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Synthesis of 5′-Amino- and 5′-Azido-2′,5′-dideoxy Nucleosides from Thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione

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Summary. Thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**4**) was silylated and condensed with methyl 5-azido-2,5-dideoxy-3-O-(4-methylbenzoyl)-*D-erythro*-pentofuranoside (**2**) in the presence of *TMS* triflate to afford the corresponding protected nucleoside **6** and acyclic nucleoside **7**. Deprotection of **6** with MeONa/MeOH at room temperature gave 1-(5-azido-2,5-dideoxy-α-*D-erythro*-pentofuranosyl)-thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**8**) and the corresponding β anomer **9**, whereas compound **7** yielded 5-azido-2,5-dideoxy-1-(2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-1-yl)-1-O-methyl-*D-erythro*-pentitol (**10**) under the same reaction conditions. 1-(5-Amino-2,5-dideoxy-β-*D-erythro*-pentofuranosyl)thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**11**) was obtained on treating **9** with Ph_3P in pyridine followed by hyrolysis with NH_4OH. The anomeric nucleosides **14** and **15** and the corresponding acyclic nucleoside **16** were obtained when **4** was trimethylsilylated and condensed with methyl 2-deoxy-3,5-di-O-(4-methylbenzoyl)-*D-erythro*-pentofuranoside (**3**) followed by deprotection with MeONa in MeOH. Compounds **8** and **9** were also obtained when the anomeric mixture **14/15** was treated with a mixture of NaN_3, Ph_3P, and CBr_4 in dry *DMF* at room temperature.

Keywords. HIV; Nucleoside synthesis; Nucleosides, 5′-azido-2′,5′-dideoxy; Thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione nucleosides.

Synthese von 5′-Amino- und 5′-Azido-2′,5′-dideoxynucleosiden aus Thieno[2,3-*d*]pyrimidin-2,4(1*H*,3*H*)-dion

Zusammenfassung. Die Silylierung und anschließende Kondensation von Thieno[2,3-*d*]pyrimidin-2,4(1*H*,3*H*)-dion (**4**) mit 5-Azido-2,5-dideoxy-3-O-(4-methylbenzoyl)-*D-erythro*-pentofuranosid (**2**) in Gegenwart von *TMS*-Triflat führt zum entsprechenden geschützten Nucleosid **6** und zum acyclischen Nucleosid **7**. Abspaltung der Schutzgruppe von **6** mit MeONa/MeOH bei Zimmertemperatur lieferte 1-(5-Azido-2,5-dideoxy-α-*D-erythro*-pentafuranosyl)-thieno[2,3-*d*]pyrimidin-2,4(1*H*,3*H*)-dion (**8**) und das entsprechende β-Anomere **9**, während Verbindung **7** unter den gleichen Reaktionsbedingungen 5-Azido-2,5-dideoxy-1-(2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-1-yl)-1-O-methyl-*D-erythro*-pentitol (**10**) ergab. Umsetzung von **9** mit Ph_3P in Pyridin und anschließende Hydrolyse mit

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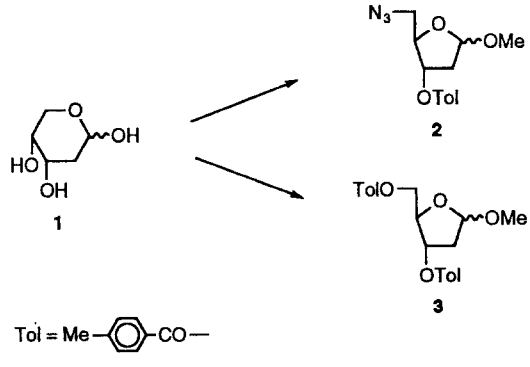
NH_4OH führte zu 1-(5-Amino-2,5-dideoxy-*β*-*D*-*erythro*-pentafuranosyl)thieno[2,3-*d*]pyrimidin-2,4-(1*H*,3*H*)-dion (**11**). Die anomeren Nucleoside **14** und **15** und das entsprechende acyclische Nucleosid **16** wurden durch Trimethylsilylierung und Kondensation von **4** mit 2-Deoxy-3,5-di-O-(4-methylbenzoyl)-*D*-*erythro*-pentofuranosid (**3**) sowie anschließende Entfernung der Schutzgruppe mit MeONa in MeOH hergestellt. Die Verbindungen **8** und **9** wurden auch durch Behandeln des anomeren Gemisches **14**/**15** mit einer Mischung von NaN_3, Ph_3P und CBr_4 in trockenem *DMF* bei Zimmertemperatur erhalten.

Introduction

5′-Amino-5′-deoxythymidine has been demonstrated to be of potent antiviral activity against herpes simplex virus type 1 (HSV-1) in the complete absence of toxicity to the uninfected host *Vero* cells in culture [1, 2]. This compound was therapeutically effective in the topical therapy of herpetic keratouveitis in rabbits and systemic administration into the neonatal mouse revealed no adverse effect *in vivo* or by the histopathological examination [3]. 5′-Amino-3′-O-acylthymidine derivatives show significant antiviral activity by inhibition of the formation of infectious HSV-1 [4]. 5′-Aminonucleosides are useful starting materials for formation of a new type of antisense oligonucleotides with a modified backbone. These oligonucleotides are of interest in therapies utilizing antisense DNAs to interrupt protein synthesis or otherwise inactivate messenger RNA (mRNA) or double stranded DNA [5]. Also, 5′-azido nucleosides are of interest and can be considered as precursors of 5′-amino nucleosides. We found it interesting to investigate the synthesis and the antiviral activity of 5′-amino and 5′-azido nucleosides with thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione as the nucleobase, *i.e.* thieno annelated analogues.

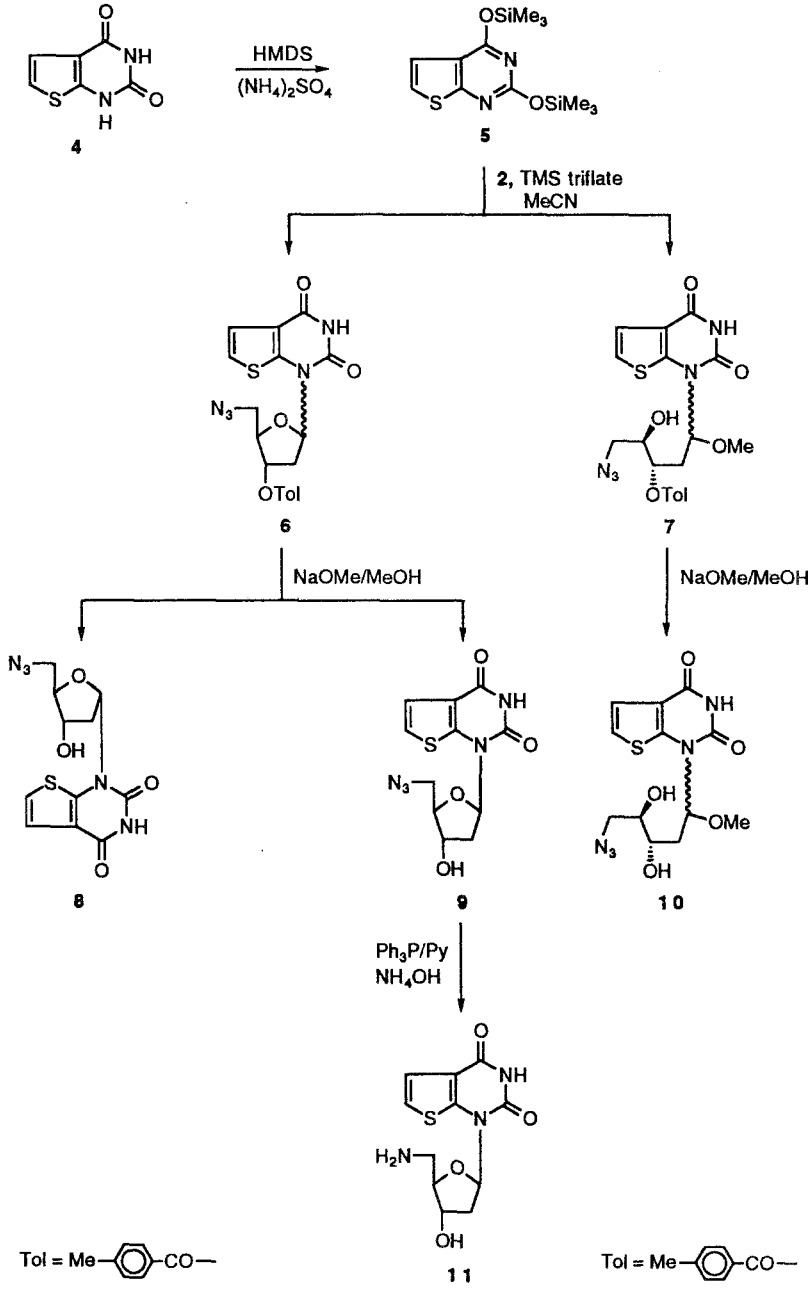
Results and Discussion

Methyl 5-azido-2,3-dideoxy-3-O-(4-methylbenzoyl)-*D*-*erythro*-pentofuranoside (**2**) was synthesized from the commercially available 2-deoxy-*D*-ribose (**1**) by consecutive methyl glycosidation [6, 7], replacement of 5-OH with N_3 [8, 9], and finally 3-OH protection with 4-methylbenzoyl chloride in pyridine [10]. Methyl 2-deoxy-3,5-di-O-(4-methylbenzoyl)-*D*-*erythro*-pentofuranoside (**3**) was prepared from **1** by glycosidation and subsequent treatment with 4-methylbenzoyl chloride in pyridine [11].



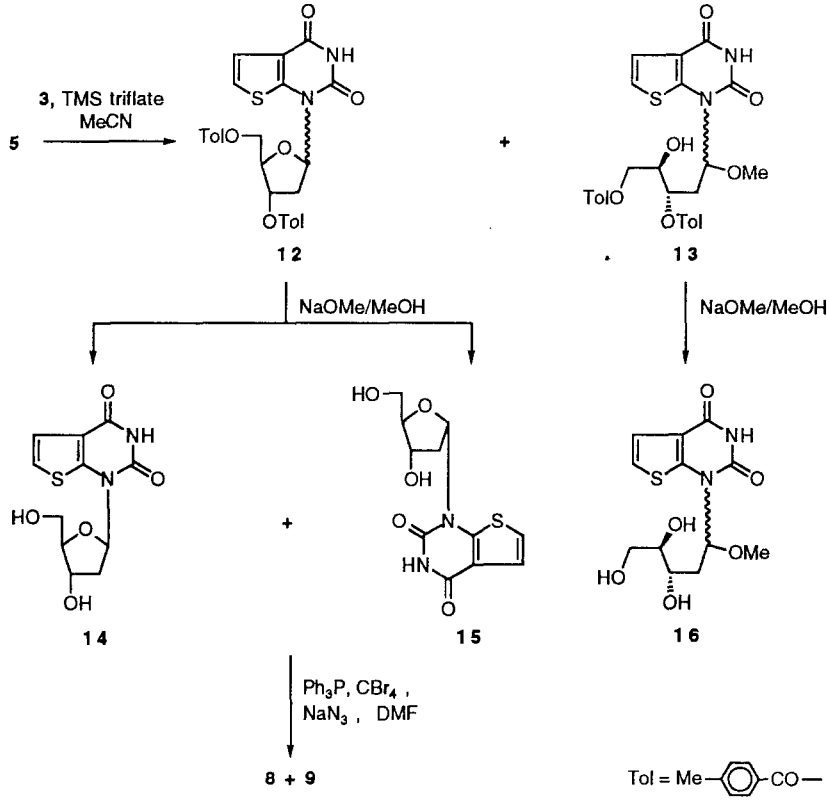
Scheme 1

The silylation of thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**4**) was accomplished with 1,1,1,3,3,3-hexamethyldisilazane (*HMDS*) in the presence of a catalytic amount of ammonium sulfate. The trimethylsilylated derivative **5** thus obtained was condensed with methyl 5-azido-2,5-dideoxy-3-O-(4-methylbenzoyl)-*D-erythro*-pentofuranoside (**2**) in acetonitrile using trimethylsilyl trifluoromethanesulfonate (*TMS* triflate) as the catalyst according to the method of *Vorbrüggen et al.* [12] to afford a 2:5 α:β anomeric mixture of the protected nucleoside **6** and the acylic nucleoside **7** in 34% and 23% yield, respectively.



Scheme 2

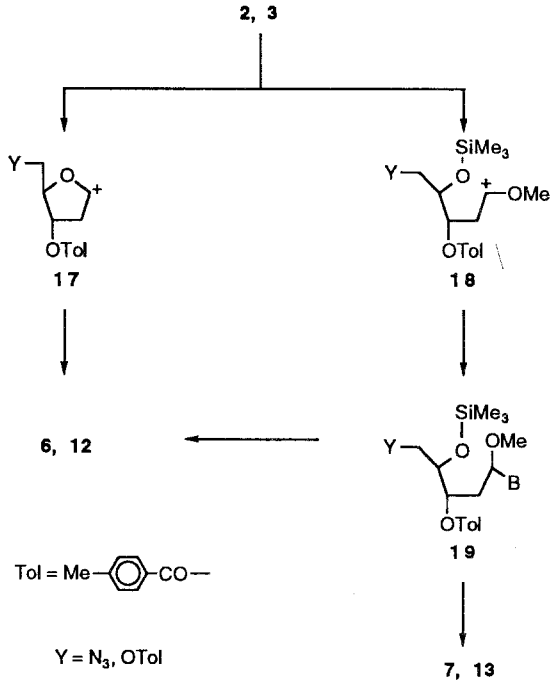
Treatment of compound **6** with sodium methoxide in methanol at room temperature gave 1-(5-azido-2,5-dideoxy-α-*D-erythro*-pentofuranosyl)thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**8**) and the corresponding β anomer **9** in 28% and 51% yield, respectively. Under the same reaction condition, the diastereomeric mixture of compound **7** afforded 5-azido-2,5-dideoxy-1-(2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-1-yl)-1-O-methyl-*D-erythro*-pentitol (**10**) which was obtained in a total yield of 69% after separation into pure stereoisomers. 1-(5-Amino-2,5-dideoxy-β-*D-erythro*-pentofuranosyl)-thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**11**) was obtained in a good yield by treatment of compound **9** with triphenylphosphine in pyridine followed by hydrolysis with ammonium hydroxide [13].



Scheme 3

The protected nucleoside **12** and the acyclic nucleoside **13** were obtained when the trimethylsilylated derivative **5** was condensed with methyl 2-deoxy-3,5-di-O-(4-methylbenzoyl)-*D-erythro*-pentofuranoside (**3**) in acetonitrile in the presence of *TMS* triflate as catalyst. Removal of the protecting group from the sugar moiety of compound **12** was achieved by treatment with sodium methoxide in methanol at room temperature. The separation of the α/β anomeric mixture on a silica gel column was partially achieved to give the pure β anomer **14** and the anomeric mixture **14**/**15** in a total yield of 73%. 2-Deoxy-1-(2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-*d*]pyrimidin-1-yl)-1-O-methyl-*D-erythro*-pentitol (**16**) was obtained as a diastereomeric mixture in 79% yield when the protected acyclic nucleoside **13** was

treated with sodium methoxide in methanol at room temperature. Treatment of the anomeric mixture **14**/**15** with triphenylphosphine, carbon tetrabromide, and sodium azide in dry N,N-dimethylformamide at room temperature afforded the corresponding 5'-azido nucleosides **8** and **9** in a moderate yield (21%).



Scheme 4

Formation of the acyclic nucleosides **7** and **13** can be explained by a mechanism in which the ring oxygen of the sugar is silylated making ring opening possible with formation of the acyclic carbenium ion **18** which, in turn, can condense with the silylated nucleobase to yield **19** [14, 15]. The intermediates, producing the acyclic nucleosides **7** and **13** on hydrolysis, may also represent an important route for the formation of the nucleosides **6** and **12**. A similar mechanism has recently been reported when $SnCl_4$ is used as the catalyst for the nucleoside condensation reaction [16].

The structures of the newly synthesized compounds were confirmed by ^1H NMR, ^{13}C NMR, IR and mass spectra. The protons in the ^1H NMR spectra were assigned by ^1H-^1H homonuclear shift-correlated (COSY) 2D NMR. ^1H Nuclear *Overhauser* Effects (NOE difference spectroscopy) proved **14** to be a β anomer. A typical decisive feature was irradiation of $2'_\alpha$-H at the α-face of the sugar which resulted in a strong NOE enhancement in 1′-H (11%), whereas $2'_\beta$-H at the β-face resulted in a strong NOE enhancement in 3′-H (7%).

The compounds **8**, **9**, and **11** did not show any significant activity at 100 μM against HIV-1 in MT-4 cells. Expression of HIV in culture medium was quantified by HIV antigen detection ELISA. The same compounds were also devoid of any activity at 100 μM against herpes simplex virus, type 1 (HSV-1), strain *McIntyre* when tested in African green monkey kidney cell line *Vero*.

Experimental

NMR spectra were recorded on a Bruker 250 FT NMR spectrometer with *TMS* as an internal standard. Mass spectra were recorded using electron ionization (EI) on a Varian Mat 311A spectrometer and fast atom bombardment (FAB) on a Kratos MS 50 spectrometer. IR spectra were recorded on a Perkin Elmer 1720 spectrometer. The silica gel (0.040–0.063 mm) used for column chromatography was purchased from Merck.

1-[5-Azido-2,5-dideoxy-3-O-(4-methylbenzoyl)-D-erythro-pentofuranosyl]thieno[2,3-d]pyrimidine-2,4(1H,3H)-dione (**6**) *and 5-Azido-2,5-dideoxy-1-(2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidin-1-yl)-O-methyl-3-O-(4-methylbenzoyl)-D-erythro-pentitol* (**7**)

A mixture of thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**4**, 1.34 g, 8 mmol), $(NH_4)_2SO_4$ (100 mg) and 1,1,1,3,3,3-hexamethyldisilazane (*HMDS*) (60 ml) was refluxed overnight. The clear solution obtained was cooled and the solvent was removed *in vacuo*. The resulting trimethylsilylated derivative **5** was dissolved in anhydrous MeCN (20 ml), and a solution of 5-azido-2,5-dideoxy-3-O-(4-methylbenzoyl)-*D-erythro*-pentofuranoside (**2**, 1.46 g, 5 mmol) in anhydrous MeCN (20 ml) was added with stirring. The mixture was cooled to −50 °C and a solution of *TMS* triflate (1.3 ml, 6.5 mmol) in anhydrous MeCN (5 ml) was added dropwise and the mixture was stirred for 1 h at −35 °C. The mixture was diluted with CH_2Cl_2 (200 ml), washed with a cold sat. aq. $NaHCO_3$ (150 ml), then with cold H_2O (3 × 150 ml), and dried over anhydrous Na_2SO_4. The solvent was removed *in vacuo* and the residue was chromatographed on silica gel with $CHCl_3$ to afford **6** as a white form, yield 720 mg (34%, $\alpha:\beta = 2:5$), and **7** as a white foam, yield 530 mg (23%).

1-(5-Azido-2,5-dideoxy-α-D-erythro-pentofuranosyl)thieno[2,3-d]pyrimidine-2,4 (1H,3H)-dione (**8**) *and the corresponding β anomer* **9**

A suspension of the protected nucleoside **6** (470 mg, 1.1 mmol) in anhydrous MeOH (15 ml) and MeONa (65 mg, 1.12 mmol) in anhydrous MeOH (5 ml) were mixed, stirred at room temperature for 2 h, and neutralized with NH_4Cl (75 mg, 1.14 mmol). The solvent was removed *in vacuo* and the residue was chromatographed on silica gel with $MeOH/CHCl_3$ (0–2%) to afford **8** and **9**.

Compound **8**: Yield, 95 mg (28%); m.p., 177–178 °C; IR (KBr), $\nu = 2105\ cm^{-1}$ (N_3); ^1H NMR (250 MHz, *DMSO*-d_6), $\delta = 2.23$ (dt, 1H, $J = 7.2$, 13.4 Hz, 2′-H), 2.51 (td, 1H, $J = 6.4$, 12.9 Hz, 2′-H), 3.43 (dd, 1H, $J = 5.9$, 13.3 Hz, 5′-H), 3.56 (dd, 1H, $J = 3.0$, 13.2 Hz, 5′-H), 4.18 (m, 2H, 3′-H, 4′-H), 5.43 (d, 1H, $J = 4.0$ Hz, OH), 6.29 (t, 1H, $J = 6.7$ Hz, 1′-H), 7.21 (d, 1H, $J = 5.8$ Hz, 5-H), 7.24 (d, 1H, $J = 5.8$ Hz, 6-H), 11.47 (s, 1H, NH) ppm; ^{13}C NMR (62.9 MHz, *DMSO*-d_6), $\delta = 37.71$ (C-2′), 51.64 (C-5′), 70.10 (C-3′), 84.60, 86.44 (C-1′, C-4′), 117.02 (C-4a), 119.31, 121.19 ($C_{arom.}$), 148.11 (C-7a), 149.56 (C-2), 158.20 (C-4) ppm; EI MS, m/z (%) = 309 (M^+, 64.)

Compound **9**: Yield, 175 mg (51%); m.p., 168–169 °C; IR (KBr), $\nu = 2105\ cm^{-1}$ (N_3); ^1H NMR (250 MHz, *DMSO*-d_6), $\delta = 2.08$ (m, 1H, 2′-H), 2.51 (td, 1H, $J = 7.3$, 14.6 Hz, 2′-H), 3.51 (m, 2H, 5′-H), 3.86 (q, 1H, $J = 5.1$ Hz, 4′-H), 4.23 (m, 1H, 3′-H), 5.44 (broad s, 1H, OH), 6.37 (t, 1H, $J = 7.0$ Hz, 1′-H), 7.21 (m, 2H, 5′-H, 6-H) ppm; ^{13}C NMR (62.9 MHz, *DMSO*-d_6), $\delta = 36.51$ (C-2′), 51.27 (C-5′), 70.52 (C-3′), 84.54, 85.31 (C-1′, C-4′), 117.02 (C-4a), 119.02, 121.06 (C_{arom}), 149.15 (C-7a), 149.41 (C-2), 157.98 (C-4) ppm; EI MS, m/z (%) = 309 (M^+, 48).

5-Azido-2,5-dideoxy-1-(2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidin-1-yl)-1-O-methyl-D-erythro-pentitol (**10**)

The protected acyclic nucleoside **7** (360 mg, 0.78 mmol) was treated with MeONa (43 mg, 0.8 mmol) similarly was described in the preparation of **8** and **9**. Purification by column chromatography on silica gel with the gradient 0–3% MeOH in $CHCl_3$ gave **10** as a white solid, yield 183 mg (69%).

More polar anomer: Yield, 101 mg (38%); m.p., 121–122 °C; ^{1}H NMR (250 MHz, CD_3OD), $\delta = 1.69$ (ddd, 1 H, $J = 4.0$, 10,4, 14.4 Hz, 2'-H), 2.51 (ddd, 1H, $J = 1.8$, 9.2, 13.9 Hz, 2 -H), 3.30–3.52 (m, 6H, OCH_3, 5'-H, 4'-H), 3.71 (m, 1H, 3'-H), 6.17 (dd, 1H, $J = 4.1$, 9.1 Hz, 1'-H), 7.11 (d, 1H, $J = 5.6$, Hz, 5-H), 7.27 (d, 1H, $J = 5.6$ Hz, 6-H) ppm; ^{13}C NMR (62.9 MHz, CD_3OD), $\delta = 37.26$ (C-2'), 55.21 (OCH_3), 57.40 (C-5'), 70.18 (C-3'), 75.65 (C-4'), 88.51 (C-1'), 119.09 (C-4a), 120.95, 122.70 (C_{arom}) 150.71 (C-7a), 152.47 (C-2), 161.25 (C-4) ppm; FAB MS, $m/z = 342$ ($M^+ + 1$).

Less polar anomer: Yield, 82 mg (31%); m.p.; 129–131 °C; ^{1}H NMR (250 MHz, $CDCl_3$), $\delta = 2.02$ (ddd, 1H, $J = 5.5$, 8.3, 13.9 Hz, 2'-H), 2.45 (ddd, 1H, $J = 2.8$, 7.8, 14.4 Hz, 2'-H), 3.26–3.58 (m, 7H, OCH_3, 5'-H, 4'-H, 3'-H), 6.18 (dd, 1H, $J = 5.2$, 7.7 Hz, 1'-H), 7.12 (d, 1H, $J = 5.9$ Hz, 5-H), 7.28 (d, 1H, $J = 5.9$ Hz, 6-H) ppm; ^{13}C NMR (62.9 MHz, CD_3OD), $\delta = 37.81$ (C-2'), 55.29 (OCH_3), 57.22 (C-5'), 70.10 (C-3'), 75.21 (C-4'), 88.67 (C-1'), 119.28 (C-4a), 121.01, 122.77 (C_{arom}), 150.33 (C-7a), 152.93 (C-2), 161.14 (C-4) ppm; FAB MS, $m/z = 342$ ($M^+ + 1$).

1-(5-Amino-2,5-dideoxy-β-D-erythro-pentofuranosyl)thieno[2,3-d]pyrimidine-2,4(1H,3H)-dione (**11**)

1-(5-Azido-2,5-dideoxy-*β-D-erythro*-pentofuranosyl)-thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**9**, 140 mg, 0.45 mmol) and triphenylphosphine (194 mg, 0.74 mmol) were dissolved in pyridine (3 ml) and kept at room temperature for 1 h. Conc. ammonium hydroxide was added and the reaction mixture was allowed to stand for an additional 2 h. The solvent was removed *in vacuo* and the residue was chromatographed on silica gel with the gradient 0–5% MeOH in $CHCl_3$ to obtain **11**. Yield, 92 mg (72%); m.p., 178–180 °C; ^{1}H NMR (250 MHz, *DMSO*-d_6), $\delta = 2.02$ (ddd, 1 H, $J = 3.3$, 6.3, 13.5 Hz, 2'-H), 2.36 (m, 1H, 2'-H), 2.87 (d, 1H, $J = 5.9$ Hz, 5'-H), 3.68 (m, 1H, 4'-H), 4.16 (m, 1H, 3'-H), 5.45 (broad s, 3H, NH_2, OH), 6.36 (t, 1H, $J = 7.2$ Hz, 1'-H), 7.22 (s, 2H, 5-H, 6-H) ppm; ^{13}C NMR (62.9 MHz, *DMSO*-d_6), $\delta = 36.77$ (C-2'), 43.64 (C-5'), 70.79 (C-3'), 84.56 (C-4'), 88.09 (C-1'), 117.12 (C-4a), 119.27, 121.37 (C_{arom}), 148.58 (C-7a), 149.52 (C-2), 158.01 (C-4) ppm; FAB MS, $m/z = 284$ ($M^+ + 1$).

1-[2-Deoxy-3,5-di-O-(4-methylbenzoyl)-D-erythro-pentofuranosyl)thieno[2,3-d]pyrimidine-2,4(1H,3H)-dione (**12**) *and 2-Deoxy-3,5-di-O-(4-methylbenzoyl)-1-(2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidin-1-yl)-1-O-methyl-D-erythro-pentitol* (**13**)

Thieno[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**4**, 0.84 g, 5 mmol) was silylated, similarly as described in the preparation of **6** and **7**, and trimethylsilylated derivative **5** was dissolved in anhydrous MeCN (15 ml). A solution of methyl 2-deoxy-2,5-di-O-(4-methylbenzoyl)-*D-erythro*-pentofuranoside (**3**, 1.15 g, 3 mmol) in anhydrous MeCN (15 ml) was added with stirring. The reaction mixture was cooled to −50 °C and a solution of *TMS* triflate (0.75 ml, 3.9 mmol) in anhydrous MeCN (5 ml) was added dropwise. The reaction mixture was stirred for 2 h at −30 °C and 2 h at −20 °C. The reaction mixture was diluted with CH_2Cl_2, washed with $NaHCO_3$ and H_2O, and dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue was chromatographed on silica gel with $CHCl_3$ to give **12** as a white foam, yield 650 mg (42%, $\alpha:\beta = 1:3$), and **13** as a white foam, yield 120 mg (7%).

1-(2-Deoxy-β-D-erythro-pentofuranosyl)thieno[2,3-d]pyrimidine-2,4(1H,3H)-dione (**14**)

The protected nucleoside **12** (500 mg, 0.96 mmol) was treated with MeONa (106 mg, 1.96 mmol) similarly as described in the preparation of **8** and **9**. The mixture was stirred at room temperature for 5 h. After purification on silica gel with 0–5% MeOH in $CHCl_3$, the title compound **14** and a mixture of **14** and **15** were obtained in a total yield of 198 mg (73%).

Compound **14**: White solid; yield, 54 mg (20%); m.p., 166–167 °C; ^{1}H NMR (250 MHz, *DMSO*-d_6), $\delta = 2.04$ (ddd, 1H, $J = 3.2$, 6.4, 13.6 Hz, $2'_\alpha$-H), 2.38 (m, 1H, $2'_\beta$-H), 3.66 (t, 2H, $J = 5.4$ Hz, 5'-H), 3.77 (q, 1 H, $J = 5.1$, 4'-H), 4.19 (m, 3'-H), 4.88 (t, 1H, $J = 5.5$ Hz, OH), 5.34 (d, 1H, $J = 4.6$ Hz, OH), 6.37 (dd, 1H, $J = 6.5$, 8.1 Hz, 1'-H), 7.21 (d, 2H, $J = 5.6$ Hz, 5-H), 7.23 (d, 1H, $J = 5.6$ Hz, 6-H), 11.51 (s, 1H,

NH) ppm; ^{13}C NMR (62.9 MHz, *DMSO*-d_6), $\delta = 36.60$ (C-2′), 61.41 (C-5′), 70.11 (C-3′), 84.84 (C-4′), 87.42 (C-1′), 117.08 (C-4a), 119.33, 121.32 (C_{arom}), 148.76 (C-7a), 149.56 (C-2), 158.05 (C-4) ppm; EI MS, m/z (%) = 284 (M^+, 0.8); peak matching for $C_{11}H_{12}N_2O_5S$, calcd.: 284.0467, found: 284.0457.

2-Deoxy-1-(2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidin-1-yl)-1-O-methyl-D-erythro-pentitol (**16**)

The protected acyclic nucleoside **13** (100 mg, 0.18 mmol) was treated with MeONa (21 mg, 0.39 mmol) similarly as described in the preparation of **8** and **9**. The reaction mixture was stirred for 3 h at room temperature. Purification on silica gel with 5% MeOH in $CHCl_3$ afforded **16** as a white solid, yield 45 mg (79%). ^{1}H NMR (250 MHz, *DMSO*-d_6), $\delta = 1.55$, 1.84, 2.37 (3 × m, 2′-H), 3.18–3.36 (m, OCH_3, 5′-H, 4′-H, 3′-H), 4.29–4.72 (m, 3 × OH), 6.08 (m, 1H, 1′-H), 7.22 (m, 2H, 5-H, 6-H) ppm; ^{13}C NMR (62.9 MHz, *DMSO*-d_6), $\delta = 35.26$, 35.72 (C-2′), 55.62, 55.92 (OCH_3), 62.94 (C-5′), 67.59 (C-3′), 74.69 (C-4′), 86.07 (C-1′), 117.08, 117.19 (C-4a), 119.34, 121.12 (C_{arom}), 147.97 (C-7a), 150.49 (C-2), 158.27 (C-4) ppm; FAB MS, $m/z = 317$ ($M^+ + 1$).

Reaction of the anomeric mixture **14**/**15** *with* $NaN_3/Ph_3P/CBr_4$

CBr_4 (160 mg, 0.48 mmol) was added to the anomeric mixture **14**/**15** (100 mg, 0.35 mmol) Ph_3P (110 mg, 0.94 mmol), and NaN_3 (63 mg, 0.96 mmol) in dry *DMF* (5 ml). The reaction mixture was stirred 10 days at room temperature and the solvent was removed *in vacuo*. The residue was chromatographed on silica gel with 0–2% MeOH in $CHCl_3$ to afford **8** and **9** in a total yield of 23 mg (21%).

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