[Chem. Pharm. Bull. 36(10)3887—3896(1988)]

Pyrimidine Derivatives. V.[1] Synthesis and Nucleophilic Reactions of 5-Bromo-6-bromomethyl-1-(2-bromoethyl and 2-bromopropyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione

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(Received April 18, 1988)

The reaction of 1-(2-hydroxyethyl and 2-hydroxypropyl)-3,6-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (**2** and **3**) with bromine afforded 5-bromo-6-bromomethyl-1-(2-bromoethyl and 2-bromopropyl)- (**4** and **5**), 5-bromo-1-(2-bromoethyl)-6-dibromomethyl-2,4(1*H*,3*H*)-pyrimidinedione (**6**), and 8,8-dibromo-6,8a-dimethyl (or 2,6,8a-trimethyl)-5,7-dioxoperhydrooxazolo[3,2-*c*]-pyrimidine (**8** or **9**).

Compound **4** reacted with sodium methoxide to give the 5-debrominated compounds **10**, **11**, and **13** [1-(2-bromoethyl)-, 1-vinyl-, and 1-(2-hydroxyethyl)-6-bismethoxy)methyl-3-methyl-2,4-(1*H*,3*H*)-pyrimidinedione]. Treatment of **4** with sodium dithiocarbamate and potassium thiolacetate gave 1-[2-(*N*,*N*-dimethylthiocarbamoylthio)ethyl]-6-(*N*,*N*-dimethylthiocarbamoylthiomethyl)- and 1-(2-acetylthioethyl)-6-acetylthiomethyl-5-bromo-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (**14** and **15**).

The reaction of **4** with sodium benzenesulfinate yielded 5-bromo-1-(2-bromoethyl)-3-methyl-6-benzenesulfonylmethyl-2,4(1*H*,3*H*)-pyrimidinedione or 4-bromo-2-methyl-5-benzenesulfonyl-1,3(2*H*,8*H*)-dioxoperhydropyrrolo[1,2-*c*]pyrimidine (**19** or **21**).

Keywords——bromination; debromination; intramolecular cyclization; nucleophilic reaction; oxazolo[3,2-*c*]pyrimidine; pyrrolo[1,2-*c*]pyrimidine; bisalkoxymethylation

A number of papers have appeared[2] on the reactions of 5-bromouracil derivatives with nucleophiles to give 5-substituted- and/or 5-debrominated-6-substituted uracils. On the other hand, Hirota *et al.*[3] have found that 5-bromo-6-bromomethyl-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione reacts with amines to give 6-aminomethyl-2,4(1*H*,3*H*)-pyrimidinedione and the 5-debrominated Schiff's base.

There has been considerable interest in the reactivity of 5-bromo-6-bromomethyl-1-(2-bromoethyl and 2-bromopropyl)-2,4(1*H*,3*H*)-pyrimidinedione (**4** and **5**) with nucleophiles from the viewpoint of introduction of functional groups on the side chains of the 1 and 6 positions.

In this paper we describe the bromination of 1-(2-hydroxyethyl and 2-hydroxypropyl)-3,6-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (**2** and **3**) with bromine in various solvent systems and the reactions of 5-bromo-6-bromomethyl-1-(2-bromoethyl and 2-bromopropyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (referred to as the tribromo compounds: **4** and **5**) with several nucleophiles.

Bromination of 2 and 3

At first, for the preparation of **4**, 5-bromo-1-(2-hydroxyethyl)-3,6-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione[4] was treated with bromine in acetic acid at 125—135 °C by a procedure similar to that reported by Hirota *et al.*[3] A mixture of **4** and 1-(2-bromoethyl)-5-bromo-6-dibromomethyl-2,4(1*H*,3*H*)-pyrimidinedione (referred to as the tetrabromo compound: **6**) was obtained.

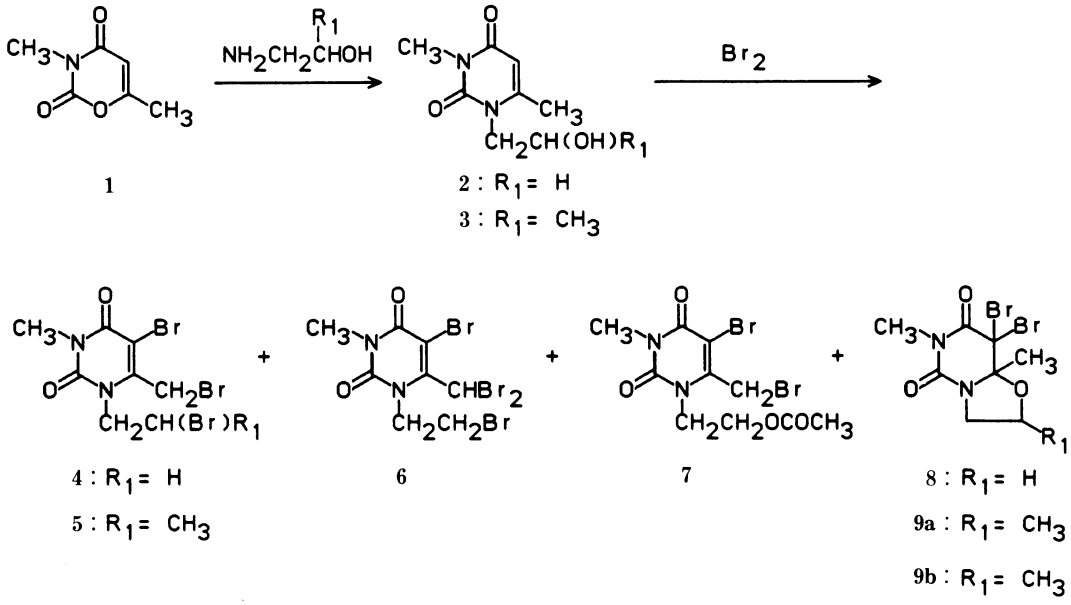

Chart 1

TABLE I. Bromination of 3,6-Dimethyl-1-(2-hydroxyethy)-2,4(1*H*,3*H*)-pyrimidinedione (**2**)

Entry No.	**2** g (mmol)	Bromine ml	Solvent ml (AcOH : H_2O)	Products[a] (%)			
				4	**6**	**7**	**8**
1[b]	3.68 (20.0)	4	50 (10:0)	43.2	10.6		
2[c]	3.68 (20.0)	4	50 (10:0)	65.4			
3[c]	3.68 (20.0)	4	20 46% HBr	45.9			
4[c]	1.84 (10.0)	2	15 (10:0) H_2O 5 drops	82.7			
5[c]	1.84 (10.0)	2	15 (8:2)	11.4		19.8	13.5
6[c]	1.84 (10.0)	2	15 (7:3)			16.4	38.5
7[c]	1.84 (10.0)	2	15 (2:8)				68.1
8[c]	1.84 (10.0)	2	15 (0:10)				57.3

a) Isolated yields are shown. *b*) Reaction was carried out at 125—135 °C for 3 h. *c*) Reaction was carried out at 90—95 °C for 3 h.

During the investigation of the bromination, it was found that **4** could be prepared directly by the reaction of **2** with bromine in acetic acid. Therefore, **2** was treated with bromine in acetic acid at 125—135 °C for 3 h to give a mixture of **4** and **6** in the ratio of 4 : 1 (Table I, entry 1). The mixture could not be separated by recrystallization, but was separated by using column chromatography.

Various reaction conditions were examined in attempts to obtain **4** more conveniently, as

shown in Table I. When the reaction was carried out in acetic acid or 46% hydrobromic acid at 90—95 °C, **4** was obtained in 65.4 or 45.9% yield almost exclusively (entries 2 and 3). However, it could not be purified by recrystallization as mentioned above. A small amount of water (5 drops) was added to the reaction solvent and the reaction was carried out in the same way as described above. Compound **4** was obtained in excellent yield (82.7%) and could be purified by recrystallization (entry 4). The reaction was carried out in 80% acetic acid, yielding three products, **4**, **7**, and **8** (entry 5). When 70% acetic acid was used as the solvent, **8** was obtained along with **7**, but no **4** was obtained (entry 6). At 20% acetic acid, compound **8** was prepared exclusively (entry 7). The yield of **8** increased with dilution of the solvent with water. Compound **8** was obtained as the sole product when the reaction was carried out in water[5] (entry 8), though the yield was slightly decreased as compared with entry 7.

The structure of compound **8** was established by elemental analysis and spectral data as follows. The UV spectrum of compound **8** showed only end absorption with no band at near 285 nm corresponding to that of 5-bromo-1,3-disubstituted uracils.[6] The proton nuclear magnetic resonance (^{1}H-NMR) spectrum in $CDCl_3$ showed signals at δ 3.83, 4.02, 4.27, and 4.52 as triple doublet splitting patterns, and those signals corresponded to the $-NCH_2CH_2O-$ part. The resonance at δ 1.65 was assigned to C-methyl protons, and was shifted to high magnetic field as compared with that of 5-bromo-6-methyl-1,3-disubstituted uracils.[7] This observation suggested that the carbon–carbon double bond on the pyrimidine ring had been converted to a single bond.

Similar intramolecular cyclization reactions have been reported by Honjo *et al.*,[5] who found that reactions of pyrimidine 6-*O*-cyclonuclosides with halogen or *N*-halosuccinimide gave 6,3′:6,5′-dianhydro-5,5-dibromo-5,6-dihydro-6,6-dihydroxy-1-(β-D-xylofuranosyl)uracil and so on.

5-Bromo-6-bromomethyl-1-(2-bromopropyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (**5**) and 8,8-dibromo-2,8,8a-trimethyl-5,7-dioxoperhydrooxazolo[3,2-*c*]pyrimidines (**9a** and **9b**) were prepared in a similar manner in acetic acid and 50% acetic acid as solvent systems, respectively. Compounds **9a** and **9b** were obtained as a mixture in a 55:45 ratio, determined from the signal integrals of C(2)-CH_3. They were separated by preparative thin layer chromatography (TLC) (Merck No. 5715) using *n*-hexane–AcOEt (1:1 mixture) as the developer. Their individual structures were assigned on the basis of spectral data and the stereochemistry was determined with the help of nuclear Overhauser effect (NOE) difference spectra (refer to the experimental section).

Reactions of 4 and 5 with Nucleophiles

Compound **4** was treated with sodium methoxide in methanol to give a mixture of **10**, **11**, and **13**. The reaction of **4** with sodium allyloxide in tetrahydrofuran (THF) afforded **12** as a colorless viscous oil. Compounds of **10**, **11**, **12**, and **13** were identified by elemental analysis and/or spectral data as 6-bismethoxymethyl-5-debrominated-3-methyl-1-substituted uracils. The debromination and its reaction mechanism have been reported by Hirota *et al.*[3]; 5-bromo-6-bromomethyl-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione reacted with aromatic amines to give 6-(*N*-phenyliminomethyl)-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione. However, no reports have appeared on the formation of the bismethoxymethyl group from the bromomethyl group.

A plausible mechanism for this reaction is assumed as follows. 5-Bromo-6-methoxymethyl compounds (A) may be formed first, and then tautomerized to a methylene intermediate (B). This is followed by a second methoxide anion attack on the electron-deficient methylene group at the 6-position and the bromine at the 5-position is eliminated simultaneously as the bromo anion through the S_N2' mechanism.

When **4** was treated with sodium *N*,*N*-dimethylamino dithiocarbamate or potassium

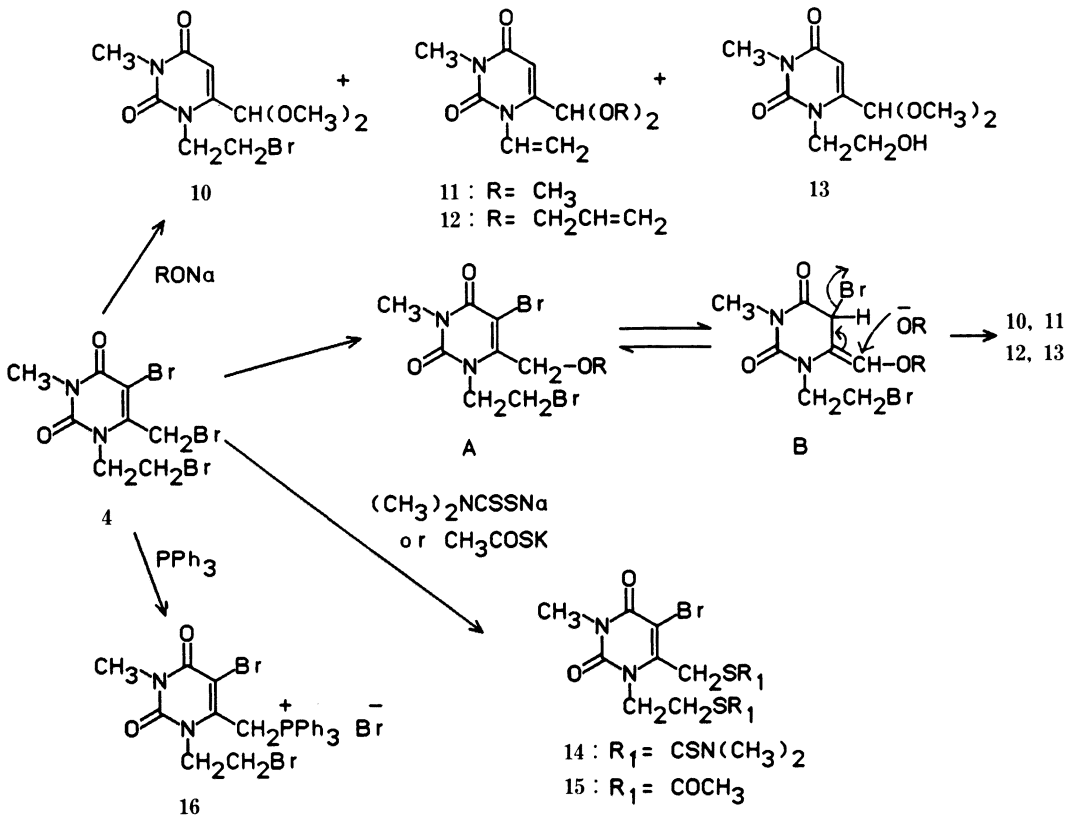

Chart 2

thiolacetate, which shows weak basicity and high nucleophilicity, the disubstituted compound (**14** or **15**) was obtained. The reaction of **4** with 1 eq of triphenylphosphine gave the 6-substituted compound (**16**). When 2 eq of triphenylphosphine was used, only a gummy product was obtained. Compound **4** or **5** was treated with sodium succinimide, giving the mono-substituted compound **17** or **18**, even when 2 eq of reagent was used.

The reaction of **4** with sodium benzenesulfinate or *p*-toluenesulfinate afforded the mono-substituted compound (**19a** or **19b**), when 1.2 eq of the reagent was used. However, the reaction with 2.9—3.23 eq of the reagent gave a novel bicyclic compound (**21a** or **21b**).

The structures of **21a** and **21b** were determined from the results of elemental analysis and spectral data as follows. The carbon-13 nuclear magnetic resonance (^{13}C-NMR) [distortionless enhancement by polarization transfer (DEPT) method] spectrum of **21a** showed signals at δ 69.66 (CH), 24.64 (CH_2), and 49.14 (CH_2), other than those of phenyl, *p*-tolyl, *N*-methyl, and pyrimidine ring moieties. The ^{1}H-NMR spectrum of **21a** showed signals at δ 2.60 and 3.05 due to CH–C$\underline{H}_2$–CH_2, δ 4.71 due to C$\underline{H}CH_2$, and δ 4.15—4.3 due to N–CH_2. The above NMR data indicate that compound **21a** possesses a rigid ring with the –NCH_2CH_2CH– moiety. A similar spectral pattern was recognized in the ^{1}H-NMR spectrum of compound **21b**.

In the case of **5**, 1.2 eq of benzenesulfinate and *p*-toluenesulfinate gave the normal mono-substituted compounds **20a** and **20b**, respectively. When 2.2—2.4 eq of sulfinates was used, bicyclic compounds such as **21a** and **21b** were not obtained but hydrolyzed products (**22a** and **22b**) were found.

The mechanism for the formation of **21** and **22** is postulated to be as follows.

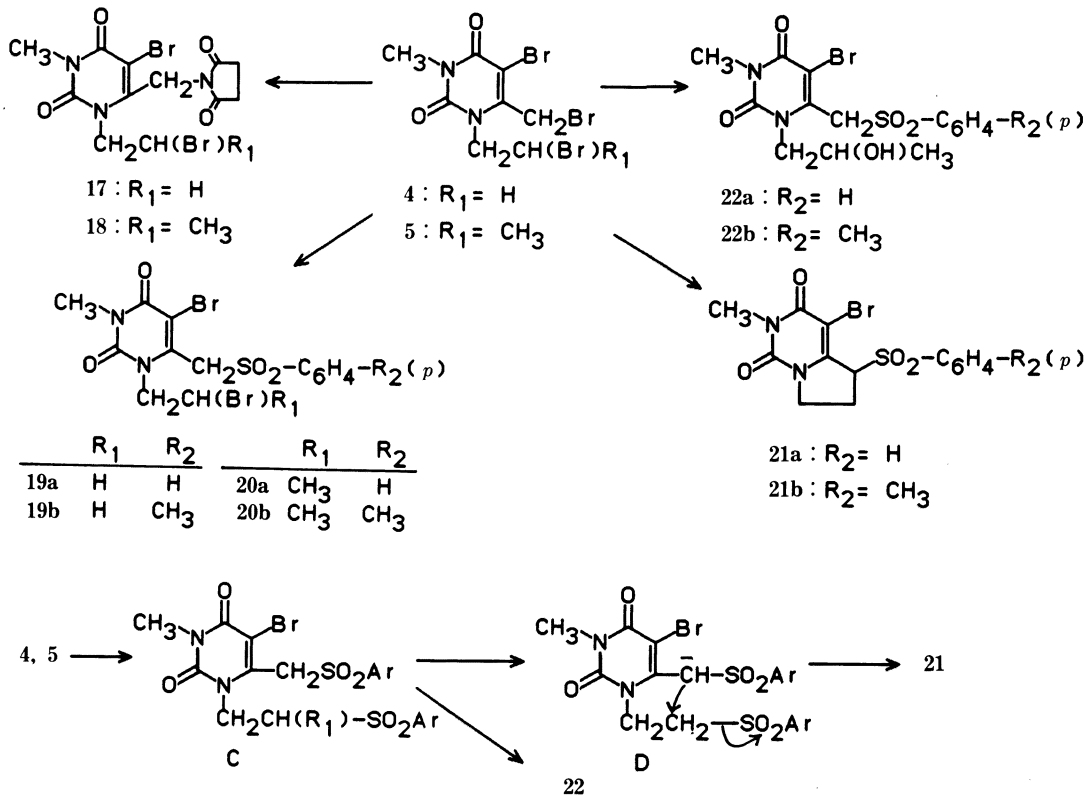

Chart 3

TABLE II. Reactions of Tribromo Compounds (**4** and **5**) with Sodium Arylsulfinate

Entry No.	Tribromo		Sulfinate			DMF	Reaction		Reaction products		
	Compd. No.	g (mmol)	R	g (mmol)	eq	ml	time h	Temp. °C	Compd.	R	g (%)
1	**4**	0.50 (1.25)	H	0.30 (1.50)	1.20	15	24	rt	**19a**	H	0.40 (69.5)
2	**4**	0.50 (1.25)	Me	0.25 (1.50)	1.20	15	24	rt	**19b**	Me	0.25 (40.0)
3	**5**	2.00 (4.77)	H	1.05 (5.25)	1.10	12	24	rt	**20a**	H	0.96 (44.5)
4	**5**	2.00 (4.77)	Me	1.02 (5.72)	1.20	20	24	rt	**20b**	Me	1.16 (49.2)
5	**4**	0.50 (1.25)	H	0.81 (4.04)	3.23	20	24	rt	**21a**	H	0.27 (57.0)
6	**4**	1.00 (2.50)	Me	1.24 (7.50)	2.90	30	13.5	95—100	**21b**	Me	0.52 (50.3)
7	**5**	2.00 (4.77)	H	2.30 (11.45)	2.40	20	24	rt	**22a**	H	0.60 (31.1)
8	**5**	3.00 (7.16)	Me	2.80 (15.70)	2.20	30	24	rt	**22b**	Me	0.42 (14.0)

rt = room temperature.

Disubstituted compounds (C: R = H and CH_3) are formed first. Then in the case of **21**, excess sulfinate anions abstract a proton from the 6-position methylene group activated by the electron-withdrawing sulfonyl group, followed by anion attack on the electron-deficient methylene group of $ArSO_2CH_2^-$ (D) to give the intramolecular cyclization product **21**. The formation of **22** is presumed to arise by hydrolysis of compound C with water during handling of the reaction mixture.

Experimental

All melting points were measured with a Laboratory Devices Mel-temp capillary melting point apparatus or a Yanaco micro melting point apparatus, and are uncorrected. Infared (IR) spectra were measured with a JASCO IR-810 or IRA-2 spectrophotometer. Ultraviolet (UV) spectra were recorded in ethanol on a Hitachi 323 spectrophotometer. NMR spectral measurements were carried out with a Hitachi R-600 Fourier-transform spectrometer (60 MHz, ^1H), a JEOL JNM FX-90Q Fourier-transform spectrometer (90 MHz, ^1H and 22.5 MHz, ^{13}C), or a JEOL JNM GX-400 Fourier-transform spectrometer (400 MHz, ^1H and 100 MHz, ^{13}C). Chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) as an internal standard. Mass spectra (MS) were taken with a JEOL JMS-DX-303 spectrometer and a JEOL JMA-DA-5000 data processor by the electron impact (EI) or fast atom bombardment (FAB) ionization method.

1-(2-Hydroxyethyl)-3,6-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione[4,8] (2)——Ethanolamine (9.1 g, 150 mmol) was added dropwise to a stirred solution of 3,6-dimethyl-1,3-oxazine-2,4(3*H*)-dione (**1**) (14.1 g, 100 mmol) in CH_2Cl_2 (20 ml) and the mixture was stirred at room temperature for 1 h. After removal of the solvent, the residue was heated at 95—100 °C for 2 h. The reaction mixture was acidified with 10% hydrochloric acid and stirred for 30 min. The mixture was extracted with $CHCl_3$ 3 times and the combined extract was dried over $MgSO_4$. After removal of the solvent, the solidified residue was washed with ether and recrystallized from MeOH to give 12.9 g (70%) of colorless prisms, mp 136—137 °C.

3,6-Dimethyl-1-(2-hydroxypropyl)-2,4(1*H*,3*H*)-pyrimidinedione (3)——Reaction and work-up were similar to the above case. Reaction of **1** (10.0 g, 71.0 mmol) with 2-hydroxypropylamine (10.64 g, 142.0 mmol) gave 9.11 g (64.8%) of colorless needles, mp 103—104 °C. *Anal.* Calcd for $C_9H_{14}N_2O_3$: C, 54.53; H, 7.12; N, 14.13. Found: C, 54.29; H, 7.09; N, 14.05. IR (KBr): 1685, 1655 (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm (log ε): 268 (4.03). ^1H-NMR (90 MHz, $CDCl_3$) δ: 1.27 (3H, d, J=6.15 Hz, CH(OH)–C$\underline{H}_3$), 2.32 (3H, s, C6-CH_3), 3.21 (1H, s, OH), 3.26 (3H, s, N-CH_3), 3.88 (2H, dd, J=2.85, 9.23 Hz, N-CH_2), 4.19 (1H, m, CH_2–C$\underline{H}$(OH)–CH_3), 5.52 (1H, s, C(5)-H).

Bromination of 1-(2-Hydroxyethyl)pyrimidinedione (Refer to Table I)——General Procedure is as Follows: Bromine was added dropwise to stirred solution of **2** or **3** in a solvent, and the mixture was heated at 90—95 °C for 3 h. After removal of the excess solvent and bromine *in vacuo*, water (20 ml) was added to the residue and removed *in vacuo* 3 times. The residue was alkalized with 5% $NaHCO_3$ aqueous solution and extracted with $CHCl_3$ (3 times). The combined extract was washed with 10% sodium thiosulfate aqueous solution and dried over $MgSO_4$ and then the solvent was removed. The residue was chromatographed on a silica gel column and eluted with $CHCl_3$–CH_3CN (gradient).

5-Bromo-1-(2-bromoethyl)-6-bromomethyl-2,4(1*H*,3*H*)-pyrimidinedione (4)——mp 126—127 °C; colorless cubes (ether or acetone). *Anal.* Calcd for $C_8H_9Br_3N_2O_2$: C, 23.73; H, 2.24; Br, 59.21; N, 6.92. Found: C, 23.68; H, 2.23; Br, 58.83; N, 6.99. IR (KBr): 1702, 1657—1640 (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm (log ε): 299 (3.92). ^1H-NMR (90 MHz, $CDCl_3$) δ: 3.41 (3H, s, N-CH_3), 3.73 (2H, dd, J=5.83, 6.70 Hz, N-CH_2), 4.39 (2H, dd, J=5.83, 6.70 Hz, CH_2–C$\underline{H}_2$Br), 4.70 (2H, s, C6-CH_2Br). ^{13}C-NMR (100 MHz, $CDCl_3$, C–H correlation spectroscopy (C–H COSY)) δ: 27.06 (C(6)-$\underline{C}H_2$–Br), 28.85 (Br–$\underline{C}H_2$–CH_2N), 29.56 (N-CH_3), 47.87 (N–$\underline{C}H_2$–CH_2Br), 101.13 (C(5)), 146.86 (C(6)), 150.65 (C=O (2)), 158.39 (C=O (4)). EI-MS m/z: 408, 406, 404, 402 (M^+), 327, 325, 323 [$(M-Br)^+$].

5-Bromo-6-bromomethyl-1-(2-bromopropyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (5)——Reaction and work-up were similar to the above bromination of 1-(2-hydroxyethyl)-pyrimidinedione. Compound **3** (3.0 g, 15.2 mmol) and bromine (3.1 ml) in AcOH (30 ml) gave 4.8 g (75.7%) of a colorless viscous oil. An analytical sample was purified by silica gel column chromatography with $CHCl_3$ as an eluent. *Anal.* Calcd for $C_9H_{11}Br_3N_2O_2$ (0.3 $CHCl_3$): C, 24.56; H, 2.51; N, 6.16. Found: C, 24.65; H, 2.52; N, 5.98. IR (neat): 1770, 1708, 1660 (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm (log ε): 210 (3.88), 300 (3.87). ^1H-NMR (400 MHz, $CDCl_3$) δ: 1.82 (3H, d, J=6.60 Hz, CH–C$\underline{H}_3$), 3.42 (3H, s, N-CH_3), 4.02 (1H, dd, J=10.63, 14.65 Hz, N–CH), 4.41 (1H, dd, J=3.74, 15.02 Hz, N–CH), 4.59 (1H, m, CH_2–C$\underline{H}$), 4.70 (1H, d, J=11.73 Hz, one of Br–CH_2), 4.87 (1H, d, J=11.73 Hz, one of Br-CH_2). EI-MS m/z: 422, 420, 418, 416 (M^+), 300, 298, 296 [$(M-CHCH(Br)CH_3)^+$]. HR-MS m/z: Calcd for $C_9H_{11}Br_3N_2O_2$ = 415.8371 (Br = 79). Found = 415.8397.

5-Bromo-1-(2-bromoethyl)-6-dibromomethyl-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (6)——mp 204 °C, colorless prisms (acetone). *Anal.* Calcd for $C_8H_8Br_4N_2O_2$: C, 19.86; H, 1.67, Br, 66.07; N, 5.79. Found: C, 19.93; H, 1.73; Br, 65.26; N, 5.50. IR (KBr): 1701, 1660 (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm (log ε): 303 (3.99). ^1H-NMR (90 MHz, $CDCl_3$) δ: 3.43 (3H, s, N–CH_3), 3.74 (2H, m, CH_2–C$\underline{H}_2$Br), 4.69 (2H, m, N–CH_2), 7.47 (1H, s, C6-$CHBr_2$). ^{13}C-NMR (100 MHz,

$CDCl_3$, C–H COSY) δ: 26.22 (Br–$\underline{C}H_2$–CH_2N), 29.80 (N–CH_3), 30.94 (Br_2–$\underline{C}H$), 48.44 (N-$\underline{C}H_2$–CH_2), 97.99 (C(5)), 145.51 (C(6)), 150.72 (C=O (2)), 157.61 (C=O (4)). EI-MS *m/z*: 488, 486, 484, 482, 480 (M^+).

1-(2-Acetoxyethyl)-5-bromo-6-bromomethyl-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (7)——mp 136—137 °C, colorless prisms (acetone). *Anal.* Calcd for $C_{10}H_{12}Br_2N_2O_4$: C, 31.28; H, 3.15; Br, 41.62; N, 7.29. Found: C, 31.38; H, 3.12; Br, 41.69; N, 7.29. IR (KBr): 1738, 1710, 1660 (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm (log ε): 212 (3.99), 300 (3.96). ^{1}H-NMR (60 MHz: $CDCl_3$) δ: 2.03 (3H, s, CO–CH_3), 3.39 (3H, s, N–CH_3), 4.30 (4H, s, CH_2CH_2), 4.66 (2H, s, Br–CH_2).

8,8-Dibromo-6,8a-dimethyl-5,7-dioxoperhydrooxazolo[3,2-*c*]pyrimidine (8)——mp 142—143 °C, colorless cubes (AcOEt). *Anal.* Calcd for $C_8H_{10}Br_2N_2O_3$: C, 28.10; H, 2.95; N, 8.19. Found: C, 28.07; H, 2.95; N, 8.12. IR (KBr): 1717, 1680 (C=O) cm^{-1}. UV: end absorption. ^{1}H-NMR (400 MHz: $CDCl_3$) δ: 1.65 (3H, s, C-CH_3), 3.27 (3H, s, N-CH_3), 3.83 (1H, ddd, J=5.86, 7.33, 10.26 Hz, one of N-CH_2), 4.02 (1H, ddd, J=6.60, 7.33, 10.26 Hz, one of N–CH_2), 4.27 (1H, ddd, J=6.60, 7.33, 7.69 Hz, one of O–CH_2), 4.52 (1H, ddd, J=5.86, 6.60, 7.69 Hz, one of O–CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$, DEPT) δ: 21.76 (C–CH_3), 29.72 (N–CH_3), 45.09 (CH_2), 65.27 (C(5)), 66.34 (CH_2), 93.41 (C(6)), 148.39 (C=O (2)), 162.79 (C=O (4)). EI-MS *m/z*: 344, 342, 340 (M^+), 202, 200, 198 [(Br_2C=C=O)$^+$].

8,8-Dibromo-2,6,8a-trimethyl-5,7-dioxoperhydrooxazolo[3,2-*c*]pyrimidine (9a and **9b)**——Reaction and work-up were similar to those in the case of **8**. Compound **3** (2.0 g, 10 mmol) and bromine (2.2 ml) in AcOH–H_2O (1 : 1, 40 ml) gave 1.94 g (54.5%) of colorless prisms, mp 160—166 °C. The product was a mixture of the two diastereoisomers (the ratio was about 55 : 45 by NMR). The isomers were separated by preparative TLC (Merck No. 5717) using *n*-hexane–AcOEt (1 : 1 mixture) as a developer and independently characterized. a) Major product (**9a**) TLC upper: mp 149—150 °C colorless prisms (acetone). The relative configuration of the two methyl groups (2 and 8a) was determined to be *cis* by examination of the NOE difference spectrum. *Anal.* Calcd for $C_9H_{12}Br_2N_2O_3$: C, 30.36; H, 3.40; N, 7.87. Found: C, 30.35; H, 3.31; N, 7.85. IR (KBr): 1732 and 1695 (C=O) cm^{-1}. UV: end absorption. ^{1}H-NMR (400 MHz: $CDCl_3$) δ: 1.45 (3H, d, J=6.23 Hz, CH–$C\underline{H}_3$), 1.65 (3H, s, C(8a)-CH_3), 3.25 (1H, dd, J=9.16, 10.62 Hz, one of CH–$C\underline{H}_2$), 3.26 (3H, s, N–CH_3), 4.33 (1H, dd, J=5.86, 10.62 Hz, one of CH–$C\underline{H}_2$), 4.92 (1H, ddq, J=5.86, 6.23, 9.16 Hz, CH_2–$C\underline{H}$–CH_3). NOE difference spectrum: 1.45⇒3.26 (2.98), 4.92 (6.43), 4.92⇒1.45 (4.64), 4.33 (6.92). ^{13}C-NMR (100 MHz, $CDCl_3$, DEPT) δ: 19.95 (C(2)-CH_3), 24.23 (C(8a)-CH_3), 29.68 (N–CH_3), 50.77 (CH_2), 65.99 (C (8)), 76.23 (CH), 94.05 (C (8a)), 148.66 (C=O (5)), 162.81 (C=O (7)). b) Minor product (**9b**) TLC lower: mp 165—166 °C colorless prisms (acetone). The relative configuration of the two methyl groups (2 and 8a) was determined to be *trans* by examination of the NOE difference spectrum. *Anal.* Calcd for $C_9H_{12}Br_2N_2O_3$: C, 30.36; H, 3.40; N, 7.87. Found: C, 30.41; H, 3.38; N, 7.92. IR (KBr): 1733, 1698 (C=O) cm^{-1}. UV: end absorption. ^{1}H-NMR (400 MHz: $CDCl_3$) δ: 1.54 (3H, d, J=6.23 Hz, CH–$C\underline{H}_3$), 1.67 (3H, s, C(8a)-CH_3), 3.26 (3H, s, N–CH_3), 3.35 (1H, t, J=9.90 Hz, one of CH–$C\underline{H}_2$), 4.00 (1H, dd, J=5.86, 9.90 Hz, one of CH–$C\underline{H}_2$), 4.60 (1H, ddq, J=5.86, 6.23, 9.90 Hz, CH_2–CH–CH_3). NOE difference spectrum: 1.54⇒3.35 (3.11), 4.60 (4.53), 4.60⇒1.54 (4.10), 3.35 (3.09), 4.00 (7.04). ^{13}C-NMR (100 MHz, $CDCl_3$, DEPT) δ: 18.14 (C(2)-CH_3), 20.94 (C(8a)-CH_3), 29.68 (N-CH_3), 52.49 (CH_2), 65.06 (C (8)), 73.07 (CH), 93.14 (C (8a)), 147.84 (C=O (5)), 163.04 (C=O (7)).

Reaction of 4 with Sodium Methoxide——A solution of **4** (5.0 g, 12.5 mmol) and 1 M NaOMe (37.5 ml) in dry MeOH (50 ml) was stirred at room temperature for 6 h. The excess solvent was removed *in vacuo* at room temperature. The residue was dissolved in water (10 ml) and extracted with $CHCl_3$ (3 times). The combined extract was dried over $MgSO_4$ and the solvent was removed. The residue was separated into three components by silica gel column chromatography using 20—25% CH_3CN in $CHCl_3$ mixture (gradient) as an eluent. From the former fractions, **10** (460 mg, 12.1%) was obtained. The middle fractions gave 160 mg (5.7%) of **11**, and the later fractions afforded 50 mg (1.6%) of **13**.

a) [6-(Bismethoxy)methyl-1-(2-bromoethyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione] (**10**): mp 77.5—78 °C, colorless crystals (ether). *Anal.* Calcd for $C_{10}H_{15}BrN_2O_4$: C, 39.11; H, 4.92; N, 9.12. Found: C, 39.43; H, 4.88; N, 8.96. IR (KBr): 1713, 1670 (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm (log ε): 267 (3.98). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 3.34 (3H, s, N–CH_3), 3.43 (6H, s, 2 × O–CH_3), 3.58 (2H, t, J=7.0 Hz, Br–CH_2), 4.29 (2H, t, J=7.0 Hz, N–CH_2), 5.12 (1H, s, C(6)-$C\underline{H}(OCH_3)_2$), 5.95 (1H, s, CH ring olefin). ^{13}C-NMR (100 MHz, $CDCl_3$, C–H COSY) δ: 27.86 (Br–$\underline{C}H_2$–CH_2N), 27.92 (N–CH_3), 46.26 (N–$\underline{C}H_2$–CH_2–Br), 54.47, 54.57 (O–CH_3), 100.74 (C(6)-$\underline{C}H(OCH_3)_2$), 101.80 (C (5)), 147.99 (C (6)), 152.24 (C=O (2)), 162.21 (C=O (4)). EI-MS *m/z*: 308, 306 (M^+), 278, 276 [(M − CH_2O)$^+$], 75 [($CH(OCH_3)_2$)$^+$].

b) [6-(Bismethoxy)methyl-3-methyl-1-vinyl-2,4(1*H*,3*H*)-pyrimidinedione] (**11**): A colorless viscous oil. IR (neat): 1710, 1670 br, 1640 sh (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm (log ε): 270 (3.88). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 3.53 (3H, s, N-CH_3), 3.54 (6H, s, 2 × O-CH_3), 5.12 (1H, s, $C\underline{H}(OCH_3)_2$), 5.51 (1H, dd, J=0.7, 15.6 Hz, vinyl), 5.53 (1H, dd, J=0.7, 7.9 Hz, vinyl), 6.08 (1H, s, CH ring olefin), 6.47 (1H, dd, J=7.9, 15.6 Hz, vinyl). EI-MS *m/z*: 226 (M^+), 211 [(M − CH_3)$^+$], 196 [(M − CH_2O)$^+$], 75 [($CH(OCH_3)_2$)$^+$]. HR-MS *m/z*: Calcd for $C_{10}H_{14}N_2O_4$ = 226.0953. Found = 226.0958.

c) [6-(Bismethoxy)methyl-1-(2-hydroxyethyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione] (**13**): mp 118—119 °C, colorless needles (AcOEt). *Anal.* Calcd for $C_{10}H_{16}N_2O_5$: C, 49.18; H, 6.60; N, 11.47. Found: C, 49.21; H, 6.47; N, 11.14. IR (KBr): 3380 (OH), 1708, 1665 (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm (log ε): 270 (3.98). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 2.90 (1H, t, J=5.1 Hz, OH, disappeared by D_2O), 3.32 (3H, s, N–CH_3), 3.39 (6H, s, 2 × O-CH_3), 3.80 (2H, m, O-CH_2), 4.18 (2H, t, J=5.1 Hz, N-CH_2), 5.39 (1H, s, C(6)-$C\underline{H}(OCH_3)_2$), 5.98 (1H, s, C–H ring olefin). ^{13}C-NMR (100 MHz, $CDCl_3$ C–H COSY) δ: 28.01 (N–CH_3), 47.17 (N–$\underline{C}H_2$–CH_2–OH), 54.09, 54.18 (O–CH_3), 61.27 (O–$\underline{C}H_2$–

CH_2–N), 100.13 (C(6)-$\underline{C}H(OCH_3)_2$), 101.50 (C (5)), 148.81 (C (6)), 153.13 (C=O (2)), 162.45 (C=O (4)). EI-MS *m/z*: 244 (M^+), 214 [$(M-CH_2O)^+$], 75 [$(CH(OCH_3)_2)^+$].

6-(Bisallyloxy)methyl-3-methyl-1-vinyl-2,4(1*H*,3*H*)-pyrimidinedione (12)——A mixture of NaH (50% mineral oil dispersion, 2.2 g, 54.2 mmol) and allyl alcohol (2.6 g, 44.8 mmol) in THF (20 ml) was stirred for 3 h at room temperature. A solution of **4** (6.0 g, 14.8 mmol) in THF (30 ml) was added to the sodium allyloxide obtained above and then the mixture was stirred for 24 h at room temperature. The reaction mixture was filtered and the filtrate was concentrated *in vacuo*. Water (15 ml) was added to the residue and the mixture was extracted with $CHCl_3$ (3 times). The combined extract was dried over $MgSO_4$ and the solvent was removed. The residue was chromatographed on a silica gel column using 3% CH_3CN in $CHCl_3$ as an eluent, giving 0.44 g (10.7%) as a colorless viscous oil. The product was purified to obtain an analytical sample by preparative TLC (Merck No. 5717) using 0.5% EtOH in AcOEt as a developer. *Anal.* Calcd for $C_{14}H_{18}N_2O_4$: C, 60.42; H, 6.52; N, 10.07. Found: C, 60.26; H, 6.43; N, 10.15. IR (neat): 1715, 1670, 1650 sh (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm ($\log\varepsilon$): 271 (3.93). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 3.34 (3H, s, N–CH_3), 4.06 (4H, d, J=5.94 Hz, 2×CH–$C\underline{H}_2$–O), 5.1—5.4 (4H, m, 2×$OCH_2CH=C\underline{H}_2$), 5.49 (1H, dd, J=0.66, 15.60 Hz, one of $NCH=C\underline{H}_2$), 5.50 (1H, dd, J=0.66, 7.91 Hz, one of $NCH=C\underline{H}_2$), 5.88 (2H, ddt, J=5.30, 10.00, 17.36 Hz, 2×CH_2–$C\underline{H}=CH_2$), 6.15 (1H, s, ring olefin), 6.48 (1H, dd, J=7.91, 15.60 Hz, $CH_2=C\underline{H}$). EI-MS *m/z*: 278 (M^+), 237 [$(M-CH_2CH=CH_2)^+$], 180 [$(237-OCH_2CH=CH_2)^+$], 127 [$(CH(OCH_2CH=CH_2)_2^+$]. HR-MS *m/z*: Calcd for $C_{14}H_{18}N_2O_4$=278.1266. Found=278.1301.

5-Bromo-1-[2-(*N*,*N*-dimethylthiocarbamoylthio)ethyl]-6-(*N*,*N*-dimethylthiocarbamoylthiomethyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (14)——A solution of **4** (1.0 g, 2.5 mmol) and sodium *N*,*N*-dimethyldithiocarbamate (0.79 g, 5.5 mmol) in a mixture of EtOH and $CHCl_3$ (40 ml and 5 ml) was refluxed for 7 h. After cooling, the separated crystalline mass was collected and recrystallized from MeOH–$CHCl_3$ to give 0.45 g (37.1%) of colorless plates, mp 201—203 °C. *Anal.* Calcd for $C_{14}H_{21}BrN_4O_2S_4$: C, 34.63; H, 4.36; N, 11.54; S, 26.42. Found: C, 34.58; H, 4.32; N, 11.48; S, 26.50. IR (KBr): 1702, 1657 (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm ($\log\varepsilon$): 216 (sh, 4.69), 240 (sh, 4.46). ^{1}H-NMR (90 MHz, DMSO-d_6) δ: 3.23, 3.34, 3.36, 3.43, 3.47 (each 3H, s, N–CH_3), 3.55 (2H, t, J=7.3 Hz, S-CH_2), 4.13 (2H, t, J=7.3 Hz, N–CH_2), 4.71 (2H, s, S–CH_2).

1-(2-Acetylthioethyl)-6-acetylthiomethyl-5-bromo-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (15)——A mixture of **4** (1.0 g, 2.47 mmol) and potassium thiolacetate (0.71 g, 6.17 mmol) in CH_3CN (100 ml) was refluxed for 4 h. After evaporation of the solvent, water (15 ml) was added to the residue and the mixture was extracted with $CHCl_3$ (3 times). The combined organic layer was dried over $MgSO_4$ and the solvent was removed. The residue was crystallized from acetone to give 0.5 g (51.2%) of pale brown prisms, mp 150—151 °C. If necessary, the product was chromatographed on silica gel for purification with $CHCl_3$ as an eluent. *Anal.* Calcd for $C_{12}H_{15}BrN_2O_4S_2$: C, 36.46; H, 3.83; Br, 20.21; N, 7.09; S, 16.22. Found: C, 36.45; H, 3.82; Br, 20.25; N, 6.75; S, 16.36. IR (KBr): 1682, 1645, 1630 (sh, C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm ($\log\varepsilon$): 222 (4.11), 293 (4.01). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 2.39 (3H, s, $COCH_3$), 2.42 (3H, s, $COCH_3$), 3.16 (2H, dd, J=6.8, 7.9 Hz, S-CH_2), 3.40 (3H, s, N-CH_3), 4.06 (2H, dd, J=6.8, 7.9 Hz, N–CH_2), 4.49 (2H, s, S–CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$, C–H COSY) δ: 27.26 (S–$\underline{C}H_2$–CH_2–N), 29.45 (N–CH_3), 30.09 (CO–CH_3), 30.47 (CO–CH_3), 30.83 (C(6)-S–CH_2), 46.08 (N–$\underline{C}H_2$–CH_2–S), 100.79 (C (5)), 147.91 (C (6)), 150.79 (C=O (2)), 158.36 (C=O (4)), 192.54 (S–$\underline{C}OCH_3$), 195.02 (S–$\underline{C}OCH_3$). EI-MS *m/z*: 396, 394 (M^+), 353, 351 [$(M-COCH_3)^+$], 321, 319 [$(353, 351-CH_2=C=O)^+$].

6-[5-Bromo-1-(2-bromoethyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedionyl]methyltriphenylphosphonium Bromide (16)——A solution of triphenylphosphine (1.3 g, 5 mmol) in THF (20 ml) was added to a stirred solution of **4** (2.0 g, 5 mmol) in THF (20 ml) and the mixture was allowed to stand at room temperature for 3.5 h. The separated crystalline mass was collected and recrystallized from AcOEt–MeOH to give 1.87 g (58.8%) of colorless cubes, mp 180 °C (dec.). *Anal.* Calcd for $C_{26}H_{24}Br_3N_2O_2P$: C, 46.81; H, 3.63; N, 4.20. Found: C, 46.54; H, 3.69; N, 4.10. IR (KBr): 1702, 1653 (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm ($\log\varepsilon$): 300 (3.89). 352 (4.15).

5-Bromo-1-(2-bromoethyl)-3-methyl-6-(succinimidylmethyl)-2,4(1*H*,3*H*)-pyrimidinedione (17)——A solution of **4** (2.0 g, 5.0 mmol) in dry THF (20 ml) was added to a mixture of sodium succimide [prepared from NaH (0.42 g, 60% in mineral oil dispersion, 10.0 mmol) and succimide (1.0 g, 10.1 mmol) in dry THF (20 ml)] and the mixture was refluxed for 5 h. After removal of the precipitate, the filtrate was concentrated *in vacuo* and water (10 ml) was added to the residue, then it was extracted with $CHCl_3$ (3 times). The combined extract was dried over $MgSO_4$ and the solvent was removed. The residue (1.17 g) was chromatographed on a silica gel column using 2% CH_3CN in $CHCl_3$ as an eluent, giving 0.67 g (31.7%) of colorless cubes, mp 196—198 °C. *Anal.* Calcd for $C_{12}H_{13}Br_2N_3O_4$: C, 34.07; H, 3.10; N, 9.93. Found: C, 34.14; H, 3.08; N, 9.99. IR (KBr): 1770 (w), 1702, 1650 (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm ($\log\varepsilon$): 287 (3.98). ^{1}H-NMR (90 MHz, $CDCl_3$–TFA 3 drops) δ: 2.90 (4H, s, CH_2CH_2), 3.48 (3H, s, N–CH_3), 3.69 (2H, t, J=5.94, 6.37 Hz, Br–CH_2), 4.55 (2H, J=5.94, 6.15 Hz, N–CH_2), 4.93 (2H, s, SO_2–CH_2). EI-MS *m/z*: 425, 423, 421 (M^+). FAB-MS *m/z*: 426, 424, 422 [$(M+1)^+$].

5-Bromo-1-(2-bromopropyl)-3-methyl-6-succimidylmethyl-2,4(1*H*,3*H*)-pyrimidinedione (18)——A solution of **5** (2.0 g, 4.8 mmol) in dry THF (30 ml) was added to a mixture of sodium succimide [prepared from NaH (0.4 g, 60% in mineral oil) and succimide (0.95 g, 9.6 mmol)] and the mixture was refluxed for 5 h. After removal of the precipitate, the filtrate was concentrated *in vacuo*. Water (10 ml) was added to the residue and then the mixture was extracted with $CHCl_3$ (3 times). The combined extract was dried over $MgSO_4$ and the solvent was removed. The residue was

TABLE III. Physical Data for **19**, **20**, **21**, and **22**

Compd. No.	mp (°C)	Appearance Recryst. solvent	Formula	Analysis (%) Calcd (Found) C	H	N	IR (KBr) cm^{-1} C=O	SO_2	UV $\lambda_{max}^{ethanol}$ nm (log ε)
19a	176—178	Prisms $CHCl_3$–AcOEt	$C_{14}H_{14}Br_2N_2O_4S$	36.07 (36.25)	3.03 (3.16)	6.01 (6.08)	1700 1662	1320 1160	218 (4.31) 295 (3.99)
19b	178—180	Needles AcOEt	$C_{15}H_{16}Br_2N_2O_4S$	37.52 (37.58)	3.36 (3.32)	5.83 (5.74)	1698 1660	1310 1159	229 (4.68) 295 (4.67)
20a	166—168	Cubes Acetone	$C_{15}H_{16}Br_2N_2O_4S$	37.76 (37.69)	3.38 (3.34)	5.87 (5.86)	1710 1660	1321 1160	219 (4.25) 296 (3.96)
20b	168—170	Prisms Acetone	$C_{16}H_{18}Br_2N_2O_4S$	38.89 (39.01)	3.67 (3.64)	5.67 (5.72)	1705 1660	1333 1159	229 (4.24) 296 (3.93)
21a	184—185	Powder MeOH–AcOEt	$C_{14}H_{13}BrN_2O_4S$	43.65 (43.45)	3.40 (3.41)	7.27 (7.25)	1700 1650	1308 1140	218 (4.36) 294 (3.99)
21b	277—279	Prisms $CHCl_3$–AcOEt	$C_{15}H_{15}BrN_2O_4S$	45.12 (44.80)	3.78 (3.74)	7.02 (6.86)	1698 1643 1630	1315 1140	223 (100)[a] 229 (100) 295 (48)
22a	164—168	Prisms Acetone	$C_{15}H_{17}BrN_2O_5S$	43.17 (43.25)	4.11 (4.03)	6.71 (6.81)	1715 1655 3490	1331 1160 (OH)	218 (4.27) 297 (3.94)
22b	191—193	Powder $CHCl_3$–AcOEt	$C_{16}H_{19}BrN_2O_5S$	44.56 (44.69)	4.44 (4.41)	6.50 (6.46)	1695 1650 3475	1323 1150 (OH)	229 (4.27) 296 (3.97)

a) Relative absorption percentages are shown, because this compound is insoluble in EtOH and log ε values could not be calculated.

chromatographed on a silica gel column using 10% CH_3CN in $CHCl_3$ as an eluent, giving 1.0 g (47.6%) of crystals. The product was recrystallized from AcOEt to give 0.46 g (21.9%) of a colorless powder, mp 177—179 °C. *Anal.* Calcd for $C_{13}H_{15}Br_2N_3O_4$: C, 35.72; H, 3.46; N, 9.61. Found: C, 35.77; H, 3.40; N, 9.63. IR (KBr): 1780, 1708, 1658 (C=O) cm^{-1}. UV $\lambda_{max}^{ethanol}$ nm (log ε): 287 (3.98). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.78 (3H, d, J=6.60 Hz, CH–C$\underline{H}_3$), 2.78 (4H, s, 2 × CH_2), 3.42 (3H, s, N–CH_3), 4.23 (1H, dd, J=9.89, 15.39 Hz, one of CH–C$\underline{H}_2$), 4.43 (1H, dd, J=11.73, 15.39 Hz, one of CH–C$\underline{H}_2$), 4.56 (1H, ddq, J=6.60, 9.89, 11.73 Hz, CH_2–C$\underline{H}$–CH_3), 4.77 (1H, d, J=15.76 Hz, one of N–C$\underline{H}_2$), 5.02 (1H, d, J=15.76 Hz, one of N–C$\underline{H}_2$).

Reaction of Sodium Benzenesulfinate (or *p*-Toluenesulfinate) with 4 or 5: General Procedure is as Follows——A solution of **4** or **5** and sodium benzenesulfinate (*p*-toluenesulfinate) in DMF was stirred for 24 h at room temperature. The reaction mixture was concentrated to dryness *in vacuo* and the residue was extracted with $CHCl_3$ (3 times). The extract was dried over $MgSO_4$ and the solvent was removed. The crystalline residue was recrystallized from suitable solvents. If necessary, the products were purified by column chromatography.

6-Benzenesulfonylmethyl-5-bromo-1-(2-bromoethyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (19a)——^{1}H-NMR (90 MHz, $CDCl_3$) δ: 2.16 (acetone), 3.42 (3H, s, N–CH_3), 3.73 (2H, t, J=5.71 Hz, Br–CH_2), 4.66 (2H, t, J=5.71 Hz, N–CH_2), 4.99 (2H, s, SO_2–CH_2), 7.4—8.0 (5H, m, phenyl). EI-MS m/z: 468, 466, 464 (M^+), 387, 385 [$(M-Br)^+$].

5-Bromo-1-(2-bromoethyl)-3-methyl-6-*p*-toluenesulfonylmethyl-2,4(1*H*,3*H*)-pyrimidinedione (19b)——^{1}H-NMR (90 MHz, $CDCl_3$) δ: 2.47 (3H, s, phenyl-CH_3), 3.43 (3H, s, N–CH_3), 3.73 (2H, t, J=5.49, 5.72 Hz, Br–CH_2), 4.67 (2H, t, J=5.49, 5.72 Hz, N–CH_2), 4.96 (2H, s, SO_2–CH_2), 7.38, 7.76 (4H, AB-q, J=8.46 Hz, phenyl).

6-Benzenesulfonylmethyl-5-bromo-1-(2-bromopropyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (20a)——^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.83 (3H, d, J=6.23 Hz, CH–C$\underline{H}_3$), 3.43 (3H, s, N–CH_3), 4.40 (1H, m, CH_2–C$\underline{H}$–CH_3), 4.56 (2H, m, N–CH_2), 5.08 (2H, m, SO_2–CH_2), 7.6—8.0 (5H, m, phenyl).

5-Bromo-1-(2-bromopropyl)-3-methyl-6-*p*-toluenesulfonylmethyl-2,4(1*H*,3*H*)-pyrimidinedione (20b)——^{1}H-NMR (90 MHz, $CDCl_3$) δ: 1.83 (3H, d, J=6.15 Hz, CH–C$\underline{H}_3$), 2.47 (3H, s, phenyl-CH_3), 3.43 (3H, s, N–CH_3), 4.3—4.7 (3H, m, CH_2–C$\underline{H}$ and CH–C$\underline{H}_2$), 5.04 (2H, s, SO_2–CH_2), 7.3—7.8 (4H, AB-q, phenyl).

5-Benzenesulfonyl-4-bromo-2-methyl-1,3(2*H*,8*H*)-dioxoperhydropyrrolo[1,2-*c*]pyrimidine (21a)——^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.60 (1H, ddt, J=8.03, 10.63, 14.29 Hz, one of CH–C$\underline{H}_2$), 3.05 (1H, ddd, J=0.88, 5.71, 14.29 Hz, one of CH–C$\underline{H}_2$), 3.40 (3H, s, N–CH_3), 4.15—4.3 (2H, m, N–CH_2), 4.71 (1H, dd, J=0.88, 8.03 Hz, CH_2–C$\underline{H}$), 7.6—8.0 (5H, m, phenyl). ^{13}C-NMR (100 MHz, $CDCl_3$, DEPT) δ: 24.64 (CH_2 (2)), 29.14 (N–CH_3), 49.14 (CH_2 (3)), 69.66 (CH (1)), 96.45 (C (8)), 129.49 (2 × CH, phenyl), 129.98 (2 × CH, phenyl), 135.21 (CH, phenyl), 137.39 (C phenyl), 146.32 (C (8a)), 149.01 (C=O (5)), 159.61 (C=O (7)). FAB-MS m/z: 387, 385 [$(M+1)^+$].

4-Bromo-2-methyl-5-*p*-toluenesulfonyl-1,3(2*H*,8*H*)-dioxoperhydropyrrolo[1,2-*c*]pyrimidine (21b)——^{1}H-NMR (90 MHz, $CDCl_3$–TFA 3 drops) δ: 2.50 (3H, s, phenyl-CH_3), 2.65 (1H, m, CH), 3.02 (1H, m, CH), 3.46 (3H, s, N–CH_3), 4.26 (2H, dd, J=3.95, 6.15 Hz, CH_2), 4.78 (1H, d, J=7.03 Hz, CH), 7.4—7.9 (4H, AB-q, J=8.4 Hz, phenyl). HR-MS m/z: Calcd for $C_{15}H_{15}BrN_2O_4S$=397.9936 (Br=79). Found: 397.9929.

6-Benzenesulfonylmethyl-5-bromo-1-(2-hydroxypropyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (22a)——^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.31 (3H, d, J=5.86 Hz, CH–C$\underline{H}_3$), 2.99 (1H, br s, OH), 3.36 (3H, s, N–CH_3), 4.16 (2H, br s, one of CH–C$\underline{H}_2$ and CH_2–C$\underline{H}$), 4.40 (1H, d, J=12.82 Hz, one of CH–C$\underline{H}_2$), 4.87 (1H, d, J=14.84 Hz, one of SO_2–C$\underline{H}_2$), 5.33 (1H, d, J=14.84 Hz, one of SO_2–C$\underline{H}_2$), 7.6—8.0 (5H, m, phenyl).

5-Bromo-1-(2-hydroxypropyl)-3-methyl-6-*p*-toluenesulfonylmethyl-2,4(1*H*,3*H*)-pyrimidinedione (22b)——^{1}H-NMR (90 MHz, $CDCl_3$) δ: 1.30 (3H, d, J=5.5 Hz, CH–C$\underline{H}_3$), 2.46 (3H, s, phenyl-CH_3), 2.92 (1H, s, OH), 3.34 (3H, s, N–CH_3), 4.0—4.6 (3H, m, CH_2 and CH), 4.81 (1H, d, J=14.72 Hz, one of SO_2–CH_2), 5.31 (1H, d, J=14.72 Hz, one of SO_2–CH_2), 7.3—7.8 (4H, AB-q, phenyl).

Acknowledgment The authors are indebted to Mrs. H. Mazume for the elemental analysis, and also to Messrs. K. Inada, M. Ohnishi, N. Yamaguchi, and M. Ohwatari for the measurements of NMR, MS, IR, and UV spectra, respectively.

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7) Unpublished data: for example 5-bromo-3,6-dimethyl-1-(2-hydroxyethyl and 2-bromoethyl)-2,4(1*H*,3*H*)-pyrimidinedione showed C-methyl signals at δ 2.63 and 2.62.
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