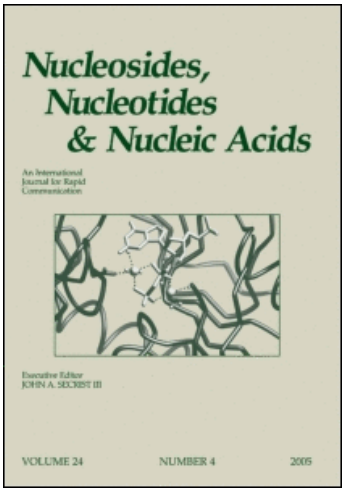

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REACTIONS OF 9-SUBSTITUTED 1-AMINOADENINES WITH NUCLEOPHILES AND SYNTHESES OF 3-SUBSTITUTED 3*H*-IMIDAZO[4,5-*e*][1,2,4]TRIAZOLO[1,5-*c*][1,2,3]TRIAZINES

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Abstract: Reactions of 1-aminoadenines (**2**) with NH_2OH gave adenine 1-oxides (**6**). Alkaline treatment of **2** afforded 5-amino-4-(1,2,4-triazol-3-yl)imidazoles (**3**), which were converted to 3*H*-imidazo[4,5-*e*][1,2,4]triazolo[1,5-*c*][1,2,3]triazines (**5**), aza analogues of 3*H*-[1,2,4]triazolo[3,2-*i*]purines (**4**), by treatment with $NaNO_2$.

INTRODUCTION

As we previously reported, electrophilic amination reactions towards nucleic acid bases have been extensively studied in relation to the chemical carcinogenesis of arylamines and arylhydroxylamines.[1-6] 9-Substituted 1-aminoadenines are one type of product which can be obtained from reactions of adenine derivatives with dinitrophenoxyamine (DNPA) in DMF.[6] Reaction of 1-aminoadenosine (**2b**) with H_2S in DMF gave 1-amino-6-thiopurine riboside.[6] On the other hand, reaction of **2b** with aqueous alkali afforded 5-amino-1-(ß-D-ribofuranosyl)-4-(1,2,4-triazol-3-yl)imidazole (**3b**) but not 6-hydrazinopurine riboside, a Dimroth-type rearranged product.[6] It was reported that the 6-hydrazinopurine derivative was obtained by reaction of 1-amino-9-benzyladenine with hydrazine hydrate.[7] Treatment

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This paper is dedicated to Professor Emeritus Morio Ikehara of Osaka University on the occasion of his 70th birthday.

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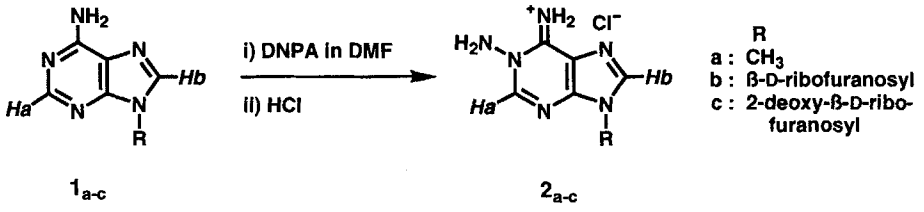
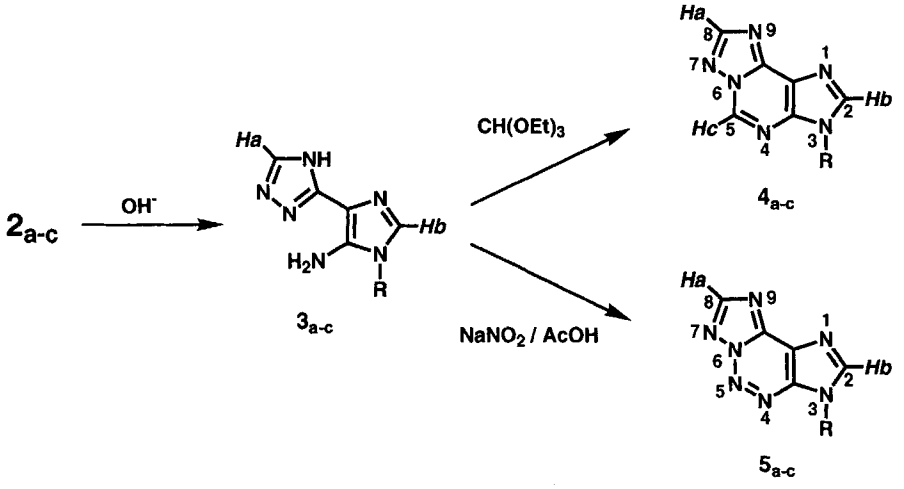
of **3b** with ethyl orthoformate gave 3-(ß-D-ribofuranosyl)-3*H*-[1,2,4]triazolo[3,2-*i*]purine (**4b**), which was also formed by the reaction of **2b** with ethyl orthoformate.[6] In this report, syntheses of compounds **2c** - **5c** from 2'-deoxyadenosine (**1c**), reactions of 9-substituted (methyl, ß-D-ribofuranosyl, 2-deoxy-ß-D-ribofuranosyl) 1-aminoadenines (**2**) with NH_2OH and reactions of 1-substituted 5-amino-4-(1,2,4-triazol-3-yl)imidazoles (**3**) with $NaNO_2$ are described. The reaction of **2** with NH_2OH gave adenine 1-oxide derivatives (**6**) and the reaction of **3** with $NaNO_2$ gave 3*H*-imidazo[4,5-*e*][1,2,4]triazolo[1,5-*c*][1,2,3]triazine derivatives (**5**), aza analogues of 3*H*-[1,2,4]triazolo[3,2-*i*]purine derivatives (**4**).

RESULTS AND DISCUSSION

Reactions of 9-substituted adenines (**1**) with 1.5 equimolecular amounts of DNPA in DMF gave 1-amino derivatives (**2**) in almost quantitative yields (Scheme 1). Heating **2** in aqueous alkali quantitatively afforded 1-substituted 5-amino-4-(1,2,4-triazol-3-yl)imidazoles (**3**) (Scheme 2). Reaction of **3** with ethyl orthoformate afforded 3-substituted 3*H*-[1,2,4]triazolo[3,2-*i*]purine derivatives (**4**) which are compounds having a fused three-ring system. Compound **4** was also obtained by reaction of **2** with ethyl orthoformate. These reactions have already been reported by us for 9-methyladenine (**1a**) and adenosine (**1b**).[6] In this study, we demonstrated that 2'-deoxyadenosine (**1c**) also gave good yields of the corresponding derivatives (**2c, 3c, 4c**) using procedures similar to those reported.[6] Treatment of **3a** with $NaNO_2$ in 50% aqueous acetic acid gave a product whose NMR spectra demonstrated the disappearance of the NH_2 group. From the elemental analysis, and NMR and Mass spectra, the structure of the product was presumed to be **5a**, however, it was not evident which nitrogen (N2 or N4) of the triazole moiety of **3a** was involved in ring closure. X-ray diffraction analysis of **5a** revealed a typical structure in which four nitrogens are consecutively bonded (Table I and Fig. I). The greater reactivity of N2 than N4 of **3** is also supported by the fact that **4** was formed by the reaction of **3** with ethyl orthoformate. The bond lengths of **5a** showed a tendency towards localization of π-electrons on the three heterocyclic rings. These three rings form a plane having a high



Scheme 1



Scheme 2

TABLE I. Crystal Data for Compound 5a

formula	$C_6H_5N_7$	crystal system	monoclinic
formula wt.	175.15	space group	$P2_1/a$
a (Å)	14.708(2)	*Z*	4
b (Å)	6.892(1)	μ (Cu *K*α) (cm^{-1})	9.09
c (Å)	7.346(1)	*Dc* (g cm^{-3})	1.582
ß (°)	99.19(1)	*R*	0.039
V ($Å^3$)	735.2(2)	No. of reflections (F≠0)	1082

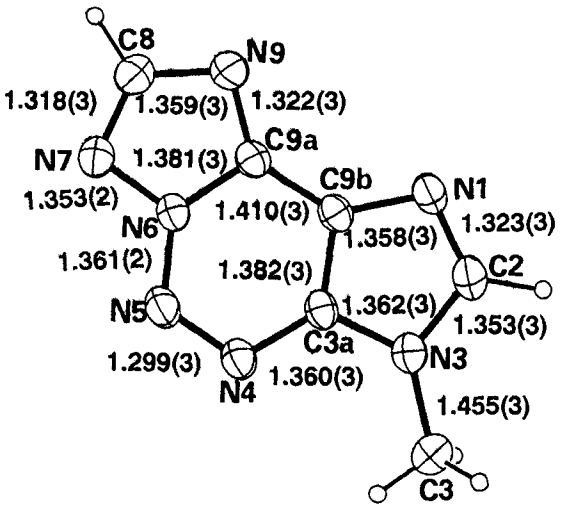


FIGURE I. ORTEP[16] drawing of **5a** with atomic numberings and bond lengths (Å).

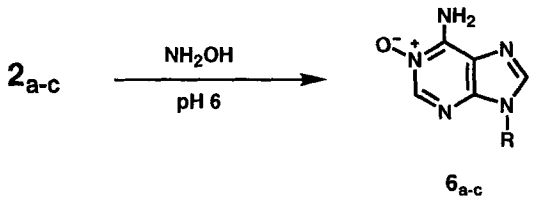
degree of planarity with a maximum deviation of 0.015(2) Å at N7 from the best plane formed by all non-hydrogen atoms. Assignments of the CH protons of **3a**, **4a**, **5a** were achieved using the 8-D compound of **2a** as a starting material which was prepared by a previously reported procedure[6] (Scheme 2 and Table II). The CH protons of the fused ring-compounds (**4a** and **5a**) resonated at much lower fields than those of **3a**. The CH protons of compound **5a**, an aza analogue of **4a**, resonated at lower fields than those of **4a**. The significantly greater down field shift (0.42 ppm) of Hb for **5a** may be attributed to an electron-withdrawing effect of the N5 nitrogen through the five consecutive resonating bonds. UV spectra of **5** were quite characteristic, *i.e.* λmax's around 220 nm (intense) and 285 nm (less intense with a relative absorbance of 0.2) in media of pH 1 to 12, and these UV spectra were similar to those of the nitrosation product of 5-amino-1-benzyl-4-(1,2,4-triazol-3-yl)imidazole reported.[8] UV spectra of **4** and **5** were quite different, *i.e.* compound **4** has a λmax around 278 nm in media of pH 1 to 12. These results indicate that both compounds have different electronic configurations for UV absorption. Protonation of **4** and **5** seems to take place in pH region as reflected by changes in the UV spectra obtained

TABLE II. Chemical Shifts of Compounds 1a-5a

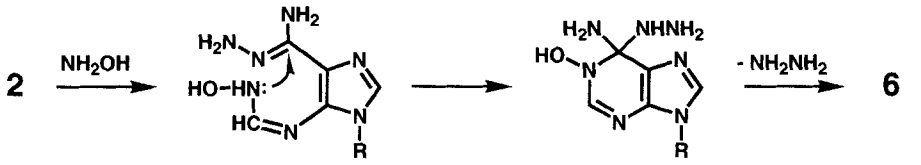
Proton	Chemical shift (ppm)				
	1a	**2a**	**3a**	**4a**	**5a**
Ha	8.10	8.64	7.81	8.61	8.86
Hb	8.06	8.47	7.24	8.47	8.89
Hc	–	–	–	9.67	–
Me	3.72	3.83	3.46	3.95	4.16

with acidic and neutral media, but these changes are too small to determine the p*K*a values. ^{1}H-NMR spectra of **4a** and **5a** were taken in D_2O and the changes in their chemical shifts were examined by addition of a drop of conc. DCl. Results showed that protons of **4a** actually moved down field (Ha 8.54 ppm, Hb 8.34, Hc 9.41, Me 4.00 in D_2O; Ha 8.78, Hb 9.32, Hc 9.71, Me 4.20 in acidic media), but only slight changes were observed for **5a** (Ha 8.76 ppm, Hb 8.73, Me 4.25 in D_2O; Ha 8.77, Hb 8.78, Me 4.25 in acidic media). These results support an evidence that **4** has a protonation site in acidic media, but it is not clear whether **5** has a similar site. Compounds **3b,c** also gave **5b,c**, respectively, by the same $NaNO_2$ treatment and the structures of the products were identified from their spectral data by comparing with those of **5a**.

Treatment of **2** with an excess of NH_2OH in aqueous solution at pH 6 at 37°C yielded adenine 1-oxide derivatives (**6**) (Scheme 3). The structures of these derivatives were identified by comparing their spectral data with those of authentic specimens. A possible mechanism for the formation of adenine 1-oxides is that the nitrogen of NH_2OH attacks at the C2 carbon of **2** in a nucleophilic manner to form a 1,2-bond-cleaved intermediate. Subsequently, the nitrogen of the C(2)-NHOH group attacks at the C6 to form a ring-closed intermediate, followed by release of the -$NHNH_2$ group and then by aromatization to form **6** (Scheme 4). Alternatively, an initial attack of the NH_2OH nitrogen at C6 carbon of **2** may



Scheme 3



Scheme 4

also lead to **6** by 1,2-bond cleavage, concomitant ring re-closure, release of the -NHNH2 group and aromatization. It has been reported that *N*-aminopyridine forms pyridine *N*-oxide by treatment with NH2OH by means of a similar mechanism.[9] Treatment of 1-methyladenosine with NH2OH is also known to produce adenosine 1-oxide.[10] The conversion rates of 1-aminoadenosine (**2b**) and 1-methyladenosine to adenosine 1-oxide (**6b**) were compared under conditions of 150 equimolecular amounts of NH2OH at pH 6 at 37°C using HPLC. The reaction proceeded with pseudo-first order kinetics (data not shown) and **2b** was converted to **6b** about 6 times faster than 1-methyladenosine (k_{obs} = 2.0 x 10^{-4} sec^{-1} for **2b** and k_{obs} = 3.6 x 10^{-5} sec^{-1} for 1-methyladenosine). This can be explained by the fact that the *N*-amino group withdraws electrons as reported previously[5] making it easy for NH2OH to attack the aromatic system.

EXPERIMENTAL

^{1}H-NMR spectra were recorded on a JEOL EX 270 or GSX 400 spectrometer and chemical shifts were reported in parts per million (ppm) using tetramethylsilane as the internal standard. Mass spectra were obtained with a JEOL DX-300 spectrometer. UV

spectra were recorded on a Shimadzu UV-2100 spectrophotometer. Melting points were measured with a Yanagimoto micro-melting point apparatus and are uncorrected.

1-Amino-2'-deoxyadenosine (2c). 2'-Deoxyadenosine monohydrate (**1c**, 1.08 g, 4 mmol) and DNPA (1.19 g, 6 mmol) were dissolved in 14 mL of DMF and the mixture was kept standing at 37°C for 24 h. After the solvent was removed by evaporation to half the original volume, 2 mL of 1 N HCl and 10 mL of ether were added. After the precipitate of the crude product which appeared was filtered, the aqueous layer was washed with ether three times and EtOH and ether were then added to obtain more product. The crude products obtained as precipitates were combined and dissolved in 3 mL of water. Addition of EtOH and ether to the solution yielded light brown needles of 1-aminodeoxyadenosine HCl salt in a 972 mg (78 %) yield. mp 241-242°C (dec); ^{1}H-NMR (Me$_2$SO-*d*$_6$) δ 10.1 and 9.20 (each, br s, 1 H, 6-NH$_2$), 8.71 (s, 1 H, 2-H), 8.65 (s, 1 H, 8-H), 6.73 (s, 2 H, N-NH$_2$), 6.37 (dd, 1 H, $J_{1',2'a}$ = 6.6 Hz, $J_{1',2'b}$ = 6.3 Hz, 1'-H), 5.43 (d, 1 H, $J_{3',3'\text{-OH}}$ = 4.0 Hz, 3'-OH), 5.00 (t, 1 H, $J_{5',5'\text{-OH}}$ = 5.0 Hz, 5'-OH), 4.43 (dddd, 1 H, $J_{2'a,3'}$ = 5.6 Hz, $J_{2'b,3'}$ = 3.6 Hz, $J_{3',4'}$ = 3.3 Hz, 3'-H), 3.90 (ddd, 1 H, $J_{4',5'a}$ and $J_{4',5'b}$ = 4.3 Hz, 4'-H), 3.60 (ddd, 1 H, $J_{5'a,5'b}$ = 11.9 Hz, 5'-Ha), 3.52 (ddd, 1 H, 5'-Hb), 2.68 (ddd, 1 H, $J_{2'a,2'b}$ = 13.2 Hz, 2'-Ha), 2.38 (ddd, 1 H, 2'-Hb); UV λ_{max} nm (ε) (pH 1 and H$_2$O) 257 (12,600), (pH 12) 257 (13,100), 264 (sh), 290 (sh); FAB-MS *m/z* 267 $(M+H)^+$ free form, 151 $(B+H)^+$. Anal. Calcd for C$_{10}$H$_{14}$N$_6$O$_3$·HCl·1/2H$_2$O (dried *in vacuo* at 20°C for 12 h): C, 38.53; H, 5.01; N, 26.95. Found: C, 38.40; H, 5.15; N, 26.56.

5-Amino-1-(2-deoxy-ß-D-ribofuranosyl)-4-(1,2,4-triazol-3-yl)imidazole (3c). 1-Amino-2'-deoxyadenosine·HCl·1/2H$_2$O (**2c**, 150 mg, 0.5 mmol) was dissolved in 5 mL of water and the pH of the solution was adjusted to 12 with 1 N NaOH. The mixture was then heated at 60°C for 2 h. TLC showed one major and several minor spots but no starting material. A part of the reaction mixture was purified by silica gel PLC (isopropanol/1% aqueous (NH$_4$)$_2$SO$_4$) and Sephadex LH20 column chromatography (MeOH) and a powder of **3c** was obtained. ^{1}H-NMR (Me$_2$SO-*d*$_6$) δ 13.68 (br s, 1 H, NH), 7.82 (s, 1 H, triazole-CH), 7.50 (s, 1 H, imidazole-CH), 5.98 (dd, 1 H, $J_{1',2'a}$ = 8.2

Hz, $J_{1',2'b}$ = 5.9 Hz, 1'-H), 5.78 (s, 2 H, NH_2), 5.27 (d, 1 H, $J_{3',3'\text{-}OH}$ = 3.9 Hz, 3'-OH), 5.13 (t, 1 H, $J_{5',5'\text{-}OH}$ = 5.0 Hz, 5'-OH), 4.35 (dddd, 1 H, $J_{2'a,3'}$ = 6.0 Hz, $J_{2'b,3'}$ = 2.8 Hz, $J_{3',4'}$ = 2.6 Hz, 3'-H), 3.82 (ddd, 1 H, $J_{4',5'a}$ and $J_{4',5'b}$ = 3.8 Hz, 4'-H), 3.56 (dd, 2 H, 5'-H), 2.47 (ddd, 1 H, $J_{2'a,2'b}$ = 13.2 Hz, 2'-Ha), 2.1 (ddd, 1 H, 2'-Hb); UV λ_{max} nm (pH 1) 247, 268 (sh), (H_2O) 260, (pH 12) 249.

3-(2-Deoxy-ß-D-ribofuranosyl)-3*H*-[1,2,4]triazolo[3,2-*i*]purine (4c). 1-Amino-2'-deoxyadenosine·HCl·1/2H_2O (**2c** ,62 mg, 0.2 mmol) and K_2CO_3 (693 mg, 5 mmol) were suspended in 1.5 mL of DMF. Ethyl orthoformate (0.7 mL, 4 mmol) was added to the solution and the mixture was refluxed for 5 min. After precipitates were removed by filtration, the filtrate was evaporated *in vacuo* and products were purified by silica gel column chromatography. Elution with $CHCl_3$/MeOH (19/1) yielded glycosidic bond cleaved 3*H*-[1,2,4]triazolo[3,2-*i*]purine (**4d**) as a powder (1.4 mg, 4.4 %) and subsequent elution with $CHCl_3$/MeOH (9/1) afforded 3-(2-deoxy-ß-D-ribofuranosyl)-3*H*-[1,2,4]triazolo[3,2-*i*]purine (**4c**) as a powder (15.3 mg, 28 %). **4d**: ^{1}H-NMR (Me_2SO-d_6) δ 9.60 (s, 1 H, 5-H), 8.61 (s, 1 H, 8-H), 8.49 (s, 1 H, 2-H); UV λ_{max} nm (pH 1) 275, 261(sh), (H_2O) 278, 263(sh), (pH 12) 289. **4c**: ^{1}H-NMR (Me_2SO-d_6) δ 9.70 (s, 1 H, 5-H), 8.74 (s, 1 H, 8-H), 8.64 (s, 1 H, 2-H), 6.54 (dd, 1 H, $J_{1',2'a}$ = 7.0 Hz, $J_{1',2'b}$ = 6.2 Hz, 1'-H), 5.39 (d, 1 H, $J_{3',3'\text{-}OH}$ = 4.2 Hz, 3'-OH), 4.97 (t, 1 H, $J_{5',5'\text{-}OH}$ = 5.5 Hz, 5'-OH), 4.45 (dddd, 1 H, $J_{2'a,3'}$ = 6.2 Hz, $J_{2'b,3'}$ = 3.8 Hz, $J_{3',4'}$ = 3.3 Hz, 3'-H), 3.91 (ddd, 1 H, $J_{4',5'a}$ and $J_{4',5'b}$ = 4.6 Hz, 4'-H), 3.64 (ddd, 1 H, $J_{5'a,5'b}$ = 11.9 Hz, 5'-Ha), 3.55 (ddd, 1 H, 5'-Hb), 2.75 (ddd, 1 H, $J_{2'a,2'b}$ = 13.7, 2'-Ha), 2.41 (ddd, 1 H, 2'-Hb); UV λ_{max} nm (pH 1) 279, (H_2O) 278, (pH 12) 279 (dec); FAB-MS *m/z* 277 $(M+H)^+$.

Reaction of 1-substituted 5-amino-4-(1,2,4-triazol-3-yl)imidazoles (3) with $NaNO_2$.

3-Methyl-3*H*-imidazo[4,5-*e*][1,2,4]triazolo[1,5-*c*][1,2,3]triazine (5a): 5-Amino-1-methyl-4-(1,2,4-triazol-3-yl)imidazole (**3a**, 41 mg, 0.25 mmol) was dissolved in 4 mL of 50 % aqueous acetic acid solution and then $NaNO_2$ (21 mg, 0.3 mmol) dissolved in 0.5 mL of water was added dropwise with stirring at room temperature. After the stirring

was continued for 20 min, the solvent was removed by evaporation. The main product was separated by silica gel column chromatography ($CHCl_3$/MeOH = 9/1) and recrystallized from EtOH to yield light brown needles of **5a** in a 22 mg (50 %) yield. mp 238-247°C (dec); ^{1}H-NMR (Me_2SO-*d*$_6$) δ 8.89 (s, 1 H, 8-H), 8.86 (s, 1 H, 2-H), 4.16 (s, 3 H, CH_3); UV λ_{max} nm (ε) (pH 1) 218 (25,500), 225 (sh), 286 (5,300), (H_2O) 218 (25,300), 225 (sh), 286 (5,200), (pH 12) 218 (25,900), 225 (sh), 286 (5,300); MS *m/z* 175 (M^+). Anal. Calcd for $C_6H_5N_7$: C, 41.14; H, 2.88; N, 55.98. Found: C, 41.25; H, 3.04; N, 56.20.

3-(ß-D-Ribofuranosyl)-3*H*-imidazo[4,5-*e*][1,2,4]triazolo[1,5-*c*][1,2,3]-triazine (5b): After treatment of 5-amino-1-(ß-D-ribofuranosyl)-4-(1,2,4-triazol-3-yl)imidazole (**3b**, 94 mg, 0.3 mmol) with $NaNO_2$ as described for the synthesis of **5a**, the product was separated by silica gel column chromatography ($CHCl_3$/MeOH = 9/1) and recrystallized from EtOH yielding transparent needles of **5b** in a 35 mg (36 %) yield. mp 189-194°C (color change of the crystal began at 183°C); ^{1}H-NMR (Me_2SO-*d*$_6$) δ 9.21 (s, 1 H, 8-H), 8.89 (s, 1 H, 2-H), 6.32 (d, 1 H, $J_{1',2'}$ = 4.2 Hz, 1'-H), 5.76 (d, 1 H, $J_{2',2'\text{-OH}}$ = 5.5 Hz, 2'-OH), 5.33 (d, 1 H, $J_{3',3'\text{-OH}}$ = 5.4 Hz, 3'-OH), 5.15 (t, 1 H, $J_{5',5'\text{-OH}}$ = 5.3 Hz, 5'-OH), 4.63 (ddd, 1 H, $J_{2',3'}$ = 4.9 Hz, 2'-H), 4.25 (ddd, 1 H, $J_{3',4'}$ = 4.8 Hz, 3'-H), 4.07 (ddd, 1 H, $J_{4',5'a} = J_{4',5'b}$ = 3.8 Hz, 4'-H), 3.66 (ddd, 1 H, $J_{5'a,5'b}$ = 12.1 Hz, 5'-Ha), 3.63 (ddd, 1 H, 5'-Hb); UV λ_{max} nm (ε) (pH 1) 219 (28,100), 281 (5,200), 315 (sh), (H_2O) 219 (27,700), 281 (5,000), 315 (sh), (pH 12) 220 (28,000), 283 (5,200), 315 (sh); FAB-MS *m/z* 294 $(M+H)^+$. Anal. Calcd for $C_{10}H_{11}N_7O_4$: C, 40.96; H, 3.78; N, 33.44. Found: C, 40.78; H, 3.82; N, 33.34.

3-(2-Deoxy-ß-D-ribofuranosyl)-3*H*-imidazo[4,5-*e*][1,2,4]triazolo[1,5-*c*][1,2,3]triazine (5c): Compound **2c** (60 mg, 0.2 mmol) was treated with alkali as described for the preparation of **3c**. After the mixture was neutralized with 1 N HCl, the solvent was removed by evaporation. Without purification of **3c**, the residues were dissolved in 4 mL of 50 % aqueous acetic acid and $NaNO_2$ was then added as described above. Purification of products by silica gel column chromatography ($CHCl_3$/MeOH = 9/1)

and recrystallization from EtOH-hexane yielded transparent needles of **5c** in a 16 mg (30 %) yield. mp 162-167°C (dec); ^{1}H-NMR (Me$_2$SO-d_6) δ 9.14 (s, 1 H, 8-H), 8.88 (s, 1 H, 2-H), 6.74 (dd, 1 H, $J_{1',2'a}$ = 5.9 Hz, $J_{1',2'b}$ = 6.3 Hz, 1'-H), 5.42 (d, 1 H, $J_{3',3'\text{-OH}}$ = 4.6 Hz, 3'-OH), 4.97 (t, 1 H, $J_{5',5'\text{-OH}}$ = 5.0 Hz, 5'-OH), 4.50 (dddd, 1 H, $J_{2'a,3'}$ = 5.9 Hz, $J_{2'b,3'}$ = 4.3 Hz, $J_{3',4'}$ = 3.3 Hz, 3'-H), 3.97 (ddd, 1 H, $J_{4',5'a}$ and $J_{4',5'b}$ = 4.3 Hz, 4'-H), 3.68 (ddd, 1 H, $J_{5'a,5'b}$ = 12.1 Hz, 5'-Ha), 3.57 (ddd, 1 H, 5'-Hb), 2.84 (ddd, 1 H, $J_{2'a,2'b}$ = 13.5 Hz, 2'-Ha), 2.54 (ddd, 1 H, 2'-Hb); UV λ_{max} nm (ε) (pH 1) 219 (28,600), 282 (5,300), 305 (sh), (H$_2$O) 219 (29,200), 282 (5,400), 305 (sh), (pH 12) 218 (29,900), 282 (5,400), 305 (sh); FAB-MS *m/z* 278 $(M+H)^+$. Anal. Calcd for $C_{10}H_{11}N_7O_3$: C, 43.32; H, 4.00; N, 35.37. Found: C, 43.03; H, 3.87; N, 35.44.

Reactions of 9-substituted 1-aminoadenines (2a-c) with NH$_2$OH. (Formation of 9-substituted adenine 1-oxides (6)). Hydroxylamine·HCl (209 mg, 3 mmol) was dissolved in 1 mL of H$_2$O and the pH was adjusted to 6.0 with 40% aqueous NaOH solution. The hydrochloride salt of 1-aminoadenines (**2**, 0.3 mmol) was then added and the mixture was kept at 50°C for 2 days. Products were isolated by column chromatography.

6a: Product was isolated by silica gel column chromatography (CHCl$_3$/MeOH = 9/1) and further purified by Sephadex LH 20 column chromatography (MeOH). Recrystallization of the product from MeOH afforded white needles of 9-methyladenine 1-oxide (**6a**) in a 46 mg (92 %) yield. mp 294-297°C (dec) [lit.[11] mp 292-294°C (dec)]. ^{1}H-NMR (Me$_2$SO-d_6) δ 9.0-7.5 (br s, 2 H, NH$_2$), 8.57 (s, 1 H, 2-H), 8.24 (s, 1 H, 8-H), 3.76 (s, 3 H, CH$_3$); UV λ_{max} nm (pH 1) 215, 260, (H$_2$O and pH 12) 232, 262; MS *m/z* 165 (M^+), 149 (M^+-O or NH$_2$).

6b: Product was isolated by silica gel column chromatography (CHCl$_3$/MeOH = 4/1) and further purified by Sephadex LH 20 column chromatography (MeOH). Recrystallization of the product from MeOH gave white needles of adenosine 1-oxide (**6b**) in a 44 mg (52 %) yield. mp 214-225°C (dec) [lit.[12] mp 217-220°C (dec)]. ^{1}H-NMR (Me$_2$SO-d_6) δ 9.0-7.5 (br s, 2 H, NH$_2$), 8.63 (s, 1 H, 2-H), 8.54 (s, 1 H, 8-H), 5.88 (d, 1 H, $J_{1',2'}$ = 5.6 Hz, 1'-

H), 5.54 (d, 1 H, $J_{2',2'\text{-OH}}$ = 6.0 Hz, 2'-OH), 5.23 (d, 1 H, $J_{3',3'\text{-OH}}$ = 5.1 Hz, 3'-OH), 5.05 (t, 1 H, $J_{5',5'\text{-OH}}$ = 5.6 Hz, 5'-OH), 4.53 (ddd, 1 H, $J_{2',3'}$ = 4.6 Hz, 2'-H), 4.25 (ddd, 1 H, $J_{3',4'}$ = 3.8 Hz, 3'-H), 4.07 (ddd, 1 H, $J_{4',5'a} = J_{4',5'b}$ = 4.0 Hz, 4'-H), 3.66 (ddd, 1 H, $J_{5'a,5'b}$ = 12.1 Hz, 5'-Ha), 3.63 (ddd, 1 H, 5'-Hb); UV λ_{max} nm (pH 1) 215, 260, (H_2O and pH 12) 232, 262; FAB-MS *m/z* 284 $(M+H)^+$, 268 $((M\text{-}O \text{ or } NH_2)+H)^+$.

6c: Product was isolated by silica gel column chromatography ($CHCl_3$/MeOH = 3/1) and further purified by Sephadex LH 20 column chromatography (MeOH). Recrystallization of the product from MeOH afforded white needles of 2'-deoxyadenosine 1-oxide (**6c**)[13] in a 72 mg (84 %) yield. mp 228-232°C (dec). ^{1}H-NMR (Me_2SO-*d*6) δ 9.0-7.5 (br s, 2 H, NH_2), 8.61 (s, 1 H, 2-H), 8.51 (s, 1 H, 8-H), 6.32 (d, 1 H, $J_{1',2'a}$ = 7.2 Hz, $J_{1',2'b}$ = 6.3 Hz, 1'-H), 5.36 (d, 1 H, $J_{3',3'\text{-OH}}$ = 4.2 Hz, 3'-OH), 4.96 (t, 1 H, $J_{5',5'\text{-OH}}$ = 5.4 Hz, 5'-OH), 4.40 (dddd, 1 H, $J_{2'a,3'}$ = 6.1 Hz, $J_{2'b,3'}$ = 3.5 Hz, $J_{3',4'}$ = 3.1 Hz, 3'-H), 3.86 (ddd, 1 H, $J_{4',5'a}$ and $J_{4',5'b}$ = 4.7 Hz, 4'-H), 3.59 (ddd, 1 H, $J_{5'a,5'b}$ = 11.8 Hz, 5'-Ha), 3.51 (ddd, 1 H, 5'-Hb), 2.69 (ddd, 1 H, $J_{2'a,2'b}$ = 13.5 Hz, 2'-Ha), 2.31 (ddd, 1 H, 2'-Hb); UV λ_{max} nm (pH 1) 258, (H_2O and pH 12) 232, 260; FAB-MS *m/z* 268 $(M+H)^+$, 252 $((M\text{-}O \text{ or } NH_2)+H)^+$.

X-ray analysis. The crystal data for **5a** are listed in Table I. Intensity data were collected on a Rigaku AFC-5R diffractometer with graphite-monochromated Cu *Kα* radiation using the ω-2θ scan mode ($2\theta_{max}$ = 120°) at 293K. The structure was solved by direct methods[14] and refined by the full matrix least-squares method.[15] Discrimination between C and N atoms was based on values of temperature factors. The correctness of the assignment was confirmed by the positions of all H atoms located on a difference Fourier map after anisotropic refinement of the non-H atoms. The final refinement including H atoms with isotropic temperature factors reduced the *R* value to 0.039. The final atomic parameters, bond lengths and angles will be deposited in the Cambridge Crystallographic Data Centre. All numerical calculations were carried out on an ACOS S930 computer at the Protein Engineering Research Center, Institute for Protein Research, Osaka University.

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