Pergamon

Tetrahedron, Vol. 53, No. 30, pp. 10643-10658, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00675-3

Convenient Preparation of α- and β-Glycosides of Novel Isomeric 3-Deoxy-hept-2-ulosaric Acids Diesters

Jacek Młynarski and Anna Banaszek*

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

Abstract: Methyl 3-deoxy-α and β-D-*ribo*, D-*xylo* and D-*lyxo*-hept-2-ulosonic acids were obtained from the individual α and β anomers of the same methyl (methyl 3-deoxy-D-*arabino*-hept-2-ulopyranosid)-onate in a sequential epimerisation at C-4 and/or C-5 of their appropriate *O*-trifluoromethanesulfonic derivatives, using cesium acetate. Subsequent oxidation of the 7-OH group in these compounds lead to the new isomeric 3-deoxy-hept-2-ulosaric acids derivatives. © 1997 Elsevier Science Ltd.

INTRODUCTION

3-Deoxy-hept-2-ulosaric acids are, to our knowledge, represented in Nature by only one isomer: the 3-deoxy-D-*lyxo*-hept-2-ulosaric acid (DHA). DHA has been reported to occur as a component of rhamnogalacturonane[1a] and of the glycoprotein cell wall of algae.[1b] Besides, DHA was isolated from the lipopolysaccharides (LPS) of Gram-negative bacteria *Acinobacter calcoaceticus*,[1c] *Rhizobium leguminosarum bv. trifolii* 24 and its exo⁻ mutant AR20.[1d,e] In the LPSs of the mutant AR20, DHA was estimated[1e] to be a constituent of the trisaccharide repeating unit. These interesting biological and chemical properties of DHA, being side-chain shortened 3-deoxy-D-*manno*-oct-2-ulosonic acid (KDO) with an additional carboxy group at C-7, prompted us to synthesize all isomeric 3-deoxy-hept-2-ulosaric acids.

In our recent paper[2] we have already reported on the synthesis of DHA. In this paper, we describe the preparation of three remaining hitherto unreported stereoisomers of the α-series and four of the β-series. We assume that these compounds would be valuable for biological investigations,[3,4] as was the case of KDO[5] and neuraminic acid (Neu5Ac)[6], modified either at C-4 and C-5, or the side-chain-shortened.[7]

RESULTS AND DISCUSSION

Our strategy for the construction of the isomeric sugars was based on a sequential epimerisation at C-4 and/or C-5. The key precursors, methyl (methyl 3-deoxy-α and β-D-*arabino*-hept-2-ulopyranosid)onates (**1a** and **1b**, respectively) were prepared by the methoxymercuration-demercuration of 1-carbomethoxy-D-glucal, according to our previously described methodology.[8] The α and β anomers thus obtained (4:1) were separated by chromatography and served for the preparation of both the α and β-series of 3-deoxy-hept-2-ulosaric acids.

Among the known methods of inversion at different carbon atoms of the pyranose ring the Mitsunobu reaction[9] (TPP, DEAD, RCO_2H) is the most commonly used. This very useful reaction is, however, very sensitive to the steric hindrance prohibiting inversion or causing undesired side-reactions.[9] More promising seemed to be the nucleophilic displacement of the triflate group by cesium acetate in the presence of 18-crown-6 in toluene.[10] A limited number of applications of this methodology in sugars has been reported.[11] In this context utilization of this reaction for C-4, C-5 epimerisation in the sialic acids-type compounds was highly desirable.

Introduction of the triflate at C-4 position was preceded by a selective protection of 5,7-OH groups as the benzylidene derivative,[12] to give **2a,b**. Esterification of 4-OH in **2a,b** with triflic anhydride in dichloromethane and pyridine at -10 °C afforded the 4-triflate in 92% yield. This derivative of the α anomer, when treated with CsOAc in toluene, furnished the methyl (methyl 4-*O*-acetyl-5,7- *O*-benzylidene-3-deoxy-α-D-*ribo*-hept-2-ulopyranosid)onate (**3a**) in 60% yield, accompanied by the 3,4-unsaturated product **4** (~15%) (Scheme 1).

Using tetraethylammonium acetate as a nucleophile in the reaction with the same substrate (**2a**) led to **3a** and **4** in a ratio 2:3, respectively; this confirms the better nucleophilicity and lower basicity of cesium acetate in this substitution reaction as compared to those of tetraethylammonium acetate. In contrast, 4-triflyl group in the β-anomer **2b** underwent the substitution with cesium acetate in 96% yield, and none of the elimination product was observed in the reaction mixture. This difference in the reaction with cesium acetate of both these anomers cannot be explained by steric effects, because both C-2 substituents are in similar proximity to the C-4 reactive center. A more reliable explanation seems to be the influence of electronic factors due to repulsion of the negatively charged nucleophile by the electron rich α methoxy oxygen.[13]

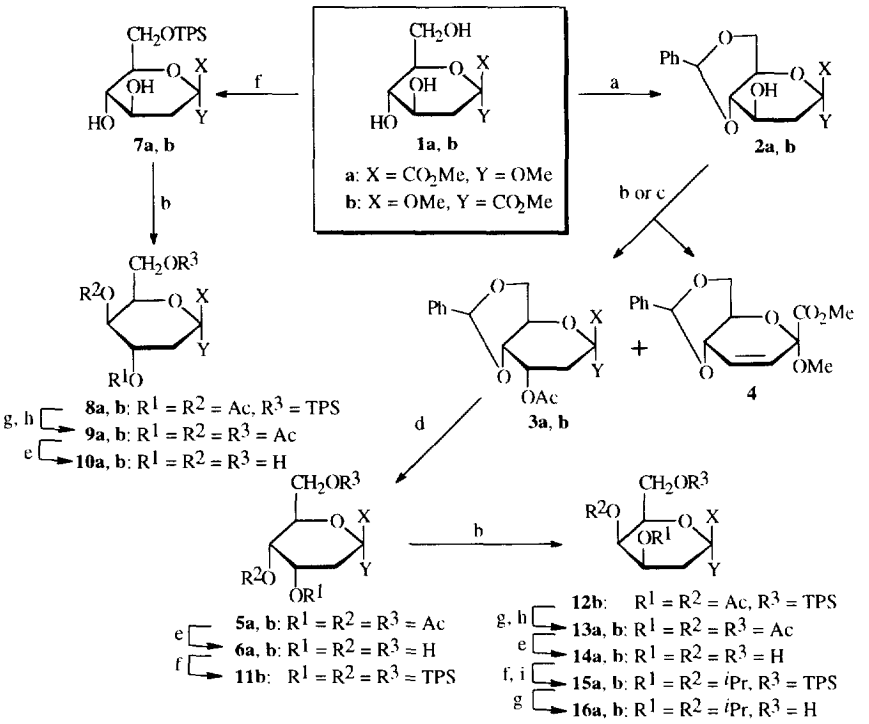
Hydrolysis of the 5,7-*O*-benzylidene residue in **3a** with aqueous trifluoroacetic acid in dichloromethane was accompanied by a partial acetyl migration, to give a mixture of 4- and 5-*O*-acetyl derivatives which after acetylation afforded the fully acetylated product **5a**.

A more efficient procedure applied to deprotection of the 5,7-*O*-benzylidene group involves treatment of **3** with cupric chloride dihydrate in THF-ethanol,[14] followed by acetylation, leading to **5** in 95% yield.

For the preparation of the *xylo* isomer **9a** and **9b**, 7-OH group in both anomers **1a** and **1b** was protected as 7-*O*-TPS (*t*-butyldiphenylsilyl) derivative **7a** and **7b**, respectively. Epimerisation of two centers in one step

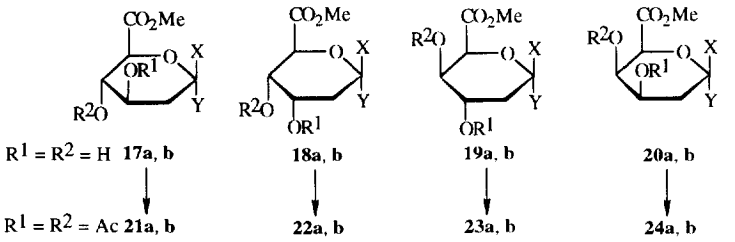
allowed introduction of two triflate groups at C-4 and C-5. This was done in a similar way as mentioned above. Thus, treatment of **7a** or **7b** with triflic anhydride-pyridine in dichloromethane, followed by cesium acetate and 18-crown-6, furnished the doubly inverted at C-4 and C-5 methyl (methyl 4,5-di-*O*-acetyl-7-*O*-(*t*-butyldiphenylsilyl)-3-deoxy-α-D-*xylo*- or β-D-*xylo*-hept-2-ulopyranosid)onate (**8a** or **8b**), both in high yield.

The double displacement process was applied also for the conversion of the β-D-*ribo* isomer **11b** into the methyl (methyl 4,5-di-*O*-acetyl-7-O-(*t*-butyldiphenylsilyl)-3-deoxy-β-D-*lyxo*-hept-2-ulopyranosid)onate (**12b**).



Scheme 1. Reagents: (a) PhCHO-TFA; (b) Tf_2O-Py, CH_2Cl_2 / CsOAc, $PhCH_3$, 70 °C; (c) Tf_2O-Py, CH_2Cl_2 / Et_4N OAc, $PhCH_3$, 70 °C; (d) $CuCl_2 \cdot 2H_2O$, THF, EtOH, reflux; (e) $NaHCO_3$-MeOH; (f) TPSCl-TEA, CH_2Cl_2; (g) TBAF, THF; (h) Ac_2O-Py; (i) DMP, CSA, DMF.

For the removal of acetyl residues in the prepared compounds sodium bicarbonate in methanol was applied.[8] These mild conditions prevented hydrolysis of the C-1 methyl ester. Crucial oxidation of the primary 7-OH group to the carboxyl one in the α and β-anomers of the isomeric heptulosonic acids derivatives **1**, **6**, **10** and **14**, was carried out with an excess of sodium hypochlorite catalysed by 2,2,6,6-tetramethylpipe-ridine 1-oxyl, radical (TEMPO), in aqueous acetone solution.[15] In all cases but one, the oxidation reaction led to the 7-heptulosaric acids, which were *in situ* transformed into their 1,7-dicarbomethoxy derivatives **17-20** by treatment with trimethylsilyl chloride in methanol. (Scheme 2).



Scheme 2. a: X = CO_2Me, Y = OMe; b: X = OMe, Y = CO_2Me.

In contrast, oxidation of the *β-lyxo* isomer **14b** under the same conditions gave a mixture of unresolved products. The oxidation of this isomer succeeded, however, leading to the desired heptulosaric acid **20b**, when the reaction was performed with the substrate **16b**, having 4,5-OH groups blocked by the *O*-isopropylidene ring. This, to our knowledge, is the first observation on the necessity of protected of secondary hydroxyl groups in substrate, whose primary OH group has to be oxidized by NaOCl-TEMPO.[15]

It is worth noting, that esterification of this oxidation product, using methanol-trimethylsilyl chloride affected the isopropylidene ring,[2] this resulted in obtention of the 4,5-*O*-deprotected methyl ester of heptulosaric acid **20b**.

The α or β configuration of the prepared compounds arises from the known configuration of their substrates **1a** and **1b**. It is important to stress, however, that ^{1}H NMR spectra of the all anomeric pairs demonstrate the general feature, i.e., the chemical shifts of H-3_{eq} and H-6 are shifted further downfield in the β-anomers than in the α-anomers (Table 1). This observation is compatible with the analogous data for KDO.[16] An exclusion concerns the *ribo* isomers **22a** and **22b**, where the δ value of H-3_{eq} (δ 2.34 ppm) in the β-anomer occurs in the higher field than that of the α-anomer (δ 2.44 ppm). This anomaly can be considered in terms of a distortion of $^5C_2$ chair conformation (typical of a nearly all 3-deoxy-2-ulosonic acids[17]) as it is indicated by the magnitude of the coupling constants value: $J_{3eq,4}$ 7.4 and 8.8 Hz in **18b** and **22b**, respectively, as compared to those of 7-OAc and 7-OH (**6b** and **5b**) counterparts: $J_{3eq,4}$ 5.4 Hz. The reason for such phenomenon is somewhat difficult to explain in terms of influence of the 7-carbomethoxy group, because all other diesters (**17a,b**; **19a,b - 24a, b**) present typical $^5C_2$ conformation. A similar anomaly was reported[18] for modified sialic acids bearing the carbonyl group at C-7.

In conclusion, the proposed methodology allows ready construction of isomeric 3-deoxy-2-ulosonic and ulosaric acids. The ^{1}H NMR spectral data are valuable for determination of α and β configuration in the anomeric pair.

Table 1. Chemical shifts of H-3_{eq} and H-6.

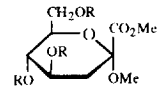
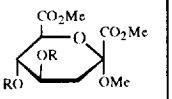
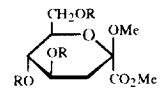
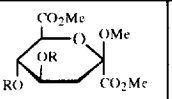
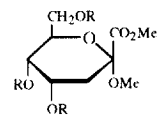
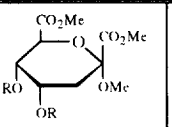
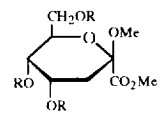
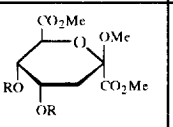
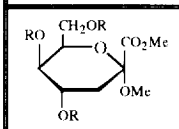
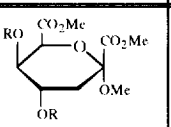
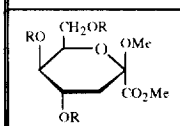
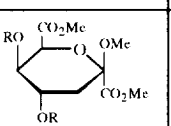
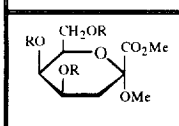
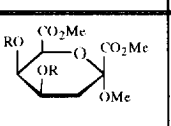
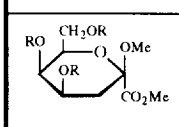
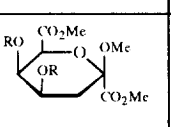
	R = Ac		R = H			R = Ac		R = H	
	3_{eq}	6	3_{eq}	6		3_{eq}	6	3_{eq}	6
 **1a**[8]	2.52	3.89	2.36	3.50	 **17a, 21a**	2.54	4.20	2.40	4.15
 **1b**[8]	2.66	4.01	2.45	3.50	 **17b, 21b**	2.62	4.41	2.64	4.24
 **5a, 6a**	2.41	4.30	2.29	3.90	 **18a, 22a**	2.44	4.60	2.18	4.32
 **5b, 6b**	2.57	4.47	2.52	4.15	 **18b, 22b**	2.34	4.71	2.40	4.70
 **9a, 10a**	2.30	4.36	2.04	4.11	 **19a, 23a**	2.34	4.77	2.17	4.80
 **9b, 10b**	2.52	4.56	2.35	4.33	 **19b, 23b**	2.54	5.02	2.36	4.99
 **13a, 14a**	2.17	4.08	2.09	3.85	 **20a, 24a**	2.20	4.47	2.19	4.30
 **13b, 14b**	2.36	4.23	2.36	3.90	 **20b, 24b**	2.36	4.74	2.36	4.63

Table 2. The distance between H-3_{eq} and H-3_{ax}.

entry	a	b	entry	a	b
1[8] 4,5-OH	0.61	0.82	**17**	0.59	0.76
1[8] 4,5-OAc	0.64	0.71	**21**	0.64	0.61
6	0.23	0.55	**18**	0.19	0.32
5	0.32	0.49	**22**	0.32	0.10
10	0.10	0.23	**19**	0.11	0.20
9	0.25	0.43	**23**	0.26	0.40
14	0.18	0.38	**20**	0,27	0,36
13	0.07	0.22	**24**	0.07	0,16

EXPERIMENTAL

General methods: Optical rotations were measured with a JASCO DIP Digital Polarimeter at room temperature. ^{1}H NMR spectra were recorded on Bruker AM-500 (500 MHz) and Varian AC-200 (200 MHz) spectrometers with Me_4Si as internal standard. Mass spectra were taken on a AMD-604 mass spectrometer. Reactions were controlled using TLC on silica [Merck alu-plates (0.2 mm)]. All reagents and solvents were purified and dried according to common methods. All organic solutions were dried over $MgSO_4$. Reaction products were purified by flash chromatography, using Merck's Kieselgel 60 (240-400 mesh or 70-230 mesh). All acetylation reactions were performed using acetic anhydride-pyridine (1:1) at room temperature (with catalytic amount of DMAP if necessary). Cesium acetate was dried by stirring with acetic anhydride overnight and evaporation with toluene. Solvents: A-hexane-ether (1:1+5% MeOH), B - hexane-ether (1:1), C - CH_2Cl_2-MeOH (9:1), D - CH_2Cl_2-MeOH (95:5).

Methyl (methyl 5,7-*O*-benzylidene-3-deoxy-α-D-*arabino*-hept-2-ulopyranosid)onate (2a) — The ester **1**[8] (470 mg, 2 mmol) in benzaldehyde (5mL) was treated with trifluoroacetic acid (0.5 mL) at room temperature. The mixture was stirred at this temperature for 1 h (TLC - solvent A), then CH_2Cl_2 was added, and the mixture was neutralized with triethylamine. Purification by chromatography afforded **2a** (630 mg, 98%) as white crystals: m.p. 104 °C; $[\alpha]_D$ +53.0° (c 1.05, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.82 (dd, 1H, H-3_{ax}), 2.42 (d, 1H, OH, *J* 2.7 Hz), 2.49 (dd, 1H, H-3_{eq}), 3.28 (s, 3H, OMe), 3.83 (s, 3H, CO_2Me), 3.56 (t, 1H, H-5), 3.74 (ddd, 1H, H-6), 3.92 (dd, 1H, H-7a), 4.24 (m, 1H, H-4), 4.36 (dd, 1H, H-7b), 5.59 (s, 2H, PhCH_2), 7.35-7.55 (m, 5H,

Ar); $J_{3ax,3eq}$ 13.3, $J_{3ax,4}$ 11.1, $J_{3eq,4}$ 5.3, $J_{4,5}$ 9.5, $J_{6,5}$ 9.1, $J_{6,7a}$ 1.0 Hz, $J_{6,7b}$ 4.5, $J_{7a,7b}$ 10.1 Hz; HR-MS (LSIMS) calcd for $C_{16}H_{21}O_7$ $[M+H]^+$ 325.1287 found 325.1264.

Methyl (methyl 5,7-*O*-benzylidene-3-deoxy-β-D-*arabino*-hept-2-ulopyranosid)onate (2b). — The reaction of ester **1b**[8] (470 mg, 2 mmol) with benzaldehyde (5mL) and trifluoroacetic acid (0.5 mL) was processed as described for the preparation of **2a**. Chromatography gave **2b** (620 mg, 96%) as a colorless oil: $[\alpha]_D$ +7.9° (c 0.86, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 1.90 (dd, 1H, H-3_{ax}), 2.51 (d, 1H, OH, *J* 2.9 Hz), 2.78 (dd, 1H, H-3_{eq}), 3.39 (s, 3H, OMe), 3.86 (s, 3H, CO_2Me), 3.50-4.00 (m, 4H, H-5, H-6, H-7a), 4.42 (dd, 1H, H-7b), 5.58 (s, 2H, PhCH_2), 7.35-7.55 (m, 5H, Ar); $J_{3ax,3eq}$ 13.3, $J_{3ax,4}$ 10.9, $J_{3eq,4}$ 5.1, $J_{7b,6}$ 4.2 Hz; HR-MS (LSIMS) calcd for $C_{16}H_{21}O_7$ $[M+H]^+$ 325.1287 found 325.1288.

A — General procedure for the preparation of triflates and their displacement with cesium acetate

To a solution of 3-deoxy-hept-2-ulosonic acid derivative (1.0 mmol) in CH_2Cl_2 (5-10 mL) containing pyridine (0.25 mL, 3 mmol) was added dropwise triflic anhydride (0.2 mL, 1.1 mmol) at -10 °C under argon. The mixture was allowed to stir for ~10 min (TLC, solvent A), then filtered through a short column of silica gel. The filtrate was evaporated *in vacuo* to yield the corresponding triflate.

The crude triflate obtained in the previous step was dried under high vacuum and dissolved in anhydrous toluene (20 mL) containing 18-crown-6 (790 mg, 3 mmol). Freshly prepared dry cesium acetate (580 mg, 3 mmol) was added, and the reaction mixture was stirred at 60-70 °C under argon until the reaction was complete (TLC, solvent A). The solvent was then evaporated *in vacuo* and the product was isolated by column chromatography.

Methyl (methyl 4-*O*-acetyl-5,7-*O*-benzylidene-3-deoxy-α-D-*ribo*-hept-2-ulopyranosid)onate (3a) and **methyl (methyl 3,4-dideoxy-α-D-erythro-hept-3-en-2-ulopyranosid)onate (4).** — (a) Prepared according to the general procedure from **2a** (420 mg, 1.3 mmol). Chromatography (solvent B) gave **3a** in the second fraction (280 mg, 60%): colorless oil; $[\alpha]_D$ +88.1° (c 0.63, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 2.04 (dd, 1H, H-3_{ax}), 2.11 (s, 3H, Ac), 2.58 (dd, 1H, H-3_{eq}), 3.29 (s, 3H, OMe), 3.81 (s, 3H, CO_2Me), 3.75-3.95 (m, 2H, H-7a, H-7b), 3.20-3.45 (m, 2H, H-5, H-6), 5.32 (q, 1H, H-4) 5.60 (s, 2H, PhCH_2), 7.35-7.50 (m, 5H, Ar); $J_{3ax,3eq}$ 15.3, $J_{3ax,4}$ 3.5, $J_{3eq,4}$ 2.8 Hz; HR-MS (LSIMS) calcd for $C_{18}H_{22}O_8$ $[M+Na]^+$ 389.1212 found 389.1203.

Eluted first was **4** (60 mg, 15%): m.p. 87-88 °C; $[\alpha]_D$ +142.8° (c 1.55, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 3.63 (s, 3H, OMe), 3.83 (s, 3H, CO_2Me), 3.90-4.04 (m, 2H, H-7a, H-7b), 4.20-4.42 (m, 2H, H-5, H-6), 5.85 (dd, 1H, H-4, $J_{4,3}$ 10.2, $J_{4,5}$ 2.6 Hz), 6.26 (d, 1H, H-3, $J_{3,4}$ 10.2), 5.61 (s, 2H, PhCH_2), 7.30-7.60 (m, 5H, Ar); HR-MS (LSIMS) calcd for $C_{16}H_{18}O_6$ $[M+H]^+$ 307.1182 found 307.1173.

(b) The crude 4-*O*-triflyl derivative prepared from **2a** (420 mg, 1.3 mmol), dissolved in toluene (20 mL), was treated with triethylammonium acetate (470 mg, 2.5 mmol) and the mixture was stirred at 70 °C for 1 h under argon. Flash chromatography of the products (solvent B) gave **3a** (170 mg, 35%), and **4** (200 mg, 50%) which were identical (TLC, $[\alpha]_D$, NMR) with the previously obtained compounds.

Methyl (methyl 4-*O*-acetyl-5,7-*O*-benzylidene-3-deoxy-β-D-*ribo*-hept-2-ulopyranosid)onate (3b). — From **2b** (320 mg, 1 mmol) based on the procedure A, after isolation by chromatography **3b** was obtained as a sole product (330 mg, 90%): m.p. 102-103 °C; $[\alpha]_D$ +46.7° (c 2.02, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.00 (dd, 1H, H-3_{ax}), 2.05 (s, 3H, Ac), 2.86 (dd, 1H, H-3_{eq}), 3.32 (s, 3H, OMe), 3.85 (s, 3H, CO_2Me), 3.70-3.85 (m, 2H, H-7a, H-7b), 4.25-4.55 (m, 2H, H-5, H-6), 5.40 (q, 1H, H-4) 5.58 (s, 2H, PhCH_2), 7.30-7.50 (m, 5H, Ar); $J_{3ax,3eq}$ 14.8, $J_{3ax,4}$ 2.7, $J_{3eq,4}$ 3.5 Hz; HR-MS (LSIMS) calcd for $C_{18}H_{22}O_8$ $[M+H]^+$ 367.1393 found 367.1393.

Methyl (methyl 4,5,7-tri-*O*-acetyl-3-deoxy-α-D-*ribo*-hept-2-ulopyranosid)onate (5a) — A mixture of **3a** (100 mg, 0,27 mmol) and cupric chloride dihydrate (420 mg, 2.5 mmol) in THF-ethanol 1:1 (5 mL) was refluxed for 1 h (TLC - solvent C). The solvents were evaporated under reduced pressure, and the solid was acetylated *in situ*. The product was poured into water and extracted with CH_2Cl_2. The organic layer was dried and concentrated *in vacuo*. Column chromatography of the residue (solvent B) afforded **5a** (90 mg, 92%): colorless oil; $[\alpha]_D$ +114.3° (c 1.67, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.09 (dd, 1H, H-3_{ax}), 2.03, 2.09 2.11 (3s, 3×3H, Ac), 2.41 (dd, 1H, H-3_{eq}), 3.30 (s, 3H, OMe), 3.81 (s, 3H, CO_2Me), 4.21-4.35 (m, 3H, H-6, H-7a, H-7b), 4.96 (m, 1H, H-5), 5.36 (q, 1H, H-4); $J_{3ax,3eq}$ 15.3, $J_{3ax,4}$ 3.7, $J_{3eq,4}$ 3.1, $J_{4,5}$ 3.3 Hz; ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.63, 20.76, 21.04, 35.34, 51.12, 52.75, 62.63, 65.92, 65.97, 66.45, 97.89, 168.18, 169.53, 170.43, 170.76; HR-MS (LSIMS) calcd for $C_{15}H_{22}O_{10}$ $[M+Na]^+$ 385.1111 found 385.1115.

Methyl (methyl 4,5,7-tri-*O*-acetyl-3-deoxy-β-D-*ribo*-hept-2-ulopyranosid)onate (5b). — This compound was obtained from **3b** (100 mg, 0,27 mmol) by a procedure above described to give 96 mg (98%) of **5b**: m.p. 68-69 °C; $[\alpha]_D$ +59.1° (c 1.38, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.08 (dd, 1H, H-3_{ax}), 2.02, 2.03 2.10 (3s, 3×3H, Ac), 2.57 (dd, 1H, H-3_{eq}), 3.30 (s, 3H, OMe), 3.83 (s, 3H, CO_2Me), 4.29 (dd, 1H, H-7a), 4.31 (dd, 1H, H-7b), 4.47 (m, 1H, H-6), 4.98 (dd, 1H, H-5), 5.44 (m, 1H, H-4); $J_{3ax,3eq}$ 14.4, $J_{3ax,4}$ 3.1, $J_{3eq,4}$ 5.4, $J_{4,5}$ 3.0, $J_{5,6}$ 8.8, $J_{6,7a}$ 3.6, $J_{6,7b}$ 4.3, $J_{7a,7b}$ 12.1 Hz; ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.68, 20.69, 20.78, 35.64, 51.65, 52.40, 62.67, 66.18, 66.63, 70.42, 97.93, 168.66, 169.37, 169.73, 170.76; HR-MS (LSIMS) calcd for $C_{15}H_{22}O_{10}$ $[M+Na]^+$ 385.1111 found 385.1115.

B — General procedure for the removal of acetyl residues

To a solution of ester (1 mmol) in methanol (5 mL) was added $NaHCO_3$ (2 g) and the resulting suspension was stirred at room temperature for 1 h (TLC - solvent C). The mixture was then diluted with CH_2Cl_2 and filtered through a short column of silica gel to give the desired product in almost quantitative yield.

Methyl (methyl 3-deoxy-α-D-*ribo*-hept-2-ulopyranosid)onate (6a) . — Based on the procedure B the ester **5a** (100 mg, 0.28 mmol) was converted into **6a** (65 mg, 97%): colorless oil; $[\alpha]_D$ +103.9° (c 1.10, MeOH); ^{1}H NMR (500 MHz, D_2O): δ 2.06 (dd, 1H, H-3_{ax}), 2.29 (dd, 1H, H-3_{eq}), 3.25 (s, 3H, OMe), 3.68 (dd, 1H, H-5), 3.84 (dd, 1H, H-7b), 3.86 (s, 3H, CO_2Me), 3.90 (ddd, 1H, H-6), 3.95 (dd, 1H, H-7a), 4.14 (m, 1H, H-4); $J_{3ax,3eq}$ 15.2, $J_{3ax,4}$ 3.7, $J_{3eq,4}$ 3.1, $J_{5,4}$ 3.4, $J_{5,6}$ 10.1, $J_{6,7a}$ 2.0, $J_{6,7b}$ 5.5, $J_{7a,7b}$ 12.2 Hz; ^{13}C NMR (500 MHz, D_2O): δ 39.93, 53.77, 56.31, 63.74, 68.60, 69.27, 77.47, 101.34, 173.47.

Methyl (methyl 3-deoxy-β-D-*ribo*-hept-2-ulopyranosid)onate (6b). — Based on the procedure B the ester **5b** (100 mg, 0.28 mmol) was converted into **6b** (63 mg, 95%): colorless oil; $[\alpha]_D$ +50.2° (c 0.95, MeOH); ^{1}H NMR (500 MHz, D_2O): δ 1.97 (dd, 1H, H-3_{ax}), 2.52 (dd, 1H, H-3_{eq}), 3.32 (s, 3H, OMe), 3.74 (dd, 1H, H-5), 3.79 (dd, 1H, H-7b), 3.85 (s, 3H, CO_2Me), 3.91 (dd, 1H, H-7a), 4.13-4.19 (m, 1H, H-6, H-4); $J_{3ax,3eq}$ 14.1, $J_{3ax,4}$ 2.7, $J_{3eq,4}$ 5.6, $J_{4,5}$ 5.4, $J_{5,6}$ 8.9, $J_{6,7a}$ 3.1, $J_{6,7b}$ 5.3, $J_{7a,7b}$ 12.3 Hz; ^{13}C NMR (500 MHz, D_2O): δ 40.30, 54.11, 55.92, 64.05, 68.71, 68.90, 77.33, 100.90, 173.71.

Methyl [methyl 7-O-(*t*-butyldiphenylsilyl)-3-deoxy-α-D-*arabino*-hept-2-ulopyranosid]onate (7a). — To a solution of **2a** (100 mg, 0.42 mmol) in anhydrous CH_2Cl_2 (5 mL) was added triethylamine (0.07 mL, 0.5 mmol) and 4-dimethylaminopyridine (10 mg) and *t*-butyldiphenylsilyl chloride (0.13 mL, 0.5 mmol). The solution was stirred overnight at room temperature (TLC - solvent A), then evaporated, and the residue was chromatographed on silica gel (solvent B) to give **7a** (180 mg, 90%): colorless oil; $[\alpha]_D$ +16.9 (c 1.85, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.08 (s, 9H, *t*-Bu), 1.70 (dd, 1H, H-3_{ax}), 2.39 (dd, 1H, H-3_{eq}), 2.45 (bs, 1H, OH), 3.18 (s, 3H, OMe), 3.28 (bs, 1H, OH), 3.52-3.62 (m, 2H), 3.80 (s, 3H, CO_2Me), 3.98 (m, 3H), 7.35-7.75 (m, 10H, Ar); HR-MS (LSIMS) calcd for $C_{25}H_{34}SiO_7$ $[M+Na]^+$ 497.1971 found 497.1980.

Methyl [methyl 7-O-(*t*-butyldiphenylsilyl)-3-deoxy-β-D-*arabino*-hept-2-ulopyranosid]onate (7b). — The compound was prepared from **2b** (100 mg, 0.42 mmol) applying the procedure described for **7a** to give 188 mg (94%) of **7b**: colorless oil; $[\alpha]_D$ +4.4 (c 1.15, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.09 (s, 9H, *t*-Bu), 1.77 (dd, 1H, H-3_{ax}), 2.52 (d, 1H, OH, *J* 2.4 Hz), 2.63 (dd, 1H, H-3_{eq}), 3.23 (s, 1H, OH), 3.32 (s, 3H, OMe), 3.55-3.80 (m, 3H, H-4, H-5, H-6), 3.81 (s, 3H, CO_2Me), 3.90 (dd, 1H, H-7b), 4.04 (dd, 1H, H-7a), 7.35-7.80 (m, 10H, Ar); $J_{3ax,3eq}$ 12.6, $J_{3ax,4}$ 11.7, $J_{3eq,4}$ 4.8, $J_{6,7a}$ 3.9, $J_{6,7b}$ 5.5, $J_{7a,7b}$ 10.3 Hz; HR-MS (LSIMS) calcd for $C_{25}H_{34}SiO_7$ $[M+Na]^+$ 497.1971 found 497.1976.

Methyl [methyl 4,5-di-*O*-acetyl-7-O-(*t*-butyldiphenylsilyl)-3-deoxy-α-D-*xylo*-hept-2-ulopyranosid]onate (8a). — Based on the procedure A the compound **7a** (200 mg, 0.42 mmol) was converted into **8a** (200 mg, 85%): colorless oil; $[\alpha]_D$ +20.3 (c 1.00, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.08 (s, 9H, *t*-Bu), 2.00 (dd, 1H, H-3_{ax}), 2.04, 2.14 (2s, 2×3H, Ac), 2.35 (ddd, 1H, H-3_{eq}), 3.24 (s, 3H, OMe), 3.82 (s, 3H, CO_2Me), 3.85 (m, 2H, H-7a, H-7b), 4.26 (m, 1H, H-6), 4.92-5.06 (m, 2H, H-4, H-5), 7.35-7.80 (m, 10H, Ar); HR-MS (LSIMS) calcd for $C_{29}H_{38}SiO_9$ $[M+Na]^+$ 581.2183 found 581.2170.

Methyl [methyl 4,5-di-*O*-acetyl-7-O-(*t*-butyldiphenylsilyl)-3-deoxy-β-D-*xylo*-hept-2-ulopyranosid]onate (8b). — Based on the procedure A the compound **7b** (160 mg, 0.34 mmol) was converted into **8b** (160 mg, 86%): colorless oil; $[\alpha]_D$ +13.0 (c 1.19, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.05 (s, 9H, *t*-Bu), 2.00 (dd, 1H, H-3_{ax}), 1.99, 2.04 (2s, 2×3H, Ac), 2.57 (ddd, 1H, H-3_{eq}), 3.27 (s, 3H, OMe), 3.80 (s, 3H, CO_2Me), 3.76 (dd, 1H, H-7a), 3.90 (dd, 1H, H-7b), 4.48 (dd, 1H, H-6), 4.97 (m, 1H, H-5), 5.10 (q, 1H, H-4), 7.30-7.70 (m, 10H, Ar); $J_{3ax,3eq}$ 14.7, $J_{3ax,4}$ 3.3, $J_{3eq,4}$ 3.2, $J_{3eq,5}$ 0.9, $J_{6,7a}$ 1.7, $J_{6,7b}$ 6.0 $J_{7a,7b}$ 9.8 Hz; HR-MS (LSIMS) calcd for $C_{29}H_{38}SiO_9$ $[M+Na]^+$ 581.2183 found 581.2164.

Methyl (methyl 4,5,7-tri-*O*-acetyl-3-deoxy-α-D-*xylo*-hept-2-ulopyranosid)onate (9a). — Tetra-*n*-butylammonium fluoride (95 mg, 0.3 mmol) was added to a solution of **8a** (110 mg, 0.2 mmol) in THF (5 mL). The reaction mixture was stirred at rt for ~1 h (TLC solvent C). Evaporation of the solvent and acetylation *in situ* gave compound **9a** which was purified by column chromatography (solvent B) (70 mg, 97%): colorless oil; $[\alpha]_D$ +78.0° (c 1.09, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 2.05 (dd, 1H, H-3_{ax}), 2.08, 2.09 2.12 (3s, 3×3H, Ac), 2.30 (ddd, 1H, H-3_{eq}), 3.27 (s, 3H, OMe), 3.81 (s, 3H, CO_2Me), 4.20 (dd, 1H, H-7b), 4.26 (dd, 1H, H-7a), 4.36 (m, 1H, H-6), 4.89 (m, 1H, H-5), 4.93 (m, 1H, H-4); $J_{3ax,3eq}$ 15.3, $J_{3ax,4}$ 4.1, $J_{3eq,4}$ 2.7, $J_{3eq,5}$ 0.9, $J_{4,5}$ 3.3, $J_{5,6}$ 1.5, $J_{6,7a}$ 5.5, $J_{6,7b}$ 7.5, $J_{7a,7b}$ 11.5 Hz; ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.76, 20.78, 21.10, 30.82, 51.15, 52.96, 62.65, 65.74, 65.96, 66.17, 97.74, 168.30, 169.65, 169.80, 170.54; HR-MS (LSIMS) calcd for $C_{15}H_{22}O_{10}$ $[M+Na]^+$ 385.1111 found 385.1108.

Methyl (methyl 4,5,7-tri-*O*-acetyl-3-deoxy-β-D-*xylo*-hept-2-ulopyranosid)onate (9b). — From **8b** (110 mg, 0.2 mmol) - processed as described for **9a** to yield 69 mg (96%) of **9b**: colorless oil; $[\alpha]_D$ +64.4 (c 1.13, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 2.09 (dd, 1H, H-3_{ax}), 2.02, 2.08 2.13 (3s, 3×3H, Ac), 2.52 (ddd, 1H, H-3_{eq}), 3.33 (s, 3H, OMe), 3.81 (s, 3H, CO_2Me), 4.22 (dd, 1H, H-7b), 4.26 (dd, 1H, H-7a), 4.56 (td, 1H, H-6), 4.85 (m, 1H, H-5), 5.08 (q, 1H, H-4); $J_{3ax,3eq}$ 14.7, $J_{3ax,4}$ 3.3, $J_{3eq,4}$ 3.5, $J_{3eq,5}$ 0.9, $J_{4,5}$ 3.9, $J_{5,6}$ 1.9, $J_{6,7a}$ 6.5, $J_{6,7b}$ 6.7, $J_{7a,7b}$ 11.2 Hz; ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.71, 20.72, 20.74, 32.30, 51.46, 52.34, 62.15, 65.16, 66.97, 69.61, 97.60, 168.65, 168.72, 169.69, 170.55; HR-MS (LSIMS) calcd for $C_{15}H_{22}O_{10}$ $[M+Na]^+$ 385.1111 found 385.1112.

Methyl (methyl 3-deoxy-α-D-*xylo*-hept-2-ulopyranosid)onate (10a). — Based on the procedure B the compound **9a** (50 mg, 0.14 mmol) was converted into **10a** (32 mg, 97%): m.p. 85-90 °C; $[\alpha]_D$ +76.2° (c 0.85, MeOH); ^1H NMR (500 MHz, D_2O): δ 2.04 (ddd, 1H, H-3_{eq}), 2.14 (dd, 1H, H-3_{ax}), 3.25 (s, 3H, OMe), 3.69 (bd, 1H, H-5), 3.80 (dd, 1H, H-7a), 3.86 (s, 3H, CO_2Me), 3.89 (dd, 1H, H-7b), 4.00 (m, 1H, H-4), 4.11 (ddd, 1H, H-6); $J_{3ax,3eq}$ 15.3, $J_{3ax,4}$ 4.1, $J_{3eq,4}$ 2.5, $J_{3eq,5}$ 0.7, $J_{5,4}$ 3.5, $J_{6,5}$ 1.3, $J_{6,7a}$ 4.3, $J_{6,7b}$ 7.7, $J_{7a,7b}$ 12.0 Hz; ^{13}C NMR (500 MHz, D_2O): δ 35.00, 53.75, 56.22, 64.30, 69.21, 69.63, 72.05, 101.35, 173.42.

Methyl (methyl 3-deoxy-β-D-*xylo*-hept-2-ulopyranosid)onate (10b). — Based on the procedure B the compound **9b** (50mg, 0.14 mmol) was converted into **10b** (30mg, 90%): $[\alpha]_D$ +42.4° (c 1.33, MeOH); ^1H NMR (500 MHz, D_2O): δ 2.12 (dd, 1H, H-3_{ax}), 2.35 (ddd, 1H, H-3_{eq}), 3.34 (s, 3H, OMe), 3.67 (m, 1H, H-5), 3.81 (dd, 1H, H-7a), 3.84 (dd, 1H, H-7b), 3.84 (s, 3H, CO_2Me), 4.09 (m, 1H, H-4), 4.33 (ddd, 1H, H-6); $J_{3ax,3eq}$ 14.3, $J_{3ax,4}$ 2.9, $J_{3eq,4}$ 3.5, $J_{3eq,5}$ 0.4, $J_{5,4}$ 4.0, $J_{5,6}$ 1.5, $J_{6,7a}$ 4.8, $J_{6,7b}$ 7.4, $J_{7a,7b}$ 11.7 Hz; ^{13}C NMR (500 MHz, D_2O): δ 36.74, 53.91, 55.81, 64.35, 68.95, 69.83, 76.27, 100.84, 173.74.

Methyl [methyl 7-O-(*t*-butyldiphenylsilyl)-3-deoxy-β-D-*ribo*-hept-2-ulopyranosid]onate (11b). — From **6b** (100 mg, 0.42 mmol) by the procedure described for the preparation of **7**, to give **11b** (163 mg, 82%): colorless oil; $[\alpha]_D$ 0.0° (c 0.60, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 1.12 (s, 9H, *t*-Bu), 1.86 (dd, 1H, H-3_{ax}), 2.60 (d, 1H, OH, *J* 1.7 Hz), 2.70 (dd, 1H, H-3_{eq}), 3.26 (s, 3H, OMe), 3.84 (s, 3H, CO_2Me), 3.70-3.94 (m, 2H, H-7a,

H-7b), 4.05-4.20 (m, 2H, H-5, H-6), 4.33 (ddd, 1H, H-4), 7.35-7.80 (m, 10H, Ar); $J_{3ax,3eq}$ 14.3, $J_{3ax,4}$ 2.1, $J_{3eq,4}$ 4.1 Hz; HR-MS (LSIMS) calcd for $C_{25}H_{34}SiO_7$ $[M+Na]^+$ 497.1972 found 497.1971.

Methyl [methyl 4,5-di-*O*-acetyl-7-O-(*t*-butyldiphenylsilyl)-3-deoxy-β-D-*lyxo*-hept-2-ulopyranosid]onate (12b). — Based on the procedure A the compound **11b** (60 mg, 0.13 mmol) was converted into **12b** (63 mg, 87%): colorless oil; $[\alpha]_D$ +11.7° (c 0.65, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 1.10 (s, 9H, *t*-Bu), 2.05 (dd, 1H, H-3_{ax}), 2.07, 2.17 (2s, 2×3H, Ac), 2.45 (dd, 1H, H-3_{eq}), 3.35 (s, 3H, OMe), 3.84 (s, 3H, CO_2Me), 3.98 (dd, 1H, H-7a), 4.10 (dd, 1H, H-7b), 4.15 (m, 1H, H-6), 4.95 (m, 1H, H-4), 5.40 (m, 1H, H-5), 7.35-7.70 (m, 10H, Ar); $J_{3ax,3eq}$ 14.3, $J_{3ax,4}$ 2.1, $J_{3eq,4}$ 4.1 Hz.

NMR data for methyl (methyl 4,5,7-tri-*O*-acetyl-3-deoxy-α-D-*lyxo*-hept-2-ulopyranosid)onate (13a).[2] — ^1H NMR (500 MHz, $CDCl_3$): δ 1.98, 2.05, 2.14 (3s, 3×3H, Ac), 2.10 (m, 1H, H-3_{ax}), 2.17 (ddd, 1H, H-3_{eq}), 3.28 (s, 3H, OMe), 3.83 (s, 3H, CO_2Me), 4.08 (td, 1H, H-6), 4.20 (m, 2H, H-7a, H-7b), 5.30-5.35 (m, 2H, H-4, H-5); $J_{3ax,3eq}$ 12.7, $J_{4,3ax}$ 11.9, $J_{3eq,4}$ 5.2, $J_{3eq,5}$ 0.9, $J_{4,5}$ 3.1 $J_{6,5}$ 1.2 Hz; ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.70, 20.77, 32.03, 51.19, 52.73, 62.11, 65.66, 66.44, 68.80, 98.90, 167.79, 169.89, 170.30, 170.44.

Methyl (methyl 4,5,7-tri-*O*-acetyl-3-deoxy-β-D-*lyxo*-hept-2-ulopyranosid)onate (13b). — From **12b** (56 mg, 0.10 mmol) by the procedure similar to that described for the preparation of **9** to give **13b** (32 mg, 89%): colorless oil; $[\alpha]_D$ +62.3° (c 1.20, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.99, 2.05, 2.14 (3s, 3×3H, Ac), 2.14 (t, 1H, H-3_{ax}), 2.36 (ddd, 1H, H-3_{eq}), 3.39 (s, 3H, OMe), 3.84 (s, 3H, CO_2Me), 4.19 (m, 2H, H-7a, H-7b), 4.23 (m, 1H, H-6), 4.93 (ddd, 1H, H-4), 5.30 (m, 1H, H-5); $J_{3ax,3eq}$ 12.6, $J_{3ax,4}$ 13.0, $J_{3eq,4}$ 4.7, $J_{3eq,5}$ 1.0, $J_{4,5}$ 2.9 Hz; ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.67, 20.74, 20.74, 31.90, 51.82, 52.82, 61.68, 65.19, 67.22, 71.08, 99.42, 168.44, 169.89, 170.26, 170.44; HR-MS (LSIMS) calcd for $C_{15}H_{22}O_{10}$ $[M+Na]^+$ 385.1111 found 385.1123.

NMR data for methyl (methyl 3-deoxy-α-D-*lyxo*-hept-2-ulopyranosid)onate (14a).[2] — ^1H NMR (500 MHz, D_2O): δ 1.91 (dd, 1H, H-3_{ax}), 2.09 (dd, 1H, H-3_{eq}), 3.25 (s, 3H, OMe), 3.77-3.90 (m, 4H, H-5, H-6, H-7a, H-7b), 3.87 (s, 3H, CO_2Me), 4.10 (ddd, 1H, H-4); $J_{3ax,3eq}$ 13.0, $J_{3ax,4}$ 12.1, $J_{3eq,4}$ 5.1 Hz; ^{13}C NMR (500 MHz, D_2O): δ 36.34, 53.76, 56.32, 64.31, 68.03, 69.68, 76.26, 101.95, 173.18.

Methyl (methyl 3-deoxy-β-D-*lyxo*-hept-2-ulopyranosid)onate (14b). — Based on the procedure B compound **13b** (30 mg, 0.08 mmol) was converted into **14b** (18 mg, 93%): colorless oil; $[\alpha]_D$ +52.5° (c 1.89, MeOH); ^1H NMR (500 MHz, D_2O): δ 1.98 (td, 1H, H-3_{ax}), 2.36 (ddd, 1H, H-3_{eq}), 3.39 (s, 3H, OMe), 3.87 (s, 3H, CO_2Me), 3.75-3.85 (m, H-4, H-5, H-6, H-7a, H-7b); $J_{3ax,3eq}$ 12.4, $J_{3ax,4}$ 12.4, $J_{3eq,4}$ 4.6 Hz; ^{13}C NMR (500 MHz, D_2O): δ 35.70, 54.34, 56.17, 64.38, 69.30, 69.32, 78.53, 102.58, 173.02.

Methyl [methyl 7-*O*-(*t*-butyldiphenylsilyl)-3-deoxy-4,5-*O*-isopropylidene-β-D-*lyxo*-hept-2-ulopyranosid]onate (15b)— To a solution of **14b** (50 mg, 0.21 mmol) in anhydrous CH_2Cl_2 (1 mL) was added triethylamine (0.04 mL, 0.3 mmol) and 4-dimethylaminopyridine (10 mg) and *t*-butyldiphenylsilyl chloride (0.08 mL, 0.3 mmol). The solution was stirred overnight at room temperature (TLC - solvent A). The reaction mixture was then evaporated, and the residue was filtered through silica gel. The crude product was redissolved in DMF

(2 mL). To this solution dimethoxypropane (0.05 mL, 0.4 mmol) and camphorosulphonic acid (2 mg) was added. The solution was stirred at 50 °C for 1 h, then evaporated (with toluene). The residue was chromatographed on silica gel to afford **15b** (90 mg, 85%) as a colorless oil: $[\alpha]_D$ +4.9 (c 1.10, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 1.06 (s, 9H, *t*-Bu), 1.33, 1.48 (2s, 2×3H, *i*-Pr), 2.05-2.20 (m, 2H, H-3_{ax}, H-3_{eq}), 3.32 (s, 3H, OMe), 3.77 (s, 3H, CO_2Me), 3.94 (m, 3H, H-6, H-7a, H-7b), 4.32 (m, 1H, H-5), 4.46 (m, 1H, H-4) 7.30-7.80 (m, 10H, Ar).

Methyl [methyl 3-deoxy-4,5-*O*-isopropylidene-β-D-*lyxo*-hept-2-ulopyranosid]onate (16b). — Tetra-*n*-butylammonium fluoride (47 mg, 0.15 mmol) was added to a solution of **15b** (50 mg, 0.1 mmol) in THF (3 mL). The reaction mixture was stirred at rt for ~1 h. Evaporation of the solvent and column chromatography gave **16b** (25 mg, 98%): colorless oil; $[\alpha]_D$ +6.4° (c 1.45, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 1.32, 1.51 (2s, 2×3H, *i*-Pr), 2.09 (dd, 1H, H-3_{ax}), 2.25 (dd, 1H, H-3_{eq}), 3.37 (s, 3H, OMe), 3.80 (s, 3H, CO_2Me), 3.81 (m, 2H, H-7a, H-7b), 3.92 (m, 1H, H-6), 4.19 (dd, 1H, H-5), 4.50 (m, 1H, H-4).

C — General procedure for the oxidation of the primary hydroxyl group to the carboxyl function

The heptulosonic acid derivative (1 mmol) was dissolved in a mixture of acetone (5 mL) and saturated aqueous $NaHCO_3$ (8mL), containing KBr (12 mg) and TEMPO (12 mg). The suspension was cooled in the ice-bath, and NaOCl (6.8 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature. After disappearance of the substrate (TLC - solvent C) the mixture was acidified with acetic acid, and evaporated to dryness. The residue was redissolved in methanol (10 mL) and trimethylsilyl chloride was added (~0.5 mL). The mixture was stirred overnight. After this the mixture was neutralized with solid $NaHCO_3$, filtered through Celite and purified on a silica gel column (solvent D) to afford diester of heptulosaric acid. Additional elution of the column with CH_2Cl_2-MeOH (1:1) followed by esterification gave the next portion of diester.

Methyl (methyl 7-carbomethoxy-3-deoxy-α-D-*arabino*-hept-2-ulopyranosid)onate (17a). — From compound **1a**[8] (100 mg, 0.42 mmol) according to the procedure C to give **15a** (68 mg, 62%): colorless oil; $[\alpha]_D$ +61.4° (c 1.26, $CHCl_3$); ^1H NMR (500 MHz, D_2O): δ 1.81 (dd, 1H, H-3_{ax}), 2.40 (dd, 1H, H-3_{eq}), 3.27 (s, 3H, OMe), 3.59 (t, 1H, H-5), 3.87, 3.88 (2s, 2×3H, CO_2Me), 3.97 (ddd, 1H, H-4), 4.15 (d, 1H, H-6); $J_{3ax,3eq}$ 13.5, $J_{3ax,4}$ 11.5, $J_{3eq,4}$ 5.1, $J_{4,5}$ 9.3, $J_{5,6}$ 9.9 Hz; ^{13}C NMR (500 MHz, D_2O): δ 41.46, 54.04, 56.03, 56.49, 70.39, 74.60, 75.69, 102.40, 172.06, 173.74; HR-MS (LSIMS) calcd for $C_{10}H_{16}O_8$ $[M+Na]^+$ 287.0743 found 287.0738.

Methyl (methyl 7-carbomethoxy-3-deoxy-β-D-*arabino*-hept-2-ulopyranosid)onate (17b). — From compound **1b**[8] (50 mg, 0.21 mmol) according to the procedure C **15b** was obtained in 55% yield (30 mg): colorless oil; $[\alpha]_D$ +18.0° (c 0.78, $CHCl_3$); ^1H NMR (500 MHz, D_2O): δ 1.88 (dd, 1H, H-3_{ax}), 2.64 (dd, 1H, H-3_{eq}), 3.38 (s, 3H, OMe), 3.66 (t, 1H, H-5), 3.69 (ddd, 1H, H-4), 3.86, 3.91 (2s, 2×3H, CO_2Me), 4.24 (d, 1H, H-6); $J_{3ax,3eq}$ 13.3, $J_{3ax,4}$ 11.3, $J_{3eq,4}$ 4.7, $J_{4,5}$ 9.4, $J_{5,6}$ 9.3 Hz; ^{13}C NMR (500 MHz, D_2O): δ 40.62, 54.80, 56.00, 56.47, 70.85, 74.44, 77.97, 102.65, 172.18, 173.79; HR-MS (LSIMS) calcd for $C_{10}H_{16}O_8$ $[M+Na]^+$ 287.0743 found 287.0750.

Methyl (methyl 4,5-di-*O*-acetyl-7-carbomethoxy-3-deoxy-α-D-*arabino*-hept-2-ulopyranosid)onate (21a). — colorless oil; $[\alpha]_D$ +44.9° (c 2.53, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.91 (dd, 1H, H-3_{ax}), 2.02, 2.04 (2s, 2×3H, Ac), 2.54 (dd, 1H, H-3_{eq}), 3.32 (s, 3H, OMe), 3.77, 3.83 (2s, 2×3H, CO_2Me), 4.20 (d, 1H, H-6), 5.18 (t, 1H, H-5), 5.37 (ddd, 1H, H-4); $J_{3ax,3eq}$ 13.0, $J_{3ax,4}$ 11.5, $J_{3eq,4}$ 5.4, $J_{4,5}$ 9.5, $J_{5,6}$ 10.1 Hz; ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.53, 20.81, 36.68, 51.38, 52.87, 52.89, 68.14, 69.50, 70.62, 98.87, 167.02, 167.67, 169.60, 169.87.

Methyl (methyl 4,5-di-*O*-acetyl-7-carbomethoxy-3-deoxy-β-D-*arabino*-hept-2-ulopyranosid)onate (21b). — colorless oil; $[\alpha]_D$ +24.4° (c 1.10, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 2.01 (dd, 1H, H-3_{ax}), 2.03, 2.04 (2s, 2×3H, Ac), 2.62 (dd, 1H, H-3_{eq}), 3.39 (s, 3H, OMe), 3.76, 3.87 (2s, 2×3H, CO_2Me), 4.41 (d, 1H, H-6), 5.03 (ddd, 1H, H-4), 5.22 (t, 1H, H-5); $J_{3ax,3eq}$ 13.3, $J_{3ax,4}$ 11.0, $J_{3eq,4}$ 5.0, $J_{4,5}$ 8.9, $J_{5,6}$ 8.9 Hz; ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.61, 20.85, 35.83, 52.22, 52.71, 52.97, 67.98, 69.52, 72.78, 98.92, 167.94, 167.98, 169.74, 169.89.

Methyl (methyl 7-carbomethoxy-3-deoxy-α-D-*ribo*-hept-2-ulopyranosid)onate (18a). — From **6a** (50 mg, 0.21 mmol), applying procedure C **16a** was obtained in 70% yield (39 mg): colorless oil; $[\alpha]_D$ +66.7° (c 0.80, $CHCl_3$); ^1H NMR (500 MHz, D_2O): δ 1.99 (dd, 1H, H-3_{ax}), 2.18 (dd, 1H, H-3_{eq}), 3.12 (s, 3H, OMe), 3.71 (dd, 1H, H-5), 3.72, 3.73 (2s, 2×3H, CO_2Me), 4.06 (q, 1H, H-4), 4.32 (d, 1H, H-6); $J_{3ax,3eq}$ 15.2, $J_{3ax,4}$ 3.7, $J_{3eq,4}$ 3.2, $J_{4,5}$ 3.2, $J_{5,6}$ 10.2 Hz; ^{13}C NMR (500 MHz, D_2O): δ 39.59, 54.14, 55.96, 56.41, 68.94, 70.38, 71.74, 101.53, 172.52, 174.55; HR-MS (LSIMS) calcd for $C_{10}H_{16}O_8$ $[M+Na]^+$ 287.0743 found 287.0746.

Methyl (methyl 7-carbomethoxy-3-deoxy-β-D-*ribo*-hept-2-ulopyranosid)onate (18b). — From **6b** (30 mg, 0.13 mmol), applying procedure C **16b** was obtained in 53% yield (18 mg): colorless oil; $[\alpha]_D$ +7.7° (c 0.83, $CHCl_3$); ^1H NMR (500 MHz, D_2O): δ 2.08 (dd, 1H, H-3_{ax}), 2.40 (dd, 1H, H-3_{eq}), 3.29 (s, 3H, OMe), 3.84, 3.88 (2s, 2×3H, CO_2Me), 4.06 (dd, 1H, H-5), 4.23 (m, 1H, H-4), 4.70 (d, 1H, H-6); $J_{3ax,3eq}$ 13.9, $J_{3ax,4}$ 3.4, $J_{3eq,4}$ 7.4, $J_{4,5}$ 2.9, $J_{5,6}$ 6.9 Hz; ^{13}C NMR (500 MHz, D_2O): δ 39.07, 54.87, 55.78, 56.21, 67.32, 70.00, 76.79, 102.02, 172.72, 174.52; HR-MS (LSIMS) calcd for $C_{10}H_{16}O_8$ $[M+Na]^+$ 287.0743 found 287.0745.

Methyl (methyl 4,5-di-*O*-acetyl-7-carbomethoxy-3-deoxy-α-D-*ribo*-hept-2-ulopyranosid)onate (22a). — colorless oil; $[\alpha]_D$ +96.9° (c 1.17, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 2.12 (dd, 1H, H-3_{ax}), 2.03, 2.11 (2s, 2×3H, Ac), 2.44 (dd, 1H, H-3_{eq}), 3.33 (s, 3H, OMe), 3.80, 3.81 (2s, 2×3H, CO_2Me), 4.60 (d, 1H, H-6), 5.17 (dd, 1H, H-5), 5.37 (m, 1H, H-4); $J_{3ax,3eq}$ 15.3, $J_{3ax,4}$ 3.7, $J_{3eq,4}$ 3.3, $J_{4,5}$ 3.4, $J_{5,6}$ 10.2 Hz; ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.54, 21.02, 34.97, 51.51, 52.79, 52.89, 65.79, 67.18, 67.64, 98.08, 167.69, 168.15, 169.33, 170.33.

Methyl (methyl 4,5-di-*O*-acetyl-7-carbomethoxy-3-deoxy-β-D-*ribo*-hept-2-ulopyranosid)onate (22b). — colorless oil; $[\alpha]_D$ +12.3° (c 0.75, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 2.03, 2.08 (2s, 2×3H, Ac), 2.24 (ddd, 1H, H-3_{ax}), 2.34 (dd, 1H, H-3_{eq}), 3.29 (s, 3H, OMe), 3.80, 3.85 (2s, 2×3H, CO_2Me), 4.71 (d, 1H, H-6), 5.44 (ddd, 1H, H-5), 5.51 (m, 1H, H-5); $J_{3ax,3eq}$ 13.5, $J_{3ax,4}$ 4.0, $J_{3ax,5}$ 0.7, $J_{3eq,4}$ 8.8, $J_{5,4}$ 3.0, $J_{5,6}$ 5.3 Hz; ^{13}C NMR (500

MHz, $CDCl_3$): δ 20.76, 20.77, 34.09, 52.52, 52.55, 52.68, 64.90, 67.03, 72.70, 99.38, 167.90, 168.43, 169.40, 169.87.

Methyl (methyl 7-carbomethoxy-3-deoxy-α-D-*xylo*-hept-2-ulopyranosid)onate (17a). — Compound **10a** (50 mg, 0.21 mmol) was oxidized as described in procedure C to give **17a** (28 mg, 51 %): colorless oil; $[\alpha]_D$ +34.9° (c 0.60, $CHCl_3$); ^1H NMR (500 MHz, D_2O): δ 2.06 (dd, 1H, H-3_{eq}), 2.17 (dd, 1H, H-3_{ax}), 3.25 (s, 3H, OMe), 3.86, 3.88 (2s, 2×3H, CO_2Me), 4.04-4.08 (m, 2H, H-4, H-5), 4.80 (d, 1H, H-6); $J_{3ax,3eq}$ 15.3, $J_{3ax,4}$ 3.8, $J_{3eq,4}$ 2.3, $J_{3eq,5}$ 1.0, $J_{5,6}$ 1.5 Hz; ^{13}C NMR (500 MHz, D_2O): δ 34.65, 54.22, 55.73, 56.33, 69.31, 70.23, 71.76, 72.70, 101.91, 172.73, 174.34; HR-MS (LSIMS) calcd for $C_{10}H_{16}O_8$ $[M+Na]^+$ 287.0743 found 287.0751.

Methyl (methyl 7-carbomethoxy-3-deoxy-β-D-*xylo*-hept-2-ulopyranosid)onate (19b). — Oxidation of **10b** (30mg, 0.13 mmol) according to procedure C led to **17b** in 60% yield (20 mg): colorless oil; $[\alpha]_D$ -0.6° (c 0.95, $CHCl_3$); ^1H NMR (500 MHz, D_2O): δ 2.16 (dd, 1H, H-3_{ax}), 2.36 (ddd, 1H, H-3_{eq}), 3.38 (s, 3H, OMe), 3.84, 3.85 (2s, 2×3H, CO_2Me), 4.00 (m, 1H, H-5), 4.16 (q, 1H, H-4), 4.99 (d, 1H, H-6); $J_{3ax,3eq}$ 14.4, $J_{3ax,4}$ 2.7, $J_{3eq,4}$ 3.4, $J_{3eq,5}$ 0.7, $J_{6,5}$ 2.0 Hz; ^{13}C NMR (500 MHz, D_2O): δ 36.05, 54.24, 55.70, 56.03, 69.64, 69.68, 75.90, 101.23, 173.38, 174.36; HR-MS (LSIMS) calcd for $C_{10}H_{16}O_8$ $[M+Na]^+$ 287.0743 found 287.0803.

Methyl (methyl 4,5-di-*O*-acetyl-7-carbomethoxy-3-deoxy-α-D-*xylo*-hept-2-ulopyranosid)onate (23a). — colorless oil; $[\alpha]_D$ +21.5° (c 0.60, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 2.08 (dd, 1H, H-3_{ax}), 2.09 (s, 2×3H, Ac), 2.34 (ddd, 1H, H-3_{eq}), 3.30 (s, 3H, OMe), 3.79, 3.83 (2s, 2×3H, CO_2Me), 4.77 (d, 1H, H-6), 4.98 (m, 1H, H-4), 5.20 (m, 1H, H-5); $J_{3ax,3eq}$ 15.4, $J_{3ax,4}$ 4.1, $J_{3eq,4}$ 2.5, $J_{3eq,5}$ 1.1, $J_{6,5}$ 1.7 Hz; ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.75, 21.05, 29.69, 30.33, 51.66, 52.66, 52.83, 66.02, 66.40, 67.72, 98.24, 167.78, 167.97, 169.48.

Methyl (methyl 4,5-di-*O*-acetyl-7-carbomethoxy-3-deoxy-β-D-*xylo*-hept-2-ulopyranosid)onate (23b). — m.p. 109-111 °C; $[\alpha]_D$ +63.7° (c 0.85, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 2.03, 2.09 (2s, 2×3H, Ac), 2.14 (dd, 1H, H-3_{ax}), 2.54 (ddd, 1H, H-3_{eq}), 3.39 (s, 3H, OMe), 3.78, 3.81 (2s, 2×3H, CO_2Me), 5.02 (d, 1H, H-6), 5.10-5.15 (m, 2H, H-4, H-5); $J_{3ax,3eq}$ 14.8, $J_{3ax,4}$ 3.0, $J_{3eq,4}$ 3.0, $J_{3eq,5}$ 0.9, $J_{6,5}$ 1.7 Hz; ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.66, 20.67, 31.94, 51.86, 52.45, 52.52, 66.11, 66.91, 71.47, 97.95, 167.85, 168.41, 168.65, 169.35.

NMR data for methyl (methyl 7-carbomethoxy-3-deoxy-α-D-*lyxo*-hept-2-ulopyranosid)onate (20a).[2] — ^1H NMR (500 MHz, $CDCl_3$): δ 1.92 (dd, 1H, H-3_{ax}), 2.19 (ddd, 1H, H-3_{eq}), 3.29 (s, 3H, OMe), 3.84, 3.86 (2s, 2×3H, CO_2Me), 4.11 (ddd, 1H, H-4), 5.21 (bs, 1H, H-5), 4.30 (d, 1H, 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.

NMR data for methyl (methyl 4,5-di-*O*-acetyl-7-carbomethoxy-3-deoxy-α-D-*lyxo*-hept-2-ulopyranosid) onate (24a).[2] — ^1H NMR (500 MHz, $CDCl_3$): δ 1.99, 2.10 (2s, 2×3H, Ac), 2.13 (t, 1H, H-3_{ax}), 2.20 (ddd, 1H, H-3_{eq}), 3.31 (s, 3H, OMe), 3.77, 3.86 (2s, 2×3H, CO_2Me), 4.47 (d, 1H, H-6), 5.37 (ddd, 1H, H-4), 5.69 (m, 1H, H-5); $J_{3ax,3eq}$ 12.8, $J_{3ax,4}$ 12.2, $J_{3eq,4}$ 5.3, $J_{3eq,5}$ 1.0, $J_{4,5}$ 3.1, $J_{6,5}$ 1.6 Hz.

Methyl (methyl 7-carbomethoxy-3-deoxy-β-D-*lyxo*-hept-2-ulopyranosid)onate (20b). — Compound **16b** (30 mg, 0.11 mmol) was oxidized as described in procedure B to give **20b** (18 mg, 63%): colorless oil; $[\alpha]_D$ +27.2° (c 0.48, $CHCl_3$); ^1H NMR (500 MHz, D_2O): δ 2.04 (t, 1H, H-3_{ax}), 2.36 (dd, 1H, H-3_{eq}), 3.44 (s, 3H, OMe), 3.84, 3.88 (2s, 2×3H, CO_2Me), 3.90 (m, 1H, H-4), 4.19 (m, 1H, H-5), 4.63 (d, 1H, H-6); $J_{3ax,3eq}$ 12.7, $J_{3ax,4}$ 12.7, $J_{3eq,4}$ 4.7, $J_{3eq,5}$ 0.7, $J_{6,5}$ 1.5 Hz; ^{13}C NMR (500 MHz, D_2O): δ 35.20, 54.62, 55.75, 56.32, 68.46, 70.02, 77.79, 102.81, 172.43, 173.38; HR-MS (LSIMS) calcd for $C_{10}H_{16}O_8$ $[M+Na]^+$ 287.0743 found 287.0751.

Methyl (methyl 4,5-di-*O*-acetyl-7-carbomethoxy-3-deoxy-β-D-*lyxo*-hept-2-ulopyranosid)onate (24b). — colorless oil; $[\alpha]_D$ +91.3° (c 0.80, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 2.01, 2.10 (2s, 2×3H, Ac), 2.21 (t, 1H, H-3_{ax}), 2.36 (ddd, 1H, H-3_{eq}), 3.46 (s, 3H, OMe), 3.76, 3.85 (2s, 2×3H, CO_2Me), 4.74 (d, 1H, H-6), 4.95 (ddd, 1H, H-4), 5.62 (m, 1H, H-5); $J_{3ax,3eq}$ 12.7, $J_{3ax,4}$ 12.8, $J_{3eq,4}$ 4.7, $J_{3eq,5}$ 1.0, $J_{4,5}$ 2.9, $J_{6,5}$ 1.6 Hz; ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.60, 20.70, 31.80, 52.26, 52.56, 52.93, 66.42, 66.74, 73.00, 99.65, 167.03, 168.40, 169.80, 169.84.

REFERENCES

1. a) Stevenson, T.T.; Darvill, A.G.; Albersheim, P. *Carbohydr. Res.* **1989**, *179*, 269; b) Becker, E; Hard, K.; Melkonian, M.; Kamerling, J.P. Vliegenthart, J.F.G. *Eur. J. Biochem.* **1989**, *82*, 153; c) Brade, H.; Rietschel, E.Th. *Eur. J. Biochem.* **1985**, *153*, 249; d) Russa, R.; Urbanik-Sypniewska, T.; Choma, A.; Mayer, H. *FEMS Microbiol. Lett.* **1991**, *84*, 337; e) Russa, R.; Urbanik-Sypniewska, T.; Shashkov, A.S.; Banaszek, A.; Zamojski, A.; Mayer, H. *System. Appl. Microbiol.* **1996**, *19*, 1.
2. Banaszek, A. *Tetrahedron* **1995**, *51*, 4231.
3. Fitz, W.; Schwark, J.-R.; Wong, Ch.-H. *J. Org. Chem.* **1995**, *60*, 3663.
4. Lin, Ch.Ch.; Shimazaki, M.; Heck, M.-P.; Aoki, S.; Wang, R.; Kimura, T.; Ritzen, H.; Takayama, S.; Wu, S.-H.; Weitz-Schmidt, G.; Wong, Ch.-H. *J. Am. Chem. Soc.* **1996**, *118*, 6826.
5. Krülle, T.; Schmidt, R.R.; Brade, H.; Holst, O. *Carbohydr. Res.* **1994**, *254*, 141.
6. a) Hartman, M.; Christian, R.; Zbiral, E. *Liebigs Ann. Chem.* **1990**, 83; b) Dondoni, A.; Boscarto, A.; Marra, A. *Tetrahedron: Asymmetry*, **1994**, *5*, 2209; c) Koppert, K.; Brossmer, R. *Tetrahedron Lett.* **1992**, *33*, 8031.
7. a) David, S.; Malleron, A.; Cavayé, B. *New J. Chem.* **1992**, *16*, 751; b) Halcomb, R.L., Fitz, W.; Wong, C.-H. *Tetrahedron: Asymmetry* **1994**, *5*, 2437; c) Bamford, M.J.; Pichel, J.C.; Husman, W.; Patel, B.; Storrer, R.; Weir, N.G. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1181.

8. Młynarski, J; Banaszek, A. *Carbohydr. Res.* **1996**, *295*, 69.

9. a) Mitsunobu, O. *Synthesis* **1981**, 1; b) Alfredson, G.; Garegg, P.J. *Acta Chem. Scand.* **1973**, *27*, 724; c) Grynkiewicz, G. *Rocz. Chem.* **1976**, *50*, 1449; d) Banaszek, A.; Szechner, B.; Mieczkowski, J.; Zamojski, A. *Rocz. Chem.* **1976**, *50*, 105.

10. a) Torisawa, Y.; Okabe, H.; Ikegami, S. *Chem. Lett.* **1984**, 1555; b) Willis, C.L. *Tetrahedron Lett.* **1987**, *28*, 6705.

11. a) Nashed, M.A.; El-Sokkary, R.J.; Rateb, L. *Carbohydr. Res.* **1984**, *131*, 47; b) Sato, K.; Yoshimoto, A. *Chem. Letters* **1995**, 39.

12. Tabeur, Ch.; Machetto, F.; Mallet, J.-M.; Duchaussoy, P.; Petiton, M.; Sinaÿ, P. *Carbohydr. Res.* **1996**, *281*, 253.

13. a) Binkley, R.W.; Ambrose, M.G. *J. Carbohydr. Chem.* **1984**, 1; b) Su, T.-L.; Klein, R.S.; Fox, J.J. *J. Org. Chem.* **1981**, *46*, 1790.

14. Ichikawa, Y.; Monden, R.; Kuzuhara, H. *Carbohydr. Res.* **1988**, *172*, 37.

15. a) Davies, N.J.; Flitsch, S.L. *J. Chem. Soc., Perkin Trans. 1* **1994**, 359; b) Györgydeák, Z.; Thiem, J. *Carbohydr. Res.* **1995**, *268*, 85.

16. Paulsen, H.; Hayauchi, Y.; Unger, F.M. *Liebigs Ann. Chem.* **1984**, 1270; 1278; Unger, F.M.; Stix, D.; Schulz, G. *Carbohydr. Res.* **1980**, *80*, 191.

17. Charon, D.; Szabó, L.; Cesario, M.; Guilhem, J. *J. Chem. Soc., Perkin Trans. 1* **1982**, 3055.

18. Bandgar, B.P.; Hartmann, M.; Schmid, W.; Zbiral, E. *Liebigs Ann. Chem.* **1990**, 1185.

(*Received in UK* 13 *May* 1997; *revised* 4 *June* 1997; *accepted* 5 *June* 1997)