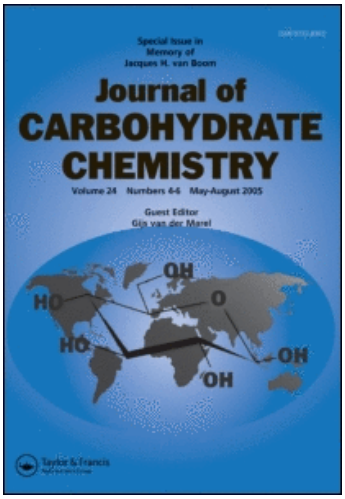

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CHAIN ELONGATION OF ALDONOLACTONES*

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ABSTRACT

As an alternative to the classical *Reformatsky*-type branching reaction of aldonolactones, ethyl trimethylsilylacetate, methyl 2-trimethylsilyl-propionate, trimethylsilylacetonitrile or alkyl 2-(trimethylsilylmethyl)-acrylates in the presence of catalytic amounts of tetra-*n*-butyl-ammonium fluoride can be used. The corresponding chain elongated monosaccharides are obtained in high yields.

INTRODUCTION

The synthesis of chain-elongated monosaccharides has been of synthetic interest for many years. Several approaches to *C*-glycosyl compounds[1] have been proposed and investigated, among them the reaction

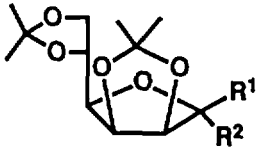
* Dedicated to *Professor Dr. R. Neidlein* on the occasion of his 60th birthday.

of carbohydrate esters with allylsilanes under Lewis acid catalysis,[2] the generation of carbanions[3] or radicals at C-1,[4] and the use of 1-deoxy-1-nitro-sugars[5] or pyridylthioglycosides by related strategies.[6] Among all of these approaches the use of aldonolactones as starting materials seems very promising since these compounds are readily available. In spite of this advantage for synthetic strategy, only a few reports about the use of aldono-lactones for the synthesis of *C*-glycosyl compounds have been published so far.[7-9] A direct synthesis of *C*-glycosyl compounds by the reaction of aldonolactones with *Grignard* or organolithium reagents has been proposed.[8] In addition, the *Reformatsky*-type branching[9] has recently been re-investigated[10] and significantly improved by the use of a highly activated zinc-silver couple dispersed on the surface of graphite.[11] As an alternative to this approach which requires strictly anhydrous conditions similar transformations of aldonolactones can be achieved by the use of organosilicon based reagents.

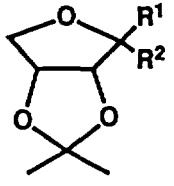
RESULTS AND DISCUSSION

Since the tetra-*n*-butylammonium ester enolates, reasonably assumed to be formed in the reaction of ethyl trimethylsilylacetate (**5**) with fluoride anion were shown to react with uloses to yield the corresponding β-hydroxy esters[12] the reaction of lactones **1-4** with this reagent as an easy-to-prepare alternative to the corresponding *Reformatsky*-reagent derived from **6** was investigated.

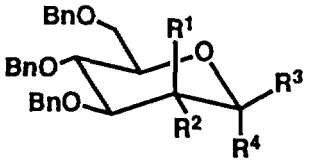
Reaction of lactone **1** in anhydrous tetrahydrofuran with **5** in the presence of catalytic amounts (ca 5 mol %) of anhydrous tetra-*n*-butylammonium fluoride (TBAF) afforded a mixture of silylated **11** and **12**. Subsequent desilylation of either this mixture (performed as a one-pot sequence) or of isolated **11** or **12** by aqueous TBAF yielded the octulosonate



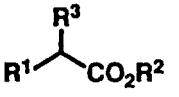
1 R^1, R^2= O
7 R^1= CH_2CO_2Et, R^2= OH
11 R^1= CH_2CO_2Et, R^2= $OSi(CH_3)_3$
12 R^1= $OSi(CH_3)_3$, R^2= CH_2CO_2Et
14 R^1= OH, R^2= $CH(CH_3)CO_2Me$
16 R^1= $CH_2C(=CH_2)CO_2C(CH_3)_3$, R^2 = OH
18 R^1= CH_2CN, R^2= $OSi(CH_3)_3$
19 R^1=CH_2CN, R^2= OH



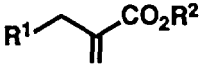
2 R^1, R^2= O
8 R^1= OH, R^2= CH_2CO_2Et
15 R^1= OH, R^2= $CH(CH_3)CO_2Me$
17 R^1= OH, R^2= $CH_2C(=CH_2)CO_2Et$
20 R^1= $OSi(CH_3)_3$, R^2 = CH_2CN
21 R^1= OH, R^2 = CH_2CN



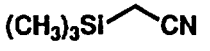
3 R^1= H, R^2= OBn, R^3, R^4= O
4 R^1= OBn, R^2= H, R^3, R^4= O
9 R^1= H, R^2= OBn, R^3= CH_2CO_2Et, R^4= OH
10 R^1= OBn, R^2= H, R^3= CH_2CO_2Et, R^4= OH



5 R^1= $Si(CH_3)_3$, R^2= Et, R^3= H
6 R^1= Br, R^2 = Et, R^3 = H
13 R^1= $Si(CH_3)_3$, R^2= Me, R^3 = Me



23 R^1= $Si(CH_3)_3$, R^2= Et
24 R^1= $Si(CH_3)_3$, R^2= $C(CH_3)_3$



25

7 in high yield. Similarly, the corresponding hex- and octulosonates **8-10** were obtained from lactones **2-4.**

Surprisingly, the analogous sequence of reactions of methyl 2-trimethylsilylpropionate[13] (**13**) with lactones **1** or **2** under the same conditions yielded for each of the lactones only one single stereoisomer **14** and **15**, respectively. The reason for this stereodifferentiation remains unclear, as the absolute configuration obtained at C-2 for these compounds could not unambiguously assigned either from NMR spectroscopic experiments or by comparison of the specific rotation of these compounds with simple analogs.

In order to exploit the applicability of this novel chain elongation reaction of lactones, the reaction of trimethylsilylacetonitrile (**25**) under TBAF-catalysis was investigated. As recently shown,[14] reaction of **25** with aldehydes or ketones in the presence of tris(dimethylamino)sulphonium-difluoro-trimethylsiliconate (TASF) leads to the formation of trimethylsilyloxy-nitriles or after elimination of trimethylsilanol to the corresponding alkene-nitriles.[14]

As compared to the reaction of **5** or **13** with lactones **1** or **2** the rate of formation of **18** or **20** was significantly slower albeit after prolonged reaction time similar high yields could be obtained. Interestingly, whereas reaction of **1** with **5** afforded a mixture of diastereomers **11** and **12** only one diastereoisomer could be isolated from the reaction of **1** or **2** with **25** under similar conditions. As for **11** and **12**, rapid desilylation can be achieved by treatment of the trimethylsilyloxynitriles with aqueous TBAF in methanol/tetrahydrofuran as exemplified for **18** to yield **19** in 87% yield.

In addition, silylated compounds **11, 12,** or **18** may be envisaged as excellent starting materials for performing a second C-branching at the anomeric centre by applying *Mukaiyama's* procedure thus leading to *C*-glycosides of ketoses.[15]

Table: ^{1}H-NMR Spectral Data

H (δ)	7	11	12	14[a]	18	19
H-2	2.72	3.03	2.42	2.95	2.79	2.86
H-2´	2.82	2.76	2.42	---	2.92	2.86
H-4	4.51	4.68	4.70	4.47	4.54	4.57
H-5	4.84	4.78	4.64	4.83	4.82	4.88
H-6	4.09	3.95	3.55	4.09	4.02	4.27
H-7	4.35	4.35	4.26	4.35	4.35	4.39
H-8	3.99	4.04	3.89	4.03	3.97	4.10
H-8´	4.06	3.98	3.95	3.96	3.97	4.02
Me	1.29	1.31	1.18	1.32	1.32	1.34
Me	1.37	1.35	1.19	1.37	1.36	1.38
Me	1.42	1.42	1.25	1.41	1.43	1.46
Me	1.46	1.43	1.37	1.46	1.48	1.50
Me of ester	1.29	1.25	1.10	3.72		
CH_2 of ester	4.20	4.13	4.00			
$SiMe_3$		0.13	0.10		0.23	
OH	4.89			4.56		2.94

J (Hz)	7	11	12	14[a]	18	19
2,2´	16.6	16.1	0.0	---	16.6	0.0
4,5	5.8	5.9	6.0	5.9	5.9	5.8
5,6	3.7	3.9	4.1	3.8	3.8	3.7
6,7	8.0	7.4	7.7	7.7	6.9	7.6
7,8	6.1	6.2	4.6	6.2	4.7	6.2
7,8´	4.5	4.6	6.2	4.7	6.3	4.2
8,8´	8.7	8.8	8.6	8.7	8.8	8.9
ester	7.2	7.2	7.1			

a) Me-(C-2): δ= 1.30 ppm, J(H-(C2)-Me-(C-2)= 7.2 Hz

Access to higher monosaccharides, *e.g.* synthetic precursors to analogs of sialic acids, can be achieved by reaction of **1** with a twofold molar excess of **24** for 24h to yield 93% of **16**.[16] Similarly, upon reaction with **23**, **2** afforded chain elongated **17** in fairly good yield. All of these reactions show strong decrease in yields as well as increase in reaction time upon dilution of the reaction mixture.[17]

Attempts to make C-1 alkylidene branched carbohydrates by reaction of the lactones with ethyl lithiotrimethylsilylacetate[18] failed. Reaction of **1-4** with this reagent even at -78 °C caused formation of complex reaction mixtures containing only minor amounts of the desired products.[19] In addition, 30-40% of the β-hydroxy esters **7-10** could be isolated, the formation of which can either be explained by a deprotonation/reprotonation sequence *via* a carbohydrate derived enolate or by assuming a Brook-rearrangement.

EXPERIMENTAL

General procedures. Melting points are uncorrected (*Tottoli*), optical rotations were obtained using a Perkin-Elmer 241 polarimeter, NMR spectra for solutions in $CDCl_3$ (internal Me_4Si) were recorded using Bruker WM-250, and AM-400 instruments, IR spectra (3 % solution in $CHCl_3$) on a Perkin-Elmer 298. TLC was performed on silica gel (Merck, 5554, detection by spraying with a 5 % solution of vanillin in concd sulphuric acid followed by heating at 150 °C). Anhydrous TBAF was obtained by drying commercially available trihydrate at 80 °C for 3 days *in vacuo*.

Procedure A. To a solution of the lactone (2 mmol) and **5** (0.42 g, 2.6 mmol) in anhydrous tetrahydrofuran (5-10 mL) catalytic amounts of anhydrous TBAF (ca 5 mol %) were added at 0 °C under argon. The reaction mixture was allowed to warm up to room temp. and stirred further for 60 min. Methanol/water (90:10 (*v/v*), 1 mL) and a catalytic amount of TBAF trihydrate

were added, the mixture was allowed to stand at room temp for 20-60 min, then diluted with ethyl acetate (25 mL), washed with ice water and brine (2 mL each), and dried over sodium sulphate. The solvents were evaporated and the residue subjected to flash chromatography (hexane/ethyl acetate 5:1 (*v/v*)).

Procedure B. To a solution of the lactone (2 mmol) and **13**, **23-25** (4 mmol) in anhydrous tetrahydrofuran (5 mL) 5 mol % of anhydrous TBAF were added at room temp. After stirring for 24 h desilylation and work-up was performed analogously to procedure A.

Ethyl 2-Deoxy-4,5:7,8-di-O-isopropylidene-α-D-manno-3,6-furanoso-3-octulosonate (**7**). By procedure A 0.64 g (92 %) of **7** were obtained from **1** and **5**.

By desilylation of **11** or **12** – To a solution of **11** (0.22 g, 0.53 mmol) in tetrahydrofuran/methanol (2 mL, 9:1 (*v/v*)) TBAF trihydrate (0.17 g, 0.55 mmol) was added. After stirring for 20 min the reaction mixture was diluted with ethyl acetate (50 mL), washed twice with ice water and brine (2 mL each), and dried over sodium sulphate. The solvents were evaporated and the residue subjected to chromatography (hexane/ethyl acetate 5:1 (*v/v*)) to yield 165 mg (91 %) of **7**.

Analogous desilylation of **12** afforded 160 mg (89 %) of **7** as an oil: $[\alpha]_D^{25}$ = +5.7° (*c* 2.5, chloroform); Lit.[10] +5.6° (*c* 2.7, chloroform); MS (c.i., isobutane) 329 (M-H_2O+1).

Anal. Calcd for $C_{16}H_{26}O_8$: C, 55.48; H, 7.57. Found: C, 55.51; H, 7.66.

Ethyl 2-Deoxy-4,5:7,8-di-O-isopropylidene-3-O-trimethylsilyl-α-D-manno-3,6-furanoso-3-octulosonate (**11**) and **Ethyl 2-Deoxy-4,5:7,8-di-O-isopropylidene-3-O-trimethylsilyl-β-D-manno-3,6-furanoso-3-octulosonate** (**12**). To a solution of **1** (0.52 g, 2 mmol) in anhydrous tetrahydrofuran (5 mL) **5** (0.42 g, 2.6 mmol) catalytic amounts of

dry TBAF were added at 0 °C under argon. The yellowish solution was allowed to warm to room temp. After completion (ca 40 min as checked by TLC) ethyl acetate (25 mL) was added and the reaction mixture was washed with ice water and brine (2 mL each), dried over sodium sulphate and the solvents were evaporated *in vacuo* to yield a yellow oil which was subjected to flash chromatography (hexane/ethyl acetate gradient 20:1 to 10:1, (*v/v*)) to yield 480 mg (57.3 %) of **11** as an oil: $[\alpha]_D^{25}$ = +23.4° (*c* 2.2, chloroform); IR 1740 cm^{-1} (ester); ^{13}C NMR ($CDCl_3$) δ 1.38 ($(CH_3)_3Si$), 14.07 (CH_3, ester), 24.39, 25.27, 25.78, 26.83 (CH_3, isopropylidene), 40.15, 60.23, 66.42 (CH_2), 73.19, 78.94, 79.54, 86.44 (CH), 106.16, 108.94, 112.18 ($C_{quat.}$), 168.92 (COO); MS (c.i., isobutane) 419 (M+1).

Anal. Calcd for $C_{19}H_{34}O_8Si$: C, 54.52; H, 8.19; Si, 6.71. Found: C, 54.38; H, 8.28; Si, 6.72.

Further elution gave 280 mg (33.4%) of **12** as an oil: $[\alpha]_D^{25}$ = -7.5° (*c* 1.8, chloroform); IR 1730 cm^{-1} (ester). ^{13}C NMR ($CDCl_3$) δ 1.78 ($(CH_3)_3Si$), 14.12 (CH_3, ester), 24.28, 25.20, 25.55, 26.95 (CH_3, isopropylidene), 44.12, 60.72, 66.86 (CH_2), 73.17, 78.32, 79.39, 82.11 (CH), 104.77, 109.31, 112.87 ($C_{quat.}$), 169.17 (COO); MS (c.i., ammonia) 436 ($M+1+NH_3$).

Anal. Calcd for $C_{19}H_{34}O_8Si$: C, 54.52; H, 8.19; Si, 6.71. Found: C, 54.30; H, 8.34; Si, 6.74.

Ethyl 2-Deoxy-4,5-O-isopropylidene-β-D-erythro-3,6-furanoso-3-hexulosonate (8). By procedure B 0.45 g (92 %) of **8** were obtained from **2** and **5** as an oil: $[\alpha]_D^{25}$ = -56.1° (*c* 3.0, chloroform); Lit.[10] -55.9° (*c* 4.1, chloroform); MS (c.i., isobutane) 229 ($M-H_2O+1$).

Anal. Calcd for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found: C, 53.45; H, 7.51.

Ethyl 2-Deoxy-4,5,6,8-tetra-O-benzyl-α-D-gluco-3,7-pyranoso-3-octulosonate (9). Compound **9**, 1.2 g (95%), was obtained

from **3** and **5** by procedure A as an oil: $[\alpha]_D^{25}$ = -5.4° (*c* 1.0, chloroform); Lit.[10] -5.3° (*c* 1.3, chloroform); MS (c.i., isobutane) 609 ($M-H_2O+1$).

Anal. Calcd for $C_{38}H_{42}O_8$: C, 72.82; H, 6.75. Found: C, 72.98; H, 6.84.

Ethyl 2-Deoxy-4,5,6,8-tetra-O-benzyl-α-D-manno-3,7-pyranoso-3-octulosonate (10). Compound **10**, 1.1 g (87%), was obtained from **4** and **5** by procedure A as an oil: $[\alpha]_D^{25}$ = +8.9° (*c* 2.4, chloroform); Lit.[10] +8.7° (*c* 4.1, chloroform); MS (c.i., isobutane) 609 ($M-H_2O+1$).

Anal. Calcd for $C_{38}H_{42}O_8$: C, 72.82; H, 6.75. Found: C, 73.00; H, 6.84.

Methyl 2-Deoxy-4,5;7,8-di-O-isopropylidene-2-C-methyl-α-D-manno-3,6-furanoso-3-octulosonate (14). Compound **14**, 0.72 g (91 %), was obtained as an oil from **1** and **13** according to procedure B: $[\alpha]_D^{25}$ = -4.8° (*c* 1.1, chloroform); IR 3480 (hydroxy), 1710 (ester) cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 13.50 (CH_3), 24.20, 25.23, 25.63, 26.56 (CH_3, isopropylidene), 41.05, 51.72 (CH, CH_3), 66.56 (C-8), 72.94, 79.02, 79.04, 83.96 (CH), 106.10, 108.03, 112.44 (C-3, $C_{quat.}$), 176.52 (ester); MS (c.i., isobutane) 329 ($M-H_2O+1$).

Anal. Calcd for $C_{16}H_{26}O_6$: C, 55.48; H, 7.57. Found: C, 55.60; H, 7.50.

Methyl 2-Deoxy-4,5-O-isopropylidene-2-C-methyl-β-D-erythro-3,6-furanoso-3-hexulosonate (15). Compound **15**, 0.44 g (89%), was obtained as an oil from **2** and **13** according to procedure B: $[\alpha]_D^{25}$ = -29.0° (*c* 1.2, chloroform); IR 3480 (hydroxyl), 1710 (ester) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (d, 3H, J = 7.2 Hz, CH_3), 1.34 (s, 3H, CH_3 of isopropylidene), 1.47 (s, 3H, CH_3 of isopropylidene), 3.01 (q, 1H, J = 7.2 Hz, H-2), 3.74 (s, 3H, OCH_3), 3.91 (d, 1H, $J_{6,6'}$=10.2 Hz, H-6′), 4.03 (dd, 1H, $J_{5,6}$= 3.7, $J_{6,6'}$=10.2 Hz, H-6), 4.42 (d, 1H, $J_{4,5}$=5.8 Hz, H-4), 4.51 (s, 1H, OH, exchangeable with D_2O), 4.86 (dd, $J_{4,5}$=5.8, $J_{5,6}$= 3.7 Hz, H-5); ^{13}C NMR

($CDCl_3$) δ 13.65 (CH_3), 24.74, 26.12 (CH_3, isopropylidene), 42.02, 51.89 (CH, CH_3), 71.25 (C-6), 80.74, 83.62 (CH), 107.08, 112.30 (C-3, $C_{quat.}$), 176.96 (ester); MS (c.i., ammonia) 229 (M-H_2O+1).

Anal. Calcd for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found: C, 53.82; H, 7.28.

2-Deoxy-4,5;7,8-di-O-isopropylidene-3-O-trimethylsilyl-3,6-furanoso-α-D-manno-3-octulononitrile (18). To a solution of **1** (0.52 g, 2 mmol) in anhydrous tetrahydrofuran (5 mL) **25** (0.45 g, 4 mmol) and catalytic amounts of dry TBAF were added at 0 °C under argon. After stirring for 24 h at room temp, ethyl acetate (25 mL) was added and the reaction mixture was washed with ice water and brine (2 mL each), dried over sodium sulphate and the solvents were evaporated *in vacuo* to yield a yellow oil which was subjected to flash chromatography (hexane/ethyl acetate 10:1 (*v/v*)) to give 0.67 g (90 %) of **18**, mp: 52-54°; $[\alpha]_D^{25}$ = +14.7° (*c* 1.3, chloroform); IR 2250 (nitrile) cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 1.35 ($(CH_3)_3Si$), 24.16, 25.18, 25.56, 26.78 (CH_3, isopropylidene), 25.39 ($\underline{C}H_2$-CN), 66.18 (C-8), 72.92, 79.71, 80.06, 86.41 (CH), 105.09, 109.06, 113.13, 116.16 (C-1, C-3, $C_{quat.}$); MS (c.i., ammonia) 372 (M+1).[20]

Anal. Calcd for $C_{17}H_{29}NO_6Si$: C, 54.96; H, 7.87; N, 3.77; Si, 7.56. Found: C, 54.79; H, 7.95; N, 3.72; Si, 7.66.

2-Deoxy-4,5;7,8-di-O-isopropylidene-3,6-furanoso-α-D-manno-3-octulononitrile (19). Compound **19**, 0.51 g (86 %), was obtained by procedure B from **1** and **25**, or by desilylation of **18**. To a solution of **18** (0.186 g, 0.5 mmol) in tetrahydrofuran/methanol (2 ml, 9:1 (*v/v*)) TBAF trihydrate (0.17 g, 0.55 mmol) was added. After stirring for 30 min at room temp the mixture was diluted with ethyl acetate (25 mL), washed with ice water and brine (2 mL each), and dried over sodium sulphate. The solvents were evaporated and the residue subjected to chromatography (hexane/ ethyl

acetate 5:1 (*v/v*)) to yield 0.13 g (87%) of **19**: mp 104-107 °C; $[\alpha]_D^{25}$ = +27.5° (*c* 0.5, chloroform); IR 3500 (hydroxy), 2440 (nitrile), 1730 (ester) cm^{-1}; ^{13}C NMR ($CDCl_3$): 24.23, 25.05, 25.63, 26.79 (CH_3, isopropylidene), 25.83 ($\underline{C}H_2$-CN), 66.46 (C-8), 72.80, 79.89, 80.08, 84.78 (CH), 103.08, 109.39 (C-1, C-3), 113.42, 116.11 ($C_{quat.}$); MS (c.i., ammonia) 300 (M+1).[20]

Anal. Calcd for $C_{14}H_{21}NO_6$: C, 56.18; H, 7.07; N, 4.68. Found: C, 56.01; H, 7.20; N, 4.76.

2-Deoxy-4,5-O-isopropylidene-3-O-trimethylsilyl-β-D-erythro-3-hexulononitrile (20). Compound **20**, 0.48 g (88%), was obtained as an oil from **2** and **25** according to the procedure given for the synthesis of **18**: $[\alpha]_D^{25}$ = -46.13° (*c* 0.3, chloroform); IR 2260 (nitrile) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.24 (s, 9H, $Si(CH_3)_3$), 1.58 (s, 3H, CH_3 of isopropylidene), 1.58 (s, 3H, CH_3 of isopropylidene), 2.71 (s, 2H, H-2, H-2′), 3.9-4.1 (m, 2H, H-6, H-6′), 4.55 (d, 1H, $J_{4,5}$= 6.4 Hz, H-4), 4.86 (ddd, 1H, $J_{4,5}$=6.4, $J_{5,6}$= 4.8, $J_{5,6'}$= 2.4 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 1.62 ($(CH_3)_3Si$), 24.95, 25.96 (CH_3, isopropylidene), 28.97 ($\underline{C}H_2$-CN), 70.88 (C-6), 79.69, 82.93 (C-4, C-5), 103.35, 114.53, 116.07 (C-1, C-3, $C_{quat.}$); MS (c.i., ammonia) 272 (M+1).[20]

Anal. Calcd for $C_{12}H_{21}NO_4Si$: C, 53.115; H, 7.80; N, 5.16; Si, 10.35. Found: C, 52.85; H, 7.72; N, 5.19; Si, 10.50.

Tert-butyl 2,3-Dideoxy-2-C-methylene-5,6:8,9-di-O-isopropylidene-α-D-manno-4,7-furanoso-4-nonulosonate (16). Compound **16**, 0.74g (93%), was obtained by procedure B from **1** and **24**: [21] mp 62-64 °C, $[\alpha]_D^{25}$ = +7.4° (*c* 1.5, chloroform); Lit.[10] mp 62-64 °C, $[\alpha]_D^{25}$ +7.5 °C (*c* 1.6, chloroform); MS (c.i., isobutane) 383 ($M-H_2O+1$).

Anal. Calcd for $C_{20}H_{32}O_8$: C, 59.99 H, 8.05. Found: C, 60.15; H, 7.97.

Ethyl 2,3-Dideoxy-5,6-O-isopropylidene-2-C-methylene-β-D-erythro-4,7-furanoso-4-heptulosonate (17). Compound 17, 0.47 g (87%), was obtained as an oil from 2 and 23[21] by procedure B: $[\alpha]_D^{25} = -41.4^o$ (*c* 0.3, chloroform); Lit.[10] $[\alpha]_D^{25} = -41.8^o$ (*c* 0.6, chloroform) ; MS (c.i., isobutane) 255 (M-H_2O+1).

Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.39; H, 7.58.

REFERENCES AND FOOTNOTES

1. For reviews on *C*-glycosides: G. Doyle-Daves, Jr. and C. C. Cheng, *Progr. Med. Chem.*, **13**, 304 (1976); S. Hanessian and A. G. Pernet, *Adv. Carbohydr. Chem. Biochem.*, **33**, 111 (1976).

2. S. Danishefsky and J. F. Kerwin Jr, *J. Org. Chem.*, **47**, 3803 (1982); A. P.Kozikowski and K. L. Sorgi, *Tetrahedron Lett.*, **23**, 2281 (1982); T. L. Cupps, D. S. Wise, and L. B. Townsend, *J. Org. Chem.*, **47**, 5115 1982).

3. P. DeShong, G. A. Slough, V. Elango, and G. L. Trainor, *J. Am. Chem. Soc.*, **107**, 7788 (1985).

4. G. Descotes, *J. Carbohydr. Chem.*, **7**, 1 (1988); J. Dupuis, B. Giese, J. Hartung, M. Leising, H.-G. Korth, and R. Sustmann, *J. Am. Chem. Soc.*, **107**, 4332 (1985).

5. F. Baumberger and A. Vasella, *Helv. Chim. Acta*, **69**, 1205 (1986); R. Julina, I. Müller, A. Vasella, and R. Wyler, *Carbohydr. Res.*, **164**, 415 (1987); for other "Umpolung" reactions at the anomeric centre by means of strong electron-withdrawing groups such as sulfonyl or phosphonium: *e.g.* J.-M. Beau and P. Sinaÿ, *Tetrahedron Lett.*, **26**, 6185, 6189 and 6193 (1985); J. B. Ousset, C. Mioskowski, Y. L. Yang, and J. R. Falck, *Tetrahedron Lett.*, **25**, 5903 (1984).

6. A. O. Stewart and R. M. Williams, *J. Am. Chem. Soc.*, **107**, 4289 (1985); R. R. Schmidt and M. Hoffmann, *Tetrahedron Lett.*, **23**, 409 (1982).

7. A. Bandzouzi and Y. Chapleur, *Carbohydr. Res.*, **171**, 13 (1987); H. Ogura and H. Takahashi, *J. Org. Chem.*, **39**, 1374 (1974).

8. G. A. Kraus and M. T. Molina, *J. Org. Chem.*, **53**, 752 (1988); R. R. Schmidt and W. Frick, *Tetrahedron*, **44**, 7163 (1988); S. B. Rosenblum and H. A. Bates, *194th ACS National Meeting*, New Orleans, 1987, abstract of papers ORGN 188.

9 Yu. A. Zhdanov, Yu. E. Alexeev, and Ch. A. Khourdanov, *Carbohydr. Res.*, **14**, 422 (1970); Yu. A. Zhdanov and Yu. E. Alexeev, *Zh. Obshch. Khim.*, **42**, 2776-80 (Engl. translation 2767-2770) (1972); V. K. Srivastava and L. M. Lerner, *J. Org. Chem.*, **44**, 3368 (1979).

10. R. Csuk and B. I. Glänzer, preceeding paper this issue.

11. R. Csuk, B. I. Glänzer, and A. Fürstner, *Adv. Organomet. Chem.*, **28**, 5 (1988).

12. R. Csuk, A. Fürstner, and H. Weidmann, *J. Carbohydr. Chem.*, **5**, 77 (1986).

13. Prepared in 54% yield (after distillation) from methyl propanoate by reaction with trimethylsilyltrifluormethane sulfonate according to H. Emde, G. Simchen, *Synthesis* **1987**, 867 .

14. C. Palomo, J. M. Aizpurna, M. C. López, and B. Lecea, *J. Chem. Soc., Perkin Trans. 1*, **1989**, 1692.

15. T. Mukaiyama, K. Homma, and H. Takenoshita, *Chem. Lett.* ,**1988**, 1725; this aspect is presently under investigation.

16. $NaBH_4$ reduction of **16**, subsequent cleavage of the acetals under acidic conditions followed by ozonolysis affords a mixture of 3-deoxy-**D**-*glycero*-**D**-*galacto*-2-nonulosonic acid, KDN, and its 4-epimer, the ratio of both compounds strongly depending on the conditions used in the reduction (R. Csuk and A. Vasella, unpublished results). KDN itself has been found to be located at the non-reducing end of sialyl chains of rainbow trout egg polysialoglycoprotein [D. Nadano, Y. Inone, *J. Biol. Chem.*, **261**, 11550 (1986)]. Its straightforward enzymic synthesis from **D**-mannose and sodium pyruvate has recently been described [C. Auge, C. Gautheron, S. David, A. Malleron, B. Cavayé, B. Bouxom,*Tetrahedron*, **46**, 201 (1990)].

17. The same observation was made for the reaction of carbohydrate derived uloses, *e.g.* methyl 4,6-*O*-benzylidene-3-deoxy-α-**D**-*erythro*-2-hexulopyranoside or 1,2;5,6-di-*O*-isopropylidene-α-**D**-*ribo*-3-hexo-furanos-ulose, gave upon reaction with **23** (2 equivs) and TBAF(catalytic amount) in the minimum amount of tetrahydrofuran for 48h, followed by TBAF mediated desilylation/lactonization, the known spiro α-methylene-γ-lactonized derivatives in yields of 80-90%, respectively [R. Csuk, A. Fürstner, H. Sterk, and H. Weidmann, *J. Carbohydr. Chem.*, **5**, 459 (1986)]. Inferior yields from extremely prolonged reaction times (1-2 weeks!) were observed for more diluted solutions.

18. G. Sauvé and P. Deslongchamps, *Synth. Commun.*, **15**, 201 (1985).

19. Treatment of **7-10** or **21** with 1.1 equiv. of methanesulfonyl chloride and triethylamine leads to (*Z,E*)-mixtures of the corresponding α,β-

unsaturated esters or nitriles in excellent yields (80-90%): R. Csuk, B. I. Glänzer, presented in part: *5th IUPAC Symposium on OrganoMetallic Chemistry directed towards Organic Synthesis*, Florence, Italy, October 1989.

20. The configuration at the anomeric centre was assigned by performing semi-empirical MO-calculations [MOPAC by QCPE; for AM1 see: M. J. J. Dewar, E. G. Zoebisch, F. F. Healy, and J. J. P. Steward, *J. Am. Chem. Soc.*, **107**, 3902 (1985)]. It can be assumed that for each of the possible products both anomers might be in equilibrium *via* their open chain form. AM1 calculations were performed and the calculated values for the heat of formation of the respective anomers were compared. Significant differences (3-7 Kcal/mol) in the heat of formation of the respective couples were found, hence clearly indicating the preferred anomer.

21. Prepared according to A. Haider, *Synthesis*, **1985**, 271.