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Note

Direct transformation of D-idose and D-altrose with potassium cyanate into cyclic carbamates of derived glycosylamines

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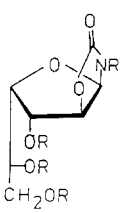
The reaction of aldoses with potassium cyanate in water in the presence of weakly acidic buffers (NH_4Cl, NaH_2PO_4) yields 1,2-*cis*-(cyclic carbamates) [*N,O*-carbonyl derivatives] of glycosylamines [1,2]. We now report these transformations for D-idose and D-altrose, thus completing our studies in the series of hexoses.

The reaction of D-idose, prepared in situ [3] from 1-deoxy-1-nitro-D-iditol [4], with potassium cyanate (1.5 mol) in the presence of sodium dihydrogen phosphate (2 mol) at 60°C was complete within 2 h (pH 6.5 → 7.5) and gave β-D-idofuranosylamine 1,2-(cyclic carbamate) (**1**) in 60% yield. No identifiable by-products were observed.



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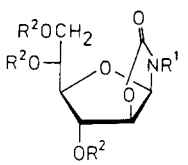
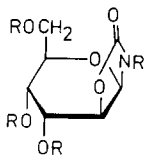
2 R = Ac



3 $R^1 = R^2 = H$

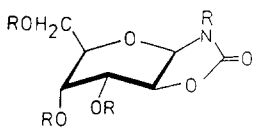
4 $R^1 = R^2 = Ac$

5 $R^1 = H$, $R^2 = Ac$



6 R = H

7 R = Ac



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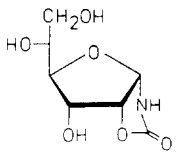
Treatment of **1** with hot acetic anhydride and sodium acetate gave the *N*-acetyl-tri-*O*-acetyl derivative **2**. Both **1** and **2** were identified by comparison of their NMR spectra with those of the corresponding L enantiomers [2] obtained as by-product from the analogous reaction of L-gulose.

Unlike D-idose, transformation of D-altrose under the same conditions gave a mixture of three isomeric cyclic carbamates besides unreacted D-altrose, which was present even after prolonged times of reaction. The mixture of products was separated by column chromatography into two fractions: an inseparable mixture (54%) of 1-*N*,2-*O*-carbonyl-β-D-altrofuranosylamine (**3**) and its β-D-pyranoid analogue **6** in the ratio of 7:2 (NMR data), and 1-*N*,2-*O*-carbonyl-α-D-allofuranosylamine (**8**, 2%) [2].



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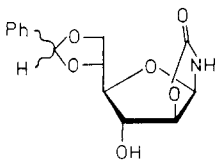
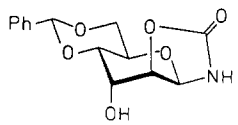


9a, b



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Although compounds **3** and **6** could not be separated even by HPLC, their structures were elucidated by the ^{1}H and ^{13}C NMR spectra of a solution of the mixture in D_2O (Tables 1 and 2). The assignments of the carbon signals were corroborated by $^{1}H/^{13}C$-correlated NMR spectra (2D-COSY) with the exception of the very close signals of C-1 and C-2 (δ 80.61 and 80.54) for **6**. The signal for C-1 in **3** appeared at significantly lower field (δ 87.60, furanoid system) than that for **6** (δ 80.61 or 80.54, pyranoid system), in agreement with the ^{13}C NMR data [5] of aldofuranoses and aldopyranoses and those of the analogous cyclic carbamates [1,2,6]. The β-D-altrofuranose configura-

Table 1
^{1}H NMR data [a] for the cyclic carbamates

Compound	Chemical shifts (δ)						
	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b
1	5.745	4.883	4.238	3.796	3.832	3.587	3.477
3	5.904	5.056	4.611	4.007	3.594	3.760	3.607
6	5.432	4.676	4.101	3.921	3.75 –3.81		3.686
8	5.742	5.069	4.293	3.830	4.000	3.711	3.632
	Coupling constants (Hz)						
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
1	5.5	0	2.5	7.7	3.2	5.7	−12.1
3	5.7	~0	~1	8.4	3.0	6.2	−11.85
6	4.9	5.7	3.15	4.35		6.4	−12.1
8	5.4	5.6	9.15	3.35	3.8	7.2	−11.9

[a] Recorded at 500 MHz for solutions in D_2O.

Table 2
^{13}C NMR data [a] for the cyclic carbamates

Compound	Chemical shifts (δ)						
	C-1	C-2	C-3	C-4	C-5	C-6	NCOO
1	85.97 [b]	85.86 [b]	73.10	79.71	70.50	62.82	160.27
3	87.60	87.00	75.15	86.26	71.19	63.02	159.79
6	80.61 [b]	80.54 [b]	68.77	67.75	77.14	62.14	160.79
8	85.64	80.32	70.17	78.20	70.91	62.40	160.64

[a] Recorded at 125.8 MHz for solutions in D_2O. [b] Assignments may have to be interchanged.

tion of **3** was deduced from the very small values of $J_{2,3}$ (~ 0 Hz) and $J_{3,4}$ (~ 1 Hz) indicative of the *trans* dispositions of H-2,3 and H-3,4 as found for analogous systems with the β-L-arabinofuranose and α-D-galactofuranose configurations [1]. On the other hand, medium $^3J_{H,H}$ values for **6** accord with neither the $^1C_4$ nor the $^4C_1$ conformation of the pyranoid ring and strongly indicate a conformation near $^{O,3}B$, permitting maximum distances between the substituents. In other related cases [2,6] heavily distorted pyranoid rings were observed.

Treatment of the mixture of **3** and **6** with hot acetic anhydride and sodium acetate furnished the corresponding tetra-*N*,*O*-acetyl derivatives **4** and **7**, respectively, which could be separated by column chromatography. During the separation the main component **4** was partially *N*-deacetylated, affording the triacetate **5**. NMR spectra of the acetylated derivatives (Tables 3 and 4) corroborated the structures of **3** and **6**. In agreement with the furanoid structure of **3** acetylation caused small downfield shifts (0.237 and 0.196 ppm, respectively) of the resonance for H-4, but significant shifts (1.524 and 1.558 ppm, respectively) of the resonances for H-5 in the spectra of **4** and **5**. In contrast, the resonance of H-4 was shifted downfield by 1.383 ppm, but that of H-5 underwent only a small shift (0.27 ppm) in the conversion of **6** into **7** in accordance with the pyranoid system (Tables 1 and 3). The $^3J_{H,H}$ coupling constants from the ^1H NMR spectrum of **7** (Table 3) suggest either an $^{O,3}B$ or another related, strongly distorted conformation of the pyranoid ring.

In order to establish a rigid conformation of the pyranoid ring, the mixture of **3** and **6** was benzylidenated [7] by treatment with benzaldehyde dimethyl acetal in the presence of catalytic amounts of *p*-toluenesulfonic acid. The furanoid 5,6-*O*-benzylidene derivatives **9a** and **9b**, as main components, were separated by column chromatography from the pyranoid 4,6-*O*-benzylidene compound **10**. All benzylidenated cyclic carbamates were characterised by their ^1H and ^{13}C NMR spectra (Tables 3 and 4). However, a decision between the diastereomers of structure **9a,b** could not be made. According to the $^3J_{H,H}$ coupling constants the pyranoid compound **10** adopts a regular $^4C_1$ conformation, due to the fixation by the 4,6-*O*-benzylidene protecting group.

These results are in accord with our observation [2] that the outcome of the reaction of aldoses with potassium cyanate is controlled by the relative configuration at C-2 and C-4 of the parent sugar. If C-2 and C-4 have the same relative configuration, the reaction affords only one furanose derivative (e.g., **1** from D-idose). This is stereochemically favourable because the oxazolidine ring and the large substituent at C-4 are on

Table 3
^{1}H NMR data [a] for the protected cyclic carbamates

Compound	Chemical shifts (δ)							
	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	Others
2 [b]	6.307	4.846	5.420	4.367	5.322	4.374	4.019	2.545 (NAc), 2.160, 2.099, 2.056 (OAc)
4 [b]	6.276	4.893	5.432	4.244	5.073	4.419	3.986	2.508 (NAc), 2.115, 2.082, 2.010 (OAc)
5 [b]	5.794	4.956	5.387	4.203	5.107	4.404	4.148	6.888 (NH), 2.101, 2.096, 2.038 (OAc)
7 [b]	5.910	4.604	5.371	5.304	4.050	4.388	4.174	2.536 (NAc), 2.125, 2.097, 2.092 (OAc)
9a [c]	5.703	4.796	4.289	3.822	3.954	4.049	3.986	8.814 (NH), 5.758(2) (HO-3, PhC*H*), 7.38–7.42(3), 7.45–7.48(2) (Ph)
9b [c]	5.702	4.807	4.301	3.98–4.07		4.202	3.851	8.796 (NH), 5.776 (HO-3), 5.914 (PhC*H*), 7.37–7.43(4), 7.45–7.49(1) (Ph)
10 [c]	5.230	4.330	4.218	3.730	3.866	4.192	3.637	8.727 (NH), 5.704 (PhC*H*), 5.696 (HO-3) 7.34–7.37(3), 7.44–7.47(2) (Ph)
	Coupling constants (Hz)							
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	$J_{3,HO-3}$
2 [b]	5.6	0.9	3.8	6.8	3.8	5.7	−12.2	
4 [b]	5.7	0	2.05	6.55	3.8	5.75	−12.2	
5 [b]	5.7	0	1.9	7.3	3.3	5.15	−12.2	
7 [b]	4.8	6.25	2.9	2.5	3.8	2.85	−12.1	
9a [c]	5.5	0	1.5	8.5	6.7	4.4	−8.0	4.5
9b [c]	5.6	0			5.9	6.0	−8.5	4.4
10 [c]	3.3	2.5	3.0	9.4	5.5	10.2	−10.3	

[a] Recorded at 500 MHz. [b] For solutions in $CDCl_3$. [c] For solutions in $(CD_3)_2SO$.

Table 4
^{13}C NMR data [a] for the protected derivatives of cyclic carbamates

Compound	Chemical shifts (δ)							
	C-1	C-2	C-3	C-4	C-5	C-6	NCOO	Others
2 [b]	85.29	80.13	77.11	74.67	68.99	62.26	151.74	170.32, 169.66, 169.45, 169.31 (COO,CON), 23.64 (*Me*CON), 20.92, 20.57(2) (*Me*COO)
4 [b]	86.68	83.81	76.23	81.39	70.06	62.25	151.29	170.17, 169.79, 169.37, 169.22 (COO,CON), 23.38 (*Me*CON), 20.51(2), 20.44 (*Me*COO)
5 [b]	87.14	84.30	76.92	82.87	70.05	62.35	156.50	170.54, 170.11, 169.37 (COO), 20.58, 20.55(2) (*Me*COO)
7 [b]	79.60	75.07	69.38	68.40	74.51	63.30	151.99	170.51, 169.39, 169.23, 168.92 (COO,CON), 23.42 (*Me*CON), 20.59, 20.53(2) (*Me*COO)
9a [c]	86.68	86.49	75.16	85.73	74.93	67.66	156.75	136.96, 129.34, 128.15(2), 126.77(2) (Ph), 103.74 (Ph*C*H)
9b [c]	86.59	85.95	75.36	85.77	75.13	67.87	156.81	137.72, 129.16, 128.20(2), 126.43(2) (Ph), 103.21 (Ph*C*H)
10 [c]	78.90	78.78	63.14	75.77	59.17	68.00	157.90	137.66, 128.73, 127.87(2), 126.29(2) (Ph), 100.72 (Ph*C*H)

[a] Recorded at 125.8 MHz. Assignments are tentative only.
[b] For solutions in $CDCl_3$.
[c] For solutions in $(CD_3)_2SO$.

opposite sides of the furanoid ring. On the other hand, opposite relative configurations of C-2 and C-4 in the aldoses involve the formation of a mixture of isomeric cyclic carbamates (*e.g.*, **3**, **6**, **8** from D-altrose). In these cases the furanoid 1,2-*cis*-carbamates derived from the parent sugar are sterically more crowded because of steric hindrance of the oxazolidine moiety and the side chain at C-4, thus giving a chance for the formation of other isomers, including even those involving epimerisation at C-2.

1. Experimental

General methods.—TLC was performed on Silica Gel F_{254} (Merck) with *A*, 7:2:1 EtOAc–EtOH–H_2O; *B*, 9:1 $CHCl_3$–acetone; *C*, 4:1 $CHCl_3$–acetone; and *D*, 1:1 toluene–EtOAc; and detection by charring with H_2SO_4. Silica gel (230–400 mesh) was used for column chromatography and dry-column flash chromatography [8]. HPLC was carried out with a Knauer 64 apparatus using a column (500 × 8 mm) of LiChrosorb RP-18, 5 μm (Merck) and H_2O as eluent. Optical rotations were measured with a Zeiss Polamat A polarimeter at 25°C and IR spectra with a Nicolet 205 FT spectrometer. A Bruker AMXR-500 spectrometer was used to obtain ^1H NMR spectra [solutions in D_2O, internal HOD; solutions in $CDCl_3$ and $(CD_3)_2SO$, internal Me_4Si] at 500 MHz and ^{13}C NMR spectra [solutions in D_2O, internal acetone; solutions in $CDCl_3$ and $(CD_3)_2SO$, internal Me_4Si] at 125.8 MHz.

Aldosylamine 1,2-(cyclic carbamates).—To a solution of the aldose (5 mmol) in water (7 mL) were added potassium cyanate (0.61 g, 7.5 mmol) and $NaH_2PO_4 \cdot H_2O$ (1.38 g, 10 mmol), and the mixture was heated at 60°C until in the TLC no more changes were observed (2 to 6 h, pH 6.5 → 7.5). The solution was then concentrated together with silica gel (3 g) and the residue was dried by the evaporation of toluene. Separation of the products was performed by dry-column flash chromatography [8] by repeated elution with solvent *A* (18 mL) from a short column (70 × 30 mm) and, if necessary, by column chromatography.

Acetylation of the cyclic carbamates.—A mixture of the cyclic carbamate (1 mmol) and anhyd NaOAc (0.25 g, 3 mmol) in Ac_2O (3 mL) was boiled under reflux for 1.5 h, then poured into ice–water and extracted with $CHCl_3$. The extract was dried and concentrated, then the residue was purified by column chromatography (solvent *B*).

Benzylidenation of the cyclic carbamates [7].—To a solution of the cyclic carbamate (1 mmol) in *N*,*N*-dimethylformamide (3 mL) were added benzaldehyde dimethyl acetal (0.25 g, 1.6 mmol) and *p*-toluenesulfonic acid (2 mg), and the mixture was heated to 55°C on a rotary evaporator in vacuo for 3 h, while the solvent was removed. The residue was treated with aq 3% $NaHCO_3$ (10 mL) and extracted with $CHCl_3$ (20 mL). The combined organic phase was washed with aq $NaHCO_3$, then dried with Na_2SO_4, concentrated, and purified by column chromatography.

β-D-Idofuranosylamine 1,2-(cyclic carbamate) (**1**, *1*-N,*2*-O-*carbonyl*-*β*-D-*idofuranosylamine).*—An aqueous solution (18 mL) of D-idose freshly prepared [3] from 1-deoxy-1-nitro-D-iditol semihydrate [4] (2.7 g, 12.3 mmol) was treated with potassium cyanate according to the general procedure for 2 h. TLC (solvent *A*) then showed one main product (R_f 0.55) but no starting sugar. Work-up with dry-column flash chromatography (solvent *A*) afforded first a negligible multicomponent mixture (51 mg, R_f 0.65

–0.75), then **1** (1.50 g, 60%) as a syrup; R_f 0.55 (solvent *A*); $[\alpha]_D$ +12° (*c* 2.6, H_2O); ν_{max}^{MeOH} 1760 cm^{-1} (C = O). Anal. Calcd for $C_7H_{11}NO_6$: C, 40.98; H, 5.40; N, 6.83. Found: C, 40.83; H, 5.72; N, 6.85.

The tetra-acetyl derivative (**2**, 67%) of **1** was a syrup; R_f 0.35 (solvent *B*); $[\alpha]_D$ −41° (*c* 3.4, $CHCl_3$) {lit.[2] for the L enantiomer: $[\alpha]_D$ +45° (*c* 1, $CHCl_3$)}. Anal. Calcd for $C_{15}H_{19}NO_{10}$: C, 48.26; H, 5.13; N, 3.75. Found: C, 48.17; H, 5.10; N, 3.61.

Reaction of D-*altrose with potassium cyanate.*—Reaction of D-altrose (0.90 g, 5 mmol) for 6.5 h by the general procedure gave (TLC) a complex mixture that contained products with R_f 0.65 and 0.4 together with D-altrose, R_f 0.3 (solvent *A*). Column chromatography (solvent *A*) gave, first, an inseparable mixture (554 mg, 54%) of 1-*N*,2-*O*-carbonyl-β-D-altrofuranosylamine (**3**) and 1-*N*,2-*O*-carbonyl-β-D-altropyranosylamine (**6**) in the ratio 7:2 (NMR); R_f 0.65 (solvent *A*); $[\alpha]_D$ −10° (*c* 2, H_2O); ν_{max}^{MeOH} 1763 cm^{-1} (C = O). Attempts to separate **3** and **6** by HPLC failed.

Eluted second was 1-*N*,2-*O*-carbonyl-α-D-allofuranosylamine (**8**; 20 mg, 2%); syrup; R_f 0.4 (solvent *A*); $[\alpha]_D$ +61° (*c* 1.2, H_2O), identical (NMR) with an authentic sample {lit. [2] $[\alpha]_D$ +62° (*c* 1.9, H_2O)}.

Eluted third was D-altrose (198 mg, 22%); R_f 0.3 (solvent *A*); identified by ^{13}C NMR spectroscopy [5].

Acetylation of the first fraction (**3** + **6**) furnished (TLC) a mixture of the corresponding tetra-acetyl derivatives **4** and **7**, R_f 0.35 and 0.4, respectively (solvent *B*). Column chromatography (solvent *B*) gave, first, **7** (13%); syrup; R_f 0.4; $[\alpha]_D$ −52° (*c* 1.8, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 1803 (carbamate C = O), 1750 (OAc), 1720 cm^{-1} (NAc). Anal. Calcd for $C_{15}H_{19}NO_{10}$: C, 48.26; H, 5.13; N, 3.75. Found: C, 48.60; H, 5.54; N, 3.71.

Eluted second was **4** (29%); syrup; R_f 0.35; $[\alpha]_D$ −73° (*c* 1.3, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 1804 (carbamate C = O), 1751 (OAc), 1720 cm^{-1} (NAc). Anal. Found: C, 48.42; H, 5.39; N, 3.58.

Eluted third (solvent *C*) was the triacetate **5** (34%); R_f 0.25 (solvent *C*); mp 109°C (from EtOH); $[\alpha]_D$ −37° (*c* 2, $CHCl_3$); ν_{max}^{KBr} 1803 (carbamate C = O), 1750, 1738 cm^{-1} (OAc). Anal. Calcd for $C_{13}H_{17}NO_9$: C, 47.13; H, 5.17; N, 4.23. Found: C, 46.82; H, 5.18; N, 4.25.

Reacetylation of **5** gave **4** (89%); syrup; R_f 0.35 (solvent *B*), identical with the product described above.

Benzylidenation of the mixture of **3** and **6** afforded (TLC) a mixture of the corresponding acetals **9** (R_f 0.10–0.15, 2 spots) and **10** (R_f 0.35), respectively (solvent *D*). Column chromatography (solvent *D*) gave, first, 4,6-*O*-benzylidene-β-D-altropyranosylamine 1,2-(cyclic carbamate) (**10**, 17%); R_f 0.35; mp 187°C (from $CHCl_3$); $[\alpha]_D$ −37° (*c* 1.4, EtOAc); ν_{max}^{KBr} 1778 cm^{-1} (C = O). Anal. Calcd for $C_{14}H_{15}NO_6$: C, 57.34; H, 5.16; N, 4.78. Found: C, 57.70; H, 5.29; N, 4.70.

Eluted second was a chromatographically pure 5,6-*O*-benzylidene-β-D-altrofuranosylamine 1,2-(cyclic carbamate) (**9a**, 12%); R_f 0.15 (solvent *D*), mp 102–103°C (from $CHCl_3$–hexane); $[\alpha]_D$ −48° (*c* 1.1, EtOAc); ν_{max}^{KBr} 1753, 1739 cm^{-1} (C = O). Anal. Found: C, 57.62; H, 5.33; N, 4.59.

Eluted third was a mixture of diastereomers **9a** and **9b** (27%); syrup; R_f 0.10–0.15 (solvent *D*).

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