38. Nucleosides

Part LV[1])

Efficient Synthesis of Arabinoguanosine Building Blocks

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From guanosine (**1**) as starting molecule, protected arabinoguanosine derivatives such as phosphoramidite precursors and arabinoguanosine (**18**) itself were prepared in high yields. Inversion of the configuration at C(2′) was achieved by introduction of the (trifluoromethyl)sulfonyl residue and subsequent displacement by nucleophiles like acetate, bromide, and azide. The guanine moiety was protected at the amide function by the 2-(4-nitrophenyl)ethyl (npe) group on O^6 and at the NH_2 function by the 2-(4-nitrophenyl)ethoxycarbonyl (npeoc) group.

1. Introduction. – During our ongoing research in oligoarabinonucleotide chemistry, we required larger amounts of 9-(β-D-arabinofuranosyl)guanine (= arabinoguanosine; aGuo; **18**) and partially protected derivatives [2]. While the synthesis of the pyrimidine arabinosides aUrd and aCyd from the corresponding ribosides *via* the anhydronucleosides is well established, the preparation of purine arabinosides, especially of aGuo, causes still difficulties.

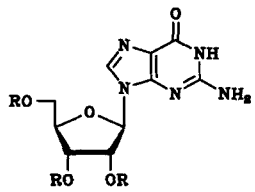
Since the first synthesis of arabinoguanosine published by *Reist* and *Goodman* in 1964 [3], several attempts were made to find practicable synthetic routes, either by glycosylation of purine bases with appropriately protected *arabino*-sugar moieties [4] [5] or by conversion of guanosine into aGuo *via* a 2′-ketonucleoside [6] [7]. In our experience, these methods led to unseparable mixtures of α/β-D-anomers or arabino/ribonucleosides, and the approach described by *Chattopadhyaya* and *Reese* [8] *via* 8,2′-anhydroguanosine [9] offers a reproducible but multistep route with low overall yield from guanosine. Published methods applying enzymatically catalyzed transglycosidations [10] [11] can not be carried out by usual means.

In consideration of this unsatisfactory situation, we searched for more convenient methods to synthesize arabinoguanosine building blocks. A first trial to invert the configuration at C(2′) of guanosine by application of the *Mitsunobu* reaction, which is often used in steroid chemistry for configurational inversions, failed. More favorable seemed the conversion of the 2′-OH function into a good leaving group and subsequent nucleophilic displacement involving an S_N2 mechanism, already used for the synthesis of aAdo [12] [13], neplanocinA [14], and deaza-arabinoadenosines [15] [16].

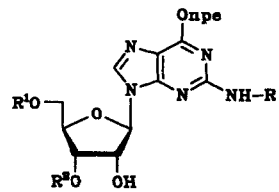
[1]) Part LIV: [1].

2. Syntheses. – Starting from 9-(β-D-ribofuranosyl)guanine (**1**), the aglycon-protected nucleosides **3** and **4** [17] were synthesized *via* 9-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-guanine (**2**) [18] by O^6-alkylation under *Mitsunobu* conditions with 2-(4-nitrophenyl)-ethanol and subsequent reaction with 2-(4-nitrophenyl)ethyl chloroformate to give **4** by known procedures. O^6-Protection turned out to be essential in avoiding side reactions in the consecutive sulfonation step which worked also without harming an unprotected 2-amino group.

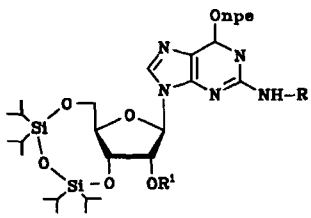
Further blocking was then achieved by 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (tipdsCl$_2$; *Markiewicz*'s reagent) in abs. pyridine to give O^6-[2-(4-nitrophenyl)ethyl]-9-[3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-ribofuranosyl]guanine (**5**) and its



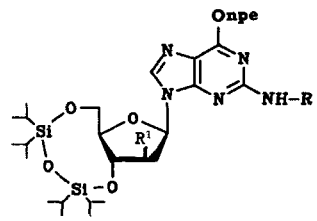
1 R = H
2 R = ac



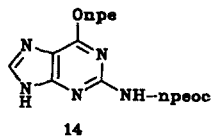
3 R = R^1 = R^2 = H
4 R = npeoc, R^1 = R^2 = H
5 R = H, R^1, R^2 = tipds
6 R = npeoc, R^1, R^2 = tipds



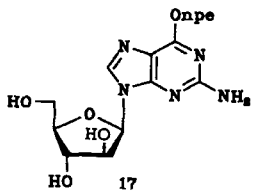
7 R = H, R^1 = ts
8 R = H, R^1 = tf
9 R = npeoc, R^1 = tf



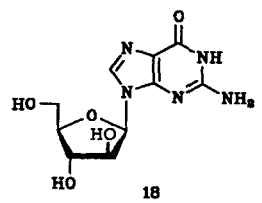
10 R = H, R^1 = acO
11 R = H, R^1 = N_3
12 R = H, R^1 = Br
13 R = npeoc, R^1 = acO
15 R = H, R^1 = OH
16 R = npeoc, R^1 = OH



14



17



18

ac = acetyl; tipds = 1,1,3,3-tetraisopropyldisiloxane-1,3-diyl; npe = 2-(4-nitrophenyl)ethyl; npeoc = 2-(4-nitrophenyl)ethoxycarbonyl; ts = (tol-4-yl)sulfonyl; tf = (trifluoromethyl)sulfonyl

N^2-[2-(4-nitrophenyl)ethoxycarbonyl] derivative **6** in high yields. Treatment of **5** with toluene-4-sulfonyl chloride at 0° led, after purification, to the corresponding 2′-*O*-[(tol-4-yl)sulfonyl] derivative **7** in 66% yield, but this molecule showed no tendency to react with nucleophiles under mild conditions. Therefore, we changed to the more reactive (trifluoromethyl)sulfonyl residue as leaving group. Its introduction into the 2′-OH nucleosides **5** and **6** worked best with trifluoromethanesulfonic anhydride as sulfonylating agent and pyridine and 4-(dimethylamino)pyridine as bases in excess in CH_2Cl_2 as solvent. The crude products **8** and **9**, respectively, were obtained in almost quantitative yield and turned out to be pure enough for further reactions. Chromatographic purification of these labile compounds on silica gel was possible, but the isolated yield decreased drastically.

Subsequent nucleophilic displacement reactions of **8** with AcO^-, N_3^-, or Br^- ions, preferably as their lithium salts, worked well in hexamethylphosphoramide (HMPA) or HMPA/DMF to form the corresponding arabinonucleosides **10–12** in yields of 85–96% as amorphous powders; besides precipitation by ice-water, extraction by AcOEt was also successful. Triflate substitution in **9** with LiOAc afforded, besides the desired fully protected nucleoside **13**, a by-product in 26% yield, which could be identified as N^2-[2-(4-nitrophenyl)ethoxycarbonyl]-O^6-[2-(4-nitrophenyl)ethyl]guanine (**14**). Compounds **10** and **13** represent universal building blocks for a variety of synthetic approaches, since each blocking group can be selectively cleaved without harming the others, by simple procedures. Deacetylation with NH_3 in MeOH/dioxane/H_2O gave the 2′-OH free arabinonucleosides **15** and **16**, respectively. A straightforward synthesis of **15** was achieved by a three-step reaction sequence without isolation and purification of intermediates consisting of sulfonylation of **5** (→**8**), nucleophilic substitution of **8** (LiOAc) (→**10**), and subsequent cleavage of the 2′-*O*-acetyl group. This important key compound **15** in the synthesis of aGuo phosphoramidites [2] is now available in *ca.* 30% overall yield from Guo (**1**) as starting material, instead of 7% by the conventional method (Guo→8,2′-anhydroGuo→aGuo→**15**). A further advantage of this new strategy is the losing O^6-alkylation on the level of the cheap guanosine (**1**) instead of the valuable aGuo (**18**).

Cleavage of the 1,1,3,3-tetraisopropyldisiloxane-1,3-diyl group in **15** with F^- ions, deactivated by AcOH, in THF solution afforded **17** in 72% yield, and the final deblocking step to remove the 2-(4-nitrophenyl)ethyl group of **17** was performed in the usual manner by 0.5M 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dry MeCN *via* a β-elimination. After recrystallization from H_2O, 9-(β-D-arabinofuranosyl)guanine (**18**) was obtained in 64% yield.

3. Physical Data. – The newly synthesized nucleosides were characterized by C,H,N analyses and UV and ^{1}H-NMR spectra. The arabinonucleosides **15–18** were also identified by comparison with authentic samples, prepared by another route [2]. Usually the ^{1}H-NMR spectra can be analyzed properly according to the characteristic structural features. The introduction of the (trifluoromethyl)sulfonyl group (**8**, **9**) causes a typical down-field shift of H–C(2′). Comparisons of the corresponding ribonucleosides and arabinonucleosides show a typical down-field shift of the anomeric proton in the latter. Furthermore, $J(1',2')$ coupling constants of 3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)-protected nucleosides permit exact assignments to *ribo* ($J(1',2') = 0$–1.5 Hz) or *arabino* ($J(1',2') = 6$–6.5 Hz) configuration. This result is in accordance with earlier observations of *Robins et al.* [19].

Experimental Part

General. Products were dried under high vacuum. TLC: precoated silica-gel thin layer sheets *60 F 254* from *Merck*. Prep. column chromatography (CC): silica gel (*Merck 60*, 0.063–0.2 mesh). Flash chromatography (FC): silica gel (*Baker*, 30–60 μm); 0.2–0.3 bar. M.p.: *Gallenkamp* melting-point apparatus; no corrections. UV/VIS: *Perkin-Elmer, Lambda 15*; λ_{max} in nm ($\log\varepsilon$). ^{1}H-NMR: *Bruker AC 250*; δ in ppm rel. to Me_4Si, J in Hz.

1. *O^6-[2-(4-Nitrophenyl)ethyl]-9-[3′,5′-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-*D*-ribofuranosyl]guanine* (**5**). To a soln. of **3** (2.15 g, 5 mmol) in abs. pyridine (30 ml) was added 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (1.63 ml, 5.2 mmol) and stirred at r.t. for 6 h. The soln. was evaporated and the residue partitioned between AcOEt (150 ml) and H_2O (150 ml). The org. layer was washed subsequently with 0.2M HCl (70 ml), sat. $NaHCO_3$ (70 ml), and NaCl soln. (70 ml), dried ($MgSO_4$), and evaporated. A light yellow foam, pure enough for further reactions, was obtained in quantitative yield. Crystallization from toluene/hexane (50 ml) gave 2.68 g (79%) of **5**. M.p. 99–100°. TLC (SiO_2, toluene/AcOEt/MeOH 5:4:1): R_f 0.58. UV (MeOH): 251 (4.18), 279 (4.26). ^{1}H-NMR ((D$_6$)DMSO): 8.17 (*d*, 2 H *o* to NO_2); 7.89 (*s*, H–C(8)); 7.62 (*d*, 2 H *m* to NO_2); 6.47 (*s*, NH_2); 5.74 (*d*, J = 1.5, H–C(1′)); 5.62 (*d*, OH–C(2′)); 4.65 (*t*, OCH_2CH_2); 4.35 (*m*, H–C(2′), H–C(3′)); 4.00 (*m*, H–C(4′), 2 H–C(5′)); 3.23 (*t*, OCH_2CH_2); 0.98 (*m*, 4 i-Pr). Anal. calc. for $C_{30}H_{46}N_6O_8Si_2$ (674.9): C 53.39, H 6.87, N 12.45; found: C 53.17, H 6.88, N 12.33.

2. *N^2-[2-(4-Nitrophenyl)ethoxycarbonyl]-O^6-[2-(4-nitrophenyl)ethyl]-9-[3′,5′-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-*D*-ribofuranosyl]guanine* (**6**). As described in *Exper. 1*, with **4** (10 g, 16 mmol) and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (5.17 ml, 16.5 mmol) in abs. pyridine (70 ml). Evaporation of the org. layer gave 13.9 g (100%) of colorless foam. TLC (SiO_2, toluene/AcOEt 1:1): R_f 0.40. UV (MeOH): 268 (4.54). ^{1}H-NMR ($CDCl_3$): 8.15 (*m*, 2 H *o* to NO_2); 7.95 (*s*, H–C(8)); 7.48, 7.40 (2*d*, 4 H *m* to NO_2); 7.27 (*s*, NH); 5.92 (*d*, J = 1.5, H–C(1′)); 4.78 (*m*, H–C(2′), OCH_2CH_2); 4.44 (*m*, H–C(3′), OCH_2CH_2); 4.08 (*m*, H–C(4′), 2 H–C(5′)); 3.28 (*t*, OCH_2CH_2); 3.10 (*t*, OCH_2CH_2); 1.05 (*m*, 4 i-Pr). Anal calc. for $C_{39}H_{53}N_7O_{12}Si_2 \cdot 0.5\ H_2O$ (877.1): C 53.41, H 6.20, N 11.17; found: C 53.10, H 6.12, N 10.94.

3. *O^6-[2-(4-Nitrophenyl)ethyl]-9-{3′,5′-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2′-O-[(tol-4-yl)sulfonyl]-β-*D*-ribofuranosyl}guanine* (**7**). To a cooled (0°) soln. of **5** (0.337 g, 0.5 mmol), 4-(dimethylamino)pyridine (0.12 g, 1 mmol), and abs. pyridine (0.12 ml, 1.5 mmol) in abs. CH_2Cl_2 (6 ml) was added TsCl (115 mg, 0.6 mol). The stirred soln. was slowly warmed to r.t., and after 4 h, another 30 mg of TsCl were added and stirred for further 2 h. The mixture was diluted with CH_2Cl_2 (50 ml), washed successively with 0.2M HCl (30 ml), sat. $NaHCO_3$ (30 ml), and NaCl soln. (30 ml), dried ($MgSO_4$), and evaporated. Purification by FC (2 × 9 cm, toluene/AcOEt 5:1) gave 272 mg (66%) of a colorless foam. TLC (SiO_2, toluene/AcOEt 1:1): R_f 0.46. UV (MeOH): 253 (4.17), 278 (4.23). ^{1}H-NMR ($CDCl_3$): 8.18 (*d*, 2 H *o* to NO_2); 7.77 (*d*, 2 H *o* to Me); 7.63 (*s*, H–C(8)); 7.49 (*d*, 2 H *m* to NO_2); 7.24 (*d*, 2 H *m* to Me); 5.87 (*d*, J = 1.1, H–C(1′)); 5.50 (*d*, H–C(2′)); 4.83 (*dd*, H–C(3′)); 4.75 (*t*, OCH_2CH_2); 4.07 (*m*, H–C(4′), 2 H–C(5′)); 3.28 (*t*, OCH_2CH_2); 2.40 (*s*, Me); 0.95 (*m*, 4 i-Pr). Anal. calc. for $C_{37}H_{52}N_6O_{10}SSi_2$ (829.1): C 53.60, H 6.32, N 10.12; found: C 53.70, H 6.45, N 10.12.

4. *O^6-[2-(4-Nitrophenyl)ethyl]-9-{3′,5′-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2′-O-[(trifluoromethyl)sulfonyl]-β-*D*-ribofuranosyl}guanine* (**8**). A soln. of **5** (16.5 g, 24.4 mmol), 4-(dimethylamino)pyridine (11.8 g, 97 mmol), and abs. pyridine (17.7 ml, 220 mmol) in abs. CH_2Cl_2 (250 ml) was stirred in an ice-bath for 1 h. After addition of 6.4 ml (39 mmol) of trifluoromethanesulfonic anhydride during 5 min, the mixture was stirred for another h, diluted with CH_2Cl_2 (250 ml), successively washed with H_2O (300 ml), 0.4M HCl (2 × 400 ml), sat. $NaHCO_3$ (300 ml), and NaCl soln. (300 ml), dried ($MgSO_4$), and evaporated: 18.79 g (95%) of **8**, pure enough for further reactions. An anal. sample was obtained by FC (toluene/AcOEt 6:1). TLC (SiO_2, toluene/AcOEt 1:1): R_f 0.70. UV (MeOH): 252 (4.21), 279 (4.27). ^{1}H-NMR ((D$_6$)DMSO): 8.17 (*d*, 2 H *o* to NO_2); 7.95 (*s*, H–C(8)); 7.62 (*d*, 2 H *m* to NO_2); 6.32 (*s*, NH_2); 6.23 (*s*, J = 0, H–C(1′)); 5.99 (*d*, H–C(2′)); 4.82 (*dd*, H–C(3′)); 4.67 (*t*, OCH_2CH_2); 3.98 (*m*, H–C(4′), 2 H–C(5′)); 3.24 (*t*, OCH_2CH_2); 1.02 (*m*, 4 i-Pr). Anal. calc. for $C_{31}H_{45}F_3N_6O_{10}SSi_2$ (807.0): C 46.14, H 5.62, N 10.41; found: C 46.46, H 5.74, N 10.08.

5. *N^2-[2-(4-Nitrophenyl)ethoxycarbonyl]-O^6-[2-(4-nitrophenyl)ethyl]-9-{3′,5′-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2′-O-[(trifluoromethyl)sulfonyl]-β-*D*-ribofuranosyl}guanine* (**9**). As described in *Exper. 4*, with **6** (2.6 g, 3 mmol), 4-(dimethylamino)pyridine (1.47 g, 12 mmol), abs. pyridine (2.2 ml, 27 mmol) in CH_2Cl_2 (35 ml), and trifluoromethanesulfonic anhydride (0.78 ml, 4.8 mmol). Workup with CH_2Cl_2 (200 ml), H_2O, 0.2M HCl, sat. $NaHCO_3$ and NaCl soln. (100 ml of each), and $MgSO_4$. Purification by FC (3 × 16 cm, toluene/AcOEt 7:1) gave 2.32 g (76%) of a colorless foam. TLC (SiO_2, toluene/AcOEt 1:1): R_f 0.71. UV (MeOH): 268 (4.51). ^{1}H-NMR ($CDCl_3$): 8.15 (*m*, 4 H *o* to NO_2); 7.98 (*s*, H–C(8)); 7.49 (*d*, 2 H *m* to NO_2); 7.40 (*d*, 2 H *m* to NO_2); 6.07 (*s*, J = 0, H–C(1′)); 5.60 (*d*, H–C(2′)); 4.91 (*m*, H–C(3′)); 4.80 (*t*, OCH_2CH_2); 4.45 (*t*, OCH_2CH_2); 4.22–3.99 (*m*, H–C(4′),

2 H–C(5')); 3.29 (*t*, OCH_2CH_2); 3.11 (*t*, OCH_2CH_2); 1.01 (*m*, 4 i-Pr). Anal. calc. for $C_{40}H_{52}F_3N_7O_{14}SSi_2$ (1000.1): C 48.04, H 5.24, N 9.80; found: C 48.00, H 5.47, N 9.75.

6. *9-[2'-O-Acetyl-3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-arabinofuranosyl]-O⁶-[2-(4-nitrophenyl)ethyl]guanine* (**10**). To a soln. of **8** (0.403 g, 0.5 mmol) in DMF (5 ml) and hexamethylphosphoric triamide (HMPA; 2 ml) was added LiOAc (0.2 g, 3 mmol) and stirred overnight at r.t. Under vigorous stirring, the mixture was dropped into ice-water (40 ml) and the precipitate filtered off by suction, washed with H_2O, and dried under high vacuum: 314 mg (85%) of light yellow powder. TLC (SiO_2, toluene/AcOEt 1:1): R_f 0.45. UV (MeOH): 252 (4.18), 279 (4.25). ^{1}H-NMR ($CDCl_3$): 8.14 (*d*, 2 H *o* to NO_2); 7.89 (*s*, H–C(8)); 7.47 (*d*, 2 H *m* to NO_2); 6.32 (*d*, J = 6.4, H–C(1')); 5.52 (*t*, H–C(2')); 5.49 (*s*, NH_2); 4.68 (*m*, H–C(3'), OCH_2CH_2); 4.06 (*m*, 2 H–C(5')); 3.85 (*m*, H–C(4')); 3.26 (*t*, OCH_2CH_2); 1.73 (*s*, Me); 1.00 (*m*, 4 i-Pr). Anal. calc. for $C_{32}H_{48}N_6O_9Si_2 \cdot H_2O$ (735.0): C 52.29, H 6.86, N 11.43; found: C 52.09, H 6.99, N 11.45.

7. *9-[2'-Azido-2'-deoxy-3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-arabinofuranosyl]-O⁶-[2-(4-nitrophenyl)ethyl]guanine* (**11**). As described in *Exper. 6*, with **8** (0.403 g, 0.5 mmol), HMPA (5 ml), and LiN_3 (49 mg, 1 mmol; 1.5 h, r.t.). Workup with ice-water (50 ml). The product was dried over P_4O_{10}: 337 mg (96%) of light yellow powder. TLC (SiO_2, toluene/AcOEt 1:1): R_f 0.39. UV (MeOH): 252 (4.18), 279 (4.27). ^{1}H-NMR ($CDCl_3$): 8.13 (*d*, 2 H *o* to NO_2); 7.87 (*s*, H–C(8)); 7.46 (*d*, 2 H *m* to NO_2); 6.29 (*d*, J = 6.1, H–C(1')); 4.89 (*s*, NH_2); 4.72 (*t*, OCH_2CH_2); 4.40 (*m*, H–C(2'), H–C(3')); 4.06 (*m*, 2 H–C(5')); 3.85 (*m*, H–C(4')); 3.26 (*t*, OCH_2CH_2); 1.04 (*m*, 4 i-Pr). Anal. calc. for $C_{30}H_{45}N_9O_7Si_2$ (699.9): C 51.48, H 6.48, N 18.01; found: C 51.11, H 6.62, N 17.30.

8. *9-[2'-Bromo-2'-deoxy-3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-arabinofuranosyl]-O⁶-[2-(4-nitrophenyl)ethyl]guanine* (**12**). As described in *Exper. 6*, with **8** (0.806 g, 1 mmol), HMPA (8 ml), and LiBr (174 mg, 2 mmol; 2 h, r.t.). Workup with ice-water (150 ml): 0.641 g (87%) of light orange powder. TLC (SiO_2, toluene/AcOEt 1:1): R_f 0.48. UV (MeOH): 252 (sh, 4.13), 278 (4.22). ^{1}H-NMR ((D$_6$)DMSO): 8.15 (*d*, 2 H *o* to NO_2); 7.84 (*s*, H–C(8)); 7.62 (*d*, 2 H *m* to NO_2); 6.55 (*s*, NH_2); 6.24 (*d*, H–C(1')); 5.03 (*t*, H–C(2')); 4.68 (*m*, H–C(3'), OCH_2CH_2); 4.20–3.87 (*m*, H–C(4'), 2 H–C(5')); 3.22 (*t*, OCH_2CH_2); 1.00 (*m*, 4 i-Pr). Anal. calc. for $C_{30}H_{45}N_6O_7Si_2$ (737.8): C 48.84, H 6.15, N 11.39; found: C 50.05, H 6.64, N 10.73.

9. *9-[2'-O-Acetyl-3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-arabinofuranosyl]-N²-[2-(4-nitrophenyl)ethoxycarbonyl]-O⁶-[2-(4-nitrophenyl)ethyl]guanine* (**13**) *and N²-[2-(4-Nitrophenyl)ethoxycarbonyl]-O⁶-[2-(4-nitrophenyl)ethyl]guanine* (**14**). As described in *Exper. 4*, with **6** (15 g, 17.25 mmol), 4-(dimethylamino)pyridine (8.43 g, 69 mmol), abs. pyridine (12.5 ml, 0.155 mmol), abs. CH_2Cl_2 (220 ml), and trifluoromethanesulfonic anhydride (4.5 ml, 27.6 mmol). Workup with CH_2Cl_2 (280 ml), 0.2M HCl, sat. $NaHCO_3$ and NaCl soln. (300 ml of each) and $MgSO_4$. The resulting oil was dissolved in DMF (250 ml) and HMPA (45 ml) and, after addition of LiOAc (6.4 g, 97 mmol), stirred for 48 h at r.t., and then poured into cold NaCl soln. (2.5 l). The precipitate was filtered off by suction, washed with H_2O, dried, and dissolved in dioxane/MeOH 1:1 (70 ml). Shortly thereafter, **14** separated which was filtered off by suction, washed with dioxane/MeOH, and dried: 2.35 g (26%) of **14**. The filtrate gave, on evaporation, 11.19 g (71%) of **13** as a light yellow foam. An anal. sample was further purified by FC (toluene→toluene/AcOEt 6:1).

13: TLC (SiO_2, toluene/AcOEt 1:1): R_f 0.56. UV (MeOH): 255 (sh, 4.49), 267 (4.57). ^{1}H-NMR ($CDCl_3$): 8.15 (*m*, 4 H *o* to NO_2); 8.03 (*s*, H–C(8)); 7.49 (*d*, 2 H *m* to NO_2); 7.41 (*d*, 2 H *m* to NO_2); 7.32 (*s*, NH); 6.37 (*d*, J = 6.4, H–C(1')); 5.52 ('*t*', H–C(2')); 4.77 (*m*, OCH_2CH_2); 4.68 (*t*, H–C(3')); 4.45 (*t*, OCH_2CH_2); 4.09 (*m*, 2 H–C(5')); 3.87 (*m*, H–C(4')); 3.29 (*t*, OCH_2CH_2); 3.10 (*t*, OCH_2CH_2); 1.68 (*s*, Me); 1.00 (*m*, 4 i-Pr). Anal. calc. for $C_{41}H_{55}N_7O_{13}Si_2$ (910.1): C 54.11, H 6.09, N 10.77; found: C 53.97, H 6.19, N 10.57.

14: UV (MeOH): 254 (sh, 4.28), 268 (4.40). ^{1}H-NMR ((D$_6$)DMSO): 13.10 (*s*, NH); 10.20 (*s*, NH); 8.14 (*m*, 4 H *o* to NO_2, H–C(8)); 7.63 (*m*, 4 H *m* to NO_2); 4.72 (*t*, OCH_2CH_2); 4.34 (*t*, OCH_2CH_2); 3.34 (*t*, OCH_2CH_2); 2.28 (*t*, OCH_2CH_2). Anal. calc. for $C_{22}H_{19}N_7O_7 \cdot 1.5\ H_2O$ (520.5): C 50.77, H 4.26, N 18.84; found: C 50.50, H 4.14, N 18.84.

10. *O⁶-[2-(4-Nitrophenyl)ethyl]-9-[3',5'-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-arabinofuranosyl]guanine* (**15**). As described in *Exper. 4*, with **5** (13.48 g, 20 mmol), 4-(dimethylamino)pyridine (9.8 g, 80 mmol), abs. pyridine (14.6 ml, 180 mmol), abs. CH_2Cl_2 (260 ml), and trifluoromethanesulfonic anhydride (5.2 ml, 32 mmol). Workup with CH_2Cl_2 (340 ml), H_2O, 0.2M HCl, sat. $NaHCO_3$ and NaCl soln. (400 ml of each), and $MgSO_4$. The resulting oil (**8**) was dissolved in DMF (200 ml) and HMPA (80 ml) and, after addition of LiOAc (4.0 g, 60 mmol), stirred at r.t. for 12 h. The mixture was poured into H_2O (1.5 l) and extracted with AcOEt (3 × 500 ml). The combined org. layer was dried ($MgSO_4$) and evaporated. The crude residue (**10**) was dissolved in dioxane/MeOH/conc. aq. NH_3 soln. 1.5:1:1 (350 ml) and stirred at r.t. for 12 h. On evaporation to *ca.* 150 ml, the product separated: 6.53 g. The mother liquor was evaporated and the residue purified by FC (4.5 × 10 cm, toluene/AcOEt 5:1,

toluene/AcOEt 1.5:1): 1.14 g. Total yield: 7.68 g (57%) of **15**. TLC (SiO_2, toluene/AcOEt/MeOH 5:4:1): R_f 0.58. UV (MeOH): 250 (4.15), 278 (4.25). ^{1}H-NMR ((D_6)DMSO): 8.17 (*d*, 2 H *o* to NO_2); 7.73 (*s*, H–C(8)); 7.62 (*d*, 2 H *m* to NO_2); 6.46 (*s*, NH_2); 6.05 (*d*, J = 6.5, H–C(1′)); 5.80 (*d*, OH–C(2′)); 4.65 (*t*, OCH_2CH_2); 4.43 (*m*, H–C(2′)); 4.30 (*t*, H–C(3′)); 3.93 (*m*, 2 H–C(5′)); 3.75 (*m*, H–C(4′)); 3.23 (*t*, OCH_2CH_2); 1.03 (*m*, 4 i-Pr). Anal. calc. for $C_{30}H_{46}N_6O_8Si_2$ (674.9): C 53.39, H 6.87, N 12.45; found: C 53.22, H 6.96, N 12.21.

11. *N^2-[2-(4-Nitrophenyl)ethoxycarbonyl]-O^6-[2-(4-nitrophenyl)ethyl]-9-[3′,5′-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-*D*-arabinofuranosyl]guanine* (**16**). A soln. of **13** (9.0 g, 9.84 mmol) in dioxane/MeOH/conc. aq. NH_3 soln. 1:1:1 (150 ml) was stirred at r.t. for 20 h and evaporated. The residue was partitioned between $CHCl_3$ and H_2O (400 ml of each), the org. layer dried ($MgSO_4$) and evaporated. FC (4.5 × 18 cm, toluene/AcOEt 7:1→5:1) gave 3.6 g (41%) of colorless foam. TLC (SiO_2, toluene/AcOEt 1:1): R_f 0.35. UV (MeOH): 268 (4.55). ^{1}H-NMR ($CDCl_3$): 8.16 (*m*, 4 H *o* to NO_2); 8.06 (*s*, H–C(8)); 7.47, 7.39 (2*d*, 4 H *m* to NO_2); 7.28 (*s*, NH); 6.05 (*d*, J = 5.8, H–C(1′)); 4.70 (*m*, H–C(2′), OCH_2CH_2); 4.54 (*t*, H–C(3′)); 4.44 (*m*, OCH_2CH_2); 3.96 (*m*, 2 H–C(5′)); 3.86 (*m*, H–C(4′)); 3.27 (*t*, OCH_2CH_2); 3.09 (*t*, OCH_2CH_2); 1.04 (*m*, 4 i-Pr). Anal. calc. for $C_{39}H_{33}N_7O_{12}Si_2$ (868.1): C 53.96, H 6.15, N 11.29; found: C 53.88, H 6.26, N 11.14.

12. *9-[β-*D*-Arabinofuranosyl]-O^6-[2-(4-nitrophenyl)ethyl]guanine* (**17**). To a soln. of **15** (0.33 g, 0.5 mmol) in abs. THF (6 ml) were added AcOH (0.21 ml, 3.75 mmol) and $(Bu_4N)F \cdot 3\,H_2O$ (0.31 g, 1 mmol) and stirred for 2.5 h at r.t. The mixture was poured into H_2O (30 ml) and the precipitate filtered off by suction, washed with AcOEt and Et_2O, and dried under high vacuum: 0.155 g (72%) of **17**. TLC (SiO_2, $CHCl_3$/MeOH 9:1): R_f 0.18. UV (MeOH): 250 (4.18), 278 (4.26). ^{1}H-NMR ((D_6)DMSO): 8.17 (*d*, 2 H *o* to NO_2); 7.90 (*s*, H–C(8)); 7.63 (*d*, 2 H *m* to NO_2); 6.45 (*s*, NH_2); 6.10 (*d*, J = 4.2, H–C(1′)); 5.60, 5.50 (2*d*, OH–C(2′), OH–C(3′)); 5.06 (*t*, OH–C(5′)); 4.66 (*t*, OCH_2CH_2); 4.06 (*m*, H–C(2′), H–C(3′)); 3.73 (*m*, H–C(4′)); 3.61 (*m*, 2 H–C(5′)); 3.24 (*t*, OCH_2CH_2). Anal. calc. for $C_{18}H_{19}N_6O_7$ (431.4): C 50.12, H 4.44, N 19.48; found: C 49.60, H 4.58, N 19.80.

13. *9-(β-*D*-Arabinofuranosyl)guanine* (**18**). A suspension of **17** (0.215 g, 0.5 mmol) in 0.5M DBU in MeCN (2 ml) was stirred at r.t. for 24 h, then neutralized with AcOH (0.057 ml, 1 mmol). The precipitate was filtered off by suction, washed with MeCN, MeOH, and Et_2O, and dried. Recrystallization from H_2O (2 ml) gave **18** (95 mg, 64%). TLC (cellulose, PrOH/aq. NH_3 soln./H_2O 55:10:35): R_f 0.46. UV (pH 7): 252 (4.12), 266 (sh, 3.99). ^{1}H-NMR ((D_6)DMSO): 10.60 (br. *s*, NH); 7.74 (*s*, H–C(8)); 6.46 (br. *s*, NH_2); 5.99 (*d*, J = 4.4, H–C(1′)); 5.60, 5.49 (2*d*, OH–C(2′), OH–C(3′)); 5.05 (*t*, OH–C(5′)); 4.03 (*m*, H–C(2′), H–C(3′)); 3.73 (*m*, H–C(4′)); 3.59 (*m*, 2 H–C(5′)). Anal. calc. for $C_{10}H_{13}N_5O_5 \cdot 0.75\,H_2O$ (296.8): C 40.47, H 4.92, N 23.60; found: C 40.21, H 4.97, N 23.97.

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