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Oxidation of Pyrimidine Base Derivatives with *m*-Chloroperbenzoic Acid

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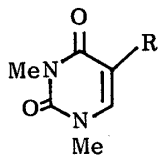
Oxidations of 1,3-dimethylthymine (**1**), 3′,5′-diacetylthymidine (**2**), 1,3-dimethyluracil (**3**), 5-fluoro-1,3-dimethyluracil (**4**), and 2′,3′,5′-triacetyluridine (**5**) with *m*-chloroperbenzoic acid were investigated. Dimethylthymine (**1**) gave the hydroxy ester (**6**), the stereostructure of which was determined by an X-ray analysis, while diacetylthymidine (**2**) gave **10a** and **10b**. Dimethyluracil (**3**) provided **11**, **12**, and **13**, and 5-fluoro-dimethyluracil (**4**) provided **11**. Triacetyluridine (**5**) afforded **16** in dichloromethane and **17** in benzene. A plausible mechanism for formation of these oxidation products is presented.

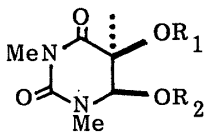
Keywords——*m*-chloroperbenzoic acid oxidation; 1,3-dimethylthymine; 3′,5′-diacetylthymidine; 1,3-dimethyluracil; 5-fluoro-1,3-dimethyluracil; 2′,3′,5′-triacetyluridine; *cis*-1,3-dimethyl-5,6-dihydroxy-5,6-dihydrothymine

In connection with the damage and repair of nucleic acids, the oxidation of nucleic acids and related compounds has received considerable attention.[1-13] Our interest has been focused on the oxidation of nucleic acids, particularly pyrimidine bases, with active oxygen species such as hydrogen peroxide, singlet oxygen, lipohydroperoxide and so on, in order to understand the mechanisms of oxidative decomposition of these bases. As part of a research program aimed in this direction, we briefly described the results of oxidation of 1,3-dimethylthymine (**1**), 3′,5′-diacetylthymidine (**2**), 1,3-dimethyluracil (**3**), 5-fluoro-1,3-dimethyluracil (**4**), and 2′,3′,5′-triacetyluridine (**5**) with *m*-chloroperbenzoic acid (MCPBA) as a representative acyl peroxide.[14,15] The details of these oxidation reactions are the subject of this paper.

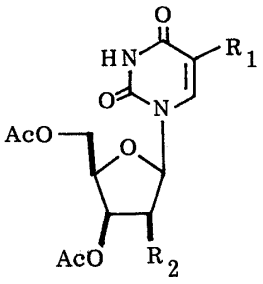
Oxidation of **1** with MCPBA in dichloromethane (CH_2Cl_2) gave the hydroxy ester (**6**) in 76.4% yield, while in the presence of sodium acetate (AcONa), oxidation of **1** with MCPBA gave **6** and the monoacetate (**7**) in 18.2% and 26.7% yields, respectively. Hydrolysis of **6** with ammonia (NH_3) in dioxane at room temperature afforded the diol (**8**) in 54.6% yield. Compound **6** was regenerated by acylation of **8** with the mixed anhydride prepared from isobutyl chloroformate and *m*-chlorobenzoic acid.[16] Acetylation of **8** with acetic anhydride in pyridine at room temperature afforded the diacetate (**9**) in 22.5% yield along with the monoacetate (**7**). The facile acetylation of the tertiary hydroxy group in **8** at room temperature, which may be caused by acyl migration, suggests that the two hydroxy groups have a *cis* relationship. The *cis* relationship of the C_5-hydroxy group and the C_6-acyloxy group in **6** was ultimately established by an X-ray analysis of the compound (**6**) (see Fig. 1 and Experimental). Therefore, the stereostructures of the hydroxy ester, the monoacetate, and the diol can be represented by the formulas **6**, **7**, and **8**, respectively. The present method (oxidation and hydrolysis) provides another procedure for stereoselective preparation of the *cis* diol (**8**), in addition to the previous methods.[4,5,17] Oxidation of diacetylthymidine (**2**) with MCPBA in CH_2Cl_2 under reflux gave the hydroxy esters (**10a** and



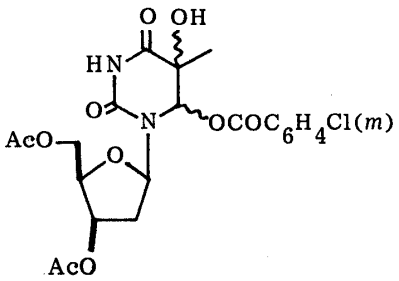
1 : R=Me
3 : R=H
4 : R=F
13 : R=Cl
15 : R=OCOC$_6$H$_4$Cl(*m*)



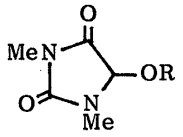
6 : R$_1$=H, R$_2$=COC$_6$H$_4$Cl(*m*)
7 : R$_1$=H, R$_2$=Ac
8 : R$_1$=R$_2$=H
9 : R$_1$=R$_2$=Ac



2 : R$_1$=Me, R$_2$=H
5 : R$_1$=H, R$_2$=OAc
16 : R$_1$=Cl, R$_2$=OAc
17 : R$_1$=OCOC$_6$H$_4$Cl(*m*), R$_2$=OAc



10a,b



11 : R=COC$_6$H$_4$Cl(*m*)
14 : R=Ac

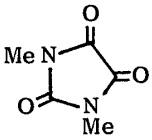


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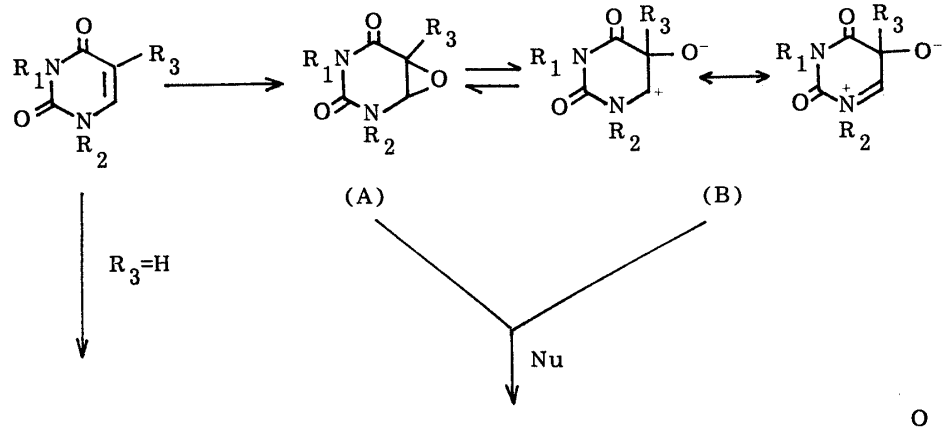
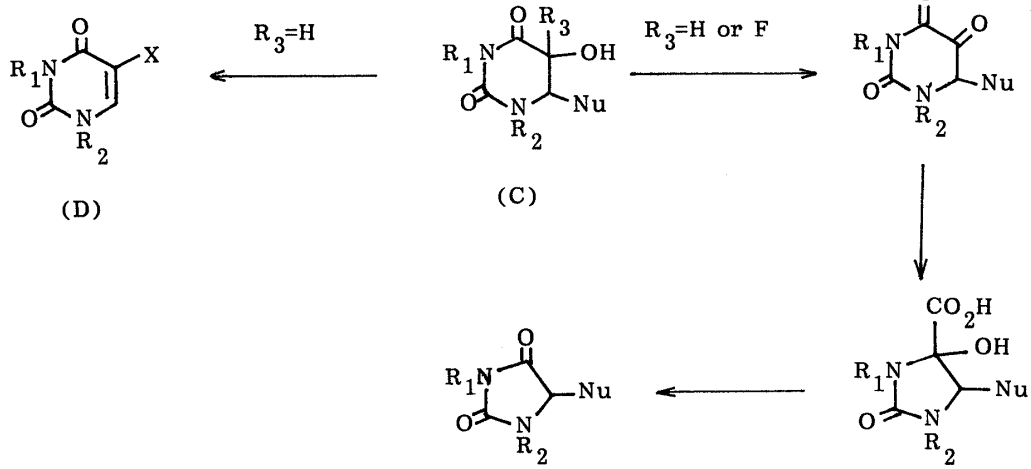
Chart 1



(A) (B)



(D) (C) (E)

Chart 2

10b) in 59% and 16.8% yields, respectively. Although the results mentioned above seem to suggest that the newly introduced hydroxy and acyloxy groups in **10a** and **10b** have a *cis* relationship, the stereostructures could not be determined difinitively.

Next, oxidation of uracil derivatives with MCPBA was investigated. Thus, oxidation of **3** with MCPBA in CH_2Cl_2 under reflux gave the ester (**11**), 1,3-dimethylparabanic acid (**12**),[18] and the chloride (**13**)[19] in 3.0, 6.4, and 1.0% yields, respectively, along with 35% recovery of **3**. No diol derivative of **3** was isolated. Oxidation of **4** under similar conditions afforded **11** in 43% yield, and in the presence of AcONa, oxidation of **4** gave **11**, the acetate (**14**), and the ester (**15**) in 9.0, 2.1, and 2.0% yields, respectively, along with 62.2% recovery of **4**. Oxidation of **5** with MCPBA in CH_2Cl_2 under reflux afforded the chloride (**16**) in 12.6% yield along with 59.1% recovery of **5**. On the other hand, the oxidation of **5** in benzene under reflux afforded the ester (**17**) in 4.3% yield along with 47.7% recovery of **5**. It can therefore be presumed that

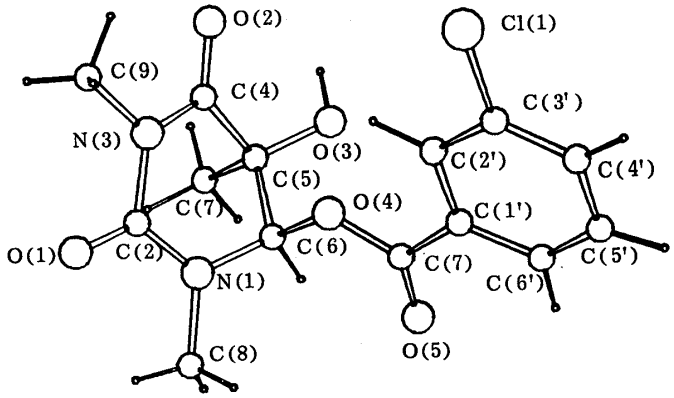


Fig. 1. Molecular Structure of the Hydroxy Ester (**6**)

TABLE I. Atomic Parameters for Non-hydrogen Atoms in the Hydroxy Ester (**6**)

Atom	x	y	z	B_{eq}
Cl(1)	0.5821 (1)	0.4987 (2)	0.8174 (1)	8.33 (9)
N(1)	0.8007 (3)	0.6910 (4)	0.4321 (2)	4.82 (18)
C(2)	0.7037 (4)	0.7461 (6)	0.4106 (2)	4.93 (22)
N(3)	0.6300 (3)	0.6182 (5)	0.4087 (2)	5.67 (19)
C(4)	0.6475 (4)	0.4392 (7)	0.4124 (3)	5.92 (23)
C(5)	0.7579 (3)	0.3826 (6)	0.4172 (3)	5.08 (19)
C(6)	0.8207 (3)	0.5183 (6)	0.4663 (2)	4.51 (19)
C(7)	0.7853 (5)	0.3685 (9)	0.3228 (3)	7.29 (30)
C(8)	0.8824 (5)	0.8206 (8)	0.4356 (5)	6.90 (32)
C(9)	0.5249 (5)	0.6832 (11)	0.3978 (5)	8.98 (41)
O(1)	0.6824 (3)	0.9001 (4)	0.3939 (2)	6.85 (18)
O(2)	0.5809 (3)	0.3314 (5)	0.4095 (3)	9.14 (24)
O(3)	0.7724 (3)	0.2216 (4)	0.4608 (2)	7.08 (18)
O(4)	0.7960 (2)	0.5139 (4)	0.5556 (1)	4.60 (13)
O(5)	0.9579 (2)	0.4959 (6)	0.6075 (2)	7.43 (20)
C(1')	0.8358 (3)	0.4791 (5)	0.7066 (2)	4.26 (18)
C(2')	0.7347 (3)	0.4948 (6)	0.7173 (2)	4.50 (19)
C(3')	0.7086 (3)	0.4790 (6)	0.8014 (3)	5.10 (19)
C(4')	0.7789 (4)	0.4485 (7)	0.8707 (3)	6.14 (24)
C(5')	0.8770 (4)	0.4302 (8)	0.8581 (3)	6.84 (26)
C(6')	0.9062 (3)	0.4446 (7)	0.7765 (3)	5.77 (21)
C(7')	0.8710 (3)	0.4961 (6)	0.6186 (2)	4.61 (19)

Estimated standard deviations are given in parentheses. B_{eq} is the isotropic equivalent of the anisotropic thermal parameter (Hamilton 1959).

TABLE II. Fractional Coordinates and Isotropic Thermal Parameters ($Å^2$) for Hydrogen Atoms in the Hydroxy Ester (**6**)

Atom	x	y	z	B_{iso}
H(3)	0.730 (3)	0.128 (7)	0.430 (3)	8.8 (14)
H(6)	0.894 (3)	0.494 (5)	0.467 (2)	5.6 (10)
H(7A)	0.776 (3)	0.489 (7)	0.288 (3)	7.9 (13)
H(7B)	0.739 (3)	0.275 (7)	0.286 (3)	8.1 (13)
H(7C)	0.859 (4)	0.330 (6)	0.326 (3)	8.4 (14)
H(8A)	0.908 (3)	0.845 (7)	0.497 (3)	9.1 (14)
H(8B)	0.859 (4)	0.924 (7)	0.407 (3)	8.6 (15)
H(8C)	0.938 (4)	0.771 (6)	0.410 (3)	8.7 (13)
H(9A)	0.504 (4)	0.734 (7)	0.339 (3)	8.8 (14)
H(9B)	0.483 (4)	0.573 (6)	0.406 (3)	9.1 (14)
H(9C)	0.508 (4)	0.764 (7)	0.447 (3)	9.0 (14)
H(2′)	0.680 (3)	0.517 (5)	0.666 (2)	5.7 (10)
H(4′)	0.763 (3)	0.435 (5)	0.932 (3)	6.4 (10)
H(5′)	0.924 (3)	0.396 (5)	0.913 (3)	6.5 (10)
H(6′)	0.978 (3)	0.440 (5)	0.767 (2)	6.1 (10)

TABLE III. Anisotropic Thermal Parameters (10^4) for Non-H Atoms in the Hydroxy Ester (**6**)

Atom	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Cl(1)	105 (1)	493 (5)	75 (1)	19 (2)	52 (1)	16 (2)
N(1)	85 (3)	193 (7)	46 (2)	−11 (4)	24 (2)	−4 (3)
C(2)	103 (4)	185 (9)	35 (2)	7 (5)	9 (2)	−4 (3)
N(3)	81 (3)	257 (9)	55 (2)	0 (4)	−4 (2)	−2 (3)
C(4)	107 (4)	243 (11)	48 (2)	−43 (6)	3 (2)	−6 (4)
C(5)	99 (3)	185 (9)	44 (2)	1 (5)	15 (2)	1 (3)
C(6)	78 (3)	203 (9)	39 (2)	6 (4)	23 (2)	0 (3)
C(7)	152 (6)	314 (15)	44 (2)	1 (8)	21 (3)	−31 (5)
C(8)	106 (5)	243 (12)	87 (4)	−40 (6)	42 (3)	−8 (6)
C(9)	91 (5)	457 (21)	101 (5)	24 (8)	−16 (4)	−4 (8)
O(1)	137 (3)	210 (7)	63 (2)	29 (4)	5 (2)	4 (3)
O(2)	117 (3)	363 (11)	113 (3)	−81 (5)	5 (2)	−14 (4)
O(3)	147 (3)	190 (7)	69 (2)	0 (4)	13 (2)	20 (3)
O(4)	60 (2)	289 (7)	33 (1)	8 (3)	13 (1)	3 (2)
O(5)	60 (2)	574 (12)	55 (2)	9 (4)	19 (1)	3 (4)
C(1′)	70 (3)	188 (8)	38 (2)	−5 (4)	9 (2)	−2 (3)
C(2′)	71 (3)	209 (9)	41 (2)	−1 (4)	15 (2)	1 (3)
C(3′)	84 (3)	216 (9)	51 (2)	−1 (5)	28 (2)	−4 (4)
C(4′)	125 (4)	284 (12)	34 (2)	−8 (6)	13 (2)	2 (4)
C(5′)	105 (4)	385 (15)	43 (2)	−5 (6)	−5 (2)	7 (5)
C(6′)	71 (3)	326 (12)	50 (2)	4 (5)	0 (2)	1 (4)
C(7′)	63 (3)	235 (9)	44 (2)	5 (4)	14 (2)	−7 (4)

Estimated standard deviations are given in parentheses. The temperature factor is expressed by the formula, $T=\exp[-(B_{11}h^2+B_{22}k^2+B_{33}l^2+2B_{12}hk+2B_{13}hl+2B_{23}kl)]$.

the chlorine atom in **16** originated from CH_2Cl_2.

The formation of these products could be readily explained by assuming that an initially formed epoxide (A) or a cationic intermediate (B) was attacked by nucleophiles to give their adducts (C). In the case that R_3 is hydrogen or fluorine, the adducts could undergo elimination and/or further oxidative degradation *via* benzylic acid type rearrangement to yield

TABLE IV. Bond Lengths (Å) and Valence Angles (°) in the Hydroxy Ester (**6**)

Bond	Length	Bond	Length
Cl(1)–C(3′)	1.743 (4)	N(1)–C(2)	1.367 (6)
N(1)–C(6)	1.421 (5)	N(1)–C(8)	1.462 (7)
C(2)–N(3)	1.377 (6)	C(2)–O(1)	1.217 (5)
N(3)–C(4)	1.371 (6)	N(3)–C(9)	1.479 (8)
C(4)–C(5)	1.530 (7)	C(4)–O(2)	1.203 (7)
C(5)–C(6)	1.480 (6)	C(5)–C(7)	1.554 (7)
C(5)–O(3)	1.393 (5)	C(6)–O(4)	1.461 (4)
O(4)–C(7′)	1.326 (4)	O(5)–C(7′)	1.193 (5)
C(1′)–C(2′)	1.385 (6)	C(1′)–C(6′)	1.379 (5)
C(1′)–C(7′)	1.500 (5)	C(2′)–C(3′)	1.394 (6)
C(3′)–C(4′)	1.366 (6)	C(4′)–C(5′)	1.354 (8)
C(5′)–C(6′)	1.371 (7)		

Bond	Angle	Bond	Angle
C(2)–N(1)–C(6)	120.2 (4)	C(2)–N(1)–C(8)	119.3 (4)
C(6)–N(1)–C(8)	119.4 (4)	N(1)–C(2)–N(3)	116.7 (4)
N(1)–C(2)–O(1)	122.3 (5)	N(3)–C(2)–O(1)	121.0 (5)
C(2)–N(3)–C(4)	124.8 (4)	C(2)–N(3)–C(9)	116.0 (5)
C(4)–N(3)–C(9)	119.1 (5)	N(3)–C(4)–C(5)	115.9 (4)
N(3)–C(4)–O(2)	122.9 (5)	C(5)–C(4)–O(2)	121.2 (5)
C(4)–C(5)–C(6)	108.7 (4)	C(4)–C(5)–C(7)	107.6 (4)
C(4)–C(5)–O(3)	110.3 (4)	C(6)–C(5)–C(7)	110.7 (4)
C(6)–C(5)–O(3)	108.3 (3)	C(7)–C(5)–O(3)	111.3 (4)
N(1)–C(6)–C(5)	111.7 (3)	N(1)–C(6)–O(4)	108.8 (3)
C(5)–C(6)–O(4)	107.3 (3)	C(6)–O(4)–C(7′)	118.0 (3)
C(2′)–C(1′)–C(6′)	120.7 (3)	C(2′)–C(1′)–C(7′)	120.8 (3)
C(6′)–C(1′)–C(7′)	118.5 (4)	C(1′)–C(2′)–C(3′)	117.1 (3)
Cl(1)–C(3′)–C(2′)	118.4 (3)	Cl(1)–C(3′)–C(4′)	119.6 (4)
C(2′)–C(3′)–C(4′)	122.0 (4)	C(3′)–C(4′)–C(5′)	119.6 (5)
C(4′)–C(5′)–C(6′)	120.4 (4)	C(1′)–C(6′)–C(5′)	120.1 (4)
O(4)–C(7′)–O(5)	124.1 (3)	O(4)–C(7′)–C(1′)	113.1 (3)
O(5)–C(7′)–C(1′)	122.8 (3)		

products (D) and/or (E), as shown in Chart 2. The product (D) may be formed directly from uracil derivatives ($R_3 = H$). Furthermore, the predominant formation of *cis* products, **6** and **7**, is explicable in terms of a *gauche* effect, as it has been demonstrated that the *gauche* conformer is more stable than the *trans* conformer in certain highly electronegatively substituted systems (*gauche* effect).[3,20,21] Hence, it would be reasonable to assume that the nucleophile attacks the intermediate (B) from an energetically favorable direction to yield the *cis* product.

Thus, the formation of such oxidative products as **6** and **7** strongly suggested the possibility of cross-coupling of pyrimidine bases with amines and amino acids by taking advantage of the reactivity of the epoxide (A) or its equivalent (B), and the reactions of this system and related systems are being pursued.[22]

Experimental

Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. The

infrared spectra (IR ν_{max}) were determined on a Shimadzu IR-400 spectrophotometer in chloroform. The proton nuclear magnetic resonance (^{1}H-NMR) spectra were obtained in chloroform-*d* at 200 MHz on a JEOL FX 200 instrument with chemical shifts being reported in parts per million downfield from a tetramethylsilane internal standard (δ 0.0) and couplings in hertz unless otherwise stated. Mass spectra (MS) were taken on a JEOL JMS O1SG-2 instrument (direct inlet) at 70 eV. All reactions were carried out under an atmosphere of argon. The reaction mixture was diluted with CH_2Cl_2 and washed with 10% $Na_2S_2O_3$, 5% $NaHCO_3$, and brine, unless otherwise noted. The extracts were dried over K_2CO_3, and filtered, then the filtrates were concentrated to dryness *in vacuo*. Column chromatography was carried out with Silica gel 60 (E. M. Merck, 70—230 mesh) or Florisil (Floridin Co., 60—100 mesh). Preparative thin-layer chromatography (prep. TLC) was run on 20 × 20 cm plates coated with a 0.25 mm layer of Merck Silica gel PF_{254} and GF_{254}.

Oxidation of 1,3-Dimethylthymine (1) with MCPBA——MCPBA (7 g, 41 mmol) was added to a solution of 2 g (13 mmol) of **1** in 200 ml of dry CH_2Cl_2, and the mixture was stirred for 6 d at room temperature or refluxed for 24 h. The residue was subjected to column chromatography on silica gel (eluted with $CHCl_3$) to give 3.24 g (76.4% yield) of the hydroxy ester (**6**). Recrystallization from hexane–ether produced colorless prisms, mp 110—112 °C. IR: 3500, 1725, 1680 cm^{-1}. ^{1}H-NMR δ: 1.57 (3H, s, C_5-CH_3), 3.21 (3H, s, N-CH_3), 3.30 (3H, s, N-CH_3), 6.16 (1H, s, C_6-H), 7.37 (1H, t, J=7.5), 7.55 (1H, dt, J=7.5, 1.5), 7.82 (1H, dt, J=7.5, 1.5), 7.89 (1H, t, J=1.5). *Anal.* Calcd for $C_{14}H_{15}ClN_2O_5$: C, 51.46; H, 4.62; N, 8.57. Found: C, 51.75; H, 4.66; N, 8.69.

X-Ray Analysis of the Hydroxy Ester (6)——Single crystals of **6** were prepared by slow crystallization from hexane–Et_2O. The crystals were monoclinic, space group $P2_1/n$, with the unit cell dimensions a=13.365 (3), b=7.545 (1), c=15.524 (4) Å, β=96.47 (2)°, and D_{calcd}=1.395 gcm^{-3} for Z=4 ($C_{14}H_{15}ClN_2O_5$, M_r 326.55). A crystal with dimensions of 0.15 × 0.20 × 0.20 mm was used for data collection. The intensity data were collected on a Rigaku AFC-5 RU diffractometer with monochromated CuK_α radiation (λ=1.54178 Å), using the $\omega-2\theta$ scan method at an ω scan speed of 16° min^{-1}. Three standard reflections were measured every 56 reflections to monitor intensity fluctuations. Absorption corrections were not applied (μ=24.21 cm^{-1}). A total of 2077 reflection data were collected for $0<\theta<60°$, of which 1840 reflections were considered to be usable ($F_o>3\sigma(F_o)$). The structure was solved by the direct method using the RANTAN program, and was refined by the full-matrix least-squares method, minimizing the function $\Sigma_\omega(F_c-F_o)^2$ with ω=1. The last cycles of refinement, which included anisotropic thermal parameters for non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms, converged the discrepancy factors R and R_ω to 0.056 and 0.050, respectively. The final difference map has no peaks greater than ±0.2 eÅ^{-3}. All computations were performed on a FACOM M 382 computer in the Data Processing Center of Kyoto University, using the KPPXRAY programs.

Oxidation of 1,3-Dimethylthymine (1) with MCPBA in the Presence of Sodium Acetate——MCPBA (354 mg, 2 mmol) and AcONa (400 mg, 4.9 mmol) were added to a solution of 99.8 mg (0.65 mmol) of **1** in dry CH_2Cl_2 (6 ml). The mixture was stirred overnight at room temperature and then refluxed for 21 h. Separation of the residue by prep. TLC using a hexane–AcOEt (1 : 1) solvent system gave 38.5 mg (18.2% yield) of **6**, mp 110—112 °C, from the upper zone and 39.5 mg (26.7% yield) of the monoacetate (**7**) from the lower zone. **7**, mp 130—132 °C (colorless plates from ether–hexane). IR: 3500, 1745, 1720, 1680 cm^{-1}. ^{1}H-NMR (d_6-DMSO) δ: 1.37 (3H, s, C_5-CH_3), 2.03 (3H, s, OCOCH_3), 2.98 (3H, s, N-CH_3), 3.05 (3H, s, N-CH_3), 5.88 (1H, s, C_6-H), 6.05 (1H, s, C_5-OH, disappeared by adding D_2O). *Anal.* Calcd for $C_9H_{14}N_2O_5$: C, 46.95; H, 6.13. Found: C, 47.21; H, 6.20.

Hydrolysis of the Hydroxy Ester (6) with NH_3——A solution of 1.13 g (3.47 mmol) of **6** in 50 ml of dry dioxane was treated with 10 ml of 28% NH_3. The mixture was stirred for 7 h at room temperature and concentrated to dryness *in vacuo*. A solution of the residue in AcOEt was washed with 5% $NaHCO_3$. The residue in $CHCl_3$ was chromatographed on silica gel. Elution with 3% MeOH–$CHCl_3$ gave 355.5 mg (54.6% yield) of the diol (**8**). Slow recrystallization from H_2O–MeOH in a freezer produced colorless prisms, mp 95—96 °C. IR: 3500, 1720, 1675 cm^{-1}. ^{1}H-NMR (d_6-DMSO) δ: 1.25 (3H, s, C_5-CH_3), 2.95 (3, s, N-CH_3), 3.00 (3H, s, N-CH_3), 4.49 (1H, d, J=3, C_6-H, changed to a singlet on adding D_2O), 5.54 (1H, s, C_5-OH, disappeared on adding D_2O), 6.45 (1H, d, J=3, C_6-OH, disappeared on adding D_2O). MS Calcd for $C_7H_{12}N_2O_4$: 188.0796 (M^+). Found: 188.0795.

Formation of the Hydroxy Ester (6) from the Diol (8)——A solution of 48 mg (0.31 mmol) of *m*-chlorobenzoic acid and 30.6 mg (0.31 mmol) of NEt_3 in 1 ml of tetrahydrofuran (THF) was cooled to −10 °C and 40.8 mg (0.31 mmol) of isobutyl chloroformate was added. After 1 h, a solution of 20 mg (0.11 mmol) of **8** in 1.5 ml of THF was added and the mixture was stirred overnight at room temperature, then refluxed for 24 h. The reaction mixture was diluted with AcOEt and washed with brine. The organic layer was dried over $MgSO_4$, filtered and evaporated. The residue was purified by prep. TLC to give 17.1 mg (51.1% yield) of **6**, mp 109—111 °C.

Acetylation of 8 with Acetic Anhydride in Pyridine——Acetic anhydride (2 ml) was added to a solution of 80 mg (4.3 mmol) of **8** in 2 ml of pyridine, and the reaction mixture was left to stand at room temperature overnight. The mixture was concentrated *in vacuo*, diluted with water, and extracted with CH_2Cl_2. The extract was washed with brine. The residue was separated by prep. TLC using a hexane–AcOEt (1 : 1) solvent system. The upper zone gave 26 mg (22.5% yield) of the diacetate (**9**), which was recrystallized from hexane to afford colorless prisms, mp 131—133 °C. IR: 1755, 1730, 1680 cm^{-1}. ^{1}H-NMR δ: 1.65 (3H, s, C_5-CH_3), 2.06 (3H, s, OCOCH_3), 2.09 (3H, s, OCOCH_3), 3.11 (3H, s, N-CH_3), 3.24 (3H, s, N-CH_3), 6.51 (1H, s, C_6-H). *Anal.* Calcd for $C_{11}H_{16}N_2O_6$: C, 48.52; H, 5.92. Found:

C, 48.42; H, 5.94. The lower zone afforded 51 mg (52.2% yield) of the monoacetate (**7**), mp 129—131 °C.

Oxidation of Diacetylthymidine (2) with MCPBA——A mixture of 326 mg (1 mmol) of **2**, 864 mg (5 mmol) of MCPBA and 20 ml of dry CH_2Cl_2 was refluxed for 97 h. Column chromatography of the residue on silica gel (eluted with 15% AcOEt in hexane) gave 293.6 mg (59% yield) of **10a** from the first eluate and 83.5 mg (16.8% yield) of **10b** from the second eluate. **10a**, colorless oil. IR: 3550, 3400, 3200, 1730, 1575 cm^{-1}. ^{1}H-NMR δ: 1.57 (3H, s, C_5-CH_3), 2.08 (3H, s, $OCOCH_3$), 2.26 (3H, s, $OCOCH_3$), 5.23 (1H, dt, J=6.1, 1.8, $C_{3'}$-H), 6.29 (1H, dd, J=9.5, 5.6, $C_{1'}$-H), 6.56 (1H, s, C_6-H), 7.38 (1H, t, J=8.0), 7.56 (1H, ddd, J=8.0, 2.0, 1.2), 7.84 (1H, dt, J=8.0, 1.2), 7.91 (1H, dd, J=2.0, 1.2), 8.88 (1H, s, NH). MS m/z: 343 ($M^+ - OCOC_6H_4Cl$). **10b**, colorless oil. IR: 3520, 3390, 3200, 1735, 1575 cm^{-1}. ^{1}H-NMR δ: 1.61 (3H, s, C_5-CH_3), 2.02 (3H, s, $OCOCH_3$), 2.10 (3H, s, $OCOCH_3$), 5.19 (1H, dt, J=6.4, 2.0, $C_{3'}$-H), 6.22 (1H, dd, J=8.9, 6.0, $C_{1'}$-H), 6.51 (1H, s, C_6-H), 7.36 (1H, t, J=8.0), 7.54 (1H, ddd, J=8.0, 1.9, 1.2), 7.83 (1H, dt, J=8.0, 1.2), 7.89 (1H, dd, J=1.9, 1.2), 8.54 (1H, s, NH). MS m/z: 343 ($M^+ - OCOC_6H_4Cl$).

Oxidation of 1,3-Dimethyluracil (3) with MCPBA——A mixture of 197 mg (1.4 mmol) of **3**, 1.217 g (7.05 mmol) of MCPBA, and 20 ml of dry CH_2Cl_2 was refluxed for 40 h. The residue was subjected to column chromatography on Florisil. Elution with 40% AcOEt in hexane gave a mixture of the ester (**11**) and 1,3-dimethylparabanic acid (**12**). The mixture was separated by prep. TLC using a $CHCl_3$–CH_3CN (5 : 1) solvent system. The upper zone gave 11.8 mg (3.0% yield) of **11** and the lower zone gave 12.7 mg (6.4% yield) of **12**. Further elution with 40% AcOEt in hexane afforded 2.4 mg (1.0% yield) of the chloride (**13**). Elution with AcOEt gave 68.8 mg (35% recovery) of **3**. **11**, mp 158—160 °C (colorless prisms from CH_2Cl_2–ether). IR: 1795, 1730 cm^{-1}. ^{1}H-NMR δ: 3.03 (3H, s, N-CH_3), 3.12 (3H, s, N-CH_3), 6.34 (1H, s, C_5-H), 7.43 (1H, t, J=8.0), 7.61 (1H, ddd, J=8.0, 1.7, 1.2), 7.95 (1H, dt, J=8.0, 1.2), 8.03 (1H, dd, J=1.7, 1.2). *Anal.* Calcd for $C_{12}H_{11}ClN_2O_4$: C, 50.99; H, 3.92; N, 9.91. Found: C, 51.03; H, 3.84; N, 10.05. **12**, mp 156—158 °C (lit.[18] 155 °C) (colorless flakes from ether). IR: 1775, 1730 cm^{-1}. ^{1}H-NMR δ: 3.19 (6H, s, N–CH_3). MS m/z: 142 (M^+). **13**, mp 150—152 °C (lit.[19] 150—150.2 °C) (colorless plates from $CHCl_3$). IR: 1710, 1660 cm^{-1}. ^{1}H-NMR δ: 3.41 (3H, s, N-CH_3), 3.44 (3H, s, N–CH_3), 7.43 (1H, s, C_6-H). MS Calcd for $C_6H_7ClN_2O_2$: 174.0196 (M^+). Found: 174.0197.

Oxidation of 5-Fluoro-1,3-dimethyluracil (4) with MCPBA——MCPBA (1.297 g, 7.51 mmol) was added to a solution of 238 mg (1.5 mmol) of **4** in 15 ml of dry CH_2Cl_2, and the mixture was refluxed for 37 h. The residue was subjected to column chromatography on silica gel. Elution with 20% AcOEt in hexane afforded 182.3 mg (43% yield) of the ester (**11**), mp 158—160 °C.

Oxidation of 4 with MCPBA in the Presence of AcONa——A mixture of 300 mg (1.9 mmol) of **4**, 1.634 g (9.5 mmol) of MCPBA, and 934.8 mg (11.4 mmol) of AcONa in 20 ml of dry CH_2Cl_2 was refluxed for 45 h. The residue was chromatographed on silica gel. Elution with 10% AcOEt in hexane gave 48.4 mg of **11** in 9.0% yield. Elution with 10—20% AcOEt in hexane afforded 7.3 mg (2.1% yield) of the acetate (**14**). Successive elution with 20% AcOEt in hexane afforded 11.3 mg (2.0% yield) of the ester (**15**). Elution with 50% AcOEt in hexane gave 186.7 mg (62.2% recovery) of the starting material (**4**). **14**, colorless oil. IR: 1795, 1760, 1730 cm^{-1}. ^{1}H-NMR δ: 2.19 (3H, s, $OCOCH_3$), 2.97 (3H, s, N-CH_3), 3.06 (3H, s, N-CH_3), 6.10 (1H, s, C_5-H). MS m/z: 186 (M^+). **15**, mp 146—148 °C (colorless plates from hexane–ether). IR: 1725, 1660 cm^{-1}. ^{1}H-NMR δ: 3.41 (3H, s, N-CH_3), 3.45 (3H, s, N-CH_3), 7.35 (1H, s, C_6-H), 7.44 (1H, t, J=8.0), 7.61 (1H, ddd, J=8.0, 2.2, 1.2), 8.04 (1H, dt, J=8.0, 1.2), 8.13 (1H, dd, J=2.2, 1.2). MS Calcd for $C_{13}H_{11}ClN_2O_4$: 294.0407 (M^+). Found: 294.0404.

Oxidation of Triacetyluridine (5) with MCPBA——a) In CH_2Cl_2: A mixture of 218 mg (0.57 mmol) of **5**, 518 mg (3 mmol) of MCPBA in 15 ml of dry CH_2Cl_2 was refluxed for 120 h. The residue was subjected to column chromatography on silica gel. Elution with 50% AcOEt in hexane gave 29 mg (12.6% yield) of the chloride (**16**). Elution with AcOEt gave 129.1 mg (59.1% recovery) of the starting material (**5**). **16**, colorless oil. IR: 1745, 1700 cm^{-1}. ^{1}H-NMR δ: 2.12 (3H, s, $OCOCH_3$), 2.13 (3H, s, $OCOCH_3$), 2.21 (3H, s, $OCOCH_3$), 4.16 (1H, m, $C_{4'}$-H), 4.38 (2H, br s, $C_{5'}$-H), 6.09 (1H, d, J=4.9, $C_{1'}$-H), 7.75 (1H, s, C_6-H), 9.28 (1H, s, NH). MS Calcd for $C_{15}H_{17}ClN_2O_9$: 404.0623 (M^+). Found: 404.0635.

b) In Benzene: A mixture of 297 mg (0.8 mmol) of **5** and 689 mg (4.0 mmol) of MCPBA in 20 ml of dry benzene was refluxed for 135 h. The residue was subjected to column chromatography on silica gel. Elution with 60% AcOEt in hexane gave 18 mg (4.3% yield) of the ester (**17**). Elution with AcOEt afforded 141.4 mg (47.7% recovery) of the starting material (**5**). **17**, colorless oil. IR: 3350, 1750, 1710 cm^{-1}. ^{1}H-NMR δ: 2.08 (3H, s, $OCOCH_3$), 2.13 (6H, s, 2 × $OCOCH_3$), 6.12 (1H, d, J=4.6, $C_{1'}$-H), 7.45 (1H, t, J=8.0), 7.62 (1H, ddd, J=8.0, 2.2, 1.7), 7.69 (1H, s, C_6-H), 8.03 (1H, dt, J=8.0, 1.7), 8.12 (1H, dd, J=2.2, 1.7). MS Calcd for $C_{22}H_{21}ClN_2O_{11}$: 524.0833 (M^+). Found: 524.0820.

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