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Biocatalytic Separation of *N*-7/*N*-9 Guanine Nucleosides

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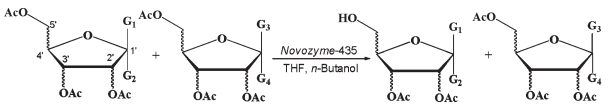

β-D-ribofuranosyl guanine:
G_1 = N^2-isobutanoylguanin-9-yl, G_2 = H, C-2' & C-3' OAc (α), C-4' CH_2OAc (β)
G_3 = N^2-isobutanoyl-7-yl, G_4 = H, C-2' & C-3' OAc (α), C-4' CH_2OAc (β)
α-D-arabinofuranosyl guanine:
G_1 = H, G_2 = N^2-isobutanoylguanin-9-yl, C-2' OAc (β), C-3' OAc (α), C-4' CH_2OAc (β)
G_3 = H, G_4 = N^2-isobutanoylguanin-7-yl, C-2' OAc (β), C-3' OAc (α), C-4' CH_2OAc (β)
α-L-arabinofuranosyl guanine:
G_1 = N^2-isobutanoylguanin-9-yl, G_2 = H, C-2' OAc (α), C-3' OAc (β), C-4' CH_2OAc (α)
G_3 = N^2-isobutanoylguanin-7-yl, G_4 = H, C-2' OAc (α), C-3' OAc (β), C-4' CH_2OAc (α)

Vorbrüggen coupling of trimethylsilylated 2-*N*-isobutanoylguanine with peracetylated pentofuranose derivatives generally gives inseparable *N*-7/*N*-9 glycosyl mixtures. We have shown that the *two* isomers can be separated biocatalytically by Novozyme-435-mediated selective deacetylation of the 5′-*O*-acetyl group of peracetylated *N*-9 guanine nucleosides.

The discovery of 9-[(2-hydroxyethoxy)methyl]guanine (acyclovir) against herpes simplex type 1 and type 2 viruses and its low mammalian toxicity triggered the synthesis of a series of guanine nucleosides, e.g., penciclovir, famciclovir, valaciclovir, valganciclovir, abacavir, etc., for the treatment of various viral diseases.[1,2] The most problematic chemistry and difficulties in manipulation of all five common bases found in DNA and RNA occur with the polyfunctional guanine (pK_{a1} −1.7, pK_{a2} −9.2) nucleosides and nucleotides. The coupling of guanine with peracetylated sugar derivatives generally produces *N*-7/*N*-9 isomeric mixtures of nucleosides that are difficult to separate.[3,4] The changes in experimental variables and the use of a selectively modified guanine moiety, such as 2-*N*-acetyl-6-*O*-diphenylcarbamoylguanine in nucleoside coupling reactions, affect the isomeric ratio but do not eliminate the formation of the *N*-7 isomer together with the desired *N*-9 isomer.[5] In this paper, we report the synthesis of guanine nucleosides (mixture of 9- and 7-glycosyl derivatives) derived from D-ribose, D-arabinose, and L-arabinose sugars and for the first time their highly efficient separation mediated by Novozyme-435 lipase-catalyzed removal of one of the acetoxy functions of the peracetylated *N*-9 guanine nucleosides.

The coupling of 2-*N*-isobutanoylguanine (**2**)[6] with 1,2,3,5-tetra-*O*-acetyl-D-ribofuranose (**3**),[7,8] 1,2,3,5-tetra-*O*-acetyl-D-arabinofuranose (**4**),[9] or 1,2,3,5-tetra-*O*-acetyl-L-arabinofuranose (**5**)[8−10] in the presence of TMSOTf as Lewis acid catalyst following a standard Vorbrüggen[5,11] coupling protocol afforded mixtures of 2,3,5-tri-*O*-acetylated 9- and 7-β-D-ribofuranosylguanines **6** and **7**, 9- and 7-α-D-arabinofuranosylguanines **8** and **9**, and 9- and 7-α-L-arabinofuranosylguanines **10** and **11** in ratios of 87:13, 63:37, and 76:24, respectively, in 60−65% yields (Scheme 1 and Table 1). The ratio of regioisomers *N*-9 and *N*-7 in the above guanine nucleoside mixtures **6** and **7**, **8** and **9**, and **10** and **11** were calculated on the basis of the integration of the corresponding anomeric protons in the ^{1}H NMR spectra (400 MHz) of the mixtures (Table 1). Our various attempts of separation of *N*-9 and *N*-7 guanine nucleosides from the mixtures **6** and **7**, **8** and **9**, and **10** and **11** by repeated column chromatography on silica gel were unsuccessful.

Some lipases have been found to selectively acylate/deacylate primary hydroxyl over secondary hydroxyl group(s) of sugars[12]

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SCHEME 1. Procedure for the Synthesis of Guanine Nucleosides

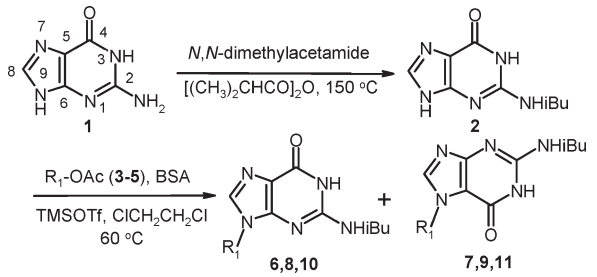


TABLE 1. Glycosylation of 2-*N*-Isobutanoylguanine with Peracetylated Sugar Derivatives 3−5

reactants	reaction time (h)	products	ratio[a] of *N*-9/ *N*-7 nucleosides	yields (%)
2 + **3**	4	**6** and **7**	87:13	60
2 + **4**	6	**8** and **9**	63:37	62
2 + **5**	6	**10** and **11**	76:24	65

[a]Ratios of *N*-9 and *N*-7 nucleoside regioisomers were calculated from the ^{1}H NMR spectral (400 MHz) data of the mixtures.

and nucleosides.[13] In the recent past, lipases have been used for the separation of the nucleosides from their anomeric mixtures[14] and for the resolution of β-D/L-2′- deoxynucleosides.[15] Stimulated by these results, we decided to explore an enzymatic route for the separation of *N*-9 and *N*-7 guanine nucleosides. Five lipases, viz. *Candida antarctica* lipase-B immobilized on polyacrylate, Lewatit (Novozyme-435 or CAL-B), *Theremomyces lanuginosus* lipase immobilized on silica (Lipozyme TL IM), Amano PS lipase, *Candida rugosa* lipase (CRL), and porcine pancreatic lipase (PPL) were screened for the selective deacetylation of one regioisomer over the other in *N*-9/*N*-7 guanine nucleoside mixtures **6** and **7**, **8** and **9**, and **10** and **11** in five sets of organic solvents, i.e., tetrahydrofuran (THF), acetonitrile (CH_3CN), toluene, diisopropyl ether (DIPE), and acetone using *n*-butanol as acetyl acceptor at 40−42 °C and at 150 rpm in an incubator shaker (Figure 1).

It was observed that lipase Novozyme-435 in THF at 40−42 °C selectively and most efficiently deacetylates the acetoxy group at the C-4′-hydroxymethyl moiety of *N*-9-glycosylguanine over the other acetoxy groups of *N*-9 and *N*-7 isomers of nucleosides (Scheme 2). The Novozyme-435-catalyzed deacetylation reaction carried out in other solvents, i.e., acetonitrile, toluene, DIPE, and acetone, did not yield any product. Although PPL in THF initially showed selectivity for the deacetylation of the C-4′-acetoxymethyl group of *N*-9-glycosylguanine, the reaction was too slow to be of any practical use, and deacetylation of other acetoxy groups of the *N*-7 and *N*-9 regioisomers were observed leading to the formation of a mixture of compounds. When the Novozyme-435 catalyzed reaction was conducted at a higher temperature than 40−42 °C, the enhancement in the rate was observed, but it resulted in the formation of multiple

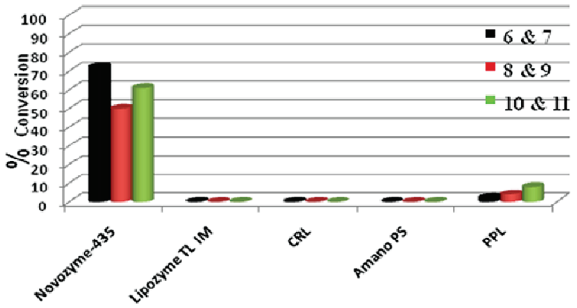
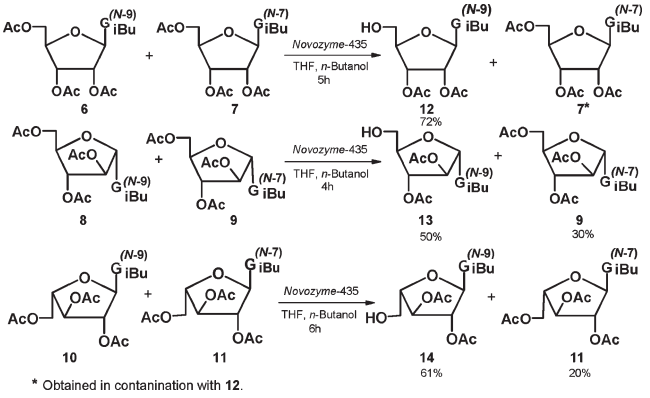


FIGURE 1. Selective deacetylation studies on nucleosides **6** and **7**, **8** and **9**, and **10** and **11** in THF at 40−42 °C catalyzed by Novozyme-435 and other lipases.

SCHEME 2. Novozyme-435-Catalyzed Deacetylation Reaction: Separation of *N*-7 and *N*-9 Guanine Nucleosides



products. Lipozyme TL IM, Amano PS, and CRL did not show any reaction on the peracetylated *N*-9-, *N*-7-glycosylguanine nucleoside substrate mixtures.

In a typical reaction, a solution of *N*-9/*N*-7 nucleoside mixture **6** and **7** (200 mg) in tetrahydrofuran (20 mL) containing a small amount of *n*-butanol was incubated with Novozyme-435 (substrate−enzyme ratio 1:0.5 w/w) in an incubator shaker at 40−42 °C. The reaction mixture was shaken for 4−6 h until a prominent spot of the product appeared on analytical TLC at much lower R_f value than the starting compounds.[16] The reaction was quenched by filtering off the enzyme, and the solvent was removed under reduced pressure. The crude product thus obtained was purified by silica gel column chromatography using methanol in chloroform as gradient solvent system to afford the pure *N*-9 glycosylguanine **12** having a C-5′ hydroxyl group in 72% yield (Scheme 2). Similarly, lipase-catalyzed deacetylation reactions on nucleoside mixtures **8** and **9** and **10** and **11** led to the formation of the selectively deacetylated compounds **13** and **14** in 50 and 61% yields, respectively, along with the unreacted peracetylated pure *N*-7 glycosylated guanines **9** and **11** in 30 and 20% yields, respectively.[17] These reactions did not yield any product when carried out in the absence of lipase. All the enzymatically deacetylated *N*-9 glycosylguanine nucleosides **12**−**14**

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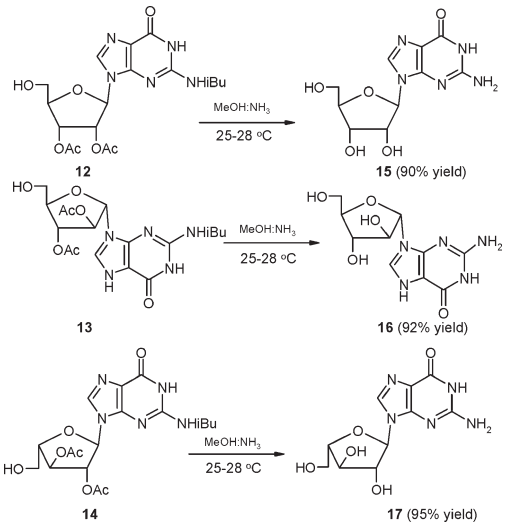
(16) Completion of the reaction was monitored by TLC in methanol−chloroform as solvent system. Partial separation in *N*-9- and *N*-7-glycosylated nucleosides was observed after five to six runs of the TLC plate in the solvent.

(17) Yields of *N*-9 glycosylated guanines **12**−**14** and *N*-7 glycosylated guanines **9** and **11** were calculated on the basis of the consideration of *N*-9 and *N*-7 regioisomers as 100% in the mixtures.

SCHEME 3. Deacetylation of Guanine Nucleosides 12−14



and unreacted, recovered peracetylated *N*-7 glycosylguanine nucleosides **9** and **11** were unambiguously identified on the basis of their spectral (IR, ^{1}H and ^{13}C NMR) and HRMS data.

The 5′-OH group of selectively deacetylated *N*-9-glycosylated guanine nucleosides **12**−**14** was acetylated using acetic anhydride and DMAP as a catalyst in THF resulting in the formation of 2′,3′,5′-tri-*O*-acetylated guanine nucleosides **6**, **8**, and **10** in 82, 84, and 85% yields, respectively. The NMR spectral data of pure tri-*O*-acetylated *N*-9 glycosylguanines **6**,[18] **8**, and **10** and pure *N*-7 glycosylguanines **9** and **11** were compared with the NMR spectral data of *N*-9/*N*-7 glycosylated guanine mixtures **6** and **7**, **8** and **9**, and **10** and **11** to further confirm the identity of the individual compounds.

To confirm the structures of Novozyme-435 deacetylated nucleosides, hydrolysis of compounds **12**−**14** was performed in methanolic ammonia to yield guanosine (**15**),[5] α-D-arabinofuranosylguanine **16**,[9] and α-L-arabinofuranosylguanine **17** in 90, 92, and 95% yields, respectively (Scheme 3). The hydrolyzed products **15**−**17** were unambiguously identified on the basis of their spectral (IR, ^{1}H and ^{13}C NMR spectra) and HRMS data analysis. The physical and spectral data of known compounds **15** and **16** were found to be identical to the reported data; the spectral data of compound **17** has not been previously reported.

In summary, it has been established that the lipase Novozyme-435 can selectively hydrolyze the acetoxy function derived from the primary hydroxyl group at the C-5′-position of tri-*O*-acetylated *N*-9 glycosylated guanines over the acetoxy moieties derived from the two secondary hydroxyl groups present in the same molecule and also over three acetoxy functions of *N*-7 glycosylguanines. This enzymatic methodology enables efficient separation of mixtures of *N*-9 and *N*-7 glycosylated guanines, which are otherwise almost impossible to separate by column chromatography or other techniques.

Experimental Section

General Procedure of Lipase-Catalyzed Selective Deacetylation of Mixtures of *N*-9/*N*-7 Nucleosides 6 and 7, 8 and 9, and 10 and 11. The solution of *N*-9/*N*-7 guanine nucleosides **6** and **7**, **8** and **9**, or **10** and **11** (200 mg, 0.42 mmol) in tetrahydrofuran (20 mL) containing a small amount of *n*-butanol as acetyl acceptor was incubated with *C. antarctica* lipase B (Novozyme-435, 100 mg) in an incubator shaker at 40−42 °C. After 4−6 h of incubation, a prominent spot of the product appeared at much lower R_f value than the starting compounds.[16] The reaction was stopped by filtering off the enzyme, and the solvent was removed under reduced pressure. The crude product thus obtained was purified through a silica gel column using a gradient solvent system of methanol in chloroform (1:99 to 1.5:98.5) to afford pure 5′-hydroxylated *N*-9 glycosylguanine nucleosides **12**, **13**, and **14** in 72%, 50%, and 61% yields, respectively. The recovered unreacted *N*-7 guanine nucleosides **9** and **11** were isolated in pure form in 30 and 20% yields, respectively, whereas the recovered *N*-7 nucleoside **7** was contaminated with *N*-9 guanine nucleoside.

9-(2′,3′-Di-*O*-acetyl-β-D-ribofuranosyl)-N^2-isobutanoylguanine (12). Compound **12** was obtained as a white sticky solid (0.13 g, 72% yield): R_f = 0.5 (10% methanol in chloroform); $[\alpha]^{25}_D$ = +2.2 (*c* 0.07, methanol); IR (KBr) ν_{max} 3220, 2936, 1751, 1684, 1609, 1560, 1405, 1375, 1250, 1157, 1105, 949, 785 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.23 (6H, d, *J* = 6.8 Hz), 2.03, 2.12 (6H, 2s), 2.70−2.73 (1H, m), 3.78−3.88 (2H, m), 4.26−4.28 (1H, m), 5.56−5.58 (1H, m), 5.82 (1H, t, *J* = 5.6 Hz), 6.18 (1H, d, *J* = 6.0 Hz), 8.29 (1H, s); ^{13}C NMR (CD_3OD, 100.6 MHz): δ 19.36, 20.11, 20.50, 37.03, 62.35, 72.78, 75.38, 87.11, 85.34, 121.44, 139.74, 150.07, 150.63, 157.49, 171.11, 171.64, 181.81; HR-ESI-TOF-MS *m*/*z* 460.1432 ([M + Na]$^+$), calcd for [$C_{18}H_{23}N_5O_8$ + Na]$^+$ 460.1439.

9-(2′,3′-Di-*O*-acetyl-α-D-arabinofuranosyl)-N^2-isobutanoylguanine (13). Compound **13** was obtained as a white solid (90 mg, 50% yield): R_f = 0.5 (10% methanol in chloroform); mp 180−182 °C; $[\alpha]^{25}_D$ = +3.9 (*c* 0.1, methanol); IR (KBr) ν_{max} 3196, 2975, 2935, 1737, 1718, 1690, 1615, 1567, 1370, 1247, 1137, 1043, 908, 800 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz): δ 1.22 (6H, d, *J* = 6.8 Hz), 2.05, 2.09 (6H, 2s), 2.71−2.74 (1H, m), 3.73−3.83 (2H, m), 4.56−4.59 (1H, m), 5.43−5.45 (1H, m), 5.85 (1H, t, *J* = 4.0 Hz), 6.22 (1H, d, *J* = 3.6 Hz) and 8.13 (1H, s); ^{13}C NMR (CD_3OD, 100.6 MHz) δ 19.36, 20.02, 20.05, 36.99, 62.41, 76.93, 81.08, 86.16, 89.04, 121.65, 139.85, 150.06, 150.68, 157.49, 170.54, 171.49, 181.87; HR-ESI-TOF-MS *m*/*z* 460.1426 ([M + Na]$^+$), calcd for [$C_{18}H_{23}N_5O_8$ + Na]$^+$ 460.1439.

9-(2′,3′-Di-*O*-acetyl-α-L-arabinofuranosyl)-N^2-isobutanoylguanine (14). Compound **14** was obtained as a white solid (0.11 g, 61% yield): R_f = 0.5 (10% methanol in chloroform); mp 176−178 °C; $[\alpha]^{25}_D$ = −4.2 (*c* 0.1, methanol); IR (KBr) ν_{max} 3193, 2976, 2950, 1737, 1719, 1691, 1612, 1566, 1407, 1370, 1247, 1137, 1071, 909, 801 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.22 (6H, d, *J* = 6.8 Hz), 2.09, 2.05 (6H, 2s), 2.71−2.74 (1H, m), 3.76−3.80 (2H, m), 4.57−4.59 (1H, m), 5.43−4.45 (1H, m), 5.85 (1H, t, *J* = 4.0 Hz), 6.22 (1H, d, *J* = 4.0 Hz), 8.13 (1H, s); ^{13}C NMR (CD_3OD, 100.6 MHz) δ 19.36, 20.02, 20.05, 36.99, 62.41, 76.93, 81.08, 86.16, 89.04, 121.65, 139.85, 150.06, 150.68, 157.49, 170.54, 171.49, 181.87; HR-ESI-TOF-MS *m*/*z* 460.1426 ([M + Na]$^+$), calcd for [$C_{18}H_{23}N_5O_8$ + Na]$^+$ 460.1439.

7-(2′,3′,5′-Tri-*O*-acetyl-α-D-arabinofuranosyl)-N^2-isobutanoylguanine (9). Compound **9** was obtained as a white sticky solid (59 mg, 30% yield): R_f = 0.5 (7% methanol in chloroform); $[\alpha]^{25}_D$ = +1.7 (*c* 0.1, methanol); IR (KBr) ν_{max} 3188, 2976, 1751, 1686, 1610, 1375, 1226, 1054, 781 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.21 (6H, d, *J* = 6.8 Hz), 1.99−2.10 (9H, 3s), 2.70−2.74 (1H, m), 4.27−4.40 (2H, m), 4.85−4.86 (1H, m), 5.37−5.39 (1H, m), 5.88 (1H, t, *J* = 4.0 Hz), 6.41 (1H, d, *J* = 4.0 Hz), 8.35 (1H, s); ^{13}C NMR (CD_3OD, 100.6 MHz) δ 19.36, 20.13, 20.70, 20.92, 36.96, 64.39, 76.98, 81.59, 83.35, 91.38, 112.03, 144.30, 149.61, 154.81, 160.03, 171.51, 172.39,

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181.93; HR-ESI-TOF-MS m/z 502.1535 ([M + Na]$^+$), calcd for [$C_{20}H_{25}N_5O_9$ + Na]$^+$ 502.1544.

7-(2′,3′,5′-Tri-*O*-acetyl-α-L-arabinofuranosyl)-N^2-isobutanoylguanine (11). Compound **11** was obtained as a white sticky solid (40 mg, 20% yield): R_f = 0.5 (7% methanol in chloroform); $[\alpha]^{25}_D$ = −1.5 (c 0.1, methanol); IR (KBr) ν_{max} 3434, 2927, 1751, 1685, 1611, 1551, 1372, 1224, 1055, 781 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.24 (6H, d, J = 6.8 Hz), 2.03−2.15 (9H, 3s), 2.83−2.85 (1H, m), 4.29−4.38 (2H, m), 4.79 (1H, brs), 5.31 (1H, t, J = 3.6 Hz), 5.83 (1H, t, J = 3.2 Hz), 6.43 (1H, d, J = 3.0 Hz), 8.01 (1H, s), 9.86 (1H, brs), 12.36 (1H, brs); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 19.05, 20.68, 20.79, 36.15, 62.95, 75.96, 80.36, 82.55, 90.26, 111.31, 141.58, 148.14, 152.99, 157.84, 169.36, 169.74, 170.61, 179.65; HR-ESI-TOF-MS m/z 502.1537 ([M + Na]$^+$), calcd for [$C_{20}H_{25}N_5O_9$ + Na]$^+$ 502.1544.

General Procedure of Acetylation of Enzymatically Selectively Deacetylated Guanine Nucleosides 12−14. To a stirred solution of nucleosides **12**−**14** (0.1 g, 0.21 mmol) in THF (8 mL) was added acetic anhydride (0.25 mmol), followed by the addition of catalytic amount of DMAP, and the reaction mixture was stirred for 4−5 h at 28 °C. On completion (examination on analytical TLC), crushed ice was added, and the reaction mixture was extracted with ethyl acetate (2 × 30 mL). The combined organic layer was washed with saturated aqueous $NaHCO_3$ solution (2 × 30 mL) and dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The residue thus obtained was purified by column chromatography on silica gel using methanol/chloroform (1:99) as eluent to afford the pure triacetylated guanine nucleosides **6**,[17] **8**, and **10** in 82, 84, and 85% yields, respectively.

9-(2′,3′,5′-Tri-*O*-acetyl-β-D-ribofuranosyl)-N^2-isobutanoylguanine (6)[18]. Compound **6** was obtained as a white sticky solid (90 mg, 82% yield): R_f = 0.5 (7% methanol in chloroform); $[\alpha]^{25}_D$ = +5.2 (c 0.1, methanol); HR-ESI-TOF-MS m/z 502.1533 ([M + Na]$^+$), calcd for [$C_{20}H_{25}N_5O_9$ + Na]$^+$ 502.1544.

9-(2′,3′,5′-Tri-*O*-acetyl-α-D-arabinofuranosyl)-N^2-isobutanoylguanine (8). Compound **8** was obtained as a white sticky solid (92 mg, 84% yield): R_f = 0.5 (7% methanol in chloroform); $[\alpha]^{25}_D$ = +4.2 (c 0.1, methanol); IR (KBr) ν_{max} 3167, 2976, 2936, 1749, 1683, 1609, 1560, 1403, 1373, 1224, 1101, 1053, 907, 785 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.22 (6H, d, J = 6.8 Hz), 2.05, 2.06, 2.10 (9H, 3s), 2.73 (1H, m), 4.32−4.36 (2H, m), 4.79−4.86 (1H, m), 5.36−5.38 (1H, m), 5.84 (1H, t, J = 3.6 Hz), 6.23 (1H, d, J = 3.2 Hz), 8.11 (1H, s); ^{13}C NMR (CD_3OD, 100.6 MHz) δ 19.36, 20.54, 20.68, 37.01, 64.07, 77.17, 80.79, 83.56, 89.23, 121.67, 139.60, 150.07, 150.37, 157.48, 171.29, 171.38, 172.39, 181.86; HR-ESI-TOF-MS m/z 502.1526 ([M + Na]$^+$), calcd for [$C_{20}H_{25}N_5O_9$ + Na]$^+$ 502.1544.

9-(2′,3′,5′-Tri-*O*-acetyl-α-L-arabinofuranosyl)-N^2-isobutanoylguanine (10). Compound **10** was obtained as a white sticky solid (93 mg, 85% yield): R_f = 0.5 (7% methanol in chloroform); $[\alpha]^{25}_D$ = −4.6 (c 0.1, methanol); IR (thin film) ν_{max} 3153, 2928, 1747, 1683, 1609, 1563, 1402, 1373, 1225, 1158, 1053, 908, 757 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.22 (6H, d, J = 6.8 Hz), 2.05, 2.06, 2.10 (9H, 3s), 2.73 (1H, m), 4.32−4.36 (2H, m), 4.79−4.86 (1H, m), 5.36−5.38 (1H, m), 5.83−5.85 (1H, m), 6.23 (1H, d, J = 3.2 Hz), 7.90 (1H, s); ^{13}C NMR (CD_3OD, 100.6 MHz) δ 19.36, 20.54, 20.68, 37.01, 64.07, 77.17, 80.79, 83.56, 89.23, 121.67, 139.60, 150.07, 150.37, 157.48, 171.29, 171.38, 172.39, 181.86; HR-ESI-TOF-MS m/z 502.1538 ([M + Na]$^+$), calcd for [$C_{20}H_{25}N_5O_9$ + Na]$^+$ 502.1544.

General Procedure for the Hydrolysis of Nucleosides 12−14. A solution of selectively deacetylated nucleosides **12**−**14** (0.1 g, 0.22 mmol) in 20% methanolic ammonia solution (15 mL) was stirred at 25−28 °C for 10 h. On completion of the reaction (examination on analytical TLC), the excess solvent was removed under reduced pressure and the residue thus obtained was washed with hot ethyl acetate several times to afford guanosine (**15**),[5] 9-α-D-arabinofuranosyl guanine (**16**),[9] and 9-α-L-arabinofuranosyl guanine (**17**) as white solids in 90, 92, and 95% yields, respectively.

Guanosine (15)[5]. Compound **15** was obtained as a white solid (57.6 mg, 90% yield): mp 238−240 °C dec (lit.[5] mp 240 °C dec); $[\alpha]^{25}_D$ = −40.7 (c 0.1, CH_3SOCH_3); HR-ESI-TOF-MS m/z 284.0988 ([M + H]$^+$), calcd for [$C_{10}H_{13}N_5O_5$ + H]$^+$ 284.0989.

9-α-D-Arabinofuranosylguanine (16)[9]. Compound **16** was obtained as a white solid (58.9 mg, 92% yield): R_f = 0.3 (25% methanol in chloroform); mp 210 °C dec; $[\alpha]^{32}_D$ = +21.8 (c 0.1, MeOH); HR-ESI-TOF-MS m/z 306.0804 ([M + Na]$^+$), calcd for [$C_{10}H_{13}N_5O_5$ + Na]$^+$ 306.0809.

9-α-L-Arabinofuranosylguanine (17). Compound **17** was obtained as a white solid (60.8 mg, 95% yield); R_f = 0.3 (25% methanol in chloroform); mp 238 °C dec; $[\alpha]^{32}_D$ = −25.6 (c 0.1, MeOH); IR (KBr) ν_{max} 3368, 3200, 2933, 1729, 1693, 1609, 1534, 1398, 1052, 781 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz) δ 3.44−3.59 (2H, m), 3.93−3.96 (1H, m), 4.06−4.10 (1H, m), 4.46−4.48 (1H, m), 5.67 (1H, d, J = 4.8 Hz), 7.91 (1H, s); ^{13}C NMR (CD_3OD, 100.6 MHz): δ 60.90, 75.03, 79.38, 84.84, 87.31, 116.53, 135.96, 151.09, 153.32, 156.26; ESI-TOF-MS m/z 306.0805 ([M + Na]$^+$), calcd for [$C_{10}H_{13}N_5O_5$ + Na]$^+$ 306.0809.

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Supporting Information Available: General experimental methods, procedure for the preparation of compounds **6** and **7**, **8** and **9**, and **10** and **11**, and ^{1}H- and ^{13}C NMR spectra of mixtures of **6** and **7**, **8** and **9**, and **10** and **11**, **6**, and **8**−**17**. This material is available free of charge via the Internet at http://pubs.acs.org.