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Novel observation concerning the nitrobenzenesulfonamide protecting group

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Abstract—In an ongoing work directed towards the synthesis of nucleoside derivatives containing an L-alanine residue, we report herein a novel observation concerning the Ns-protecting group: the epimerization of the α-hydrogen in acylation conditions.

1. Introduction

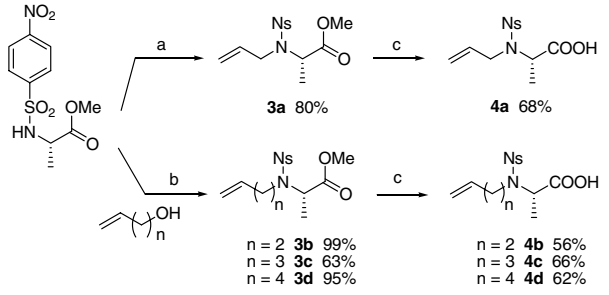
As a part of an ongoing programme directed to the synthesis of a modified adenosine bearing a 2′,3′-cyclized peptidic moiety,[1] we needed to prepare compounds **5**. As depicted in Scheme 1 this required the acylation of the 3′-O by a N-protected L-alanyl residue suitably N-alkylated.

Such functionalized amino acids can be readily obtained using the methodology recently developed by Fukuyama and co-workers,[2] according to Scheme 2.

It is important to notice that racemization was never observed during the alkylation step.[3]

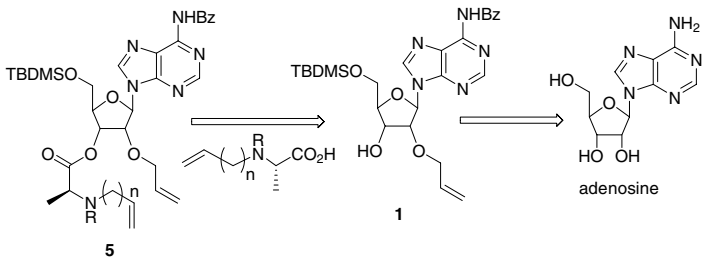
2. Results and discussion

The final acylation step at 3′-O of the protected adenosine **1** was first conducted using EDCI in the presence of DMAP in refluxing dichloromethane (Scheme 3).



Scheme 2. Reagents and conditions: (a) allylbromide, K_2CO_3; (b) DEAD, $P(Ph)_3$; (c) (i) LiOH, (ii) HCl.

Surprisingly NMR analysis of the so obtained derivatives revealed the presence of two compounds, which could not be separated by column chromatography.



Scheme 1.

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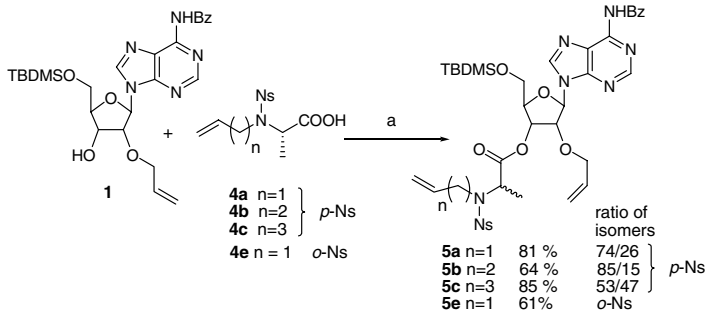
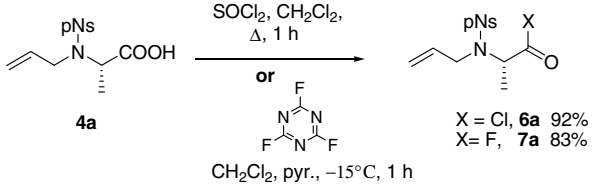


Scheme 3. Reagents and conditions: (a) EDCI, DMAP, CH_2Cl_2, Δ.

For **5a** and **5b** mass spectrometry showed a single peak at $m/z = 822.4$ and 836.4, respectively, although in ^1H NMR, two characteristic doublets appear for H1′ (this differentiation was used to quantify the two isomers and the ratio was done in Scheme 3 for each compound). For compound **5e** (protected by the *ortho*-nitrobenzenesulfonamide group *o*-Ns) the two signals corresponding to the H1′ overlap, but the result seems comparable to that obtained for compound **5a** (about 20% in conditions of Table 1, entry 1). All those facts suggest the partial epimerization of the chiral centre on the amino acid moiety. To reduce this side effect, many acylation conditions were tested and described in Table 1. We observed that an excess of EDCI (Table 1, entry 2) increased the epimerization and a shortened reaction time decreased the epimerization. Unfortunately, the yield appeared very low in the latter (Table 1, entry 3). This method (EDCI, DMAP) is known to be problematic,[4] so a variety of coupling reagents were tested.

The phosphonium reagent: 'BOP reagent'[5] (Table 1, entry 7) known as a racemization suppressant, gave no acylation product. With additives like HOAt (1-hydroxy-7-azabenzotriazole) in the presence of carbodiimide reagent, or HBTU (Table 1, entries 4 and 5) the percentage of epimerization is very high. It is known that the highly reactive aminoacyl chloride protected at the nitrogen atom by an arene or heteroarenesulfonyl group can be used for peptide coupling and can avoid the risk of racemization.[6] In our case, the lower percentage of epimerization was obtained from the corresponding amino acid chloride **6a** (Table 1, entry 8; Scheme 4),



Scheme 4.

but the yield was dramatically low (24%) and if we run the condensation by refluxing in CH_2Cl_2, the percentage of epimerization increased. With the method developed by Carpino et al.[7] (Table 1, entry 9) using acid fluoride as intermediate (the acid fluoride was obtained under mild nonacidic conditions by reaction of the carboxylic acid with cyanuric fluoride and pyridine, Scheme 4), the result was not any better.

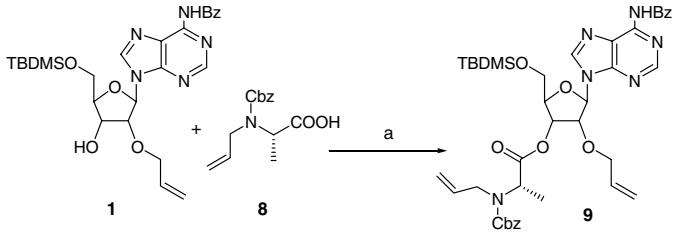
At this stage, it seems that the presence of Ns-protecting group increases the acidity of the α-hydrogen in the amino acid moiety, and in many conditions of acylation, substantial epimerization was observed at the chiral centre of the amino acid part. To be sure that the presence of Ns-protecting group is responsible for this side reaction, the acylation was done with the NCbz L-alanine derivative **8**[8] and the desired product **9** was obtained without epimerization[9] (Scheme 5).

In conclusion, even if the use of Ns-strategy presents a lot of advantages, the organic chemist has to be aware that during the acylation process, the presence of this protecting group could induce unfavourable side effects.

Table 1. Coupling of optically pure **4a** under different conditions

Entry		Yield (%)	Ratio of isomers **5a**
1	EDCI (1.2 equiv), DMAP (1.2 equiv)[a]	81	74/26
2	EDCI (1.7 equiv), DMAP (1.2 equiv)[a]	78	54/46
3	EDCI (1.1 equiv), DMAP (1.2 equiv)[b]	32	86/14
4	EDCI (1.1 equiv), HOAt (0.9 equiv), NMM (1 equiv)[c]	32	51/49
5	HBTU (0.9 equiv), DIPEA (1 equiv)[c]	32	60/40
6	'Bop reagent'	—	—
7	Acid chloride, pyr. (1.1 equiv)[c]	24	99/01
8	Acid chloride, pyr. (1.1 equiv)[a]	40	95/05
9	Acid fluoride, pyr.[a]	25	89/11
10	Symmetrical anhydride	50	76/24

[a] Δ, 18 h.
[b] Δ, 2 h.
[c] Room temperature, 2 h.



Scheme 5. No epimerization observed during the acylation step. Reagents and conditions: (a) EDCI, DMAP, CH_2Cl_2, Δ.

In our particular case, new strategies have to be developed to prepare adenosine derivatives **5**.

3. Experimental

3.1. General methods

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution. All assignments were confirmed by 2D experiments and Dept 135. Moisture-sensitive reactions were conducted under argon in oven-dried glassware. All chemical reagents were purchased from Aldrich Chemical Co. and used without further purification. THF was distilled over sodium and benzophenone. Dichloromethane was distilled over P_2O_5. Column chromatography was performed on E. Merck Silica gel 60 (230–400 mesh). Analytical thin layer chromatography was performed on E. Merck aluminium plates of Silica Gel 60F-254 with detection by UV and by spraying with 6 N H_2SO_4 and heating for about 1 min at 300 °C.

3.2. General procedure for hydrolysis of esters

To a solution of **3** (2 mmol) in THF (10 mL) was added LiOH 0.5 M (4 mmol). The reaction mixture was stirred at room temperature for 30 min. and concentrated under reduced pressure. Ether and saturated aqueous $NaHCO_3$ were added. The layers were separated, and the ether layer was washed with saturated aqueous $NaHCO_3$. The combined aqueous layer was acidified with concentrated HCl and extracted with Ether. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure to give acid **4**.

3.2.1. (*S*)-2-[Allyl-(4-nitro-benzenesulfonyl)-amino]-propionic acid 4a. Preparation as described in the general procedure afforded **4a** as a yellowish solid in 68% yield. $[\alpha]_D$ −24.4 (*c* 1.25, CH_2Cl_2). Mp 100 °C. ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 1.48$ (d, 3H, $J = 7.2$ Hz, CH_3); 3.75–4.05 (m, 2H, CH_2); 4.65 (m, 1H, CH); 5.13–5.26 (m, 2H, CH_2=); 5.68–5.82 (m, 1H, CH=); 7.98–8.03 (m, 2H, HAr); 8.29–8.35 (m, 2H, HAr); 8.80 (br s, 1H, CO_2H) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): $\delta = 15.5$ (CH_3); 47.7 (CH_2); 54.5 (CH); 117.8 (CH_2=); 123.1; 127.6 (4 × CHAr); 132.9 (CH=); 144.7; 149.0 (2 × CqAr); 175.8 (CO) ppm. MS (IC NH_3^+): 332 ($M+NH_4^+$).

3.2.2. (*S*)-2-[But-3-enyl-(4-nitro-benzenesulfonyl)-amino]-propionic acid 4b. Preparation as described in the general procedure afforded **4b** as a yellowish oil in 56% yield. $[\alpha]_D$ −31.3 (*c* 1.03, CH_2Cl_2). ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 1.51$ (d, 3H, $J = 7{,}4$ Hz, CH_3); 2.22–2.61 (2 m, 2H, $CH_2\beta_N$); 3.07–3.41 (m, 2H, $CH_2\alpha_N$); 4.63 (m, 1H, CH); 5.07 (m, 2H, CH_2=); 5.68 (m, 1H, CH=); 7.97–8.06 (m, 2H, 2 × CHAr); 8.30–8.38 (m, 2H, 2 × CHAr); 9.77 (br s, 1H, CO_2H) ppm ^{13}C NMR ($CDCl_3$, 63 MHz): $\delta = 16.7$ (CH_3); 35.2 ($CH_2\beta_N$); 45.9 ($CH_2\alpha_N$); 55.6 (CH); 117.5 (CH_2=); 124.1; 128.5 (4 × CHAr); 133.9 (CH=); 145.3; 150.0 (2 × CqAr); 176.8 (CO) ppm. Ms (IC NH_3^+): 346 ($M+NH_4^+$).

3.2.3. (*S*)-2[Pent-4-enyl-(4-nitro-benzenesulfonyl)-amino]-propionic acid 4c. Preparation as described in the general procedure afforded **4c** as a yellowish solid in 66% yield. $[\alpha]_D$ −31 (*c* 0.93, CH_2Cl_2). ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 1.48$ (d, 3H, $J = 7.2$ Hz, CH_3); 1.56–1.97 (2m, 2H, $CH_2\beta_N$); 2.07 (m, 2H, $CH_2\gamma_N$); 3.02–3.36 (2m, 2H, $CH_2\alpha_N$); 4.63 (q, 1H, $J = 7.5$ Hz, CH); 4.97–5.20 (m, 3H, CH_2=, CO_2H); 5.73 (m, 1H, CH=); 7.97–8.02 (m, 2H, 2 × CHAr); 8.29–8.34 (m, 2H, 2 × CHAr) ppm ^{13}C NMR ($CDCl_3$, 63 MHz): $\delta = 17.0$ (CH_3); 30.1 ($CH_2\beta_N$); 31.0 ($CH_2\gamma_N$); 46.1 ($CH_2\alpha_N$); 55.7 (CH); 115.8 (CH_2=); 124.3; 128.7 (4 × CHAr); 137.2 (CH=); 145.7; 150.1 (2 × CqAr); 175.2 (CO) ppm. Ms (IC NH_3^+): 360 ($M+NH_4^+$).

3.2.4. (*S*)-2-[Hex-5-enyl-(4-nitro-benzenesulfonyl)-amino]-propionic acid 4d. Preparation as described in the general procedure afforded **4d** as a yellowish solid in 62% yield. ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 1.38$ (m, 2H, $CH_2\gamma_N$); 1.49 (d, 3H, $J = 7{,}5$ Hz, CH_3); 1.50–1.84 (2m, 2H, $CH_2\beta_N$); 2.02 (m, 2H, $CH_2\delta_N$); 3.05–3.35 (2m, 2H, $CH_2\alpha_N$); 4.62 (q, 1H, $J = 7{,}5$ Hz, CH); 4.92–5.01 (m, 2H, CH_2=); 5.50–5.81 (m, 2H, CH=, CO_2H); 7.97–8.02 (m, 2H, 2 × CHAr); 8.29–8.34 (m, 2H, 2 × CHAr) ppm ^{13}C NMR ($CDCl_3$, 63 MHz): $\delta = 16.9$ (CH_3); 26.1 ($CH_2\gamma_N$); 30.4 ($CH_2\beta_N$); 33.2 ($CH_2\delta_N$); 46.6 ($CH_2\alpha_N$); 55.7 (CH); 115.1 (CH_2=); 124.2; 128.6 (4 × CHAr); 138.2 (CH=); 145.7; 150.1 (2 × CqAr); 175.4 (CO) ppm. MS (IC NH_3^+): 374 ($M+NH_4^+$).

3.2.5. (*S*)-2-[Allyl-(2-nitro-benzenesulfonyl)-amino]-propionic acid 4e. Preparation as described in the general procedure afforded **4e** as a yellowish solid in 91% yield. ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 1.53$ (d, 3H, $J = 7.5$ Hz, CH_3); 3.44–4.17 (m, 2H, CH_2); 4.82 (q, 1H, CH); 5.06–5.22 (m, 2H, CH_2=); 5.82 (m, 1H, CH=); 7.68 (m, 3H, HAr); 8.06 (m, 1H, HAr) ppm. ^{13}C NMR ($CDCl_3$, 63 MHz): $\delta = 15.5$ (CH_3); 47.7 (CH_2); 54.5 (CH); 117.8 (CH_2=); 123.1; 127.6

(4 × CHAr); 132.9 (CH=); 144.7; 149.0 (2 × CqAr); 175.8 (CO) ppm.

3.3. General procedure for the acylation step

Acid **4** (0.55 mmol) was dissolved in DCM (3 mL) and cooled to 0 °C, at which point DMAP (68 mg, 0.55 mmol) and EDCI (106 mg, 0.55 mmol) were added. After stirring the reaction mixture at 0 °C for 15 min, alcohol **1** (242 mg, 0.46 mmol) was added. The cooling bath was removed and the solution was heated to 40 °C for 12 h. The crude reaction was concentrated in vacuo and purified using silica gel chromatography (EtOAc/cyclohexane).

3.3.1. 6-*N*-Benzoyl-9-{2′-*O*-allyl-3′-*O*-[1-oxo-2-[allyl,(4-nitrobenzenesulfonyl)]amino]propyl-5′-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl}adenine 5a. Preparation as described in the general procedure afforded **5a** as a white powder in 81% yield. Spectroscopic data of the major isomer ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 0.11$ (s, 6H, 2 × CH_3–Si); 0.92 (s, 9H, *t*-Bu); 1.56 (d, 3H, $J = 7.2$ Hz, CH_3); 3.77–4.24 (m, 7H, 2 × CH_2, 2H-5′, H-4′); 4.62 (m, 1H, H-2′); 4.78 (m, 1H, CH); 5.05–5.27 (m, 4H, 2 × CH_2=); 5.39 (m, 1H, H-3′); 5.53–5.90 (2m, 2H, 2 × CH=); 6.08 (d, 1H, $J = 6.7$ Hz, H-1′); 7.50–7.62 (m, 3H, HBz); 8.02–8.12 (m, 4H, HBz, 2 × CHAr); 8.31–8.40 (m, 3H, 2 × CHAr, H-2 or H-8); 8.83 (s, 1H, H-2 or H-8); 9.08 (br s, 1H, NH) ppm ^{13}C NMR ($CDCl_3$, 63 MHz): $\delta = -5.2$ (2 × CH_3–Si); 17.2 (CH_3); 18.5 (Cq/*t*-Bu); 26.1 (3 × CH_3/*t*-Bu); 49.1 (NCH_2); 56.2 (CH); 63.1 (C-5′); 72.1 (OCH_2); 72.8 (C-3′); 79.9 (C-2′); 83.5 (C-4′); 85.6 (C-1′); 118.7; 119.1 (CH_2=); 124.4 (CHAr); 128.0 (CHBz); 128.7 (CHAr); 128.9; 132.9 (CHBz); 133.7; 134.4 (CH=); 141.0 (C-2 or C-8); 146.2; 149.7 (CqAr); 150.1; 152.1 (CqBz); 153.0 (C-2 or C-8); 164.8; 170.3 (CO) ppm. MS (IC NH_3^+): 822 ($M+H^+$).

3.3.2. 6-*N*-Benzoyl-9-{2′-*O*-allyl-3′-*O*-[1-oxo-2-[(3-butenyl),(4-nitrobenzenesulfonyl)]amino]propyl-5′-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl}adenine 5b. Preparation as described in the general procedure afforded **5b** as a white powder in 64% yield. Spectroscopic data of the major isomer ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 0.12$ (s, 6H, 2 × CH_3–Si); 0.93 (s, 9H, *t*-Bu); 1.58 (d, 3H, $J = 7.2$ Hz, CH_3); 2.26–2.61 (m, 2H, $NCH_2\beta$); 3.13–3.27 (m, 1H, $NCH_2\alpha$); 3.40–3.68 (m, 2H, $NCH_2\alpha$, OCH_2); 3.72–4.02 (m, 4H, H-4′, 2H-5′, OCH_2); 4.58 (dd, 1H, $J = 6.8$; 5.2 Hz, H-2′); 4.78 (q, 1H, $J = 7.4$ Hz, CH); 5.02–5.10 (m, 4H, 2 × CH_2=); 5.37 (dd, 1H, $J = 4.9$; 2.1 Hz, H-3′); 5.49–5.78 (m, 2H, 2 × CH=); 6.03 (d, 1H, $J = 6.8$ Hz, H-1′); 7.49–7.61 (m, 3H, HBz); 8.01–8.11 (m, 4H, HBz, 2 × CHAr); 8.28–8.38 (m, 3H, 2 × CHAr, H-2 or H-8); 8.83 (s, 1H, H-2 or H-8); 9.11 (br s, 1H, NH) ppm ^{13}C NMR ($CDCl_3$, 63 MHz): $\delta = -5.2$ (2 × CH_3–Si); 17.5 (CH_3); 18.5 (Cq/*t*-Bu); 26.1 (CH_3/*t*-Bu); 35.3 ($NCH_2\beta$); 46.3 ($NCH_2\alpha$); 56.4 (CH); 63.1 (C-5′); 72.2 (OCH_2); 72.9 (C-3′); 79.9 (C-4′); 83.4 (C-2′); 85.6 (C-1′); 117.5; 119.2 (CH_2=); 124.5 (CHAr); 128.0 (CHBz); 128.6 (CHAr); 129.0; 132.9 (CHBz); 133.7; 134.2 (CH=); 141.0 (C-2 or C-8); 146.0; 149.7 (CqAr); 150.2; 152.1 (CqBz); 153.0 (C-2 or C-8); 170.3 (CO) ppm. MS (FAB): 836 ($M+H^+$).

3.3.3. 6-*N*-Benzoyl-9-{2′-*O*-allyl-3′-*O*-[1-oxo-2-[(4-pentenyl),(4-nitrobenzenesulfonyl)]amino]propyl-5′-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl}adenine 5c. Preparation as described in the general procedure afforded **5c** as a white powder in 85% yield. Spectroscopic data of the major isomer ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 0.13$ (s, 6H, 2 × CH_3–Si); 0.94 (s, 9H, *t*-Bu); 1.58 (d, 3H, $J = 7.2$ Hz, CH_3); 1.65–1.98 (m, 2H, $NCH_2\beta$); 2.05 (m, 2H, $NCH_2\gamma$); 3.08–3.50 (m, 2H, $NCH_2\alpha$); 3.75–4.22 (m, 5H, H-4′, 2H-5′, OCH_2); 4.60 (m, 1H, H-2′); 4.76 (m, 1H, CH); 4.98–5.11 (m, 4H, 2 × CH_2=); 5.37 (s, 1H, H-3′); 5.50–5.85 (m, 2H, 2 × CH=); 6.04 (d, 1H, $J = 6.7$ Hz, H-1′); 7.50–7.62 (m, 3H, HBz); 8.03–8.11 (m, 4H, HBz, 2 × CHAr); 8.30–8.40 (m, 3H, 2 × CHAr, H-2 or H-8); 8.83 (s, 1H, H-2 or H-8); 9.11 (br s, 1H, NH) ppm ^{13}C NMR ($CDCl_3$, 63 MHz): $\delta = -5.2$ (CH_3–Si); 17.5 (CH_3); 18.5 (Cq/*t*-Bu); 26.1 (CH_3/*t*-Bu); 30.0 ($NCH_2\beta$); 31.1 ($NCH_2\gamma$); 46.1 ($NCH_2\alpha$); 56.0 (CH); 63.2 (C-5′); 72.2 (OCH_2); 72.9 (C-3′); 79.9 (C-4′); 83.5 (C-2′); 85.6 (C-1′); 115.9; 118.9 (CH_2=); 124.5 (CHAr); 128.0 (CHBz); 128.6 (CHAr); 129.0; 133.0 (CHBz); 133.7; 137.1 (CH=); 141.2 (C-2 ou C-8); 146.5; 149.6 (CqAr); 150.2; 152.3 (CqBz); 153.0 (C-2 or C-8); 164.6; 170.4 (CO) ppm.

3.3.4. 6-*N*-Benzoyl-9-{2′-*O*-allyl-3′-*O*-[1-oxo-2-[allyl,(2-nitrobenzenesulfonyl)]amino]propyl-5′-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl}adenine 5e. Preparation as described in the general procedure afforded **5a** as a white powder in 61% yield. Spectroscopic data of the major isomer ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 0.09$ (s, 6H, 2 × CH_3–Si); 0.91 (s, 9H, *t*-Bu); 1.57 (d, 3H, $J = 7.5$ Hz, CH_3); 3.80–4.11 (m, 7H, 4 × CH_2, 2H-5′, H-4′); 4.63 (t, 1H, H-2′); 4.93 (q, 1H, CH); 5.02–5.19 (m, 4H, 2 × CH_2=); 5.41 (m, 1H, H-3′); 5.57–5.85 (2m, 2H, 2 × CH=); 6.11 (d, 1H, $J = 6{,}5$ Hz, H-1′); 7.71–7.47 (m, 6H, HBz, CHAr); 8.0–8.12 (m, 3H, HBz, CHAr); 8.31 (s, 1H, H-2 or H-8), 8.80 (s, 1H, H-2 or H-8); 9.3 (br s, 1H, NH) ppm ^{13}C NMR ($CDCl_3$, 63 MHz): $\delta = -4.95$ (2 × CH_3–Si); 17.08 (CH_3); 18.8 (Cq/*t*-Bu); 26.3 (3 × CH_3/*t*-Bu); 49.3 (NCH_2); 56.8 (CH); 63.2 (C-5′); 72.4 (OCH_2); 72.6 (C-3′); 80.1 (C-2′); 83.7 (C-4′); 86.3 (C-1′); 118.5; 119.3 (CH_2=); 124.6 (CHAr); 128.3 (CHBz); 129.4 (CHAr); 131.8; 132.4, 133.5, 134.06 (CHBz); 135; 134.4 (CH=); 141.6 (C-2 or C-8); 148.2; 149.9, 152.3 (CqAr–CqBz); 153.1 (C-2 or C-8); 165; 171.1 (CO) ppm. MS (IC NH_3^+): 822 ($M+H^+$).

3.3.5. 6-*N*-Benzoyl-9-{2′-*O*-allyl-3′-*O*-[1-oxo-2-[allyl-benzyloxycarbonyl-amino]]propyl-5′-*O*-(*tert*-butyldimethylsilyl)-β-D-ribofuranosyl}adenine 9. Preparation as described in the general procedure (using acid **8** instead of **4**) afforded **9** as a white powder in 67% yield. $[\alpha]_D$ −15 (*c* 1.2, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 0.08$ (s, 6H, 2 × CH_3–Si); 0.89 (s, 9H, *t*-Bu); 1.50 (d, 3H, $J = 7.5$ Hz, CH_3); 3.65–4.20 (m, 7H, H-4′, 2H-5′, OCH_2, NCH_2); 4.29 (m, 1H, H-2′); 4.62 (m, 1H, CH); 5.04–5.23 (m, 6H, 2 × CH_2=, CH_2); 5.43 (br s, 1H, H-3′); 5.62 (m, 1H, CH=); 5.90 (m, 1H, CH=); 6.19 (br d, 1H, H-1′); 7.29 (s, 5H, HAr); 7.47–7.52 (m, 3H, HBz); 7.99 (m, 2H, HBz); 8.29 (br s, 1H, H-2 or H-8); 8.77 (s, 1H, H-2 or H-8); 9.13 (br s, 1H, NH) ppm ^{13}C

NMR ($CDCl_3$, 63 MHz): $\delta = -4.9$ (CH_3–Si); 18.8 (CH_3); 26.4 (CH_3/*t*-Bu); 30.1 (Cq/*t*-Bu); 48.4 (NCH_2); 54.2 (CH); 61.9 (C-5′); 66.45 (CH_2); 70.8 and 70.9 (C-3′, OCH_2); 78.8 (C-2′); 82.8 (C-4′); 84.8 (C-1′); 115.7 (NCH_2=); 117.6 (OCH_2=); 126.9, 127.4, 127.8 (CHAr); 131.7 (CH=); 132.3 (CHAr); 133.6 (CH=); 135.3 (CHAr); 140.0 (C-2 or C-8); 148.5; 151.0 (CqHAr); 151.8 (C-2 or C-8);154.98 (CO); 158.15 (CqAr); 163.6; 170.3 (CO) ppm. MS (IC NH_3^+): 771 ($M+H^+$).

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References and notes

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9. A verification was done by reacting nucleoside **1** with a racemic mixture of NCbz D–L alanine **8** and the NMR spectrum of stereoisomers **9** showed two characteristic signals in ^{13}C NMR for the CH_2= of the *O*-allyl group and two characteristic signals in ^{13}C NMR for the CH_2= of the *N*-allyl group. This was not observed in the NMR spectrum of compound **9** after the acylation step with the optically pure L-alanine derivative **8**.