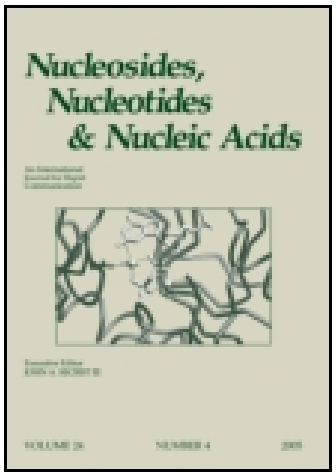

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EFFICIENT SYNTHESIS OF FUSED ISOTHIAZOLO C-NUCLEOSIDES. III. SYNTHESIS OF 7-SUBSTITUTED ISOTHIAZOLO[4,5-d]PYRIMIDINE C-NUCLEOSIDES*

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NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS, 20(3), 229–241 (2001)

EFFICIENT SYNTHESIS OF FUSED ISOTHIAZOLO C-NUCLEOSIDES. III. SYNTHESIS OF 7-SUBSTITUTED ISOTHIAZOLO[4,5-d]PYRIMIDINE C-NUCLEOSIDES*

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ABSTRACT

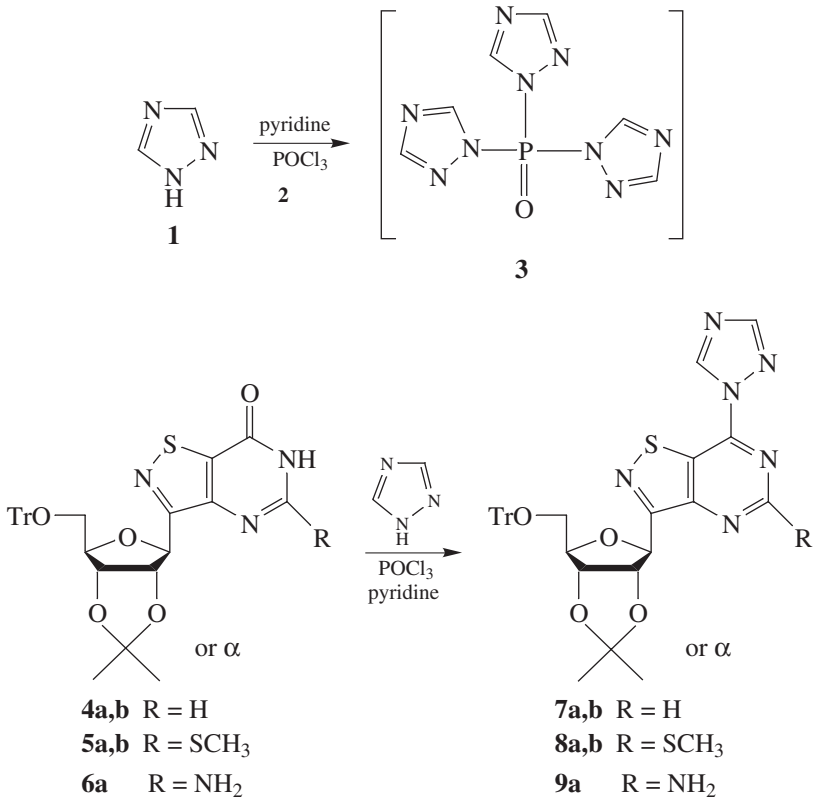
The Divakar-Reese procedure has been successfully applied for transforming 7-oxo-isothiazolo[4,5-d]pyrimidine C-nucleosides (**4a**,**b**, **5a**,**b**, **6a**) *via* 1,2,4-triazol-1-yl intermediates (**7a**,**b**, **8a**,**b**) into various 7-substituted C-nucleosides **15a**,**b**, **16a**,**b**, **17a**, **18a**, **19a**,**b**, **20a**,**b**; their subsequent deprotection provides novel types of unusual C-glycosides **22b**, **23a**, **24a**,**b**, **25b**, **26b**.

C-Nucleosides, possessing on its heterocyclic base other than naturally occuring oxo- or amino substituents, are important model compounds for biological or medicinal studies (2,3). We want to report on the synthesis of novel 7-substituted isothiazolo = [4,5-d]pyrimidine C-nucleosides. As we could show in previous papers (1,4), there exists a simple approach to the protected C-glycosides **4**–**6**.

RESULTS AND DISCUSSIONS

The activation of the 4-CO-function with subsequent nucleophilic substitution by a broad choice of N- and S-nucleophiles opens a efficient access to manifold potentially active and novel C-glycosides. This activation method was introduced

*See reference 1.



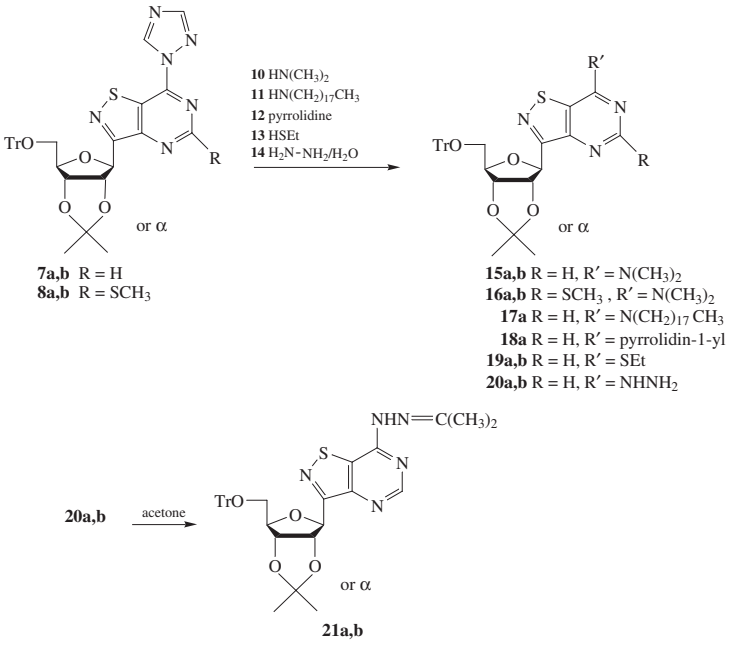
Scheme 1.

by Divakar and Reese (5) on uracils and consists in the activation of an uracil nucleoside (6) with a 1,2,4-triazole moiety **1** *via* a putative (5) tris-(1H-1,2,4-triazol-1-yl)phosphinoxide **3** which has been isolated in pure state by reaction of 1,2,4-triazole **1** and phosphorooxytrichloride **2** (7).

An alterated application of this Reese-Divakar procedure has been already reported by Wamhoff and Berressem to afford the adenosine isostere (7-aminoisothiazolo[4,5-d]pyrimidine C-nucleoside) in high yield (1,4). Pedersen applied this reaction to 2′,3′-Dideoxyuridine derivatives (8), and Robins et al. (9), however, applied the 1,2,4-triazol-4-yl substituent for converting the amino group of adenosine by treatment with bis-[(dimethylamino)methylene]hydrazine dihydrochloride into a versatile leaving group. Recently, this method has been applied to the synthesis of bicyclic *N* (4)-amino-2′-deoxycytidine derivatives (10).

We have treated the 4-C═O group in **4a**,**b**, **5a**,**b** and **6a** (11) with this system 1H-1,2,4-triazole, $POCl_3$ (2:1) in pyridine as a base and obtained the appropriate 7-(1,2,4-triazol-1-yl)-derivatives **7a**,**b**, **8a**,**b** and **9a** after chromatographic purification in 30–60% yield.

The isolated (12) 1,2,4-triazolyl-1-yl derivatives **7a**,**b**, **8a**,**b** enabled us to exchange this heterocyclic substituent smoothly and under mild reaction conditions for



Scheme 2.

several S- and N-nucleophiles and to generate a broad number of novel isothiazolo [4,5-d]pyrimidine C-glycosides.

Thus, employing dimethylamine **10**, octadecylamine **11**, pyrrolidine **12**, ethylmercaptan **13**, and hydrazine hydrate we converted **7a**,**b** and **8a**,**b** into the 4-substituted C-glycosides **15a**,**b**, **16a**,**b, 17a**, **18a**, **19a**,**b**, **20a**,**b**. The nucleophilic displacement reaction was carried out at room temp. in absol. MeCN with DBU as catalyst. After 6–12 h reaction time the products were purified by chromatography.

The reaction of hydrazine hydrate **14** with **7a**,**b** in methylenechloride at room temp. was accomplished already after 1.5 **h** duration to afford **20a**,**b**. During the chromatography with ethyl acetate/acetone these primary products **20a**,**b** were converted into the acetone hydrazones **21a**,**b**.

Deprotection of **15b**, **16a**,**b**, **18a**, **19a**,**b**, **20a**,**b**, and **21b** to afford the free C-glycosides **22b**, **23a**, **24a**,**b**, **25b**, **26b** and **27a**,**b** was effected by MeOH/HCl; **25b**, **26b** and **27a**,**b** were obtained as monohydrochlorides.

EXPERIMENTAL

General Materials and Methods

1-β-D-Cyanomethylribofuranose was kindly supplied by Dr. Hagemann, BAYER AG, Leverkusen; 5-Methylthio- and 5-Amino-3-(2,3-*O*-isopropylidene-5-*O*-trityl-$\alpha(\beta)$-D-ribofuranosyl)-isothiazolo[4,5-d]pyrimidine-7(6H)-ones **5a**,**b** and

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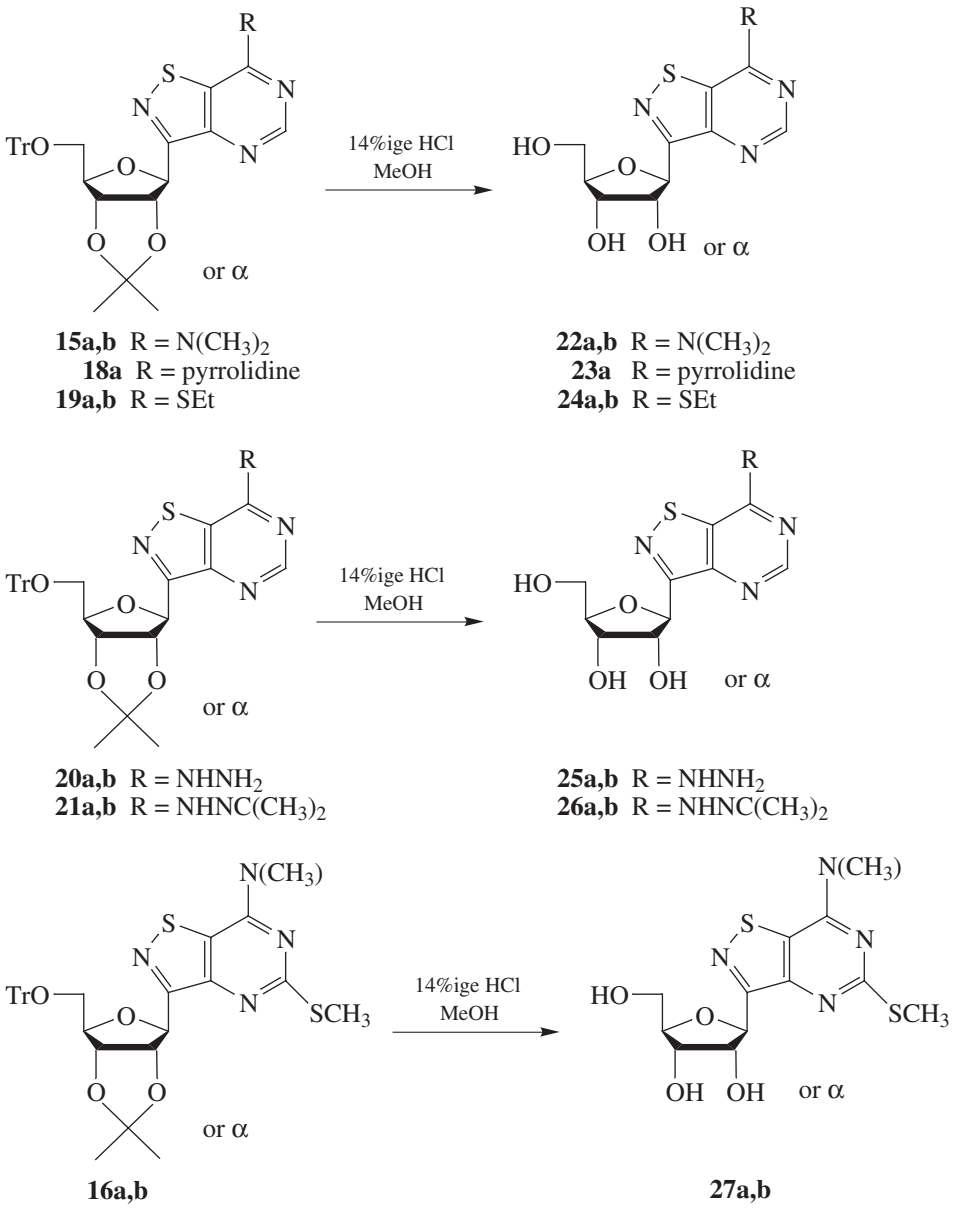

Scheme 3.

6a were prepared according to Lit (1,4,13). - ^{1}H, ^{13}C NMR spectra: Bruker AC-200 (200/50.29 MHz), WM-250 (250.13/62.19 MHz), AM-400 (400/100.62 MHz).

In some cases additionally DEPT 135 spectra were run, and CH-GEKO-, NOE- and/or H, H-COSY measurements were undertaken. UV spectra: Beckman, DU-640. IR spectra: Perkin-Elmer 1576 (in KBr). MS 50: FAB 70eV, 300 μA, DE

180° with 3-nitrobenzylalcohol as matrix. Melting points: SMP-20 of Büchi and apparatus of Leitz, Wetzlar. Microanalyses were performed in the Microanalytical Laboratory of the Institute. TLC: on precoated plates Silica gel $60F_{254}$. Column chromatography* was carried out on Silica gel 63–200 μm.

7-(1,2,4-Triazol-1-yl)isothiazolo[4,5-d]pyrimidines (7a,b, 8a,b, 9a)

General Procedure. To a solution of 1,2,4-1H-triazole **1** (1.8 g, 12.89 mmol) in absol. pyridine (45 mL) phosphoroxidtrichloride **2** (0.65 mL, 6.44 mmol) was added under ice-cooling and inert gas; then the reaction mixture was stirred for 30 min. at 25°C, and then **4a**,**b**, **5a**,**b** or **6a** (1.97 mmol) were added and stirred for additional 24 h at ambient temperature. The reaction mixture showed a color change from yellow to lilac blue. Then ethyl acetate (50 mL) was added and the solution was stirred for 2 h at room temp.. After evaporation to dryness, the oily residue was purified firstly by flash-chromatography (PE/EE, 1:3) the obtained product was dissolved in MeOH and further purified by chromatography.

7-(1,2,4-Triazol-1-yl)-3-(2,3-*O*-isopropylidene-5-*O*-trityl-α-D-ribofuranosyl)-isothiazolo[4,5-d]pyrimidine (**7a**) From 1.2 g (8.05 mmol of **1**, 0.45 ml (4.45 mmol) of **2**, and 0.67 g (1.23 mmol) **4a** in pyridine (30 mL); after chromatography (PE/EE 1:1) and recrystallization from MeOH yield 378 mg (54%), white needles of mp 122–125°C. IR ν 2990, 2915, 1570, 1500. UV ($CHCl_3$) λ_{max} (log ε) 253 (3.97), 328 (3.85). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.18/1.24 (ss, 6H), 3.25 (dd, 1H, J = 10.4, 3.2), 3.58 (dd, 1H, J = 10.0, 3.2), 4.59 (m, 1H), 4.83 (d, 1H, J = 6.0), 5.57 (t, 1H, J = 4.8), 6.22 (d, 1H, J = 4.4), 7.48–7.21 (m, trityl), 8.31 (s, 1H), 9.42 (s, 1H), 9.15 (s, 1H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 25.34, 26.09, 65.25, 82.60, 82.93, 83.80, 83.90, 87.75, 113.01, 127.34, 128.13, 128.79, 131.50, 142.30, 143.63, 149.20, 154.15, 154.30, 156.55, 162.23. MS (FAB) m/z (rel. intens.) 619.2 (M + 1; 5.5), 618.2 (1.24), 243.1 (trityl; 5). HR-MS Calcd for $C_{34}H_{30}N_6O_4S$: 618.2049; Found: 618.2042. Anal. Calcd for $C_{34}H_{30}N_6O_4S \cdot H_2O$: C, 64.13; H, 5.06; N, 13.18. Found: C, 63.98; H, 4.60; N, 13.26.

β-D-ribofuranosyl-isomer (7b). After chromatography (PE/EE 1:1) and recrystallization from isopropanol yield 430 mg (35.0%), mp 93–95°C. IR ν 3060, 2980, 2940, 1575, 1525, 1445. UV ($CHCl_3$) λ_{max} (log ε) 252 (3.83), 356 (3.84). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.43, 1.66 (ss, 6H), 3.08–3.25 (m, 2H), 4.48 – 4.56 (m, 1H), 4.87 (dd, 1H, J = 6.25, 2.76), 5.59 (d, 1H, J = 6.25, 3.86), 5.69 (d, 1H, J = 3.86), 7.12–7.36 (m, 15H), 8.32 (s, 1H), 9.13 (s, 1H), 9.40 (s, 1H). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 25.70, 27.48, 63.87, 81.62, 83,15, 83.34, 85.11, 86.60, 114.04, 126.90, 127.70, 128.61, 132.01, 142.36, 143.70, 149.13, 154.07, 154.47, 156.81, 163.17. MS (FAB) m/z (rel. intens.) 619.2, (M + 1; 11.2) 243.1 (trityl; 100). Anal. Calcd for $C_{34}H_{30}N_6O_4S$: C, 66.00; H, 4.89; N, 13.58. Found: C, 65.49; H, 4.82; N, 13.29.

*Abbreviations for solvents: EE: ethyl acetate; PE: petroleum ether.

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5-Methylthio-7-(1,2,4-triazol-1-yl)-3-(2,3-*O*-isopropylidene-5-*O*-trityl-α-D-ribofuranosyl)-isothiazolo[4,5-d]pyrimidine (8a). From 400 mg (0.65 mmol) of **5a**; after chromatography (EE/cyclohexane 2:1) and recrystallization from isopropanol/ MeOH yield 163 mg (37.8 %), mp 160–162°C. IR ν 3050, 2980, 2920, 1560, 1490, 1445. UV ($CHCl_3$) λ_{max} (log ε) 244 (4.11), 269 (4.23), 373 (3.53). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.15/1.21 (ss, 6H), 2.59 (s, 3H), 3.15 (dd, 1H, J = 10.33, 2.96), 3.55 (dd, 1H, J = 10.34, 3.20), 4.48–4.52 (m, 1H), 4.82 (d, 1H, J = 5.90), 5.51 (t, 1H, J = 5.42), 6.07 (d, 1H, J = 4.68), 7.10–7.36 (m, 15H), 8.17 (s, 1H), 9.22 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 14.69, 25.37, 26.09, 65.69, 82.69, 82.92, 83.72, 83.89, 87.67, 113.05, 127.22, 127.91, 128.70, 129.69, 142.36, 143.55, 148.49, 154.00, 156.87, 161.02, 169.11. MS (FAB) m/z (rel. intens.) 665.2 (M + 1; 15.7) 243.1 (trityl; 100). Anal. Calcd for $C_{35}H_{32}N_6O_4S \cdot 0.5$ MeOH: C, 62.62; H, 4.99; N, 12.34; S, 9.40. Found: C, 62.33; H, 4.76; N, 12.14; S, 9.40.

β-D-ribofuranosyl isomer (8b). From 410 mg (0.67 mmol) of **5b**; after chromatography (PE/EE 1:1) and recrystallization from isopropanol/MeOH yield 268 mg (60.4 %), mp 102–103 °C. IR ν 3060, 2970, 2920, 1560, 1520, 1445. UV ($CHCl_3$) λ_{max} (log ε) 244 (4.40), 270 (4.55), 370 (3.86). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.22/1.40 (s, 6H), 2.65 (s, 3H), 3.75–4.06 (m, 2H), 4.46–4.52 (m, 1H), 5.02 (d, 1H, J = 5.88), 5.13 (t, 1H, J = 5.40), 5.63 (d, 1H, J = 4.70), 7.12–7.41 (m, 15H), 8.28 (s, 1H), 9.31 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 14.65, 25.63, 27.50, 64.30, 82.70, 83.79, 83.89, 84.71, 86.70, 114.11, 127.26, 128.05, 128.35, 129.70, 142.43, 143.78, 148.48, 154.00, 157.44, 162.22, 169.59. MS (FAB) m/z (rel. intens.) 665.2 (M+1; 8.92), 243.1 (trityl; 100). Anal. Calcd for $C_{35}H_{32}N_6O_4S_2 \cdot 0.5$ MeOH: C, 62.62; H, 4.99; N, 12.34; S, 9.40. Found: C, 62.64; H, 5.08; N, 12.15; S, 9.45.

5-Amino-7-(1,2,4-triazol-1-yl)-3-(2,3-*O*-isopropylidene-5-*O*-trityl-α-D-ribo-furanosyl)-isothiazolo[4,5-d]pyrimidine (9a). From 180 mg (0.31 mmol) of **6a**; after chromatography (EE) and recrystallization from isopropanol yield 60 mg (30.6%), mp 120–125°C (dec.). IR ν 3470, 3330, 3200, 3050, 2970, 2920, 1590, 1490, 1445. UV ($CHCl_3$) λ_{max} (log ε) 244 (4.18), 372 (3.66). ^{1}H NMR ($CDCl_3$) δ 1.14/1.27 (s, 6H), 3.19 (dd, 1H, J = 10.34, 3.69), 3.50 (dd, 1H, J = 10.09, 3.69), 4.52 (d, 1H, J = 3.45), 4.75 (d, 1H, J = 5.91), 5.28 (s, 2H), 5.41 (t, 1H, J = 5.42), 5.92 (d, 1H, J = 4.92), 7.03–7.43 (m, 15H), 8.16 (s, 1H), 9.15 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 25.41, 26.11, 65.13, 82.19, 82.65, 83.59, 83.68, 87.57, 113.06, 127.23, 127.99, 128.73, 129.98, 142.05, 143.61, 149.68, 153.70, 158.46, 160.03, 160.80. MS (FAB) m/z (rel. intens.): 634.2 (M + 1: 8.5), 243.1 (trityl; 100). Anal. Calcd for $C_{34}H_{31}N_7O_4S$: C, 64.44; H, 4.93; N, 15.47; S, 5.06. Found: C, 64.24; H, 5.08; N, 15.78; S, 5.28.

7-Substituted Isothiazolo[4,5-d]pyrimidine C-glycosides 15a,b, 16a,b, 17a, 18a, 19a,b, 20a,b

General Procedure. A suspension of the 7-(1,2,4-triazol-1-yl) derivatives **7a,b, 8a**,**b** (1.13 mmol) and the nucleophiles **10**-**14** (140 mmol) was stirred for

12 h at ambient temperature; then ethyl acetate (10 mL) was added and the reaction mixture evaporated, purified by column chromatography, and recrystallization.

7-Dimethylamino-3-(2,3-*O*-isopropylidene-5-*O*-trityl-α-D-ribofuranosyl)-isothiazolo[4,5-d]pyrimidine (15a). Obtained from **7a** (400 mg, 0.65 mmol) and aq. (40%) dimethylamine **10** (3 mL, 60 mmol); after chromatography (PE/EE 1:1) and recrystallization from isopropanol/methanol yield 45 mg (11.7%), mp 78–80°C. IR ν 3050, 3010, 2960, 2920, 1560, 1445. UV ($CHCl_3$) λ_{max} (log ε) 242 (3.88), 271 (4.03), 332 (3.96). ^{1}H NMR ($CDCl_3$) δ 1.12/1.22 (s, 6H), 3.35 (s, 6H), 3.18–3.41 (m, 2H), 4.52–4.58 (m, 1H), 4.76 (d, 1H, $J = 6.16$), 5.38–5.44 (m, 1H), 5.86 (d, 1H, $J = 4.68$), 7.11–7.49 (m, 15H), 8.51 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 25.36, 26.12, 38.50, 64.26, 82.10, 82.45, 83.57, 83.60, 87.41, 112.95, 127.15, 127.90, 128.69, 130.22, 143.62, 154.95, 154.99, 157.71, 161,78. MS (FAB) m/z (rel. intens.): 595.2 (M + 1; 24.1), 243.1 (trityl; 100). Anal. Calcd for $C_{34}H_{34}N_4O_4S$•0.5 MeOH: C, 67.84; H, 5.89; N, 9.17; S, 5.24. Found: C, 67.90; H, 5.59; N, 9.41; S, 5.50.

β-D-Ribofuranosyl isomer (15b). After chromatography (PE/EE 1:1) and recrystallization from methanol yield 422 mg (62.9%), mp 188°C. IR ν 3050, 3020, 2980, 2930, 1570, 1500, 1445. UV ($CHCl_3$) λ_{max} (log ε) 244 (3.88), 272 (4.12), 332 (3.88). ^{1}H NMR ($CDCl_3$) δ 1.31/1.55 (s, 6H), 3.07–3.13 (m, 2H), 3.28 (s, 2H), 4.38–4.44 (m, 1H), 4.73–4.80 (m, 1H), 5.47–5.58 (m, 1H), 7.03–7.38 (m, 15H), 8.52 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 25.58, 25.81, 38.45, 64.14, 81.65, 83.26, 84.96, 86.59, 113,87, 127.72, 127.92, 128.72, 130.79, 143.91, 153.63, 155.51, 157.56, 163.28. MS (FAB) m/z (rel. intens.): 595.2 (M + 1; 89.3), 243.1 (trityl; 100). Anal. Calcd for $C_{34}H_{34}N_4O_4S$: C, 68.67; H, 5.76; N, 9.42; S, 5.39. Found: C, 68.44; H, 5.79; N, 9.26; S, 5.23.

7-Dimethylamino-5-methylthio-3-(2,3-*O*-isopropylidene-5-*O*-trityl-α-D-ribofuranosyl)-isothiazolo[4,5-d]pyrimidine (16a). Preparation from **8a** (130 mg, 0.2 mmol) and aq. (40%) dimethylamine **10** (3 mL, 60 mmol); after chromatography (PE/EE 1:1) and recrystallization from isopropanol yield 50 mg (39%), mp 108–110°C. IR ν 3050, 2920, 1560, 1500. UV ($CHCl_3$) λ_{max} (log ε) 244 (4.54), 270 (4.36), 307 (3.63), 338 (4.01). ^{1}H NMR ($CDCl_3$) δ 1.18/1.25 (ss, 6H), 2.49 (s, 3H), 3.13–3.48 (m, 2H), 3.30 (s, 6H), 4.46–4.52 (m, 1H), 5.02 (d, 1H, $J =$ 5.88), 5.13 (t, 1H, $J = 5.40$), 5.63 (d, 1H, $J = 4.70$), 7.12–7.41 (m, 15H).^{13}C NMR ($CDCl_3$): δ 14.39, 25.35, 26.18, 38.32, 65.18, 82.90, 83.57, 83.72, 83.89, 87.66, 112.78, 127.25, 127.80, 128.03, 129.69, 143.64, 156.87, 161.07, 168.59, 169.13. MS (FAB) m/z (rel. intens.) 641.1 (M + ; 100), 243.1 (trityl; 100). Anal. Calcd for $C_{35}H_{36}N_6O_4S_2$: C, 65.60; H, 5.66; N, 8.74; S, 10.01. Found: C, 65.20; H, 5.96; N, 8.35; S, 10.06.

β-D-ribofuranosyl isomer (16b). Obtained as **16a** from **8b** (140 mg, 0.21 mmol), aq. (44%) dimethylamine **10** (3 mL, 60 mmol); after chromatography (PE/EE 1:1) and recrystallization from isopropanol yield 76 mg (56.7%), mp 82–85°C. IR ν 3050, 3020, 2980, 2920, 1560, 1500, 1445. UV ($CHCl_3$) λ_{max} (log ε) 242 (3.87), 271 (4.08), 329 (4.00). ^{1}H NMR ($CDCl_3$) δ 1.28/1.54 (ss, 6H), 2.41 (s, 3H), 3.07–3.22 (m, 2H), 3.22 (s, 6H), 4.32–4.38 (m, 1H), 4.72–4.78 (m, 1H), 5.26–5.33 (m, 1H), 5.63 (d, 1H, $J = 3.45$), 7.05–7.37 (m, 15H). ^{13}C NMR

($CDCl_3$) δ 14.23, 25.69, 27.53, 38.35, 65.36, 81.30, 83.49, 83.75, 85.04, 86.64, 113.80, 126.98, 127.81, 128.77, 129.70, 143.95, 154.47, 156.59, 162.50, 160.09. MS (FAB) m/z (rel. intens.) 641.1 (M + ; 80.3), 243.1 (trityl; 100). Anal. Calcd for $C_{35}H_{36}N_4O_4S_2$: C, 65.60; H, 5.66; N, 8.74; S, 10.01. Found: C, 65.16; H, 5.83; N, 8.27; S, 10.06.

7-Octadecylamino-3-(2,3-*O*-isopropylidene-5-*O*-trityl-α-D-ribofuranosyl) -isothiazolo[4,5-d]pyrimidine (17a). Obtained from **7a** (190 mg, 0.3 mmol) in absol. MeCN (15 mL) and octadecylamine **11** (1.0 g, 3.7 mmol) and DBU (0.2 mL, 1.3 mmol) and 12 h stirring at ambient temperature and in an argon atmosphere. After evaporation, chromatography (PE/EE 7:3) and recrystallization from EtOH yield 98 mg (40%), mp 68–70°C. IR ν 3310, 3050, 3010, 2910, 2840, 1560, 1530, 1480, 1445. UV ($CHCl_3$) λ_{max} (log ε) 244 (3.91), 302 (3.91). ^{1}H NMR ($CDCl_3$) δ 0.82–1.44 (m, 43H, alkyl, 2 CH_3), 3.13–3.55 (m, 2H), 4.50–4.60 (m, 1H), 4.75 (d, 1H, $J = 6.16$), 5.44 (t, 1H, $J = 5.08$), 6.02 (d, 1H, $J = 4.68$), 7.10–7.45 (m, 15H), 8.71 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 14.33, 22.72, 25.35, 26.08, 26.13, 26.94, 29.31, 29.39, 29.56, 29.61, 29.68, 29.73, 31.95, 54.62, 63.74, 82.50, 82.69, 83.64, 83.69, 87.55, 113.05, 127.20, 128.01, 128.79, 132.58, 143.58, 154.50, 155.23, 162.21, 163.06. MS (FAB) m/z (rel. intens.) 819.5 (M + 1; 57.1), 243.1 (trityl; 100), Anal. Calcd for $C_{50}H_{66}N_4O_4S \cdot EtOH$: C, 72.18; H, 8.02; N, 6.47. Found: C, 71.81; H, 7.44; N, 6.51.

7-Pyrrolidino-3-(2,3-*O*-isopropylidene-5-*O*-trityl-α-D-ribofuranosyl)-iso-thiazolo[4,5-d]pyrimidine (18a). Obtained from **7a** (470 mg, 0.75 mmol) in absol. MeCN (40 mL), pyrrolidine (**12**) (1.03 mL, 12.22 mmol), and DBU (0.47 mL, 3.1 mmol) with 6 h stirring at 25°C in an argon atmosphere; after evaporation the residue was recrystallized from isopropanol; yield 440 mg (94.4%), mp 176–178°C. IR ν 3050, 3020, 2970, 2930, 2860, 1560, 1500, 1445. UV ($CHCl_3$) λ (qualit.) 248, 274, 330. ^{1}H NMR ($CDCl_3$) δ 1.14/1.20 (ss, 6H), 1.91–2.06 (m, 4H), 3.15–3.38 (m, 2H), 3.61–3.90 (m, 4H), 4.50–4.55 (m, 1H), 4.76 (d, 1H, $J = 6.16$), 5.36–5.41 (m, 1H), 5.81 (d, 1H, $J = 4.68$), 7.11–7.41 (m, 15H), 8.49 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 24.55, 25.35, 26.00, 26.14, 47.37, 47.78, 64.21, 82.10, 82.42, 83.57, 87.39, 112.93, 127.17, 127.98, 128.69, 131.10, 143.63, 155.32, 154.99, 161.78. MS (FAB) m/z (rel. intens.): 621.3 (M + 1; 29.0), 243.1 (trityl; 100). Anal. Calcd for $C_{36}H_{36}N_4O_4S$: C, 69.66; H, 5.85; N, 9.03; S, 5.16. Found: C, 69.38; H, 5.85; N, 8.85; S, 5.31.

7-Ethylthio-3-(2,3-*O*-isopropylidene-5-*O*-trityl-α-D-ribofuranosyl)-iso-thiazolo[4,5-d]pyrimidine (19a). Obtained from **7a** (500 mg, 0.81 mmol), ethyl-mercaptan (1.0 mL, 13 mmol), DBU (0.43 mL, 2.8 mmol) in absol. MeCN (50 mL). The solvent was removed *in vacuo* and the residue chromatographed (PE/EE 7:2); recrystallization from isopropanol; yield 346 mg (70%) colorless needles of mp 135°C. IR ν 2990, 2915, 1585, 1510. UV ($CHCl_3$) λ_{max} (log ε) 239 (3.91), 270 (3.92), 324 (4.15). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.18/1.25 (ss, 6H), 1.46 (t, 3H, $J = 7.3$), 3.22 (dd, 1H, $J = 10.1, 3.6$), 3.52 (dd, 1H, $J = 10.2, 4.0$), 3.69 (q, 2H, $J = 6.9$), 4.55 (m, 4′-H), 4.81 (d, 1H, $J = 6.1$), 5.50 (t, 1H, $J = 4.7$), 6.06 (d, 1H, $J = 4.6$),

7.12–7.45 (m, trityl), 8.97 (s, 1H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 14.58, 24.33, 25.44, 26.18, 64.96, 82.65, 82.82, 83.74, 83.82, 87.66, 113.17, 127.30, 128.10, 128.78, 141.62, 143.65, 150.94, 154.25, 162.80, 164.17. MS m/z (rel. intens.): 611 (M+; 0.13), 368 (0.98), 243 (2). HR-MS Calcd. for $C_{34}H_{33}N_3O_4S_2$: 611.1913; Found: 611.1913. Anal. Calcd for $C_{34}H_{33}N_3O_4S_2$: C, 66.75; H, 5.44; N, 6.87. Found C, 66.62; H, 5.53; N, 6.92.

β-D-ribofuranosyl-isomer (19b). Obtained from **7a** (320 mg, 0.52 mmol) in absol. MeCN (50 mL); ethylmercaptan (0.7 mL, 9.1 mmol) and DBU (0.3 mL, 2 mmol) with 6 h stirring at 25°C in an argon atmosphere. Evaporating of the solvent and chromatography (PE/EE 7:2) of the yellow sirupous residue and recrystallization from isopropanol gave 240 mg (76%) of colorless crystals of mp 75°C. IR ν 3060, 2990, 2930, 1590, 1530, 1445. UV ($CHCl_3$) λ_{max} (log ε) 244 (3.91), 271 (3.90), 325 (4.07). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.48 (t, 3H, $J = 7.38$), 1.48/1.63 (ss, 6H), 3.13 (d, 2H, $J = 5.26$), 3.43 (q, 2H, $J = 7.35$), 4.45–4.51 (m, 1H), 4.85 (dd, 1H, $J = 6.18, 2.74$), 5.59 (dd, 1H, $J = 6.18, 3.65$), 5.61 (d, 1H, $J = 3.58$), 7.15–7.34 (m, 15H), 8.99 (s, 1H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 15.06, 24.92, 26.36, 28.90, 64.66, 82.55, 83.88, 83.98, 85.79, 87.24, 114.52, 127.54, 128.32, 129.27, 142.72, 144.40, 152.15, 155.02, 164.68, 164.87. MS (FAB) m/z (rel. intens.): 612.2 (M+1; 1.55), 596.2 (M-15; 0.52), 243.1 (trityl; 32.8). Anal. Calcd for $C_{34}H_{33}N_3O_4S_2$: C, 66.75; H, 5.44; N, 6.87. Found: C, 66.25; H, 5.26; N, 6.67.

7-Hydrazino-3-(2,3-*O*-isopropylidene-5-*O*-trityl-α-D-ribofuranosyl)-isothiazolo[4,5-d]pyrimidine (20a). Obtained by treatment of **7a** (250 mg, 0.4 mmol) in CH_2Cl_2 (30 mL) with hydrazine hydrate (98%, 2 mL), and stirring for 4 h at 25°C. Evaporation of the solvent; after chromatography (EE) and recrystallization from isopropanol; yield 21.4 mg (7.4%), mp 205–210°C. IR ν 3340, 3230, 2930, 1650, 1560, 1540. UV ($CHCl_3$) λ_{max} (log ε) 239 (3.75), 260 (3.80), 317 (3.87). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.24/1.32 (ss, 6H), 3.24 (dd, 1H, $J =$ 10.0, 4.4), 3.44 (dd, 1H, $J = 10.1, 4.6$), 4.12 (s, br, NH_2), 4.59 (m, 4′-H), 4.80 (d, 1H, $J = 5.8$), 5.43 (t, 1H, $J = 4.9$), 5.91 (d, 1H, $J = 4.2$), 7.46–7.18 (m, trityl), 8.44 (s, 1H), 8.58 (s, br, NH). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 25.48, 26.28, 64.39, 81.81, 82.59, 83.63, 83.70, 87.63, 113.10, 127.34, 128.14, 128.44, 128.84, 143.73, 153.00, 153.93, 160.60, 160.96. MS m/z (rel. intens.): 581 (M+; 0.40), 243 (trityl; 5). HR-MS Calcd for $C_{32}H_{31}N_5O_4S_2$: 581.2097; Found 581.2104. Anal. Calcd for $C_{32}H_{31}N_5O_4S$: C, 66.08; H, 5.37; N, 12.04. Found: C, 67.70; H, 5.30; N, 11.52.

β-D-ribofuranosyl isomer (20b). Obtained by treatment of a solution of **7b** (650 mg, 1.05 mmol) in CH_2Cl_2 (100 mL) with hydrazine hydrate **14** (98%, 4 mL) and stirring for 1.5 h at room temp. Evaporation of the solvent is followed by chromatography (EE/EtOH 8:1) of the residue and recrystallization from isopropanol/MeOH; yield 210 mg (34.4%), mp 200–203°C. IR ν 3330, 3210, 3050, 2970, 2930, 1660, 1560, 1445. UV ($CHCl_3$) λ (qualit.): 259, 319. ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.36/1.62 (ss, 6H), 3.17 (dd, 1H, $J = 5.15, 9.93$), 3.28 (dd, 1H, $J = 4.96$, 9.93), 4.06 (s, br, 2H), 4.41–4.49 (m, 1H), 4.78–4.84 (m, 1H), 5.53–5.57 (m, 2H),

7.13–7.42 (m, 15H), 8.44 (s, 1H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 25.66, 27.48, 64.22, 80.97, 82.78, 83.19, 84.80, 86.82, 114.25, 127.05, 127.83, 128.67, 128.90, 143.68, 153.36, 155.00, 160.71, 161.17. MS (FAB) m/z (rel. intens.): 582.2 (M + 1; 98), 243.1 (trityl; 100). Anal. Calcd for $C_{34}H_{33}N_3O_4S_2 \cdot 0.5$ MeOH: C, 65.25; H, 5.52; N, 11.71. Found: C, 65.18; H, 5.68; N, 11.70.

7-Isopropylidenehydrazino-3-(2,3-*O*-isopropylidene-5-*O*-trityl-α-D-ribo-furanosyl)-isothiazolo[4,5-d]pyrimidine (21a). 7a (250 mg, 0.4 mmol) was treated with hydrazine hydrate (98%, 2 mL) in CH_2Cl_2 (100 mL) for 1.5 h at room temp. After evaporation the residue was treated with acetone for 1 h at ambient temp., and the mixture concentrated *in vacuo*; chromatography (EE/acetone 2:1) and recrystallization from Petroleum ether 60/90/ethyl acetate; yield 62.3 mg (25%), mp 215°C. IR ν 3340, 3240, 2940, 1630, 1560. UV ($CHCl_3$) λ_{max} (log ε) 239 (3.7), 277 (3.85), 330 (3.95).^{1}H NMR (250 MHz, $CDCl_3$) δ 1.21/1.28 (ss, 6H), 2.01/2.18 (s, 6H), 3.23 (dd, 1H, J = 10.0, 4.1), 3.45 (dd, 1H, J = 10.0, 4.7), 4.57 (t, 1H, J = 4.2), 4.82 (d, 1H, J = 6.2), 5.47 (t, 1H, J = 4.9), 5.97 (d, 1H, J = 4.6), 7.47–7.16 (m, trityl), 8.58 (s, 1H), 8.64 (s, NH).^{13}C NMR (62.9 MHz, $CDCl_3$) δ 16.77, 25.47, 25.56, 26.26, 64.60, 82.14, 82.76, 83.66, 83.78, 87.58, 113.09, 127.29, 128.10, 128.84, 129.95, 143.76, 151.43, 154.27, 156.63, 160.97, 162.97. MS (FAB) m/z (rel. intens.): 622.2 (M + 1; 70), 243.1 (trityl; 55). Anal. Calcd for $C_{35}H_{35}N_3O_4S_2$: C, 67.61; H, 5.67; N, 11.26. Found: C, 65.63; H, 5.00; N, 12.11.

β-D-ribofuranosyl isomer (21b). A solution of **7b** (250 mg, 0.40 mmol) in CH_2Cl_2 (100 mL) was stirred with hydrazine hydrate **14** (98%, 2 mL) for 1.5 h at room temp. After evaporation the residue was treated with acetone for 1 h at ambient temp., and the mixture concentrated *in vacuo*; after chromatography (EE/acetone 2:1) and recrystallization from ethyl acetate; yield 210 mg (89.4%), mp 245–256°C (dec). IR ν 3250, 3060, 2990, 2930, 1660, 1560, 1490, 1445. UV ($CHCl_3$) λ_{max} (log ε) 244 (4.11), 276 (4.47), 331 (4.61). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.39/1.63 (ss, 6H), 1.99 (s, 3H), 2.19 (s, 3H), 3.11–3.18 (m, 2H), 4.44–4.52 (m, 1H), 4.82–4.86 (m, 1H), 5.58–5.62 (m, 2H), 7.16–7.38 (m, 15H), 8.50 (s, 1H), 8.59 (s, 1H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 16.94, 24.20, 24.45, 26.43, 63.06, 79.83, 81.89, 82.20, 83.75, 85.16, 112.19, 125.85, 126.65, 127.37, 129.30, 142.71, 147.60. 151.50, 155.80, 160.75. MS (FAB) m/z (rel. intens.): 622.2 (M + 1; 4.23), 243.1 (trityl; 41.5). Anal. Calcd for $C_{34}H_{33}N_3O_4S_2$: C, 67.61; H, 5.67; N, 11.26. Found: C, 67.14; H, 5.64; N, 11.48.

Synthesis of the Free C-Glycosides 22b, 23a, 24a,b, 25b, 26b, 27a,b by Deprotection.

General Procedure. A solution of the protected nucleoside was stirred in methanolic HCl (14% HCl) for 1–2 h at room temp. Then the solvent was removed in vacuo and the residue was treated with ether. The solid obtained was recrystallized.

7-Dimethylamino-3-β-D-ribofuranosylisothiazolo[4,5-d]pyrimidine (22b). Prepared from **15b** (500 mg, 0.84 mmol) in HCl/MeOH (15 mL) by 1 h stirring;

recrystallization from MeOH; yield 200 mg (75.7%), white crystals of mp 213−215°C. IR ν 3260, 2920, 1600, 1570. UV ($CHCl_3$) λ (qualit.) 271, 332. ^{1}H NMR (DMSO-d_6) δ 3.45 (s, br, 6H), 3.35–5.41 (m, br 9H), 8.61 (s, 1H). ^{13}C NMR (DMSO-d_6) δ 38.98, 61.88, 71.86, 74.35, 80.46, 85.92, 131.57, 146.69, 152.37, 157.17, 161.84. MS (FAB) m/z (rel. intens.) 313.1 (M + 1; 31.2). Anal. Calcd for $C_{12}H_{10}N_4O_4S$: C, 46.13; H, 5.12; N, 17.94. Found: C, 45.85; H, 4.99; N, 17.78.

7-Pyrrolidino-3-α-D-ribofuranosylisothiazolo[4,5-d]pyrimidine (23a). Obtained from **18a** (434 mg, 0.7 mmol) in MeOH/HCl (20 mL) by stirring for 2 h, and recrystallization from ethanol; yield 200 mg (84.7%), mp 112–115 °C. IR ν 3030–3400, 2900, 1580, 1540, 1445. UV ($CHCl_3$) λ (qualit.) 276, 322, 336. ^{1}H NMR (DMSO-d_6) δ 1.98–2.20 (m, 4H), 3.51 (d, 1H, J = 11.57), 3.69 (d, 1H, J = 11.32), 3.82–4.11 (m, 4H), 4.23 (m, 2H), 4.43 (m, 1H), 5.23 (s, br. 3H), 5.53 (d, 1H, J = 3.94), 8.71 (s, 1H). ^{13}C NMR (DMSO-d_6) δ 23.79, 25.38, 48.88, 49.65, 61.20, 71.87, 73.48, 80.57, 83.18, 132.80, 144.00, 150.15, 154.20, 159.17. MS (FAB) m/z (rel. intens.) 339.1 (M + 1; 100). Anal. Calcd for $C_{14}H_{18}N_4O_4S$•MeOH: C, 48.63; H, 5.94; N, 15.13. Found: C, 48.43; H, 5.72; N, 14.69.

7-Ethylthio-3-α-D-ribofuranosylisothiazolo[4,5-d]pyrimidine (24a) From **19a** (320 mg, 0.52 mmol) in MeOH/HCl (5 mL); recrystallization from ethanol; yield 142 mg (83%) of colorless crystals of mp 145°C. IR ν 3390, 3250, 2910, 1570, 1545. UV (EtOH) λ_{max} (log ε) 271 (3.71), 324 (3.94). ^{1}H NMR (250 MHz, DMSO-d_6) δ), 1.39 (t, 3H, J = 5.2), 3.4 (s, br. OH), 3.45 (q, 2H, J = 5.0), 3.97 (m, 1H), 4.14 (m, 1H), 4.54 (q, 1H, J = 3.2), 4.74 (m, 1H), 4.99 (d, 1H, J = 5.2), 5.63 (d, 1H, J = 3.0) 9.08 (s, 1H).^{13}C NMR (62.9 MHz, DMSO-d_6) δ 14.45, 23.80, 61.32, 71.87, 72.68, 80.41, 82.48, 140.20, 151.07, 154.21, 163.21, 165.25. MS (FAB) m/z (rel. intens.): 330.0 (M + 1; 13). Anal. Calcd for $C_{12}H_{15}N_3O_4S_2$: C, 43.76; H, 4.59; N, 12.76. Found: C, 44.10; H, 4.42; N, 12.58.

β-D-ribofuranosylisothiazolo isomer (24b). Obtained from **19b** (150 mg, 16 mmol) in MeOH/HCl (5 mL); recrystallization from ethanol; yield 69.95 mg (86.4%) of white pearly crystals of mp 156–158°C. IR ν 3380, 3250, 2940, 2900, 2880, 1530. UV (EtOH) λ_{max} (log ε) 203 (4.26), 225 (4.34), 270 (3.87), 324 (4.20). ^{1}H NMR (250 MHz, DMSO-d_6) δ 1.39 (t, 3H, J = 7.32), 3.45 (q, 2H, J = 7.32), 3.51–3.66 (m, 2H), 3.94 (q, 1H, J = 4.26), 4.12 (q, 1H, J = 5.0), 4.55 (q, 1H, J = 6.09), 4.87–4.92 (m, 1H), 5.05 (d, 1H, J = 5.19), 5.18 (d, 1H, J = 6.29), 5.24 (d, 1H, J = 6.28), 9.11 (s, 1H). ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 14.36, 23.91, 62.26, 71.81, 74.16, 79.85, 85.78, 141.24, 150.97, 154.25, 163.85, 165.51. MS (FAB) m/z (rel. intens.): 330.0 (M + 1; 100). Anal. Calcd for $C_{12}H_{15}N_3O_4S_2$: C, 43.76; H, 4.59; N, 12.76. Found: C, 44.02; H, 4.47; N, 12.50.

7-Hydrazino-3-β-D-ribofuranosylisothiazolo[4,5-d]pyrimidine (25b). Obtained from **20b** (150 mg, 0.25 mmol) in HCl/MeOH (5 mL) after stirring 1 h; recrystallization from MeOH; yield 51.0 mg (68.9%), mp 205–208°C. IR ν 3380, 3250, 2930, 1590. UV (EtOH) λ (qualit.) 203, 269, 322. ^{1}H NMR (250 MHz, DMSO-d_6) δ 3.61–3.70 (m, 2H), 4.00–4.06 (m, 1H), 4.09 (dd, 1H, J = 3.49, 4.78),

4.18 (s, br, 3H), 4.32 (dd, 1H, $J = 5.33, 6.22$), 5.08 (d, 1H, $J = 6.80$), 5.33 (s, br, 2H), 8.58 (s, 1H), 11.41 (s, br, 1H). ^{13}C NMR measurements turned out to be impossible due to the poor solubility. MS (FAB) m/z (rel. intens.): 300.0 (M+1; 57.9). Anal. Calcd for $C_{10}H_{13}N_5O_4S \cdot HCl \cdot 0.5$ MeOH: C, 34.28; H, 4.35; N, 19.05. Found: C 34.37; H, 4.40; N, 19.59.

7-Isopropylidenehydrazino-3-β-D-ribofuranosylisothiazolo[4,5-d]pyrimidine (26b). By treatment of **21b** (140 mg, 0.23 mmol) in MeOH/HCl (5 mL); recrystallization from MeOH; yield 53.0 mg (67.9%), mp 195–198°C. IR ν 3330, 3120, 2930, 1590, 1560. UV (EtOH) λ_{max} (log ε) 204 (4.20), 281 (3.70), 333 (3.87). ^{1}H NMR (200 MHz, DMSO-d_6) δ 2.11, 2.15 (ss, 2H), 3.57 (dd, 1H, $J = 11.95$, 3.31), 3.67 (dd, 1H, $J = 11.95, 3.12$), 3.97 (d, 1H, $J = 3.31$), 4.08 (dd, 1H, $J = 4.78$, 3.86), 4.41 (dd, 1H, $J = 6.62, 5.15$), 4.48 (s, br, 3H), 5.14 (d, 1H, $J = 6.80$), 8.67 (s, 1H), 11.68 (s, br, 1H).^{13}C NMR (62.9 MHz, DMSO-d_6) δ 18.68, 25.23, 61.78, 71.85, 74.73, 81.29, 85.81, 130.78, 150.16, 151.97, 157.49, 159.45, 160.49. MS (FAB) m/z (rel. intens.): 340 (M + 1; 100). Anal. Calcd for $C_{13}H_{17}N_5O_4S \cdot HCl$: C, 41.58; H, 4.79; N, 18.66. Found: 41.10; H, 4.29; N, 18.43.

7-Dimethylamino-5-methylthio-3-α-D-ribofuranosylisothiazolo[4,5-d] pyrimidine (27a). By treatment of **16a** (150 mg, 0.23 mmol) in MeOH/HCl (10 mL) for 1 h. The solid obtained was recrystallized from EtOH; yield 48 mg (65.7%), mp 173–175°C. IR ν 3400–3100, 2900, 1590, 1560, 1445. UV (EtOH) δ (qualit.) 252, 266, 322, 342.^{1}H NMR (DMSO-d_6) δ 2.52 (s, 3H), 3.22 (s, 6H), 3.48–3.71 (m, 2H), 3.94–4.00 (m, 1H), 4.12–4.18 (m, 1H), 4.56 (t, 1H, J-4.18), 4.94 (s, br, 3H), 5.49 (d, 1H, J-4.18). ^{13}C NMR (DMSO-d_6) δ 13.60, 51.48, 61.31, 80.47, 82.09, 82.47, 86.32, 143.55, 147.68, 155.93, 161.96, 167.06. MS (FAB) m/z (rel. intens.) 359.0 (M+1; 52.7). Anal. Calcd for $C_{13}H_{18}N_4O_4S_2 \cdot HCl$: C, 39.48, H, 4.80; N, 14.17. Found: C, 39.10; H, 4.57; N, 14.10.

β-D-ribofuranosylisothiazolo isomer (27b). Obtained like **27a** from **16b** (200 mg, 0.31 mmol) in MeOH/HCl (20 mL); recrystallization from ethanol; yield 80 mg (72.7%), mp 168–170°C. IR ν 3050–3400, 2930, 1570, 1445. UV ($CHCl_3$) λ (qualit.) 250, 276, 332. ^{1}H NMR (DMSO-d_6) δ 2.52 (s, 3H), 3.35 (s, 6H), 3.48–3.98 (m, 3H), 4.11 (t, 1H, $J = 4.68$), 4.50 (t, 1H, $J = 5.67$), 5.15 (d, 1H, $J = 5.91$), 5.59 (s, br, 3H). ^{13}C NMR (DMSO-d_6) δ 13.70, 51.49, 62.16, 79.67, 80.47, 85.32, 86.31, 143.55, 147.68, 155.88, 162.22, 167.43. MS (FAB) m/z (rel. intens.) 359.1 (M + 1; 22.4). Anal. Calcd for $C_{13}H_{18}N_4O_4S_2 \cdot HCl$: C, 39.48; H, 4.80; N, 14.17. Found: C, 39.15; H, 4.72; N, 14.05.

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REFERENCES

1. Part 2: Wamhoff, H.; Berressem, R.; Nieger, M. *J. Org. Chem*. **1994**, *59*, 1912–1917.
2. cf. Hanessian, S.; Pernet, A.G. *Adv. Carbohydr. Chem. Biochem*. **1976**, *32*, 111– 188; Mizuno, Y. *The Organic Chemistry of Nucleic Acids*, Elsevier, Amsterdam **1986**; Huryn, D.M.; Okabe, M. *Chem. Rev*. **1992**, *92,* 1745–1768; Häbich, D. *Chem. in uns. Zeit* **1991**, *25*, 295–307; Uhlmann, E.; Peyman, A. *Chem. Rev*. **1990**, *90*, 543–584; Thuong, N.T.; Helene, C. *Angew. Chem*. **1993**, *105*, 697–723; *Angew. Chem. Int. Ed. Engl*. **1993**, *33*, 666–690; Yarchoan, R.; Mitsuya, H.; Zhomas, R.V.; Pluda, J.M.; Hartman, N.R.; Perno, C.F.; Marczyk, K.S.; Allain, J.P.; Johns, D.G.; Broder, S. *Science* **1989**, *245*, 412– 414; Tanaka, H.; Baba, M.; Hayakawa, H.; Sakamaki, T.; Miyasaka, T. Ubasawa, M.; Takashima, H.; Sekiya, E.; Nitta, I.; Shigeta, S.;Walker, R.T.; Balzarini, J.; De Clerq, E. *J. Med. Chem*. **1991**, *34*, 349–357.
3. Some C-glycosides with antibiotic, antiviral (HIV), and anticancer activities: Koyama, G.; Maeda, K.; Umezawa, H.; Iitaka, Y. *Tetrahedron Lett*. **1966**, 597–602; Hori, M.; Wakashiro, T.; Ito, E.; Sawa, T.; Takeuchi, T.; Umezawa, H.J. *J. Antibiot*. **1968**, *21A*, 264–270 [*Chem. Abstr*. **1968**, *69,* 11356j]; Farkas, J.; Šorm, *F. Collect. Czech. Chem. Commun*. **1972,** *37,* 2798–2803; Acton, E.M.; Ryan, K.J.; Henry, D.W.; Goodman, L. *J. Chem. Soc., Chem. Commun*. **1971**, 986–988; Nakagawa, Y.; Kano, H.; Tsukuda, Y. Koyama, H. *Tetrahedron Lett*. **1967**, 4105–4109; Inoue, I.; Kuwaijama, I. *J. Chem. Soc., Chem. Commun*. **1980**, 251–253; Buchanan, J.G.; Stobie, A.; Wightman, R.H. *ibid.* **1980**, 916–917; Hildebrand, S.; Leumann, C. *Angew. Chem*. **1996**, *108*, 2100–2102; *Angew. Chem. Int. Ed. Engl*. **1996**, *35,* 1968–1970.
4. Wamhoff, H.; Berressem, R.; Nieger, *M. J. Org. Chem*. **1993**, *58*, 5181– 5185.
5. Divakar, K.J.; Reese, C.B. *J.C.S., Perkin Trans. 1*, **1982**, 1171–1176.
6. Wigerinck, P.; Pannecouque; Snoeck, R.; Claes, P.; De Clerq, E.; Herdewijn, *P. J. Med. Chem*. **1991**, *34,* 2380–2389.
7. Kraszewski, A.; Stawinsky, J. *Teterahedron Lett*. **1980**, *21*, 2935–2936. Here the isolated phosphoryl tris-triazole was used as phosphorylating agent.
8. Abdel-Megied, A.E.-S.; Pedersen, H.; Pedersen, E.B.; Nielsen, C. *Heterocycles* **1993**, *36*, 681– 692.
9. Miles, R.W.; Samano, V.; Robins, M.J. *J. Am. Chem. Soc*. **1995**, *117*, 5951–5957; *J. Org. Chem*. **1995**, *60*, 7066–7069.
10. Loakes, D.; Bazzanini, R.; Brown, D.M. *Helv. Chim. Acta* **1999**, *82*, 2028–2036.
11. The different configurations have been assigned with a and b for the α-and β-isomers, respectively.
12. Other isolated C4-triazole derivatives of zidovudine and other pyrimidine nucleosides *cf.* Wallis, M.P.; Mahmood, N.; Fraser, W. *Il Farmaco* **1999**, *54*, 83-89; Lin, T.-S.; Gao, Y.-S.; Mancini, W.R. *J. Med. Chem.* **1983**, *26*, 1691–1696.
13. Berressem, R. Dissertation, University of Bonn **1992**.

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