Chemistry of Natural Compounds and Bioorganic Chemistry

Synthesis of (1→5)-β-D-galactofuranan and cyclo[(1→5)-β-D-galactofurano]oligosaccharides

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Synthesis of a linear (1→5)-β-D-galactofuranan was accomplished by trityl-cyanoethylidene polycondensation. On 10-fold reduction in the monomer concentration, the condensation products are cyclic oligosaccharides; the formation of 1,5-anhydro-α-D-galactofuranose was also demonstrated.

Key words: 3,6-di-*O*-benzoyl-5-*O*-trityl-1,2-*O*-[(1-cyano)ethylidene]-α-D-galactofuranose, polycondensation; (1→5)-β-D-galactofuranan, cyclooligomerization, concentration dependence; cyclooligosaccharides; 1,5-anhydro-α-D-galactofuranose.

The general method for the synthesis of regular polysaccharides with the 1,2-*trans*-configuration of the internal glycosidic linkages, based on the use of trityl-cyanoethylidene polycondensation,[1] was recently successfully applied to the synthesis of galactofuranans built of (1→3)-, (1→6)-, and alternating (1→3)- and (1→6)-β-D-galactofuranose residues.[2,3] This gave evidence of high reactivity of trityl ethers formed both by primary and secondary hydroxyl groups of a furanose ring and of the stereospecificity of the glycosylation reaction (an elementary act of polycondensation) in these cases. During these syntheses the formation of cyclic oligosaccharide structures, arising from intramolecular glycosylation of the growing polymer chain, was observed for the first time.

To develop these studies and with the goal of synthesizing (1→5)-β-D-galactofuranan, the polycondensation of the 1,2-*O*-(1-cyano)ethylidene derivative of D-galactofuranose bearing a trityl group at the secondary exocyclic oxygen atom was investigated. It appeared possible to direct the process towards the formation of a linear polysaccharide or cyclic oligosaccharides by changing the initial monomer concentration.

Linear (1→5)-β-D-galactofuranan is a glycopeptide component produced by *Penicillium charlesii*,[4] 5-substituted residues of β-D-galactofuranose form a part of the mannogalactans of the cell walls of micelia and conidia of *Aspergillus fumigatus*,[5] and a part of the arabinogalactans of the cell walls of *Micobacterium leprae*[6] and M. *tuberculosis*. Recently the step-by-step synthesis

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Table 1. ^{1}H NMR data for compounds **1**, **3**—**6**

Compound	δ								
	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	CH_3S	$COOCH_3$
1	6.10(d)	4.95(d)	5.88(d)	4.44(d)	4.20(d)	4.36(d)	4.25(dd)	1.66(s)	—
3	6.28(d)	5.00(d)	5.14(d)	4.28(br.d)	4.44(ddd)	4.19(dd)	3.99(dd)	1.78(s)	3.78(s)
4	6.26(d)	5.02(d)	5.30(s)	4.34(d)	3.95(m)	3.85(dd)	3.75(dd)	1.72(s)	3.73(s)
5	6.31(d)	5.09(d)	5.46(d)	4.44(d)	4.1(m)	4.61(dd)	4.49(dd)	1.76(s)	3.77(s)
6	6.10(d)	4.91(d)	5.79(d)	4.41(dd)	4.04(m)	4.35(dd)	4.25(dd)	1.51(s)	3.72(s)

Table 2. Coupling constants in ^{1}H NMR spectra of compounds **1**, **3**—**6**

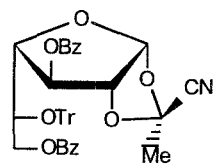
Compound	*J*/Hz					
	$J_{H-1,H-2}$	$J_{H-3,H-4}$	$J_{H-4,H-5}$	$J_{H-5,H-6a}$	$J_{H-5,H-6b}$	$J_{H-6a,H-6b}$
1	4.0	3.5	6.5	3.4	4.5	12.5
3	4.0	1.2	8.5	6.2	6.6	8.5
4	4.2	0	8.5	3.8	4.6	11.9
5	4.2	1.5	7.5	4.4	5.5	11.5
6	4.0	4.2	6.2	3.5	4.3	12.5

Note. For all compounds $J_{H-2,H-3} = 0$.

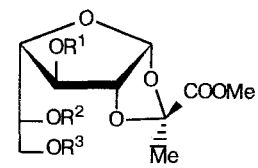
Table 3. ^{13}C NMR data for compounds **1**, **5**, and **6**

Compound	δ									
	C-1	C-2	C-3	C-4	C-5	C-6	$\underline{C}H_3$—$\underline{C}$——$\underline{C}N(\underline{C}OO\underline{C}H_3)$			
1	105.7	87.8	75.3	87.8	71.25	63.6	24.5	101.4	116.5	
5	107.4	86.4	78.3	88.3	69.9	65.5	21.2	108.0		(168.9 52.5)
6	106.3	86.1	76.0	87.6	71.6	63.9	21.8	108.9		(169.3 52.5)

of short oligosaccharide fragments of (1→5)-β-D-galactofuranan was described.[7,8]



1



2—**6**

2: R^1 = H, $R^2 + R^3 = CMe_2$
3: R^1 = Bz, $R^2 + R^3 = CMe_2$
4: R^1 = Bz, $R^2 = R^3$ = H
5: $R^1 = R^3$ = Bz, R^2 = H
6: $R^1 = R^3$ = Bz, R^2 = Tr

The initial mponomer for the synthesis of (1→5)-β-D-galactofuranan was 3,6-di-*O*-benzoyl-5-*O*-trityl-1,2-*O*-(1-cyano)-ethylidene-α-D-galactofuranose **(1)** obtained using methodology proposed earlier[9] by the introduction of the cyanoethylidene function through the masked precursor, 1,2-*O*-(1-methoxycarbonyl)ethylidene group. Benzoylation of the known[2] 1,2-*O*-(1-methoxycarbonyl)ethylidene derivative **2** led to benzoate **3**, which was deacetonated with 90 % trifluoroacetic acid in chloroform to give diol **4**. Its selective benzoylation under the action of *N*-benzoylimidazole according to the method in ref. 10 resulted in 3,6-dibenzoate **5**, as indicated by the ^{1}H NMR data (Tables 1 and 2). Trityl ether **6** was prepared by the tritylation of compound **5** with triphenylmethylium perchlorate in the presence of 2,4,6-collidine in 89 % yield, and then it was converted to the target monomer **1** by ammonolysis followed by treatment with benzoyl chloride in pyridine.[9] The structure of monomer **1** was determined from the NMR spectra (Tables 1—3) and by comparison of them with the spectra of the monomers used for the synthesis of (1→3)- and (1→6)-β-D-galactofuranans which had been reported earlier.

The polycondensation of monomer **1** was carried out in dichloromethane at 20 °C using a vacuum technique. Under standard conditions of trityl-cyanoethylidene polycondensation (monomer concentration 0.24 *M*, catalyst concentration 0.02 *M*), the protected polysaccharide **7** was obtained in 94 % yield after isolation by chromatography on silica gel. Removal of the protecting groups by methanolysis in the presence of a catalytic amount of sodium methoxide followed by treatment with aqueous NaOH afforded the free polysaccharide **8**. Only six signals corresponding to the 5-substituted β-D-galactofuranose residue were observed in its ^{13}C NMR spectrum (Table 4) which confirmed

Table 4. ^{13}C NMR data for polysaccharides **7** and **8**, anhydroderivative **12**, and cyclotetraose **14**

Compound	δ					
	C-1	C-2	C-3	C-4	C-5	C-6
7	105.4	81.7	77.3	82.7	72.8	65.0
8	108.2	82.6	77.65	82.65	76.8	62.3
12	101.0	82.7	77.85	85.25	76.75	64.0
14	108.1	82.5	80.2	83.7	78.3	61.6

Table 5. ^1H NMR data for compounds **9—14**

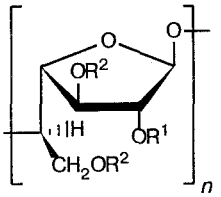
Compound	δ							
	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	SH_3SO
9	5.88(d)	4.94(m)	4.86(d)	5.04(d)		4.18—4.40(m)		2.16(s)
10	5.37(s)	5.18(d)	5.44(dd)	4.99(t)		4.33—4.53(m)		2.09(s)
11	5.37(s)	5.25(d)	5.48(dd)	4.60(dd)	4.48(m)	4.25(m)	4.34(m)	2.00(s)
12	5.59(d)	3.94(ddd)	3.76(d)	4.57(d)	3.82(t)	3.58(dd)	3.51(dd)	—
13	5.14(d)	4.10(dd)	3.92(dd)	4.27(t)	3.88(m)	3.82(dd)	3.69(dd)	—
14	5.23(s)	4.14(d)	3.98(dd)	4.29(dd)	3.88(m)	3.81(dd)	3.67(dd)	—

Table 6. Coupling constants in ^1H NMR spectra of compounds **9—14**

Compound	*J*/Hz						
	$J_{H-1,H2}$	$J_{H-2,H-3}$	$J_{H-3,H-4}$	$J_{H-4,H-5}$	$J_{H-5,H-6a}$	$J_{H-5,H-6b,}$	$J_{H-6a,H-6b}$
9*	2.5	1.5	0	0	—	—	—
10	0	2.5	7.4	6.5	—	—	—
11	0	1.0	5.0	6.2	—	—	—
12**	2.7	1.1	0	0	5.2	6.0	11.7
13	2.5	4.3	7.4	6.7	3.0	7.2	12.0
14	0	2.3	5.7	7.7	3.1	6.5	12.2

*$J_{H-2,H-4}$ = 1.5 Hz. **$J_{H-2,H-4}$ = 1.9 Hz.

the high regio- and stereoregularity of the polysaccharide obtained. The absence of signals due to a terminal monosaccharide residue indicated a high degree of polymerization. In fact, polysaccharide **8** eluted in the gel chromatography in the same range as (1→6)-β-D-galactofuranan with $\overline{DP}_n$ ~30 (*cf.* ref. 2). Thus, the polycondensation of monomer **1** proceeded rather effectively and gave regular (1→6)-β-D-galactofuranan with a reasonably high molecular weight.



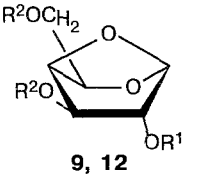
7, 8

7: R^1 = Ac, R^2 = Bz

8: $R^1 = R^2$ = H

However, it appeared that the character of the polycondensation of monomer **1** changed crucially as the monomer concentration in the reaction mixture decreased. A mixture of three products, which did not incorporate a trityl group and possessed essentially higher TLC mobility than polysaccharide **7**, was obtained upon 10-fold dilution of the reaction mixture with respect to the monomer (0.014 *M*), and the polymer fraction corresponding to the polysaccharide was absent.

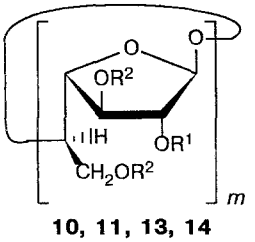
Compounds **9—11**, which were isolated individually, were converted by deacetylation to the free saccharides **12—14**, respectively (their NMR spectra are listed in Tables 4—6).



9, 12

9: R^1 = Ac, R^2 = Bz

12: $R^1 = R^2$ = H



10, 11, 13, 14

10: R^1 = Ac, R^2 = Bz, m = 3

11: R^1 = Ac, R^2 = Bz, m = 4

13: $R^1 = R^2$ = H, m = 3

14: $R^1 = R^2$ = H, m = 4

The character of the spin-spin interaction and coupling constants, particularly the $J_{H-2,H-4}$ constants, in the ^1H NMR spectra of compounds **9** and **12** (Tables 5 and 6) are similar to those for the known derivatives of 1,5-anhydro-α-D-galactofuranose (1,4-anhydro-β-D-galactopyranose[12]). The signal for the C-1 atom in the ^{13}C NMR spectrum of compound **12** has a chemical shift of 101 ppm (see Table 4), which is equally typical of both α-D-galactofuranosides and β-D-galactopyranosides.

The cyclic structure of oligosaccharides **10**, **11** and, respectively, **13**, **14** was derived from the presence in their NMR spectra of only one set of signals, corresponding to the 5-substituted galactofuranose residue, and the absence of signals that could be attributed to terminal monosaccharide units. These data pointed unambiguously to the internal symmetry of the oligosaccharide molecules. Similar spectral features were observed for cyclo[(1→3)- and (1→6)-β-D-galactofurano]oligosaccharides[9,13,14] as well. Mass-spectral (LSIMS) data gave evidence in favor of a cyclic nature of compounds **10**, **11**, **13**, and **14**. The number of galactofuranoside units in a cycle, determined on the basis of these spectra, was 3 for **13** and 4 for **14**. The molecular ion peaks, their clusters with sodium and potassium ions, and also peaks corresponding to the ejection of one or more monosaccharide units were present in the spectra (a similar fragmentation pattern for cyclooligosaccharides was observed earlier[15]).

Thus, a linear polysaccharide and cyclic oligosaccharides are formed during the polycondensation of cyanoethylidene derivatives of galactofuranose with a trityl group in any possible position (3, 5, or 6). It should be mentioned that the conditions which permit one to selectively obtain one of these two types of products have been found in the present work. The effect of the monomer concentration on the ratio of intra- and intermolecular polycondensation products is commonly known, but interestingly, in this case the selectivity of the process is achieved only with a 10-fold change in the concentration.

The formation of a 1,2-*trans*-glycosidic bond occurs, apparently, according to the ordinary mechanism both during the linear polycondensation of monomer **1** and during the closure of the oligosaccharide cycles, which is cofirmed by the stereospecificity of the glycosylation. At the same time, the formation of 1,5-anhydro derivative **9** cannot be explained in terms of the common mechanism of glycosylation using cyanoethylidene derivatives (the known examples of anhydrosugar formation from tritylated cyanoethylidene derivatives belong to pyranose systems[16,17]). Probably, the appearance of this product is preceded by the isomerization of the bicyclic dioxolenium ion into the monocyclic glycosyl cation, as was assumed in the formation of the 1,5-anhydro-β-L-arabinofuranose derivative from the corresponding 1,2,5-orthoester.[18]

Experimental

For the general procedures see ref. 2. Column chromatography was performed on Silasorb silica gel (Czechoslovakia), TLC was performed on Kieselgel-60F_{254} plates (Merck, Germany). The gel-permeation chromatography (Fractogel TSK HW-40, 1.6 × 78 cm, V_0 = 46 mL) was monitored using a Knauer 88.00 differential refractometer (Germany). Positive-ion mass spectra (LSIMS) were obtained using a glycerol matrix and cesium ions as the source of ionization at 5-30 keV on an AMD-600 apparatus (Germany).*

3-*O*-Benzoyl-5,6-*O*-isopropylydene-1,2-*O*-[1-(*exo*-methoxycarbonyl)ethylidene]-α-D-galactofuranose (3). Benzoyl chloride (0.812 mL, 7.0 mmol) was added over 2 h to a solution of monohydroxyl derivative **2** (ref. 2) (1.75 g, 5.7 mmol) in pyridine (10 mL). Conventional work-up, column chromatography (elution with benzene—ether, 1:0 →9:1), and crystallization from a benzene—hexane mixture afforded benzoate **3**, yield 2.0 g (86 %), m.p. 91—94 °C, $[\alpha]_D^{28}$ +12° (*c* 1.14). Found (%): C, 59.36; H, 6.02. $C_{20}H_{24}O_9$. Calculated (%): C, 58.82; H, 5.92.

3-*O*-Benzoyl-1,2-*O*-[1-(*exo*-methoxycarbonyl)ethylidene]-α-D-galactofuranose (4). Aqueous (90 %) trifluoroacetic acid (10 mL) was added to a solution of isopropylidene derivative **3** in chloroform (10 mL). The mixture was kept for 10 min, poured into a saturated aqueous solution of $NaHCO_3$, diluted with chloroform (100 mL), and washed with $NaHCO_3$ solution until the total removal of acid. Then the solvent was evaporated. The yield of diol **4** is 1.77 g (88 %), $[\alpha]_D$ +45° (*c* 1.05). Found (%): C, 55.42; H, 5.60. $C_{17}H_{20}O_9$. Calculated (%): C, 55.43; H, 5.47.

3,6-Di-*O*-benzoyl-1,2-*O*-[1-(*exo*-methoxycarbonyl)-ethylidene]-α-D-galactofuranose (5). A solution of benzoyl chloride (0.36 mL, 2.25 mmol) in chloroform (2 mL) was added to a solution of imidazole (305 mg, 4.5 mmol) in chloroform (4 mL). The precipitate was filtered off, washed with dry chloroform (2.5 mL), and the combined filtrates were poured in one portion to a solution of diol **4** (1.07 g, 2.02 mmol) in anhydrous chloroform (10 mL). The mixture was refluxed for 24 h, diluted with chloroform (25 mL), and washed with $NaHCO_3$ solution (2 × 20 mL). The solvent was evaporated, and the residue was chromatographed to give dibenzoate **5** as a syrup, yield 1.48 g (73 %), $[\alpha]_D^{20}$ +17° (*c* 1.04).

3,6-Di-*O*-benzoyl-1,2-*O*-[1-(*exo*-methoxycarbonyl)ethylidene]-5-*O*-trityl-α-D-galactofuranose (6). Triphenylmethylium perchlorate (500 mg, 1.5 mmol) was added in portions to a stirred solution of dibenzoate **5** (700 mg, 1.5 mmol) and 2,4,6-collidine (0.2 mL, 1.5 mmol) in dichloromethane (5 mL). After 0.5 h, more collidine (0.07 mL) and triphenylmethylium perchlorate (170 mg) were added. The mixture was stirred until it became colorless, diluted with chloroform (30 mL), and washed with water (2 × 15 mL). The solvent was evaporated, and the residue was chromatographed in benzene—ethyl acetate (1:0 → 9:1). Trityl ether **6** was obtained as a white foam, yield 950 mg (89 %), $[\alpha]_D$ −30° (*c* 0.84). Found (%): C, 72.05; H, 5.19. $C_{43}H_{38}O_{10}$. Calculated (%): C, 72.26; H, 5.35.

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3,6-Di-*O*-benzoyl-1,2-*O*-[1-(*exo*-cyano)ethylidene]-5-*O*-trityl-α-D-galactofuranose (1). A solution of derivative **6** (760 mg, 1.06 mmol) in a methanol—chloroform mixture (10:1, 20 mL) was saturated with ammonia at 0—5 °C and kept for 5 h at 20 °C. The mixture was concentrated, a small amount of pyridine was added, and after repeated evaporation the residue was dissolved in pyridine (15 mL) and treated with benzoyl chloride (1.2 mL, 10.3 mmol). After 18 h the mixture was diluted with chloroform (60 mL), washed with $NaHCO_3$ solution (3 × 20 mL) and water. The solvent was evaporated, and the residue was chromatographed in benzene—ether (1:0 → 9:1). Crystallization from an ether—hexane mixture afforded cyanoethylidene derivative **1**, yield 620 mg (86 %), m.p. 128—130 °C, $[\alpha]_D^{28}$ −41° (*c* 1.0). Found (%): C, 74.06; H, 4.78; N, 1.85. $C_{42}H_{35}NO_8$. Calculated (%): C, 73.99; H, 5.17; N, 2.05.

Polycondensation of monomer 1. In one limb of a tuning-fork-shaped tube (⅄) was placed a solution of monomer **1** (810 mg, 1.19 mmol) in benzene (3 mL), and a solution of triphenylmethylium perchlorate (33 mg, 0.096 mmol) was placed in the other limb. The tube was connected to a vacuum apparatus (10^{-3} Torr) and the solutions were lyophilized. The monomer was repeatedly lyophilized from benzene which had been distilled from CaH_2 in the same apparatus. Dichloromethane (distilled from CaH_2) (5.0 mL) was condensed into the tube, the reagents in the two limbs were dissolved, mixed, and left for 24 h at 20 °C. After tube opening the mixture was treated with pyridine (0.3 mL), diluted with chloroform (60 mL), washed with water (3 × 20 mL), and concentrated. 2-*O*-Acetyl-6-*O*-benzoyl-(1→5)-β-D-galactofuranan was izolated from the residue using column chromatography in toluene—methanol (1:0 → 9:1), yield 460 mg (94 %), R_f 0.25—0.5 (toluene—methanol, 9:1), $[\alpha]_D^{28}$ −71° (*c* 1.6).

(1→5)-β-D-Galactofuranan (8). Protected polysaccharide **7** (460 mg) was dissolved in anhydrous dichloromethane (4 mL) followed by addition of abs. methanol (6 mL) and 1 mL of 1 *M* methanolic MeONa. The suspension which formed after 10 min was stirred for 2 h, concentrated, water (10 mL) was added to the residue, and stirring was continued for an additional 4 h. Completion of the debenzoylation was monitored by UV-absorption of the zone containing carbohydrates (TLC). The mixture was neutralized with acetic acid and polysaccharide **8** was isolated using gel-permeation chromatography (it eluted with a void volume of the column), yield 150 mg (84 %), $[\alpha]_D^{25}$ −124° (*c* 0.66, water). (For linear nona(deca)saccharide:[19] $[\alpha]_{578}$ −84°.)

1,5-Anhydro-2-*O*-acetyl-3,6-di-*O*-benzoyl-α-D-galactofuranose (9), cyclo[(1→5)-(2-*O*-acetyl-3,6-di-*O*-benzoyl-β-D-galactofurano)]triose (10), and cyclo[(1→5)-(2-*O*-acetyl-3,6-di-*O*-benzoyl-β-D-galactofurano)]tetraose (11). The cyclooligomerization of monomer **1** (315 mg, 0.46 mmol) was performed in dichloromethane (18 mL) in the presence of triphenylmethylium perchlorate (85 mg, 0.25 mmol) under the polycondensation conditions described for 40 h. The reaction mixture was worked up as above. Column chromatography (benzene—ether, 1:0 → 4:1) afforded anhydro derivative **9**, yield 50 mg (26 %), R_f 0.65 (toluene—ethyl acetate, 4:1), $[\alpha]_D^{29}$ +100° (*c* 1.02) and a mixture of cyclooligosaccharides **10** and **11**, combined yield 110 mg (58 %), R_f 0.58 and 0.50, which was separated by HPLC (Silasorb-600, heptane—ethyl acetate, 2:1) to yield pure samples of compounds **10** ($[\alpha]_D^{26}$ −52° (*c* 0.95)) and **11** ($[\alpha]_D^{24}$ −88°(*c* 1.36)).

1,5-Anhydro-α-D-galactofuranose (12). A 0.1 *M* methanolic solution of MeONa (3.5 mL) was added to a solution of compound **9** (50 mg) in dichloromethane (1 mL) and the mixture was left for 4 h, neutralized with acetic acid, diluted with water (40 mL), and deionized by a KU-2 (H^+) cation-exchanger. Evaporation of the solution and drying gave anhydride **12**, yield 15 mg (76 %), $[\alpha]_D^{27}$ +126° (*c* 1.02, water).

Cyclo[(1→5)-β-D-galactofurano)]triose (13). Acylated oligosaccharide **10** was saponified by 0.1 *M* methanolic solution of MeONa for 3 h, methanol was evaporated, water (2 mL) was added, and the solution was kept for an additional hour. The mixture was deionized by cation-exchanger KU-(H^+), and cyclotrisaccharide **13** was isolated using gel-chromatography on a column with TSK-gel (elution maximum is 106 mL). MS, *m/z* (I_{rel} (%)): 525 $[Gal_3 + K]^+$ (2), 509 $[Gal_3 + Na]^+$ (3), 487 $[Gal_3 + H]^+$ (3.5), 325 $[Gal_2 + H]^+$ (5).

Cyclo[(1→5)-β-D-galactofurano)]tetraose (14). The deacylation of the derivative **11** was performed as described above, and cyclotetrasaccharide **14** was obtained, $[\alpha]_D^{26}$ −90° (c 1.04, water), maximum of the pick under elution from the column with TSK-gel is 102 mL. MS, *m/z* (I_{rel} (%): 687 $[Gal_4 + K]^+$ (7.5), 671 $[Gal_4 + Na]^+$ (21), 649 $[Gal_4 + H]^+$ (9), 525 $[Gal_3 + K]^+$ (1), 509 $[Gal_3 + Na]^+$ (2), 487 $[Gal_3 + H]^+$ (4), 325 $[Gal_2 + H]^+$ (18), 163 $[Gal_1 + H]^+$ (3).

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Reactivity of 1,2-*O*-cyanoalkylidene sugar derivatives in trityl-cyanoalkylidene condensation

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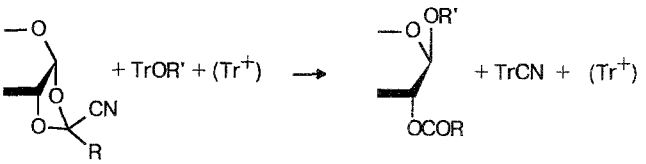
The rate-determining step of trityl-cyanoalkylidene condensation is the interaction between the cyanoalkylidene derivative (CD) and the triphenylmethyl cation. The rate of the reaction follows first-order kinetics with respect to both CD and the catalyst (Tr^+) and is independent of the nature and concentration of the trityl ether. Glycosylation rate constants have been determined for CD's of most common monosaccharides.

Key words: trityl-cyanoalkylidene condensation; cyanoalkylidene derivatives, mechanism of glycosidation.

The method of trityl-cyanoalkylidene condensation has found wide application for the synthesis of regular polysaccharides containing 1,2-*trans*-glycosidic linkages between the repeating units.[1,2] For effective control of the polycondensation process it is necessary to have information about the elementary step of trityl-cyanoalkylidene condensation and the relative reactivities of the cyanoalkylidene derivatives (CD). The estimation of the latter is also decisively important for the synthesis of block-polysaccharides.[3] Some suggestions regarding the difference between the reactivities of CD's have been made on the basis of X-ray structural analysis data;[4] the reactivities of the *exo*- and *endo*-cyanoethylidene derivatives (CED) of D-galactose, D-glucose and D-xylose have also been compared.[5] However, no systematic studies in this field have been carried out. To refine the existing mechanistic concepts we have investigated the kinetics of the glycosidation and the relative reactivity of a series of CD's.

The synthesis of *O*-glycosides by trityl-cyanoalkylidene condensation is the interaction of 1,2-*O*-(1-cyano)alkylidene sugar derivatives as glycosyl donors with trityl ethers as glycosyl acceptors in the presence of triphenylmethylium perchlorate as a promoter and a catalyst[6] (Scheme 1).

Scheme 1



Tr = Ph_3C

The glycosidation kinetics of the condensation of D-mannose CED (**1**) (ref. 7) with trityl ethers **2** (ref. 8) and **3** (ref. 9) and *exo*-D-galactose CED **4** with trityl ether **5** (ref. 10) were studied under conditions typical for this reaction: in dichloromethane in the presence of catalytic amount of triphenylmethylium perchlorate. The reaction was monitored by determining the amount TrCN formed (GLC). GLC analysis demonstrated that the disaccharide/TrCN ratio was constant during the reaction. Thus, the rates of formation of the disaccharide and trityl cyanide were the same (it should be noted that the amount of trityl cyanide has served as a measure of the extent of trityl-cyanoalkylidene polycondensation[11]).

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