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The First Synthesis of 3-Deoxy-D-*lyxo*-2-heptulosaric Acid (DHA) Derivatives

Anna Banaszek

Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw, Poland

Abstract: Synthetic route to the methyl ester of methyl glycoside of 3-deoxy-D-*lyxo*-heptulosaric acid (**13**) starting from 1-cyanogalactal **2** is described. The latter substance was prepared by direct elimination of acetic acid from **1** using 1,8-diazabicyclo[5.4.0]undec-7-ene in dichloromethane.

INTRODUCTION

A 3-deoxy-2-heptulosaric acid has originally been detected[1] as a partner of 3-deoxy-D-*manno*-octulosonic acid (KDO) in the lipopolysaccharides (LPS) of the Gram-negative bacterium *Acinetobacter calcoaceticus*, but neither the relative nor the absolute configuration of the sugar was determined.

Soon after, 3-deoxy-D-*lyxo*-2-heptulosaric acid (DHA) has been found in the rhamnogalacturonan II (RG-II) of different angiosperms and gymnosperms[2], in the cell wall (theca) of the green alga *Tetraselmis striata*[3] , and in some Gram-negative *Rhizobiaceae* bacteria[4,5]. Because of the lack of a standard for DHA, its the *lyxo* configuration has been deduced[2-5] from comparison of the chemical shifts and coupling constants of its protons with those of KDO.

It seems probable that 3-deoxy-2-heptulosaric acid isolated from *A. calcoaceticus*[1] and that found in RG-II[2] and *T. striata*[3] may be the same DHA.

It remains unclear whether DHA is a constituent of the LPS repeating units[1,3-6] or of the core region of carbohydrates.

As concerns 3-deoxyheptulosonic acid, some preparations have been reported[7,8]. In contrast, no synthetic approaches to DHA have been described. Bearing in mind the intended synthesis of the trisaccharide chains of *Rhizobium* LPS[5,6], it was essential to develop a simple method for preparation of the title component.

RESULTS AND DISCUSSION

Our strategy for the stereoselective synthesis of heptulosaric acid involved a pyranosidic one-carbon homologation procedure. Some of the methods applied for a such an elongation employ glycals as target molecules. Thus, Crich and Ritchie[7] have treated glycals with hydrogen chloride, thiophenol and ethyl diisopropylamine, and then with m-chloroperbenzoic acid to obtain phenyl sulfones. Valverde and Garcia-Ochoa[8] have converted glycals into phenyl sulfones of 2,3-deoxy-hex-2-enopyranoside by treatment with thiophenol and boron trifluoride etherate, followed by oxidation with m-chloroperbenzoic acid. Further transformations of these sulfones into methyl (methyl 3-deoxy-3-heptulopyranosid)onates have involved tedious synthetic procedures[7,8]. Horton *et al*[9] have converted oxidatively glycals into 2-deoxyaldonolactones which with the 1,3-dithian-2-yl anion gave the corresponding dithioacetals of 3-deoxyalduloses; the dithianyl group was then transformed into methyl ester by the reaction with mercuric salts in wet methanol.

As regards the strategies for DHA synthesis, our attention was focused on Horton's methodology[9]. Unfortunately, this procedure applied to 2-deoxy-D-*lyxo*-hexono-1,5-lactone led in our hands to the desired ulosonic acid in a very low yield. We, therefore, revised the strategy and investigated a protocol in which the cyanide **1**[10] was processed according to scheme 1. Thus, treatment of the cyanide **1** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dichloromethane[11] led to direct elimination of acetic acid and afford the target 1-cyanogalactal **2** in 69% yield. The compound **2** was then converted to ester **3**; the latter, after exhaustive treatment with mercuric trifluoroacetate in methanol followed by potassium chloride, gave the adduct **4** as a sole product. The exclusive addition of chloromercuri at C-3 position across the double bond was demonstrated by the upfield shift of H-3 (δ 2.58 in C_6D_6). A small coupling constant ($J_{3,4}$ = 5.4 Hz) between the chloromercuri substituent and the adjacent 4-*O*-acetyl group supported *trans*-diaxial arrangement of chloromercuri and the 2-methoxy group, and thus formation of the α-glucoside **4**. In the adduct **4** additional methoxy group was present (δ 3.05).

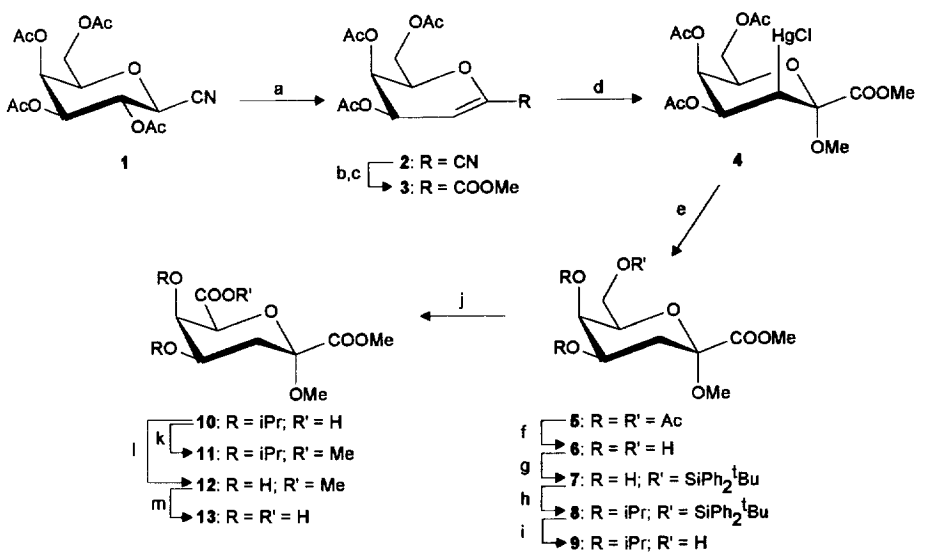
This result was fully consistent with the studies of Thiem *et al.*[12], who have well documented the preference of the *trans*-diaxial addition in glycals of the sialic acid series.

Although it is known[13] that reductive removal of the mercuric substituent may be accompanied by an elimination process which could then lead to the starting **3**, it was possible to perform selective reduction of the mercuric residue by the use of triphenyl- or tributyltin hydride/sodium acetate (excess) in benzene, thus obtaining the required **5** in a high yield.

The introduction of the carbonyl group into the C-7 position should be obviated by differentiating the protection of C-7-OH. Consequently, **5** was deacetylated with potassium carbonate in dry methanol at -20°C this leading to **6**, whereas under room temperature the reaction was accompanied by deblocking of the C-1-carboxymethyl group. The C-7-OH group in **6** was then protected as its tertbutyldiphenylsilyl ether **7** which reacted with dimethoxypropane to give the 4,5-*O*-isopropylidene derivative **8**. For introduction of the final

carboxylic group, the C-7-OH group was liberated by treatment with tetrabutylammonium fluoride, and the resulting alcohol **9** was subjected to the Sharpless oxidation procedure[14] summarized in Scheme 1. The single product **10** thus obtained was isolated as its methyl ester **11**. It is worth noting that esterification of **10** using methanol-trimethylsilyl chloride[15] affected the isopropylidene ring, this resulting in obtainment of the *O*-deprotected methyl ester of heptulasaric acid **12**. On the other hand, the 4,5-*O*-isopropylidene blocking in **10** is readily removable with a trifluoroacetic acid solution in dry dichloromethane, leading to **13**.

SCHEME 1



(a) DBU, CH_2Cl_2, 0°C → r.t.; (b) aq. 1 N NaOH, EtOH, 80°C; (c) 1. aq. HCl , 2. Ac_2O- Py; (d) 1. $Hg(COOCF_3)_2$-MeOH, 2.KCl; (e) AcONa, Ph_3SnH, benzene, r.t. →40°C; (f) K_2CO_3, dry MeOH, -20°C; (g) $Ph_2{}^tBuSiCl$, CH_2Cl_2, Et_3N, DMAP; (h) dimethoxypropane, CSA, DMF, r.t. → 40°C; (i) $Bu_4NF \cdot 3H_2O$, THF; (j) $NaIO_4$-$RuCl_3 \cdot 3H_2O$, MeCN-CCl_4-H_2O; (k) CH_2N_2-MeOH-Et_2O; (l) Me_3SiCl-MeOH; (m) CF_3COOH, CH_2Cl_2

The D-*lyxo*-configuration of **12**, arising from the D-*galacto* configuration of the substrate **1**, was confirmed by the parameters $J_{3ax,4}$ = 11.3 Hz; $J_{3eq,4}$ = 5.5 Hz; $J_{4,5}$ = 3.1 Hz; $J_{5,6}$ = 1.5 Hz. The α-configuration of the C-1-OMe group was supported by $J_{3,4}$ = 5.4 Hz found for the 3-mercuric derivative **5**.

The presented NMR data are in perfect agreement with those reported[3] for the methyl ester of methyl glycoside of 3-deoxy-D-*lyxo*-heptulosaric acid, isolated from a methanolysate of the *Tetraselmis striata* theca.

EXPERIMENTAL

Optical rotations were measured with JASCO DIP 360 Digital Polarimeter. ^{1}H NMR spectra were measured with Bruker AM-500 (500 MHz) and Varian AC-200 (200 MHz) spectrometers with TMS as internal standard. High resolution mass spectra (HR-MS) were measured with AMD-604 mass-spectrometer. Reactions were controlled using TLC on Merck's alu-plates (0.2 mm). All reagents and solvents were purified and dried according to common methods[16]. Organic solutions were dried with anhydrous magnesium sulfate. Reaction products were purified by column chromatography (flash), using Merck's Kieselgel 60 (230-400 mesh).

4,5,7-Tri-*O*-acetyl-2-anhydro-3-deoxy-D-*lyxo*-hept-2-enononitrile (2). - To a stirred solution of cyanide **1**[10] (2 g, 6.68 mmol) in dry CH_2Cl_2 (50 mL) were added molecular sieves (~2 g). The mixture was stirred for 30 min., and then DBU (2 mL, 13.3 mmol) was added at 0°C under argon. Stirring was continued for 20 h at room temperature, then the mixture was filtered, and the filtrate was washed with saturated ammonium chloride solution, dried and evaporated. The residue was purified by column chromatography (hexane-ether, 1:1) to give **2** (1.15 g, 69 %) as crystals; m.p. 115-116°C; $[\alpha]_D^{20}$ -52.2° (*c* 1.3, $CHCl_3$); lit.[11]: m.p. 115-116°C; $[\alpha]_D^{20}$ -52° (c 1.2, $CHCl_3$).

Methyl 4,5,7-tri-*O*-acetyl-2-anhydro-3-deoxy-D-*lyxo*-hept-2-enoate (3). - To a solution of nitrile **2** (2.8 g, 9.36 mmol) in ethanol (100 mL) was added 1 N aqueous sodium hydroxide (80 mL). The reaction mixture was heated to ~80°C for 40 h, then cooled to room temperature, and acetic acid was added to neutralize the solution (pH ~6). The solution was evaporated under reduced pressure, and the solid was treated with pyridine (15 mL), acetic anhydride (15 mL) and left overnight. 1 N Aqueous hydrochloric acid was added (pH 3) and the aqueous extracts were dried and concentrated, then redissolved in methanol. Solution of diazomethane in ether was added, and the resulting mixture was left for 1 h. Evaporation of solvents left the sole product (TLC, hexane-acetone, 3:2), which crystallized from ether to give **3** (2.66 g, 86 %); m.p. 130-131°C; $[\alpha]_D^{20}$ -72.5° (*c* 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.04, 2.09, 2.12 (3 s × 3 H, 3 OAc); 3.83 (s, 3 H, $COOCH_3$); 4.31 (ddd, 2 H, H-4); 5.92 (dd, 1 H, H-3); $J_{3,4}$ = 2.6; $J_{3,5}$ = 1.64; $J_{4,5}$ = 3.87; $J_{4,6}$ = 1.2; $J_{5,6}$ = 1.5; $J_{6,7}$ = 6.6; $J_{6,7'}$ = 10.7; $J_{7,7'}$ = 11.6 Hz.

Anal. Calcd for $C_{14}H_{18}O_9$ (330.28): C, 50.91; H, 5.49. Found: C, 51.00; H, 5.47.

Methyl [methyl 4,5,7-tri-*O*-acetyl-3-chloromercuri-3-deoxy-α-D-*lyxo*-2-heptulopyranosid)onate (4). - Mercuric trifluoroacetate (4.39 g, 10.30 mmol) was added to a stirred suspension of the ester **3** (1.70 g, 5.15 mmol) in dry methanol (30 mL). After being stirred for 30 min at room temperature, TLC (hexane-acetone, 3:2) showed disappearance of the substrate. Potassium chloride (1 g, 13.4 mmol) was then added

and stirring was continued for 2 h. Solids were filtered off and the solution was concentrated. The residue was treated with ether and filtered again to remove unresolved solids. Evaporation of the solvent, followed by filtration through a short column (hexane-acetone, 17:3) gave the title **4** (2.9 g, 100%), which was used directly in the next step. A sample of pure **4** was obtained by chromatography; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.01, 2.06, 2.26 (3 s × 3 H, 3 OAc), 2.99 (dd, 1 H, H-3); 3.30 (s, 3 H, OCH_3); 3.38 (s, 3 H, $COOCH_3$); 4.15-4.25 (m, 3 H, H-6, H-7, H-7'); 5.42 (dt, H-5); 5.89 (dd, H-4); ^{1}H NMR (200 MHz, C_6D_6): δ 1.57, 1.58, 1.90 (3 × 3 OAc); 2.52 (dd, 1 H, H-3); 3.05 (s, 3 H, OCH_3); 3.22 (s ,3 H, $COOCH_3$); 3.69 (ddd, 1 H, H-6); 4.06 (s, 1 H, H-7); 4.09 (s, 3 H, H-7'); 5.36 (ddd, 1 H, H-5); 5.83 (dd, 1 H, H-4); $J_{3,4}$ = 5.3, $J_{3,5}$ = 0.7, $J_{4,5}$ = 3.3, $J_{5,6}$ = 1.1, $J_{6,7}$ = 6.0, $J_{6,7'}$ = 6.2 Hz.

Methyl (methyl 4,5,7-tri-*O*-acetyl-3-deoxy-α-D-*lyxo*-2-heptulopyranosid)onate (5). - A solution of **4** (2.8 g, 4.98 mmol) and dry sodium acetate (1.7 g, 20.7 mmol) in dry benzene (20 mL) was treated with triphenyltin hydride (2.5 g, 5.87 mmol) and AIBN (10 mg) under argon. The reaction mixture was heated to 40°C with stirring until TLC showed disappearance of the substrate (TLC, hexane-acetone, 7:3) and then evaporated to dryness. The residue was dissolved in ether, 60% aqueous solution of potassium fluoride was added, and the resulting suspension was stirred overnight. The mixture was diluted with ether and filtered through Celite, and the organic phase was separated. The aqueous phase was extracted with ether, dried and concentrated. Column chromatography of the residue (hexane-acetone, 17:3) provided **5** (1.6 g, 86%) as a colorless oil; $[\alpha]_D^{20}$ +56.6° (*c* 0.62, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.0-2.13 (m, H-3_{ax}); 2.02, 2.04, 2.06 (3 s, 3 × 3 H, 3 OAc); 2.3 (dd, 1 H, H-3_{eq}); 3.26 (s, 3 H, OCH_3); 3.86 (s, 3 H, $COOCH_3$), 4.15-4.33 (m, 3 H, H-6, H-7, H-7'); 5.24 (dt, 1 H, H-5); 6.33 (dd, 1 H, H-4); $J_{3eq,4}$ = 6.1, $J_{3eq,5}$ = 0.7, $J_{4,5}$ = 3.2, $J_{5,6}$ = 1.0 Hz.

Anal. Calcd for $C_{15}H_{22}O_{10}$ (362.33): C, 49.72; H, 6.12. Found: C, 49.76; H, 6.09.

Methyl (methyl 3-deoxy-α-D-*lyxo*-2-heptulopyranosid)onate (6). - To a cooled (-20°C) solution of **5** (3.62 g, 10 mmol) in dry methanol (50 mL) was added potassium carbonate (2.76 g, 20 mmol) and the resulting mixture was stirred at the same temperature for 1 h (TLC, $CHCl_3$-methanol, 9:1). The mixture was filtered through Celite, then through a short column of silica gel to give **6** (2.04 g, 86%); m.p. 114-115°C; $[\alpha]_D^{20}$ +89.1° (*c* 1.0, methanol).

Anal. Calcd for $C_9H_{16}O_7$ (236.22): C, 45.76; H, 6.83. Found: C, 45.78; H, 7.00.

Methyl [methyl 7-*O*-(*t*-butyldiphenylsilyl)-3-deoxy-α-D-*lyxo*-2-heptulopyranosid]onate (7). - To a cold (0°C) solution of **6** (0.364 g, 1.54 mmol), triethylamine (0.19 g, 0.25 mL, 1.88 mmol), and 4-dimethylaminopyridine (20 mL) in dry CH_2Cl_2 (25 mL) was added *t*-butyldiphenylsilyl chloride (0.466 g, 0.434 mL, 1.69 mmol). The solution was allowed to reach room temperature, and stirred overnight (TLC,

hexane-acetone, 3:2). The reaction mixture was then evaporated and the residue was chromatographed on silica gel (hexane-acetone, 7:3) to afford **7** (0.64 g, 88%) as colourless oil; $[\alpha]_D^{20}$ +38° (*c* 0.8, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.07 (s, 3 H, *t*-Bu); 1.87 (dd, 1 H, H-3_{ax}); 2.14 (d, 1 H, OH); 2.26 (d, 1 H, OH); 2.84 (d, 1 H, H-3_{eq}); 3.17 (s, 3 H, OCH_3); 3.68 (td, 1 H, H-6); 3.78 (s, 3 H, $COOCH_3$), 3.97 (dddd, 2 H, H-7, H-7'); 3.97-4.05 (m, 2 H, H-4, H-5); 7.38-7.45 (m, 5 H, Ph); 7.73 (dddd, 5 H, Ph); $J_{3ax,4}$ = 11.0, $J_{3eq,4}$ = 2.8, $J_{5,6}$ = 0.9, $J_{6,7}$ = 4.9, $J_{6,7'}$ = 5.9, $J_{7,7'}$ = 10.7 Hz.

Anal. Calcd for $C_{25}H_{34}O_7Si$ (474.61): C, 63.26; H, 7.22. Found: C, 63.19; H, 7.03.

Methyl [methyl 7-*O*-(*t*-butyldiphenylsilyl)-3-deoxy-4,5-*O*-isopropylidene-α-D-*lyxo*-2-heptulopyranosid]onate (8). - To a solution of **7** (0.462 g, 1 mmol) in dry N,N-dimethylformamide (5 mL) was added dimethoxypropane (0.208 g, 0.245 ml, 2 mmol) and camphorsulphonic acid (5 mg). The solution was stirred at 40°C (bath) for ~1 h, then cooled to 0°C. Ether and water were added, and the organic phase was separated. The aqueous phase was extracted with ether, and the combined organics were washed with saturated sodium bicarbonate solution, dried and concentrated. Chromatography of the residue (hexane-acetone, 17:3) provided **8** (0.447 g, 87%) as a colourless oil; $[\alpha]_D^{20}$ -21.0° (*c* 0.96, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.06 (s, 9 H, *t*-Bu); 1.28, 1.38 (2 s, 2 × 3 H, *i*-Pr); 1.93 (dd, 1 H, H-3_{ax}); 2.58 (dd, 1 H, H-3_{eq}); 3.21 (s, 3 H, OCH_3); 3.79 (s, 3 H, $COOCH_3$); 3.82 (td, 1 H, H-6); 3.95 (ddd, 2 H, H-7, H-7'); 4.21 (dd, 1 H, H-5); 4.47 (ddd, 1 H, H-4); 7.38-7.45 (m, 5 H, Ph); 7.73 (dddd, 5 H, Ph); $J_{3ax,3eq}$ = 15.0, $J_{3a,4}$ = 3.7, $J_{3eq,4}$ = 5.0, $J_{4,5}$ = 7.1, $J_{5,6}$ = 2.0, $J_{6,7}$ = 6.4, $J_{7a,7b}$ = 10.3 Hz.

Anal. Calcd for $C_{28}H_{38}O_7Si$ (514.67): C, 65,33; H, 7.44. Found: C, 65.10; H, 7.21.

Methyl (methyl 3-deoxy-4,5-*O*-isopropylidene-α-D-*lyxo*-2-heptulopyranosid)onate (9). - Tetra-n-butylammonium fluoride (0.27 g, 0.85 mmol) was added to a solution of **8** (0.355 g, 0.69 mmol) in tetrahydrofuran (15 mL). The reaction mixture was stirred at room temperature for ~0.5 h. The reaction was then diluted with ether and washed with brine. the organic phase was dried, concentrated and the residue was purified on a short column of silica gel (hexane-acetone, 4:1) to give the crystalline **9** (0.18 g, 94%); m.p. 111.5-112°C; $[\alpha]_D^{20}$ +51.8° (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.30, 1.44 (2 s × 3 H, O-iPr); 1.96 (dd, 1 H, H-3_{ax}); 2.27 (bs, 1 H, OH); 2.60 (dd, 1 H, H-3_{eq}); 3.25 (s, 3 H, OCH_3); 3.80 (s, 3 H, $COOCH_3$); 3.80-3.90 (m, 2 H, H-7, H-7'); 4.00 (ddd, 1 H, H-6); 4.18 (dd, 1 H, H-5); 4.50 (ddd, 1 H, H-4); $J_{3ax,3eq}$ = 15.1, $J_{3ax,4}$ = 3.7, $J_{3eq,4}$ = 5.0, $J_{4,5}$ = 7.1, $J_{5,6}$ = 1.9, $J_{6,7}$ = 4.5, $J_{6,7'}$ = 7.5 Hz; HR-MS calcd. for $C_{12}H_{20}O_7Na$ $(M+Na)^+$: 299.1107. Found: 299.1104.

Methyl (methyl 7-carboxy-3-deoxy-4,5-*O*-isopropylidene-α-D-*lyxo*-2-heptulopyranosid)onate (10). - To a stirred solution of **9** (0.19 g, 0.69 mmol) in acetonitrile (1.5 mL) carbon tetrachloride (1.5 mL) and

water (2.28 mL) were added. The mixture was cooled in the ice-bath, and sodium periodide (0.665 g, 3.12 mmol) was slowly added, followed by rhutenium chloride (16 mg, 0.072 mmol). The reaction mixture was allowed to warm to room temperature for. After disappearance of substrate (TLC, CH_2Cl_2-acetone, 3:2) the mixture was diluted with $CHCl_3$ (10 mL), quenched by the addition of diluted aqueous sodium bisulfite, and stirred for an additional 30 min. The organic phase was separated and the aqueous phase was extracted by $CHCl_3$ (5 × 20 mL). The organic layers were dried, filtered and concentrated. The residue was purified on a silica gel column (CH_2Cl_2-methanol, 43:2) to yield the acid **10** (0.13 g, 65%) as crystals; m.p. 182.5-183°C; $[\alpha]_D^{20}$ +3.92° (*c* 0.79, $CHCl_3$); IR (KBr): 1240 cm^{-1} (COOH); ^1H NMR (500 MHz, $CDCl_3$): δ 1.29, 1.41 (2 s × 3 H, O-iPr); 1.90 (dt, 1 H, H-3_{ax}); 2.82 (dt, 1 h, H-3_{eq}); 3.26 (s, 3 H, OCH_3); 3.84 (s, 3 H, $COCH_3$); 4.36 (t, 1 H, H-6); 4.57 (t, 2 H, H-4, H-5); $J_{3ax,3eq}$ = 15.5, $J_{3ax,4}$ = 2.3, $J_{3eq,5}$ = 0.9, $J_{4,5}$ = 7.0, $J_{5,6}$ = 1.7 Hz.

HR-MS calcd. for $C_{12}H_{18}O_8$ $(M+H)^+$: 291.1080. Found: 291.1063.

Methyl (methyl 7-carbomethoxy-3-deoxy-4,5-*O*-isopropylidene-α-D-*lyxo*-2-heptulopyranosid)onate (11). - Diazomethane (solution in ether) was added to a cold solution of **10** (30 mg, 0.1 mmol) in methanol. The reaction was left at 0°C for 30 min (TLC, hexane-acetone, 3:2). The solvents were evaporated to give the crude ester **11** as a pale yellow gum; ^1H NMR (500 MHz, $CDCl_3$): δ 1.30, 1.40 (2 s × 3 H, O-iPr); 1.90 (dt, 1 H, H-3_{ax}); 2.69 (dt, 1 H, H-6); 4.70 (dd, 1 H, H-5); 4.60 (ddd, 1 H, H-4); $J_{3ax,3eq}$ = 15.3, $J_{3ax,4}$ = 2.7, $J_{3ax,5}$ = 1.5, $J_{3eq,4}$ = 3.3, $J_{4,5}$ =6.6, $J_{5,6}$ = 1.8 Hz.

Methyl (methyl 7-carbomethoxy-3-deoxy-α-D-*lyxo*-2-heptulopyranosid)onate (12). - Trimethylsilyl chloride (1 M solution in methanol, 0.25 mL) was added dropwise at 0°C to a solution of **10** (29 mg, 0.1 mmol) in dry methanol (2 mL). The reaction mixture was raised to room temperature and mainted overnight (TLC, CH_2Cl_2-methanol, 4:1). The solution was concentrated and the residue was purified on a silica gel column (CH_2Cl_2-acetone, 1:1) to give **12** (20 mg, 76%) as a clear syrup; $[\alpha]_D^{20}$ +60.5° (*c* 1.26, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.92 (dd, 1 H, H-3_{ax}); 2.19 (ddd, 1 H, H-3_{eq}); 2.33 (d, 1 H, OH); 2.81 (bs, 1 H, OH); 3.29 (s, 3 H, OCH_3); 3.84, 3.86 (2 s × 3 H, 2 $COOCH_3$); 4.11 (ddd, 1 H, H-4); 4.21 (bs, 1 H, H-5); 4.30 (d, 1 H, H-6); $J_{3ax,3eq}$ = 13.0, $J_{3ax,4}$ = 11.7, $J_{3eq,4}$ = 5.2, $J_{3eq,5}$ = 0.8, $J_{4,5}$ = 4.9, $J_{5,6}$ = 1.5 Hz.

HR-MS calcd. for $C_{10}H_{17}O_8$ $(M+H)^+$: 265.0923. Found: 265.0919.

Methyl (methyl 7-carboxy-3-deoxy-α-D-*lyxo*-2-heptulopyranosid)onate (13). - To a solution of **10** (29 mg, 0.1 mmol) in dry dichlorometane (1 mL) was added trifluoroacetic acid (10% solution in dry CH_2Cl_2, 1 mL). The reaction mixture was stirred at room temperature until TLC (CH_2Cl_2-methanol, 7:3) indicated disappearance of the substrate (~1 h). The mixture was diluted with toluene, and evaporated in vacuo. The resultant syrup (sole compound, TLC: propanol-water-acetic acid, 20:5:0.2) was triturated with ether, and dried under high vacuo to give **13** (20 mg, 80%) as a foam; $[\alpha]_D^{20}$ +6.2° (*c* 1.2, MeOH); ^1H NMR (500 MHz,

$CDCl_3$): δ 1.94 (dd, 1 H, OH); 1.99 (ddd, 1 H, H-3eq); 3.23 (s, 3 H, OCH_3); 3.82 (s, 3 H, $COOCH_3$); 3.88 (m, 1 H, OH), 4.03 (ddd, 1 H, H-4); 4.14 (ddd, 1 H, H-5); 4.29 (d, 1 H, H-6); $J_{3ax,4}$ = 11.4; $J_{3ax,3eq}$ = 12.8, $J_{3eq,4}$ = 5.3, $J_{4,5}$ = 3.1, $J_{5,6}$ 1.5 Hz. HR-MS calcd. for $C_9H_{14}O_8$ $(M-H+2Na)^+$: 295.0363. Found: 295.0384.

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