

Synthesis of 6-C-Substituted Purine Nucleosides: α -(Aminomethylene)-9- β -D-ribofuranosylpurine-6-acetic Acid Derivatives

Norimitsu HAMAMICHI*¹⁾ and Tadashi MIYASAKA

School of Pharmaceutical Sciences, Showa University, Hatanodai 1-5-8, Shinagawa-ku, Tokyo 142, Japan. Received April 8, 1991

α -(Aminomethylene)- β -D-ribofuranosylpurine-6-acetamide (4) and the ethyl acetate (9) have been synthesized by catalytic hydrogenation of 6-cyanomethylenepurine derivatives (3 and 7). 6-Cyanomethylenepurines were obtained by substitution of 6-chloro-9-(2,3-*O*-isopropylidene- β -D-ribofuranosyl)purine (1) with α -cyanoacetamide and ethyl cyanoacetate, followed by deprotection of the isopropylidene group. Substitution of 4 and 9 with benzylamine and aniline gave the corresponding *N*-benzyl- and *N*-phenyl-substituted α -(aminomethylene)- β -D-ribofuranosylpurine-6-acetamides (5) and the ethyl acetate (10), respectively.

Keywords purine; enamino-amide; enamino-ethyl ester; catalytic hydrogenation; ribofuranose

*N*⁶-Alkyladenosines are important intermediates in the study of the A₁ and A₂ adenosine receptors.²⁾ 6-C-Alkylpurine ribonucleosides are also useful as biological probes in studies of the mechanism of adenylosuccinate synthetase.³⁾ It is known that enamino-acetic acid derivatives are versatile starting materials for the synthesis of *N*-alkyl side chains by the substitution of amines.⁴⁾ However, there is only one report of a method for the introduction of an enamine moiety into purine at position 6.⁵⁾ Although 6-cyanomethylene purine derivatives can be prepared in high yield by reaction of the sodium salt of an activated cyanomethylene such as α -cyanoacetamide or ethyl cyanoacetate with 6-chlorinated or methylsulfonated purine derivatives,⁶⁾ the conversion of the cyano group to an enamine has not been described.

In a previous publication, we described⁷⁾ the synthesis of α -(aminomethylene)purine-6-acetonitrile via 6-dicyanomethylenepurine derivatives, which exist as an equilibrium mixture of the enamino-nitrile isomers.⁸⁾ However, α -(aminomethylene)-9-*H*-purine-6-acetamides are only found in the *Z* form.^{7c,d)} Also, it was found that an *N,N*-dimethylformamide (DMF)–benzene solvent system was most successful for the catalytic hydrogenation of 6-dicyanomethylenepurine derivatives. In the present paper, we have extended our work to the synthesis of α -(aminomethylene)-9- β -D-ribofuranosylpurine-6-acetamide (4) and the ethyl acetate (9) and their *N*-substituted purine derivatives (5 and 10) via 6-cyanomethylene derivatives (2 and 6).

The syntheses of (*Z*)- α -(aminomethylene)-9- β -D-ribofuranosylpurine-6-acetamide (4) and its amino-substituted derivatives 5 are summarized in Chart 1. Initial attempts

to substitute 6-chloro-9-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)purine with α -cyanoacetamide using sodium hydride were unsuccessful. Reaction of 6-chloro-9-(2,3-*O*-isopropylidene- β -D-ribofuranosyl)purine (1)⁹⁾ with α -cyanoacetamide in the presence of sodium hydride in DMF gave α -cyano-9-(2,3-*O*-isopropylidene- β -D-ribofuranosyl)purine-6-acetamide (2) in 71% yield, and this product was treated

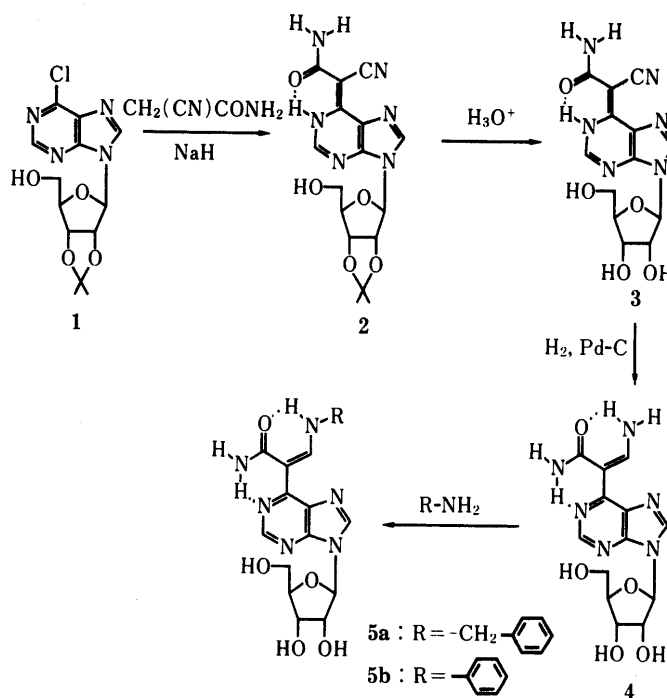


Chart 1

TABLE I. ¹H-NMR Data for 4 and 5 in DMSO-*d*₆

Compd. No.	Chemical shifts of aglycone moiety (ppm) (<i>J</i> in Hz)						Others and H-1' of ribofuranosyl
	H-2 (s)	H-8 (s)	C=CH (d)	CONH (br s)	CONH (br s)	C=CNH (m)	
4	8.61	8.59	9.61 ^{a)}	6.96	9.94–10.15 ^{b)}		8.30 (br s, NH), 5.98 (1H, d, <i>J</i> = 5 Hz, H-1')
5a	8.63	8.60	9.73 (<i>J</i> = 13)	7.06	10.09	11.11	4.48–4.64 (2H, m, CH ₂), 7.36 (5H, s, Ph-H), 6.00 (1H, d, <i>J</i> = 5 Hz, H-1')
5b	8.80	8.74	10.26 (<i>J</i> = 13)	7.13	10.16	12.71 ^{c)} (<i>J</i> = 12)	7.07–7.45 (5H, m, Ph-H), 6.00 (1H, d, <i>J</i> = 5 Hz, H-1')

a) dd, *J* = 16 Hz, *J* = 8 Hz. b) m. c) d.

with 40% aqueous trifluoroacetic acid to give α -cyano-9- β -D-ribofuranosylpurine-6-acetamide (**3**) in 84% yield. Catalytic hydrogenation of **3** over 5% Pd-C in DMF-benzene under medium pressure (4 atm) gave **4** in 75% yield. In the proton nuclear magnetic resonance ($^1\text{H-NMR}$) spectrum the vinyl proton was found at δ 9.61 as a doublet of doublets which collapsed to a singlet on adding deuterium oxide (Table I). Although the signal of the vinyl proton of an enamine moiety generally appears at δ 7–8,⁴⁾ in this case the large downfield shift of the vinyl proton is due to the anisotropic effect of the purine ring.^{7c,d)} From this, the configuration of the vinyl proton was concluded to be *Z*. Interestingly, although α -(aminomethylene)-9-(methoxymethyl)-9*H*-purine-6-acetonitrile exists in an enamino-nitrile tautomeric equilibrium (*E/Z*),⁸⁾ the enamino-amide moiety of **4** is only found in the *Z* form.

Substitution of **4** with benzylamine or aniline under heating gave the corresponding *N*-substituted enamines **5a** and **5b** in 95% yield and 66% yield, respectively. In the $^1\text{H-NMR}$ spectra the vinyl protons of **5a** and **5b** were found at δ 9.73 (1H, d) and δ 10.26 (1H, d), respectively, indicating that both **5a** and **5b** are in the *Z* form.

Substitution of **1** with ethyl cyanoacetate in the presence of sodium hydride in DMF gave ethyl α -cyano-9-(2,3-*O*-isopropylidene- β -D-ribofuranosyl)purine-6-acetate (**6**) in 81% yield. Its isopropylidene group was removed with acid to give **7** in 81% yield. Catalytic hydrogenation of **7** over 5% Pd-C in DMF-benzene under medium pressure (4 atm) gave ethyl 2-(9- β -D-ribofuranosylpurin-6-yl)propionate (**8**)

in 21% yield as an over-reduced by-product and ethyl α -(aminomethylene)-9- β -D-ribofuranosylpurine-6-acetate (**9**) in 75% yield (Chart 2). In the $^1\text{H-NMR}$ spectrum the vinyl protons of **9** exhibited two sets of signals at δ 7.67 (m, *E*) as the minor signal and at δ 7.99 (brs, *Z*) as the major signal which collapsed to a singlet on adding deuterium oxide.^{7c,d)} On the basis of the chemical shift of the vinyl proton, **9** seems to exist in an enamino ester tautomeric equilibrium.^{7c,d)} The ratio of geometrical isomers (*E/Z*) in deuteriodimethyl sulfoxide ($\text{DMSO-}d_6$) is 38:62 based on the integration ratios of the H-2 and vinyl proton signals of the isomers in the $^1\text{H-NMR}$ spectrum.

Substitution of **9** with benzylamine under heating for 5 h gave ethyl α -(*N*-benzylaminomethylene)-9- β -D-ribofuranosylpurine-6-acetate (**10a**) in 89% yield. In the $^1\text{H-NMR}$ spectrum ($\text{DMSO-}d_6$) the vinyl proton signal was found at δ 7.84 (*E*) and δ 8.01 (*Z*).^{7c,d)} The amino proton signal was found at δ 9.36 (*E*) and δ 8.98 (*Z*). On the basis of the chemical shifts of the amino and vinyl protons, the geometrical isomers (*E/Z*) of *N*-substituted **10a** seem to exist in an enamino ester tautomeric equilibrium. The ratio of geometrical isomers was 47:53 based on the integration ratios of signals due to the two isomers in the $^1\text{H-NMR}$ spectrum. Similarly, after reaction of **9** with aniline, the *N*-substituted phenylamine **10b** was obtained in 55% yield. The ratio of geometrical isomers (*E/Z*) in $\text{DMSO-}d_6$ was 48:52. In this reaction ethyl 9- β -D-ribofuranosylpurine-6-acetate (**11**) was obtained in 21% yield as a by-product by addition of aniline at the α -position of the enamine, followed by cleavage of the carbon-carbon bond of the enamine moiety, with concomitant formation of the amidine fragment.¹⁰⁾

In conclusion, the present work demonstrates that catalytic hydrogenation of 6-cyanomethylene purine derivatives (**3** and **7**) to the corresponding α -(aminomethylene)-9- β -D-ribofuranosylpurine-6-acetamide (**4**) and the ethyl acetate (**9**) in DMF-benzene is highly chemoselective, because the enamine moiety and purine ring are unaffected. Compounds **4** and **9** are versatile intermediates for the preparation of 6-enaminopurine ribonucleosides having alkyl or aryl substituents.

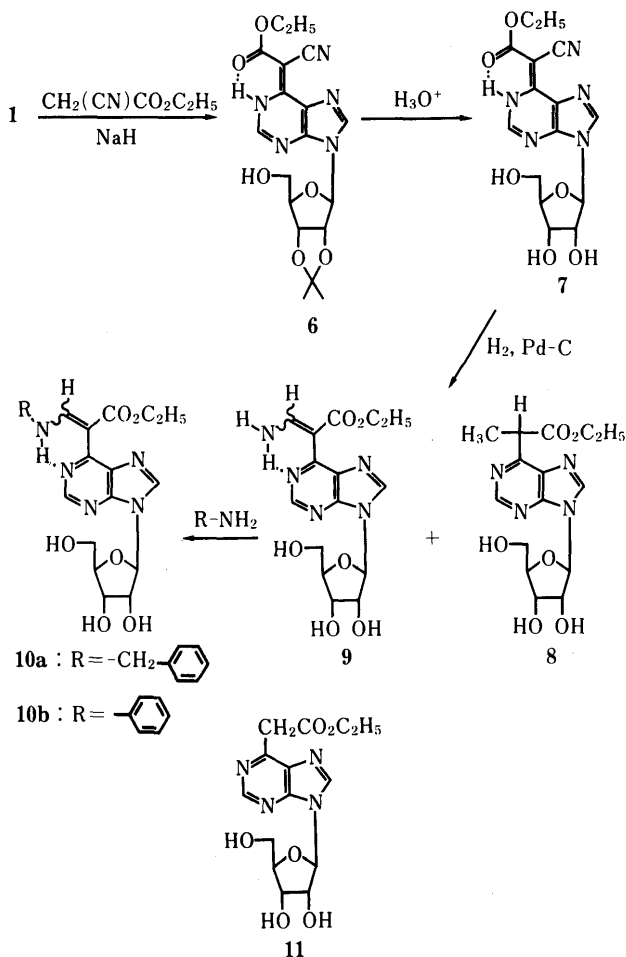


Chart 2

Experimental

All melting points were determined on a Yamato capillary melting point apparatus, MP-21, and are uncorrected. Infrared (IR) spectra were taken on a JASCO A-102 spectrophotometer. Ultraviolet (UV) spectra were measured using a Hitachi EPS-3T spectrophotometer. $^1\text{H-NMR}$ spectra were recorded on a JEOL JNM-FX 100 spectrometer using tetramethylsilane as an internal standard. Mass spectra (MS) were measured on a JEOL JMS-D300 spectrometer. The following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; sh, shoulder; and dd, doublet of doublets.

α -Cyano-9-(2,3-*O*-isopropylidene- β -D-ribofuranosyl)purine-6-acetamide (2**)** A solution of α -cyanoacetamide (4.290 g, 0.05 mol) in dry DMF (30 ml) was added to a cold (0–5 °C) stirred suspension of 60% sodium hydride (2.0 g, 0.05 mol) in dry DMF (60 ml) over a period of 30 min under argon, and stirring was continued for 20 min at room temperature. At this time a solution of **1** (3.267 g, 0.01 mol) in DMF (30 ml) was added and the solution was stirred for 7 h at room temperature. The solvent was evaporated *in vacuo*, and the residue was adjusted to pH 7 with 3% hydrochloric acid. The solution was allowed to stand overnight, and the resulting precipitate was collected by filtration, and washed with water. Recrystallization from DMF-MeOH gave **2** (2.671 g, 71%) as colorless needles, mp 221–224 °C. IR (KBr): 3480, 3400, 2195 (CN), 1645 cm^{-1} . UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 329 (33000 sh), 338 (37000). $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 1.33 (3H, s, Me), 1.54 (3H, s, Me), 6.13 (1H, d, $J=2\text{ Hz}$, H-1'), 7.01

(2H, brs, NH₂), 8.46 (2H, s, H-2, H-8), 14.98 (1H, brs, NH). MS *m/z*: 374 (M⁺), 332. *Anal.* Calcd for C₁₆H₁₈N₆O₅: C, 51.33; H, 4.85; N, 22.45. Found: C, 51.05; H, 4.96; N, 22.32.

α -Cyano-9- β -D-ribofuranosylpurine-6-acetamide (3) A solution of 2 (1.872 g, 5 mmol) in 40% aqueous trifluoroacetic acid (60 ml) was stirred for 1.5 h at room temperature. The resulting precipitate was collected by filtration, and recrystallized from DMSO-MeOH to give 3 (1.409 g, 84%) as colorless needles, mp 202–205 °C (dec.). IR (KBr): 2180 (CN) cm⁻¹. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 329 (33000 sh), 338 (36300). ¹H-NMR (DMSO-*d*₆) δ : 5.91 (1H, d, *J* = 5 Hz, H-1'), 7.00 (2H, brs, NH₂), 8.44 (1H, brs, H-2), 8.54 (1H, s, H-8), 14.96 (1H, brs, NH). MS *m/z*: 334 (M⁺), 261, 202 (B+1). *Anal.* Calcd for C₁₃H₁₄N₆O₅: C, 46.70; H, 4.22; N, 25.14. Found: C, 46.75; H, 4.29; N, 24.80.

(Z)- α -(Aminomethylene)-9- β -D-ribofuranosylpurine-6-acetamide (4) A solution of 3 (1.003 g, 3 mmol) in DMF-benzene (1:1 v/v, 200 ml) was hydrogenated over 5% Pd-C (900 mg) for 24 h at room temperature under 4 atm pressure. The catalyst was filtered off, and the filtrate was evaporated *in vacuo*. The residue was recrystallized from MeOH to give 4 (0.752 g, 75%) as yellow needles, mp 167–168 °C. IR (KBr): 3370, 3220, 3170, 1638 (CO) cm⁻¹. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 237 (14400), 265 (10500), 332 (26300). MS *m/z*: 336 (M⁺), 224, 204 (B+1). *Anal.* Calcd for C₁₃H₁₆N₆O₅: C, 46.42; H, 4.80; N, 24.99. Found: C, 46.05; H, 4.76; N, 24.60.

(Z)- α -(N-Benzylaminomethylene)-9- β -D-ribofuranosylpurine-6-acetamide (5a) A solution of 4 (0.336 g, 1 mmol) and benzylamine (0.297 g, 3 mmol) in ethanol (15 ml) was refluxed with stirring for 24 h. After cooling, the resulting precipitate was collected by filtration and recrystallized from MeOH to give 5a (0.399 g, 95%) as colorless needles, mp 116–117 °C. IR (KBr): 3350, 1635 (CO) cm⁻¹. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 240 (15800), 274 (10700), 343 (27500), 351 (26900 sh). MS *m/z*: 426 (M⁺), 294 (B+1). *Anal.* Calcd for C₂₀H₂₂N₆O₅: C, 56.33; H, 5.20; N, 19.71. Found: C, 56.23; H, 5.11; N, 19.53.

(Z)- α -(N-Phenylaminomethylene)-9- β -D-ribofuranosylpurine-6-acetamide (5b) A solution of 4 (0.336 g, 1 mmol) and aniline (0.279 g, 3 mmol) in ethanol (15 ml) was refluxed with stirring for 14 d. After cooling, the resulting precipitate was recrystallized from tetrahydrofuran-MeOH to give 5b (0.272 g, 66%) as yellow needles, mp 120–121 °C. IR (KBr): 3350, 1640 (CO) cm⁻¹. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 241 (17000), 281 (16200), 371 (36300). MS *m/z*: 412 (M⁺), 280 (B+1). *Anal.* Calcd for C₁₉H₂₀N₆O₅: C, 55.33; H, 4.89; N, 20.38. Found: C, 55.03; H, 4.94; N, 20.64.

Ethyl α -Cyano-9-(2,3-O-isopropylidene- β -D-ribofuranosyl)purine-6-acetate (6) A solution of ethyl cyanoacetate (1.018 g, 9 mmol) in dry DMF (5 ml) was added dropwise to a cold (0–5 °C) stirred suspension of 60% sodium hydride (0.264 g, 6.6 mmol) in dry DMF (15 ml) over a period of 15 min, and the solution was stirred for 5 min at room temperature under argon. A solution of 1 (0.980 g, 3 mmol) in dry DMF (10 ml) was added, and the mixture was stirred for 15 h at 80 °C. After cooling, the solvent was evaporated *in vacuo* and the residue was acidified to pH 4 with 10% acetic acid. The resulting precipitate was collected by filtration and recrystallized from ethanol to give 6 (0.987 g, 81%) as colorless needles, mp 223–225 °C (dec.). IR (KBr): 3270, 3125, 2200 (CN), 1650 (CO) cm⁻¹. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 338 (37100), 328 (32300). ¹H-NMR (DMSO-*d*₆) δ : 1.28 (3H, t, *J* = 7 Hz, Me), 1.33 (3H, s, Me), 1.54 (3H, s, Me), 4.23 (2H, q, CH₂), 6.16 (1H, d, *J* = 2 Hz, H-1'), 8.51 (1H, s, H-2), 8.48 (1H, s, H-8). MS *m/z*: 403 (M⁺), 314, 231 (B+1). *Anal.* Calcd for C₁₈H₂₁N₅O₆: C, 53.59; H, 5.24; N, 17.36. Found: C, 53.57; H, 5.28; N, 17.66.

Ethyl α -Cyano-9- β -D-ribofuranosylpurine-6-acetate (7) A solution of 6 (4.034 g, 1 mmol) in 40% aqueous trifluoroacetic acid (70 ml) was stirred for 4 h at room temperature. The resulting precipitate was collected by filtration and recrystallized from DMF-chloroform to give 7 (2.935 g, 81%) as colorless needles, mp 218–221 °C (dec.). (lit.^{6c}) mp 230–233 °C (dec.). IR (KBr): 3375, 3225, 2200 (CN), 1650 (CO) cm⁻¹. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 338 (38000), 328 (33000). ¹H-NMR (DMSO-*d*₆) δ : 1.28 (3H, t, *J* = 7 Hz, Me), 4.23 (2H, q, CH₂), 5.94 (1H, d, *J* = 5 Hz, H-1'), 8.50 (1H, s, H-2), 8.62 (1H, s, H-8), 13.58 (1H, brs, NH). MS *m/z*: 363 (M⁺), 231 (B+1).

Catalytic Hydrogenation of 7 A solution of 7 (0.726 g, 0.002 mol) in DMF-benzene (1:1 v/v, 80 ml) was hydrogenated over 5% Pd-C (0.5 g) for 48 h at room temperature under 4 atm pressure. The catalyst was filtered off, and the filtrate was evaporated *in vacuo*. The residue was purified by column chromatography on Florisil (60 g) using 9% ethanol in dichloromethane as eluent and the eluate was evaporated *in vacuo* to give ethyl 2-(9- β -D-ribofuranosylpurin-6-yl)propionate (8) (0.150 g, 21%) as a foam (lit.^{6c}) foamy. IR (KBr): 3375, 1730 (CO), 1595 cm⁻¹.

UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 262 (8710). ¹H-NMR (DMSO-*d*₆) δ : 1.09 (3H, t, *J* = 7 Hz, Me), 1.53 (3H, d, *J* = 7 Hz, Me), 4.08 (2H, q, CH₂), 4.51 (1H, q, *J* = 7 Hz, CH), 6.04 (1H, d, *J* = 6 Hz, H-1'), 8.81 (1H, s, H-8), 8.88 (1H, d, *J* = 6 Hz, H-2). MS *m/z*: 352 (M⁺), 249 (B+30), 221 (B+2). High-resolution MS *m/z*: 352.1360 (M⁺, Calcd for C₁₅H₂₀N₄O₆: 352.1385).

Further elution with the same solvent gave ethyl α -(aminomethylene)-9- β -D-ribofuranosylpurine-6-acetate (9) (0.551 g, 75%), which was recrystallized from acetone-hexane to give colorless prisms, mp 100–101 °C. IR (KBr): 3325, 1665 (CO), 1635, 1580 cm⁻¹. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 323 (186000), 263 (11700), 236 (11700). ¹H-NMR (DMSO-*d*₆) δ : 1.14 (3H, t, *J* = 7 Hz, Me), 3.95–4.23 (2H, m, CH₂), 5.98 (1H, d, *J* = 5 Hz, H-1'), 7.70 (0.38H, m, C=CH, *E*), 7.99 (1.62H, brs, NH, C=CH, *Z*), 8.59 (1H, s, H-8), 8.66 (0.62H, s, H-2, *Z*), 8.74 (0.38H, s, H-2, *E*). MS *m/z*: 365 (M⁺), 306, 233 (B+1). High-resolution MS *m/z*: 365.1336 (M⁺, Calcd for C₁₅H₁₉N₅O₆: 365.1337).

Ethyl α -(N-Benzylaminomethylene)-9- β -D-ribofuranosylpurine-6-acetate (10a) A solution of 9 (0.181 g, 0.5 mmol) and benzylamine (0.160 g, 1.50 mmol) in ethanol (7 ml) was refluxed with stirring for 5 h. After cooling, the solvent was evaporated *in vacuo*. The residue was purified by column chromatography on Florisil (20 g) using 4% ethanol in dichloromethane as eluent and the eluate was evaporated *in vacuo* to give 10a (0.201 g, 89%) as a foam. IR (KBr): 3400, 3300, 1665 (CO), 1620 cm⁻¹. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 238 (15000), 273 (17800), 333 (32300). ¹H-NMR (DMSO-*d*₆) δ : 1.13 (3H, t, *J* = 7 Hz, Me), 3.95–4.23 (2H, m, CH₂), 4.53–4.71 (2H, m, CH₂), 5.98 (1H, d, *J* = 5 Hz, H-1'), 7.34 (5H, brs, phenyl-H), 7.84 (0.47H, d, *J* = 14 Hz, C=CH, *E*), 8.01 (0.53H, d, *J* = 14 Hz, C=CH, *Z*), 8.60 (1H, s, H-8), 8.66 (0.53H, s, H-2, *Z*), 8.73 (0.47H, s, H-2, *E*), 8.98 (0.53H, brs, NH, *Z*), 9.36 (0.47H, brs, NH, *E*). MS *m/z*: 455 (M⁺), 351, 323 (B+1). High-resolution MS *m/z*: 455.1796 (M⁺, Calcd for C₂₂H₂₅N₅O₆: 455.1807).

Reaction of 9 with Aniline A solution of 9 (0.181 g, 0.5 mmol) and aniline (0.139 g, 1.5 mmol) was refluxed with stirring for 4 d, then allowed to cool. The solvent was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel (30 g) using 4% ethanol in dichloromethane as eluent and the eluate was evaporated *in vacuo* to give ethyl α -(N-phenylaminomethylene)-9- β -D-ribofuranosylpurine-6-acetate (10b) (0.120 g, 55%) as a foam. IR (KBr): 3375, 3300, 1665 (CO), 1625 cm⁻¹. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 232 (10500), 284 (10700), 353 (25700). ¹H-NMR (DMSO-*d*₆) δ : 1.19 (3H, t, *J* = 7 Hz, Me), 4.13–4.34 (2H, m, CH₂), 6.03 (1H, d, *J* = 5 Hz, H-1'), 7.04–7.33 (5H, m, phenyl-H), 8.20 (0.48H, d, *J* = 13 Hz, C=CH, *E*), 8.53 (0.52H, d, *J* = 13 Hz, C=CH, *Z*), 8.71 (1H, s, H-8), 8.77 (0.52H, s, H-2, *Z*), 8.91 (0.48H, s, H-2, *E*), 10.31 (0.52H, d, *J* = 13 Hz, NH, *Z*), 10.52 (0.48H, d, *J* = 13 Hz, NH, *E*). MS *m/z*: 441 (M⁺), 309 (B+1). High-resolution MS *m/z*: 441.1643 (M⁺, Calcd for C₂₁H₂₃N₅O₆: 441.1650).

Further elution with the same solvent gave ethyl 9- β -D-ribofuranosylpurine-6-acetate (11) (45 mg, 21%) as a foam (lit.^{6c}) glassy solid. IR (KBr): 3325, 1730 (CO), 1600 cm⁻¹. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (ϵ): 262 (7200), 334 (1660). ¹H-NMR (DMSO-*d*₆) δ : 1.18 (3H, t, *J* = 7 Hz, Me), 3.96–4.25 (2H, m, CH₂), 4.17 (2H, s, CH₂), 6.03 (1H, d, *J* = 6 Hz, H-1'), 8.81 (1H, s, H-8), 8.87 (1H, s, H-2). MS *m/z*: 338 (M⁺), 249, 207 (B+2). High-resolution MS *m/z*: 338.1236 (M⁺, Calcd for C₁₄H₁₈N₄O₆: 338.1228).

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