# SYNTHETIC USE OF THE RIBOSYL DERIVATIVES OF 2,4- AND 2,5-THIAZOLIDINEDIONES*

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On ribosidation of 2,4-thiazolidinedione (2,5-thiazolidinedione, respectively), the 3-β-D-ribofuranosyl derivative is formed in high yield, either the benzoyl derivative *Ia* (*IIa*) or the acetyl derivative *Ib* (*IIb*). The unsubstituted ribosyl derivative *Ic* is formed from the acetyl derivative *Ib* by methanolic hydrogen chloride. The benzoylated ribosyl-2,4-thiazolidinedione *Ia* affords the benzoylated ribosylurea *III* on reaction with aqueous ammonia, the hydroxyethylurea derivative *IVa* with 2-aminoethanol, the semicarbazide derivative *Va* with hydrazine hydrate, the ribosylhydroxyurea derivative *VIa* on reaction with hydroxylamine hydrochloride and triethylamine, the benzoyl derivative of ribosylbiuret *VII* with O-methylisourea hydrochloride and triethylamine, and (analogously) ribosylisothiobiuret *VIII* with S-methylisothiourea. Methanolysis of the benzoyl derivative of hydroxyethylurea *IVa* with sodium methoxide affords the unprotected riboside *IVb*. Ribosylhydroxyurea *VIb* is formed on debenzoylation of compound *VIa* with methanolic ammonia. Acetylation of compound *VIb* furnishes the pentaacetyl derivative *VIc*.

2,4-Thiazolidinediones and 2,5-thiazolidinediones exhibit a relatively high reactivity; under cleavage of the heterocyclic ring, they can afford a number of products. Besides, the alkyl derivatives of 2,4-thiazolidinedione exhibit some important biological effects (as insecticides[1] and repellents[2]).

The glycosyl derivatives of these compounds were not yet described. It seemed convenient, therefore, to prepare the ribosyl derivative of 2,4-thiazolidinedione and that of 2,5-thiazolidinedione at first and, subsequently, to exploit their reactivity. The silylation method was found to be suitable for the preparation of the ribosyl derivatives; high yields were obtained in both cases. The silylation method was used earlier for the ribosidation[3] of a related 5-amino-1,2,4-thiadiazol-3-one under the use of the tetraacetylribofuranose and tin tetrachloride. Silylation of 2,4- and 2,5-thiazolidinedione was performed by a modified method according to Wittenburg[4], namely, by heating in a mixture of chlorotrimethylsilane and hexamethyldisilazane. Condensation of the silylated base with the triacylribofuranosyl bromide was performed in acetonitrile under catalysis of mercuric bromide. The benzoylated haloge-

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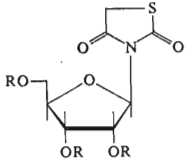
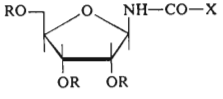
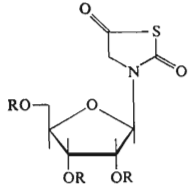
nose led to the benzoyl derivatives *Ia* and *IIa* while the acetylated halogenose afforded the acetyl derivatives *Ib* and *IIb*. An acidic methanolysis of *Ib* by methanolic hydrogen chloride succeeded in yielding the free 3-(β-D-ribofuranosyl)-2,4-thiazolidinedione (*Ic*). In the case of the benzoyl derivative *Ia*, acidic methanolysis was not efficient enough to split off the benzoyl groups while the basic one led to the cleavage of thiazolidine ring. In 2,5-thiazolidinedione series, no success was encountered either on acidic or on alkaline methanolysis of the benzoyl derivative *IIa* and the acetyl derivative *IIb*, due to the instability of the heterocyclic ring.



*Ia*, R = Bz
*Ib*, R = Ac
*Ic*, R = H



*III*, R = Bz, X = $NH_2$
*IVa*, R = Bz, X = $NH(CH_2)_2OH$
*IVb*, R = H, X = $NH(CH_2)_2OH$
*Va*, R = Bz, X = $NHNH_2$
*Vb*, R = Ac, X = $N(Ac)NAc_2$
*VIa*, R = Bz, X = NHOH
*VIb*, R = H, X = NHOH
*VIc*, R = Ac, X = N(Ac)OAc
*VII*, R = Bz, X = $N{=}C(OCH_3)NH_2$
*VIII*, R = Bz, X = $N{=}C(SCH_3)NH_2$



*IIa*, R = Bz
*IIb*, R = Ac

It is known that the 2,4- and especially the 2,5-thiazolidinedione ring is very reactive towards the alkaline agents. The cleavage of 2,4-thiazolidinedione with ammonia[5] forms urea while the reaction of 3-alkyl-2,4-thiazolidinediones with hydrazine hydrate[6,7] is known to give alkylsemicarbazides. In peptide chemistry the formation and reactivity of 2,5-thiazolidinediones is used for the synthesis of peptides[8]. The alkyl derivatives of 2,4-thiazolidinedione are known to react with hydrazine[6,7] under formation of products identical with those obtained on reaction of hydrazine with corresponding alkyl isocyanates.

On the basis of these literature data, a series of reactions was performed in which the ribosyl-2,4-thiazolidinedione *Ia* (*Ib*) was used as a suitable compound to replace

ribosyl isocyanate. At the same time, some advantages of the thiazolidine derivative *Ia* (*Ib*) in comparison with ribosyl isocyanate were demonstrated. Compound *Ia* (*Ib*) is accessible in a high yield and exhibits a higher stability than ribosyl isocyanate what enables to prepare this compound on a large scale and store it for a long time. Even somewhat lower reactivity of *Ia* (*Ib*) gives an advantage over ribosyl isocyanate in some reactions. Thus, the reactions of *Ia* (*Ib*) with ammonia, 2-aminoethanol, hydrazine, hydroxylamine, O-methylisourea, and S-methylisothiourea were performed. Acetonitrile was found to be a suitable solvent for the reaction. On reaction of ribosyl-2,4-thiazolidinedione *Ia* with aqueous ammonia in acetonitrile, the benzoylated β-D-ribofuranosylurea *III* was formed in 88% yield. Physical constants of *III* are in accordance with literature[9] data. Analogously, the benzoyl derivative of ribosylhydroxyethylurea *IVa* was prepared in 69% yield by the action of 2-aminoethanol. Debenzoylation with 0·1M sodium methoxide afforded free hydroxyethylurea derivative *IVb*. The benzoylated ribosylsemicarbazide *Va* was prepared in 80% yield on reaction of *Ia* with hydrazine hydrate. The action of methanolic ammonia gives rise to the deprotected ribosylsemicarbazide; however, the compound was not isolated in pure state. On its acetylation with acetic anhydride in pyridine, the hexaacetate *Vb* was formed which represented (according to NMR spectra) a mixture of isomers that were not separated. The benzoylated N-ribosylhydroxyurea *VIa* was prepared on reaction of hydroxylamine with *Ia* in 65% yield. Hydroxylamine was liberated from its hydrochloride by triethylamine directly in the reaction mixture. On methanolysis of hydroxyurea derivative *VIa* with methanolic ammonia, the unprotected ribosylhydroxyurea *VIb* was prepared in 57% yield. Compound *VIb* is the ribosyl derivative of the biologically active hydroxyurea[10,11]. Acetylation of *VIb* with acetic anhydride in pyridine afforded the pentaacetate *VIc*. The benzoylated ribosylmethylisobiuret *VII* was prepared from *Ia* by the action of O-methylisourea (liberated from parent hydrochloride by triethylamine) for 5 days at room temperature. In analogy, the benzoylated ribosylmethylisothiobiuret *VIII* was prepared on reaction of *Ia* with S-methylisothiourea. Both compounds *VII* and *VIII* are intermediates for the preparation of 5-aza analogues of pyrimidine nucleosides[12].

## EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block). The UV spectra were recorded on a CF-4 apparatus (Optica, Milano). The IR spectra were taken on a UR-20 apparatus (Carl Zeiss, Jena). The $^1$H-NMR spectra were measured on a Varian HA-100 apparatus at 100 MHz with hexamethyldisiloxane as internal standard; chemical shifts ($\delta$ values) are expressed in ppm and the coupling constants in Hz. Optical rotations were measured on an automatic Perkin–Elmer 141 MC polarimeter. Mass spectra were taken on A.E.I. type MS 902 apparatus. Analytical samples were dried at 0·5 Torr. Column chromatography was performed on the Pitra silica gel (particle size, 30 – 60 μm; produced by Service Laboratories of this Institute). The reactions and column separations were checked by thin-layer chromatography which was

performed on ready-for-use Silufol[R] UV 254 silica gel sheets (Kavalier Glassworks, Votice, Czechoslovakia); the spots were detected by UV light or by a gentle heating in flame.

3-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-2,4-thiazolidinedione (*Ia*)

Powdered 2,4-thiazolidinedione[13] (702 mg; 6 mmol) was coevaporated with toluene (10 ml). Then toluene (10 ml), hexamethyldisilazane (2·5 ml), and chlorotrimethylsilane (6·5 ml) were added to the residue; the mixture was heated to reflux for 8 h, evaporated *in vacuo*, and the residue was coevaporated with toluene (15 ml). To the resulting silylated 2,4-thiazolidinedione, a solution of 2,3,5-tri-O-benzoyl-D-ribofuranosyl bromide [prepared from 2·53 g (5 mmol) of 1-O-acetyl-2,3,5-tri-O-benzoyl-D-ribofuranose] in acetonitrile (10 ml), mercuric bromide (500 mg), and Potasit 3 molecular sieves (1 g) were added. The mixture was stirred at room temperature for 4 h, molecular sieves and the insoluble materials were filtered off and washed with acetonitrile (2 × 5 ml). The combined filtrates were evaporared *in vacuo* and the residue was dissolved in chloroform (50 ml). The solution was washed with a 10% solution of potassium iodide (3 × × 20 ml) and water (2 × 20 ml), dried over anhydrous magnesium sulfate, and evaporated. The residue was chromatographed on a silica gel column (250 g) in the system benzene–ethyl acetate 10 : 1 to afford 2·35 g (83·5%) of the chromatographically homogeneous *Ia* in the form of a solid foam. $[\alpha]_D^{25}$ −13·5° (*c* 0·28; ethyl acetate). UV spectrum (ethanol): $\lambda_{max}$ 231 and 275 nm (log ε 4·39 and 3·27), $\lambda_{min}$ 261 nm (log ε 3·04). IR spectrum (chloroform): 1705 and 1767 $cm^{-1}$ (C=O thiazolidinedione), 1728 $cm^{-1}$ (C=O benzoate). $^1$H-NMR spectrum (deuteriochloroform): 3·99 (s, 2 H, 2 $H_5$), 4·40–4·80 (m, 3 H, 2 $H_5$, $H_{4'}$), 5·70–6·20 (m, 3 H, $H_{1'}$, $H_{2'}$, $H_{3'}$), 7·20–7·60, 7·75–8·10 (m, m, 15 H, arom. protons). For $C_{29}H_{23}NO_9S$ (561·55) calculated: 62·02% C, 4·13% H, 2·49% N, 5·71% S; found: 62·18% C, 4·25% H, 2·68% N, 5·61% S.

3-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-2,5-thiazolidinedione (*IIa*)

A solution of 2,3,5-tri-O-benzoyl-D-ribofuranosyl bromide (10 mmol) in acetonitrile (25 ml), Potasit 3 molecular sieves (2 g), and mercuric bromide (1 g) were added to the residue of silylated 2,5-thiazolidinedione [prepared from 2,5-thiazolidinedione[8] (1·404 g; 12 mmol) in the same manner as in the case of silylated 2,4-thiazolidinedione]. The mixture was stirred for 15 min and kept at room temperature for 4 h. The deposited crystals were dissolved by the addition of chloroform (150 ml). The molecular sieves were filtered off and washed with chloroform (3 × 5 ml). The combined filtrates were washed with a 10% solution of potassium iodide (3 × 50 ml) and water (2 × 50 ml), dried over anhydrous magnesium sulfate, and evaporated *in vacuo*. On crystallization of the residue from ethyl acetate, 3·87 g of *IIa* (m.p. 191–192°C) were obtained. Chromatography of mother liquors on a silica gel column (120 g) in chloroform followed by crystallization from ethyl acetate afforded additional 620 mg of *IIa* of the same m.p. Total yield, 80% of *IIa*. $[\alpha]_D^{20}$ −95·9° (*c* 0·41; chloroform). IR spectrum (chloroform): sh 1694, sh 1710 $cm^{-1}$ (C=O 2,5-thiazolidinedione). For $C_{29}H_{23}NO_9S$ (561·55) calculated: 62·02% C, 4·13% H, 2·49% N, 5·71% S; found: 62·19% C, 4·28% H, 2·59% N, 6·05% S.

3-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-2,4-thiazolidinedione (*Ib*)

The title compound was prepared from silylated 2,4-thiazolidinedione (6 mmol) and 2,3,5-tri-O-acetyl-D-ribofuranosyl bromide [prepared[14] from 1·60 g (5 mmol) of guanosine dihydrate] in the same manner as in the case of the benzoylated compound *Ia*. Chromatography on a column of silica gel (100 g) in the system benzene–acetone 8 : 1 afforded 1·16 g (62%) of the chromatographically homogeneous *Ib* in the form of a solid foam. $[\alpha]_D^{25}$ +9·9° (*c* 0·24; ethyl acetate). IR

spectrum (chloroform): 1705, sh 1767 $cm^{-1}$ (C=O 2,4-thiazolidinedione); 1751 $cm^{-1}$ (C=O acetate). For $C_{14}H_{17}NO_9S$ (375·4) calculated: 44·79% C, 4·57% H, 3·73% N, 8·54% S; found: 44·54% C, 4·64% H, 3·71% N, 8·59% S.

3-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-2,5-thiazolidinedione (*IIb*)

Compound *IIb* was prepared from silylated 2,5-thiazolidinedione (6 mmol) and 2,3,5-tri-O-acetyl-D-ribofuranosyl bromide (5 mmol) by the same procedure as in the case of compound *Ib*. Chromatography on a silica gel column (100 g) in the system benzene–acetone (5 : 1) afforded 1·12 g (60%) of the syrupy product *IIb*, homogeneous on TLC. IR spectrum (chloroform): sh 1696 and 1706 $cm^{-1}$ (C=O 2,5-thiazolidinedione), 1754 $cm^{-1}$ (C=O acetate). For $C_{14}H_{17}NO_9S$ (375·4) calculated: 44·79% C, 4·57% H, 3·73% N, 8·54% S; found: 44·49% C, 4·75% H, 3·75% N, 8·82% S.

3-(β-D-Ribofuranosyl)-2,4-thiazolidinedione (*Ic*)

A solution of *Ia* (563 mg; 1·5 mmol) in 0·025M methanolic hydrogen chloride (20 ml) was kept at room temperature for 20 h. The solution was neutralized with sodium acetate and evaporated *in vacuo*. The residue was chromatographed on a column of silica gel (50 g) in the system ethyl acetate–acetone 5 : 1. Yield, 282 mg (75%) of syrupy *Ic*, homogeneous on TLC. UV spectrum (water): $\lambda_{max}$ 228 nm (log 3·50), $\lambda_{min}$ 213 nm (log ε 3·35). IR spectrum (KBr): sh 1652, 1678, 1752, 1762 $cm^{-1}$ (C=O), 3381 and 3448 $cm^{-1}$ (OH). For $C_8H_{11}NO_6S$ (249·25) calculated: 38·55% C, 4·45% H, 5·62% N, 12·86% S; found: 38·67% C, 4·61% H, 5·71% N, 12·65% S.

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)urea (*III*)

To a solution of *Ia* (281 mg; 0·5 mmol) in acetonitrile (4 ml), a 26% aqueous ammonia (0·3 ml) was added and the mixture was kept at room temperature for 2 h. The crystalline product was filtered off and washed with acetonitrile (2 × 1 ml). Yield, 103 mg of ribosylurea *III*. The combined filtrates were diluted with ethyl acetate (25 ml) and washed with water (3 × 5 ml) and a saturated solution of sodium chloride (5 ml). Ethyl acetate solution was dried over anhydrous magnesium sulfate and evaporated *in vacuo*. Crystallization of the residue from ethanol afforded additional 58 mg of ribosylurea *III*. Mother liquors were chromatographed on a silica gel column (25 g) in the system benzene–acetone 2 : 1 to give 23 mg of ribosylurea *III* and 48 mg of the starting *Ia*. Total yield of *III*, 88% (referred to the reacted *Ia*), m.p. 188·5—190·5°C. UV spectrum (ethanol): $\lambda_{max}$ 231 and 275 nm (log ε 4·33 and 3·48), $\lambda_{min}$ 260 nm (log ε 3·34). IR spectrum (chloroform): 1536 $cm^{-1}$ (amide II of urea), 1602 $cm^{-1}$ ($NH_2$), 1678, 1691, and 1710 $cm^{-1}$ (amide I of urea), 1726 $cm^{-1}$ (C=O), 3424 $cm^{-1}$ (NH), 3523 $cm^{-1}$ ($NH_2$). For $C_{27}H_{24}N_2O_8$ (504·5) calculated: 64·28% C, 4·80% H, 5·55% N; found: 64·39% C, 4·90% H, 5·57% N.

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-3-(2-hydroxyethyl)urea (*IVa*)

To a solution of ribosylthiazolidinedione *Ia* (562 mg; 1 mmol) in acetonitrile (8 ml), water (0·1 ml) was added. Then 2-aminoethanol (0·25 ml) was added under stirring in small portions over 10 min. The solution was kept at room temperature for 30 min, diluted with ethyl acetate (40 ml), washed with water (3 × 10 ml) and a saturated solution of sodium chloride (10 ml), dried over anhydrous magnesium sulfate, and evaporated *in vacuo*. The residue was chromatographed on a silica gel column (40 g) in the system toluene–acetone 1 : 1. Crystallization of the residue of the main UV absorbing fraction (from ethanol) yielded 323 mg (59%) of *IVa*, m.p. 161—164°C.

Mother liquors afforded additional 54 mg (10%) of the same compound. $[\alpha]_D^{25}$ −33·3° (*c* 0·42; ethyl acetate). IR spectrum (chloroform), $c = 3 \cdot 10^{-3}$M: 3629 $cm^{-1}$ (OH), 3403 $cm^{-1}$ (NH); $c = 2\%$: 1727 $cm^{-1}$ (C=O benzoate), 1684 $cm^{-1}$ (amide I), 1603, 1584, 1496, 1435 $cm^{-1}$ (benzoate ring), 1556 $cm^{-1}$ (amide II), 1271 $cm^{-1}$ (C—O benzoate). For $C_{29}H_{28}N_2O_9$ (548·5) calculated: 63·50% C, 5·14% H, 5·11% N; found: 63·33% C, 5·00% H, 5·17% N.

1-(β-D-Ribofuranosyl)-3-(2-hydroxyethyl)urea (*IVb*)

A solution of *IVa* (274 mg; 0·5 mmol) in 0·1M methanolic sodium methoxide (10 ml) was kept at room temperature for 2 h and then neutralized with Dowex 50 ($H^+$) which was prewashed with methanol. The resin was filtered off and washed with methanol (30 ml). The combined filtrates were evaporated *in vacuo*. Crystallization of the residue from 2-propanol–methanol (9 : 1) afforded 60 mg (47%) of *IVb*, m.p. 178—180°C. Mother liquors yielded additional 23 mg (19·5%) of the same compound. $[\alpha]_D^{25}$ −27·4° (*c* 0·37; water). IR spectrum (KBr): 3518, 3373, 3351, sh 3320, sh 3210 $cm^{-1}$ (OH, NH), 1649 $cm^{-1}$ (amide I), 1581 $cm^{-1}$ (amide II). For $C_8H_{16}N_2O_6$ (236·2) calculated: 40·67% C, 6·83% H, 11·68% N; found: 40·56% C, 6·83% H, 11·78% N.

4-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)semicarbazide (*Va*)

To a solution of *Ia* (562 mg; 1 mmol) in acetonitrile (8 ml), an 80% hydrazine hydrate (1 ml) was added over 10 min and the solution was kept at room temperature for 30 min. The solution was diluted with chloroform (40 ml), washed with water (3 × 10 ml) and a saturated solution of sodium chloride (10 ml), dried over anhydrous magnesium sulfate, and evaporated. Crystallization of the residue from ethanol yielded 415 mg (80%) of *Va*, m.p. 171—172°C. $[\alpha]_D^{25}$ −37·5° (*c* 0·51; ethyl acetate). UV spectrum (ethanol): $\lambda_{max}$ 231 and 275 nm (log ε 4·58 and 3·62), $\lambda_{min}$ 262 nm (log ε 3·49). IR spectrum (chloroform): 3405 and sh 3392 $cm^{-1}$ (NH), 1726 $cm^{-1}$ (C=O benzoate), 1695 $cm^{-1}$ (amide I), 1525 $cm^{-1}$ (amide II), 1603, 1585, 1493, 1453 $cm^{-1}$ (benzoate ring). For $C_{27}H_{25}N_3O_8$ (519·5) calculated: 62·42% C, 4·85% H, 8·09% N; found: 62·68% C, 4·88% H, 7·89% N.

1,1,2-Triacetyl-4-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)semicarbazide (*Vb*)

A solution of *Va* (519 mg; 1 mmol) in methanolic ammonia (40 ml of a 17% solution) was kept at room temperature for 40 h and evaporated *in vacuo*. The residue was washed with ether and dissolved in a mixture of pyridine (5 ml) and acetic anhydride (2·5 ml). The solution was allowed to stand at room temperature for 16 h and methanol (4 ml) was added. After 10 min, the solution was evaporated *in vacuo*. The residue was coevaporated with toluene (3 × 5 ml) and chromatographed on a silica gel column (80 g) in the system benzene–acetone (4 : 1). Yield, 296 mg (64·5%) of *Vb* in the form of a solid foam. Mass spectrum (*m/e*): 399 ($M-CH_3COOH$), 386 ($M-CH_2.OCOCH_3$), 259 (acetylated sugar). For $C_{18}H_{25}N_3O_{11}$ (459·4) calculated: 47·06% C, 5·49% H, 9·15% N; found: 47·23% C, 5·62% H, 8·93% N.

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-3-hydroxyurea (*VIa*)

To a solution of *Ia* (1·123 g; 2 mmol) in acetonitrile (16 ml), pulverized hydroxylamine hydrochloride (1·4 g; 20 mmol) and water (0·4 ml) were added under stirring; then triethylamine (2·8 ml) was added dropwise over 5 min under stirring. The mixture was stirred for additional 30 min, diluted with ethyl acetate (100 ml), extracted with 0·1M hydrochloric acid (50 ml), water

(2 × 50 ml), and a saturated solution of sodium chloride (50 ml), dried over anhydrous magnesium sulfate, and evaporated. The residue was chromatographed on a silica gel column (50 g) in the system benzene–acetone (2 : 1). On crystallization of the UV-absorbing fraction from ethanol, 528 mg (51%) of *VIa* were obtained, m.p. 166–168°C. Mother liquors afforded additional 150 mg (14%) of the same compound. $[\alpha]_D^{25}$ −32·2° (*c* 0·38; ethyl acetate). UV spectrum (ethanol): $\lambda_{max}$ 231 and 275 nm (log ε 4·37 and 3·46), $\lambda_{min}$ 260 nm (log ε 3·33). IR spectrum (chloroform): 3 542 $cm^{-1}$ (OH), 3422 and 3 371 $cm^{-1}$ (NH), 1 726 $cm^{-1}$ (C=O), sh 1 691 $cm^{-1}$ (amide I). For $C_{27}H_{24}N_2O_9$ (520·5) calculated: 62·30% C, 4·65% H, 5·38% N; found: 62·32% C, 4·77% H, 5·39% N.

1-(β-D-Ribofuranosyl)-3-hydroxyurea (*VIb*)

A solution of *VIa* (520 mg; 1 mmol) in methanolic ammonia (20 ml of a 17% solution) was kept at room temperature for 20 h and evaporated *in vacuo*. The residue was chromatographed on a silica gel column (20 g) in 2-propanol. Evaporation of the main fraction afforded a strongly hygroscopic residue which was dried in vacuum desiccator over potassium hydroxide for 48 h. Yield, 125 mg (57%) of *VIb*. $[\alpha]_D^{25}$ −30° (*c* 0·67; water). IR spectrum (KBr): 3 350 and 2915 $cm^{-1}$ (OH, NH), 1 669 $cm^{-1}$ (amide I), 1 547 $cm^{-1}$ (amide II). Mass spectrum (*m/e*): 176 (M−NHOH), 60 (CONHOH). For $C_6H_{12}N_2O_6$ (220·2) calculated: 34·61% C, 5·81% H, 13·46% N; found: 34·21% C, 6·00% H, 13·07% N.

3-Acetyl-3-O-acetyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)-3-hydroxyurea (*VIc*)

The hydroxyurea derivative *VIb* (66 mg; 0·3 mmol) was dissolved in a mixture of pyridine (1·5 ml) and acetic anhydride (0·5 ml). The solution was kept at room temperature for 20 h and then methanol (1 ml) was added. The mixture was allowed to stand at room temperature for 10 min, evaporated *in vacuo*, and coevaporated with toluene (3 × 4 ml). Chromatography of the residue on a column of silica gel (15 g) in the system benzene–acetone (2 : 1) afforded 90 mg (72%) of *VIc* in the form of a solid foam. $[\alpha]_D^{25}$ +62·2° (*c* 0·51, ethyl acetate). IR spectrum (chloroform): 3 305 $cm^{-1}$ (NH), 1 812, 1 755, 1 747, sh 1 731, and sh 1 710 $cm^{-1}$ (C=O), 1 521 $cm^{-1}$ (amide II), 1 246 $cm^{-1}$ (C—O). $^1$H-NMR spectrum (deuteriochloroform): 2·03, 2·08. 2·20, 2·25, 2·31 (4 × s, 4 × 3 H, 4 × $COC\underline{H}_3$), 5·50–5·75 (m, 2 H, $H_{1'}$, $H_{3'}$), 3·60–4·10 (m, 2 H, $H_{5'}$), 5·02 (m, 1 H, $H_{4'}$), 5·15 (dd, 1 H, $H_{2'}$, $J_{1',2'}$ = 4·5, $J_{2',3'}$ = 3·5), 9·45 (bd, 1 H, N$\underline{H}$). Mass spectrum: M = 418·1223; calculated: 418·1221. For $C_{16}H_{22}N_2O_{11}$ (418·4) calculated: 45·93% C, 5·50% H, 6·70% N; found: 45·98% C, 5·44% H, 6·62% N.

1-(2,3,5-Tri-O benzoyl-β-D-ribofuranosyl)-4-O-methylisobiuret (*VII*)

To a stirred mixture of *Ia* (562 mg; 1 mmol), acetonitrile (8 ml), O-methylisourea hydrochloride (221 mg; 2 mmol), and water (0·2 ml), triethylamine (1·4 ml) was added dropwise over 30 min. The mixture was allowed to stand at room temperature for 5 days, diluted with ethyl acetate (80 ml), extracted with water (2 × 20 ml) and a saturated solution of sodium chloride (20 ml), dried over anhydrous magnesium sulfate, and evaporated *in vacuo*. Crystallization of the residue from 2-propanol yielded 174 mg of *VII*, m.p. 169–171·5°C. Mother liquors furnished additional 156 mg of the same compound. Total yield, 59%. $[\alpha]_D^{25}$ −36·7° (*c* 0·32, ethyl acetate). IR spectrum (chloroform): *c* 3 . $10^{-3}$M: 3 501 and 3 326 $cm^{-1}$ ($NH_2$), 3 438 $cm^{-1}$ (NH); *c* 2%: 1 729 and 1 714 $cm^{-1}$ (C=O benzoate), 1 659 $cm^{-1}$ ($NH_2$), 1 624 $cm^{-1}$ (C=N), 1 530 $cm^{-1}$ (amide II). For $C_{29}H_{27}O_9N_3$ (561·5) calculated: 62·03% C, 4·85% H, 7·48% N; found: 62·07% C, 4·93% H, 7·36% N.

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-4-S-methylisothiobiuret (*VIII*)

Title compound was prepared from *Ia* (562 mg; 1 mmol) and S-methylisothiourea hydrochloride (254 mg; 2 mmol) in the same manner as in the case of *VII*; crystallization from 2-propanol–methanol afforded 185 mg of *VIII*, m.p. 161—163°C. Chromatography of the residue of mother liquors on a silica gel column (30 g) in the system benzene–ethyl acetate (3 : 2) and subsequent crystallization from 2-propanol–methanol yielded additional 160 mg of the same compound. Total yield, 60%. $[\alpha]_D^{25}$ −51·2° (*c* 0·38, ethyl acetate). IR spectrum (chloroform): *c* 3 . $10^{-3}$M: 3482 and 3293 $cm^{-1}$ ($NH_2$), 3435 $cm^{-1}$ (NH); *c* 2%: 1730 and 1714 $cm^{-1}$ (C═O benzoate), 1647 $cm^{-1}$ ($NH_2$), 1598 $cm^{-1}$ (C═N), 1522 $cm^{-1}$ (amide II). For $C_{29}H_{27}N_3O_8S$ (577·6) calculated: 60·30% C, 4·71% H, 7·27% N, 5·55% S; found: 60·21% C, 4·80% H, 7·39% N, 5·84% S.

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