SYNTHESIS OF 5-AMINO-5-DEOXYPENTONOLACTAMS

Karel KEFURT[1], Zdenka KEFURTOVA, Vera MARKOVA and Karla SLIVOVA

Department of Natural Compounds, Prague Institute of Chemical Technology, 166 28 Prague 6, Czech Republic; e-mail: [1] karel.kefurt@vscht.cz

Received March 8, 1996
Accepted April 23, 1996

5-Azido-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose (**4**) and 5-azido-5-deoxy-1,2-*O*-isopropylidene-β-D-arabinofuranose (**10**) were prepared starting from D-xylose and D-arabinose, respectively. Using the oxidation-reduction way for the C-3 epimerization, 5-azido-5-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**15**) and 5-azido-5-deoxy-1,2-*O*-isopropylidene-β-D-lyxofuranose (**17**) were obtained from **4** and **10**, respectively. The derivatives **4**, **10**, **15** and **17** afforded by acid hydrolysis, oxidation with bromine and catalytic hydrogenation successively the corresponding 5-azido-5-deoxy-D-pentofuranoses **6**, **11**, **18**, **19**, 5-azido-5-deoxy-D-pentonolactones **7**, **12**, **20**, **21** and 5-amino-5-deoxy-D-pentonolactams **8**, **13**, **22**, **23**.

Key words: 5-Azido-5-deoxypentoses; 5-Amino-5-deoxypentonolactams; Synthesis.

Some time ago we prepared[1–3] and assembled the complete set of eight diastereoisomeric 6-amino-6-deoxyhexonolactams and their tetra-*O*-acetyl derivatives. Later, we studied structures of these seven-membered cyclic compounds by NMR, CD and IR spectroscopy[4,5] as well as by X-ray measurements[6–8]. Some non-answered questions, namely rised from the CD spectra measurements[4] demanded to perform similar studies also on analogical six-membered cyclic compounds, i.e. on 5-amino-5-deoxypentonolactams. From the four possible 5-amino-5-deoxy-D-pentonolactams only D-*ribo* diastereoisomer prepared from 5-azido-2,3-*O*-benzylidene-5-deoxy-β-D-ribofuranose[9,10] or 1,2-*O*-isopropylidene-D-ribono-1,4-lactone[11] is known until now (L-*arabino* diastereoisomer which was without any data mentioned in the patent[12] is not here considered). A different way, in comparison with the methods mentioned above[9–11], leading to D-*ribo* diastereoisomer and further three diastereoisomers, is presented in this paper.

As follows, our synthetic routes to all 5-amino-5-deoxy-D-pentonolactams employ corresponding 5-azido-5-deoxy-1,2-*O*-isopropylidene-α/β-D-pentofuranoses as advantageous key intermediates.

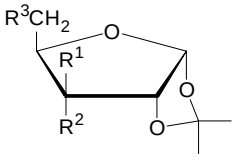
Partial tosylation of the readily accessible[13] 1,2-*O*-isopropylidene-α-D-xylofuranose (**1**) gave a mixture of 1,2-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-α-D-xylofuranose (**2**) and 1,2-*O*-isopropylidene-3,5-di-*O*-*p*-toluenesulfonyl-α-D-xylofuranose (**3**) in a ratio ca 7 : 1. This mixture was converted without separation to the corresponding 5-azido-derivatives by displacement reaction with sodium azide on C-5. Separation on silica gel

column afforded pure 5-azido-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose (**4**) and 5-azido-5-deoxy-1,2-*O*-isopropylidene-3-*O*-*p*-toluenesulfonyl-α-D-xylofuranose (**5**) in a ratio ca 6 : 1. Azide **4** exhibited consistent melting point, but reversed specific rotation by comparison with the data reported for **4** in literature[14,15]. Structures of **4** and **5** were also confirmed by elemental analysis and NMR spectra (Table I). Acid hydrolysis of **4** in the presence of Dowex 50 W (H^+) afforded syrupous 5-azido-5-deoxy-D-xylose (**6**) which was oxidized with bromine to give 5-azido-5-deoxy-D-xylono-1,4-lactone (**7**) in form of the colourless syrup. The assignment of the structure to **7** is based on the stretching frequencies of the carbonyl and azido groups in its IR spectrum, on elemental analysis and ^1H and ^{13}C NMR spectra. Hydrogenation of **7** produced desired 5-amino-5-deoxy-D-xylonolactam (**8**), possibly in the mixture with corresponding 5-amino-5-deoxy-D-xylonic acid (according to TLC). By crystallization from hot methanol crystalline lactam **8** was obtained, which exhibited characteristic bands of both hydroxy and amido groups in the IR spectra, proper elemental analysis and confirming NMR spectra. NMR spectra of all 5-amino-5-deoxy-D-pentonolactams and their derivatives will be in detail discussed in the next paper concerning conformation of a six-membered lactam ring.

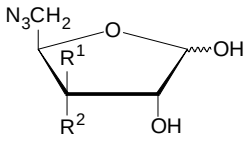
The diastereoisomeric D-*arabino* isomer was prepared in the similar manner. Reaction of 1,2-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-β-D-arabinofuranose[16] (**9**) with sodium azide in *N*,*N*-dimethylformamide afforded the corresponding 5-azido-5-deoxy-1,2-*O*-isopropylidene-β-D-arabinofuranose (**10**) in a form of slightly yellow syrup. Its IR and NMR spectra, as well as elemental analysis confirmed the structure **10** in agreement with formerly described compound **10** which was characterized[17] by its boiling point and IR spectra. Acid hydrolysis of the **10** in the presence of a cation-exchange resin afforded the free sugar, 5-azido-5-deoxy-D-arabinofuranose (**11**) as a colourless syrup with strongly positive specific rotation, confirming IR and NMR spectra and elemental analysis. Azide **11** was oxidized with bromine in water to give a syrupous 5-azido-5-deoxy-D-arabinono-1,4-lactone (**12**) whose structure confirmed its IR spectra and elemental analysis. By hydrogenation of **12** in methanol on Pd/C catalyst 5-amino-5-deoxy-D-arabinonolactam (**13**) was obtained with a trace of corresponding acid (according to TLC). Crystallization from methanol afforded solid lactam **13**, exhibiting strongly negative specific rotation, appropriate IR, NMR spectra and elemental analysis.

For the preparation of D-*ribo* and D-*lyxo* diastereoisomers of 5-azido-5-deoxy-1,2-*O*-isopropylidene-α/β-D-pentofuranose we used reversal of the configuration on C-3 of derivatives **4** and **10**, respectively, via their 3-furanosuloses. This way was already used for the corresponding 5-*O*-*p*-toluenesulfonyl derivatives[18]. 5-Azido-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose (**4**) was oxidized by ruthenium dioxide–sodium periodate way[19] to 5-azido-5-deoxy-1,2-*O*-isopropylidene-α-D-*erythro*-3-pentofuranosulose (**14**). The structure of **14** was confirmed by IR spectra exhibiting stretching absorption on 1 778 cm^{-1} (C=O), 2 112 cm^{-1} (azide), bending doublet on 1 386 and 1 378 cm^{-1} ($C(CH_3)_2$), and by

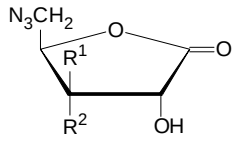
^{1}H and ^{13}C NMR spectra (Table I). Reduction of **14** with sodium borohydride in water–methanol afforded stereoselectively 5-azido-5-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**15**) isolated in crystalline state. Its IR spectrum exhibited stretching bands of hydroxy and azido groups. Further proofs of structure of **15** gave NMR spectra (Table I).



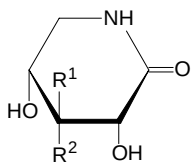
	R^1	R^2	R^3
1	OH	H	OH
2	OH	H	OTs
3	OTs	H	OTs
4	OH	H	N_3
5	OTs	H	N_3
14	O		N_3
15	H	OH	N_3



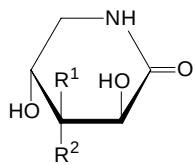
	R^1	R^2
6	OH	H
18	H	OH



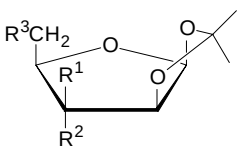
	R^1	R^2
7	OH	H
20	H	OH



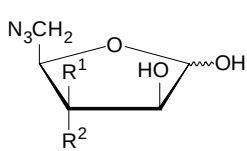
	R^1	R^2
8	OH	H
22	H	OH



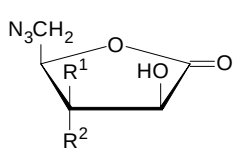
	R^1	R^2
13	H	OH
23	OH	H



	R^1	R^2	R^3
9	H	OH	OTs
10	H	OH	N_3
16	O		N_3
17	OH	H	N_3



	R^1	R^2
11	H	OH
19	OH	H



	R^1	R^2
12	H	OH
21	OH	H

TABLE I

Chemical shifts (δ-scale, ppm) and *J*(H,H) coupling constants (Hz) of the ^{1}H and ^{13}C nuclei of 1,2-*O*-isopropylidene derivatives **4, 5, 10, 14, 15–17** in $CDCl_3$

Parameter	Compound[a]						
	4	**5**	**10**	**14**	**15**	**16**	**17**
				Chemical shifts			
H-1	5.96 d	5.92 d	5.95 d	6.15 d	5.85 d	6.08 d	5.80 d
H-2	4.53 d	4.67 d	4.57 d	4.39 dd	4.59 dd	4.50 dd	4.68 dd
H-3	4.24 dd	4.78 d	4.22 d	–	3.93–3.88 m	–	4.32 ddd
H-4	4.29 ddd	4.29 ddd	4.10 ddd	4.51 ddd	3.93–3.88 m	4.33 dd	4.16 ddd
H-5	3.63 dd	3.54 dd	3.62 dd	3.69 dd	3.70 dd	3.61 dd	3.65 dd
H-5′	3.59 dd	3.24 dd	3.42 dd	3.55 dd	3.40 dd	3.55 dd	3.49 dd
H-O	2.61 d	–	3.21 s	–	2.39 d	–	2.68 d
C-1	104.8	104.8	105.8	103.1	104.7	102.8	105.1
C-2	85.4[b]	83.1[b]	86.8[b]	77.8[b]	80.1[b]	80.2[b]	81.1[b]
C-3	78.4[b]	81.7[b]	86.0[b]	208.2	79.1[b]	206.9	79.3[b]
C-4	75.2[b]	77.5[b]	76.3[b]	76.1[b]	72.8[b]	80.2[b]	69.9[b]
C-5	49.2	48.8	52.2	51.4	51.4	52.1	50.6
				Coupling constants (H,H)			
J(1,2)	3.7	3.7	3.9	4.4	3.8	4.3	4.2
J(2,3)	0	0	0	–	4.4	–	6.2
J(3,4)	2.8	2.8	2.2	–	–[c]	–	6.2
J(4,5)	6.1	7.3	7.3	3.2	2.4	6.3	8.4
J(4,5′)	5.9	5.7	6.1	3.3	4.1	4.0	4.8
J(5,5′)	–12.7	–12.7	–12.7	–13.2	–13.4	–13.3	–12.9
J(3,OH)	5.1	–	0	–	9.2	–	7.1
J(2,4)	–	–	–	~1	–	~0.6	–

[a] Other ^{1}H singlets in regions 1.47–1.57 ppm and 1.28–1.43 ppm, as well as ^{13}C signals in regions 112.6–115.1, 26.6–27.4 and 25.0–27.1 ppm were assigned to ^{1}H or ^{13}C nuclei of isopropylidene groups; [b] may be interchanged; [c] undeterminable valve.

Oxidation of 5-azido-5-deoxy-1,2-*O*-isopropylidene-β-D-arabinofuranose (**10**) was carried out with RuO_2–$NaIO_4$ reagent and also with pyridinium dichromate[3,20]. The obtained syrupous ketone, 5-azido-5-deoxy-1,2-*O*-isopropylidene-β-D-*threo*-3-pentofuranosulose (**16**) exhibited stretching bands at 1 776 cm^{-1} (C=O) and 2 108 cm^{-1} (azide) in IR spectra and confirming signals in NMR spectra (Table I). Raw ketone **16** was reduced in water–ethanol with sodium borohydride to 5-azido-5-deoxy-1,2-*O*-isopropylidene-β-D-lyxofuranose (**17**) which was obtained in crystalline state after purification by chromatography on silica gel. IR, ^1H and ^{13}C NMR spectra confirmed the assumed structure of **17** (Experimental and Table I).

Synthetic route from **15** and **17** to corresponding 5-amino-5-deoxy-D-ribono/lyxonolactams followed the usual procedure. Derivatives **15** and **17** were hydrolyzed to 5-azido-5-deoxy-D-ribofuranose (**18)** and 5-azido-5-deoxy-D-lyxofuranose (**19**), respectively. Both azidopentoses were obtained as homogeneous (TLC) colourless syrups with the proper IR data. Their oxidation with bromine in water afforded 5-azido-5-deoxy-D-ribonolactone (**20**) and 5-azido-5-deoxy-D-lyxonolactone (**21**), respectively. Crystalline lactone **20** as well as syrupous lactone **21** possessed expected bands and signals in IR and NMR spectra. Hydrogenolysis of azido group in **20** and **21** on Pd/C catalyst in methanol provided 5-amino-5-deoxy-D-ribonolactam (**22**) or 5-amino-5-deoxy-D-lyxonolactam (**23**), respectively, as major products in addition to minor 5-amino-5-deoxy-D-ribonic/lyxonic acid (TLC). Lactam **22** agreed in its m.p. and specific rotation with the described one[10]. Conclusively, structure of both lactams was confirmed also using IR and NMR spectra.

The above described synthetic route seems to be useful mainly in the case of preparation of all four diastereoisomers of 5-amino-5-deoxy-D-pentonolactam. Of course, more advantageous ways, including the quoted[10,11] syntheses of lactam **22**, could be found for the exclusive preparation of the certain single diastereoisomer.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured with an Opton photoelectric polarimeter at 20 °C. Reactions were monitored by TLC on silica gel G (Merck) using benzene–ethanol 20 : 1 (S1), benzene–acetone 1 : 1 (S2), chloroform–methanol 20 : 1 (S3), chloroform–methanol 10 : 1 (S4) and chloroform–methanol 5 : 1 (S5) mixtures for elution, and 1% solution of cerium(IV) sulfate in 10% H_2SO_4 for detection of the plates. Column chromatography was carried out on silica gel (100–200 μm, Lachema Brno). NMR spectra were recorded at 400 MHz (^1H) and 100 MHz (^{13}C) with a Bruker AM-400 instrument in deuteriochloroform, deuterium oxide or hexadeuterioacetone solutions with tetramethylsilane as internal reference. Chemical shifts are given in ppm (δ-scale) and coupling constants (*J*) in Hz. Assignments of ^{13}C signals are tentative and are based on APT experiments and on comparison with published data of structural analogs. IR spectra (wavenumbers in cm^{-1}) were measured with FT IR Nicolet 740 instrument in $CHCl_3$ solutions, KBr pellets or film, according to the state and solubility of measured matter.

1,2-*O*-Isopropylidene-5-*O*-*p*-toluenesulfonyl-α-D-xylofuranose (**2**) and 1,2-*O*-Isopropylidene-3,5-di-*O*-*p*-toluenesulfonyl-α-D-xylofuranose (**3**)

p-Toluenesulfonyl chloride (13.3 g, 70 mmol) was added during 1 h to the stirred solution of 1,2-*O*-isopropylidene-α-D-xylofuranose[13] (**1**; 12.4 g, 65 mmol) in pyridine (55 ml) at room temperature. Reaction was monitored by TLC in S2 (**1**: R_F 0.15, **2**: R_F 0.56, **3**: R_F 0.84). Relative intensity of spots of compounds **1**, **2** and **3** on TLC was constant after 2 h. Reaction mixture was poured into ice water (700 ml), crystalline product was filtered, washed and dried to obtain 19.1 g mixture **2** and **3** (TLC) in relation ca 7 : 1, according to specific rotation compared with the data[21,22] for pure compounds **2** and **3**. This mixture was used in the next step.

5-Azido-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose (**4**) and 5-Azido-5-deoxy-1,2-*O*-isopropylidene-3-*O*-*p*-toluenesulfonyl-α-D-xylofuranose (**5**)

A solution of the up described mixture of **2** and **3** (3.06 g) in *N*,*N*-dimethylformamide (30 ml) was stirred under nitrogen with water (1.7 ml), sodium azide (0.85 g, 13 mmol) and urea (0.07 g) for 20 h at 110 °C. Products **4** and **5** were distinguishable from the starting compounds **2** and **3** only according to yellow/brown colour change during carbonization of spots in the system S1 as well as in other tested systems. Reaction mixture was poured into ice water (40 ml), extracted with chloroform (3 × 50 ml) which was washed with cold solution of sodium bicarbonate and water and dried ($MgSO_4$). After filtration and evaporation of solvent 1.73 g mixture of **4** and **5** was obtained which was separated on silica gel column in system S1. Recrystallization of the product obtained by evaporation of combined fractions from chloroform–hexane 1 : 5 gave 1.2 g of **4**, m.p. 60 °C, $[\alpha]_D$ –42° (*c* 1.0, methanol). Literature[14,15] gives m.p. 58.5–60 °C, $[\alpha]_D$ +44° (*c* 1.0, methanol). NMR spectrum: see Table I. For $C_8H_{13}N_3O_4$ (215.2) calculated: 44.65% C, 6.09% H, 19.53% N; found: 44.83% C, 6.15% H, 19.65% N.

Syrupous 3-*O*-tosyl derivative **5** (0.28 g) showed $[\alpha]_D$ –8.6° (*c* 2.0, chloroform); NMR spectrum: see Table I. For $C_{15}H_{19}N_3O_6S$ (369.4) calculated: 48.77% C, 5.18% H, 11.38% N, 8.68% S; found: 48.80% C, 5.15% H, 11.11% N, 8.24% S.

5-Azido-5-deoxy-D-xylofuranose (**6**)

A solution of **4** (850 mg, 3.9 mmol) in water (7.5 ml) was stirred with Dowex 50 W (H^+, 100/200 mesh, 3.5 ml) for 45 min at 60 °C. TLC in system S4: **4**: R_F 0.68, **6**: R_F 0.2. Decolorization of filtrate, evaporation, and drying of residue afforded 653 mg (94%) syrupous azido pentose **6**, $[\alpha]_D$ +52° (*c* 1.0, water). IR spectrum (film): 3 372 broad (OH assoc.); 2 932 (CH); 2 108 (azide). For $C_5H_9N_3O_4$ (175.2) calculated: 34.29% C, 5.18% H, 23.99% N; found: 34.28% C, 5.51% H, 23.91% N.

5-Azido-5-deoxy-D-xylono-1,4-lactone (**7**)

A solution of **6** (490 mg, 2.8 mmol) in water (15 ml) was stirred with bromine (0.2 ml) and barium carbonate (1.8 g) for 1 h at 0 °C and than 2 h at room temperature. Oxidation was followed by TLC in system S5 (**6**: R_F 0.55, **7**: R_F 0.68). After filtration of insoluble salts and removal of the excess bromine with a stream of air, the colourless solution was stirred for 1 h with silver carbonate (2.5 g) and desalted on a column of Dowex 50 W (H^+ form, 10 ml). The combined filtrates on evaporation gave 437 mg (90%) colourless syrupous lactone **7**, $[\alpha]_D$ +50° (*c* 1.2, chloroform). IR spectrum (film): 3 378 broad (OH assoc.); 2 932 (CH); 2 116 (azide); 1 778 (C=O). ^{1}H NMR spectrum (D_2O): 4.67 d, 1 H, *J*(2,3) = 8.7 (H-2); 4.59 dd, 1 H, *J*(3,4) = 7.3 (H-3); 3.79 dd, 1 H, *J*(5,4) = 3.4, *J*(5,5′) = –13.9 (H-5); 3.73 dd, 1 H, *J*(5′,4) = 4.7 (H-5′). Signal of the H-4 (≈4.83 ppm) is overlapped by DOH. ^{13}C NMR spectrum (D_2O): 176.5 (C-1); 79.5, 73.6, 72.7 (C-2, C-3, C-4); 50.5 (C-5). For $C_5H_7N_3O_4$ (173.1) calculated: 34.69% C, 4.08% H, 24.27% N; found: 34.34% C, 4.50% H, 23.99% N.

5-Amino-5-deoxy-D-xylonolactam (**8**)

A solution of lactone **7** (1.11 g, 6.4 mmol) in methanol (50 ml) was stirred with 5% Pd/C (0.5 g) in a renewed hydrogen atmosphere. TLC in system S5 showed gradually disappearing spot of the starting **7** (R_F 0.68) and strengthening spot of lactam **8** (R_F 0.1) in addition to the slight spot of R_F 0 (possibly corresponding amino acid). Removal of the catalyst and evaporation of the solvent afforded 950 mg partially crystalline residue which was recrystallized from methanol to give 180 mg (19%) of **8**, m.p. 177–178 °C, $[\alpha]_D$ +6° (*c* 1.0, water). Further crystalline compound **8** (225 mg, 24%) was obtained after concentration of mother liquors. IR spectrum (KBr pellet): 3 600–3 200 broad (OH, NH assoc.); 2 952, 2 919 (CH); 1 684, 1 634 (CONH free, assoc.). For $C_5H_9NO_4$ (147.1) calculated: 40.82% C, 6.17% H, 9.52% N; found: 40.86% C, 6.27% H, 9.46% N.

5-Azido-5-deoxy-1,2-*O*-isopropylidene-β-D-arabinofuranose (**10**)

A mixture of 1,2-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-β-D-arabinofuranose[16] (**9**; 1.8 g, 5.2 mmol), sodium azide (0.43 g, 6.6 mmol) and urea (0.04 g) was stirred in *N*,*N*-dimethylformamide (12 ml) for 12 h at 110 °C. Solvent was evaporated and the residue was purified by chromatography on silica gel column in S4, affording 1.0 g (90%) of syrupous azido derivative **10**, $[\alpha]_D$ +56.6° (*c* 1.0, chloroform). IR spectrum (film): 3 450 broad (OH); 2 103 (azide); 1 378, 1 385 doublet ($C(CH_3)_2$). NMR spectrum: see Table I. For $C_8H_{13}N_3O_4$ calculated: 44.65% C, 6.02% H, 19.53% N; found: 44.23% C, 6.24% H, 19.20% N.

5-Azido-5-deoxy-D-arabinofuranose (**11**)

Solution of isopropylidene derivative **10** (0.86 g, 4 mmol) in water (7.5 ml) was stirred with Dowex 50 W (H^+, 7 ml) for 45 min at 60 °C. Course of hydrolysis was followed by TLC in S4 (**10**: R_F 0.66, **11**: R_F 0.25). The filtrate from ion exchanger was decolorized and after evaporation afforded 0.625 g (89%) of syrupous azido pentose **11**, $[\alpha]_D$ +159.2° (*c* 1.0, water). IR spectrum (film): 3 370 broad (OH); 2 932 (CH); 2 108 (azide). For $C_5H_9N_3O_4$ (175.2) calculated: 34.29% C, 5.18% H, 23.99% N; found: 34.28% C, 5.5 1% H, 23.86% N.

5-Azido-5-deoxy-D-arabinono-1,4-lactone (**12**)

Solution of azido pentose **11** (0.5 g, 2.86 mmol) in water (15 ml) was stirred with barium carbonate (1.8 g) and bromine (0.2 ml) for 2 h at 0 °C. Oxidation was followed by TLC in S5 (**11**: R_F 0.54, **12**: R_F 0.65). After similar treatment of reaction mixture as described for **6**, syrupous lactone **12**, $[\alpha]_D$ +98.4° (*c* 1.0, ethanol), was obtained (0.47 g, 95%). IR spectrum (film): 3 374 broad (OH); 2 933 (CH); 2 111 (azide); 1 765 (C=O). ^{1}H NMR spectrum (D_2O): 4.62 d, 1 H, J(2,3) = 9.2 (H-2); 4.44 m, 1 H, ΣJ = 16.1 (H-4); 4.27 dd, 1 H, J(3,4) = 8.6 (H-3); 3.87 dd, 1 H, J(5,4) = 2.5, J(5,5′) = –14.2 (H-5); 3.62 dd, 1 H, J(5′,4) = 5.3 (H-5′). ^{13}C NMR spectrum (D_2O): 176.4 (C-1); 80.3, 74.6, 74.4 (C-2, C-3, C-4); 51.1 (C-5). For $C_5H_7N_3O_4$ (173.1) calculated: 34.69% C, 4.08% H, 24.27% N; found: 34.45% C, 4.36% H, 23.62% N.

5-Amino-5-deoxy-D-arabinonolactam (**13**)

Azido lactone **12** (0.41 g, 2.3 mmol) was hydrogenated by the way described for **8**. Recrystallization of the crude product (0.34 g, 98%) from methanol afforded 0.14 g (40%) of lactam **13**, m.p. 178 °C, $[\alpha]_D$ –172° (*c* 1.0, water). IR spectrum (KBr pellet): 3 600–3 200 broad (OH, NH); 2 961, 2 906 (CH); 1 647 (CONH assoc.). For $C_5H_9NO_4$ (147.1) calculated: 40.82% C, 6.17% H, 9.52% N; found: 40.70% C, 6.35% H, 9.43% N.

5-Azido-5-deoxy-1,2-*O*-isopropylidene-α-D-*erythro*-3-pentofuranosulose (**14**)

Solution of sodium periodate (3.0 g, 14 mmol) in water (30 ml) was added dropwise to the stirred mixture of the derivative **4** (1.6 g, 7.4 mmol), ruthenium dioxide (0.145 g) and sodium carbonate (0.5 g) in tetrachloromethane (60 ml). Mixture of two liquid phases was shaked at room temperature for 8 h and followed by TLC in system S1 (**4**: R_F 0.28, **14**: R_F 0.45). Further sodium periodate (0.86 g) was added during this period. Superfluous ruthenium tetraoxide was finally decomposed by 2-propanol (1 ml), reaction mixture was diluted with water (10 ml) and extracted with chloroform (6 × 50 ml). Syrupous product **14** (1.12 g, 71%) was obtained after evaporation of the dried chloroform phase. IR spectrum (chloroform): 3 026, 2 996, 2 939 (CH); 2 112 (azide); 1 778 (C=O); 1 386, 1 378 doublet ($C(CH_3)_2$). NMR spectrum: see Table I.

5-Azido-5-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**15**)

Ketone **14** (2.1 g, 9.9 mmol) in mixture ethanol–water (95 ml, 9 : 1) was stirred at 0–5° C with sodium tetrahydridoborate (0.850 g, 22.4 mmol) for 3 h. Reduction was monitored by TLC in S1 (**14**: R_F 0.45, **15**: R_F 0.31). The excess of hydride was decomposed by acetic acid (1.0 ml), reaction mixture was evaporated and the residue extracted with ether (6 × 40 ml). Evaporating of the solution gave crystalline compound **15** (2.01 g, 95%), m.p. 50.5–51.5 °C (ether–light petroleum 1 : 2), $[\alpha]_D$ +65.5° (*c* 0.5, chloroform). IR spectrum (chloroform): 3 558 broad (OH); 3 024–2 938 (CH); 2 105 (azide); 1 384, 1 375 doublet ($C(CH_3)_2$). NMR spectrum: see Table I. For $C_8H_{13}N_3O_4$ (215.2) calculated: 44.65% C, 6.09% H, 19.53% N; found: 44.58% C, 6.29% H, 19.53% N.

5-Azido-5-deoxy-1,2-*O*-isopropylidene-β-D-*threo*-3-pentosulose (**16**)

A) Solution of 4.5 g (21 mmol) of sodium periodate in water (50 ml) was dropped to the stirred mixture of the derivative **10** (2.15 g, 10 mmol), sodium carbonate (1.2 g), ruthenium dioxide (0.12 g), tetrachloromethane (80 ml) and water (20 ml). Oxidation was monitored by TLC in S3 (**10**: R_F 0.50, **16**: R_F 0.59). Further portion of sodium periodate (2.1 g) was added in parts during 90 min always when the yellow-green soluble ruthenium tetraoxide was changed to the black insoluble ruthenium dioxide. Finally, the superfluous ruthenium tetraoxide was decomposed by 2-propanol (1 ml) and reaction mixture was extracted with chloroform (6 × 50 ml). Syrupous product **16** (1.4 g, 65%) was obtained by evaporation of the dried organic phase. IR spectrum (chloroform): 3 026, 2 996, 2 941 (CH); 2 108 (azide); 1 776 (C=O); 1 375, 1 384 doublet ($C(CH_3)_2$). NMR spectrum: see Table I.

B) Solution of acetic anhydride (1.7 ml) in dichloromethane (5 ml) was dropped to the mixture of derivative **10** (2.01 g, 9.4 mmol), pyridinium dichromate[20] (7.05 g, 18.8 mmol) and sodium acetate (1.92 g) stirred at room temperature in dichloromethane (120 ml). Reaction was monitored in S3. After 75 h, reaction mixture was filtered through a short column of silica gel and the remaining acetic anhydride was removed from filtrate by shaking with water solution of sodium bicarbonate. Evaporation of the dried dichloromethane phase afforded 1.92 g (96%) of syrupous pentosulose **16**, conforming in IR spectra with the compound prepared by the way *A*.

5-Azido-5-deoxy-1,2-*O*-isopropylidene-β-D-lyxofuranose (**17**)

Ketone **16** (345 mg, 1.62 mmol) in mixture ethanol–water (12 ml, 10 : 2) was stirred at 0–5 °C with sodium tetrahydridoborate (110 mg, 2.92 mmol) for 3 h. Reduction was monitored by TLC in S1 (**16**: R_F 0.54, **17**: R_F 0.07). Excessing hydride was destroyed with acetic acid (0.1 ml) to the pH 6.5, reaction mixture was evaporated and the residue was extracted with ether. Evaporating of the ether solution gave 308 mg (88%) colourless crystalline compound **17**, m.p. 48–49 °C (ether–light petroleum 1 : 1), $[\alpha]_D$ +45° (*c* 1.3, $CHCl_3$). IR spectrum (chloroform): 3 534 broad (OH); 3 024, 2 997, 2 943

(CH); 2 105 (azide); 1 386, 1 378 doublet ($C(CH_3)_2$). NMR spectrum: see Table I. For $C_8H_{13}N_3O_4$ (215.2) calculated: 44.65% C, 6.02% H, 19.53% N; found: 44.37% C, 6.16% H, 19.32% N.

5-Azido-5-deoxy-D-ribofuranose (**18**)

By way of hydrolysis used for azido pentoses **6** or **11**, isopropylidene derivative **15** (0.84 g, 3.9 mmol) afforded azido pentose **18** (0.61 g, 88%) in syrupous form, $[\alpha]_D$ +105° (*c* 1.2, water). For $C_5H_9N_3O_4$ (175.2) calculated: 34.29% C, 5.18% H, 23.99% N; found: 34.51% C, 5.17% H, 23.72% N.

5-Azido-5-deoxy-D-lyxofuranose (**19**)

By the up described way used for hydrolyses of **4**, **10** or **15**, isopropylidene derivative **17** (1.01 g, 4.7 mmol) afforded azidopentose **19** (0.72 g, 87%) in syrupous form, $[\alpha]_D$ +13° (*c* 0.4, water). IR spectrum (film): 3 308 broad (OH); 2 926 (CH); 2 099 (azide). For $C_5H_9N_3O_4$ (175.2) calculated: 34.29% C, 5.18% H, 23.99% N; found: 34.35% C, 5.31% H, 23.80% N.

5-Azido-5-deoxy-D-ribono-1,4-lactone (**20**)

By way described for preparation of lactones **7** or **12,** pentose **18** (1 g, 5.7 mmol) afforded 0.78 g (79%) lactone **20**, m.p. 81–82 °C (ethanol–light petroleum), $[\alpha]_D$ +96.8° (*c* 0.8, ethanol). IR spectrum (KBr pellet): 3 451–3 330 broad (OH); 2 118 (azide); 1 765 (C=O). ^{1}H NMR spectrum (D_2O): 4.81 d, 1 H, *J*(2,3) = 5.6 (H-2); 4.68 dd, 1 H, *J* = 9 (H-4); 4.42 d, 1 H, *J*(3,2) = 5.5 (H-3); 3.79 dd, 1 H, *J*(5,4) = 3.6, *J*(5,5′) = –13.7 (H-5); 3.72 dd, 1 H, *J*(5′,4) = 5.5 (H-5′). ^{13}C NMR spectrum (hexadeuterioacetone): 176.2 (C-1); 84.2, 71.2, 70.0 (C-2, C-3, C-4); 53.1 (C-5). For $C_5H_7N_3O_4$ (173.1) calculated: 34.69% C, 4.08% H, 24.27% N; found: 34.34% C, 4.09% H, 23.95% N.

5-Azido-5-deoxy-D-lyxono-1,4-lactone (**21**)

By way used for preparation of the up described lactones, pentose **19** (0.72 g, 4.1 mmol) afforded 0.71 g (99%) of syrupous lactone **21,** $[\alpha]_D$ +41° (*c* 0.3, ethanol). IR spectrum (film): 3 456 broad (OH); 2 941 (CH); 2 106 (azide); 1 776 (C=O). ^{1}H NMR spectrum (D_2O): 4.76 d, 1 H, *J*(2,3) = 4.8 (H-2); 4.70 ddd, 1 H, Σ*J* = 15.6 (H-4); 4.56 dd, 1 H, *J*(3,4) = 2.9 (H-3); 3.74 dd, 1 H, *J*(5,4) = 7.5, *J*(5,5′) = –13.6 (H-5); 3.69 dd, 1 H, *J*(5′,4) = 5.0 (H-5′). For $C_5H_7N_3O_4$ (173.1) calculated: 34.69% C, 4.08% H, 24.27% N; found: 34.33% C, 4.28% H, 23.81% N.

5-Amino-5-deoxy-D-ribonolactam (**22**)

By way described for hydrogenolysis of the azido lactones **7** or **12**, lactone **20** (0.7 g, 4.1 mmol) afforded lactam **22** (0.3 g, 50%), m.p. 244–250 °C (decomp.), $[\alpha]_D$ +33.6° (*c* 0.5, water). IR spectrum (KBr pellet): 3 600–3 200 broad (OH, NH); 2 921 (CH); 1 641 (CONH assoc.). Refs[9,10] give for lactam **22** m.p. above 240 °C (decomp.), $[\alpha]_D$ +33° (*c* 0.3, water). For $C_5H_9NO_4$ (147.1) calculated: 40.82% C, 6.17% H, 9.52% N; found: 40.55% C, 6.28% H, 9.32% N.

5-Amino-5-deoxy-D-lyxonolactam (**23**)

By way used for preparation of the up described lactams, lactone **21** (0.7 g, 4 mmol) afforded 586 mg (100%) of the crude lactam **23**. Foam product crystallized from methanol (10 ml) provided pure compound **23** (240 mg, 41%), m.p. 188–189 °C (decomp.), $[\alpha]_D$ –54.7° (*c* 1.0, water). IR spectrum (KBr pellet): 3 600–3 170 broad (OH, NH); 2 925, 2 884 (CH); 1 677, 1 634 (CONH free, assoc.). For $C_5H_9NO_4$ (147.1) calculated: 40.82% C, 6.17% H, 9.52% N; found: 40.61% C, 6.41% H, 9.23% N.

The authors are indebted to members of Laboratory of NMR Spectroscopy (Dr R. Hrabal, Head), Laboratory of Infrared Spectroscopy (Dr M. Novotna, Head) and Laboratory of Organic Analysis (Dr L. Helesic, Head) of the Prague Institute of Chemical Technology for careful spectral measurements and analyses.

REFERENCES

1. Kefurt K., Capek K., Kefurtova Z., Jary J.: Collect. Czech. Chem. Commun. *44*, 2526 (1979).
2. Kefurt K., Capek K., Kefurtova Z., Jary J.: Collect. Czech. Chem. Commun. *51*, 391 (1986).
3. Kefurt K., Kefurtova Z., Jary J.: Collect. Czech. Chem. Commun. *53*, 1795 (1988).
4. Kefurt K., Kefurtova Z., Trska P., Blaha K., Fric I., Jary J.: Collect. Czech. Chem. Commun. *54*, 2156 (1989).
5. Havlicek J., Kefurt K., Volka K., Ksandr Z.: Vibrational Spectrosc. *3*, 139 (1992).
6. Ondracek J., Novotny J., Kefurt K., Havlicek J.: Acta Crystallogr., C *48*, 929 (1992).
7. Ondracek J., Havlicek J., Kefurt K., Jary J., Novotny J., Kratochvil B.: Collect. Czech. Chem. Commun. *57*, 2367 (1992).
8. Havlicek J., Kefurt K., Husak M., Novotny J., Kratochvil B.: Collect. Czech. Chem. Commun. *58*, 1600 (1993).
9. Hanessian S., Haskell T. H.: J. Heterocycl. Chem. *1*, 55 (1964).
10. Hanessian S.: J. Org. Chem. *34*, 675 (1969).
11. Herdeis C., Waibel D.: Arch. Pharm. *324*, 269 (1991).
12. Gibson W. T.: Eur. Pat. Appl. 334586 (1989); Chem. Abstr. *113*, 11926 (1991).
13. Moravcova J., Capkova J., Stanek J.: Carbohydr. Res**.** *263***,** 61 (1994).
14. Szarek W. A., Jones J. K. N.: Can. J. Chem. *43*, 2345 (1965).
15. *Beilstein's Handbook of Organic Chemistry*, Fifth Suppl. Series, Vol. 19/9, p. 308.
16. Levene P. A., Compton J.: J. Biol. Chem. *116*, 189 (1936).
17. Hanessian S.: J. Org. Chem. *32*, 163 (1967).
18. Defaye J., Horton D., Muesser M.: Carbohydr. Res. *20*, 305 (1971).
19. Parikh V. M., Jones J. K. N.: Can. J. Chem. *43*, 3452 (1965).
20. Corey E. J., Schmidt G.: Tetrahedron Lett. *1979*, 399.
21. Levene P. A., Raymond A. L.: J. Biol. Chem. *102*, 317 (1933).
22. Karrer P., Boettcher A.: Helv. Chim. Acta *36*, 837 (1953).