141. 3′,4′-Diethynyl-2′,3′,5′-trideoxy-5′-noruridine: A New Self-polymerizable 2′-Deoxyribonucleoside Analogue

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Dedicated to Prof. Dr. *Richard Neidlein*, Heidelberg, on the occasion of his 65th birthday

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In 10 steps, 3′,4′-diethynyl-2′,3′,5′-trideoxy-5′-noruridine (**14**) was synthesized in 5% overall yield from commercial uridine, using conventional methods of nucleoside chemistry. As two functional groups capable to react with each other are present in the same molecule, the synthetic compound is able to form polymers, similar to the polynucleotides, by an acetylene coupling reaction.

Introduction. – Recently, the total syntheses of self-polymerizable carbocyclic analogues of 2′-deoxythymidine and 2′-deoxyadenosine, both as racemates, were reported from our laboratory [1]. Until now, however, the investigation of the intermolecular condensation of these nucleoside analogues has been delayed by the lack of an efficient synthesis suitable for the preparation of the pure enantiomers in sufficent quantities.

The present work deals with the enantioselective synthesis of a derivative of 2′-deoxyuridine, in which the hydroxymethyl and OH substituents at the 4′- and 3′-positions of the ribose ring, respectively, are replaced by ethynyl groups. As terminal alkynes can be coupled in the presence of a cuprous or cupric salt (*Glaser* or *Eglinton* reaction, resp.), the new nucleoside analogue **14** should be a suitable monomer for the preparation of polymeric chains similar to polyuridylic acid.

Although nucleoside analogues in which ethynyl groups are bound to the positions C(2′) [2], C(3′) [3–7], or C(4′) [8–10] of the ribose moiety are known, **14** appears to be the first such analogue to be described in which two ethynyl groups are present in the same molecule.

Results and Discussion. – *Attempted Synthesis of* **14** *from Acetate* **6b**. For a partial synthesis of **14**, two possible routes were taken into consideration, both starting with commercially available materials, namely 2′-deoxyuridine (**1**) and uridine (**4**), respectively (*Scheme 1*). In both cases, the transformation of the $HOCH_2$(5′) substituent into an ethynyl group was considered to be practicable using a well-established *Wittig*-type reaction in nucleoside chemistry [8]. For the introduction of the ethynyl group at C(3′) (*via* **2** and **5**, resp.), the known 1-(3′-deoxy-3′-ethynyl-5′-*O*-tritylarabinosyl)uracil **6a** [3]

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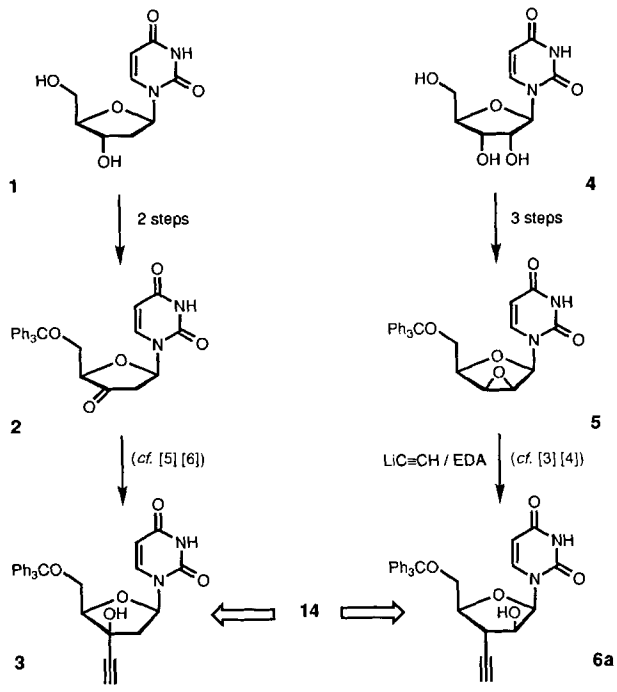
Scheme 1. *Two Possible Pathways for a Short Partial Synthesis of 3′,4′-Diethynyl-2′,3′,5′-trideoxy-5′-noruridine* (**14**)

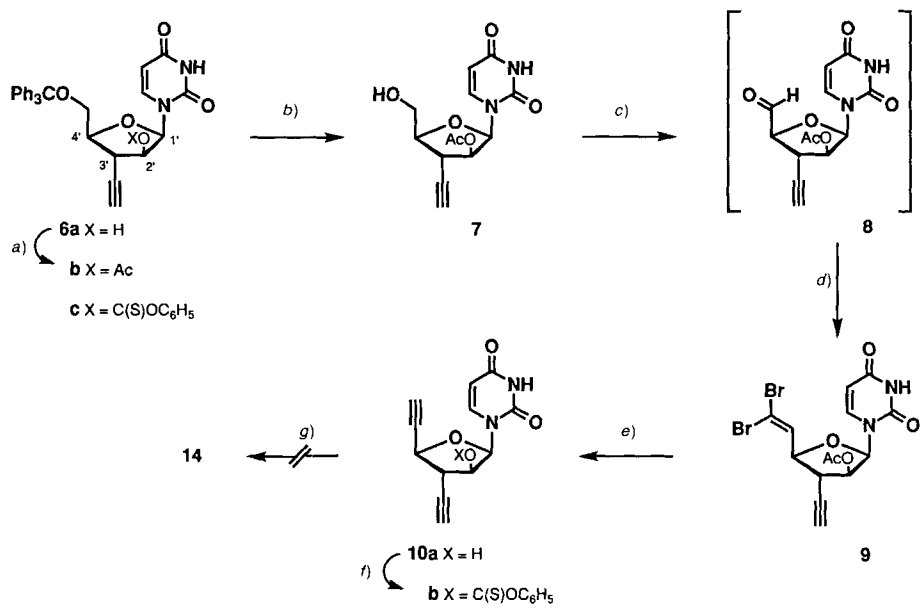


[4] was preferred to its 2′-deoxy-*xylo*-isomer **3** (*cf.* [5] [6]) as an intermediate, in order to avoid the risk of epimerization and/or elimination during radical deoxygenation of the propargylic OH group bound to C(3′) of the latter. Both side reactions were observed previously in a similar case [2]. On the other hand, enantiomerically pure **6a** was readily accessible in four steps from uridine *via* the 2′,3′-epoxy-*lyxo*-derivative **5** [4], a synthetic route which is substantially shorter than the reported stereospecific synthesis of 2′,3′-dideoxy-3′-ethynylthymidine [7], even though an additional step for the elimination of the HO–C(2′) group has to be taken into consideration. Last but not least, uridine is considerably less expensive than 2′-deoxyuridine, as starting material.

In a first attempt, elimination of the HO–C(2′) group was postponed to the last step of the synthesis of **14** (*Scheme 2*). Thus, epoxide **5** was reacted with the ethylenediamine complex of ethynyllithium according to the procedure given in [4], which was slightly modified using 4 instead of 3 equiv. of the reagent. In this way, the reaction time could be reduced from 48 to 3 h making available **6a** in 73% yield (*cf. Exper Part*). After transformation of **6a** into the corresponding 2′-acetate **6b** and subsequent deprotection of HO–C(5′), the obtained primary alcohol **7** was transformed into aldehyde **8** by *Moffatt* oxidation (*cf.* [11]). The desired diethynyl-nucleoside **10a** was obtained from **8** through *Wittig* reaction with (dibromomethylidene)triphenylphosphorane (→ **9**) and subsequent base-catalyzed dehydrohalogenation (*cf.* [8]).

Finally, substitution of the HO–C(2′) group of **10a** by a H-atom was attempted by *Barton* deoxygenation [12] of the corresponding phenoxy(thiocarbonyl) derivative **10b**

Scheme 2. *Attempted Synthesis of 3',4'-Diethynyl-2',3',5'-trideoxy-5'-noruridine* (**14**)



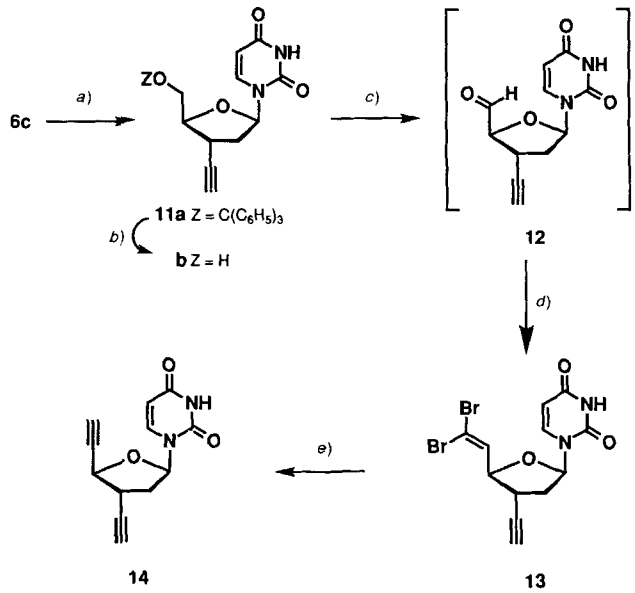
a) Ac_2O/Py. *b*) AcOH, *c*) DMSO, DCC. *d*) $Ph_3P{=}CBr_2$. *e*) BuLi, THF. *f*) $Ph_5OC(S)Cl$, MeCN, 4-(dimethylamino)pyridine. *g*) Bu_3SnH, AIBN.

according to the procedure described in [13]. Unfortunately, however, reaction of **10b** with Bu_3SnH in the presence of 2,2'-azobis[isobutyronitrile] (AIBN) in hot toluene led to an intractable mixture, in which the desired product **14** could not be detected. A similar experience was made by *Matsuda et al.* [14] on the attempted radical deoxygenation of a (2'-ethynylarabinosyl)uracil derivative, in which the terminal C-atom of the ethynyl group was not protected.

Synthesis of **14** *from* O-*Phenyl Thiocarbonate* **6c**. Despite the above mentioned failure, removal of HO–C(2') was attempted again, this time before introduction of the second ethynyl group in the molecule. Thus, alcohol **6a** was transformed into the corresponding phenoxy(thiocarbonyl) derivative **6c**, which, in its turn, was reacted with Bu_3SnH. This time, the critical reaction step proceeded satisfactorily yielding 46% of the deoxygenated product **11a**. The next steps, which paralleled those described above (→ **12** → **13**), resulted in the synthesis of the desired diethynyl-nucleoside **14**, which was obtained as a colorless crystalline compound (*Scheme 3*).

Molecular Structure of Diethynylnucleoside **14**. In view of a study of the polymerization of **14**, knowledge of the preferred conformation of the molecule appeared to be important. Actually, owing to intramolecular electronic repulsion between the two ethynyl groups, a diaxial (*i.e.* 3'-*endo*-2'-*exo*) conformer seemed to be favored *a priori*,

Scheme 3. *Synthesis of 3',4'-Diethynyl-2',3',5'-trideoxy-5'-noruridine* (**14**)



a) Bu_3SnH, AIBN. *b*) AcOH. *c*) DMSO, DCC. *d*) $Ph_3P{=}CBr_2$. *e*) BuLi, THF.

an assumption which was confirmed by X-ray diffraction analysis of crystalline **14**[3]) (*Fig.*).

Conclusion. – As mentioned before, compound **14** is the first nucleoside derivative in which two ethynyl groups are present in the same molecule. The two reactive groups replace the substituents which are involved in the polymerization process of natural monomeric subunits of DNA. Preliminary experiments carried out with **14** in the presence of cuprous chloride and *N,N,N',N'*-tetramethylethylenediamine (tmen, *cf.* [18]) reveal that oligomers are formed, the size of which is limited by their solubility in the solvent used. The elucidation of the structure of these oligomers is being investigated in our laboratory, at present.

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[3]) Crystal data for **14**: $C_{12}H_{10}N_2O_3$, space group $P2_12_12_1$, cell dimensions $a = 4.820(1)$, $b = 8.696(1)$, $c = 26.646(6)$ Å, $V = 1116.9(4)$ Å^3, $Z = 4$, $D_c = 1.369$ Mg m^{-3}, lattice parameters determined from least-squares refinement of the $\pm\omega$ values of 12 reflections and their equivalents in the range $20 \leq 2\Theta \leq 25°$; data collection with *Stoe-AED2* 4-circle diffractometer (MoK_α radiation, $\lambda = 0.71073$ Å) ar room temperature, ω/Θ scan mode with Θ limits 2.5 to 25°; 2398 reflections measured, 1199 unique ($R_{int} = 0.107$), 468 observed ($F_o > 4\sigma(F_o)$); structure solved by direct methods and difference *Fourier* synthesis (SHELXS-86 [16]); refinement (SHELXL-93 [17]) all 17 non-H-atoms anisotropic, 10 H-atoms were included in calculated positions with $U_{iso} = 1.2 \times U_{eq}(C)$; $wR_2 = 0.062$ (all data); $R_1 = 0.044$, $wR_2 = 0.045$ (obsd. data); $w = 1/[\sigma^2(F_o^2)]$; max. shift in last refinement cycle $\Delta/\sigma - 0.001$, residual density; max. 0.149, min. −0.173 eÅ^{-3}. Tables of atomic coordinates and bond distances and angles were deposited with the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB2 1EZ, England.

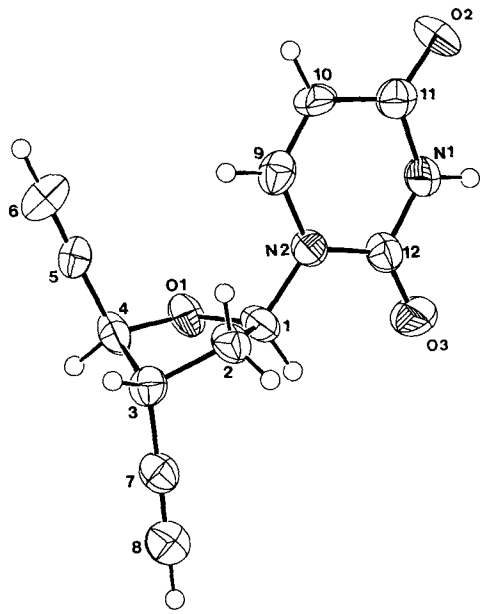

Figure. *Molecular structure of compound* **14**, *showing the crystallographic numbering scheme and ellipsoids at 50% probability level* [15]

Financial support of this work by the Agro Division of *Ciba-Geigy AG*, Basel, is gratefully acknowledged. NMR Spectra on the *Bruker-AM-360* instrument and mass spectra were recorded by *F. Fehr* and *F. Nydegger*, respectively. Elemental analyses were carried out at *Ciba-Geigy AG*, Forschungszentrum, CH-1723 Marly.

Experimental Part

General. See [1]. Uridine, lithium-acetylide-ethylenediamine complex (LiC≡CH/en), 2,2′-azobis(2-methylpropanenitrile) (AIBN), *N,N′*-dicyclohexylcarbodiimid (DCC), 4-(dimethylamino)pyridine, DMSO, CF_3COOH, tetramethylethylenediamine (tmen), and other reagents were purchased from *Fluka Chemie AG*. Solvents for chemical reactions were generally distilled over a proper drying agent prior to use. Reactions were monitored by thin-layer chromatography (TLC) on *E. Merck* silica gel $60F_{254}$ (0.2 mm) precoated aluminium foils. Column chromatography (CC): *E. Merck* silica gel *60* (230-400 mesh).

*1-[3-Deoxy-3-α-ethynyl-5-O-(triphenylmethyl)-β-*D*-arabinofuranosyl]pyrimidine-2,4(1*H*,3*H*)-dione* (**6a**). LiC≡CH/en (1.24 g, 12.8 mmol; 95%) was suspended in DMSO (12 ml), and the dark-brown mixture was stirred for 1 h at r.t. before **5** [3] (1.5 g, 3.2 mmol) was added at once. The mixture was stirred for 3 h at r.t., then poured into ice-water (150 ml) and neutralized with 1M HCl. The precipitated brown solid was filtered off and purified by CC (PhMe/Me_2CO 7:4). After evaporation of most of the solvent, the product was precipitated by addition of hexane, filtered off, and dried: 1.15 g (73%) of **6a**. M.p. 115–116° (from Et_2O/hexane). UV: as in [4]. ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.2 (*d*, *J* = 2.3, CH≡C); 3.3 (*m*, H–C(3′)); 3.5 (*m*, 2 H–C(5′)); 4.0 (*m*, H–C(4′)); 4.6–4.8 (*m*, H–C(2′), OH(2′)); 5.4 (*dd*, *J* = 8.1, 1.9, H–C(5)); 6.1 (*d*, *J* = 5.5, H–C(1′)); 7.2–7.5 (*m*, Ph_3C); 8.1 (*d*, *J* = 8.1, H–C(6)); 9.8 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 50.3 MHz): 37.31 (*d*, C(3′)); 62.14 (*t*, C(5′)); 72.91 (*d*, *C*H≡C); 77.28 (*d*, C(2′)); 80.40 (*d*, C(4′)); 81.47 (*s*, CH≡*C*); 85.89 (*d*, C(1′)); 88.11 (*s*, Ph_3C); 102.09 (*d*, C(5)); 127.86, 128.52, 129.17, 143.73 (*Ph*$_3$C); 142.05 (*d*, C(6)); 151.77 (*s*, C(4)); 164.66 (*s*, C(2)). FAB-MS: 517 (12.1, $[M + Na]^+$), 495 (14.5, $[M + H]^+$), 243 (100, Ph_3C^+), 113 (29, [uracil + H]$^+$).

*1-[2-O-Acetyl-3-deoxy-3-α-ethynyl-5-O-(triphenylmethyl)-β-*D*-arabinofuranosyl]pyrimidine-2,4(1*H*,3*H*)-dione* (**6b**). Ac_2O (1 ml, 10 mmol) was added to a soln. of **6a** (1.0 g, 2 mmol) in anh. pyridine (10 ml). After stirring

for 3 h at r.t., the mixture was poured slowly into well stirred ice-water (150 ml). The precipitate was filtered off, washed with H_2O, and dried *in vacuo*. The product was purified by CC (silica gel, AcOEt): **6b** (1.0 g, 92,6%). M.p. 104–106° (from CH_2Cl_2/hexane). UV: 212 (4.45), 260 (4.00). ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.0 (*s*, Ac); 2.25 (*d*, *J* = 2.5, CH≡C); 3.4 (*m*, H–C(3′)); 3.5 (*d*, *J* = 2.9, 2 H–C(5′)); 4.1 (*m*, H–C(4′)); 5.4 (*d*, *J* = 8.2, H–C(5)); 5.6 (*dd*, *J* = 7.6, 5.6, H–C(2′)); 6.3 (*d*, *J* = 5.5, H–C(1′)); 7.2–7.5 (*m*, Ph_3C); 7.8 (*d*, *J* = 8.2, H–C(6)); 8.7 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 50.3 MHz): 20.28 (*q*, *Me*CO); 36.14 (*d*, C(3′)); 62.05 (*t*, C(5′)); 73.81 (*d*, *C*H≡C); 76.43 (*d*, C(4′)); 78.90 (*s*, CH≡*C*); 81.56 (*d*, C(2′)); 83.82 (*d*, C(1′)); 87.97 (*s*, Ph_3C); 102.12 (*d*, C(5)); 127.9, 128.52, 129.11, 143.69 (Ph_3C); 141.14 (*d*, C(6)); 150.05 (*s*, C(4)); 164.0 (*s*, C(2)); 169.24 (*s*, Me*C*O). FAB-MS: 559 (6.5, $[M + Na]^+$), 537 (7, $[M + H]^+$), 227 (6), 243 (100, Ph_3C^+), 165 (18), 155 (11), 113 (10, [uracil + H]$^+$).

*1-{3-Deoxy-3-α-ethynyl-2-O-[phenoxy(thiocarbonyl)]-5-O-(triphenylmethyl)-β-*D*-arabinofuranosyl}pyrimidine-2,4(1*H*,3*H*)-dione* (**6c**). To a stirred soln. of **6a** (1.75 g, 3.5 mmol) and 4-(dimethylamino)pyridine (0.854 g, 7 mmol) in dry MeCN (35 ml), a soln. of *O*-phenyl chlorothioformate (0.71 ml, 5.25 mmol) in dry MeCN (20 ml) was added in one portion. The resulting yellow soln. was stirred at r.t. for 3 h. The solvent was evaporated and AcOEt/H_2O 2:1 (200 ml) added to the residue. The org. phase was washed successively with cold 1M aq. HCl (2 × 50 ml), H_2O (50 ml), 5% aq. Na_2CO_3 soln. (100 ml), and H_2O, dried (Na_2SO_4), and evaporated. The residue was purified by CC (silica gel, CH_2Cl_2, then AcOEt/CH_2Cl_2 1:4): 1.7 g (76%) of **6c**. M.p. 104–106° (from EtOH/H_2O). UV: 214 (4.34), 256 (4.02). ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.3 (*d*, *J* = 2.5, CH≡C); 3.5 (*m*, 2 H–C(5′)); 3.6 (*m*, H–C(3′)); 4.2 (*m*, H–C(4′)); 5.5 (*dd*, *J* = 8.2, 2.2, H–C(5)); 6.1 (*t*, *J* = 5.4, 5.0, H–C(2′)); 6.4 (*d*, *J* = 5.0, H–C(1′)); 7.0–7.5 (*m*, 20 arom. H); 7.7 (*d*, *J* = 8.2, H–C(6)); 9.1 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 50.3 MHz): 36.94 (*d*, C(3′)); 62.42 (*t*, C(5′)); 74.31 (*d*, *C*H≡C); 79.16 (*s*, CH≡*C*); 81.63 (*d*, C(4′)); 83.81 (*d*, C(2′)); 84.82 (*d*, C(4′)); 87.87 (*s*, Ph_3C); 102.45 (*d*, C(5)); 121.96, 127.41, 130.21, 153.77 (Ar); 142.05 (*d*, C(6)); 150.26 (*s*, C(4)); 163.17 (*s*, C(2)); 193.74 (*s*, C=S). FAB-MS: 653 (7, $[M + Na]^+$), 631 (2, $[M + H]^+$), 519 (3), 371 (4, $[M - Ph_3CO]^+$), 243 (100, Ph_3P^+), 165 (69), 154 (29), 137 (17), 105 (40), 89 (26), 77 (79). Anal. calc. for $C_{37}H_{30}N_2O_6S$ (630.72): C 70.46, H 4.79, N 4.44; found: C 70.31, H 4.99, N 4.29.

*1-(2-O-Acetyl-3-deoxy-3-ethynyl-β-*D*-arabinofuranosyl)pyrimidine-2,4(1*H*,3*H*)-dione* (**7**). A soln. of **6b** (1.0 g, 1.86 mmol) in AcOH/H_2O 4:1 (10 ml) was refluxed for 30 min. Then, abs. EtOH was added, the mixture evaporated and the residue submitted to CC (silica gel, AcOEt): **7** (0.5 g, 91%). White solid. M.p. 189–191° (from AcOEt). UV: 206 (3.93), 260 (4.01). ^{1}H-NMR ((D$_6$)DMSO, 200 MHz): 1.9 (*s*, Ac); 3.15 (*m*, H–C(3′)); 3.3 (*d*, *J* = 2.4, CH≡C); 3.5 (*m*, 1 H–C(5′)); 3.8 (*m*, 1 H–C(5′)); 4.0 (*m*, H–C(4′)); 5.3 (*t*, *J* = 5.5, OH); 5.5 (*dd*, *J* = 8.0, 6.1, H–C(2′)); 5.65 (*d*, *J* = 8.1, H–C(5)); 6.2 (*d*, *J* = 6.1, H–C(1′)); 7.8 (*d*, *J* = 8.1, H–C(6)); 11.4 (br. *s*, NH). ^{13}C-NMR ((D$_6$)DMSO, 50.3 MHz): 20.13 (*q*); 34.61 (*d*, C(3′)); 59.65 (*t*, C(5′)); 75.32 (*d*, *C*H≡C); 76.20 (*d*, C(4′)); 79.99 (*s*, CH≡*C*); 81.53 (*d*, C(2′)); 82.42 (*d*, C(1′)); 101.33 (*d*, C(5)); 141.29 (*d*, C(6)); 150.39 (*s*, C(4)); 163.13 (*s*, C(2)); 169.06 (*s*, Me*C*O). FAB-MS: 317 (14.5, $[M + Na]^+$), 295 (43.5, $[M + H]^+$), 183 (100), 113 (40, [uracil + H]$^+$). EI-MS: 294 (1.3, M^+), 234 (5, $[M - AcOH]^+$), 184 (10), 183 (100), 113 (16,7, [uracil + H]$^+$), 95 (7), 81 (9.8). Anal. calc. for $C_{13}H_{14}N_2O_6$ (294.26): C 53.06, H 4.80, N 9.52; found: C 53.09, H 4.52, N 9.40.

*1-[(2*R*,3*S*,4*R*,5*S*)-3-Acetoxy-5-(2,2-dibromoethenyl)-4-ethynyltetrahydrofuran-2-yl]pyrimidine-2,4(1*H*,3*H*)-dione* (**9**). Oxidation of **7** (0.735 g, 2.5 mmol) to the corresponding aldehyde **8** was carried out in DMSO (12 ml) containing pyridine (0.2 ml), CF_3COOH (0.09 ml), and DCC (1.53 g, 7.4 mmol), which was stirred under N_2 for 24 h at r.t. Thereafter, the mixture was added dropwise to a soln. of (dibromomethylidene)triphenylphosphorane (prepared by reaction of Ph_3P (1.311 g), CBr_4 (1.659 g), and Zn dust (0.327 g; *cf.* [19])) in 12 ml of CH_2Cl_2. After stirring for 24 h at r.t. CH_2Cl_2 (50 ml) was added, the soln. washed with H_2O (3 × 50 ml), dried (Na_2SO_4), and evaporated, and the residue submitted to CC (silica gel, AcOEt/CH_2Cl_2 1:1): product containing dicyclohexylurea as impurity. The product was redissolved in CH_2Cl_2, the solid precipitate filtered off, and the soln. evaporated: **9** (0.8 g, 71%). White solid. M.p. 184–186°. UV: 212 (4.22), 258 (4.01). ^{1}H-NMR ((D$_6$)DMSO, D_2O, 200 MHz): 1.9 (*s*, Ac); 3.2 (*d*, *J* = 2.4, CH≡C); 3.4 (*m*, H–C(4′)); 4.6 (*t*, *J* = 8.9, H–C(5′)); 5.5 (*dd*, *J* = 7.9, 6.4. H–C(3′)); 5.6 (*d*, *J* = 8.1, H–C(5)); 6.2 (*d*, *J* = 6.3, H–C(2′)); 6.9 (*d*, *J* = 8.6, CBr_2=CH); 7.6 (*d*, *J* = 8.1, H–C(6)). ^{13}C-NMR ((D$_6$)DMSO, 50.3 MHz): 20.23 (*q*); 33.60 (*d*, C(4′)); 76.03 (*d*, *C*H≡C); 76.10 (*d*, C(5′)); 78.98 (*d*,C(3′)); 79.20 (*d*, C(2′)); 82.58 (*s*, CH≡*C*); 96.04 (*s*, *C*Br=CH); 101.55 (*d*, C(5)); 135.58 (*d*, CBr_2=*C*H); 142.19 (*d*, C(6)); 150.25 (*s*, C(4)); 163.02 (*s*, C(2)); 169.13 (*s*, Me*C*O). FAB-MS: 471 (9.7, $[M + Na]^+$), 449 (29, $[M + H]^+$), 337 (29), 277 (31), 225 (100), 154 (100).

*1-[(2*R*,3*S*,4*S*,5*S*)-4,5-Diethynyltetrahydro-3-hydroxyfuran-2-yl]pyrimidine-2,4(1*H*,3*H*)-dione* (**10a**). A soln. of **9** (0.5 g, 1.1 mmol) in anh. THF was cooled to −78° before 6 ml (9.6 mmol) of 1.6M BuLi in hexane were added. The mixture was stirred for 5 h, then neutralized with AcOH. The solvent was evaporated after addition of abs. EtOH and the residue submitted to CC (silica gel, AcOEt/CH_2Cl_2 1:1): **10a** (0.18 g, 66%). White solid. M.p. 202–204° (from CH_2Cl_2/hexane). UV: 208 (4.03), 262 (4.01). ^{1}H-NMR ((D$_6$)DMSO, D_2O, 200 MHz): 3.1 (*m*,

H–C(4′)); 3.3 (*d*, *J* = 2.4, CH≡C–C(4′)); 3.6 (*d*, *J* = 2.2, CH≡C–C(5′)); 4.4 (*t*, *J* = 6.5, 6.1, H–C(3′)); 4.6 (*dd*, *J* = 8.3, 2.2, H–C(5′)); 5.6 (*d*, *J* = 8.1, H–C(5)); 6.1 (*d*, *J* = 5.8, H–C(2′)); 7.5 (*d*, *J* = 8.1, H–C(6)). ^{13}C-NMR ((D$_6$)DMSO, 50.3 MHz): 44.25 (*d*, C(4′)); 69.60 (*d*, *C*H≡C–C(5′)); 75.01 (*d*, *C*H≡C–C(4′)); 75.65 (*d*, C(3′)); 78.62 (*d*, C(5′)); 80.29 (*s*, CH≡C–C(4′)); 80.97 (*s*, CH≡C–C(5′)); 84.68 (*d*, C(2′)); 101.03 (*d*, C(5)); 142.49 (*d*, C(6)); 150.75 (*s*, C(4)); 163.32 (*s*, C(2)). FAB-MS: 269 (16, [*M* + Na]$^+$), 247 (84, [*M* + H]$^+$), 153 (24), 113 (100, [uracil + H]$^+$), 89 (40), 77 (100). EI-MS: 246 (2,8, *M*$^+$), 228 (1.7, [*M* – H$_2$O]$^+$), 192 (7.9), 163 (13.1), 141 (43.7), 135 (8.8). 113 (30, [uracil + H]$^+$), 98 (15.3), 80 (37.8), 79 (29.7), 77 (100), 70 (31).

*1-{(2*R*,3*S*,4*R*,5*S*)-4,5-Diethynyltetrahydro-3-{[phenoxy(thiocarbonyl)]oxy}furan-2-yl}pyrimidine-2,4(1*H*,3*H*)-dione* (**10b**). To a stirred soln. of **10a** (140 mg, 0.6 mmol) in dry MeCN (6 ml) containing 4-(dimethylamino)pyridine (293 mg, 2.4 mmol), a soln. of *O*-phenyl chlorothioformate (0.16 ml, 1.2 mmol) in dry MeCN (4 ml) was added in one portion. The resulting yellow soln. was stirred at r.t. for 1 h and then evaporated. AcOEt/H$_2$O 2:1 (100 ml) was added to the residue. The org. layer was separated, dried (Na$_2$SO$_4$), and evaporated and the residue submitted to CC (silica gel, CH_2Cl_2, then AcOEt/CH_2Cl_2 7:3): **10b** (0.15 g, 69%). White solid. M.p. 77–79° (from CH_2Cl_2/hexane). UV: 206 (4.26), 256 (4.01). ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.5 (*d*, *J* = 2.5, CH≡C–C(4′)); 2.8 (*d*, *J* = 2.2, CH≡C–C(5′)); 3.6 (*m*, H–C(4′)); 4.9 (*dd*, *J* = 3.7, 2.3, H–C(5′)); 5.8 (*dd*, *J* = 8.2, 1.7, H–C(5)); 5.9 (*dd*, *J* = 4.1, 2.8, H–C(3′)); 6.5 (*d*, *J* = 4.1, H–C(2′)); 6.9–7.1 (*m*, 2 arom. H); 7.2–7.5 (*m*, 4 arom. H); 7.7 (*d*, *J* = 8.2, H–C(6)); 8.8 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 50.3 MHz): 43.67 (*d*, C(4′)); 72.90 (*d*, *C*H≡C–C(5′)); 75.63 (*d*, *C*H≡C–C(4′)); 79.70 (*s*, CH≡*C*–C(4′)); 83.86 (*d*, C(5′)); 84.94 (*s*, CH≡*C*–C(5′)); 86.11 (*d*, C(2′)); 102.52 (*d*, C(5)); 121.89 127.5, 130.24 (arom. C); 141.32 (*d*, C(6)); 150.75 (*s*, C(4)); 153.63 (*s*); 163.01 (*s*, C(2)); 193.15 (*s*, CS). FAB-MS: 405 (5, [*M* + Na]$^+$), 383 (18, [*M* + H]$^+$), 271 (29), 229 (8), 154 (50), 138 (51), 113 (48, [uracil + H]$^+$), 89 (56), 77 (100).

*1-[2,3-Dideoxy-3-ethynyl-5-*O*-(triphenylmethyl)-β-*D*-ribofuranosyl]pyrimidine-2,4(1*H*,3*H*)-dione* (**11a**). To a soln. of **6c** (2.0 g, 3.2 mmol) in PhMe (70 ml), Bu_3SnH (1.3 ml, 4.8 mmol) and AIBN (106.7 mg, 0.67 mmol) were added. The soln. was degassed with N_2 during 20 min and then heated at 75° for 4 h. The solvent was evaporated and the residue submitted to CC (silica gel, AcOEt/CH_2Cl_2 1:4). After evaporation, the residue was dissolved in 5 ml of CH_2Cl_2 and the product (0.7 g, 46%) obtained by precipitation with hexane. M.p. 94–96°. UV: 214 (4.34), 262 (4.02). ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.1 (*d*, *J* = 2.4, CH≡C); 2.4–2.6 (*m*, 2 H–C(2′)); 3.2 (*m*, H–C(3′)); 3.4 (*m*, 2 H–C(5′)); 4.1 (*m*, H–C(4′)); 5.2 (*dd*, *J* = 8.1, 2.0, H–C(5)); 6.1 (*dd*, *J* = 6.2, 2.7, H–C(1′)); 7.2–7.5 (*m*, Ph_3C); 8.0 (*d*, *J* = 8.1, H–C(6)); 8.3 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 50.3 MHz): 29.04 (*t*, C(2′)); 40.74 (*d*, C(3′)); 61.62 (*t* C(5′)); 72.13 (*d*, *C*H≡C); 81.01 (*s*, CH≡*C*); 85.73 (*d*, C(4′)); 85.82 (*d*, C(1′)); 88.07 (*s*, Ph_3C); 102.23 (*d*, C(5)); 127.7, 128.37, 128.52, 129.3, 143.65 (*Ph*$_3$C); 140.58 (*d*, C(6)); 150.43 (*s*, C(4)); 163.34 (*s*, C(2)). FAB-MS: 501 (18, [*M* + Na]$^+$), 479 (2, [*M* + H]$^+$), 378 (3), 289 (8), 259 (29), 243 (100, Ph_3C^+), 215 (37), 202 (27), 177 (42), 165 (100), 136 (69), 113 (61), 105 (100), 91 (80), 77 (100).

*1-[2,3-Dideoxy-3-ethynyl-β-*D*-ribofuranosyl]pyrimidine-2,4(1*H*,3*H*)-dione* (**11b**) was obtained as a white solid (0.17 g, 76%) from 0.45 g (0.9 mmol) of **11a** as described for **7**. M.p. 139–141° (from AcOEt). UV: 208 (3.95), 262 (4.01). ^{1}H-NMR (CD_3CO_2D, 200 MHz): 2.4 (*d*, *J* = 2.3, CH≡C); 2.5 (*m*, 2 H–C(2′)); 3.15 (*m*, H–C(3′)); 3.8 (*m*, H–C(4′)); 4.0 (*m*, 2 H–C(5′)); 5.9 (*d*, *J* = 8.1, H–C(5)); 6.1 (*dd*, *J* = 5.9, 5.6, H–C(1′)); 8.0 (*d*, *J* = 8.1 H–C(6)). ^{13}C-NMR (CD_3CO_2D, 50.3 MHz): 29.4 (*t*, C(2′)); 40.16 (*d*, C(3′)); 61.08 (*t*, C(5′)); 72.39 (*d*, *C*H≡C); 812.32 (*s*, CH≡*C*); 87.01 (*d*, C(4′)); 87.23 (*d*, C(1′)); 102.44 (*d*, C(5)); 142.99 (*d*, C(6)); 152.04 (*s*, C(4)); 167.09 (*s*, C(2)). EI-MS: 237 (1, [*M* + H]$^+$), 236 (2, *M*$^+$), 205 (1.5), 125 (100), 113 (19, [uracil + H]$^+$), 81 (84), 77 (17). Anal. calc for $C_{11}H_{12}N_2O_4$ (236.23): C 55.93, H 5.12, N 11.86; found: C 55.86, H 5.06, N 11.55.

*1-[2,3-Dideoxy-3-ethynyl-β-*D*-ribodialdofuranosyl]pyrimidine-2,4(1*H*,3*H*)-dione* (**12**) was obtained by oxydation of 0.15 g (0.64 mmol) of **11b** as described for **9**. The H_2O-soluble aldehyde could not be properly purified and was, therefore, used without previous isolation for the preparation of **13**. ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.3 (*d*, *J* = 2.5, CH≡C); 2.4–2.6 (*m*, 2 H–C(2′)); 3.3 (*m*, H–C(3′)); 4.6 (*d*, *J* = 6.2, H–C(4′)); 5.8 (*dd*, *J* = 8.1, 2.3, H–C(5)); 6.2 (*t*, *J* = 6.1, 5.9, H–C(1′)); 7.7 (*d*, *J* = 8.1, H–C(6)); 8.1 (br. *s*, NH); 9.7 (*s*, CHO). CI-MS: 235 (12, [*M* + H]$^+$), 141 (12), 123 (9), 113 (100, [uracil + H]$^+$).

*1-[(2*R*,4*R*,5*S*)-5-(2,2-Dibromoethenyl)-4-ethynyltetrahydrofuran-2-yl]pyrimidine-2,4(1*H*,3*H*)-dione* (**13**) was obtained (0.15 g, 60% from **11b**) as described for **9**. M.p. 74–76°. UV: 212 (4.23), 260 (4.01). ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.2 (*d*, *J* = 2.4, CH≡C); 2.4–2.6 (*m*, 2 H–C(3′)); 3.0 (*m*, H–C(4′)); 4.7 (*t*, *J* = 8.3 H–C(5′)); 5.7 (*d*, *J* = 8.1, H–C(5)); 6.0 (*dd*, *J* = 6.9, 3.8, H–C(2′)); 6.5 (*d*, *J* = 8.3, CBr_2=CH); 7.3 (*d*, *J* = 8.1 H–C(6)); 8.9 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 50.3 MHz): 34.62 (*t*, C(3′)); 39.49 (*d*, C(4′)); 72.99 (*d*, *C*H≡C); 80.43 (*s*, CH≡*C*); 84.69 (*d*, C(5′)); 87.46 (*d*, C(2′)); 97.51 (*s*, *C*Br$_2$=CH); 103.07 (*d*, C(5)); 134.85 (*d*, CBr$_2$=*C*H); 140.27 (*d*, C(6)); 150.48 (*s*, C(4)); 163.72 (*s*, C(2)). FAB-MS: 413 (9.7, [*M* + Na]$^+$), 391 (22.6, [*M* + H]$^+$), 390 (14.5, *M*$^+$), 179 (9.7).

*1-[(2*R*,4*R*,5*S*)-4,5-Diethynyltetrahydrofuran-2-yl]pyrimidine-2,4(1*H*,3*H*)-dione* (**14**) was obtained as colorless crystals (0.24 g, 59%) from 0.4 g (1.03 mmol) of **13** as described for **10a**. M.p. 172–174° (from CH_2Cl_2).

UV: 218 (3.94); 272 (4.00). ^{1}H-NMR ($CDCl_3$, 360 MHz): 2.3 (*d*, *J* = 2.4, CH≡C–C(4′)); 2.4 (*m*, 1 H–C(3′)); 2.6 (*m*, 1 H–C(3′)); 2.7 (*d*, *J* = 2.1, CH≡C–C(5′)); 3.2 (*m*, H–C(4′)); 4.7 (*dd*, *J* = 5.8, 2.1, H–C(5′)); 5.8 (*dd*, *J* = 8.1, 1.4, H–C(5)); 6.2 (*t*, 5.7, 5.2, H–C(2′)); 7.7 (*d*, *J* = 8.1, H–C(6)); 9.1 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$, 50.3 MHz): 37.12 (*t*, C(3′)); 39.53 (*d*, C(4′)); 73.12 (*d*, *C*H≡C–C(4′)); 75.09 (*d*, C(5′)); 77.09 (*d*, *C*H≡C–C(5′)); 80.43 (*s*, CH≡*C*–C(4′)); 80.59 (*s*, CH≡*C*–C(5′)); 87.75 (*d*, C(2′)); 102.88 (*d*, C(5)); 139.89 (*d*, C(6)); 150.52 (*s*, C(4)); 163.49 (*s*, C(2)). EI-MS: 230 (6, M^+), 176 (6), 120 (9), 119 (100), 118 (7), 105 (23), 104 (38), 92 (7), 91 (55), 90 (5), 89 (18), 81 (15), 80 (11), 78 (12), 74 (13), 65 (47), 63 (36), 62 (17), 55 (42), 54 (44), 53 (89). CI-MS: 232 (17, $[M + 2\,H]^+$), 231 (88, $[M + H]^+$), 177 (7), 153 (20), 141 (71), 120 (7), 119 (75), 114 (16), 113 (100, [uracil + H]$^+$), 91 (7), 41 (19). Anal. calc. for $C_{12}H_{10}N_2O_3$ (230.22): C 62.61, H 4.38, N 12.17; found: C 62.34, H 4.38, N 12.21.

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