}, *F*(000) = 1648, *T* = 294 K, final *R* = 0.0464 for 3213 unique observed reflections. A needle-shaped crystal, 0.9 × 0.13 × 0.03 mm, was used for data collection on an Enraf-Nonius CAD-4 diffractometer with Zr-filtered Mo Kα radiation. Lattice parameters were derived from the angular settings of 25 reflections (6.69° ≤ θ ≤ 13.73°). The intensity data of 4600 reflections were collected, of which 3213 were above the 2.5σ(*I*) level [*h* 0→7, *k* 0→15, *l* −39→39, $2\theta_{max}$ = 44°, ω–2θ scan mode with $\Delta\omega = (0.60 + 0.35 \tan\theta)°$]. The *hkl* and hk$\bar{l}$ Bijvoet pairs were not merged to determine the absolute configuration. Three periodically measured standard reflections (114, 120, 034) showed rms deviations of 1.03, 0.81, and 0.68%, respectively. The structure was solved by Patterson and Fourier methods. H atoms were placed at calculated positions (C–H, 1.00 Å) riding on their carrier atoms with a general temperature factor. Anisotropic, weighted blocked full-matrix refinement of *F*(423 parameters) gave *R* = 0.0464, *wR* = 0.0459 with $w = 1.0550[\sigma^2(F_o) + 0.00269F_o^2]^{-1}$, *S* = 1.13, $(\Delta/\sigma)_{av}$ = 0.012, $(\Delta/\sigma)_{max}$ = 0.051, $(\Delta\rho)_{max}$ = 0.73, $(\Delta\rho)_{min}$ = −0.69 e Å^{-3} (around *I*). The absolute configuration was ascertained by refinement of the inverted model, which resulted in *R* = 0.0495 and *wR* = 0.0536, which established the configuration at C-7 as *S* in accordance with that of its synthetic precursor *N*-methyl-*N*-[(*S*)-α-methylbenzyl]amine. The scattering factors and anomalous-dispersion corrections were taken from *International Tables for X-ray Crystallography* (1974). Calculations were performed with SHELX76[36] (structure determination and refinement) and the EUCLID package[37] (molecular geometry and illustrations) on the CDC-Cyber-855 of the University of Utrecht: ^1H NMR (CD_3CN) δ 1.66 (d, *J* = 7 Hz, 3 H, α-Me), 2.42 (s, 3 H, C-4 Me), 2.52 (s, 3 H, C-2 Me), 2.66 (s, 3 H, anti *N*-Me), 4.19 (s, 3 H, N-1 Me), 6.13 (q, *J* = 7 Hz, 1 H, syn *N*-CH), 7.71 (d, *J* = 7.5 Hz, 1 H, H-5), 8.57 (d, *J* = 7.5 Hz, 1 H, H-6). $\Delta\epsilon$ (280 nm, MeOH): +1.3.

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A Novel Strategy for the Synthesis of Ammonium 3-Deoxy-D-*manno*-2-octulosonate (Ammonium KDO) from Lower Monosaccharides. C–C Bond Construction at C_6 of D-Mannose via Cobaloxime-Mediated Radical Alkyl–Alkenyl Cross Coupling

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Our synthesis of ammonium 3-deoxy-D-*manno*-2-octulosonate (ammonium KDO, **16**) from D-mannose (**3**) proceeds in 10 one-flask operations in 1.5–1.6% overall yield (66% per operation). The strategic reaction is a C–C bond construction at C_6 of D-mannose via photochemically induced radical cross coupling of α-ethoxyacrylonitrile with an alkyl cobaloxime derivative of D-mannose, in aqueous ethanol without protection of carbohydrate hydroxyls. In this paper we provide full experimental details of our KDO synthesis. In addition we provide some observations and insights on vanadium-catalyzed oxidations of α-hydroxy acids to α-keto acids.

Introduction

The eight-carbon monosaccharide 3-deoxy-D-*manno*-2-octulosonic acid, commonly known as KDO (**1**), is an essential component of the outer membrane lipopolysaccharide of all Gram-negative bacteria.[2] KDO is found in the core oligosaccharide, which links lipid A with the O side chain repeating oligosaccharide that protrudes into solution from the cell surface. KDO has also been found in the cell walls of plants.[3] The synthesis of KDO analogues has recently become important for studies aimed at the development of an entirely new class of Gram-negative antibacterials targeting the KDO biosynthetic pathway.[4,5]

We recently communicated a synthesis of ammonium KDO (**16**)[6,7] from D-mannose (**3**) via a novel strategy fea-

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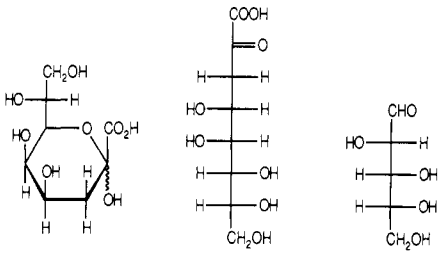
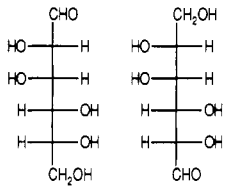
turing cobaloxime-mediated radical alkyl–alkenyl cross coupling as the key C–C bond construction. Most synthetic strategies for the preparation of KDO from lower monosaccharides have involved formation of a key C–C bond at C_1 of D-arabinose[8] (**2**) or C_1 of D-mannose[9] (**3**). Our strategy for KDO, building on C_6 of D-mannose, should allow the inexpensive preparation, from readily available aldohexoses, of KDO analogues that would otherwise be expensive to prepare, building on C_1 of aldopentoses or C_1 of aldohexoses.[10]



1
KDO
3-deoxy-D-*manno*-2-octulosonic acid

2
D-arabinose



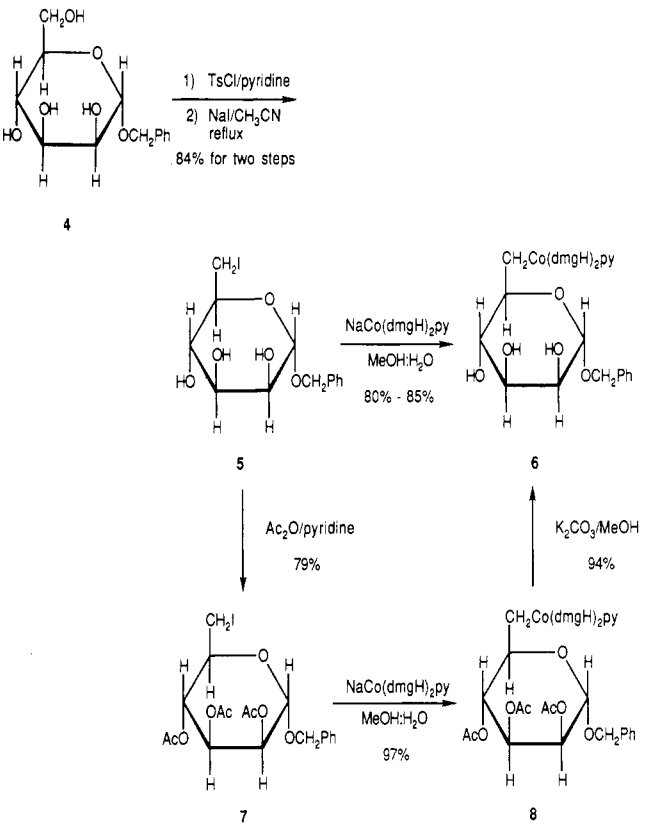
3
D-mannose

Results and Discussion

α-Benzyl-D-mannopyranoside (**4**) was prepared from D-mannose (**3**) in 35% yield with anhydrous HCl in benzyl alcohol.[11] Treatment of **4** with 1.2 equiv of *p*-toluenesulfonyl chloride in dry pyridine followed directly by refluxing the crude tosylate with NaI in dry CH_3CN for 3 h produced iodide **5** in 84% overall yield for the two steps. Treatment of **5** with $NaCo^I(dmgH)_2py$ in aqueous methanol gave cobaloxime **6** in 80–85% yield. Triacetate **7**, obtained in 79% yield from Ac_2O/pyridine acetylation of **5**, could be converted to the corresponding cobaloxime **8** in 97% yield. Treatment of **8** to base-catalyzed transesterification with K_2CO_3/MeOH removed the three acetate esters to produce cobaloxime **6** in 94% yield (Scheme I).

Alkyl–styryl cross coupling via anaeobic photolysis of 20 mM **6** and 400 mM styrene in 95% ethanol produced

Scheme I



9 in 63% yield (Scheme II). Analogous reactions using triacetate **8** produced **10** in 85% yield. In both cases, only the *E* isomer was obtained as shown by the ^1H NMR coupling constants for the olefinic C–H.

Several possible ways can be envisioned to convert **9** or **10** into KDO by using the double bond regenerated in the cross-coupling reaction as a handle for further synthetic elaboration. However, all of the routes we considered were strategically cumbersome due to extensive functional group interconversions and/or functional group protection/deprotections. We chose instead to explore a more direct route to KDO employing a latently functionalized alkene cross coupling partner designed to allow facile elaboration of the cross-coupling product into KDO.

Anaerobic photolysis of 20 mM **6** and 400 mM α-ethoxyacrylonitrile[12] in 95% EtOH produced **11** in 81% yield. Likewise, **8** was converted to **12** in 83% yield. Acetylation of **11** with Ac_2O/pyridine produced **12** in 93% yield.

Oxidative unmasking of latent functionality in the α-ethoxyacrylonitrile moiety of **12** with 1 equiv of $KMnO_4$[13] provided α-hydroxy ester **13** in 92% yield. The benzyl ether was removed from **13** by catalytic hydrogenolysis[14] to give octose **14** in 82% yield. It was more convenient to perform the oxidation of **12** to **13** and then directly convert partially purified **13** to **14** in 81% yield for the two steps (Scheme III).

Treatment of **14** with NaOH in methanol (to hydrolyze the esters), in situ treatment with $NaBH_4$ (to reduce the aldehyde to primary alcohol), and then in situ treatment with Amberlite IR-120 (H^+) ion-exchange resin (to protonate the carboxylate and promote lactonization) produced **15** in 87% overall yield. At this stage we had ac-

(6) Many of these results have been reported in preliminary form at the following conference and meetings: 42nd Northwest Regional ACS Meeting; Bellingham, WA, June 17–19, 1987; Organic no. 183. 4th IUPAC Symposium on Organometallic Chemistry Directed toward Organic Synthesis; Vancouver, BC, July 26–30, 1987; Short Talk and Poster PS1-27. 194th ACS National Meeting, New Orleans, LA, August 30–September 4, 1987; Organic no. 229.

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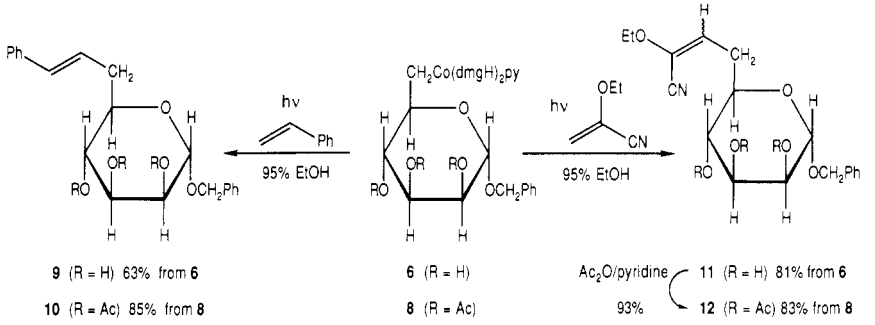
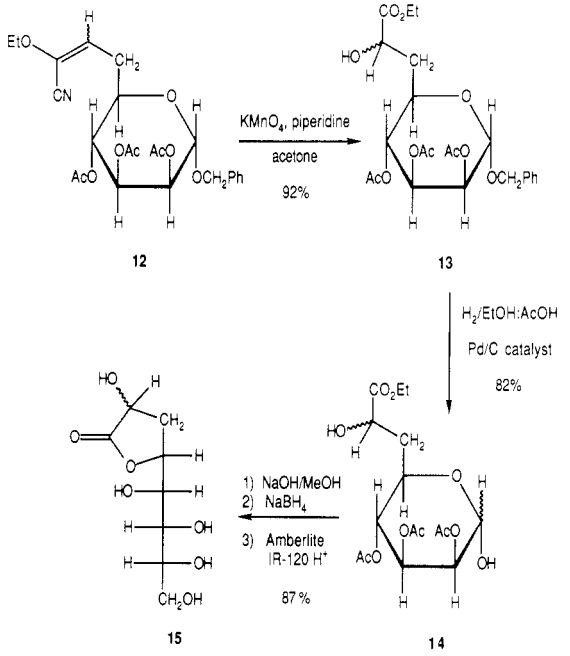
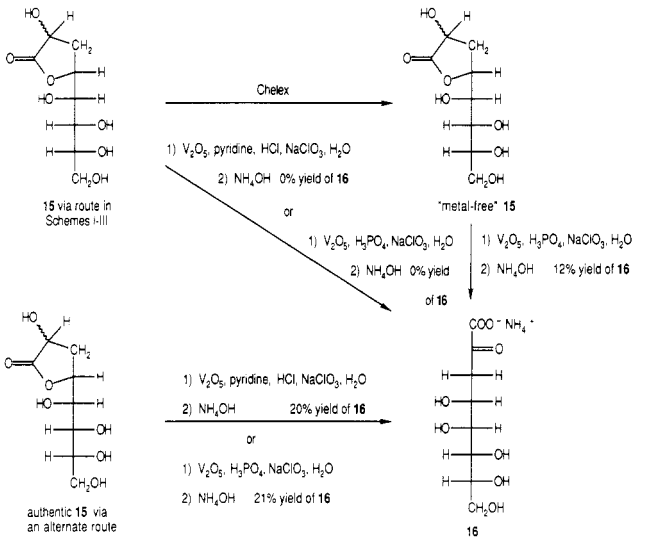
Scheme II



Scheme III



Scheme IV



complished a formal synthesis of ammonium KDO (**16**) since **15** has been prepared previously by alternate routes and has been converted to **16** by hydrolysis of the lactone in **15** and then by vanadium-catalyzed oxidation of the C_2 hydroxyl with a V_2O_5/pyridine/HCl catalyst[9b] or a V_2O_5/H_3PO_4 catalyst.[9c] We were surprised to find that numerous attempts to oxidized **15**, with either catalyst, failed in all instances. In no case could **16** be detected in even trace amounts by TLC comparison with an authentic sample of **16** (Sigma no. K 7000).

To confirm that we had indeed prepared **15**, we independently prepared an authentic sample of **15** by following a six-step literature procedure that builds on C_1 of D-mannose.[9b,c] Our synthetic **15** was shown to be the same as authentic **15** by direct ^1H NMR, ^{13}C NMR, and TLC comparisons. TLC comparisons using several solvent systems and ^1H NMR comparisons indicated that the two samples of **15** were the same, although these data were not rigorously conclusive. ^{13}C NMR spectroscopy provided an unambiguous verification that our synthetic **15** and authentic **15** were the same. By ^{13}C NMR analysis, the authentic sample contained diastereotropic lactone epimers **15** and the corresponding hydroxyl acid diastereomers (**15** + H_2O) in a 5:1 ratio of lactone to acid. Our synthetic sample contained the same compounds in a 5:1 ratio. By ^{13}C NMR analysis, the distribution of C_2 diastereomers was different but the chemical shifts of all four peaks for C_3 were identical. For the corresponding carboxylic acid sodium salts, obtained by Na_2CO_3/D_2O hydrolysis of **15**, the ^{13}C NMR chemical shifts of the two peaks for C_3 of the two diastereomers were identical. All ^1H NMR and ^{13}C NMR comparison spectra were essentially superimposable, although most data were not as diagnostic and definitive as the ^{13}C comparison of C_3.

The authentic sample of **15** could be oxidized to KDO, isolated as ammonium salt **16**, by using either the V_2O_5/pyridine/HCl method (20% isolated yield of **16**) or the V_2O_5/H_3PO_4 method (21% isolated yield of **16**). These yields are fairly typical for this reaction; literature reports range from 16%[9c] to 40%[9b] for isolated, purified **16**. The **16** that we prepared from authentic **15** and authentic **16** (Sigma no. K 7000) were found to be identical by silica gel TLC (10:10:3 methanol/chloroform/water and 4:1:1 ethanol/water/acetic acid), ^1H NMR, and ^{13}C NMR comparisons.

Why couldn't we oxidize our **15**, prepared by the cobaloxime mediated route of Schemes I–III, by using reactions that we had shown to be successful in our own hands with authentic, independently prepared **15**? One possibility was that trace metal contaminants, carried through our synthetic route complexed to polyester and polyhydroxylic intermediates, could be poisoning the vanadium catalysts or catalytically disproportionating the oxidant.

To remove any trace metal ions from our **15** prepared via the route of Schemes I–III, a sample of that **15** was dissolved in doubly distilled water and passed down a column of Chelex resin. The eluent was lyophilized, taking care to avoid contact with metal at any stage. Treatment of the resulting "metal-free" **15** to the standard V_2O_5/H_3PO_4 catalytic oxidation conditions produced **16** in 13% isolated yield, along with an 18% recovery of unreacted **15** (Scheme IV). This synthetic sample of **16** was shown

to be identical with authentic commercially available **16** (Sigma no. K 7000) by TLC, ^1H NMR, and ^{13}C NMR comparisons, as described earlier for the characterization of **16** prepared from authentic independently prepared **15**.

Our results strongly suggest that trace metals may be critical to the success or failure of vanadium-catalyzed oxidations of α-hydroxy acids to α-keto acids. Standard purification of oxidation substrates without Chelex chromatography may not be sufficient to ensure a successful oxidation. Our observations may help explain why vanadium-catalyzed oxidation of α-hydroxy acids to α-keto acids have a reputation for being capricous, unpublished carbohydrate lore which we learned informally from colleagues only after we had become stymied by the conversion of **15** to **16**.

Conclusion

We have developed a novel synthesis of ammonium KDO (**16**) from D-mannose (**3**) in 10 one-flask operations; via **4**, **5**, **6**, **11**, **12**, **13**, **14**, **15** (1.5% overall yield, 66% average per operation) or via **4**, **5**, **7**, **8**, **12**, **13**, **14**, **15** (1.6% overall yield, 66% average per operation). Unlike other strategies for the preparation of KDO from lower monosaccharides, which build on C_1 of D-mannose (**3**)[9] or C_1 or D-arabinose (**2**),[8] we have built on the C_6 end of **3**. The strategic reaction in our synthesis is a cobaloxime-mediated radical alkyl–alkenyl cross coupling of α-ethoxyacrylonitrile with cobaloxime derivatives of D-mannose **6** and **8**. Regeneration of the alkene functionality in the cross-coupling reagent incorporates the α-ethoxyacrylonitrile moiety in the product with suitable latent functionality for facile direct elaboration into **16**.

Experimental Section

All organic reagents were purchased from Aldrich Chemical Co. with the exception of dimethylglyoxime ($dmgH_2$) (Lancaster Synthesis). All inorganic reagents were purchased from J. T. Baker with the exception of $CoCl_2 \cdot 6H_2O$ (Mallinckrodt) and calcium ferrocyanide (Pfaltz and Bauer). Silica gel chromatography was performed with Baker silica gel (60–200 mesh). Flash column chromatography used Baker silica gel (40-μm particle size). Preparative thin-layer chromatography used Analtech 20 cm × 20 cm × 1 mm glass-backed silica gel plates (Analtech no. 02013). Thin-layer chromatography (TLC) used aluminum-backed silica gel plates (Merck no. 5554) with visualization of spots under UV light as well as by dipping the developed plate into a vanillin stain, followed by heating with a heat gun. The vanillin stain was prepared by dissolving 11.5 g of vanillin in 360 mL of 95% ethanol and adding 8 mL of glacial HOAc and 14 mL of concentrated H_2SO_4. The thiobarbiturate stain system[15] used to visualize **15** and **16** involved dipping the developed silica gel plate in 0.02 M aqueous $NaIO_4$ followed by heating the plate with a heat gun. The dried plate was then dipped in a 50:50:0.03 mixture of acetone/ethylene glycol/concentrated H_2SO_4, followed by heating the plate. The dried plate was then dipped in a fresh (<1 week old) 6% aqueous solution of sodium thiobarbiturate, again followed by heating. Both **15** and **16** gave pink spots on the plate after this treatment.

^1H NMR spectra were measured on a General Electric QE-300 at 300 MHz with residual $CHCl_3$ in $CDCl_3$ as internal frequency standard defined as 7.27 ppm. For spectra recorded in D_2O, the residual H_2O resonance was defined as 4.80 ppm. ^{13}C NMR spectra were measured on the QE-300 instrument at 75.48 MHz with $CDCl_3$ as an internal standard defined as 77.00 ppm. IR spectra were measured with a Nicolet 5-DXB FT instrument or a Perkin-Elmer 1400 spectrometer at the Borden Chemical Division of the Borden Co., Springfield, OR. Mass spectra were measured with a VG 12-253 automated GC–MS with a Hewlett-Packard 5890 GC or a VG ZAB-2F-HF high-field double-focusing MS both connected to a shared VG-11-250 data system. Elemental analyses were performed by Desert Analytics of Tucson, AZ. All solvents, except as noted, were purchased from J. T. Baker. Anhydrous solvents were prepared by distillation from sodium benzophenone ketyl radical under N_2 with the exception of pyridine (distilled from CaH_2 under N_2); 95% EtOH was purchased from USI Chemicals Co. and used without further purification.

Phenylmethyl α-D-Mannopyranoside (4). In a variation of a literature procedure,[11] anhydrous benzyl alcohol (80 mL) was treated with anhydrous HCl by bubbling HCl gas through the neat alcohol at room temperature for 3 min. D-Mannose (13.22 g, 73.46 mmol, mixture of anomers) was added portionwise over 10 min, and the suspension was stirred under N_2 until nearly all of the mannose had dissolved (ca. 1 h). The HCl was neutralized with excess $NaHCO_3$ (until gas evolution ceased). The solvent was then distilled off under vacuum (aspirator), and the beige residue was dissolved in ca. 60 mL of H_2O and extracted with EtOAc (8 × 50 mL). The EtOAc extracts were combined and rotary evaporated, and the crude product was recrystallized from EtOAc, furnishing **4** (6.939 g, 25.7 mmol, 35%) as a white microcrystalline powder: mp 131–132.5 °C (lit.[11] mp 131–132 °C); ^1H NMR (D_2O) δ 3.8–4.1 (m, 6 H), 4.72 (d, J = 11.6 Hz, 1 H), 4.90 (d, J = 11.6 Hz, 1 H), 7.58 (br s, 5 H); ^{13}C NMR (acetone-d_6) δ 54.3, 60.16, 62.20, 63.71, 64.34, 66.43, 92.68 (C_1, J_{C1-H1} = 171 Hz, indicates α-anomer),[16] 121.18, 121.35, 121.77, 130.65; IR (KBr) 3520, 3390, 3060, 3030, 2910, 1495, 1450, 1370, 1345, 1126, 1063, 1055, 1030, 971, 760, 705 cm^{-1}.

Phenylmethyl 6-Deoxy-6-iodo-α-D-mannopyranoside (5). A solution of **4** (3.56 g, 13.2 mmol) in 100 mL of dry pyridine was cooled to −10 °C under N_2 in an ice–salt bath. *p*-Toluenesulfonyl chloride (2.60 g, 13.6 mmol, 1.04 equiv) was added, and the mixture was stirred at 0 °C for 4 h and then at room temperature for 9 h. Another 300 mg (1.57 mmol) of TsCl was added, and the mixture was stirred at room temperature for 2 h, and then the pyridine was distilled off (0.5 mmHg). The residue was dissolved in ca. 100 mL of EtOAc, extracted once with 20 mL of H_2O, dried over anhydrous Na_2SO_4, and rotary evaporated. The crude tosylate was purified by passage through a short column of silica gel with EtOAc eluent. The filtrate was rotary evaporated, and the last traces of solvent were removed in vacuo (0.5 mmHg), leaving a white foam (5.4 g, 12.7 mmol, 97%). The foam was dissolved in 70 mL of dry CH_3CN, and NaI (7.52 g, 50.1 mmol, 3.92 equiv) was added. The solution was heated under N_2 at reflux for 1.5 h and then cooled to room temperature, and the solvent was rotary evaporated. The residue was dissolved in 100 mL of EtOAc, washed with 20 mL of H_2O and 20 mL of saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and rotary evaporated, and the residue was purified by column (gravity) chromatography on silica gel with EtOAc eluent. Iodide **5** was obtained as a slightly hygroscopic white foam (4.20 g, 11.1 mmol, 84% from **4**): mp 107.5–108.5 °C; ^1H NMR (acetone-d_6) δ 3.25 (t, J = 9.1 Hz, 1 H), 3.54 (m, 2 H), 3.69 (m, 2 H), 3.88 (m, 2 H), 3.97 (d, J = 3.9 Hz, 1 H), 4.24 (d, J = 4.2 Hz, 1 H), 4.51 (d, J = 11.7 Hz, 1 H), 4.81 (d, J = 11.7 Hz, 1 H), 4.83 (s, 1 H), 7.33 (m, 5 H); ^{13}C NMR (acetone-d_6) δ 7.92, 69.04, 71.64, 71.64, 72.22, 73.54, 99.98, 128.31, 128.72, 128.99, 138.50; IR ($CHCl_3$) 3570, 3394, 3068, 2922, 1499, 1457, 1130, 1070, 973 cm^{-1}.

Bis(dimethylglyoximato)(pyridine)(phenylmethyl 6-deoxy-α-D-mannopyranosid-6-yl)cobalt (6) from 5. In a 25-mL round-bottom flask equipped with a magnetic stir bar and a rubber septum, a suspension of $CoCl_2 \cdot 6H_2O$ (238 mg, 1.00 mmol) and $dmgH_2$ (239 mg, 2.06 mmol) in 5 mL of methanol was deoxygenated by bubbling N_2 through a syringe needle for 5 min and was treated with 50% aqueous NaOH (167 mg, 2.09 mmol) and pyridine (82 μL, 80 mg, 1.0 mmol). The dark brown suspension was deoxygenated for an additional 5 min and then treated with $NaBH_4$ (39 mg, 1.0 mmol). The resulting dark blue mixture was stirred for 5 min, and then a deoxygenated solution of iodide **5** (285 mg, 0.75 mmol) in 3 mL of deoxygenated methanol was added via cannula, and the cannula was rinsed into the reaction mixture with an additional 2 mL of deoxygenated methanol. The mixture

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was reduced again with $NaBH_4$ (30 mg) and then stirred for 3 h, the septum cap was removed, the reaction was diluted with 10 mL of acetone, and a few grams of silica gel was added. The solvents were removed with a rotary evaporator to leave a free-flowing powder. The powder was placed on top of 2 cm of silica gel in a fritted-glass funnel and suction filtered with 4:1 EtOAc/acetone. The filtrate was rotary evaporated to leave **6** as a glassy orange solid (0.44 g, 0.708 mmol, 94%). Attempts at elemental analysis were not successful, due to difficulty in removing all traces of solvent from the sample. However, this material proved to be identical by TLC, ^1H NMR, and ^{13}C NMR analyses with a sample prepared by deacetylation of **8** (vide infra): ^1H NMR ($CDCl_3$) δ 1.47 (dd, J_1 = 10.6 Hz, J_2 = 3.3 Hz, 1 H, diastereotopic C_6-H), 2.10 (s, 6 H, diastereotopic ligand methyls), 2.14 (s, 6 H, diastereotopic ligand methyls), 2.30 (dd, J_1 = 10.6 Hz, J_2 = 3.3 Hz, 1 H, diastereotopic C_6-H), 2.95 (m, 1 H, C_5-H), 3.72 (m, 2 H), 3.88 (s, 1 H), 4.41 (d, J = 12.1 Hz, 1 H), 4.61 (s, 1 H), 4.75 (d, J = 12.0 Hz, 2 H), 7.33 (m, 8 H), 7.74 (t, J = 7.6 Hz, 1 H), 8.57 (d, J = 5.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 12.11, 27.88 (broad, Co–C), 68.72, 70.71, 70.92, 71.57, 75.13, 98.88 (C_1), 125.10, 127.29, 127.77, 128.09, 137.49, 137.75, 149.63, 150.69; IR (KBr) 3410, 3060, 3025, 2920, 1600, 1560, 1490, 1445, 1230, 1094, 1063, 735, 700 cm^{-1}.

Phenylmethyl 6-Deoxy-6-iodo-α-D-mannopyranoside 2,3,4-Tri-*O*-acetate (7) from 5. Iodide **5** (1.35 g, 2.66 mmol) was dissolved in 20 mL of 4:1 Ac_2O/pyridine and stirred under N_2 for 1 h, then the mixture was poured into a beaker containing 100 mL ice and stirred for 1 h. The suspension was then extracted with diethyl ether (3 × 50 mL). The combined ether layers were stirred with aqueous $NaHCO_3$, solid $NaHCO_3$ was added until additional $NaHCO_3$ caused no evolution of gas, and then the organic phase was dried over anhydrous $MgSO_4$ and rotary evaporated. The residue was purified by flash chromatography on silica gel with 1:1 ether/petroleum ether, giving **7** as a white solid (1.06 g, 2.10 mmol, 79%): mp 129–130 °C; ^1H NMR ($CDCl_3$) δ 1.99 (s, 3 H), 2.08 (s, 3 H), 2.14 (s, 3 H), 3.25 (m, 2 H), 3.90 (dt, J_1 = 9.3 Hz, J_2 = 2.4 Hz, 1 H), 4.62 (d, J = 11.6 Hz, 1 H), 4.88 (d, J = 11.6 Hz, 1 H), 4.88 (s, 1 H), 5.13 (t, J = 9.9 Hz, 1 H), 5.28 (m, 1 H), 5.37 (dd, J_1 = 9.9 Hz, J_2 = 3.4 Hz, 1 H), 7.39 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 3.84, 20.51, 20.63, 20.68, 68.74, 69.27, 69.63, 70.03, 70.40, 96.19, 128.08, 128.24, 128.45, 136.06, 169.6, 169.67, 169.74; IR (CCl_4) 3037, 2938, 1757, 1462, 1370, 1244, 1223, 1138, 1082 cm^{-1}. A sample for elemental analysis was recrystallized three times from 5:1 EtOH/H_2O. Anal. Calcd for $C_{19}H_{23}IO_8$: C, 45.07; H, 4.58. Found: C, 45.04; H, 4.67.

Bis(dimethylglyoximato)(pyridine)(phenylmethyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-mannopyranosid-6-yl)cobalt (8). To 10 mL of methanol was added $CoCl_2 \cdot 6H_2O$ (714 mg, 3.00 mmol) and $dmgH_2$ (705 mg, 6.08 mmol). N_2 was bubbled through the suspension while 50% aqueous NaOH (500 mg, 6.25 mmol) and pyridine (245 μL, 240 mg, 3.03 mmol) were added. The brown mixture was deoxygenated by bubbling with N_2 for an additional 5 min, and then $NaBH_4$ (120 mg, 3.16 mmol) was added. The dark green mixture was stirred for 5 min, and then a solution of iodide **7** in 7 mL of THF, deoxygenated by bubbling N_2 through the solution for 10 min, was added via cannula. The cannula was rinsed into the reaction mixture with an additional 2 mL of deoxygenated THF, and then the mixture was stirred at room temperature for 1 h. The suspension was then diluted with 20 mL of acetone, and a few grams of silica gel was added. The solvents were rotary evaporated, and the dry powder obtained was applied to the top of a short column of silica gel and eluted with EtOAc. The orange band was collected and rotary evaporated to leave **8** as a glassy orange solid (1.44 g, 1.93 mmol, 97%). Recrystallization from methanol gave 1.133 g (1.52 mmol, 76%) of orange needles: mp 194–200 °C dec; ^1H NMR δ 1.27 (t, J = 8.9 Hz, diastereotopic C_6-H, 1 H), 1.98 (d, J = 10.6 Hz, C_5-H, 1 H), 1.96 (s, 3 H), 2.07 (s, 3 H), 2.06 (s, superimposed diastereotopic ligand methyl and acetate methyl, 9 H), 2.13 (s, diastereotopic ligand methyl, 6 H), 2.99 (t, J = 8.9 Hz, diastereotopic C_6-H, 1 H), 4.72 (s, C_1-H, 1 H), 4.73 (d, J = 11.0 Hz, diastereotopic benzyl methylene, 1 H), 4.98 (t, J = 9.8 Hz, 1 H), 5.13 (d, J = 11.0 Hz, diastereotopic benzyl methylene, 1 H), 5.17 (m, 1 H), 5.28 (dd, J_1 = 9.7 Hz, J_2 = 3.2 Hz, 1 H), 7.35 (m, superimposed pyridine C_3-H and benzyl aromatic ring, 7 H), 7.72 (t, J = 7.7 Hz, pyridine C_4-H, 1 H), 8.57 (d, J = 5.1 Hz, pyridine C_2-H, 2 H), 18.2 (br s, O–H–O bridge, 1 H); ^{13}C NMR ($CDCl_3$) δ 12.08, 12.13 (diastereotopic ligand methyls), 20.96 (3 superimposed lines), 26.12 (broad, Co–C), 69.11, 69.46, 69.93, 70.07, 72.07, 96.47, 125.16, 127.46 (2 superimposed lines), 128.30, 137.55, 137.59, 149.20, 149.32 (diastereotopic ligand carbons), 149.77, 170.14 (3 superimposed lines); IR (CCl_4) 3078, 3036, 2926, 1756, 1604, 1557, 1452, 1369, 1244, 1223, 1129, 1087 cm^{-1}. A sample for elemental analysis was recrystallized four times from 3:1 CH_3OH/H_2O. Anal. Calcd for $C_{32}H_{42}N_5O_{12}Co$: C, 51.41; H, 5.66; N, 9.37; Co, 7.88. Found: C, 51.07; H, 5.73; N, 9.35; Co, 7.30.

Bis(dimethylglyoximato)(pyridine)(phenylmethyl 6-deoxy-α-D-mannopyranosid-6-yl)cobalt (6) from 8. A sample of **8** (296 mg, 0.396 mmol) was suspended in 12 mL of methanol, and then K_2CO_3 (13 mg, 0.94 mmol) was added. The mixture was deoxygenated by bubbling N_2 through for 10 min, and then the reaction mixture was stirred at room temperature for 9 h before being rinsed into a one-neck flask with acetone. A few grams of silica gel was added, and the suspension was rotary evaporated to dryness. The dry powder was applied to the top of a 3-cm pad of silica gel in a 30-mL fritted-glass funnel and suction filtered with acetone. The filtrate was rotary evaporated to leave 232 mg (0.374 mmol, 94%) of **6** as a glassy orange solid. This sample was found to be identical by TLC, ^1H NMR, and ^{13}C NMR analyses with a sample prepared from iodide **5** (vide supra).

General Information on Photolyses. All photolyses were conducted with a $RCo(dmgH)_2py$ concentration of 20 mM and an alkene concentration of 400 mM in 95% EtOH. Photolyses were performed in Pyrex tubes fitted with rubber septa and equipped with magnetic stir bars. The reactions were deoxygenated by bubbling Ar through the mixture for 1 min/mL of reaction mixture, and were maintained under a positive pressure of Ar by means of syringe needles inserted through the septa. The Ar was deoxygenated by passage through a heated column of BASF catalyst R3-11 in the black (reduced) form. The light sources were 300-W Sylvania incandescent floodlamps, obtained at a local hardware store. The lamps were mounted in ceramic sockets and positioned 5 cm from a 800-mL beaker of water, in which there was immersed a coil of copper tubing (10 cm diameter, 4 turns). The water bath was magnetically stirred and tap water flowing through the copper coil was used to maintain the temperature of the water bath at 15–20 °C. The entire apparatus was wrapped in aluminum foil, and a stream of air was directed over the light bulb from the back to cool the bulb. The reactions were monitored by TLC by removing a 1-drop sample of the anaerobic reaction mixture with a long syringe needle.

Phenylmethyl 6,7,8-Trideoxy-8-phenyl-α-D-*manno*-oct-7-(*E*)-enopyranoside (9). A solution of **6** (264.2 mg, 0.425 mmol) and styrene (1.00 mL, 0.909 g, 8.74 mmol) in 21 mL of 95% ethanol was deoxygenated by bubbling Ar through the solution for 20 min and then photolyzed for 48 h. The resulting dark mixture was rinsed with acetone into a round-bottom flask, and a few grams of silica gel was added. The solvents were rotary evaporated, and the resulting dry powder was applied to a 3-cm pad of silica gel in a fritted glass funnel and suction filtered with acetone. The filtrate was rotary evaporated, and the residue was purified by flash chromatography on silica gel with 8:1 benzene/methanol as eluent, giving **9** as a colorless, sticky syrup (89.2 mg, 0.251 mmol, 59%): ^1H NMR ($CDCl_3$) δ 2.46 (m, diastereotopic C_6-H, 1 H), 2.76 (m, diastereotopic C_6-H, 1 H), 3.66 (m, 2 H), 3.81 (m, 1 H), 3.95 (s, 1 H), 4.40 (d, J = 11.8 Hz, 1 H), 4.63 (d, J = 11.8 Hz, 1 H), 4.84 (s, 1 H), 6.36, (m, 1 H, C_7-H), 6.52 (d, J = 15.6 Hz, shows *E* configuration, C_8-H, 1 H), 7.25 (m, 10 H); ^{13}C NMR (acetone-d_6) δ 35.75 (C_6), 69.25, 71.77, 72.75, 73.34, 79.12, 100.26 (C_1), 126.84, 127.64, 128.31, 128.70, 129.09, 129.26, 132.64, 138.91. A sample for elemental analysis was purified again by preparative TLC and was dried in a dessicator over Drierite under vacuum (0.005 mmHg) for several days. Anal. Calcd for $C_{21}H_{24}O_5 \cdot H_2O$: C, 67.36; H, 7.00. Found: C, 67.79; H, 6.67.

Phenylmethyl 6,7,8-Trideoxy-8-phenyl-α-D-*manno*-oct-7-(*E*)-enopyranoside 2,3,4-Tri-*O*-acetate (10). A solution of **8** (0.624 g, 0.835 mmol) and 1.9 mL (1.7 g, 16.6 mmol) of styrene in 40 mL of 95% ethanol was deoxygenated by bubbling Ar through the solution for 40 min and then photolyzed for 42 h. The reaction mixture was then rinsed into a round-bottom flask with acetone, a few grams of silica gel was added, and the solvents were rotary evaporated. The resulting dry powder was applied

to a 3-cm pad of silica gel in a fritted-glass funnel and suction filtered with EtOAc. The filtrate was rotary evaporated, and the residue was purified by flash chromatography on silica gel with 1:1 diethyl ether/petroleum ether, and **10** was obtained as a colorless syrup that slowly solidified on standing (0.344 g, 0.714 mmol, 85%): ^{1}H NMR ($CDCl_3$) δ 2.00 (s, 3 H), 2.02 (s, 3 H), 2.14 (s, 3 H), 2.47 (t, J = 6.5 Hz, 2 H, C_6-H), 3.93 (m, 1 H), 4.52 (d, J = 11.8 Hz, 1 H), 4.69 (d, J = 11.9 Hz, 1 H), 4.84 (s, 1 H), 5.21 (t, J = 9.9 Hz, 1 H), 5.30 (m, 1 H), 5.38 (dd, J_1 = 14.0 Hz, J_2 = 3.7 Hz, 1 H), 6.24 (m, 1 H, C_7-H), 6.50 (d, J = 16.2 Hz, shows *E* isomer, 1 H), 7.32 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 20.47, 20.60, 20.64, 34.99, 69.25, 69.29, 69.19, 69.77, 69.95, 96.36, 124.98, 125.95, 127.12, 127.90, 128.39, 132.68, 136.34, 137.27, 169.67, 169.79; IR (CCl_4) 3087, 3064, 3036, 2939, 1761, 1495, 1455, 1433, 1376, 1251, 1229, 1138, 1081 cm^{-1}. A sample for elemental analysis was purified by preparative TLC on silica gel. Anal. Calcd for $C_{27}H_{30}O_8$: C, 67.21; H, 6.27. Found: C, 67.34; H, 6.26.

Phenylmethyl 6,7-Dideoxy-8-*O*-ethyl-α-D-*manno*-non-7-enopyranosidurononitrile (11). A solution of **6** (0.444 g, 0.71 mmol) and α-ethoxyacylonitrile (1.36 g, 14.0 mmol) in 35 mL of 95% ethanol was deoxygenated by bubbling Ar through the solution for 30 min and then photolyzed for 74 h. The reaction mixture was then rinsed into a round-bottom flask with acetone, and a few grams of silica gel was added. The solvents were rotary evaporated, and the resultant dry powder was placed on top of a 3-cm pad of silica gel in a fritted-glass funnel and suction filtered through silica gel with EtOAc. The filtrate was rotary evaporated, and the residue was purified by preparative TLC on silica gel with 3:2 hexane/1-butanol to leave **11** (0.20 g, 0.57 mmol, 81%), a colorless thick syrup, as an inseparable mixture of isomers: ^{1}H NMR ($CDCl_3$) (mixture of isomers) δ 1.25 (overlapping methyl triplets, 3 H total), 2.47 (m, overlapping diastereotopic C_6-H, 1 H total), 2.73 (m, overlapping diastereotopic C_6-H, 1 H total), 3.55 (br m, 2 H total), 3.79 (m, 2 H total), 3.92–4.0 (m, 2 H total), 4.35–4.50 (m, 1 H total), 4.61 (m, 1 H total), 4.98 (s, 1 H), 5.65 (m, overlapping isomeric C_7-H, 1 H total), 7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 14.26, 14.73 (isomeric methyls), 27.55, 30.07 (isomeric C_6), 64.14, 65.79, 69.09, 69.36, 70.85 (broad, several superimposed lines), 71.45, 71.69, 98.99, 99.18 (isomeric C_1), 113.75, 114.36 (isomeric CN), 117.82, 124.16 (isomeric C_7), 127.83, 127.91, 128.44, 129.40, 131.70 (isomeric C_8), 136.81, 136.92 (isomeric ipso C); IR (CCl_4) 3419 (br, OH), 3066, 3033, 2992, 2935, 2221 (CN), 1639, 1270, 1212, 1056, 695 cm^{-1}.

Phenylmethyl 6,7-Dideoxy-8-*O*-ethyl-α-D-*manno*-non-7-enopyranosidurononitrile 2,3,4-Tri-*O*-acetate (12) from 8. A solution of cobaloxime **8** (500 mg, 0.669 mmol) and α-ethoxyacrylonitrile (1.28 g, 13.2 mmol) in 33 mL of 95% EtOH was deoxygenated by bubbling Ar through the solution for 30 min and then photolyzed for 77 h. The dark brown mixture was then rinsed into a flask with acetone, and a few grams of silica gel was added. The solvents were rotary evaporated, and the dry powder was placed on top of a 3-cm pad of silica gel in a fitted-glass funnel and suction filtered with diethyl ether. The filtrate was rotary evaporated, and the residue was purified by flash chromatography on silica gel with diethyl 1:1 ether/petroleum ether as eluent. The product **12**, a colorless, thick syrup (265 mg, 0.558 mmol, 83%), was obtained as a mixture of two double bond isomers, which could be separated by careful preparative TLC (10% diethyl ether in petroleum ether, 5 developments): ^{1}H NMR ($CDCl_3$) (higher R_f isomer) δ 1.29 (t, J = 7.0 Hz, 3 H), 1.99 (s, 3 H), 2.04 (s, 3 H), 2.14 (s, 3 H), 2.43 (m, 2 H), 3.83 (m, 1 H, C_5-H), 4.00 (q, J = 7.0 Hz, 2 H), 4.57 (d, J = 12.1 Hz, 1 H), 4.66 (d, J = 12 Hz, 1 H), 4.83 (s, 1 H), 5.11 (t, J = 9.9 Hz, 1 H), 5.28 (s, 1 H), 5.33 (d, J = 3.3 Hz, 1 H), 5.36 (d, J = 3.4 Hz, 1 H), 5.48 (t, J = 7.2 Hz, 1 H, C_7-H), 7.33 (m, 5 H); (lower R_f isomer) δ 1.33 (t, J = 7.0 Hz, 3 H), 1.98 (s, 3 H), 2.07 (s, 3 H), 2.12 (s, 3 H), 2.48 (m, 2 H), 3.85 (m, 1 H), 3.86 (q, J = 6.9 Hz, 2 H), 4.52 (d, J = 11.9 Hz, 1 H), 4.67 (d, J = 12 Hz, 1 H), 5.13 (t, J = 10.0 Hz, 1 H), 5.28 (m, 1 H), 5.33 (d, J = 3.3 Hz, 1 H), 5.36 (d, J = 3.5 Hz, 1 H), 5.64 (t, J = 7.9 Hz, 1 H), 7.33 (m, 5 H); ^{13}C NMR ($CDCl_3$) (high R_f isomer) δ 14.77, 20.60, 20.67, 20.81, 27.31, 67.13, 68.92, 69.04, 69.26, 69.65, 69.91, 96.80, 114.04 (CN), 121.73 (C_7), 127.91, 128.16, 128.56, 129.96 (C_8), 136.35, 169.70, 169.82, 169.93; (low R_f isomer) δ 14.21, 20.55, 20.63, 20.73, 29.61, 65.73, 68.44, 69.08, 69.39, 96.53, 113.16 (CN), 115.34 (C_7), 127.94, 128.09, 128.49, 132.53 (C_8), 136.22, 169.73, 169.78 (superimposed acetate carbonyls); IR ($CHCl_3$, mixture of isomers) 3031, 2989, 2934, 2880, 1748, 1645, 1372, 1130, 1076, 1051 cm^{-1}. A sample of recombined (1:1) isomers was used for elemental analysis. Anal. Calcd for $C_{24}H_{29}NO_9$: C, 60.62; H, 6.15; N, 2.95. Found: C, 61.00; H, 6.20; N, 2.86.

Phenylmethyl 6,7-Dideoxy-8-*O*-ethyl-α-D-*manno*-non-7-enopyranosidurononitrile (12) from 11. A sample of **11** (116 mg, 0.332 mmol) was dissolved in 1 mL of dry pyridine and 3 mL of Ac_2O and stirred overnight under N_2. The solution was then stirred while vacuum (vacuum pump) was applied. When the solvents had been removed, the residue was dissolved in 20 mL of diethyl ether, washed with 5 mL of water, 5 mL of 10% aqueous HCl, 5 mL of saturated aqueous $NaHCO_3$, and 5 mL of brine, dried over anhydrous Na_2SO_4, and rotary evaporated to leave **12** as a colorless thick syrup (146.7 mg, 0.309 mmol, 93%). By ^{1}H NMR and ^{13}C NMR analyses and by silica gel TLC in ether, 1:1 diethyl ether/petroleum ether, and 3:2 hexanes/EtOAc, this sample was identical with a sample of **12** prepared from cobaloxime **8**.

Phenylmethyl 8-Carbethoxy-7-hydroxy-6-deoxy-α-D-*manno*-octopyranoside 2,3,4-Tri-*O*-acetate (13). A solution of **12** (476 mg, 1.00 mmol) and piperidine (480 μL) in 15 mL of acetone was cooled in an ice–salt bath to −15 °C under N_2 and treated with $KMnO_4$ (163 mg, 1.03 mmol). The mixture was stirred until the ice melted, approximately 2 h, and then quenched with 1.0 g of $NaHSO_3$ in 3 mL of water. The brown suspension was diluted with 5 mL of water and 20 mL of chloroform, the phases were separated, and the aqueous layer was extracted with 5 mL of chloroform. The combined organic layers were washed with 5 mL each of 10% HCl, saturated $NaHCO_3$, and saturated brine, dried over anhydrous Na_2SO_4, and rotary evaporated to leave crude **13** as a colorless syrup (446 mg, 0.926 mmol, 92%): ^{1}H NMR ($CDCl_3$) (mixture of C_7-OH epimers) δ 1.30 (overlapping t, 3 H total), 1.71 (m, isomeric C_6-H, 1 H), 1.90–2.1 (4 apparent singlets for acetates, overlapping C_6-H, 10 H total), 4.24 (m, C_5-H, ester CH_2, 3 H), 4.51 (m, 2 H), 4.83 (m, 2 H), 5.15 (m, 1 H), 5.31 (m, 2 H), 7.30 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 14.08, 20.6–20.8 (overlapping acetate methyls), 34.79, 35.99, 61.64, 61.86, 65.81, 66.10, 66.39, 66.97, 68.98, 69.09, 69.24, 69.54, 69.59, 69.70, 69.75, 95.95, 127.92, 128.00, 128.40, 136.26, 136.55, 169.73, 169.93, 170.07, 175.10; IR ($CHCl_3$) 3467, 3025, 2983, 2940, 1748, 1433, 1371, 1221, 1076, 1051 cm^{-1}. A sample for elemental analysis was purified by preparative thin-layer chromatography on silica gel in 1:1 ether/petroleum ether (5 developments). Anal. Calcd for $C_{23}H_{30}O_{11}$: C, 57.26; H, 6.27. Found: C, 57.31; H, 6.24.

8-Carbethoxy-7-hydroxy-6-deoxy-α-D-*manno*-octopyranose 2,3,4-Tri-*O*-acetate (14). In a 250-mL Parr shaker bottle, crude **13** (446 mg, 0.925 mmol) was dissolved in 20 mL of 95% ethanol and 7 mL of glacial acetic acid, and 670 mg of 10% Pd/C (Engelhard) was added. The bottle was evacuated and flushed three times with hydrogen and then shaken at 60 psi of hydrogen pressure at room temperature for 24 h. The suspension was then suction filtered through Celite in a Büchner funnel. The filter was rinsed with 95% EtOH, and the combined filtrates were rotary evaporated to leave **14** as a white foam (306 mg, 0.754 mmol, 81% from **12**, 82% from **13**): ^{1}H NMR ($CDCl_3$, mixture of anomers and C_7 hydroxyls) δ 1.28 (overlapping t, 3 H total), 1.76 (m, 2 H, C_6), 1.98–2.15 (overlapping acetate methyls, 9 H total), 4.1–4.4 (m, 4 H), 5.0–5.40 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 13.99, 14.11 (ester methyls), 20.56, 20.66, 20.79, 20.88 (overlapping ester methyls), 34.73, 35.57 (isomeric C_6), 61.83, 62.02, 65.26, 66.20, 66.98, 67.27, 68.86, 69.35, 69.63, 70.01, 70.33, 71.18, 91.88, 92.04, 92.24, 92.63, 92.73 (isomeric acetal), 169.82, 169.97, 170.05, 170.12, 170.32, 174.91, 173.61; IR ($CHCl_3$) 3503, 2989, 2940, 1748, 1372, 1233, 1076, 1051 cm^{-1}.

3-Deoxy-D-*glycero*-D-*galacto*-octonic Acid and 3-Deoxy-D-*glycero*-D-*talo*-octonic Acid γ-Lactones (15) from 14. The mixture of anomers of **14** (46.7 mg, 0.119 mmol) was dissolved in 1 mL of MeOH, and 0.5 mL of 1 M aqueous NaOH was added. The mixture was stirred for 5 h and then treated with $NaBH_4$ (4.1 mg, 0.108 mmol) and stirred for 2 h. An additional 4 mg of $NaBH_4$ was added, the mixture was stirred for another 30 min, and then 1 mL of Amberlite IR-120 (H^+) ion exchange resin (washed repeatedly with MeOH and H_2O prior to use) was added. The suspension was stirred for 1 h and then passed down a 5 cm × 0.5 cm column of Amberlite IR-120 (H^+) resin. The filtrate was diluted with MeOH and rotary evaporated. The residue was redissolved in 2 mL of methanol and rotary evaporated to dryness

(five cycles) to remove the residual boric acid as trimethyl borate. The residue **15** was obtained as a colorless thick syrup (23.3 mg). By integration of the C_3 ^{13}C NMR resonances it was determined that the sample was a 5:1 mixture of **15** (73%) and the corresponding hydrolyzed, unlactonized hydroxy acid (**15** + H_2O, 14%) for a total yield of 87%: ^1H NMR (D_2O) δ 1.6–2.3 (m, 2 H), 3.5–4.0 (m, 7 H); ^{13}C NMR (D_2O) δ 32.14, 33.53, 63.74, 67.62, 68.66, 70.85, 71.11, 71.79, 71.84, 78.06, 79.78. TLC, ^1H NMR, and ^{13}C NMR spectral comparison of our **15** with an authentic sample of **15** prepared from 2-deoxy-D-*manno*-heptose according to the literature procedure[9b,c] confirmed that we had prepared **15**. Our yields in repeating the literature sequence to prepare authentic **15** (six steps from D-mannose **3**) were comparable to the yields reported in the literature, and all of the intermediates exhibited physical and spectroscopic properties consistent with those reported in the literature.

Ammonium 3-Deoxy-D-*manno*-2-octulosonate (16) from Authentic 15. A sample of **15** (100 mg, 0.406 mmol) was dissolved in 1 mL of H_2O, and $Na_2CO_3 \cdot H_2O$ (24 mg, 0.194 mmol) was added. The solution was heated to reflux for 3 min and then cooled to near room temperature. The mixture (pH 6 as measured by pH paper) was treated with 85% H_3PO_4 (10 μL), V_2O_5 (5 mg, 0.028 mmol), and $NaClO_3$ (17 mg, 0.16 mmol). The bright orange suspension was stirred at room temperature for 44 h, during which time it became homogeneous. Calcium ferrocyanide (50 mg) was added, and the precipitate that formed was removed by filtration through a few millimeters of Celite above a glass wool plug in the tip of a Pasteur pipet. The filter was rinsed with a few milliliters of H_2O, and the combined filtrates were treated with $Ca(OH)_2$ to increase the pH to 8 (pH paper). The suspension was filtered through a few millimeters Celite, and the filtrate was treated with 20 mg of oxalic acid. The suspension was filtered again through a few millimeters Celite, and the filtrate was made basic (pH 10) with 10% concentrated NH_4OH/H_2O. The solution was frozen in liquid N_2 and lyophilized. The residue was purified by chromatography on a 5 cm × 0.5 cm column of cellulose with 85:15 acetone/H_2O, followed by 70:30 acetone/H_2O. The fractions that tested positive with sodium thiobarbiturate on silica gel TLC were combined, frozen in liquid N_2, and lyophilized to leave 23.3 mg of a faintly green, chromatographically homogeneous solid. By integration of the C_3 ^{13}C resonances of the respective components, it was determined that the sample was a 12:1 mixture of **16** (21% yield from **15**) and the hydrolyzed, unlactonized hydroxy acid of **15** (**15** + H_2O). This sample was identical with commercially available **16** (Sigma no. K 7000) by TLC, ^1H NMR, ^{13}C NMR analyses: silica gel TLC in 10:10:3 MeOH/$CHCl_3$/H_2O and 4:1:1 95% EtOH/H_2O/glacial HOAc; ^1H NMR (D_2O) δ 1.7–2.0 (m, 2 H), 3.50–4.0 (m, 6 H); ^{13}C NMR (D_2O) δ 33.70, 43.80, 44.80, 63.10, 66.30, 66.68, 69.30, 71.27, 85.18, 85.72, 96.44.

Ammonium 3-Deoxy-2-octulosonate (16) from Our Synthetic 15. A 25-mg sample of lactones **15** was dissolved in 1 mL of doubly distilled H_2O and passed down a 0.5 × 5 cm column of Chelex ion exchange resin (Bio-Rad), which had been rinsed and packed in doubly distilled H_2O. The column was rinsed with 2 mL of doubly distilled H_2O, and the eluent was dropped directly into liquid N_2. The frozen beads were removed with Teflon-coated tweezers, placed in a tared vial, and lyophilized. The residue (22.1 mg, 0.0995 mmol) was dissolved in 1 mL of doubly distilled water, and K_2CO_3 (10 mg, 0.0725 mmol) was added. The solution was heated to reflux with a heat gun, and then it was kept hot for 10 min, during which time the pH dropped from 10 to ca. 5 as measured by pH paper. The solution was cooled to room temperature and 5 μL of 85% H_3PO_4, V_2O_5 (2 mg, 0.01 mmol), and $NaClO_3$ (10.3 mg, 0.0967 mmol) were added. The resulting bright orange solution was stirred at room temperature for 48 h. Calcium ferrocyanide (25 mg) was added to precipitate the residual vanadium. After being stirred for 15 min, the suspension was filtered through a few millimeters of Celite in a Pasteur pipet, and the filtrate was treated with $Ca(OH)_2$ to bring the pH to 10 (pH paper). The suspension was filtered through a few millimeters of Celite, and the filtrate was treated with disodium oxalate (20 mg) to remove the excess calcium. The suspension was again suction filtered through a few millimeters of Celite, and the filtrate was passed down a 3 cm × 0.5 cm column of Amberlite IR-120 (H^+) ion exchange resin. The eluent, containing KDO (**1**), was made basic to pH 10 (pH paper) with concentrated NH_4OH and then rotary evaporated to leave a pale green syrup. This material was applied to a 0.5 cm × 3 cm column of cellulose in a Pasteur pipet and eluted with 5 mL of 85% acetone/water and then 5 mL of 70% acetone/water. The fractions that contained **16** (eluted with the second solvent system) were combined and rotary evaporated to leave 5.2 mg of a pale yellow chromatographically homogeneous solid. By integration of the respective C_3 resonances in the ^{13}C NMR spectrum, it was determined that the sample was a 3:2 mixture **16** (12% yield from **15**) and hydrolyzed, unlactonized hydroxy acid of **15** (**15** + H_2O). The ammonium KDO in the sample was identical with an authentic commercially available sample (Sigma no. K 7000) by TLC in 4:1:1 95% EtOH/water/acetic acid and 10:10:3 methanol/chloroform/water, ^1H NMR, and ^{13}C NMR analyses.

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