only two of the many hydrocarbons that we have purified in this way.

We feel that this simple procedure, which has been a standard in our laboratory for years, can be of utility to other chemists who make use of organic stannanes in their synthetic work.

Experimental Part

Bulk C-18 (55-105 μm) was obtained from Waters, and C-18 TLC plates are available from Whatman ($MKC_{18}F$ reversed-phase TLC plates, 1 × 3 in., 200-μm thickness). The stannanes were obtained as follows: 1,[9] 2,[9] 3,[10] 4,[11] 7,[12] 10,[13] and 11,[14] were prepared as in the literature, and aryltins 5 and 6 were prepared from the corresponding organolithium reagents and tributyltin chloride (see supplementary material). Compound 12 is a known compound,[15] while 13 was prepared by the palladium-catalyzed coupling of (4-methoxyphenyl)tributyltin with 4-*tert*-butylcyclohexen-1-yl triflate.[16]

Model Separation: Reversed-Phase Flash Chromatography of 1 and 2. A flash chromatography column (from Aldrich, 1-in. diameter), fitted with a glass wool plug, was dry packed with C-18 up to a height of 10 in., and the column bed was equilibrated with the eluant (40% CH_2Cl_2, 60% CH_3CN) under pressure. When all the air had been removed (as shown by a change in color from white to a translucent grayish), a mixture of 1 and 2 (100 mg each) in 1 mL 1:1 CH_2Cl_2/CH_3CN was applied to the top of the C-18 bed, allowed to settle by opening the stopcock, and the walls of the column were rinsed with two 1-mL batches of the eluant. The column was then filled with the rest of the eluant, and the needle valve was adjusted so that the flow was ca. 2 cm/min. Twenty-five 12-mL fractions were collected and analyzed by C-18 TLC, staining after elution in an iodine chamber. Both compounds gave rise to bright orange spots that slowly faded when removed from the chamber. Charring with a variety of staining solutions was less satisfactory. The whole plate typically assumed an intense color that made spot detection difficult or impossible.

Fractions 9–14 contained compound 2, and fractions 16–24 contained 1. Evaporation of the solvent at the rotary evaporator and then under high vacuum gave TLC-pure 1 (89 mg) and 2 (93 mg). The column was then washed with fresh eluant (200 mL). The separation was repeated with essentially identical results.

Supplementary Material Available: Experimental procedures and spectral data for stannanes 5 and 6 (2 pages). Ordering information is given on any current masthead page.

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Ozonolyses of Cytosines and Guanine

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Damage to biological systems by a photochemical oxidant, whose major component consists of ozone, has been reported.[1] The study of the ozonization reaction of cellular substances is one of the most important subjects in ozone chemistry. On the basis of biological evidence, the relationships between mutagenesis or carcinogenesis and ozone have been reported.[2] Christensen and Giese have reported that the nucleic acid base moiety is preferentially decomposed in the reaction of ozone with DNA and RNA.[3] Fetner has reported ozone-induced chromosome breakage in human cell cultures.[4] Ishizaki et al. have reported that a direct ozone attack process on nucleic acid bases is predominant in the cases of nucleotides derived from cytidine, uridine, thymidine, and guanosine, while the reaction of a hydroxyl radical, a decomposition product of ozone in water, is important in the case of the nucleotide derived from adenosine.[5] Therefore, it is of interest to examine the reaction of nucleic acid bases with ozone. We have reported the reactions of uracils,[6] thio- and azauracils,[7] and pyrimidine nucleosides[8] with ozone. In our continuing series of studies on the reaction of nucleic acid bases with ozone, the ozonolyses of cytosines and guanine are examined in this report.

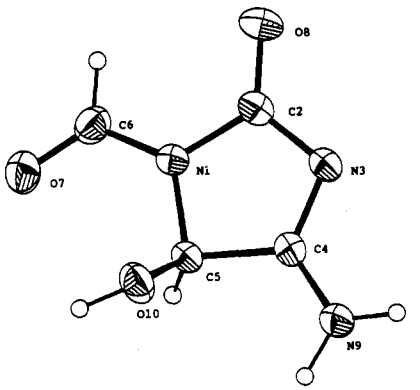

Figure 1. ORTEP view of **2a**.

Table I. Ozonolysis of Cytosines 1

run	compd	substituent R^1	R^2	R^3	yield, of 2, %[a]
1	**a**	NH_2	H	H	66
2	**b**	NHMe	H	H	45
3	**c**	NHC_5H_9	H	H	52
4	**d**	NHC_6H_{11}	H	H	36
5	**e**	NHC_7H_{13}	H	H	54
6	**f**	$NHCH(Me)C_6H_5$	H	H	30
7	**g**	NMe_2	H	H	56
8	**h**	$N(CH_2)_4$	H	H	18
9	**i**	$N(CH_2)_5$	H	H	23
10	**j**	$N(CH_2CH_2OCH_2CH_2)$	H	H	7
11	**k**	NH_2	Me	H	20
12	**l**	NH_2	H	Me	46

[a] Isolated yield.

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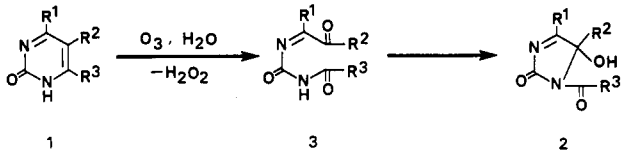
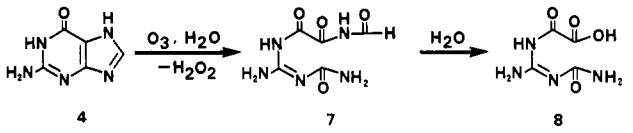
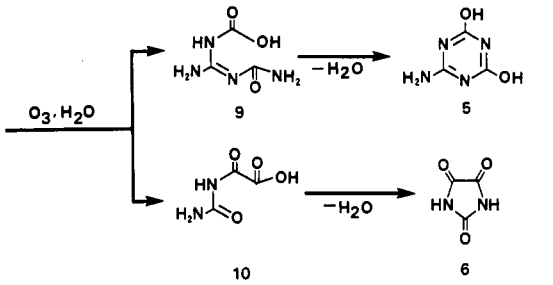
0022-3263/91/1956-4987$02.50/0

Scheme I



Scheme II





The reaction of cytosines 1 with ozone gave 1-acyl-5-hydroxy-1*H*-imidazol-2(5*H*)-ones **2**, which gave satisfactory elemental analyses and spectral data consistent with the assigned structures.

X-ray crystallography of **2a** was undertaken in order to positively determine the structure of 4-amino-1-formyl-5-hydroxy-1*H*-imidazol-2(5*H*)-one (**2a**). Figure 1 shows the ORTEP view of **2a**. 4-Amino-1*H*-imidazol-2(5*H*)-one **2a** existed as the amino form in the solid state. The imidazolone ring was planar. The deviation of the N9 atom from the planar imidazolone ring was only 0.033 Å. Table I summarizes the results of the ozonolysis of cytosines. The ORD spectroscopy of **2** showed that they were racemic.

Scheme I shows a reasonable reaction mechanism. The ozonolysis of the olefinic bond of cytosines **1** gives key intermediates **3** followed by intramolecular cyclization to afford 1-acyl-5-hydroxy-1*H*-imidazol-2(5*H*)-ones **2**. The other C–N bonds of **3** can be hydrolyzed to give unidentified products.

The reaction of guanine (**4**) with ozone gave 2-amino-4,6-dihydroxy-1,3,5-triazine (**5**) in 40% yield and a trace amount of parabanic acid (**6**) accompanied by unidentified products that were not developed by an eluent. The products **5** and **6** were identified by comparing their spectral data with those of authentic samples.

Scheme II shows the reaction mechanism. The ozonolysis of the C4–C5 bond of **4** gives an intermediate, **7**, which is hydrolyzed to afford α-keto carboxylic acid **8**. The ozonization of the purine skeleton has been reported in the reaction of caffein with ozone.[9] 2-Amino-4,6-dihydroxy-1,3,5-triazine (**5**) can be formed by the ozonization of **8** to give carboxylic acid **9**, followed by intramolecular cyclization. Since the ozonization of α-diketones to give dicarboxylic acid has been reported,[10] it is reasonable that the ozonization of α-keto carboxylic acid **8** gives **9** in water. Parabanic acid (**6**) can be formed by the hydrolysis and/or ozonization of **8** to give **10**, followed by intramolecular cyclization and dehydration. The other C–N bonds of the intermediates 7–10 can be hydrolyzed to give unidentified products.

Experimental Section

Instruments. Ozone was generated by a Nihon Ozon 0-1-2 ozonizer. Mass spectra were recorded on Shimadzu QP-1000 and 9020-DF spectrometers. NMR spectra were obtained on a JEOL JNM-GX 270 FT NMR spectrometer. Melting points were measured with a Yanagimoto micro-melting point apparatus and are uncorrected.

Materials. Commercially available cytosine (**1a**) (Kohjin Co., Ltd.), 5-methylcytosine (**1k**) (Tokyo Kasei Kogyo Co., Ltd.), and guanine (**4**) (Tokyo Kasei Kogyo Co., Ltd.) were used without further purification. The other cytosines **1c**, **1d**, **1e**, **1f**, **1i**, and **1j** were synthesized as described in the literature.[11] In a general procedure, an ethanol solution (40 mL) of 4-ethoxy-2(1*H*)-pyrimidinone (2 g, 14 mmol) and an amine (50 mmol) in a sealed tube was heated at 120 °C for 5 h. After the reaction, the solvent was evaporated. The resultant precipitate was recrystallized from ethanol. The purity of all starting materials was checked by TLC (SiO_2, AcOEt–Me_2CHOH–H_2O, 75:16:9, or Me_2CHOH–NH_4OH–H_2O, 7:1:2). The physical and spectral data of the materials follow.

4-(Methylamino)-2(1*H*)-pyrimidinone (1b): mp 287–288 °C (lit.[12] mp 270 °C); ^1H NMR (DMSO-d_6) δ 2.73 (d, J = 4.0 Hz, 3 H), 5.57 (d, J = 7.0 Hz, 1 H), 7.23 (d, J = 7.0 Hz, 1 H), 7.5 (br s, 2 H), exchanges with D_2O), 10.2 (br s, 1 H, exchanges with D_2O); EIMS m/z (rel intensity) 125 (M^+, 100).

4-(Cyclopentylamino)-2(1*H*)-pyrimidinone (1c): mp 285–287 °C; ^1H NMR (DMSO-d_6) δ 1.39–1.88 (m, 8 H), 4.21 (m, 1 H), 5.55 (d, J = 6.7 Hz, 1 H), 7.21 (d, J = 6.7 Hz, 1 H), 7.48 (d, J = 7.3 Hz, 1 H, exchanges with D_2O), 10.06 (br s, 1 H, exchanges with D_2O); EIMS m/z (rel intensity) 179 (M^+, 49), 111 (100); HRMS m/z calcd for $C_9H_{13}N_3O$ 179.1058, found 179.1052. Anal. Calcd for $C_9H_{13}N_3O$: C, 60.32; H, 7.31; N, 23.45. Found: C, 60.08; H, 7.19; N, 23.27.

4-(Cyclohexylamino)-2(1*H*)-pyrimidinone (1d): mp 271–272 °C; ^1H NMR (DMSO-d_6) δ 1.06–1.86 (m, 10 H), 3.75 (m, 1 H), 5.58 (d, J = 7.0 Hz, 1 H), 7.23 (d, J = 7.0 Hz, 1 H), 7.40 (s, 1 H, exchanges with D_2O), 10.35 (br s, 1 H, exchanges with D_2O); EIMS m/z (rel intensity) 193 (M^+, 33), 112 (100); HRMS m/z calcd for $C_{10}H_{15}N_3O$ 193.1214, found 193.1218. Anal. Calcd for $C_{10}H_{15}N_3O$: C, 62.15; H, 7.82; N, 21.74. Found: C, 61.60; H, 7.78; N, 21.80.

4-(Cycloheptylamino)-2(1*H*)-pyrimidinone (1e): mp 211–212 °C; ^1H NMR (DMSO-d_6) δ 1.41–1.84 (m, 12 H), 4.00 (m, 1 H), 5.55 (d, J = 7.9 Hz, 1 H), 7.22 (s, 1 H, exchanges with D_2O), 7.42 (d, J = 7.9 Hz, 1 H), 10.12 (s, 1 H, exchanges with D_2O); EIMS m/z (rel intensity) 207 (M^+, 31), 136 (100); HRMS m/z calcd for $C_{11}H_{17}N_3O$ 207.1371, found 207.1381. Anal. Calcd for $C_{11}H_{17}N_3O$: C, 63.74; H, 8.26; N, 20.27. Found: C, 63.48; H, 8.33; N, 20.11.

4-[(α-Methylbenzyl)amino]-2(1*H*)-pyrimidinone (1f): mp 267–268 °C; ^1H NMR (DMSO-d_6) δ 1.40 (d, J = 6.7 Hz, 3 H), 5.20 (q, J = 6.7 Hz, 1 H), 5.66 (d, J = 7.3 Hz, 1 H), 7.23 (s, 1 H, exchanges with D_2O), 7.26–7.33 (m, 5 H), 7.92 (d, J = 7.3 Hz, 1 H), 10.22 (s, 1 H, exchanges with D_2O); EIMS m/z (rel intensity) 215 (M^+, 57), 105 (100); HRMS m/z calcd for $C_{12}H_{13}N_3O$ 215.1058, found 215.1076. Anal. Calcd for $C_{12}H_{13}N_3O$: C, 66.96; H, 6.09; N, 19.52. Found: C, 66.71; H, 5.94; N, 19.59.

4-(Dimethylamino)-2(1*H*)-pyrimidinone (1g): mp 251–255 °C (lit.[13] mp 254.5–256 °C); ^1H NMR (DMSO-d_6) δ 3.01 (s, 6 H), 5.86 (d, J = 8.0 Hz, 1 H), 7.39 (d, J = 8.0 Hz, 1 H), 10.45 (br s, 1 H, exchanges with D_2O); EIMS m/z (rel intensity) 139 (M^+, 100).

4-(1-Pyrrolidinyl)-2(1*H*)-pyrimidinone (1h): mp 283–285 °C (lit.[14] mp 290–293 °C); ^1H NMR (DMSO-d_6) δ 1.87–1.93 (m, 4 H), 3.40–3.43 (m, 4 H), 5.68 (d, J = 7.3 Hz, 1 H), 7.39 (d, J = 7.3 Hz, 1 H), 10.41 (br s, 1 H, exchanges with D_2O); EIMS m/z (rel intensity) 165 (M^+, 68), 136 (100).

4-Piperidino-2(1*H*)-pyrimidinone (1i): mp 243–244 °C; ^1H NMR (DMSO-d_6) δ 1.45–1.60 (m, 6 H), 3.50–3.70 (m, 4 H), 5.98

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(d, J = 7.6 Hz, 1 H), 7.39 (d, J = 7.6 Hz, 1 H), 10.36 (br s, 1 H, exchanges with D_2O); EIMS m/z (rel intensity) 179 (M^+, 100); HRMS m/z calcd for $C_9H_{13}N_3O$ 179.1058, found 179.1041. Anal. Calcd for $C_9H_{13}N_3O$: C, 60.32; H, 7.31; N, 23.45. Found: C, 60.06; H, 7.20; N, 23.60.

4-Morpholino-2(1*H*)-pyrimidinone (1j): mp 248–250 °C; ^1H NMR (DMSO-d_6) δ 2.40–2.60 (m, 4 H), 3.50–3.70 (m, 4 H), 5.99 (d, J = 7.3 Hz, 1 H), 7.47 (d, J = 7.3 Hz, 1 H), 10.50 (br s, 1 H, exchanges with D_2O); EIMS m/z (rel intensity) 181 (M^+, 84), 124 (100); HRMS m/z calcd for $C_8H_{11}N_3O_2$ 181.0851, found 181.0855. Anal. Calcd for $C_8H_{11}N_3O_2$: C, 53.03; H, 6.12; N, 23.19. Found: C, 52.77; H, 5.91; N, 23.39.

6-Methyl-2(1*H*)-pyrimidinone (1l): mp >300 °C (lit.[15] mp 361–363 °C); ^1H NMR (DMSO-d_6) δ 2.05 (s, 3 H), 5.44 (s, 1 H), 6.96 (s, 2 H, exchanges with D_2O), 10.45 (br s, 1 H, exchanges with D_2O); EIMS m/z (rel intensity) 125 (M^+, 94), 42 (100).

Ozonolysis of Cytosines 1. In a general procedure, an aqueous solution (100 mL) of cytosine (2 mmol) was bubbled through an O_3–O_2 mixture (O_3, 0.15 mmol min^{-1}; O_2, 200 mL min^{-1}, 30–60 min) at room temperature. The end point of the reaction was monitored by TLC (SiO_2, AcOEt–Me_2CHOH–H_2O, 75:16:9). After the reaction, in order to remove the dissolved ozone, N_2 gas (100 mL min^{-1}) was bubbled through the solution for 5 min. The reaction mixture was then allowed to stand overnight. The disappearance of peroxide activity was checked by a KI test. The ozonized mixture was carefully concentrated by using a rotary pump at room temperature. The products were isolated by column chromatography (SiO_2, AcOEt–Me_2CHOH–H_2O, 75:16:9). The physical and spectral data of the isolated products follow.

4-Amino-1-formyl-5-hydroxy-1*H*-imidazol-2(5*H*)-one (2a): mp 230–231 °C dec; ^1H NMR (DMSO-d_6) δ 5.73 (d, J = 8.9 Hz, 1 H), 7.83 (d, J = 8.9 Hz, 1 H, exchanges with D_2O), 8.68 (s, 1 H, exchanges with D_2O), 8.81 (s, 1 H), 8.94 (s, 1 H, exchanges with D_2O); ^{13}C NMR (DMSO-d_6) δ 77 (d), 159 (s), 164 (s), 179 (s); EIMS m/z (rel intensity) 143 (M^+, 2), 43 (100); CIMS (C_4H_{10}) m/z 144 (MH^+, 100); HRMS m/z calcd for $C_4H_5N_3O_3$ 143.0090, found 143.0089. Anal. Calcd for $C_4H_5N_3O_3$: C, 33.57; H, 3.52; N, 29.36. Found: C, 33.76; H, 3.34; N, 29.29.

1-Formyl-5-hydroxy-4-(methylamino)-1*H*-imidazol-2-(5*H*)-one (2b): mp 217–220 °C; ^1H NMR (DMSO-d_6) δ 2.89 (s, 3 H), 5.78 (d, J = 7.9 Hz, 1 H), 7.46 (d, J = 7.9 Hz, 1 H, exchanges with D_2O), 8.82 (s, 1 H), 9.20 (br s, 1 H, exchanges with D_2O); ^{13}C NMR (DMSO-d_6) δ 29 (q), 76 (d), 159 (d), 163 (s), 177 (s); EIMS m/z (rel intensity) 157 (M^+, 4), 56 (100); CIMS (C_4H_{10}) m/z 158 (MH^+, 100); HRMS m/z calcd for $C_5H_7N_3O_3$ 157.0487, found 157.0478. Anal. Calcd for $C_5H_7N_3O_3$: C, 38.22; H, 4.49; N, 26.74. Found: C, 38.10; H, 4.55; N, 26.75.

4-(Cyclopentylamino)-1-formyl-5-hydroxy-1*H*-imidazol-2(5*H*)-one (2c): mp 223–224 °C; ^1H NMR (DMSO-d_6) δ 1.54–1.90 (m, 8 H), 4.13 (m, 1 H), 5.72 (d, J = 9.2 Hz, 1 H), 7.36 (d, J = 9.2 Hz, 1 H, exchanges with D_2O), 8.81 (s, 1 H), 9.30 (s, 1 H, exchanges with D_2O); ^{13}C NMR (DMSO-d_6) δ 23 (t), 32 (t), 54 (d), 76 (d), 157 (s), 164 (d), 174 (s); EIMS m/z (rel intensity) 211 (M^+, 9), 41 (100); CIMS (C_4H_{10}) m/z 212 (MH^+, 100); HRMS m/z calcd for $C_9H_{13}N_3O_3$ 211.0956, found 211.0975. Anal. Calcd for $C_9H_{13}N_3O_3$: C, 51.18; H, 6.20; N, 19.89. Found: C, 51.35; H, 6.15; N, 19.68.

4-(Cyclohexylamino)-1-formyl-5-hydroxy-1*H*-imidazol-2-(5*H*)-one (2d): mp 232–233 °C; ^1H NMR (DMSO-d_6) δ 1.15–1.83 (m, 10 H), 3.67 (m, 1 H), 5.72 (s, 1 H), 7.38 (s, 1 H, exchanges with D_2O), 8.81 (s, 1 H), 9.20 (s, 1 H, exchanges with D_2O); ^{13}C NMR (DMSO-d_6) δ 24 (t), 25 (t), 31 (t), 49 (d), 77 (d), 157 (s), 166 (d), 174 (s); EIMS m/z (rel intensity) 225 (M^+, 2), 144 (100); CIMS (C_4H_{10}) m/z 226 (MH^+, 100); HRMS m/z calcd for $C_{10}H_{15}N_3O_3$ 225.1113, found 225.1121. Anal. Calcd for $C_{10}H_{15}N_3O_3$: C, 53.32; H, 6.71; N, 18.65. Found: C, 53.51; H, 6.92; N, 18.61.

4-(Cycloheptylamino)-1-formyl-5-hydroxy-1*H*-imidazol-2(5*H*)-one (2e): mp 242–243 °C; ^1H NMR (DMSO-d_6) δ 1.41–1.89 (m, 12 H), 3.88 (m, 1 H), 5.70 (d, J = 8.5 Hz, 1 H), 7.35 (d, J = 8.5 Hz, 1 H, exchanges with D_2O), 8.81 (s, 1 H), 9.26 (s, 1 H, exchanges with D_2O); ^{13}C NMR (DMSO-d_6) δ 24 (t), 28 (t), 34 (t), 54 (d), 77 (d), 160 (s), 163 (s), 175 (s); EIMS m/z (rel intensity) 239 (M^+, 2), 55 (100); CIMS (C_4H_{10}) m/z 240 (MH^+, 100); HRMS m/z calcd for $C_{11}H_{17}N_3O_3$ 239.1269, found 239.1241. Anal. Calcd for $C_{11}H_{17}N_3O_3$: C, 55.22; H, 7.16; N, 17.56. Found: C, 55.04; H, 7.13; N, 17.71.

1-Formyl-5-hydroxy-4-[(α-methylbenzyl)amino]-1*H*-imidazol-2(5*H*)-one (2f): mp 221–222 °C; ^1H NMR (DMSO-d_6) δ 1.49 (d, J = 6.7 Hz, 3 H), 5.08 (m, 1 H), 5.79 (d, J = 8.6 Hz, 1 H), 6.68 (d, J = 8.6 Hz, 1 H, exchanges with D_2O), 7.25–7.50 (m, 5 H), 8.79 (s, 1 H), 9.78 (s, 1 H, exchanges with D_2O); EIMS m/z (rel intensity) 247 (M^+, 25), 105 (100); CIMS (C_4H_{10}) m/z 248 (MH^+, 100); HRMS m/z calcd for $C_{12}H_{13}N_3O_3$ 247.0956, found 247.0957. Anal. Calcd for $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.30; N, 16.99. Found: C, 58.50; H, 5.52; N, 16.77.

4-(Dimethylamino)-1-formyl-5-hydroxy-1*H*-imidazol-2-(5*H*)-one (2g): mp 210–213 °C; ^1H NMR (DMSO-d_6) δ 3.13 (s, 3 H), 3.18 (s, 3 H), 6.11 (d, J = 8.9 Hz, 1 H), 7.50 (d, J = 8.9 Hz, 1 H, exchanges with D_2O), 8.81 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 38 (q), 75 (d), 159 (d), 163 (s), 176 (s); EIMS m/z 171 (M^+, 7), 44 (100); CIMS (C_4H_{10}) m/z 172 (MH^+, 100); HRMS m/z calcd for $C_4H_9N_3O_3$ 171.0644, found 171.0653. Anal. Calcd for $C_6H_9N_3O_3$: C, 42.11; H, 5.30; N, 24.55. Found: C, 42.26; H, 5.30; N, 24.70.

1-Formyl-5-hydroxy-4-pyrrolidinyl-1*H*-imidazol-2(5*H*)-one (2h): mp 160–161 °C; ^1H NMR (DMSO-d_6) δ 1.90–1.95 (m, 4 H), 3.24–3.40 (m, 4 H), 5.08 (s, 1 H), 6.03 (s, 1 H, exchanges with D_2O), 8.81 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 24 (t), 48 (t), 76 (d), 159 (s), 162 (d), 174 (s); EIMS m/z (rel intensity) 197 (M^+, 16), 96 (100); CIMS (C_4H_{10}) m/z 198 (MH^+, 100); HRMS m/z calcd for $C_8H_{11}N_3O_3$ 197.0800, found 197.0777. Anal. Calcd for $C_8H_{11}N_3O_3$: C, 48.73; H, 5.62; N, 21.31. Found: C, 49.00; H, 5.48; N, 21.21.

1-Formyl-5-hydroxy-4-piperidino-1*H*-imidazol-2(5*H*)-one (2i): mp 125–126 °C; ^1H NMR (DMSO-d_6) δ 1.55–1.62 (m, 6 H), 2.60–2.70 (m, 4 H), 5.08 (s, 1 H), 6.70 (br s, 1 H, exchanges with D_2O), 8.32 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 23 (t), 35 (t), 47 (t), 77 (d), 157 (s), 164 (d), 174 (s); EIMS m/z (rel intensity) 211 (M^+, 3), 44 (100); CIMS (C_4H_{10}) 212 (NH^+, 100); HRMS m/z calcd for $C_9H_{13}N_3O_3$ 211.0956, found 211.0955. Anal. Calcd for $C_9H_{13}N_3O_3$: C, 51.18; H, 6.20; N, 19.89. Found: C, 51.31; H, 5.97; N, 19.71.

1-Formyl-5-hydroxy-4-morpholino-1*H*-imidazol-2(5*H*)-one (2j): mp 256–257 °C; ^1H NMR (DMSO-d_6) δ 2.20–2.60 (m, 4 H), 3.63–3.74 (m, 4 H), 6.15 (d, J = 8.3 Hz, 1 H), 7.54 (d, J = 8.3 Hz, 1 H, exchanges with D_2O), 8.83 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 75 (d), 159 (s), 163 (d), 175 (s); EIMS m/z (rel intensity) 213 (M^+, 14), 44 (100); CIMS (C_4H_{10}) 214 (MH^+, 100); HRMS m/z calcd for $C_8H_{11}N_3O_4$ 213.0749, found 213.0742. Anal. Calcd for $C_8H_{11}N_3O_4$: C, 45.07, H, 5.20; N, 19.71. Found: C, 44.78; H, 5.25; N, 19.56.

4-Amino-1-formyl-5-hydroxy-5-methyl-1*H*-imidazol-2-(5*H*)-one (2k): mp 197 °C dec; ^1H NMR (DMSO-d_6) δ 1.71 (s, 3 H), 7.24 (s, 1 H, exchanges with D_2O), 8.69 (s, 1 H, exchanges with D_2O), 8.81 (s, 1 H), 8.93 (s, 1 H, exchanges with D_2O); ^{13}C NMR (DMSO-d_6) δ 22 (q), 83 (s), 159 (d), 163 (s), 182 (s); EIMS m/z (rel intensity) 129 (M^+ – CO, 4), 43 (100); CIMS (C_4H_{10}) m/z 158 (MH^+, 100). HRMS m/z calcd for $C_5H_7N_3O_3$ 157.0487, found 157.0491. Anal. Calcd for $C_5H_7N_3O_3$: C, 38.22; H, 4.49; N, 26.74. Found: C, 38.50; H, 4.47; N, 26.59.

1-Acetyl-4-amino-5-hydroxy-1*H*-imidazol-2(5*H*)-one (2l): mp 203–205 °C; ^1H NMR (DMSO-d_6) δ 2.34 (s, 3 H), 5.73 (d, J = 7.9 Hz, 1 H), 7.20 (d, J = 7.9 Hz, 1 H, exchanges with D_2O), 8.45 (s, 1 H, exchanges with D_2O), 8.70 (s, 1 H, exchanges with D_2O); ^{13}C NMR (DMSO-d_6) δ 24 (q), 78 (d), 169 (s), 173 (s), 178 (s); EIMS m/z (rel intensity) 157 (M^+, 10), 42 (100); CIMS (C_4H_{10}) m/z 158 (MH^+, 100); HRMS m/z calcd for $C_5H_7N_3O_3$ 157.0487, found 157.0497. Anal. Calcd for $C_5H_7N_3O_3$: C, 38.22; H, 4.49; N, 26.74. Found: C, 38.12; H, 4.63; N, 26.85.

Ozonolysis of Guanine (4). An aqueous suspension (100 mL) of guanine (4) (0.5 mmol) was bubbled through an O_3–O_2 mixture (O_3; 0.4 mmol min^{-1}; O_2, 150 mL min^{-1}, 30 min) at room temperature, until the mixture turned transparent. After the reaction, nitrogen gas (100 mL min^{-1}) was bubbled through the solution for 5 min. The reaction mixture was allowed to stand overnight. The disappearance of peroxide activity was checked by a KI test. The ozonized mixture was concentrated by using a rotary evaporator and chromatographed on preparative TLC (SiO_2, Me_2CHOH–NH_4OH–H_2O, 7:1:2). 2-Amino-4,6-dihydroxy-1,3,5-triazine (5) (40%) and parabanic acid (6) (trace) were isolated. These products were identified by comparing the spectral data

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with those of authentic samples. They were also treated with bis(trimethylsilyl)trifluoroacetamide at 150 °C for 5 min to give trimethylsilyl derivatives, which were analyzed by GC–mass spectroscopy.[16] The mass spectra were consistent with those of authentic samples. The conditions of the gas chromatography are as follows: column, glass, 3 mm × 1 m, 2% Silicone OV-1 on Gas Chrom Q (60–80 mesh); column temperature, 80–240 °C (10 °C min^{-1}); injection temperature, 240 °C; carrier gas, He (30 mL min^{-1}). The physical and spectral data of the products follow.

2-Amino-4,6-dihydroxy-1,3,5-triazine:[17] mp > 300 °C; ^1H NMR (DMSO-d_6) δ 5.77 (s, 2 H, exchanges with D_2O), 10.43 (s, 2 H, exchanges with D_2O); EIMS (70 eV) m/z (rel intensity) 128 (M^+, 51), 43 (100); HRMS m/z calcd for $C_3H_4N_4O_2$ 128.0348, found 128.0334; EIMS of trimethylsilyl derivative of **5** (20 eV) m/z (rel intensity) 344 (M^+ + 3TMS, 100).

Parabanic acid (6): mp 236–240 °C (lit.[18] mp 238–244 °C); ^1H NMR (DMSO-d_6) δ 11.75 (br, 2 H, exchanges with D_2O); EIMS (70 eV) m/z (rel intensity) 114 (M^+, 72), 43 (100); EIMS of trimethylsilyl derivative of **6** (20 eV) m/z (rel intensity) 258 (M^+ + 2TMS, 12), 243 (53), 100 (100).

X-ray Measurement of 4-Amino-1-formyl-5-hydroxy-1*H*-imidazol-2(5*H*)-one (2a). All data were collected at 23 °C on a Rigaku AFC-6R diffractometer with graphite-monochromated Mo-K_α radiation in the range $2\theta < 55°$ of the ω–2θ scan mode. A total of 1460 reflections having $|F| > 3\sigma|F|$ were used in the structure refinement. Crystal data for **2a**: monoclinic, $P2_1/c$, a = 11.919 (2) Å, b = 6.969 (2) Å, c = 6.919 (10) Å, α = 90.30 (5)°, V = 574.6 (8) Å^3, D(calcd) = 1.65 g cm^{-3}, Z = 4. Crystal size: 0.2 × 0.2 × 0.4 mm^3. The structure was solved by direct method (MULTAN78) and refined by block-diagonal Fourier using the UNICS program at Osaka University. The non-hydrogen atoms in **2a** were assigned anisotropic thermal parameters. All hydrogen atoms were located on a different electron density map and were included in structure factors. The final conventional index R is 0.0509. Tables of atomic coordinates, bond distances and angles, and anisotropic temperature coefficients are available as supplementary material.

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Registry No. **1a**, 7-30-7; **1b**, 6220-47-9; **1c**, 134419-26-4; **1d**, 134419-27-5; **1e**, 134419-28-6; **1f**, 134419-29-7; **1g**, 6220-48-0; **1h**, 29840-48-0; **1i**, 62968-15-4; **1j**, 62968-21-2; **1k**, 554-01-8; **1l**, 6220-50-4; **2a**, 134419-30-0; **2b**, 134419-31-1; **2c**, 134419-32-2; **2d**, 134419-33-3; **2e**, 134419-34-4; **2f**, 134419-35-5; **2g**, 134419-36-6; **2h**, 134419-37-7; **2i**, 134419-38-8; **2j**, 134419-39-9; **2k**, 134419-41-3; **2l**, 134419-41-3; **4**, 73-40-5; **5**, 645-93-2; **6**, 120-89-8; 4-etoxy-2-(1*H*)-pyrimidinone, 6220-43-5.

Supplementary Material Available: Tables of atomic coordinates, isotropic thermal parameters, bond distances and angles, and X-ray crystallographic data for **2a** (2 pages). Ordering information is given on any current masthead page.

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A Short, Enantioselective Synthesis of the Carbocyclic Nucleoside Carbovir

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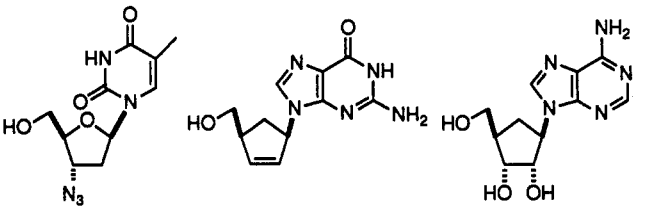
The continued interest in the synthesis of nucleosides and nucleoside analogues is reflected in the successful use of this class of compound as therapy in viral and cancerous diseases.[1] This interest has recently become more focused with the identification of the retrovirus HIV-1 as the causative agent of AIDS (Aquired Immune Deficiency Syndrome) and the finding that certain nucleoside analogues (most notably 3′-azido-2′,3′-dideoxythymidine (AZT), dideoxyinosine (ddI), dideoxyadenosine (ddA), and dideoxycytidine (ddC)) act as potent inhibitors of HIV-1 replication.[2] This antiviral activity is believed to be due to the inhibition of the key viral enzyme reverse transcriptase. In addition, these compounds, by lacking a 3′-hydroxyl function, act as terminators of the growing viral DNA chain. We recently became interested in a carbocyclic nucleoside analogue (carbovir) that was reported by Vince et al.[3] to be a potent inhibitor of reverse transcriptase and so has potential as a therapy against AIDS.



As part of our initial investigations, we required a convenient and flexible synthesis of the compound and analogues. Unfortunately, the published synthesis of carbovir is somewhat lengthy and involves a wasteful resolution procedure as the final step.[4] In order to secure a shorter, more efficient, and preferably enantioselective synthesis of carbovir our attention was focused on some organopalladium chemistry that has precedent in forming cis-1,4-substituted cyclopentenes.[5] Trost recently reported the synthesis of a related carbocyclic nucleoside (aristeromycin) via a route that involved the sequential palladium-catalyzed introduction of a purine base (adenine) followed by another nucleophilic addition of a sulfonyl-stabilized nitronate onto a cyclopentane ring.[6]

In line with this precedent, treatment of cyclopentadiene monoepoxide with 2-amino-6-chloropurine (a commonly used surrogate for the remarkably insoluble purine base guanine) under catalysis by palladium(0) gave the cis-

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