SYNTHESIS OF POLYSACCHARIDES.

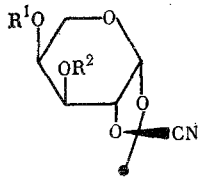
COMMUNICATION 16. SYNTHESIS OF L-ARABINOPYRANANS

N. K. Kochetkov, A. Ya. Ott,
and A. S. Shashkov

UDC 542.91:547.458

The polycondensation method for O-trityl ethers of 1,2-O-cyanoethylidene derivatives of sugars has made it possible to obtain a series of regio- and stereoregular polysaccharides [1, 2]. However, cases were recorded recently of the nonstereospecific course of this reaction with secondary O-trityl sugar ethers in [3, 4].

It seemed of interest to check whether the reason for the disturbance of the stereospecificity was the influence of the substituent on the hydroxymethyl group at C5. With the aim of assessing such a possibility the polycondensation was effected of two 1,2-O-(1-exo-cyano)ethylidene derivatives of L-arabinopyranose (I) and (II) devoid of this group.



(I)-(VI)

R^1 = Tr, R^2 = Ac(I); R^1 = Ac, R^2 = Tr(II); $R^1 = R^2$ = Ac(III),
$R^1 = R^2$ = H(IV); R^1 = Tr, R^2 = H(V); R^1 = H, R^2 = Tr(VI).

The initial (III) was synthesized by the general method of [5] from 2,3,4-tri-O-acetyl-L-arabinopyranosyl bromide obtained from a mixture of fully acetylated β- and α-arabinopyranose. As in other cases [5], (III) was obtained in a mixture with the corresponding endo-cyano isomer (IIIa) in a ratio of 64:36 (ratio of signal intensities of protons of the CH_3 group in the PMR spectrum of the mixture). Assignment of the obtained compounds to the endo and exo series was made by analogy with derivatives of D-galactopyranose. In the PMR spectrum of the endo isomer the signal of the CH_3 group is located towards high field.

Deacetylation of (III) was carried out by analogy with the D-galactose derivative of [4] using a somewhat reduced amount of 0.01 N MeONa. Tritylation of diol (IV) with one equivalent of trityl perchlorate under the usual conditions of [6, 7] led to the predominant (75%) formation of 4-O-trityl ether (V) and only 25% of 3-O-trityl ether (VI) which were acetylated and both monomers (I) and (II) were obtained.

The structures of the obtained monomers and intermediate products were established by a combination of the data of PMR and ^{13}C NMR spectra and also by x-ray structural analysis of monomers the results of which will be published in the near future. Assignment of signals in the PMR spectrum was carried out with the aid of selective homonuclear double resonance and in the ^{13}C NMR spectra with selective heteronuclear double resonance. The data of PMR and ^{13}C NMR spectroscopy are given in Tables 1 and 2.

Polycondesation of monomers (I) and (II) was carried out under the conditions described in [4] using 10 mole % $TrClO_4$ catalyst at a reaction duration of 110 h. Methanol and pyridine were then added to the reaction mixture. After deacetylation (with 1 N MeONa) the obtained polysaccharides were subjected to gel chromatography on Sephadex G-25, as a result of which two fractions were isolated. From monomer (I) 34 and 27 mg (overall yield 54%) of 1,4-arabinan was obtained, and from monomer (II) 10 and 26 mg (overall yield 43%) 1,3-arabinan (see the Experimental section).

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 1, pp. 196-199, January, 1986. Original article submitted September 11, 1984.

0568-5230/86/3501-0179$12.50

TABLE 1. Data of PMR Spectra of 1,2-O-Cyanoethylidene Derivatives* (solution in $CDCl_3$, internal standard TMS, δ ppm; J, Hz)

Compound	H^1	H^2	$H^{3'}$	H^4	H^5	$H^{5'}$	CH_3	OAc (OH)
(I)	5,53 d (3,5)	4,36 d.d (4,4)	5,16 d.d (3,4)	4,00 d.d.d. (6,1)	3,11 d.d. (11,6)	2,97 d.d. (4,0)	1,73 s	2,20 s
(II)	5,51 d (3,9)	4,05 d.d. (5,2)	3,92 d.d. (3,0)	4,26 d.d.d. (4,4)	3,80 d.d. (12,4)	3,63 d.d. (3,7)	1,64 s	2,10 s
(III)	5,57 d (3,8)	4,35 d.d (4,8)	5,26 d.d. (2,7)	5,24 d.d.d. (3,5)	4,02 d.d (12,0)	3,84 d.d (4,1)	1,89 s	2,14 2,00 2 s
(IIIa)	5,56 d (3,7)	4,26 d.d (5,9)	5,43 d.d. (3,0)	5,31 d.d.d. (4,5)	4,10 d.d (12,5)	3,77 d.d. (5,0)	1,74 s	2,05 2,02 2 s
(IV)	5,58 d (3,6)	4,34 t (3,6)	4,18 d.d. (4,2)	4,0 d.d.d. (4,2)	3,82 d.d (12,0)	3,73 d.d (6,1)	1,88 s	3,62 s 3,28 s (OH)
(V)	5,45 d (3,4)	4,21 d.d (3,0)	3,29 d.d (4,0)	3,95 d.d.d (7,0)	3,61 d.d (12,0)	3,40 d.d (5,0)	1,76 s	2,76 s (OH)
(VI)	5,58 d (4,5)	4,27 d.d (4,5)	3,90 d.d (3,5)	2,67 d.d.d. (3,1)	3,65 d.d (12,5)	3,52 d.d (3,5)	1,71 s	2,36 s (OH)

*Signals were present in the spectra of compounds (I), (II), (V), and (VI) for aromatic protons at 7.25-6.52 ppm.

TABLE 2. Data of ^{13}C NMR Spectra (solution in $CDCl_3$, internal standard TMS, δ ppm*)

Compound	C^1	C^2	C^3	C^4	C^5	$\underline{C}H_3CCN$	CN	$\underline{C}CN$	$\underline{C}H_3CO$	C=O	$\underline{C}(Ph)_3$
(I)	97,4	76,3	69,4	66,1	63,2	25,9	116,9	99,2	21,0	169,8	87,95
(II)	98,2	77,5	70,3	67,9	63,4	25,8	117,1	98,5	21,05	169,7	88,1
(III)	97,95	75,3	68,6	65,6	62,8	25,8	116,8	98,9	20,7	169,8 169,6	–
(IV)	96,9	78,8	64,4	64,7	63,5	25,8	117,0	99,5	–	–	–
(V)	96,3	78,1	65,3	66,6	61,6	25,6	116,9	99,8	–	–	88,3
(VI)	98,0	78,4	72,4	65,0	65,2	25,8	117,2	98,2	–	–	88,4

*Signals were present in the spectra of compounds (I), (II), (V), and (VI) for C_6H_5 at 127.7-144.0 ppm.

Signals were present in the ^{13}C NMR spectra of 1,4-arabinan in the region of the C1 resonance with chemical shifts of 105.65 and 98.0 ppm and of 1,3-arabinan of 105.2 and 97.4 ppm. The ratio of the integrated signal intensities for both arabinans was 3:1. By comparing the ^{13}C NMR spectra of methyl-α- and methyl-β-L-arabinopyranosides and of α,β-L-arabinopyranose [8], and also in view of the absence of a signal near 94 ppm for the free reducing terminus in the β configuration (in aqueous solution the equilibrium state for arabinopyranose was characterized by a 40% content of the β form according to [9]), it may be considered that the signals at low field belong to the C1 atom participating in 1,2-trans- and at high field to the C1 atom in 1,2-cis-glycosidic linkage.

In both synthesized arabinans there were anomalous 1,2-cis-glycosidic linkages (β-L-arabinopyranoside bonds) in a portion of which about 1/4 of all bonds occurred.

In the course of GLC mass-spectrometric analysis [10] of high-molecular-weight fractions of the obtained polysaccharides the following were detected: a) 1,5-di-O-acetyl-2,3,4-tri-O-methyl- (VII) and 1,4,5-tri-O-acetyl-2,3-di-O-methylarabitol (VIII) in a ratio of 1:10 for 1,4-arabinan and b) polyol (VII) and 1,3,5-tri-O-acetyl-2,4-di-O-methylarabitol (IX) in a ratio of 1:7 for 1,3-arabinan. The obtained results indicate the regiospecificity of the polycondensation reaction leading to the formation of (1 → 4)- and (1 → 3)-L-arabinopyranans with an average degree of polymerization of 11 and 8, respectively. However, the absence of a substituent at C5 in the monomer did not eliminate disturbance of the stereospecificity of the reaction.

EXPERIMENTAL

The PMR and ^{13}C NMR spectra were taken on a Bruker WM-250 instrument (250 MHz, West Germany). The IR spectra were obtained on a UR-20 instrument (East Germany) in KBr disks.

Optical rotation was measured on a Perkin–Elmer 141 polarimeter. Melting points were determined on a Kofler block. GLC was carried out on an LKhM-8MD chromatograph (steel column 1 m, 5% SE-30 on Chromaton N-AW, carrier gas N_2, flame-ionization detector). GLC mass-spectrometric analysis was effected on a Varian MAT-111 instrument (steel column 1.5 m, 5% SE-30 on Varoport 30, carrier gas He).

Column chromatography was carried out on SiO_2 type L 100/160 (Czechoslovakia), TLC on SiO_2 type L 5/40 (Czechoslovakia) in the systems A (benzene–ether, 1:1), B (benzene–ether, 2:3), C (chloroform–methanol, 4:1), D (benzene–ether, 4:1), E (benzene–ether, 9:1), and F (chloroform–acetone, 1:1). Detection of substances on TLC was carried out with 5% H_2SO_4 in MeOH with heating to 200°C. Solutions were evaporated at water jet pump vacuum at $\leqslant$45°C. Preparation of solvents for reactions was carried out as described previously in [11].

3,4-Di-O-acetyl-1,2,-O-[(1-exo-cyano)ethylidene]- (III) and 3,4-Di-O-acetyl-1,2-O-[(1-endo-cyano)ethylidene]-β-L-arabinopyranose (IIIa). L-Arabinose (35 g) was dissolved with heating in pyridine (300 ml). The solution was left at ∿20°C for 14 h, cooled to 0°C, AcCl (85 ml) was added with vigorous stirring and cooling, and after 20 h the mixture was diluted with $CHCl_3$ (300 ml) and poured onto ice. The chloroform extract was washed with 3 N H_2SO_4 (2 × 200 ml), with saturated $NaHCO_3$ solution (2 × 200 ml), and with water (3 × 200 ml). The chloroform solution was evaporated, and the thick syrup was dissolved in a small quantity of $CHCl_3$ (50 ml) and passed through a column (5 × 15 cm) of dry silica gel L 100/160, washing with a 1:1 mixture (600 ml) of $CHCl_3$–petroleum ether. The eluate was evaporated, and a product (64.5 g: 87%) was obtained which was homogeneous by TLC (system A). The PMR spectrum showed that a mixture was obtained of the fully acetylated β- and α-L-arabinopyranoses (two signals for H1 with δ6.30 and 5.62 ppm) at a ratio of 35.65. After drying for 15 h in vacuum over P_2O_5 the obtained syrupy product (9.0 g) was dissolved in abs. C_6H_6 (30 ml), and HBr in AcOH (60 ml) added (obtained from 34 ml AcBr, 25 ml AcOH, 4.5 ml Ac_2O, and 8.25 ml H_2O). After 1.5 h the mixture was poured into ice water (1.5 liters) and extracted with $CHCl_3$ (0.4 liter). The extract was washed with saturated $NaHCO_3$ solution (2 × 400 ml) and with cold water (400 ml), dried by filtration through glass wool, and evaporated to a thick syrup. On drying in vacuum (4 mm) the syrup crystallized (7.3g: 76%). Arabinopyranosyl bromide (21 mmoles) was dried in vacuum over KOH for 2 h, dissolved in MeCN (70 ml), KCN (7.4 g: 110 mmoles) added, and tetrabutylammonium bromide (3.7 g: 11.5 mmoles) added under conditions of absence of contact with the atmosphere. The mixture was stirred on a magnetic stirrer for 65 h (the mixture began to acquire a brown color after 40 h). The mixture was treated with ethyl acetate (500 ml) and washed with H_2O (7 × 150 ml). The solution was evaporated, and the syrup was dissolved in $CHCl_3$ (15-20 ml), applied to a column of dry silica gel L 100/160 (4 × 6 cm), and the column washed with a mixture (600 ml) of hexane–$CHCl_3$ (1:1). The solution was evaporated; the product (5.05 g, 79%) appeared on a TLC plate as two substances with R_f 0.85 and 0.80 (B). The mixture was chromatographed on a column (5 × 35 cm) in the system petroleum ether–ethyl acetate with a gradient of the latter up to 40%. Syrupy (II) (2.61 g) was obtained, R_f 0.85, $[\alpha]_D$ +52.4° (concn. 4.2, $CHCl_3$) and (IIIa) (1.20 g) of R_f 0.8, $[\alpha]_D$ +79.0° (concn. 12.0, $CHCl_3$) and a mixture (1.20 g) of (III) and (IIIa).

1,2-O-[1-(exo-Cyano)ethylidene]-β-L-arabinopyranose (IV). To a solution of (III) (2.3 g: 8 mmoles) in MeOH (30 ml) was added 0.01 N MeONa (40 ml: 0.4 mmole). The mixture was kept for 30 min at ∿20°C, neutralized with 0.1 M AcOH in MeOH (4 ml), and evaporated. The residue was chromatographed on a column (2 × 25 cm), eluting with ethyl acetate. Syrupy (IV) (1.31: ∿81%) was obtained, $[\alpha]_D$ +11.5° (concn. 1.74, CH_2Cl_2), R_f 0.7 (C).

4-O-Trityl- (V) and 3-O-Trityl-1,2,-O-[(exo-cyano)ethylidene]-β-L-arabinopyranose (VI). 2,4,6-Collidine (0.57 ml: 4.4 mmoles) and $TrClO_4$ (1.16 g: 3.4 mmoles) were added to a solution of (IV) (620 mg: 3.1 mmoles) in CH_2Cl_2 (18 ml), the mixture left for 1 h at ∿20°C then diluted with $CHCl_3$ (60 ml), and washed with H_2O (50 ml × 3). The chloroform solution was dried and evaporated, and a mixture (1.57 g) of products was obtained with R_f 0.70, 0.65, and 0.0 (D). After chromatography on a column (2 × 25 cm) in the system petroleum ether–ethyl acetate with a gradient to 15%, (V) (760 mg: 56%) was obtained as a syrup of R_f 0.70, $[\alpha]_D$ −2.1° (concn. 2.85, $CHCl_3$), also (VI) (240 mg: 17.5%) syrup $[\alpha]_D$ −21.0° (concn. 5.03, $CHCl_3$), and a mixture (70 mg: 5%) of (V) and (VI).

3-O-Acetyl-4-O-trityl- (I) and 4-O-Acetyl-3-O-trityl-1,2-O-[(1-exo-cyano)ethylidene]-β-L-arabinopyranose (II). Compound (V) (510 mg: 1.2 mmoles) was dissolved in pyridine (4 ml) with Ac_2O (1.5 ml), and (VI) (180 mg: 0.4 mmole; was dissolved in pyridine (2 ml) with

AcO_2 (1.0 ml). The mixtures were kept at ∿20°C for 20 h, then poured into MeOH (3 and 2 ml, respectively), and evaporated after 30 min. Compound (I) (525 mg: 94%) was obtained as a syrup which crystallized, R_f 0.8 (E) and (II) (180 mg: 91%) R_f 0.75. Compound (I) (430 mg) was obtained by crystallization from EtOH and had mp 122°C, $[\alpha]_D$ 26.5° (concn. 4.6, $CHCl_3$). Compound (II) (150 mg) was isolated by crystallization from MeOH and had mp 170°C, $[\alpha]_D$ −2.5° (concn. 1.2, $CHCl_3$). Found: (I), C 71.69; H 5.68; N 2.58%; (II), C 71.71; H 5.55; N 3.00%. $C_{29}H_{27}O_6N$. Calculated: C 71.74; H 5.57; N 2.88%.

Polycondensation of Monomers (I) and (II). Polycondensation of (I) (390 mg: 0.8 mmole) and (II) (300 mg: 0.6 mmole) in the presence of $TrClO_4$ (24 mg: 0.08 mmole and 18 mg: 0.06 mmole, respectively) was carried out according to [4] for 110 h. The reaction mixtures appeared on TLC plates as bands of R_f 0-0.8 (F) yellowing in appearance only at the front. A small quantity of MeOH (about 1 ml) was added to the reaction mixture and 0.5 h later pyridine (0.5 ml) was added. The mixture was kept a further 0.5 h, diluted with $CHCl_3$ (75 ml), washed with H_2O (25 ml × 3), dried, and evaporated. Residues were dissolved in a small quantity of $CHCl_3$ and precipitated with hexane. The solid was filtered off, washed with hexane, dried, and then dissolved in dry $CHCl_3$ (1.5 and 1.0 ml, respectively). Absolute MeOH (3 ml) and 1 N MeONa (1 ml) were added to the product from monomer (I) and MeOH (2 ml) and MeONa (0.7 ml) to the product from monomer (II). After stirring for 48 h at ∿20°C the mixtures were evaporated, Absorption bands at 1750 cm^{-1} were absent from the IR spectra of the dry residues.

The products of deacetylation of the sugars were dissolved in 0.1 M AcOH (1.5 ml) and chromatographed on Sephadex G-25 (column 72 × 13 cm, V_{tot} 72 ml, V_0 26 ml) in 0.1 M AcOH. Elution rate was 0.4 ml/min and fraction size ∿1.6 ml. Fractions were collected up to 59 and 63 ml, respectively. Two portions of substances were obtained, the first portions were the higher-molecular-weight portions of the products and were obtained from fractions up to the maximum of the gel chromatogram curve. For the polysaccharide from (I) product (34 mg: 30%) was obtained up to 49 ml having $[\alpha]_D$ +149° (concn. 0.85, H_2O) and 27 mg (24%). For the polysaccharide from (II) product (10 mg: 12%) was obtained up to 52 ml having $[\alpha]_D$ +123° (concn. 0.7, H_2O) and 26 mg (31%).

GLC Mass-Spectrometric Analysis of Polysaccharides. The high-molecular-weight fractions of both polysaccharides (34 and 10 mg, respectively) were methylated according to Hakomori, subjected to formolysis (85% HCOOH, 100°C, 2 h), then hydrolysis (0.13 M H_2SO_4, 100°C, 17 h), reduction with $NaBH_4$, and acetylation with AcO_2 and pyridine (17 h, 20°C). Investigation of the obtained products on the GLC/mass spectrometer showed that for the first polysaccharide polyols (VII) (mass spectrum m/z: 58, 101, 117, and 161) and (VIII) (mass spectrum m/z: 71, 87, 99, 101, 117, 129, 159, 161, and 189) were detected with a ratio of 1:10 and for the second polyols (VII) and (IX) (mass spectrum m/z: 85, 117, 127, 141, 147, 159, 173, 201, and 233) with a ratio of 1:7.

SUMMARY

The synthesis has been effected of 3-O-acetyl-4-O-trityl- and 4-O-acetyl-3-O-trityl-1,2-O-[(1-exo-cyano)ethylidene]-β-L-arabinopyranose by the polycondensation of which (1 → 4)-L-arabinopyranan and (1 → 3)-L-arabinopyranan were obtained containing 1,2-trans- and 1,2-cis-glycosidic bonds at a ratio ∿3:1.

LITERATURE CITED

1. N. K. Kochetkov, Izv. Akad. Nauk SSSR, Ser. Khim., 1543 (1982).
2. N. K. Kochetkov, Sov. Sci. Rev., Sect. B, Chemistry, 4, 1 (1982).
3. N. K. Kochetkov, N. N. Malysheva, and E. M. Klimov, Izv. Akad. Nauk SSSR, Ser. Khim., 1170 (1983).
4. N. K. Kochetkov and A. Ya. Ott, Izv. Akad. Nauk SSSR, Ser. Khim., 1177 (1983).
5. V. I. Betaneli, M. V. Ovchinnikov, L. V. Bakinovskii (Backinowsky), and N. K. Kochetkov, Carbohydr. Res., 68, C11 (1979).
6. Ya. V. Wozney and N. K. Kochetkov, Carbohydr. Res., 54, 303 (1977).
7. V. I. Betaneli, M. V. Ovchinnikov, L. V. Bakinovskii (Backinowski), and N. K. Kochetkov, Carbohydr. Res., 76, 252 (1979).
8. P. A. J. Gorin, Can. J. Chem., 52, 458 (1974).
9. S. J. Angyal, Angew. Chem., Intern. Ed., 8, 157 (1969).
10. P. E. Jansson, L. Kenne, H. Liedgren, B. Lindberg, and J. Lönngren, Chem. Commun. Univ. Stockholm, 8, 1 (1976).
11. N. K. Kochetkov, and N. N. Malysheva, Izv. Akad. Nauk SSSR, Ser. Khim., 196 (1981).