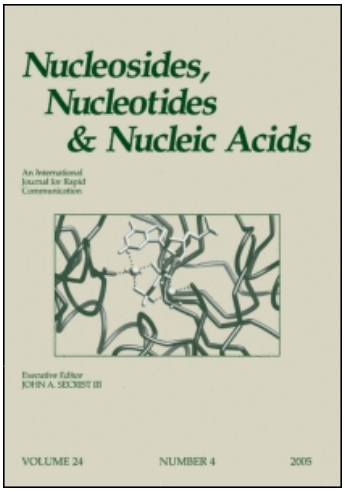

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

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Online publication date: 06 March 2002

To cite this Article Magdalena, Julia , Fernández, Susana , Ferrero, Miguel and Gotor, Vicente(2002) 'DIFFICULTIES IN THE DEPROTECTION OF 1,2-KETALS IN NUCLEOSIDES CONTAINING ALKYLIDENCARBAZOYL GROUPS', Nucleosides, Nucleotides and Nucleic Acids, 21: 1, 55 — 64
To link to this Article: DOI: 10.1081/NCN-120006530
URL: http://dx.doi.org/10.1081/NCN-120006530

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS, 21(1), 55–64 (2002)

DIFFICULTIES IN THE DEPROTECTION OF 1,2-KETALS IN NUCLEOSIDES CONTAINING ALKYLIDENCARBAZOYL GROUPS

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ABSTRACT

The synthesis of unprotected alkylidencarbazoyl nucleoside derivatives **8a**–**8d** is shown. A direct deprotection route from readily available 2′,3′-isopropylidene protected nucleosides **5a**–**5d**, prepared from a chemoenzymatic procedure, did not give the selective cleavage of the ketal function without affecting the C=N bond. The next option tried was to look at the previous compound in the retrosynthetic route: 2′,3′-protected carbazoyl nucleoside **4**. However, in all cases we obtained unsatisfactory results. Stepping further back, the hydrolysis of compound **3a** led us to unprotected carbonate nucleoside **9** in quantitative yield. With this compound available, the synthesis towards derivatives **8** was accomplished through a known procedure.

INTRODUCTION

Nucleosides are fundamental building blocks of biological systems that display a wide range of biological activities. Consequently, the search for nucleoside analogues that function as non-toxic, selective inhibitors for the control of viral diseases and cancer has been the subject of intense research[1], including their activity against the human immunodeficiency virus (HIV)[2].

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In our programme devoted to the study of the synthesis of nucleoside[3] and nucleotide[4] derivatives, we have prepared through a chemoenzymatic procedure both 3′- and 5′-alkylidencarbazoyl nucleoside analogues, both of which are promising precursors for novel types of therapeutic nucleoside derivatives. The first step was the enzymatic alkoxycarbonylation reaction, which took place with high regioselectivity and yield towards the 3′- or 5′-positions depending on the conditions[5]. The carbonate nucleosides thus obtained were then reacted with hydrazine to give carbazoyl nucleoside analogues, which through reaction with aldehydes provide the corresponding alkylidencarbazoyl nucleoside derivatives.

When applied to adenosine **1** (Chart 1) this general procedure failed because of the low solubility of this nucleoside in the solvents required for the enzymatic process. Although the reaction went with total quimio- and regioselectivity towards the 5′-hydroxyl group, the yield was approximately 20% and, as a consequence, is a limiting step in the preparation of the corresponding nucleoside derivatives **8** (Sch. 1), which was the aim of this work.

To address this limitation, commercially available 2′,3′-protected adenosine derivative **2** was used. Protecting the 1,2-*cis* diol system is a way of increasing the yield of the reaction, and not a means of directing it exclusively towards hydroxyl group in 5′-position, behaviour which is already provided by the enzyme. However, the enzyme, in addition of mild reaction conditions, also provides chemoselectivity, and the 5′-hydroxyl group reacts over the

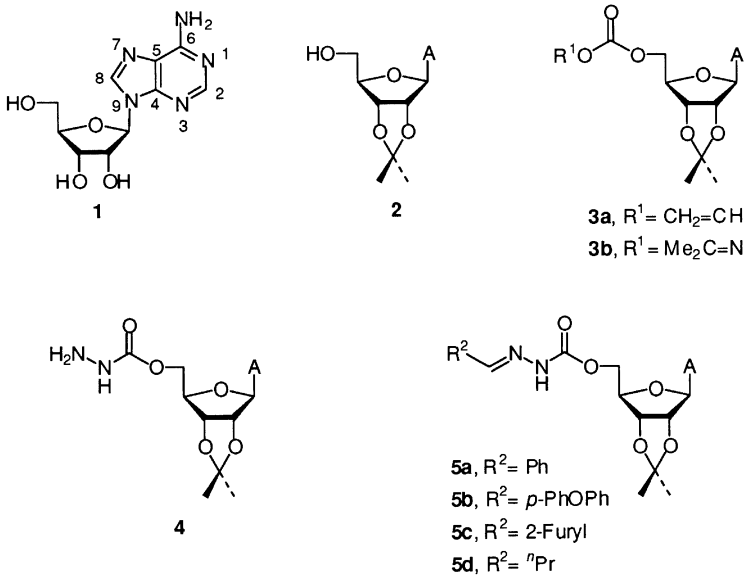
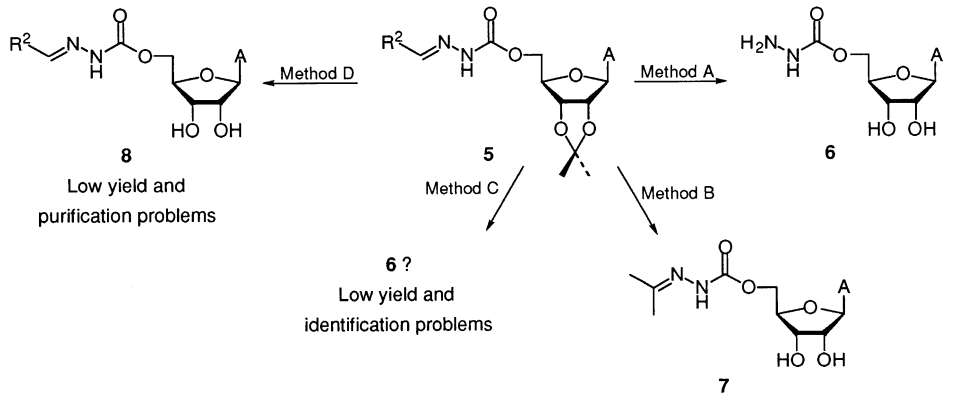


Chart 1.



Method A:[6a] CF_3CO_2H, H_2O (cat.), CH_2Cl_2, rt
Method B:[6b] CF_3CO_2H, H_2O, CH_2Cl_2, 0 °C
Method C:[7] [$FeCl_3$-SiO_2], $CHCl_3$, rt
Method D:[8] I_2 / MeOH 1% (w/v), rt and reflux

Scheme 1.

6-amino group in the adenosine base moiety. This alternative pathway led to an excellent yield of 2′,3′-isopropilyden-5′-alkylidencarbazoyl adenosine analogues **5a**–**5d**, through the formation of vinylcarbonate **3a** and/or oximecarbonate **3b**, hydrazinolysis of which give carbazoyl nucleoside **4**. This finally reacted with different aldehydes.

However, since derivatives **5** would be interesting nucleoside analogues themselves, we wanted to obtain the corresponding deprotected compounds **8**, not only to use as new nucleoside derivatives, but also for their employment in nucleotide chemistry. However, despite using several of the methods previously reported in the literature[6–8] to deprotect the ketals (and certain variants), it was found that the selective cleavage of the ketal function was impossible without affecting C=N bond. Here we report a successful route, of general interest, to obtain the target compounds **8**.

RESULTS AND DISCUSSION

The selective cleavage of ketals by acids in the presence of other acid-labile groups is difficult[6b]. To deprotect derivatives **5** (Sch. 1), we first applied the procedure described in the literature[6a] in 1,2-*cis* diols by using aqueous trifluoroacetic acid in methylene dichloride. In all cases, when using water in catalytic quantities (method A) or as co-solvent (method B), compound **6** (using method A) or nucleoside derivative **7** (using method B) were always obtained. This means that the carbon-nitrogen double bond always cleaves in

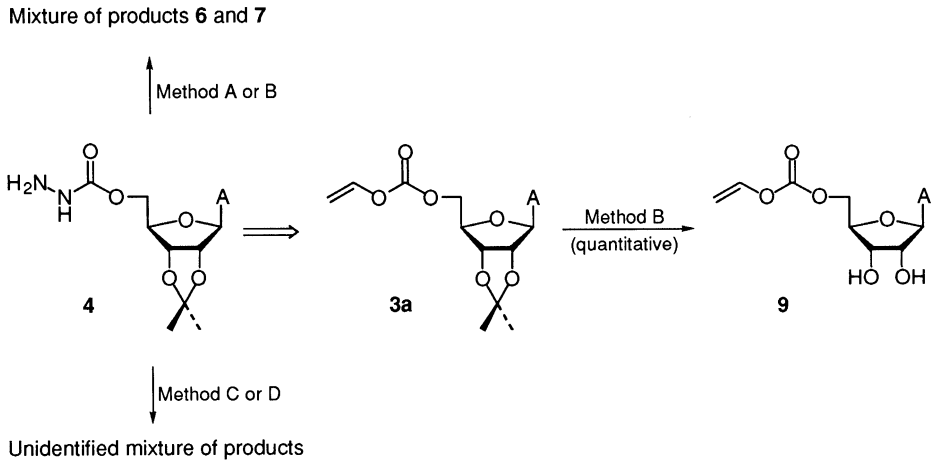
addition to the ketal group. However, in the conditions described for method B, the acetone generated in the ketal hydrolysis reacts with the terminal amino group of carbazoyl nucleoside **6** to give alkylidencarbazoyl nucleoside **7**. Various modifications in the reaction conditions did not lead to desired compounds **8a**–**8d**.

Ferric chloride-silica gel reagent (method C), a yellow powder prepared by mixing silica gel and an acetone solution of hydrated ferric chloride through evaporation of the solvent, has been reported as smoothly cleaving the ketal and acetal groups of several compounds[7]. Based on these results, it appeared that ferric chloride-silica gel reagent could be used as the selective deprotecting agent for ketal protective groups in complex molecules such as nucleoside derivatives **5**, which also contain other acid-labile groups. With this information, this methodology was applied to alkylidencarbazoyl nucleosides **5**. A very low yield of derivative **6** was obtained. In addition, we experienced identification problems because of the traces of metallic nucleus present in the NMR samples.

The reagent system, iodine and methanol, has been reported to be a facile method for cleavage of acetals and dithiocetals[8] (method D). The synthetic procedure involves keeping a solution of the ketal in 0.5–1.0% iodine in methanol (w/v) at room temperature. In these conditions no reaction was produced with our nucleoside derivatives **5**. When reflux temperature was employed only a low yield of the desired impure product was obtained even after several purification steps. Slight modifications in this method did not give satisfactory results.

Leaving the protecting group alone until the end of the synthetic process is the ideal way of maintaining the very good solubility of the nucleosides. For this reason, we have put a lot of effort into the deprotection step of compounds **5a**–**5d**. The next option to reach our objective, which is the preparation of carbazoyl derivatives **8a**–**8d**, was to look at the previous compound in the retrosynthetic route: 2′,3′-protected carbazoyl nucleoside **4** (Sch. 2). Thus, methods A and B were applied to compound **4**, but in all cases we obtained a mixture of two compounds: the desired carbazoyl nucleoside **6** and the alkylidencarbazoyl nucleoside derivative **7**. Using alternative methods C and D, a mixture of unidentified products was obtained in both cases. As previously mentioned, in all cases slight modifications of methods A to D were made with the aim of obtaining nucleoside **6**, but all of them failed.

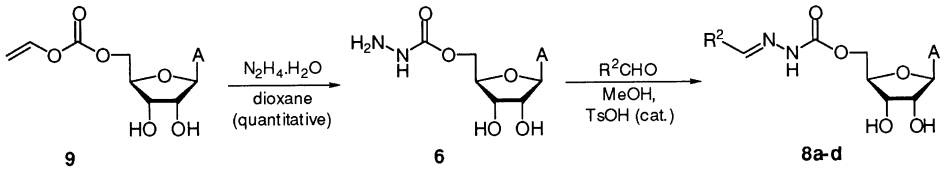
Following our retrosynthetic analysis, we took another step back and arrived at compound **3a**. Methods A and B give slow kinetics even though derivative **9** is obtained. When a variant of method B (room temperature instead of 0 °C) was applied to deprotect carbonate nucleoside **3a**, carbonate nucleoside **9** was formed in quantitative yield. With this compound in hand, the synthesis towards derivatives **8** was accomplished. Thus, Sch. 3 shows the synthetic route from carbonate **9** to alkylidencarbazoylnucleosides **8a**–**8d**.



Scheme 2.

The first step was the hydrazinolysis of **9**, which went with quantitative yield to give carbazoyl derivative **6**. This reacts with different aldehydes to give compounds **8** in yields ranging from 70 to 91%, as is shown in the table of Sch. 3. It is noteworthy that yields for the last step were around the same as those for the preparation of compounds **5a**–**5d** from **4**[3], although carbazoyl nucleoside **6** is less soluble than its counterpart **4**. The initial suspension formed when carbazoyl nucleoside **6** was dissolved in methanol started to completely solubilize when *p*-toluenesulfonic acid was added.

The structural assignment of the compounds described in this paper is based on the analysis of their ^{1}H-, ^{13}C-NMR spectra, and DEPT experiments. The correct assignment was confirmed by ^{1}H-^{13}C heteronuclear and ^{1}H-^{1}H homonuclear correlation experiments. It is noteworthy that for



	R^2	*t* (h)	Yield (%)
8a	Ph	4	91
8b	*p*-PhOPh	2	85
8c	2-Furyl	7	74
8d	^{n}Pr	6	70

Scheme 3.

compounds **8a**–**8d**, sugar moiety protons in ^{1}H-NMR spectra (except $H_{1'}$) appeared as a broad signals between 4–5 ppm due to dynamic conformational equilibrium in polar solvents as DMSO. Additionally, for compounds **8c** and **8d**, proton H_8 appears as a broad singlet probably due to relaxation problems since it is situated just on top of the sugar moiety (determine by NOESY or ROESY experiments). With respect to ^{13}C-NMR spectra, similar behaviour to that of the ^{1}H-NMR spectra was observed, the signals belonging to sugar moiety and C_8 being unusually broad in most of the cases.

The structural determination of these new compounds was carried out through different spectroscopic techniques. Thus, in the case of compound **8b**, and to confirm the presence of several carbon atoms, which appeared as broad signals in ^{13}C-NMR spectra, special NMR experiments were done. First, to clarify the chemical shifts of the sugar moiety carbon atoms (64.9, 70.7, 73.1, 82.2, and 87.2 ppm), iminic carbon (144.2 ppm), and the presence of carbonylic carbon (which was apparently missing) we tried heating the samples so as to obtain better resolved signals (for ^{13}C as well as for ^{1}H spectra)[3]. When this was done, nucleoside decomposition was observed. Next several two-dimensional NMR experiments were performed. Chemical shifts of the sugar moiety carbon atoms and the iminic carbon were confirmed with a ^{1}H-^{13}C heteronuclear correlation experiment 2D HMQC. We also performed a ^{1}H-^{13}C heteronuclear correlation experiment 2D HMBC, detecting indirectly the most sensible nucleus (^{1}H). From its analysis, it was possible to confirm the presence of the carbonylic carbon: a cross peak appears between proton $H_{3'}$ (4.33 ppm) and a carbon at 153.2 ppm, which corresponds to correlation $H_{3'}$-O-CO via $^{3}J_{CH}$. Thus, we conclude that the carbonylic carbon appears partially overlapped with the signal at 152.7 ppm which corresponds to the C_2 of the base moiety. Finally, the relative spatial arrangement of the protons was confirmed by a ROESY experiment. In this case a NOESY experiment did not show anything conclusive due to the presence of dynamic equilibrium in the molecule, which could be favoured by the polarity of the deuterated solvent used (we were obliged to use DMSO-d_6 because of the very low solubilities these compounds have in other organic solvents).

In short, a strategy to synthesise unprotected alkylidencarbazoyl nucleoside derivatives **8a**–**8d** has been shown. First of all, we tried to get these nucleoside derivatives directly from readily available 2′,3′-isopropydilene protected nucleosides **5a**–**5d**, prepared from a chemoenzymatic procedure. Neither direct deprotection techniques described in the literature, nor any of several variants, gave the selective cleavage of the ketal function without affecting C=N bond. The next option to reach our objective was to look at the previous compound in the retrosynthetic route: 2′,3′-protected carbazoyl nucleoside **4**. Thus, previously described methods were applied to compound **4**, but in all cases we obtained either a mixture of the desired carbazoyl nucleoside **6** and alkylidencarbazoyl nucleoside derivative **7**, or a mixture of unidentified products. Following our retrosynthetic analysis, we

took another step back to compound **3a**. When we used trifluoroacetic acid and stoichiometric amounts of water in methylene dichloride to deprotect carbonate nucleoside **3a**, unprotected nucleoside **9** was formed in quantitative yield. With this compound in hand, the synthesis towards derivatives **8** was accomplished. The first step was the hydrazinolysis of **9**, which went with quantitative yield to give carbazoyl derivative **6**. The later reacted with different aldehydes to give compounds **8** in yields ranging from 70 to 91%.

EXPERIMENTAL

General. Melting points were taken on samples in open capillary tubes using a Büchi melting-point apparatus and are uncorrected. NMR spectra were obtained using a Bruker AC 300 or AC 200 spectrometers for routine experiments and AMX 400 spectrometer for special measurements with deuterated DMSO as solvent. IR spectra were recorded on a UNICAM Mattson 3000 FT spectrophotometer. Microanalyses were performed on a Perkin-Elmer model 240B instrument, and mass spectra were obtained using a Finigan MAT 95 spectrometer. The solvents were dried by standard methods described in the literature.

5′-O-(Vinyloxy)carbonyladenosine 9. To a solution of 5′-*O*-(vinyloxy)-carbonyl-2′,3′-isopropylidenadenosine **3a** (377.1 mg, 1 mmol) in methylene dichloride (5 mL) was added trifluoroacetic acid (1.54 mL, 20 mmol) and water (0.36 mL, 20 mmol). The mixture reacted at room temperature until the disappearance of the starting nucleoside (approx. 6 h, TLC monitoring). Finally, the solvent was evaporated at 0°C (to avoid carbonate hydrolysis) under reduced pressure and the product was purified by filtration with silica gel using 5% MeOH/EtOAc given, in quantitative yield, nucleoside **9**. This compound has been described by us previously[9].

5′-O-Carbazoyladenosine 6. To a solution of 5′-*O*-(vinyloxy)carbonyladenosine **9** (377.1 mg, 1 mmol) in dry 1,4-dioxane (10 mL) was added hydrazine (80% aqueous) (78 μL, 2 mmol) under nitrogen atmosphere. The mixture reacted at room temperature until the disappearance of the starting nucleoside (TLC monitoring). Finally, solvent, acetaldehyde, and the excess of hydrazine were evaporated under reduced pressure. The crude product, obtained in quantitative yield, did not need additional purification. Compound **6**. M.p.: 134–135°C (syrup); IR (KBr): 3340, 3140 (N-H+O-H), and 1705 (C=O); $[\alpha]_D^{20} = -54.0$ (c 0.52, DMSO); ^{1}H-NMR (DMSO-d_6): 4.31 (m, 6H, $H_{3'}$+$H_{4'}$+$H_{5'}$+NHNH_2), 4.78 (br s, 1H, $H_{2'}$), 5.52 (br s, 1H, $OH_{3'}$), 5.66 (br s, 1H, $OH_{2'}$), 6.03 (d, 1H, $H_{1'}$, $^3J_{HH}$ 5.9 Hz), 7.44 (br s, 2H, NH_2), 8.28 (s, 1H, H_2), and 8.48 (br s, 2H, H_8+NHNH$_2$); ^{13}C-NMR (DMSO-d_6): 64.5 ($C_{5'}$), 70.7 ($C_{3'}$), 73.1 ($C_{2'}$), 82.5 ($C_{4'}$), 87.0 ($C_{1'}$), 119.1 (C_5), 139.7

(C_8), 149.8 (C_4), 152.9 (C_2), 156.2 (C_6), and 158.3 (C=O); MS (70 eV, *m/z*): 325 (M^+, 12%), 267 (2), 237 (4), 190 (1), 164 (38), 136 (100), 88 (7), and 58 (10); Anal. Calcd. (%) for $C_{11}H_{15}N_7O_5$: C, 40.60; H, 4.65; N, 30.15. Found: C, 40.6; H, 4.5; N, 29.9.

General Procedure for the Synthesis of 5′-O-Alkylidencarbazoyladenosine Derivatives 8a–8d. To a solution of 5′-*O*-carbazoyladenosine **6** (32.5 mg, 0.10 mmol) in dry methanol (2 mL) was added *p*-toluenesulfonic acid (7.6 mg, 0.04 mmol) and then the corresponding aldehyde (0.11 mmol) under nitrogen atmosphere. The mixture reacted at room temperature until disappearance of the starting nucleoside or when the process did not evolve further (TLC monitoring); data are reported in the table of Sch. 3. The solvent was evaporated under reduced pressure and the products were purified by flash column chromatography with silica gel using 5% MeOH/EtOAc. Yields are given in table of Sch. 3.

5′-[3″-(Phenyliden)carbazoyl]adenosine 8a. M.p.: 200–201°C; IR (KBr): 3431, 3259 (N-H+O-H), and 1712 (C=O); $[\alpha]_D^{20} = -95.8$ (c 0.77, DMSO); ^{1}H-NMR (DMSO-d_6): 4.26 (br s, 1H, $H_{4'}$), 4.34 (s, 1H, $H_{3'}$), 4.40 (m, 1H, $H_{5'\beta}$), 4.51 (m, 1H, $H_{5'\alpha}$), 4.84 (br s, 1H, $H_{2'}$), 5.56 (d, 1H, $OH_{3'}$, $^3J_{HH}$ 4.5 Hz), 5.69 (d, 1H, $OH_{2'}$, $^3J_{HH}$ 5.8 Hz), 6.05 (br s, 1H, $H_{1'}$), 7.40 (s, 2H, NH_2), 7.50 (m, 3H, $2H_m+H_p$), 7.73 (dd, 2H, H_o, $^3J_{HH}$ 7.4, $^4J_{HH}$ 1.6 Hz), 8.14 (s, 1H, N=CH), 8.26 (s, 1H, H_2), 8.45 (s, 1H, H_8), and 11.40 (br s, 1H, =NNH); ^{13}C-NMR (DMSO-d_6): 64.9 (br s, $C_{5'}$), 70.7 ($C_{3'}$), 73.1 ($C_{2'}$), 82.3 ($C_{4'}$), 87.0 (br s, $C_{1'}$), 119.0 (C_5), 126.8 (C_o), 128.8 (C_m), 129.7 (C_p), 134.2 (C_{ipso}), 139.4 (br s, C_8), 144.3 (C=N), 149.7 (C_4), 152.8 (C_2), 153.3 (C=O), and 156.1 (C_6); MS (70 eV, *m/z*): 413 (M^+, 9%), 164 (37), 135 (48), 90 (100), and 76 (38); HRMS (*m/z*): calcd. for $C_{18}H_{19}N_7O_5$: 413.1448. Found: 413.1445; Anal. Calcd. (%) for $C_{18}H_{19}N_7O_5$: C, 52.28; H, 4.63; N, 23.63. Found: C, 52.3; H, 4.5; N, 23.9.

5′-[3″-(*p*-Phenoxyphenyliden)carbazoyl]adenosine 8b. M.p.: 204–205°C; IR (KBr): 3337, 3224 (N-H+O-H), and 1713 (C=O); $[\alpha]_D^{20} = -92.6$ (c 0.57, DMSO); ^{1}H-NMR (DMSO-d_6): 4.26 (br s, 1H, $H_{4'}$), 4.33 (s, 1H, $H_{3'}$), 4.44 (m, 2H, $H_{5'}$), 4.84 (br s, 1H, $H_{2'}$), 5.54 (d, 1H, $OH_{3'}$, $^3J_{HH}$ 4.5 Hz), 5.69 (d, 1H, $OH_{2'}$, $^3J_{HH}$ 5.8 Hz), 6.05 (d, 1H, $H_{1'}$, $^3J_{HH}$ 5.1 Hz), 7.10 (d, 2H, H_m, $^3J_{HH}$ 7.1 Hz), 7.17 (d, 2H, $H_{o'}$, $^3J_{HH}$ 7.7 Hz), 7.28 (dd, 1H, $H_{p'}$, $^3J_{HH}$ 7.7, $^3J_{HH}$ 7.1 Hz), 7.39 (s, 2H, NH_2), 7.52 (dd, 2H, $H_{m'}$, $^3J_{HH}$ 7.7, $^3J_{HH}$ 7.7 Hz), 7.74 (d, 2H, H_o, $^3J_{HH}$ 8.4 Hz), 8.12 (s, 1H, N=CH), 8.25 (s, 1H, H_2), 8.45 (s, 1H, H_8), and 11.34 (br s, 1H, =NNH); ^{13}C-NMR (DMSO-d_6): 64.9 (br s, $C_{5'}$), 70.7 ($C_{3'}$), 73.1 (br s, $C_{2'}$), 82.2 ($C_{4'}$), 87.2 (br s, $C_{1'}$), 118.2 (C_m), 119.0 (C_5), 119.3 ($C_{o'}$), 124.1 ($C_{p'}$), 128.6 (C_o), 129.3 (C_{ipso}), 130.2 ($C_{m'}$), 139.5 (br s, C_8), 144.2 (C=N), 149.2 (C_4), 152.7 (C_2), 153.2 (C=O), 155.8 ($C_{ipso'}$), 156.1 (C_6), and 158.2 (C_p); MS (FAB$^+$, *m/z*): 506 [$(M+H)^+$,

100%], and 371 (18); Anal. Calcd. (%) for $C_{24}H_{23}N_7O_6$: C, 57.01; H, 4.59; N, 19.40. Found: C, 57.2; H, 4.6; N, 19.2.

5′-[3″-(2‴-Furyliden)carbazoyl]adenosine 8c. M.p.: 199–201°C; IR (KBr): 3430, 3220 (N-H+O-H), and 1709 (C=O); $[\alpha]_D^{20} = -78.9$ (c 0.56, DMSO); ^{1}H-NMR (DMSO-d_6): 4.24 (m, 1H, $H_{4'}$), 4.31 (m, 1H, $H_{3'}$), 4.44 (m, 2H, $H_{5'}$), 4.82 (br s, 1H, $H_{2'}$), 5.56 (d, 1H, $OH_{3'}$, $^3J_{HH}$ 5.1 Hz), 5.69 (d, 1H, $OH_{2'}$, $^3J_{HH}$ 6.4 Hz), 6.04 (br s, 1H, $H_{1'}$), 6.68 (dd, 1H, $H_{4'''}$, $^3J_{HH}$ 3.2, $^3J_{HH}$ 1.9 Hz), 6.92 (d, 1H, $H_{3'''}$, $^3J_{HH}$ 1.9 Hz), 7.40 (s, 2H, NH_2), 7.88 (d, 1H, $H_{5'''}$, $^3J_{HH}$ 1.3 Hz), 8.01 (s, 1H, N=CH), 8.25 (s, 1H, H_2), 8.45 (br s, 1H, H_8), and 11.35 (br s, 1H, =NNH); ^{13}C-NMR (DMSO-d_6): 65.1 (br s, $C_{5'}$), 70.8 ($C_{3'}$), 73.1 ($C_{2'}$), 82.4 ($C_{4'}$), 87.0 (br s, $C_{1'}$), 112.1 ($C_{4'''}$), 112.8 ($C_{3'''}$), 119.1 (C_5), 134.5 (br s, C=N), 139.5 (C_8), 144.9 ($C_{5'''}$), 149.4 ($C_{2'''}$), 149.7 (C_4), 152.9 (C_2), 153.4 (br s, C=O), and 156.1 (C_6); MS (70 eV, m/z): 403 (M^+, 1%), 164 (76), 135 (100), 110 (45), 94 (8), and 81 (22); HRMS (m/z): calcd. for $C_{16}H_{17}N_7O_6$: 403.1240. Found: 403.1228; Anal. Calcd. (%) for $C_{16}H_{17}N_7O_6$: C, 47.63; H, 4.25; N, 24.32. Found: C, 47.9; H, 4.2; N, 24.0.

5′-[3″-(Propyliden)carbazoyl]adenosine 8d. M.p.: 190–192°C; IR (KBr): 3402, 3142 (N-H+O-H), and 1718 (C=O); $[\alpha]_D^{20} = -54.6$ (c 0.56, DMSO); ^{1}H-NMR (DMSO-d_6): 0.98 (t, 3H, $H_{3'''}$, $^3J_{HH}$ 7.6 Hz), 1.55 (tq, 2H, $H_{2'''}$, $^3J_{HH}$ 7.6, $^3J_{HH}$ 6.9 Hz), 2.24 (br s, 2H, $H_{1'''}$), 4.22–4.40 (m, 3H, $H_{4'}$+$H_{5'}$), 4.28 (m, 1H, $H_{3'}$), 4.77 (ddd, 1H, $H_{2'}$, $^3J_{HH}$ 8.0, $^3J_{HH}$ 8.0, $^3J_{HH}$ 5.3 Hz), 5.50 (d, 1H, $OH_{3'}$, $^3J_{HH}$ 4.9 Hz), 5.64 (d, 1H, $OH_{2'}$, $^3J_{HH}$ 6.2 Hz), 6.03 (br s, 1H, $H_{1'}$), 7.37 (s partially overlapped, 2H, NH_2), 7.42 (t partially overlapped, 1H, N=CH, $^3J_{HH}$ 5.6 Hz), 8.25 (s, 1H, H_2), 8.44 (br s, 1H, H_8), and 10.87 (br s, 1H, =NNH); ^{13}C-NMR (DMSO-d_6): 13.6 ($C_{3'''}$), 19.5 ($C_{2'''}$), 33.7 ($C_{1'''}$), 64.6 (br s, $C_{5'}$), 70.7 ($C_{3'}$), 73.2 (br s, $C_{2'}$), 82.3 ($C_{4'}$), 87.0 ($C_{1'}$), 119.0 (C_5), 139.5 (C_8), 148.3 (C=N), 149.7 (C_4), 152.8 (C_2), 153.2 (br s, C=O), and 156.1 (C_6); MS (70 eV, m/z): 379 (M^+, <1%), 293 (2), 190 (5), 164 (95), 135 (100), and 55 (10); Anal. Calcd. (%) for $C_{15}H_{21}N_7O_5$: C, 47.47; H, 5.58; N, 25.85. Found: C, 47.5; H, 5.6; N, 26.0.

ACKNOWLEDGMENTS

We would like to express our appreciation to Novo Nordisk Co. for the generous gift of the lipase CAL-B. Financial support from Comisión Interministerial de Ciencia y Tecnología (Spain; Project BIO98-0770) is gratefully acknowledged. We would also like to thank the Ministerio de Educación y Cultura (Spain) for predoctoral (J. M.) and postdoctoral (S. F.) fellowships.

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Received September 5, 2001
Accepted November 12, 2001