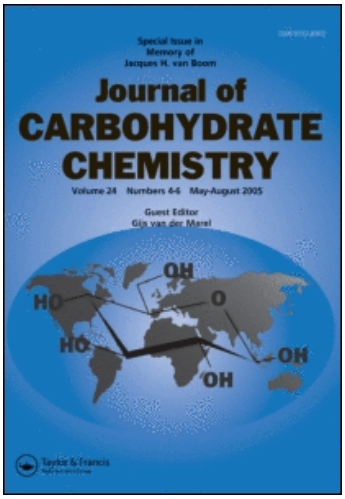

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Hydrolysis of Cyanoethylated Carbohydrates: Synthesis of New Carboxylic Derivatives of Sucrose, d-Glucose and d-Fructose

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HYDROLYSIS OF CYANOETHYLATED CARBOHYDRATES : SYNTHESIS OF NEW CARBOXYLIC DERIVATIVES OF SUCROSE, D-GLUCOSE AND D-FRUCTOSE

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ABSTRACT

Synthesis of new cyanoethylated compounds and carboxylic acids derived from sucrose, methyl D-glucopyranoside, methyl D-fructopyranoside and methyl D-fructofuranoside are described. Basic hydrolysis of these cyanoethylated compounds to the corresponding amides and carboxylates and acidic alcoholysis to the corresponding methyl esters are discussed.

INTRODUCTION

It is well-known that the use of sodium tripolyphosphate (STP) in detergent formulations as calcium and magnesium sequestering agent is subject to regulations because it leads to eutrophication of surface waters including lakes and seas.[1-5] For this reason extensive studies have been carried out with the aim to find an alternative for STP which meets all requirements. The main demands of such substitutes are : a, good performance (Ca-and Mg-binding); b, good biodegradability / biocompatibility; c, low price; d, preferentially good solubility in water, and e, non toxicity.

Up to now an intensive search for substitutes of STP has resulted in only a few systems that meet the necessary technical, commercial and environmental requirements. These substitutes include complexing agents [nitrilotriacetate (NTA) and citrate], a precipitating agent (sodium carbonate) and an inorganic ion exchanger (zeolite NaA).

Nowadays, the commonly used alternative for STP is zeolite NaA,[6-9] an inorganic ion exchanger which has several attractive properties : it is inexpensive, the calcium binding is satisfactory and the substance is nontoxic. However, there are also some drawbacks involved in its use, namely its non-water solubility and slow binding of magnesium, especially at lower washing temperature.[6,9,10] Moreover, deposits (incrustations) formed on fabrics during the washing process do not dissolve. In view of these aspects a so-called co-builder is added, which prevents the formation of incrustation and functions as a carrier, transporting the calcium and the magnesium ions to the zeolite NaA.[9]

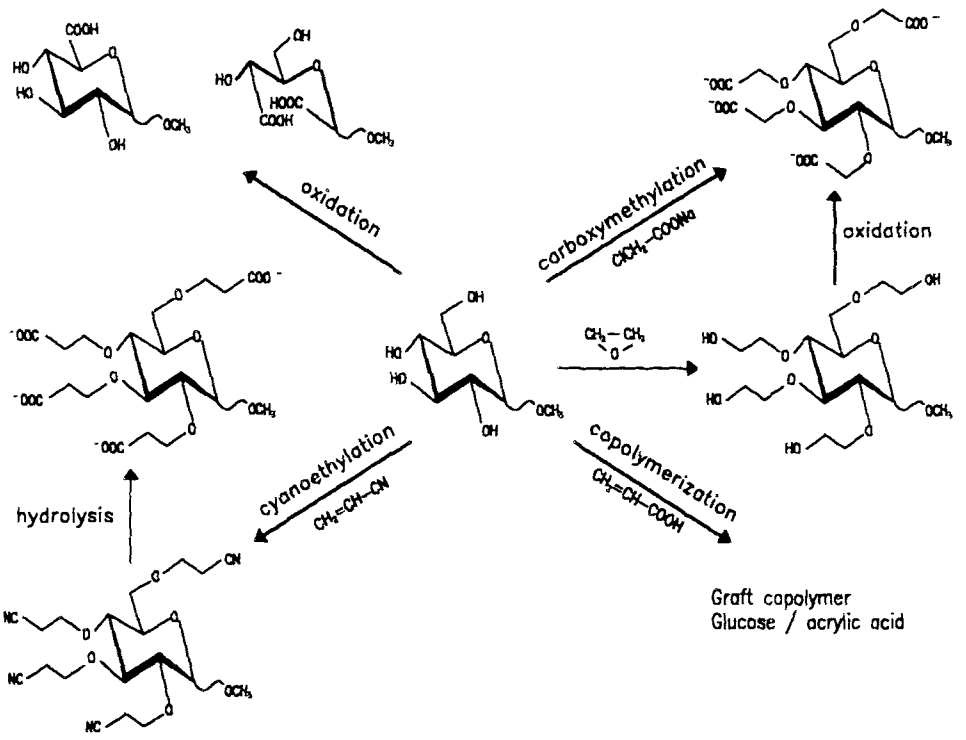
Polyacrylate and copolymers of acrylate and maleate are widely used for this purpose and they generally show optimal performance for incrustation inhibition.[11] These copolymers have been reported to be physiologically safe[11] but they are not biodegradable, which makes their long-term application unattractive.

For this reason, the development of (bio-)degradable detergent additives is of considerable importance. Carbohydrates may serve as an alternative feedstock for the preparation of polycarboxylic acides since (i) carbohydrates are relatively inexpensive renewable materials and (ii) glycoside derived products are expected to be readily (bio-) degradable via hydrolysis of the acid-labile acetal bonds.

During the past decade carboxylic acids derived from simple glycosides have gained in importance because of their multiple properties. These acids can be obtained in several ways (Scheme 1) : a, oxidation of the glycoside with or without opening of the ring; b, carboxymethylation; c, ethoxylation of carbohydrate with subsequent oxidation of hydroxyl to carboxy groups; d, graft copolymerization of carbohydrates with acrylic acid (or derivatives), and e, cyanoethylation followed by hydrolysis of nitriles to carboxy groups.

Actually the most useful and studied products are oxidized[12-19] and carboxymethylated[13,20,21] polysaccharides. The first are obtained by periodic oxidation of polysaccharide with cleavage of vicinal diol, the second by carboxymethylation of polysaccharides. These latter show better calcium sequestering capacity than STP.

Oxidation products of carbohydrate/ethylene oxide adducts present good performance, but the cost of this oxidation method limits the industrial application of this way.[22,23] Copolymerisation of carbohydrate with acrylic acid leads to a graft copolymer,

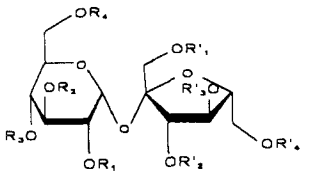


Scheme 1

with good antiincrustation properties.[24-27] Currently ether-carboxylic acids obtained by hydrolysis of cyanoethylated glycosides have not been described. This paper describes cyanoethylation of some nonreducing carbohydrates and the hydrolysis of the products to give carboxylic acids as potentially biodegradable products and good calcium complexing agents.

RESULTS AND DISCUSSION

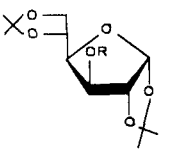
In order to try to find new opportunities in detergents for sucrose, we have synthesized cyanoethylated sucrose, **1**, **2** and **3**, with degrees of substitution of 8, 6 and 4. In addition, we have also synthesized cyanoethylated derivatives of glucose, **4-7**, with degrees of substitution 1-4, percyanoethylated methyl β-D-fructopyranoside **8** and methyl α and β-D-fructofuranoside **9** and **10** (Scheme 2). All of these compounds were then subjected to acid hydrolysis.



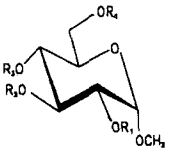
1 : $R_1-R_4=R'_1-R'_4=(CH_2)_2CN$

2 : $R_1,R_2=R'_1-R'_4=(CH_2)_2CN$, $R_3=R_4=H$

3 : $R_2=R'_2-R'_4=(CH_2)_2CN$, $R_1=R'_1=R_3=R_4=H$



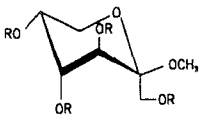
4 : $R=(CH_2)_2CN$



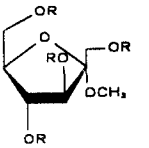
5: $R_1=R_4=H$, $R_2=R_3=(CH_2)_2CN$

6: $R_1-R_3=(CH_2)_2CN$, $R_4=H$

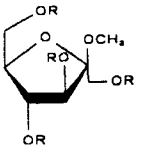
7: $R_1-R_4=(CH_2)_2CN$



8 : $R=(CH_2)_2CN$



9: $R=(CH_2)_2CN$



10: $R=(CH_2)_2CN$

Scheme 2

Cyanoethylated carbohydrates

Sucrose

Cyanoethylated derivatives were obtained by addition of acrylonitrile to an alkaline solution of protected or unprotected nonreducing sugar.[28] Cyanoethylation conditions were optimised by studying sucrose percyanoethylation. Results of this study are given in Table 1.

Under the following optimal conditions (acrylonitrile : 20 eq/sucrose, KOH 10%, 55 °C, 1.5 h) the percyanoethylated sucrose **1** was also obtained in 70% yield. 3,3'-Oxydipropionitrile (adduct-acrylonitrile/water) was also formed in limited yield.

1',2,3,3',4',6'-hexa-*O*-(2-cyanoethyl)sucrose **2** was obtained from 4,6-mono-*O*-isopropylidenesucrose[29,30] by cyanoethylation and deacetalisation (CH_3COOH 60%) in 47% yield, while 3,3',4',6'-tetra-*O*-(2-cyanoethyl)sucrose **3** was synthesized from 1',2:4,6-di-*O*-isopropylidenesucrose[29,30] using the same two-step procedure, in 40% yield.

Glucose

1,2:5,6-di-*O*-isopropylidene-3-*O*-(2-cyanoethyl)-α-D-glucofuranose **4** was obtained by direct cyanoethylation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose in 65% yield.

Methyl 2,3-di-*O*-(2-cyanoethyl)-α-D-glucopyranoside **5** was prepared from methyl α-D-glucopyranoside by acetalisation (DMP, DMF, *p*-TsOH), cyanoethylation and deacetalisation (CH_3COCl, CH_3OH) in 68% yield.

Table 1. Sucrose percyanoethylation : influence of reaction conditions

T (°C)	t (min)	Base	Base concentration (mol/l)	Molar ratio acrylonitrile/sucrose	Yield (%) of **1**
40	90	NaOH	0.15[a]	20	8
50	90	NaOH	0.15[a]	20	37
80	90	NaOH	0.15[a]	20	<5
50	180	NaOH	0.15[a]	20	19
50	90	NaOH	0.15[a]	20	67
50	90	KOH	1.80 (10%)[b]	10	27
50	90	KOH	1.80[b]	20	70
50	90	KOH	1.80[b]	30	72

Yields are given after chromatographic separation on silica gel. a. Ratio base/sucrose 2:1 (w/w). b. 1:1.

Methyl 2,3,4-tri-*O*-(2-cyanoethyl)-α-D-glucopyranoside **6** was obtained from methyl α-D-glucopyranoside by tritylation[31] (TrCl, DMAP, NEt_3, DMF), cyanoethylation and detritylation (CH_3COCl, CH_3OH) in 50% yield. During this synthesis the dicyanoethylated derivative **5** was also formed in 27% yield.

Methyl 2,3,4,6-tetra-*O*-(2-cyanoethyl)-α-D-glucopyranoside **7**, synthesized by percyanoethylation of methyl α-D-glucopyranoside, was contaminated by 3,3'-oxydipropionitrile even after purification by chromatography on silica gel.

Fructose

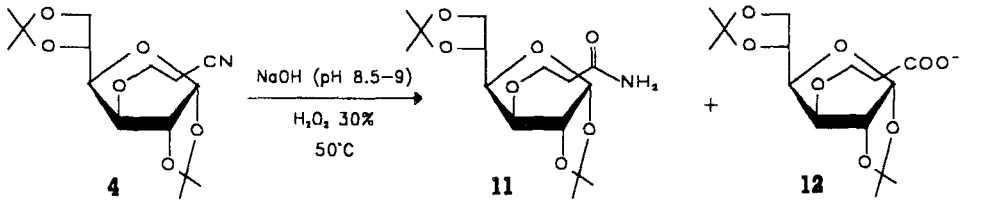
Methyl 1,3,4,5-tetra-*O*-(2-cyanoethyl)-β-D-fructopyranoside **8** was prepared 46% overall yield from D-fructose in four steps: acetalisation[32] (CH_3COCH_3, H_2SO_4), cyanoethylation of 1,2-mono-*O*-isopropylidene-β-D-fructopyranoside, deacetalisation-methylation (CH_3COCl, CH_3OH) and cyanoethylation.

Anomeric mixture of methyl 1,3,4,6-tetra-*O*-(2-cyanoethyl)-D-fructofuranoside **9** and **10** were obtained by acidic alcoholysis (CH_3COCl, CH_3OH) of 1',2,3,3',4',6'-hexa-*O*-(2-cyanoethyl)sucrose **2** in 38% yield. Compounds **9** and **10** were not separated.

Hydrolysis of cyanoethylated compounds

Monosaccharides

For direct basic hydrolysis of **4** at different temperatures, concentrations and pH conditions, traces of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **11** and 1,2:5,6-di-*O*-isopropylidene-3-*O*-(2-carboxyethyl)-α-D-glucofuranose **12** were obtained. More alkaline conditions led to total decyanoethylation of **4**.



Scheme 3

Nitriles can be converted to amides and then to carboxylic acids using basic hydrogen peroxide[33]. Indirect basic hydrolysis of **4** with hydrogen peroxide led to a mixture of the corresponding amide and carboxylic acid (Scheme 3).

The maximum yield of carboxylate **12** did not exceed 30%. Temperatures higher than 50 °C resulted in decyanoethylation of **4**. Using sodium peroxide in the presence of DMSO[34,35] the hydrolysis of amide led essentially to a desetherification to give the 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose.

Indirect basic hydrolysis of polycyanoethylated compounds did not lead to the corresponding carboxylic acids with the same substitution degree because of partial decyanoethylation under these basic conditions. This procedure was only applied for synthesis of monocarboxylic acid from monocyanoethylated compound.

Nitriles can be converted to the corresponding methyl esters by acidic alcoholysis with methanolic hydrochloric acid. Acidic alcoholysis of **4** by methanolic hydrochloric acid led to a mixture of the α and β methyl esters **13** and **14** in 52% yield. This alcoholysis, summarised in Table 2, proceeded without decyanoethylation.

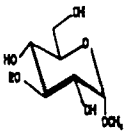
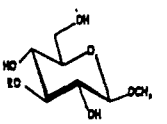
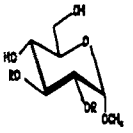
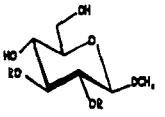
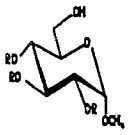
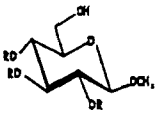
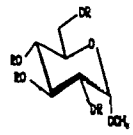
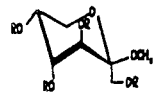
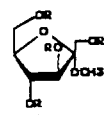
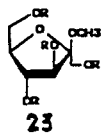
Disaccharides

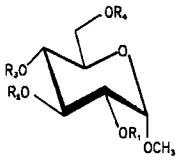
Acidic alcoholysis of **1** by methanolic HCl promoted the alcoholysis of nitrile groups and solvolysis of the glycosidic linkage leading to a mixture of methyl 2,3,4,6-tetra-*O*-[2-(methoxycarbonyl)ethyl]-α and β-D-glucopyranoside, **19** and **20**, and methyl 1,3,4,6-tetra-*O*-[2-(methoxycarbonyl)ethyl]-α and β-D-fructofuranoside, **22** and **23**. It was confirmed that hydrolysis of the glycosidic linkage was the first step of this transformation. Consequently this procedure could not be used successfully for preparing the desired carboxylic derivatives of sucrose.

Carboxylic acids

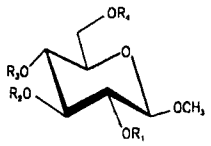
The carboxylic acids **24-35** (Scheme 4) were obtained by quantitative saponification of the methyl esters (KOH 0.2M).

Table 2. Acidic alcoholysis of cyanoethylated monosaccharides

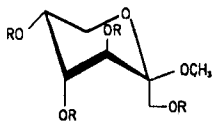
Cyanoethylated compounds	Methyl esters (yield) R = EtCOOMe	
4	 **13** (26%)	 **14** (26%)
5	 **15** (27%)	 **16** (14%)
6	 **17** (50%)	 **18** (10%)
7	 **19** (35%)	 **20** (7%)
8	 **21** (41%)	
9-10	 **22**	 **23**
	22- 23 (46%)	



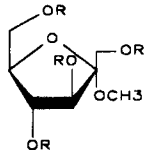
24 : $R_2=(CH_2)_2COOH$, $R_1=R_3=R_4=H$
26 : $R_1=R_2=(CH_2)_2COOH$, $R_3=R_4=H$
28 : $R_1-R_3=(CH_2)_2COOH$, $R_4=H$
30 : $R_1-R_4=(CH_2)_2COOH$



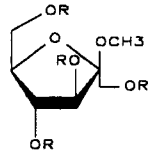
25 : $R_2=(CH_2)_2COOH$, $R_1=R_3=R_4=H$
27 : $R_1=R_2=(CH_2)_2COOH$, $R_3=R_4=H$
29 : $R_1-R_3=(CH_2)_2COOH$, $R_4=H$
31 : $R_1-R_4=(CH_2)_2COOH$



32 : $R=(CH_2)_2COOH$



33 : $R=(CH_2)_2COOH$



34 : $R=(CH_2)_2COOH$

Scheme 4

Interpretation of ^{13}C NMR spectra of cyanoethylated carbohydrates, methyl esters and carboxylic acids

For the cyanoethylated derivatives, the comparison of ^{13}C NMR spectra chemical shifts of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose and 1,2:5,6-di-O-isopropylidene-3-*O*-(2-cyanoethyl)-α-D-glucofuranose **4** showed that cyanoethylation of a hydroxyl group has a deshielding effect on the corresponding underivatized alcohol bearing carbon (Δδ 8 ppm), while the carbon in the position α experienced a shielding effect of about 3 ppm. This observation allowed assignement of the different chemical shifts listed in Tables 3, 4 and 5.

CONCLUSION

We have synthesized a number of new cyanoethylated compounds derived from sucrose, D-glucose and D-fructose. Direct basic hydrolysis of cyanoethylated compounds always led to decyanoethylation while indirect basic hydrolysis of monocyanoethylated carbohydrate resulted, via amide, in the corresponding acid in 30% maximum yield.

However the acidic alcoholysis can not be applied to cyanoethylated sucrose because of the hydrolysis of the glycosidic linkage, the acidic alcoholysis of

Table 3. Chemical shifts of cyanoethylated glucose and fructose (a. $CDCl_3$. b. D_2O)

Compounds	C1	C2	C3	C4	C5	C6	OCH_3
4[a]	105.3	82.8	**82.8**	81.1	72.3	67.5	
5[b]	97.3	**79.6**	**81.8**	66.1	71.9	60.7	55.2
6[a]	97.0	**80.7**	**80.8**	**76.8**	70.4	60.7	55.1
7[a]	97.0	**80.6**	**80.8**	**76.7**	69.6	**69.0**	55.2
8[a]	70.4	101.1	75.4	75.1	78.9	61.9	49.0
9[a]	**67.4**	106.6	**88.0**	**85.3**	79.1	**70.9**	48.7
10[a]	**70.3**	103.3	**83.8**	**83.7**	77.8	**71.3**	49.6

Table 4. Chemical shifts of methyl esters (a. D_2O. b. $CDCl_3$)

Compounds	C1	C2	C3	C4	C5	C6	OCH_3
13[a]	99.5	71.1	**82.5**	69.3	71.8	60.7	55.2
14[a]	103.3	72.8	**84.9**	69.3	76.0	60.9	57.4
15[b]	97.8	**80.3**	**82.0**	70.7	70.7	62.5	55.1
16[b]	104.5	**81.7**	**85.1**	70.7	74.8	62.7	57.1
17[b]	97.7	**80.9**	**81.5**	**76.4**	70.6	61.5	55.1
18[b]	104.4	**82.3**	**84.3**	**77.8**	74.9	61.7	57.2
19[b]	97.6	**80.6**	**81.4**	**77.3**	69.8	**69.1**	55.0
20[b]	104.2	**82.2**	**84.3**	**77.4**	74.5	**69.4**	57.0
21[b]	**70.2**	100.9	**75.6**	**78.9**	**75.8**	61.6	48.7
22[b]	**66.7**	108.1	**88.50**	**85.7**	80.5	**72.0**	49.2
23[b]	**71.5**	104.4	**85.8**	**84.4**	79.2	**72.7**	50.2

Table 5. Chemical shifts of carboxylic acids derivatives

Compounds	C1	C2	C3	C4	C5	C6	OCH_3
24	99.4	71.1	**82.6**	69.3	71.8	60.7	55.2
25	103.0	72.5	**84.8**	69.1	75.6	60.6	57.0
26	99.7	**79.5**	**81.8**	68.1	71.7	60.8	55.2
27	103.5	**81.1**	**84.1**	68.9	75.5	60.7	57.4
28	96.9	**80.0**	**81.5**	**77.7**	71.0	60.5	55.2
29	103.4	**81.5**	**83.7**	**77.5**	74.8	60.3	57.4
30	97.5	**79.7**	**81.3**	**77.5**	70.1	**68.9**	55.2
31	103.3	**81.3**	**83.4**	**77.5**	73.4	**67.6**	57.4
32	**69.5**	100.9	**75.3**	**78.5**	**76.0**	61.3	49.0
33	**65.8**	108.4	**86.3**	**84.6**	81.2	**70.9**	48.5
34	**69.6**	104.2	**85.1**	**83.8**	78.9	**72.1**	49.5

polycyanoethylated monosaccharides led to the corresponding methyl esters in 30-50% yield. Carboxylic acids were also obtained by quantitative saponification of these methyl esters.

The calcium complexing properties of those carboxylic acids derived from D-glucose and D-fructose were described elsewhere.[36]

EXPERIMENTAL

General procedures. Optical rotations were determined with a Perkin-Elmer Model 141 polarimeter. Melting points were measured on the Electrothermal 9100. ^1H (300 MHz) and ^{13}C (75.43 MHz) NMR spectra were recorded on a Bruker AC 300 spectrometer, ^1H (200 MHz) and ^{13}C (50.32 MHz) NMR spectra were recorded on a Bruker AC 200 spectrometer. Chemical shifts (δ) are referenced to the solvent ($CDCl_3$: 7.45 ppm for ^1H NMR spectra and 77.0 ppm for ^{13}C NMR spectra; CD_3COCD_3 : 29.8 ppm for ^{13}C NMR spectra; D_2O : 4.75 ppm for ^1H NMR spectra). TLC were conducted on silica gel Kieselgel 60 and visualized by spraying with 10% sulfuric acid in ethanol followed by heating. Flash chromatography was performed on silica gel Amicon 60 A. Purity of the compounds was estimated on the basis of their ^1H NMR spectra and their elementary analysis.

1',2,3,3',4,4',6,6'-octa-*O*-(2-cyanoethyl)sucrose (1). To a solution of sucrose (5.0 g, 14.6 mmol) in 10% aqueous KOH (5.0 g), acrylonitrile (2.5 eq / OH, 19.4 mL) was added and the reaction mixture stirred at 50 °C for 3 h. The reaction mixture was cooled and extracted with chloroform. The organic extracts were successively washed with diluted aqueous hydrochloric acid and water, dried over Na_2SO_4, filtered, and solvent was evaporated *in vacuo*. Purification of the residue by chromatography on silica gel (27:1, chloroform-methanol) gave the title compound **1** (7.7 g, 70%) as a crystalline product: Mp 74 °C; $[\alpha]_D^{20}$ +34.2° (*c* 1.09, chloroform); ^1H NMR (300 MHz, $CDCl_3/C_6D_6$) δ 2.00 (m, 16H, 8 CH_2CN), 3.00 (q, 1H, H-2), 3.12 (t, 1H, H-4), 3.30 (d, 1H, H-6b), 3.38 (t, 1H, G-3), 3.57 (d, 1H, H-6a), 3.74 (m, 1H, H-5), 5.31 (d, 1H, H-1), 3.00-3.85 (m, 13H); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 18.79, 18.54, 19.15, 19.18, 19.22, 19.28, 19.32 (CH_2CN), 65.29, 65.43, 65.82, 65.97, 66.10 (OCH_2), 67.32, 67.57, 69.22, 70.53, 71.31, 78.64, 80.17, 80.94, 82.02, 84.60, 89.81, 103.92 (C_1/C_6, C_1'/C_6'), 118.09, 118.45, 118.19, 118.26, 118.40, 118.66, 118.95 (CN).

Anal. Calcd for $C_{36}H_{46}N_8O_{11}$: C, 56.40; H, 6.00; N, 14.62; O 22.98. Found: C, 56.59; H, 6.02; N, 14.25; O, 23.12.

1',2,3,3',4',6'-hexa-*O*-(2-cyanoethyl)sucrose (2). To a solution of sucrose (10.0 g, 0.03 mol) in DMF (100 mL, dried over $CaSO_4$ for 24 h before distillation under an

atmosphere of nitrogen), dimethoxypropane (12eq / sucrose, 43 mL) and *p*-toluenesulfonic acid (0.3 g) were added and the reaction mixture stirred at 20 °C for 1 h. Neutralization of the reaction mixture by adding triethylamine and evaporation *in vacuo* of the solvent afforded a white solid. Purification of this solid by chromatography on silica gel (9:1, chloroform-methanol) gave 4,6-mono-*O*-isopropylidenesucrose (5.0 g, 45%) and 1',2:4,6-di-*O*-isopropylidenesucrose (5.7 g, 46%). To a solution of 4,6-mono-*O*-isopropylidenesucrose (5.0 g, 13 mmol) in 10% aqueous KOH (2.5 g), acrylonitrile (2.5 eq / OH, 13.0 mL) was added and the reaction mixture stirred at 50 °C for 2 h. The reaction mixture was treated according as above. Purification of the residue by chromatography on silica gel (30:1, chloroform-methanol) gave a mixture of 4,6-mono-*O*-isopropylidene-1',2,3,3',4',6'-hexa-*O*-(2-cyanoethyl)sucrose **2** and 3,3'-oxydipropionitrile. To a solution of this mixture (5.3 g), 60% aqueous acetic acid was added and the reaction mixture stirred at 80 °C for 20 min. Evaporation of the solvent *in vacuo* afforded a yellow syrup. Purification of this residue by chromatography on silica gel (15:1, chloroform-methanol) gave the title compound **2** (4.1 g, 47% / 4,6-mono-*O*-isopropylidenesucrose). $[\alpha]_D^{20}$ +24.5° (*c* 1.01, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.56-2.71 (m, 12 H, 6 CH_2CN), 3.32 (q, 1H, H-2), 3.45 (t, 1H, H-4), 3.56 (d, 1H, H-6b), 3.63, (t, 1H, H-3), 3.71 (d, 1H, H-6a), 4.00 (m, 1H, H-5), 5.61 (d, 1H, H-1), 3.70-4.20 (m, 21H); ^{13}C NMR (75.43 MHz, $CDCl_3$) δ 18.73, 18.84, 19.16, 19.24, 19.31, 19.36 (CH_2CN), 65.50, 65.63, 65.67, 65.78, 66.17, 67.42 (OCH_2), 62.26, 70.50, 71.11, 71.90, 72.32, 78.35, 79.43, 81.56, 81.80, 84.30, 89.47, 103.45 (C-1/C-6, C-1'/C-6'), 118.20, 118.27, 118.57, 118.71, 118.84 (CN).

Anal. Calcd for $C_{30}H_{40}O_{11}N_6$: C, 54.53; H, 6.11; N, 12.72; O, 26.64. Found: C, 53.97; H, 6.15; N, 12.40; O, 26.60.

3,3',4',6'-tetra-*O*-(2-cyanoethyl)sucrose (3). To a solution of 1'2:4,6-di-*O*-isopropylidenesucrose (5.7 g, 13.5 mmol) in 10% aqueous KOH (3.0 g), acrylonitrile (2.5 eq / OH, 8.9 mL) was added and the reaction mixture stirred at 50 °C for 2 h. The reaction mixture was treated as above. Purification of the residue by chromatography on silica gel (50:1, chloroform-methanol) gave a mixture of 1',2:4,6-di-*O*-isopropylidene-3,3',4',6'-tetra-*O*-(2-cyanoethyl)sucrose and 3,3'-oxydipropionitrile. To this mixture (4.6g), 60% aqueous acetic acid was added, and the reaction mixture was stirred at 80 °C for 20 min. Evaporation of the solvent *in vacuo* afforded a yellow syrup. Purification of this residue by chromatography on silica gel (9:1, chloroform-methanol) gave the title compound **3** (3.0 g, 40% / 1'2:4,6-di-*O*-isopropylidenesucrose). ^{1}H NMR (75.43 MHz, CD_3COCD_3) δ 2.7-2.9 (m, 8H, 4 CH_2CN), 3.37-4.52 (m, 23H), 5.35 (d, 1H, H-1); ^{13}C NMR (300 MHz, CD_3COCD_3) δ 18.65, 19.14, 19.21, 19.28 (4 CH_2CN), 62.32, 64.44, 68.01, 70.74, 72.15, 73.75, 79.67, 83.91, 84.57, 86.96, 92.27, 105.11 (C-1/C-6, C-1'/C-6' and OCH_2), 119.13, 119.43 (CN).

Anal. Calcd for $C_{24}H_{34}N_4O_{11}$: C, 52.00; H, 6.20; N, 10.10; O, 31.70. Found: C, 51.49; H, 6.13; N, 9.78; O, 31.11.

1,2:5,6-di-*O*-isopropylidene-3-*O*-(2-cyanoethyl)-α-D-glucofuranose (4). To a solution of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (5.0 g, 19.1 mmol) in aqueous NaOH 0.4 N (8 mL), acrylonitrile (4 eq / OH, 5.0 mL) was added and the reaction mixture stirred at 50 °C for 2 h. The reaction mixture was treated as above. Purification of the residue by chromatography on silica gel (i, 50:20:1, chloroform-hexane-methanol, ii, 5:1, chloroform-ethyl acetate) gave the title compound 4 (3.9 g, 65%). $[\alpha]_D^{21}$ -32.8° (*c* 0.99, chloroform); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.27, 1.31, 1.38, 1.45 (4s, 12H, 4 CH_3 of $C(CH_3)_2$), 2.59 (t, 2H, CH_2CN), 3.79 (t, 2H, OCH_2), 5.84 (d, 1H, H-1, $J_{1,2}$ = 3.7 Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 18.88 (CH_2CN), 25.17, 26.10, 26.69, 26.70 (4 CH_3 of $C(CH_3)_2$), 65.40, 67.34, 72.12, 81.00, 82.66, 82.70, 105.17 (C-1/C-6), 109.10, 111.88 (2 $C(CH_3)_2$), 117.40 (CN).

Anal. Calcd for $C_{15}H_{23}NO_6$: C, 57.51; H, 7.35; N, 4.47; O, 30.67. Found: C, 57.24; H, 7.42; N, 5.31; O, 30.45.

Methyl 2,3-di-*O*-(2-cyanoethyl)-α-D-glucopyranoside (5). To a solution of methyl α-D-glucopyranoside (5.0 g, 25.8 mmol) in anhydrous DMF (50 mL), dimethoxypropane (1.1eq / methyl α-D-glucopyranoside, 3.5 mL) and *p*-toluenesulfonic acid (0.1 g) were added and the reaction mixture stirred at 20 °C for 3 h. Neutralization of the reaction mixture by adding triethylamine and evaporation *in vacuo* of the solvent afforded a yellow syrup which was extracted with chloroform/water. The organic extract was washed with water, dried over Na_2SO_4, filtered and solvent evaporated *in vacuo*. Purification of the residue by chromatography on silica gel (15:1, chloroform-methanol) afforded methyl 4,6-mono-*O*-isopropylidene-α-D-glucopyranoside (4.5 g, 75%). To a solution of methyl 4,6-mono-*O*-isopropylidene-α-D-glucopyranoside (1.48 g, 6.2 mmol) in aqueous NaOH 0.4 N (5 mL), acrylonitrile (4 eq / OH, 3.4 mL) was added and the reaction mixture stirred at 50 °C for 3 h. The reaction mixture was treated as above. To a solution of the residue (4.6 g) in anhydrous methanol (10 mL), cooled at 0 °C, acetyl chloride was added (1 mL) and the reaction mixture stirred at 20 °C for 10 min. Solvent was evaporated *in vacuo* and the residue was extracted with chloroform/water. The aqueous extract was washed with chloroform, neutralized by adding 10% aqueous NaOH and freeze-dried. Purification of the residue by chromatography on silica gel (30:1, chloroform-methanol) gave **5** (1.29 g, 51%). $[\alpha]_D^{20}$ +106.2° (*c* 0.98, chloroform); ^{1}H NMR (200 MHz, D_2O) δ 2.75, 2.81 (t, 4H, 2 CH_2CN), 3.41 (s, 3H, α OCH_3), 3.46-3.70 (m, 4H), 3.75 (d, 1H), 3.81 (d, 1H), 3.90 (t, 2H), 4.98 (d, 1H, H-1, $J_{1,2}$ = 2.9 Hz); ^{13}C NMR (50.32 MHz, D_2O) δ 19.07, 19.09 (CH_2CN), 55.20 (α OCH_3), 60.73, 66.03, 68.13, 69.40, 71.85, 79.56, 81.79, 97.31 (C-1/C-6 and OCH_2), 120.18, 120.43 (CN).

Anal. Calcd for $C_{13}H_{20}N_2O_6$: C, 52.00; H, 6.67; N, 9.33; O, 32.00. Found: C, 49.19; H, 6.54; N, 8.64; O, 30.55.

Methyl 2,3,4-tri-*O*-(2-cyanoethyl)-α-D-glucopyranoside (6). To a solution of methyl α-D-glucopyranoside (11.6 g, 0.06 mol) in anhydrous DMF (60 mL), triphenylmethyl chloride (18.4 g, 0.066 mol), triethylamine (1.5 eq / methyl α-D-glucopyranoside, 15 mL) and 4-*N,N*-dimethylaminopyridine (0.58 g, 3.0 mmol) were added under an atmosphere of nitrogen and the reaction mixture stirred at 20 °C for 12 h. The reaction mixture was poured into a mixture of ice and water and extracted with chloroform. The organic extract was successively washed with aqueous saturated NH_4Cl solution and water, dried over Na_2SO_4, filtered, and solvent evaporated *in vacuo*. Purification of the residue by chromatography on silica gel (15:1, chloroform-methanol and triethylamine traces) gave methyl 6-mono-*O*-trityl-α-D-glucopyranoside which was recristallized in ethanol (22.3 g, 86%, mp 150 °C). To a solution of 6-mono-*O*-trityl-α-D-glucopyranoside (6.0 g, 0.014 mol) in 10% aqueous KOH (5.0 g), acrylonitrile was added (2.5 eq / OH, 6.8 mL) and the reaction mixture was stirred at 50 °C for 2 h. The reaction mixture is treated as above. To a solution of the residue (12.0 g) in anhydrous methanol (10 mL), acetyl chloride (2.0 mL) was added and the reaction mixture was stirred at room temperature for 10 min. The solvent was evaporated *in vacuo* and the residue extracted with chloroform/water. The organic extract was washed with water, dried over Na_2SO_4, filtered, and the solvent evaporated *in vacuo*. Purification of the residue by chromatography on silica gel (30:1, chloroform-methanol) gave **6** (2.9 g, 50%) and **5** (1.3 g, 27%). $[\alpha]_D^{20}$ +44.06° (*c* 2.04, chloroform); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.57-2.67 (m, 6H, 3 CH_2CN), 3.38 (s, 3H, α OCH_3), 3.32-3.44 (m, 2H), 3.53-3.65 (m, 2H), 3.69, 4.13 (m, 8H), 4.81 (d, 1H, H-1, $J_{1,2}$ = 3.4 Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 19.12, 19.17, 19.24 (CH_2CN), 55.14 (α OCH_3), 60.70, 65.63, 67.22, 67.55, 70.36, 76.78, 80.66, 80.82, 96.95 (C-1/C-6 and OCH_2), 117.78, 118.30 118.64 (CN).

Anal. Calcd for $C_{16}H_{23}N_3O_6$: C, 54.38; H, 6.52; N, 11.90; O, 27.20. Found: C, 54.13; H, 6.51; N, 11.81; O, 27.01.

Methyl 2,3,4,6-tetra-*O*-(2-cyanoethyl)-α-D-glucopyranoside (7). To a solution of methyl α-D-glucopyranoside (2.0 g, 0.01 mol) in 10% aqueous KOH, acrylonitrile (2.5eq/OH, 6.8 mL) was added and the reaction mixture stirred at 50 °C for 1.5 h. The reaction mixture was treated as above. Purification of the residue by chromatography on silica gel (40:1, chloroform-methanol) gave a mixture of **7** and β,β'-dicyanoethyl ether (5.7g). ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.54-2.64 (m, 13H instead of 8H, CH_2CN), 3.35 (s, 3H, α OCH_3), 3.32-3.46 (m, 2H), 3.56-3.94 (m, 15H), 4.00-4.11 (m, 2H), 4.76 (d, 1H, H-1, $J_{1,2}$ = 3.5 Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 18.73, 19.02, 19.14, 19.17 (CH_2CN), 55.15 (α OCH_3), 65.52, 65.93, 67.32, 67.53, 68.95, 69.55, 76.73, 80.63, 80.78, 96.98 (C-1/C-6 and OCH_2), 117.68, 117.95, 118.40, 118.54 (CN).

Methyl 1,3,4,5-tetra-*O*-(2-cyanoethyl)-β-D-fructopyranoside (8). To a solution of D-fructose (36 g, 0.2 mol) in anhydrous acetone (700 mL), concd sulfuric acid (3.5 mL) was added and the reaction mixture stirred at room temperature for 1.5 h. The reaction mixture was neutralized by adding aqueous NaOH (11 g in 10 mL water), and solvent was evaporated *in vacuo*. Purification of the residue by chromatography on silica gel (30:1, chloroform-methanol) gave 1,2-mono-*O*-isopropylidene-β-D-fructopyranoside (10.1 g, 23%) and 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranoside (33.8 g, 65%). To a solution of 1,2-mono-*O*-isopropylidene-β-D-fructopyranoside (4.5 g, 20.5 mmol) in 10% aqueous KOH (5 mL), acrylonitrile (2.5 eq / OH, 10.1 mL) was added and the reaction mixture stirred at 50 °C for 2 h. The reaction mixture was treated as above. To a solution of the residue (majority of 1,2-mono-*O*-isopropylidene-3,4,5-tri-*O*-(2-cyanoethyl)-β-D-fructopyranoside) in anhydrous methanol (30 mL), acetyl chloride (4.6 mL) was added and the reaction mixture stirred at room temperature for 1 h. The reaction mixture was neutralized with $PbCO_3$, filtered through Celite and solvent evaporated in *vacuo*. To a solution of the residue (majority of methyl 3,4,5-tri-*O*-(2-cyanoethyl)-β-D-fructopyranoside) in 10% aqueous KOH (2.5 mL), acrylonitrile (4 eq / OH, 5.4 mL) was added and the reaction mixture stirred at 50 °C for 2 h. The reaction mixture was treated as above. Purification of the residue by chromatography on silica gel (40:1, chloroform-methanol) gave the title compound **8** (3.5 g, 42%). ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 19.10, 19.26, 19.35, 19.46 ($\mathbf{CH_2}$CN), 48.95 (β $\mathbf{OCH_3}$), 61.78, 70.35, 75.40, 75.09, 78.93, 101.09 (C-1/C-6), 65.14, 65.49, 65.86, 67.66 ($\mathbf{OCH_2}$), 118.13, 118.22, 118.69 (**CN**).

Methyl 1,3,4,6-tetra-*O*-(2-cyanoethyl)-α and β-D-fructofuranoside (9 and 10). To a solution of 1',2,3,3',4',6'-hexa-*O*-(2-cyanoethyl)sucrose **2** (6.5 g, 9.8 mmol) in anhydrous methanol (30 mL), acetyl chloride (2 eq / **2**, 2.7 mL) was added and the reaction mixture stirred at room temperature for 3 h. The reaction mixture was neutralized with $PbCO_3$, filtered through Celite and solvent evaporated *in vacuo*. Purification of the residue by chromatography on silica gel (50:1, chloroform-methanol) gave **9** and **10** (38%).

1,2:5,6-di-*O*-isopropylidene-3-*O*-(2-amidoethyl)-α-D-glucofuranose (11) and 1,2:5,6-di-*O*-isopropylidene-3-*O*-(2-carboxyethyl)-α-D-glucofuranose (12). 1,2:5,6-di-*O*-isopropylidene-3-*O*-(2-cyanoethyl)-α-D-glucofuranose **4** (1.2 g, 3.8 mmol) was dispersed in aqueous hydrogen peroxide (5 mL) and the reaction was stirred at 50 °C for 3.5 h. The pH of the reaction mixture was adjusted to 8.5-9 by addition of aqueous NaOH. The reaction mixture was extracted with chloroform. The organic extract was washed with water, dried over Na_2SO_4 and filtered. Evaporation *in vacuo* of the solvent gave 1,2:5,6-di-*O*-isopropylidene-3-*O*-(2-amidoethyl)-α-D-glucofuranose **11** (1.04 g,

82%). The aqueous extract was acidified with aqueous HCl and extracted with chloroform. The organic extract was washed with water, dried over Na_2SO_4 and filtered. Evaporation *in vacuo* of the solvent gave 1,2:5,6-di-*O*-isopropylidene-3-*O*-(2-carboxyethyl)-α-D-glucofuranose **12** (0.21 g, 16%). **11**, ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.20, 1.30, 1.40, 1.50 (4s, 12H, 4 CH_3 of $C(CH_3)_2$), 2.40 (t, 2H, CH_2CONH_2), 3.58 (m, 1H), 3.85 (m, 3H), 4.07 (m, 2H), 4.25 (m, 1H), 4.50 (d, 1H), 5.80 (m, 2H, NH_2); ^{13}C NMR, (50.32 MHz, $CDCl_3$) δ 25.12, 26.08, 28.35, 36.27 (4 CH_3 of $C(CH_3)_2$), 36.31 (CH_2CONH_2), 66.05, 67.38, 72.35, 80.80, 81.81, 82.30, 105.22 (C-1/C-6 and OCH_2), 109.10, 111.79 (2 C of $(CH_3)_2$); **12**, ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.20-1.50 (4s, 12H, 4 CH_3 of $C(CH_3)_2$), 2.65 (t, 2H, CH_2CONH_2), 3.70-4.10 (m, 6H), 4.28 (m, 1H), 4.55 (d, 1H), 5.80 (d, 1H), 8.80 (COOH);^{13}C NMR (50.32 MHz, $CDCl_3$) δ 25.17, 26.15, 26.70, 26.74 (4 CH_3 of $C(CH_3)_2$), 34.66 (CH_2CO), 65.42, 67.05, 72.35, 81.91, 82.27, 82.35, 105.18 (C-1/C-6 and OCH_2), 108.98, 111.80 (2 C of $C(CH_3)_2$).

Methyl 3-*O*-[2-(carboxymethyl)ethyl)]-α and β-D-glucopyranoside (13 and 14). A solution of 1,2:5,6-di-*O*-isopropylidene-3-*O*-(2-cyanoethyl)-α-D-glucofuranose **4** (3.0 g, 9.6 mmol) in anhydrous methanol (5 mL) was hydrolyzed with acetyl chloride (1.2 eq / CN, 0.82 mL). When some cyanoethylated compound remained after 24 h of alcoholysis, or if the compound of higher Rf was not in the majority, solvents were evaporated *in vacuo* and the residue was again hydrolysed with the same quantity of reagents until complete alcoholysis was achieved. After the completion of the alcoholysis, the solvent was evaporated *in vacuo*, and the residue extracted with chloroform/water. The aqueous extracts were washed with chloroform, neutralized with diluted aqueous sodium hydroxyde and freeze-dried. Purification of the residue by chromatography on silica gel (9:1, chloroform-methanol) gave the title compounds **13** and **14** (1.2 g, 46%). To a solution of these compounds (1.2 g, 4.3 mmol) in pyridine (1.4 mL), acetyl chloride (1.5 eq / OH, 1.4 mL) was added and the reaction mixture stirred at room temperature for 12 h. Anhydrous methanol (1.5 mL) was added to the reaction mixture and solvents were evaporated *in vacuo*. The residue was extracted with chloroform/water. The organic extract was washed with water, dried over Na_2SO_4 and filtered. Acetylated anomers were separated by chromatography on silica gel (1.5:1, hexane-ethyl acetate) and deacetylated according to the Zemplen method[37] (MeONa / MeOH). **13**, $[\alpha]_D^{20}$ +111.8° (*c* 0.98, water); ^{1}H NMR (200 MHz, D_2O) δ 2.64 (t, 2H, CH_2COO), 3.35 (s, 3H, α OCH_3), 3.38 (m, 1H), 3.40-3.59 (m, 3H), 3.99 (t, 2H, OCH_2), 4.71 (d, 1H, H-1, $J_{1,2}$ = 3.1 Hz); ^{13}C NMR (50.32 MHz, D_2O) δ 34.99, (CH_2CO), 52.48 ($COOCH_3$), 55.20 (α OCH_3), 60.65, 68.48, 69.23, 71.05, 71.83, 82.51, 99.49 (C-1/C-6 and OCH_2), 175.17 (CO).

Anal. Calcd for $C_{11}H_{20}O_8$: C, 47.15; H, 7.15; O, 45.70. Found: C, 46.72; H, 7.15; O, 46.04.

14, $[\alpha]_D^{20}$ -18.9° (*c* 0.90, water); ^{1}H NMR (200 MHz, D_2O) δ 2.65 (t, 2H, CH_2COO), 3.50 (s, 3H, β OCH_3), 3.17-3.39 (m, 4H), 4.02 (t, 2H, OCH_2), 4.36 (d, 1H, H-1, $J_{1,2}$ = 7.4 Hz); ^{13}C NMR (50.32 MHz, D_2O) δ 35.03, (CH_2CO), 52.48 ($COOCH_3$), 57.38 (β OCH_3), 60.85, 68.36, 69.34, 72.83, 75.98, 84.89, 103.34 (C-1/C-6 and OCH_2), 175.12 (CO).

Anal. Calcd for $C_{11}H_{20}O_8$: C, 47.15; H, 7.15; O, 45.70. Found: C, 46.19; H, 7.14; O, 46.02.

Methyl 2,3-di-*O*-[2-(carboxymethyl)ethyl]-α and β-D-glucopyranoside (15 and 16). A solution of methyl 2,3-di-*O*-(2-cyanoethyl)-α-D-glucopyranoside **5** (5.5 g, 18.3 mmol) in anhydrous methanol (20 mL) was hydrolyzed with acetyl chloride (1.2 eq / CN, 2.9 mL) according to the process 1. After the completion of the alcoholysis, solvent was evaporated *in vacuo*, and the residue extracted with chloroform/water. The organic extracts were washed with water, dried over Na_2SO_4, filtered, and solvent was evaporated *in vacuo*. Purification of the residue by chromatography on silica gel (10:1, ethyl acetate-hexane) gave the title compounds **15** (1.7 g, 27% ; Rf 0.31, ethyl acetate) and **16** (0.9 g, 14% ; Rf 0.39, ethyl acetate). **15**, $[\alpha]_D^{22}$ +75.3° (*c* 1.00, chloroform); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.52-2.68 (m, 4H, 2 CH_2CO), 3.24 (q, 1H, H-2, $J_{2,1}$ = 3.5 Hz, $J_{2,3}$ = 9.2 Hz), 3.37 (s, 3H, α OCH_3), 3.45-3.69 (m, 3H), 3.63, 3.66 (2s, 6H, 2 $COOCH_3$), 3.69-4.03 (m, 6H), 4.76 (d, 1H, H-1, $J_{1,2}$ = 3.5 Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 34.64, 35.05 (CH_2CO), 51.57, 51.93 ($COOCH_3$), 55.07 (α OCH_3), 62.50, 66.45, 67.98, 70.72, 70.77, 80.23, 82.01, 97.76 (C-1/C-6 and OCH_2), 171.62, 173.59 (CO).

Anal. Calcd for $C_{15}H_{25}O_{10}$: C, 49.32; H, 6.84; O, 43.84. Found: C, 49.14; H, 7.14; O, 43.57.

16, $[\alpha]_D^{22}$ -11.3° (*c* 1.00, chloroform); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.34-2.64 (m, 4H, 2 CH_2CO), 2.93 (q, 1H, H-2, $J_{2,1}$ = 7.6 Hz, $J_{2,3}$ = 9.2 Hz), 3.09 (t, 1H, H-4, $J_{3,4}$ = 8.8 Hz), 3.17-3.26 (m, 1H), 3.41 (s, 3H, β OCH_3), 3.57-3.60 (2s, 6H, 2 $COOCH_3$), 3.63-3.81 (m, 4H), 3.82-4.06 (m, 2H) 4.11 (d, 1H, H-1, $J_{1,2}$ = 7.6 Hz); ^{13}C NMR, (50.32 MHz, $CDCl_3$) δ 34.58, 35.26 (CH_2CO), 51.49, 51.96 ($COOCH_3$), 57.12 (β OCH_3), 62.69, 67.71, 68.24, 70.73, 74.80, 81.73, 85.13, 104.46 (C-1/C-6 and OCH_2), 171.94, 173.62 (CO).

Methyl 2,3,4-tri-*O*-[2-(carboxymethyl)ethyl]-α and β-D-glucopyranoside (17 and 18). A solution of methyl 2,3,4-tri-*O*-(2-cyanoethyl)-α-D-glucopyranoside **6** (5.2 g, 14.7 mmol) in anhydrous methanol (20 mL) was hydrolyzed with acetyl chloride (1.2 eq / CN, 3.8 mL). The reaction mixture was treated as above. Purification of the residue by chromatography on silica gel (3:1, ethyl acetate-hexane) gave the title compounds **17** (3.3 g, 50%; Rf 0.22, 3:1, ethyl acetate-hexane) and **18** (0.7 g, 10%; Rf 0.28, 3:1 ethyl

acetate-hexane). **17**, $[\alpha]_D^{22}$ +64.3° (*c* 0.99, chloroform); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.51-3.21 (m, 6H, 3 CH_2CO), 3.25-3.30 (m, 1H), 3.33 (s, 3H, α OCH_3), 3.43-3.58 (m, 2H), 3.64 (m, 9H, 3 $COOCH_3$), 3.70-3.76 (m, 2H), 3.80-4.09 (m, 6H), 3.75 (d, 1H, H-1, $J_{1,2}$ = 3.5Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 35.04, 35.13, 35.41 (3 CH_2CO), 51.52, 51.63, 51.71 ($COOCH_3$), 55.08 (α OCH_3), 61.51, 66.74, 68.04, 68.34, 70.59, 76.43, 80.94, 81.51, 97.66 (C-1/C-6 and OCH_2), 171.98, 172.02, 172.41 (CO).

Anal. Calcd for $C_{19}H_{32}O_{12}$: C, 50.44; H, 7.08; O, 42.48. Found: C, 49.38; H, 7.09; O, 41.88.

18, $[\alpha]_D^{22}$ -13.3° (*c* 1.00, chloroform); ^{1}H NMR (200 MHZ, $CDCl_3$) δ 2.50-2.64 (m, 6H, 3 CH_2CO), 2.97-3.05 (m, 1H), 3.19-3.35 (m, 3H), 3.48 (s, 3H, β OCH_3), 3.66 (m, 9H, 3 $COOCH_3$), 3.71-4.09 (m, 8H), 4.12 (d, 1H, H-1, $J_{1,2}$ = 7.7 Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 35.13, 35.28, 35.37 (3 CH_2CO), 51.56, 51.70 ($COOCH_3$), 57.21 (β OCH_3), 61.73, 67.78, 67.96, 68.50, 74.85, 77.75, 82.43, 84.34, 104.36 (C-1/C-6 and OCH_2), 171.98, 172.01, 172.21 (CO).

Methyl 2,3,4,6-tetra-*O*-[2-(carboxymethyl)ethyl]-α and β-D-glucopyranoside (19 and 20). A solution of methyl 2,3,4,6-tetra-*O*-(2-cyanoethyl)-α-D-glucopyranoside **7** and β,β'-dicyanoethyl ether (8.74 g obtained by percyanoethylation of 5.0 g of methyl α-D-glucopyranoside) in anhydrous methanol (20 mL) was hydrolyzed with acetyl chloride (1.2 eq / CN, 7.3 mL). The reaction mixture was treated as above. Purification of the residue by chromatography on silica gel (1:1, ethyl acetate-hexane) gave the title compounds **19** (4.84 g, 35%; Rf 0.60, 4:1, ethyl acetate-hexane) and **20** (1.0 g, 7%; Rf 0.68, 4:1 ethyl acetate-hexane). **19**, $[\alpha]_D^{21}$ +62.2° (*c* 0.99, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.47-2.60 (m, 8H, 4 CH_2CO), 3.20 (t, 1H, H-4, $J_{3,4}$ = 9.5 Hz), 3.22 (q, 1H, H-2, $J_{2,1}$ = 3.6 Hz, $J_{2,3}$ = 9.6 Hz), 3.30 (s, 3H, α OCH_3), 3.48 (t, 1H, H-3, $J_{3,4}$ = 9.4 Hz), 3.54 (m, 1H, H-6b), 3.65 (m, 1H, H-6a), 3.62 (m, 12H, 4 $COOCH_3$), 3.73 (m, 3H), 3.81 (m, 3H), 3.86-4.00 (m, 3H), 4.71 (d, 1H, H-1, $J_{1,2}$ = 3.6 Hz); ^{13}C NMR (75.43 MHz, $CDCl_3$) δ 34.70, 34.97, 35.32 (CH_2CO), 51.42, 51.53 ($COOCH_3$), 54.98 (α OCH_3), 66.68, 67.79, 68.33, 69.11, 69.81, 77.27, 80.60, 81.39, 97.61 (C-1/C-6 and OCH_2), 171.80, 171.94 (CO).

Anal. Calcd for $C_{19}H_{30}O_{14}$: C, 51.30; H, 7.06; O, 41.64. Found: C, 51.38; H, 7.16; O, 41.81.

20, $[\alpha]_D^{21}$ -10.5° (*c* 1.12, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.47-2.57 (m, 8H, 4 CH_2CO), 3.43 (s, 3H, β OCH_3), 3.58 (m, 2H), 3.62 (m, 12H, 4 $COOCH_3$), 3.73 (m, 3H), 3.75-4.05 (m, 7H); ^{13}C NMR (75.43 MHz, $CDCl_3$) δ 34.75, 35.13, 35.19, 35.29 (CH_2CO), 51.47 ($COOCH_3$), 56.98 (β OCH_3), 66.76, 67.74, 68.46, 69.39, 74.48, 82.20, 84.30, 104.16 (C-1/C-6 and OCH_2), 171.80, 171.94 (CO).

Anal. Calcd for $C_{19}H_{30}O_{14}$: C, 51.30 H, 7.06; O, 41.64. Found: C, 51.40; H, 7.34; O, 41.71.

Methyl 1,3,4,5-tetra-*O*-[2-(carboxymethyl)ethyl]-β-D-fructopyranoside (21). A solution of methyl 1,3,4,5-tetra-*O*-(2-cyanoethyl)-β-D-fructopyranoside **8** (3.9 g, 9.6 mmol) in anhydrous methanol (20 mL) was hydrolyzed with acetyl chloride (1.1 eq / CN, 2.7 mL). The reaction mixture was treated as above. Purification of the residue by chromatography on silica gel (2:1, ethyl acetate-hexane) gave **21** (2.1 g, 41%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.53-2.62 (m, 8H, 4 CH_2CO), 3.21 (s, 3H, β OCH_3), 3.54 (m, 3H), 3.64-3.85 (m, 24H); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 34.72, 35.00, 35.15 (CH_2CO), 48.74 (β OCH_3), 51.34, 51.41, 51.45, 51.49 ($COOCH_3$), 61.61, 70.20, 75.55, 75.80, 78.92, 100.90 (C-1/C-6), 65.82, 65.87, 66.83, 68.30 (OCH_2), 171.86, 171.99 (CO).

Methyl 1,3,4,6-tetra-*O*-[2-(carboxymethyl)ethyl]-α and β-D-fructofuranoside (22 and 23). A solution of methyl 1,3,4,6-tetra-*O*-(2-cyanoethyl)-α and β-D-fructofuranoside **9** and **10** (3.9 g, 9.6 mmol) in anhydrous methanol (20 mL) was hydrolyzed with acetyl chloride (1.2 eq / CN, 3.3 mL). The reaction mixture was treated as above. Purification of the residue by chromatography on silica gel (1.5:1, ethyl acetate-hexane) gave **22** and **23** (2.4 g, 46%). **22** and **23**, ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.30-1.39 (m, 2x8H, 2x4 CH_2CN), 2.03 (2s, 2x3H), 2.30 (d, 2x4H), 2.29-2.74 (m, 2x23H); **22**, ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 35.53, 35.79 (CH_2COOMe), 49.24 (α OCH_3), 66.69, 71.96, 80.50, 85.67, 88.49, 108.07 (C-1/C-6), 66.37-67.80 (OCH_2); **23**, ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 35.53, 35.79 (CH_2COOMe), 50.21 (β OCH_3), 71.75, 72.67, 79.18, 84.38, 85.81, 104.44 (C-1/C-6), 66.37-67.80 (OCH_2).

Methyl 3-*O*-(2-carboxyethyl)-α and β-D-glucopyranoside (24 and 25). Methyl 3-*O*-[2-(carboxymethyl)ethyl]-α and β-D-glucopyranoside **13** and **14** were dissolved in aqueous KOH 0.2M (2 eq./ ester), and stirred at 40 °C for 1 h. The reaction mixture was neutralized with resin (Amberlite IR 120-H^+), filtered and freeze-dried. **24**, $[\alpha]_D^{21}$ +96.3° (*c* 0.94, water); ^{1}H NMR (200 MHz, D_2O) δ 2.57 (t, 2H, CH_2CO), 3.40 (s, 3H, αOCH_3), 3.46-3.74 (m, 4H), 3.77-3.81 (m, 2H), 3.99 (t, 2H, OCH_2); ^{13}C NMR (50.32 MHz, D_2O) δ 36.68 (CH_2CO), 55.20 (α OCH_3), 60.73, 69.27, 69.32, 71.06, 71.84, 82.59, 99.42 (C-1/C-6 and OCH_2), 178.95 (COOH); **25**, $[\alpha]_D^{21}$ -35.4° (*c* 0.99, water); ^{1}H NMR (200 MHz, D_2O) δ 2.53 (t, 2H, CH_2CO), 3.53 (s, 3H, βOCH_3), 3.27-3.43 (m, 4H), 3.64-3.72 (m, 1H), 3.86-3.91 (m, 1H), 3.99 (t, 2H, OCH_2), 4.36 (d, 1H, H-1, $J_{1,2}$ = 7.5 Hz); ^{13}C NMR, (50.32 MHz, D_2O) δ 36.68 (CH_2CO), 57.04 (β OCH_3), 60.61, 69.07, 72.51, 75.64, 84.77, 102.96 (C-1/C-6 and OCH_2), 179.00 (COOH).

Methyl 2,3-di-*O*-(2-carboxyethyl)-α and β-D-glucopyranoside (26 and 27). Methyl 2,3-di-*O*-[2-(carboxymethyl)ethyl]-α and β-D-glucopyranoside **15** and **16** were saponified as above. **26**, $[\alpha]_D^{21}$ +71.6° (*c* 1.02, water); ^{1}H NMR (200 MHz, D_2O) δ 2.43-2.49 (t, 4H, CH_2CO), 3.34 (s, 3H, αOCH_3), 3.30-3.46 (m, 3H), 3.51-4.05 (m, 7H), 4.89 (d, 1H, H-1, $J_{1,2}$ = 3.2 Hz); ^{13}C NMR (50.32 MHz, D_2O) δ 37.45 (CH_2CO), 55.20

(α OCH_3), 60.82, 68.11, 69.38, 69.98, 71.69, 79.50, 81.82, 97.73 (C-1/C-6 and OCH_2), 179.07, 179.65 (**COOH**); **27**, $[\alpha]_D^{21}$ =-15.4° (*c* 1.02, water); ^{1}H NMR (200 MHz, D_2O) δ 2.47-2.53 (t, 4H, CH_2CO), 3.49 (s, 3H, βOCH_3), 3.01-3.07 (m, 1H), 3.09-3.36 (m, 3H), 3.58-3.66 (m, 1H), 3.79-4.02 (m, 5H), 4.36 (d, 1H, H-1, J_{1-2}= 7.9Hz); ^{13}C NMR (50.32 MHz, D_2O) δ 36.27, 36.61 (CH_2CO), 57.40 (βOCH_3), 60.65, 68.94, 69.32, 69.55, 75.48, 81.14, 84.11, 103.47 (C-1/C-6 and OCH_2), 177.68, 178.52 (**COOH**).

Methyl 2,3,4-tri-*O*-(2-carboxyethyl)-α and β-D-glucopyranoside (28 and 29). Methyl 2,3,4-tri-*O*-[2-(carboxymethyl)ethyl]-α and β-D-glucopyranoside **17** and **18** were saponified as above. **28**, $[\alpha]_D^{21}$ +67.6° (*c* 1.02, water); ^{1}H NMR (200 MHz, D_2O) δ 2.42-2.54 (m, 6H, CH_2CO), 3.31 (s, 3H, αOCH_3), 3.17-3.36 (m, 2H), 3.45-3.54 (m, 2H), 3.64-3.98 (m, 8H), 4.86 (d, 1H, H-1, $J_{1,2}$ = 3.4 Hz); ^{13}C NMR (50.32 MHz, D_2O) δ 36.98, 37.16 (CH_2CO), 55.20 (α OCH_3), 60.51, 68.09, 69.95, 70.01, 71.01, 77.71, 79.99, 81.53, 96.93 (C-1/C-6 and OCH_2), 178.31, 178.70, 178.77 (**COOH**); **29**, $[\alpha]_D^{21}$ -12.8° (*c* 1.02, water); ^{1}H NMR (200 MHz, D_2O) δ 2.40-2.54 (m, 6H, CH_2CO), 3.51 (s, 3H, βOCH_3), 3.02-3.41 (m, 4H), 3.62-3.73 (m, 1H), 3.76-4.04 (m, 7H), 4.28 (d, 1H, H-1, $J_{1,2}$ = 7.9 Hz); ^{13}C NMR (50.32 MHz, D_2O) δ 37.05, 37.15, 37.32 (CH_2CO), 57.40 (β OCH_3), 60.29, 69.43, 69.77, 70.02, 74.84, 77.54, 81.53, 83.70, 103.35 (C-1/ C-6 and OCH_2), 178.45, 178.59, 178.99 (**COOH**).

Methyl 2,3,4,6-tetra-*O*-(2-carboxyethyl)-α and β-D-glucopyranoside (30 and 31). Methyl 2,3,4,6-tetra-*O*-[2-(carboxymethyl)ethyl]-α and β-D-glucopyranoside **19** and **20** were saponified as above. **30**, $[\alpha]_D^{22}$ +61.47° (*c* 0.98, water); ^{1}H NMR (200 MHz, D_2O) δ 2.42-2.50 (m, 8H, CH_2CO), 3.31 (s, 3H, αOCH_3), 3.20-3.36 (m, 2H), 3.44-3.53 (t, 1H), 3.60-3.97 (m, 11H), 4.85 (d, 1H, H-1, $J_{1,2}$ = 3.4 Hz); ^{13}C NMR (50.32 MHz, D_2O) δ 36.95, 37.20, 37.38 (CH_2CO), 55.20 (α OCH_3), 67.98, 68.21, 69.60, 69.90, 70.08, 77.51, 79.69, 81.33, 97.51 (C-1/C-6 and OCH_2), 178.61, 178.68, 179.00, 179.32 (**COOH**); **31**, $[\alpha]_D^{20}$ -3.01° (*c* 0.90, water); ^{1}H NMR (200 MHz, D_2O) δ 2.40-2.50 (m, 8H, CH_2CO), 3.42 (s, 3H, βOCH_3), 2.96-3.04 (m, 3H), 3.12-3.33 (m, 2H), 3.60-3.97 (m, 11H), 4.21 (d, 1H, H-1, $J_{1,2}$ = 7.9 Hz); ^{13}C NMR (50.32 MHz, D_2O) δ 36.45, 36.84, 36.77 (CH_2CO), 57.40 (β OCH_3), 67.58, 68.71, 69.15, 69.37, 73.46, 77.45, 81.31, 83.48, 103.31 (C-1/C-6 and OCH_2), 178.01, 178.13, 178.74 (**COOH**).

Methyl 1,3,4,5-tetra-*O*-(2-carboxyethyl)-β-D-fructopyranoside (32). Methyl 1,3,4,5-tetra-*O*-[2-(carboxymethyl)ethyl]-β-D-fructopyranoside **21** was saponified as above. ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.48-2.58 (m, 8H, 4 CH_2CO), 3.16 (s, 3H, β OCH_3), 3.49-3.85 (m, 15H); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 35.84, 36.10 (CH_2CO), 49.01 (β OCH_3), 61.28, 69.65, 75.27, 76.04, 78.51, 100.90 (C-1/C-6), 66.37, 66.55, 67.64, 69.53 (OCH_2), 177.51, 177.70 177.83 (**CO**).

Methyl 1,3,4,6-tetra-*O*-(2-carboxyethyl)-α and β-D-fructofuranoside (33 and 34). Methyl 1,3,4,6-tetra-*O*-[2-(carboxymethyl)ethyl]-α and β-D-fructofuranoside **22** and **23** were saponified as above. **33** and **34**, ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.62-2.68 (m, 2x8H, 2x4 CH_2CN), 3.24, 3.27 (2s, 2x3H, α et β OCH_3), 3.52-3.96 (m, 2x15H); **33**,^{13}C NMR (200 MHz, $CDCl_3$) δ 34.92, 35.22 (CH_2COOH), 48.5 (α OCH_3), 65.8, 70.9, 81.2, 84.6, 86.3, 108.4 (C-1/C-6), 176.43, 176.50, 176.60 (CO); **34**, ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 34.92, 35.22 (CH_2COOH), 49.5 (β OCH_3), 69.6, 72.1, 78.9, 883.8, 85.1, 104.2 (C-1/C-6), 176.43, 176.50, 176.60 (CO).

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