Aminosugars. XXIII. L-Idofuranose Derivatives Containing a Heterocycle at *C*-5,6 Position[1]

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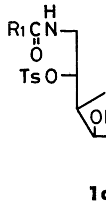
2-Aryl-(5*S*)- and -(4*S*)-(3′-*O*-benzyl- and 3′-*O*-methyl-1′,2′-*O*-isopropylidene-α-D-xylo-tetrofuranos-4′-yl)-2-oxazolines (**3** and **7**) were prepared from 6-aroylamido-6-deoxy-5-*O*-tosyl-D-glucofuranose and 5,6-aroylepimino-5,6-dideoxy-L-idofuranose derivatives, respectively. The corresponding 2-thioxo-(4*R*)- and -(5*S*)-thiazolidine derivatives (**11** and **13**) were also synthesized from 5,6-dideoxy-5,6-epimino-L-idofuranose and 6-azido-6-deoxy 5-*O*-tosyl-D-glucofuranose derivatives, respectively. 2-S-Methylated derivatives of **11** and **13** were reduced with aluminum amalgam to give the corresponding (4*R*)- and (5*S*)-thiazolidine derivatives, respectively. Formation of an intramolecular hemiaminal ring in **11** gave a new type of bicyclic derivatives; (5*S*,6*R*,8*R*)-triacetoxy-(7*S*)-substituted-2-thioxo-(8a*R*)-perhydropyrido[1,2-*c*]thiazole (**16a** and **16b**). The structure of new compounds was examined by NMR spectroscopy.

Although carbohydrate derivatives having fused heterocyclic rings at *C*-1,2 or *C*-2,3 position have been extensively studied,[2] those having a heterocycle at *C*-5,6 position have been scarcely reported, excepting oxazoline,[3,4] isoxazoline,[5] aziridine,[6,7] and triazole derivatives.[8] We have recently communicated syntheses of some isomeric pairs of L-idofuranose derivatives having 2-oxazoline or 2-thioxo-thiazolidine ring at *C*-5,6 position.[9] In this paper, syntheses of these derivatives which can be considered as a kind of reversed *C*-glycoside[5] will be reported in detail.

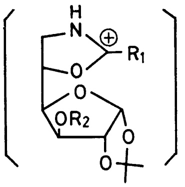
Results and Discussion

2-Phenyl-(5*S*)-(1′,2′-*O*-isopropylidene-α-D-xylo-tetrofuranos-4′-yl)-2-oxazoline was already synthesized in 50% yield by treatment of 6-benzamido-6-deoxy-5-*O*-tosyl-1,2-*O*-isopropylidene-α-D-glucofuranose with excess sodium acetate in 96% ethanol.[3] Similar treatment of the corresponding 3-*O*-benzyl derivative (**1a**) gave the corresponding oxazoline derivative (**3a**) in 52% yield, together with the corresponding hydrolyzed product; 6-benzamido-3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose (**4a**) in 19% yield. In general, **3** and **4** would be formed by deprotonation or hydrolysis of intermediate carbonium cation (**2**), respectively.[10] To avoid the hydrolysis process the above conversion was tried in an anhydrous condition. When the solution of **1a** and anhydrous sodium acetate in absolute dimethylformamide was refluxed overnight, only **3a** was obtained in 87% yield. In the same manner, the corresponding 2-anisyl derivative (**3b**), and 2-phenyl-(5*S*)-(1′,2′-*O*-isopropylidene-3′-*O*-methyl-α-D-xylo-tetrofuranos-4′-yl)-2-oxazoline (**3c**) were also prepared in good yields from the corresponding 6-aroylamido-6-deoxy derivatives, without isolation of **1b** and **1c**. The compound **1c** was prepared from 1,2-*O*-isopropylidene-3-*O*-methyl-6-*O*-tosyl-α-D-glucofuranose[11] through the corresponding 6-azido, 6-amino, and 6-benzamido derivatives successively.

Moreover, isomeric (4*S*)-2-oxazolines (**7**) were prepared by the isomerization of the corresponding 5,6-aroylepimino derivatives by treatment with sodium iodide in acetone.[12] 3-*O*-Benzyl-5,6-dideoxy-5,6-epimino-1,2-*O*-isopropylidene-β-L-idofuranose (**5**),[7] which was prepared by an improved method, was treated with equimolar amount of aroyl chloride in absolute benzene in the presence of excess triethylamine to give the 5,6-aroylepimino derivatives (**6a**,**b**,**d**) in good yields. The corresponding 3-*O*-methyl derivative (**6c**) was prepared in the same procedure, in which the 5,6-epimino derivative was obtained from the corresponding 6-azido-6-deoxy-5-*O*-tosyl or -5-*O*-mesyl derivative. Refluxing of a solution of **6** and excess amount of sodium iodide in absolute acetone overnight, followed by purification of the product by preparative tlc or by recrystallization gave the corresponding 2-aryl-(4*S*)-(3′-*O*-substituted-1′,2′-*O*-isopropylidene-α-D-xylo-tetrofuranos-4′-yl)-2-oxazolines (**7a**—**d**) in 40—96% yields. Physical constants of **6** and **7** are summarized in Table 1.



1a



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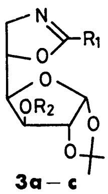
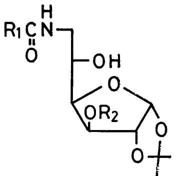
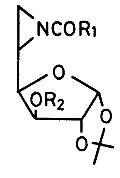


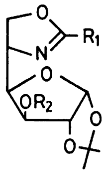
3a—c



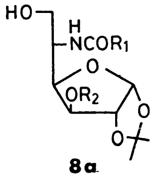
4a



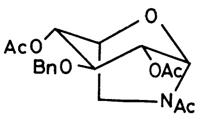
6a—d



7a—d



8a



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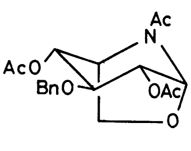

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a: R_1=phenyl, R_2=benzyl
b: R_1=anisyl, R_2=benzyl
c: R_1=phenyl, R_2=methyl
d: R_1=*p*-nitrophenyl, R_2=benzyl

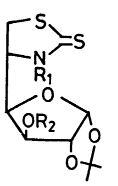
Because these oxazoline rings in **3** and **7** are labile to acid, both **3a** and **7a** were easily hydrolyzed to the corresponding benzamido derivatives (**4a** and **8a**) in

Table 1. Physical constants of compounds **6** and **7**

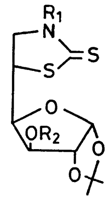
Compound	Mp (°C)	Yield (%)	$[\alpha]_D^{20}$ CHCl$_3$	Molecular formula	Anals. (Calcd) C%	H%	N%	IR[a] (cm^{-1})
6a	97—98	90	−67.4°	$C_{23}H_{25}NO_5$	69.94(69.85)	6.38(6.37)	3.48(3.54)	1670
6b	sirup	91	−55.3°	$C_{24}H_{27}NO_6$	67.98(67.75)	6.37(6.40)	3.20(3.29)	1660
6c	118—119	13	−90.3°	$C_{17}H_{21}NO_5$	64.26(63.93)	6.75(6.63)	4.50(4.39)	1670
6d	123—124	99	−51.8°	$C_{23}H_{24}N_2O_7$	62.89(62.72)	5.55(5.49)	6.27(6.36)	1670
7a	sirup	86	−44.3°	$C_{23}H_{25}NO_5$	69.31(69.85)	6.41(6.37)	3.38(3.54)	1640
7b	sirup	86	−51.0°	$C_{24}H_{27}NO_6$	67.85(67.75)	6.59(6.40)	3.19(3.29)	1640
7c	sirup	40	+1.3°	$C_{17}H_{21}NO_5$	64.21(63.93)	6.49(6.63)	4.15(4.39)	1640
7d	193—194	96	−50.3°	$C_{23}H_{24}N_2O_7$	62.74(62.72)	5.50(5.49)	6.41(6.36)	1640

a) The characteristic absorptions of **6** and **7** indicate that of the amide and C=N bond, respectively.

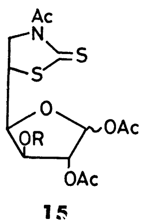
48% and 88% yields, respectively, by treatment with 80% acetic acid for two days at 30—40 °C. Conversion of **4a** into the corresponding bicyclic N,O-acetal (**9**)[13] was easily performed by successive de-N-benzoylation, de-isopropylidenation, and N,O-acetylation. To avoid the conversion into the corresponding pyridine derivatives,[13] N-benzoyl group of **8a** was previously converted into N-acetyl group, and successive de-isopropylidenation and O-acetylation gave successfully the desired N,O-acetal (**10**).



		R1	R2
11	**a**	H	Benzyl
	b	H	Methyl
12		Ac	Benzyl



		R1	R2
13	**a**	H	Benzyl
	b	H	Methyl
14		Ac	Benzyl



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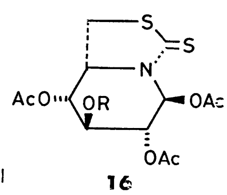
R
a Benzyl
b Methyl



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On the other hand, aziridines are known to give 2-thioxo-thiazolidines by treatment with carbon disulfide.[14] Thus, **5** was treated with carbon disulfide in a sealed tube at 98 °C for 6 hr to give crystalline 2-thioxo-(4R)-(3′-O-benzyl-1′,2′-O-isopropylidene-α-D-xylo-tetrofuranos-4′-yl)-thiazolidine (**11a**) in 84% yield. Crystalline 3′-O-methyl derivative (**11b**) was analogously obtained in 40% yield. Presence of characteristic absorptions at 3260 cm^{-1} (NH) and at 1470 cm^{-1} (NC=S) in IR spectrum supported the formation of 2-thioxo-thiazolidine ring. The structure was also confirmed by the comparison of the NMR spectrum of **11a** with that of N-acetylated derivative (**12**). N-Acetylation of **11a** caused a remarkable lower shift (1.43 ppm) of H_4 and a higher shift (0.68 ppm) of one of H_5-proton signals (*cf.* Table 2), depending on the acetylation shift[15] and the anisotropic effect of N-acetyl group, respectively. For the preparation of isomeric 2-thioxo-(5S)-thiazolidine derivatives, the synthetic procedure from a sulfate of β-aminoalcohols and carbon disulfide[16,17] was modified. Refluxing of a solution of 6-amino-3-O-benzyl-6-deoxy-5-O-tosyl-1,2-O-isopropylidene-α-D-glucofuranose,[7] large excess carbon disulfide, and two equimolar potassium hydroxide in ethanol for 2.5 hr gave 2-thioxo-(5S)-(3′-O-benzyl-1′,2′-O-isopropylidene-α-D-xylo-tetrofuranos-4′-yl)-thiazolidine (**13a**) in 98% yield. The corresponding 3′-O-methyl derivative (**13b**) was also obtained in 89% yield. Although the acetylation effect could not be clearly observed in the NMR spectrum of the corresponding N-acetate (**14**), IR spectrum and elemental analyses supported the structure of **13**. NMR parameters of typical examples of L-idofuranose derivatives having a heterocycle at C-5,6 position shown in Table 2 indicate that both the heterocyclic ring and the twist furanose ($^3T_2$) ring are generally in the *trans*-conformation with regard to the C_4–C_5 bond axis of the sugar chain, as was deduced in the isoxazoline derivatives.[5]

Hydrolysis of the isopropylidene group of **13** with 70% acetic acid at 90 °C for 5 hr and successive acetylation of the product gave a yellow sirup (**15**). Presence of one N-acetyl and two O-acetyl groups in NMR spectra, and an amide (1690 cm^{-1}) and an ester (1750 cm^{-1}) absorptions in IR spectra indicated the structure to be 3-N-acetyl-2-thioxo-(5S)-(1′,2′-di-O-acetyl-3′-O-benzyl- and -3′-O-methyl-α,β-D-xylo-tetrofuranos-4′-yl)-thiazolidine (**15a** and **15b**), respectively. While, analogous conversions of **11a** and **11b** gave crystalline and sirupy products (**16a** and **16b**), respectively, which showed no absorption of an amide. Chemical shifts and coupling constants in NMR spectrum of **16a** (Table 3) indicated that the conformation of the sugar moiety of these compounds is entirely different from those of ordinary D-xylofuranoses (Table 2). Since many long range couplings caused by the W-letter rule[18] were observed, ring protons; H_1, H_2, H_3, and H_4 should be in equatorial position (1C conformation of a pyranose ring). The values of $J_{1,4}$, $J_{1,3}$, and $J_{2,4}$ (0.5, 1.5, and 1.0 Hz) were consistent with the values of $J_{1,4}$ and $J_{1,3}$ (0.7 and 1.3 Hz) in the α-gulopyranose pentaacetate system reported by Lemieux.[19] Remarkable lower chemical shift of H_1 will be attributed to the large anisotropic effect of thiocarbonyl group of 2-thioxo-thiazolidine ring.[20] Thus **16a** and **16b** were determined to be a new class of bicyclic sugar derivatives; (5S,6R,8R)-triacetoxy-(7S)-benzyloxy- and -(7S)-

Table 2. NMR parameters of some L-idofuranose derivatives having a heterocycle at C-5,6 position

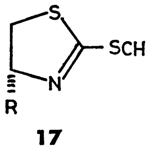
Compound	H_1	H_2	H_3	H_4	H_5	H_6	$H_{6'}$[a]
3a	6.06(d)	4.64(d)	4.00(d)	4.30(q)	4.90(m)	4.00(q)	3.51(q)
	$J_{1,2}=3.75$		$J_{3,4}=3.75$	$J_{4,5}=8.5$	$J_{5,6}=10.0$	$J_{5,6'}=8.75$	$J_{6,6'}=15.0$
3c	6.02(d)	4.60(d)	3.79(d)	4.32(q)	4.90(m)	4.20(q)	3.25(q)
	$J_{1,2}=3.75$		$J_{3,4}=3.75$	$J_{4,5}=8.75$	$J_{5,6}=10.0$	$J_{5,6'}=8.75$	$J_{6,6'}=15.0$
4c	6.05(d)	4.16(d)	3.95(d)	4.25(q)	4.73(q)	4.38(t)	4.15(t)
	$J_{1,2}=3.75$		$J_{3,4}=3.75$	$J_{4,5}=8.5$	$J_{5,6}=J_{5,6'}=J_{6,6'}=8.75$		
11a	5.97(d)	4.65(d)	3.96(d)	4.22(q)	4.40(m)	3.30(q)	3.18(q)
	$J_{1,2}=3.75$		$J_{3,4}=3.75$	$J_{4,5}=6.25$	$J_{5,6}=8.75$	$J_{5,6'}=7.5$	$J_{6,6'}=11.3$
12	5.95(d)	4.65(d)	3.96(d)	4.62(q)	5.83(q)	3.36(q)	2.50(d)
	$J_{1,2}=3.75$		$J_{3,4}=3.75$	$J_{4,5}=9.5$	$J_{5,6}=8.0$	$J_{5,6'}=0$	$J_{6,6'}=12.0$
17	6.01(d)	4.64(d)	3.94(d)	4.30(q)	4.73(q)	3.27(q)	3.05(q)
	$J_{1,2}=4.0$		$J_{3,4}=3.8$	$J_{4,5}=J_{5,6}=J_{5,6'}=9.5$			$J_{6,6'}=10.5$

a) The numbering of hydrogens indicates that of the carbon chain of L-idose.

Table 3. NMR parameters of compounds **16a** and **16b**

Compound	H_1	H_2	H_3	H_4	H_5	H_6	$H_{6'}$[a]
16a	7.09(m)	5.27(m)	3.90(m)	5.13(m)	4.92(sex)	3.35(q)	3.28(q)
	$J_{1,2}=2.0$	$J_{2,3}=3.0$	$J_{3,4}=3.0$	$J_{4,5}=2.5$	$J_{5,6}=9.0$	$J_{6,6'}=11.0$	
	$J_{1,3}=1.5$	$J_{2,4}=1.0$			$J_{5,6'}=9.0$		
	$J_{1,4}=0.5$						
16b	7.08(m)	5.20(m)	3.13(m)	5.18(m)	4.85(m)		ca. 3.3(m)

a) The numbering of hydrogens indicates that of the carbon chain of L-idose.



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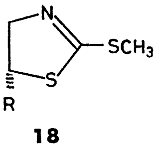

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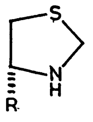

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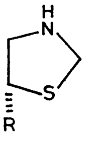

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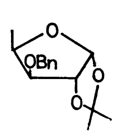

methoxy-3-thioxo-(8aR)-perhydropyrido[1,2-c]thiazole, respectively.

Conversion of **11a** and **13a** into the corresponding 2-methylthio-2-thiazoline derivatives (**17** and **18**) was easily performed by successive treatment with equimolar sodium hydride and slight excess methyl iodide under the nitrogen atmosphere. Furthermore, reduction of **17** and **18** with aluminum amalgam[21)] gave the corresponding thiazolidine derivatives (**19** and **20**) in good yields.

Because of unexpectedly stable character of heterocycles in **17**—**20**, a few attempts to synthesize S,N-analogues of **9** and **10** gave negative results, and it is still under investigation.

Experimental

All melting points were determined with Yanaco micro melting point apparatus and not corrected. The solutions were evaporated under reduced pressure at a bath temperature not exceeding 45 °C. Optical rotations were measured in a 0.5-dm tube with a Carl Zeiss LEP-A1 Polarimeter, using chloroform as a solvent unless otherwise stated. IR spectra were recorded with a Hitachi Model EPI-GS grating spectrometer. NMR spectra were taken with JEOL 4H-100 spectrometer in deuteriochloroform containing tetramethylsilane as an internal reference. Chemical shifts and coupling constants were recorded in δ and Hz units, and IR frequencies in cm^{-1}.

*6-Benzamido-3-O-benzyl-6-deoxy-1,2-O-isopropylidene-5-O-p-toluenesulfonyl-α-D-glucofuranose (**1a**).* Benzoylation of 6-amino-3-O-benzyl-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose[7)] in methanol with benzoic anhydride gave the corresponding 6-benzamide which was recrystallized from ethanol–n-hexane. Yield, 92%, mp 94—95.5 °C, $[\alpha]_{22}^{D}$ $-22.5°$ (c 0.89), IR: 3400 (NH and OH), 1640 and 1520 (amide).

Found: C, 66.38; H, 6.53; N, 3.34%. Calcd for $C_{23}H_{27}NO_6$: C, 66.81; H, 6.58; N, 3.39%.

A solution of 6-benzamide (0.84 g) and p-toluenesulfonyl chloride (0.47 g) in pyridine(4 ml) was kept for two days at room temperature, poured into ice-water, and a sirup deposited was extracted with chloroform. Treatment of the extract in a usual manner gave a sirupy product which was purified with a silica gel column, using benzene–ethyl acetate (4 : 1) as an eluent. Yield, 0.96 g (83%), $[\alpha]_D^{22}$ $-35.2°$ (c 0.95), IR: 3350 (NH), 1640 and 1520 (amide), 1360 (sulfate).

Found: C, 64.04; H, 5.97; N, 2.23%. Calcd for $C_{30}H_{33}NO_8S$: C, 63.48; H, 5.86; N, 2.47%.

*2-Aroyl-(5S)-(3′-O-benzyl-1′,2′-O-isopropylidene-α-D-xylo-tetrofuranos-4′-yl)-2-oxazoline (**3**). i) 2-Phenyl Derivative (**3a**).* (a) A solution of **1a** (220 mg) and anhydrous sodium acetate (200 mg) in 96% ethanol (10 ml) was refluxed for 20 hr, and evaporated. The residue was extracted with chloroform, after the addition of a small amount of water, and the organic layer was washed with 5% sodium chloride, dried, and evaporated to give a sirup. This sirup showed two components (R_f=0.40 and 0.11) on tlc (benzene : ethyl acetate=4 : 1 in v/v), which were separated on a preparative tlc. The both fractions gave a sirupy **3a** and crystalline **4a** in 52.5% and 19% yields, respectively.

3a: $[\alpha]_D^{22}$ −97.6° (*c* 0.68), IR: 1640 (C=N).

Found: C, 70.03; H, 6.45; N, 3.58%. Calcd for $C_{23}H_{25}NO_5$: C, 69.85; H, 6.37; N, 3.54%.

4a: mp 175 °C, $[\alpha]_D^{22}$ −62.2° (*c* 0.81), IR: 3440 and 3340 (OH and NH), 1630 and 1530 (amide).

Found: C, 66.83; H, 6.58; N, 3.28%. Calcd for $C_{23}H_{27}NO_6$: C, 66.81; H, 6.58; N, 3.39%.

(b) A suspension of **1a** (410 mg) and anhydrous sodium acetate (600 mg) in dry dimethylformamide (20 ml) was treated as above to give **3a** in 87.5% (290 mg) yield, which was identical with the authentic sirup in IR spectrum.

ii) 2-Anisyl Derivative (**3b**): Acylation of 6-amino-3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose[7] with anisoyl chloride in pyridine in a usual manner gave the corresponding 6-anisamide in 77% yield. Mp 147—147.5 °C, $[\alpha]^{22}$ −24.2° (*c* 1.05), IR: 3460 and 3340 (OH and NH), 1620 and 1530 (amide).

Found: C, 64.92; H, 6.66; N, 3.27%. Calcd for $C_{24}H_{29}NO_7$: C, 65.00; H, 6.59; N, 3.16%.

A solution of the above 6-anisamide (400 mg) and *p*-toluenesulfonyl chloride (250 mg) in pyridine (2 ml) was kept at room temperature overnight, poured into ice-water, and extracted with chloroform. The extract was treated in a usual manner to give a sirupy 5-Otosylate (**1b**, 560 mg). The sirup was dried over phosphorus pentoxide, and treated with anhydrous sodium acetate (770 mg) in DMF in the same procedure as above to give sirupy **3b** in 69% (320 mg) yield. $[\alpha]_D^{22}$ −83.0° (*c* 0.90), IR: 1640 (C=N).

Found: C, 67.70; H, 6.42; N, 3.24%. Calcd for $C_{24}H_{27}NO_6$: C, 67.75; H, 6.40; N, 3.29%.

2-Phenyl-(5S)-(1′,2′-O-isopropylidene-3′-O-methyl-α-D-xylo-tetrofuranos-4′-yl)-2-oxazoline (**3c**). Treatment of 1,2-*O*-isopropylidene-3-*O*-methyl-6-*O*-tosyl-α-D-glucofuranose[11] with sodium azide in a usual manner gave the corresponding azide in 71% yield as a sirup. Reduction of the azide in the presence of Raney-nickel, and acylation of the resulted amine with benzoic anhydride in a usual manner gave the corresponding 6-benzamide as a sirup, which was purified on a silica gel column using benzene–ethyl acetate (4 : 1 in v/v) as an eluent. Yield, 72%; $[\alpha]_D^{22}$ −25.2° (*c* 1.17), IR: 3350 (OH and NH), 1630 and 1530 (amide).

Found: C, 60.72; H, 6.95; N, 4.00%. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15%.

Tosylation of the above sirup (530 mg) in a usual manner gave 6-benzamido-6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-*O*-tosyl-α-D-glucofuranose (**1c**, 590 mg) as a sirup. Isomerization of **1c** as before, and fractionation of the product on a silicagel column gave pure **3c** in 28% yield. $[\alpha]_D^{22}$ −75.1° (*c* 0.94). IR: 1640 (C=N).

Found: C, 63.83; H, 6.60; N, 4.26%. Calcd for $C_{17}H_{21}NO_5$: C, 63.93; H, 6.63; N, 4.39%.

3-O-Benzyl-5,6-dideoxy-5,6-epimino-1,2-O-isopropylidene-β-L-idofuranose (**5**). A suspension of 3-*O*-benzyl-5,6-di-*O*-mesyl-1,2-*O*-isopropylidene-α-D-glucofuranose[22] (2.33 g) and sodium azide (1 g) in DMF (50 ml) was heated at 90—100 °C for one hr, poured into cold 5% sodium chloride after cooling, and extracted with ether. The extract was washed with 5% sodium chloride, dried, and evaporated to give a sirupy product (92%). Crystallization and recrystallization of the sirup from ethanol gave 6-azido-3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-5-*O*-mesyl-α-D-glucofuranose as prisms of mp 79.5—80.5 °C. $[\alpha]_D^{22}$ −39.0° (*c* 1.26), IR: 2100 (N_3), 1340 (sulfate), NMR: 1.29 and 1.48 (2x C–CH_3), 3.03 (SO_3CH_3), 3.60 ($H_{6'}$; q, $J_{6,6'}$=13.8, $J_{5,6'}$=10.5), 3.83 (H_6; q, $J_{5,6}$=3.1), 4.09 (H_3; d, $J_{3,4}$=3.7), 4.37 (H_4; q, $J_{4,5}$=7.75), 4.58 (H_2; d, $J_{1,2}$=3.75), 4.60 (CH_2; s), 5.13 (H_5; m), 5.86 (H_1; d), 7.35 (Ph; s).

Found: C, 49.66; H, 5.52; N, 10.08; S, 7.93%. Calcd for $C_{17}H_{23}N_3O_7S$: C, 49.39; H, 5.61; N, 10.17; S, 7.75%.

To an ice-coled solution of the above 6-azido-5-*O*-mesyl derivative (8.39 g) in dry ether (130 ml) was added lithium aluminum hydride (1.67 g) with stirring portionwise, and the mixture was stirred for one hr at room temperature, excess hydride was decomposed by adding a small volume of water, and filtered. The filtrate was evaporated to give a half crystalline mass (5.21 g, 84%), which melts at 93—94 °C (lit,[7] mp 91—94 °C, 69%), after recrystallization from benzene-*n*-hexane.

5,6-Dideoxy-5,5-epimino-1,2-O-isopropylidene-3-O-methyl-β-L-idofuranose. Treatment of 6-azido-6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose, mentioned in the preparation of **3c**, with excess *p*-tosyl chloride or methanesulfonyl chloride in the usual manner gave crystalline 5-*O*-sulfates in 90% and 99% yields, respectively.

5-*O*-Tosylate: mp 134—135 °C, $[\alpha]_D^{22}$ −53.6° (*c* 1.01).

Found: C, 49.54; H, 5.61; N, 9.60%. Calcd for $C_{17}H_{23}N_3O_7S$: C, 49.39; H, 5.60; N, 10.16%.

5-*O*-Mesylate: mp 79—80 °C, $[\alpha]_D^{22}$ −49.8° (*c* 0.98).

Found: C, 39.62; H, 5.72; N, 11.98; S, 9.69%. Calcd for $C_{11}H_{19}N_3O_7S$: C, 39.16; H, 5.68; N, 12.46; S, 9.51%.

Treatment of the above 5-*O*-tosylate or 5-*O*-mesylate in THF with lithium aluminum hydride in the same manner as **5** gave the 5,6-epimino derivative as a sirup in *ca.* 90% yield, which showed no absorption of azide. This sirup was used for preparation of **6c** and **12b** without further identification.

General procedure for preparation of 5,6-Aroylimino-5,6-dideoxy-1,2-O-isopropylidene-3-O-substituted-β-L-idofuranose (**6a-d**). To a solution of **5** or its 3-*O*-methyl derivative and excess triethylamine in dry benzene was added equimolar amount of aroyl chloride, and the precipitate was filtered off, after stirring the reaction mixture for 1—2 hr at room temperature. Evaporation of the filtrate gave the crude product, which was purified by recrystallization or by fractionation with a silica gel column chromatography.

General procedure for preparation of 2-aroyl-(4S)-(1′,2′-O-isopropylidene-3′-O-substituted-α-D-xyol-tetrofuranos-4′-yl)-2-oxazoline (**7a-d**). A solution of **6a-d** (140 mg) and dried sodium iodide (1 g) in dry acetone (5 ml) was refluxed for 15—24 hr, evaporated, and the residue was extracted with chloroform. The extract was washed with 5% sodium chloride, and evaporated to give the product, which was purified by recrystallization, by a preparative tlc, or by a silica gel column chromatography.

Ring-opening of oxazoline derivatives (**3a** *and* **7a**). A solution of **7a** (700 mg) in 80% acetic acid (40 ml) was heated at 30—36 °C for 2 days, evaporated, and the residue was triturated with ethanol to give crude crystals, which were recrystallized from ethanol to give needles of 5-benzamido-3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose (**8a**) in 48% (350 mg) yield. Mp 161—162 °C, $[\alpha]_D^{22}$ −9.4° (*c* 1.0), IR: 3460 and 3330 (OH and NH), 1620 and 1530 (amide).

Found: C, 66.80; H, 6.57; N, 3.40%. Calcd for $C_{23}H_{27}NO_6$: C, 66.81; H, 6.58; N, 3.39%.

In a similar way, **3a** was converted into **4a** in 88% yield, which was identical with that mentioned before.

*1,6-Acetylimino-3-*O*-benzyl-6-deoxy-2,4-di-*O*-acetyl-β-L-idopyranose (**9**).* A suspension of **4a** (130 mg) and potassium hydroxide (800 mg) in 90% ethanol (8 ml) was refluxed for 2 days, poured into ice-water, and extracted with chloroform. The extract was washed with 5% sodium chloride, and evaporated to give de-*N*-benzoylated sirup (80 mg). A solution of the sirup in 2*N*-sulfuric acid (30 ml) was heated at 70—80 °C for 4 hr, neutralized with barium carbonate, and then filtered after the addition of methanol. The filtrate was evaporated, and the residue was dried over phosphorus pentoxide, acetylated with acetic anhydride in a usual manner to give a sirup (30 mg), which was crystallized from ethanol. Yield, 12.5% (15 mg), mp 148—149 °C, $[\alpha]^{22}_{\mathrm{D}}$ $-12.9°$ (*c* 0.52), IR: 1740 (ester), 1640 (amide).

Found: C, 60.30; H, 6.08; N, 3.57%. Calcd for $C_{19}H_{23}NO_7$: C, 60.47; H, 6.14; N, 3.71%.

N*-Acetyl-1,6-anhydro-3-*O*-benzyl-5-deoxy-2,4-di-*O*-acetyl-β-L-idopiperidinose (**10**).* A solution of **8a** (250 mg) and potassium hydroxide (2.5 g) in 80% ethanol was refluxed overnight, and then extracted with methylene chloride in a usual manner to give the corresponding 6-amino derivative (70 mg), which was acetylated with acetic anhydride (0.2 g) and triethylamine (0.3 g) in methanol (3 ml) by the procedure reported by Paulson *et al.*[21] to give a sirup. The *N*-acetyl derivative was hydrolyzed with 0.05 M-sulfuric acid (30 ml) at 70 °C for 1 hr, and the dried product obtained by evaporation of the reaction mixture was again acetylated in a usual manner to give a sirup (120 mg) which was purified by a preparative tlc. Yield, 26% (60 mg), $[\alpha]^{22}_{\mathrm{D}}$ $+40.8°$ (*c* 0.85), IR: 1740 (ester), 1660 (amide).

Found: C, 59.85; H, 6.40; N, 3.84%. Calcd for $C_{19}H_{23}NO_7$: C, 60.47; H, 6.14; N, 3.71%.

*2-Thioxo-(4*R*)-(1′,2′-*O*-isopropylidene-3′-*O*-substituted-α-D-xylo-tetrofuranos-4′-yl)-thiazolidine (**11**).* *i) 3′-*O*-Benzyl derivative (**11a**).* A mixture of **5** (1.75 g) and carbon disulfide (5 ml) was sealed in a Pyrex glass at −70 °C, and kept with occasional shaking at room temperature for 1 hr and at 98 °C for 6 hr. The tube was opened at −70 °C, and the content was evaporated to give a sirup which was purified on a silica gel column, using benzene–ethyl acetate (9 : 1) as an eluent, to give crystals in 84% yield. Mp 140—141 °C, $[\alpha]^{22}_{\mathrm{D}}$ $-32.1°$ (*c* 0.87), IR: 3250 (NH), 1469 (NHCS).

Found: C, 55.52; H, 5.76; N, 3.73; S, 17.17%. Calcd for $C_{17}H_{21}NO_4S_2$: C, 55.55; H, 5.76; N, 3.81; S, 17.45%.

*ii) 3′-*O*-Methyl derivative (**11b**).* 5,6-Dideoxy-5,6-epimino-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-idofuranose (0.52 g) described before was treated with carbon disulfide (2.5 ml) in the same manner as above to give crystals in 40% (280 mg) yield. Mp 195—196 °C, $[\alpha]^{22}_{\mathrm{D}}$ $-29.6°$ (*c* 0.75), IR: 3220 (NH), 1470 (NHCS).

Found: C, 45.44; H, 5.83; N, 4.70; S, 21.91%. Calcd for $C_{11}H_{17}NO_4S_2$: C, 45.34; H, 5.88; N, 4.81; S, 22.01%.

*3-*N*-Acetyl-2-thioxo-(4*R*)-(3′-*O*-benzyl-1′,2′-*O*-isopropylidene-α-D-xylo-tetrofuranos-4′-yl)-thiazolidine (**12**).* A solution of **11a** (100 mg) and acetic anhydride (1 ml) in pyridine (1 ml) was kept at room temperature overnight, poured into ice-water, and the yellow sirup deposited was extracted with chloroform. A usual treatment of the extract gave a sirup (110 mg) which was purified on a silica gel column, using 5% ethyl acetate in benzene as an eluent, to give the pure sirup in 81% (90 mg) yield. $[\alpha]^{22}_{\mathrm{D}}$ $-295°$ (*c* 0.84), IR: 1700 (amide).

Found: C, 55.68; H, 5.73; N, 3.32; S, 15.44%. Calcd for $C_{19}H_{23}NO_5S_2$: C, 55.77; H, 5.67; N, 3.42; S, 15.67%.

When the acylation was performed with *p*-nitrobenzoyl chloride and triethylamine in benzene, the crystalline *N*-*p*-nitrobenzoate was obtained as yellow needles in 71% yield. Mp 154—155 °C, $[\alpha]^{22}_{\mathrm{D}}$ $-148°$ (*c* 1.18), IR: 1700 (amide).

Found: C, 55.86; H, 4.67; N, 5.49; S, 12.51%. Calcd for $C_{24}H_{24}N_2O_7S_2$: C, 55.81; H, 4.68; N, 5.42; S, 12.41%.

*2-Thioxo-(5*S*)-(1′,2′-*O*-isopropylidene-3′-*O*-substituted-α-D-xylo-tetrofuranos-4′-yl)-thiazolidine (**13**).* *i) 3′-*O*-Benzyl Derivative (**13a**):* A suspension of 6-azido-3-*O*-benzyl-6-deoxy 1,2-*O*-isopropylidene-5-*O*-tosyl-α-D-glucofuranose[7] (3.8 g) in ethanol (150 ml) was reduced in the presence of 10% palladium-charcoal (1.66 g) and acetic acid (0.56 g) for 4 hr, and the catalyst was filtered off. A mixed solution of the filtrate, carbon disulfide (4 ml), and ethanolic potassium hydroxide (1.15 g) was refluxed for 2.5 hr, evaporated, and the residue was washed with water to give crude crystals (2.81 g, 98%) which was recrystallized from ethanol. Mp 120—125 °C, $[\alpha]^{22}_{\mathrm{D}}$ $+5.8°$ (*c* 1.0, acetone), IR: 3250 (NH), 1500 (NHCS).

Found: C, 55.26; H, 5.97; N, 3.66; S, 17.19%. Calcd for $C_{17}H_{21}NO_4S_2$: C, 55.55; H, 5.76; N, 3.81; S, 17.45%.

*ii) 3′-*O*-Methyl Derivative (**13b**).* 6-Azido-6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-*O*-tosyl-α-D-glucofuranose mentioned before was treated in the same manner as above to give crystals of mp 148—150 °C in 89% yield. $[\alpha]^{22}_{\mathrm{D}}$ $+58.7°$ (*c* 1.19), IR: 3200 (NH), 1500 (NHCS).

Found: C, 45.59; H, 5.90; N, 4.60; S, 21.77%. Calcd for $C_{11}H_{17}NO_4S_2$: C, 45.34; H, 5.88; N, 4.81; S, 22.01%.

*3-*N*-Acetyl-2-thioxo-(5*S*)-(3′-*O*-benzyl-1′,2′-*O*-isopropylidene-α-xylo-tetrofuranos-4′-yl)-thiazolidine (**14**).* Acetylation of **13a** in the usual manner gave crystals of mp 156—156.5 °C in 90% yield. $[\alpha]^{22}$ $+34.5°$ (*c* 1.3), IR: 1690 (amide).

Found: C, 55.43; H, 5.48; N, 3.40; S, 15.72%. Calcd for $C_{19}H_{23}NO_5S_2$: C, 55.73; H, 5.66; N, 3.42; S, 15.66%.

*3-*N*-Acetyl-2-thioxo-(5*S*)-(1′,2′-di-*O*-acetyl-3′-*O*-substituted-α,β-D-xylo-tetrofuranos-4′-yl)-thiazolidine (**15**).* *i) 3′-*O*-Benzyl Derivative (**15a**).* A solution of **13a** (420 mg) in 70% acetic acid (20 ml) was heated at 90 °C for 5 hr, evaporated, and the residue was dried over phosphorus pentoxide, acetylated in a usual manner to give a sirup which was purified on a silica gel column using 5% ethyl acetate in benzene as an eluent. Yield, 71.5% (345 mg), $[\alpha]^{22}_{\mathrm{D}}$ $+96.5$ (*c* 1.37), IR: 1750 (ester), 1690 (amide), 1500 (NHCS), NMR: 2.05 and 2.09 (2 x OAc), 2.72 (NAc).

Found: C, 53.01; H, 5.23; N, 3.26; S, 14.32%. Calcd for $C_{20}H_{23}NO_7S_2$: C, 52.97; H, 5.11; N, 3.09; S, 14.14%.

*ii) 3′-*O*-Methyl Derivative (**15b**).* In the same manner as above **15b** was obtained from **13b** in 56% yield as a sirup. $[\alpha]^{22}_{\mathrm{D}}$ $+113.5°$ (*c* 1.4), IR: 1750 (ester), 1690 (amide), 1500 (NHCS).

Found: C, 45.41; H, 5.24; N, 3.55; S, 16.57%. Calcd for $C_{14}H_{19}NO_7S_2$: C, 44.54; H, 5.07; N, 3.71; S, 16.99%.

*(5*S*,6*R*,8*R*)-Triacetoxy-(7*S*)-alkoxy-3-thioxo-(8a*R*)-perhydropyrido[1,2-c]thiazole (**16**).* *i) (7*S*)-Benzyloxy Derivative (**16a**).* A suspension of **11a** (150 mg) in 70% acetic acid (40 ml) was heated at 90 °C for 4 hr, evaporated, and the residue was dried over phosphorus pentoxide, acetylated in a usual manner to give needles of mp 129—130 °C in 74% (230 mg) yield. $[\alpha]^{22}_{\mathrm{D}}$ $-82.0°$ (*c* 1.1), IR: 1740 (ester), 1380 (NHCS).

Found: C, 53.17; H, 5.10; N, 3.10; S, 13.92%. Calcd for $C_{20}H_{23}NO_7S_2$: C, 52.98; H, 5.11; N, 3.09; S, 14.14%.

*ii) (7*S*)-Methoxy Derivative (**16b**):* In the same manner as above, **16b** was obtained from **11b** as a sirup in 48% yield. $[\alpha]^{22}_{\mathrm{D}}$ $-56.6°$ (*c* 0.63), IR: 1740 (ester), 1370 (NHCS).

Found: C, 44.35; H, 5.07; N, 3.65; S, 16.51%. Calcd for $C_{14}H_{19}NO_7S_2$: C, 44.56; H, 5.08; N, 3.71; S, 17.00%.

*2-Methylthio-(4*R*)-(3′-*O*-benzyl-1′,2′-*O*-isopropylidene-α-D-xylo-tetrofuranos-4′-yl)-2-thiazoline (**17**).* To a suspension of sodium hydride (170 mg, dispersed in oil *ca.* 50%) in DMSO (4 ml) stirred for 1 hr under nitrogen atmosphere was added dropwise a solution of **11a** (1.2 g) in DMSO (5 ml) and then methyl iodide (2 ml). After keeping the reaction mixture at room temperature for 4 hr, it was poured into ice-water, and extracted with chloroform. The chloroform layer was washed with 5% sodium chloride, dried with magnesium sulfate, and evaporated to give a sirup which was purified on a silica gel column, using 10% ethyl acetate in toluene as an eluent, to give crystals of mp 113—114 °C in 66.5% (0.83 g) yield. $[\alpha]_D^{22}$ −50.0° (*c* 1.0), IR: 1560 (C=N).

Found: C, 56.94; H, 6.06; N, 3.60; S, 16.62%. Calcd for $C_{18}H_{23}NO_4S_2$: C, 56.68; H, 6.08; N, 3.67; S, 16.78%.

The corresponding (5*S*)-2-thiazoline (**18**) was analogously obtained from **13a** in 79% yield as a sirup. $[\alpha]_D^{22}$ −11.8° (*c* 1.22), IR: 1570 (C=N).

Found: C, 57.12; H, 6.06; N, 3.74; S, 16.29%. Calcd for $C_{18}H_{23}NO_4S_2$: C, 56.68; H, 6.08; N, 3.67; S, 16.78%.

*(4*R*)-(3′-O-Benzyl-1′,2′-O-isopropylidene-α-D-xylo-tetrofuranos-4′-yl)thiazolidine (**19**).* To a solution of **17** (0.3 g) in THF (30 ml) was added aluminum amalgam prepared from aluminum turnings (1 g) and then water (5 ml) portionwise under stirring. The reaction mixture was then stirred at 50—60 °C for 24 hr, filtered through filtercell, and the filtrate was evaporated to give crystals almost quantitatively (270 mg). Recrystallization of it from ethanol gave needles of mp 149—151 °C. $[\alpha]_D^{22}$ −95.4° (*c* 0.74), IR: 3200 (NH).

Found: C, 60.58; H, 6.85; N, 4.13; S, 9.55%. Calcd for $C_{17}H_{23}NO_4S$: C, 60.52; H, 6.87; N, 4.15; S, 9.50%.

The corresponding (5*S*)-thiazolidine (**20**) was analogously obtained from **18** in 95% yield as a sirup. $[\alpha]_D^{22}$ −7.9° (*c* 0.63), IR: 3300 (NH).

Found: C, 59.63; H, 6.81; N, 4.09; S, 9.40%. Calcd for $C_{17}H_{23}NO_4S$: C, 60.52; H, 6.87; N, 4.15; S, 9.50%.

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