# Pyrimidine Derivatives. XI.[1] Facile Carbon–Carbon Bond-Cleavage Reaction of 6-Bromomethylpyrimidinediones and (2,4-Dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)methyl Nitrate *via* 6-Formyl Derivatives

Toshio KINOSHITA,* Hiroshi OHISHI, and Youko TANIMOTO

*School of Pharmaceutical Sciences, Nagasaki University, 1–14 Bunkyo-machi, Nagasaki 852, Japan.*
Received March 22, 1993

**The reaction of 5-bromo-6-bromomethyl-1,3-dimethyl- (1a) and 5-bromo-6-bromomethyl-1-(3-bromopropyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (4a) with 1.0 and 2.0 eq of the sodium salt of 2-nitropropane yielded a mixture of 6-formyl (2 and 5a) and carbon–carbon bond-cleavage products (3 and 6a). When a large excess of the sodium salt of 2-nitropropane was used, 3 and 6a were obtained as sole products, respectively. The nitrates [(5-bromo-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)methyl nitrate (1b) and the dinitrate of 5-bromo-6-hydroxymethyl-1-(3-hydroxypropyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (4b)] were exclusively converted to 6-formylpyrimidines (2 and 5b) or 6-unsubstituted pyrimidinediones (3 and 6b) by reaction with 1.0 or 2.0 eq of sodium methoxide, respectively. The dinitrate of 5-bromo-1-(2-hydroxyethyl)-6-hydroxymethyl-3-methyl-2,4(1*H*,3*H*)-pyrimidinediones (7) was treated with sodium methoxide to yield 2-(5-bromo-6-formyl-3-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)ethyl nitrate (8), a 3,4-dihydropyrimido[6,1-*c*][1,4]oxazine derivative (9) and 2-(5-bromo-3-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)ethyl nitrate (10). A plausible reaction mechanism is presented.**

**Keywords** deformylation; (pyrimidin-6-yl)methyl nitrate; 6-bromomethylpyrimidine; 6-formylpyrimidine; reaction mechanism

Allylic and benzylic halides can be readily converted to the corresponding aldehydes by treatment with alkali metal salts of nitroalkanes.[2] In a previous paper,[3] we applied this method for the preparation of a 3,4-dihydropyrimido[6,1-*c*][1,4]oxazine derivative (**9**),[4] by treatment of 5-bromo-1-(2-bromoethyl)-6-bromomethyl-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione with the sodium salt of 2-nitropropane. The same bicyclic compound (**9**) was also prepared by reaction of the dinitrate of 5-bromo-1-(3-hydroxyethyl)-6-hydroxymethyl-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (**7**)[4] with sodium methoxide. However, when 5-bromo-1-(3-bromopropyl)-6-bromomethyl-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (**4a**)[5] reacted with the sodium salt of 2-nitropropane under the same conditions described in the previous paper,[3] the resulting product was 5-bromo-1-(3-bromopropyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione, which is apparently to the debromomethylation product of the starting material.

Decarboxylation is an important reaction in the chemistry of nitrogen heterocyclic compounds[6] (*e.g.*, pyridine-, quinoline-, isoquinoline-, and pyrimidinecarboxylic acids) for the removal of alkyl groups, which are often introduced during primary synthesis. However, this procedure requires a high temperature (180—250 °C or higher), and the products are obtained in low yields.

In this paper, we describe a carbon–carbon (C–C) bond-cleavage reaction of 6-bromomethyl-2,4-pyrimidinediones by treatment with the sodium salt of 2-nitropropane and that of (pyrimidin-6-yl)methyl nitrate with sodium methoxide. This type of reaction should be useful as a new C–C bond-cleavage reaction for the removal of unwanted functional groups (*e.g.*, methyl, hydroxymethyl, halogenomethyl, methyl nitrate) under mild reaction conditions and in high yields.

## Results and Discussion

**6-Bromomethyl Derivatives** When 5-bromo-6-bromomethyl-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (**1a**)[7] was treated with 1.0 and 2.0 eq of the sodium salt of 2-nitropropane, 5-bromo-1,3-dimethyl-6-formyl- (**2**) and 5-bromo-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (**3**)[8] were isolated (Table I, entries 1 and 2). The yield of the C–C bond-cleavage product (**3**) increased with increase in the molar ratio of the sodium salt of 2-nitropropane. When 4.0 eq of the sodium salt of 2-nitropropane was used, **3** was

TABLE I. Reactions[a] of **1a** and **4a** with Sodium Methoxide and 2-Nitropropane

| Entry No. | Compound | | | Sodium methoxide (eq) | 2-Nitropropane (eq) | Product (ratio in %) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | No. | (eq) | (g) | | | Yield (g(%)) | **1a** | **2/5a** | **3/6a** |
| 1 | **1a** | 1.0 | 0.63 | 1.0 | 1.0 | 0.43 | 24 | 64 | 12 |
| 2 | **1a** | 1.0 | 0.63 | 2.0 | 2.0 | 0.41 | — | 36 | 64 |
| 3 | **1a** | 1.0 | 0.63 | 4.0 | 4.0 | 0.35 (80) | — | — | 100 |
| 4 | **4a** | 1.0 | 1.26 | 1.0 | 1.0 | 0.75 | | 60 | 40 |
| 5 | **4a** | 1.0 | 1.26 | 2.0 | 2.0 | 0.73 (75) | | — | 100 |
| 6 | **4a** | 1.0 | 1.26 | 4.0 | 4.0 | 0.83 (85) | | — | 100 |

*a*) The reaction procedure and computation of product ratio are described in the experimental section.

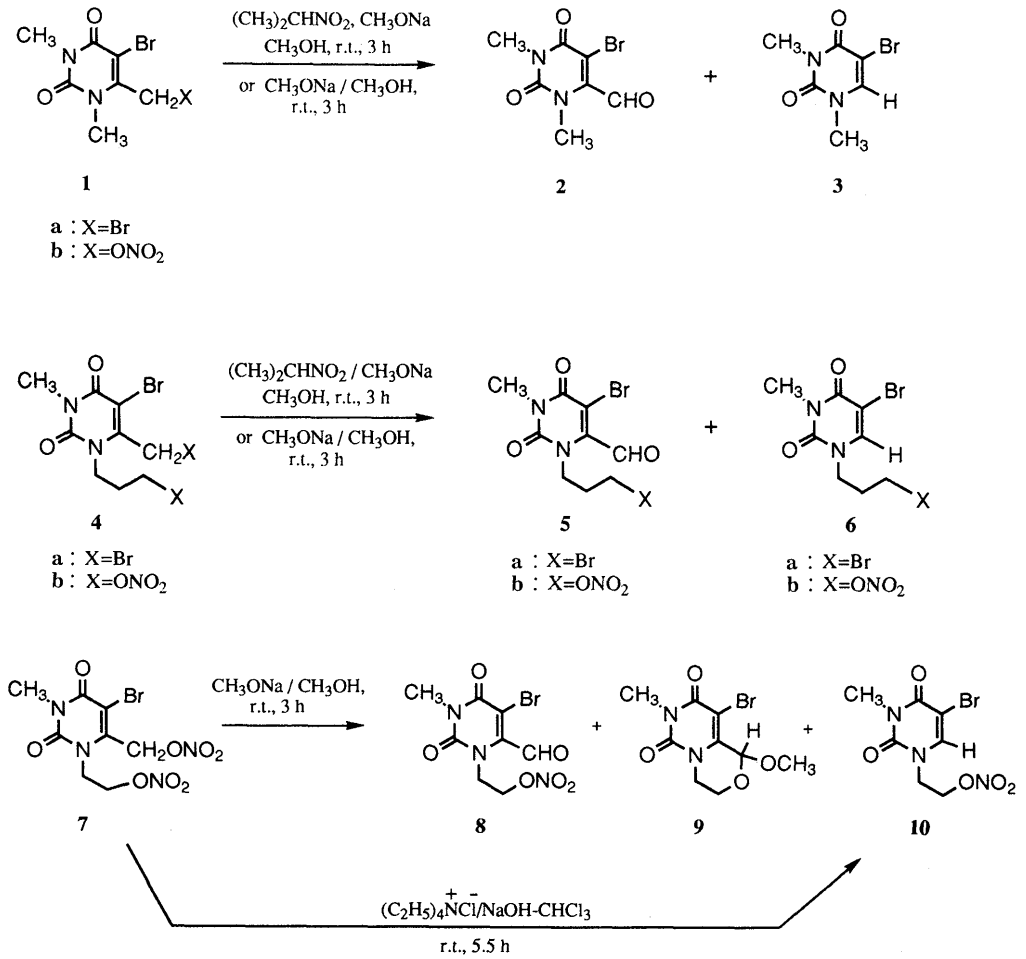


Chart 1

TABLE II. Reactions[a] of **1b** and **4b** with Sodium Methoxide

| Entry No. | Compound | | | Sodium methoxide | Product (ratio in %) | | |
|---|---|---|---|---|---|---|---|
| | No. | (eq) | (g) | (eq) | Yield (g(%)) | **2**/**5b** | **3**/**6b** |
| 1 | **1b** | 1.0 | 0.88 | 1.0 | 0.58 (78) | 100 | — |
| 2 | **1b** | 1.0 | 0.88 | 2.0 | 0.59 (80) | — | 100 |
| 3 | **4b** | 1.0 | 0.77 | 1.0 | 0.51 (82) | 100 | — |
| 4 | **4b** | 1.0 | 0.77 | 2.0 | 0.45 (73) | — | 100 |
| 5 | **4b** | 1.0 | 0.77 | 4.0 | 0.40 (65) | — | 100 |
| 6[b] | **4b** | 1.0 | 0.77 | 4.0 | 0.48 (78) | — | 100 |

*a*) The reaction procedure and computation of product ratio are described in the experimental section. *b*) The reaction was carried out at 0°C for 3 h.

TABLE III. Reactions[a] of **7** and **8** with Sodium Methoxide

| Entry No. | Compound | | | Sodium methoxide | Product (ratio in %) | | | |
|---|---|---|---|---|---|---|---|---|
| | No. | (eq) | (g) | (eq) | Yield (g) | **8** | **9** | **10** |
| 1 | **7** | 1.0 | 0.74 | 1.0 | 0.43 | 100 | — | — |
| 2 | **7** | 1.0 | 0.74 | 1.5 | 0.59 | 8 | 69 | 23 |
| 3 | **7** | 1.0 | 0.74 | 2.0 | 0.49 | — | 76 | 24 |
| 4 | **7** | 1.0 | 0.74 | 3.0 | 0.54 | — | 75 | 25 |
| 5[b] | **7** | 1.0 | 0.74 | 2.0 | 0.52 | — | 71 | 29 |
| 6 | **8** | 1.0 | 0.64 | 0.5 | 0.61 | 13 | 65 | 22 |
| 7[c] | **8** | 1.0 | 0.64 | 0.5 | 0.56 | 7 | 71 | 22 |
| 8 | **8** | 1.0 | 0.64 | 1.0 | 0.55 | — | 79 | 21 |

*a*) The reaction procedure and computation of products ratio are described in the experimental section. *b*) The reaction was carried out at 60—65 °C for 1 h. *c*) The reaction was carried out at room temperature for 12 h.

obtained exclusively (entry 3). In the case of 5-bromo-6-bromomethyl-1-(3-bromopropyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (**4a**), a mixture of **5a** and **6a** was obtained in a 6:4 ratio, even when 1.0 eq of the sodium salt of 2-nitropropane was used (entry 4). The C–C bond-cleaved compound (**6a**) was isolated as a sole product when 2.0 or 4.0 eq of the sodium salt of 2-nitropropane was used (entries 5 and 6).

**6-Pyrimidinylmethyl Nitrates** When the nitrates (**1b** and **4b**[4]) were treated with 1.0 eq of sodium methoxide, the 6-formyl compounds (**2** and **5b**) were obtained exclusively (Table II, entries 1 and 3). On the other hand, when more than 2.0 eq of sodium methoxide was used, the C–C bond-cleaved compounds (**3** and **6b**) were obtained as sole products, respectively (entries 2, 4, 5, and 6). As the reactions of the dinitrate (**7**) with sodium methoxide have been described previously,[3] the reactions were reexamined in detail and the results are summarized in Table III. When 1.0 eq of sodium methoxide was used, the 6-formyl compound (**8**) was obtained as a sole product in 66% yield (entry 1). Three compounds, *i.e.*, 6-formyl (**8**), bicyclic (**9**), and C–C bond-cleaved compounds (**10**), were identified when 1.5 eq of sodium methoxide was used (entry 2). More than 2.0 eq of sodium methoxide gave nearly the same product ratio as shown in entries 3 and 4. A slight temperature dependence was observed in the product ratio (entry

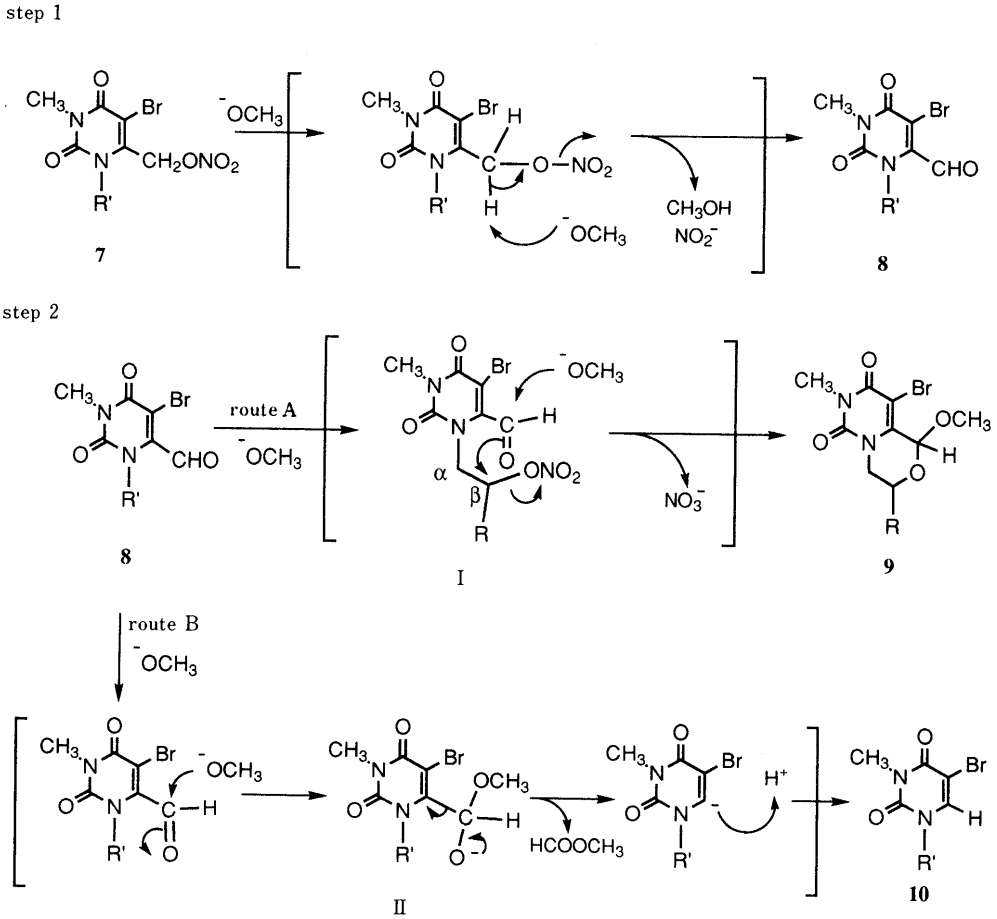


Chart 2

5).

From the above results, the 6-formyl compound (**8**) was regarded as the intermediate for the bicyclic (**9**) and the C–C bond-cleaved products (**10**). Therefore, the 6-formyl compound (**8**) was treated with sodium methoxide under various conditions as shown in Table III. In all cases, the C–C bond-cleaved product (**10**) was obtained in the same ratio (entries 6, 7, and 8). The ratio of the bicyclic compound (**9**) increased with an increase in the molar ratio of sodium methoxide (entry 8). Similarly, compound **10** was obtained in 91% yield from **7** under phase transfer-catalyzed conditions: tetraethylammonium chloride/sodium hydroxide in chloroform system.

**Reaction Mechanisms** On the basis of the above-mentioned results, a plausible reaction mechanism is presented in Chart 2. Initially, the methoxide ion attacks the hydrogen of the 6-$CH_2ONO_2$ group, then the hydrogen atom is removed followed by the loss of methanol and nitrite anion (as $NaNO_2$) to give the 6-formyl compound (**8**) (step 1: in this step, 1.0 eq of sodium methoxide is consumed). The second methoxide ion (excess anion) attacks the formyl carbon, and at this point the reaction pathway separates into routes A and B, which must be in competition (step 2).

If the compound possesses a good leaving group (such as bromine or $-ONO_2$) at the $\beta$-carbon of the 1-substituent, the oxygen atom of the carbonyl moiety (intermediate I) will simultaneously attack the $\beta$-carbon followed by the loss of nitrate ion (as $NaNO_3$) to give the bicyclic compound, and the methoxyl group becomes incorporated in the ring. A possible reaction pathway for the C–C bond-cleavage reaction being with the formation of the methoxy adduct II and the back-donation of the electron on the oxygen, followed by the loss of methyl formate to yield the final product **10**.

## Conclusion

A facile C–C bond-cleavage reaction has been found, involving the reaction of the nitrate of 6-hydroxymethylpyrimidine derivatives with sodium alkoxide, or the reaction of 6-bromomethylpyrimidine derivatives with the sodium salt of 2-nitropropane. The former reaction is better than the latter for the formation of C–C bond-cleavage products. A plausible reaction mechanism is presented, in which 6-formyl compounds are key intermediates to the final products (bicyclic compound and C–C bond-cleavage product).

### Experimental

**General** Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. The IR spectra were taken with a JASCO IR-810 spectrophotometer. The UV spectra were measured on a Hitachi 323 or a Shimadzu UV-300 spectrophotometer in EtOH. The NMR spectra were taken on a Hitachi R-600 (60 MHz for $^1H$), a JEOL JNM FX-90Q (90 MHz for $^1H$, 22.5 MHz for $^{13}C$), and a JEOL JNM GX-400 (400 MHz for $^1H$, 100 MHz for $^{13}C$) Fourier-transform spectrometer, and were measured in $CDCl_3$ solution unless otherwise mentioned. Chemical shifts are reported in ppm ($\delta$) relative to tetramethylsilane as an internal standard. The MS were obtained on a JEOL JMS-DX-303 instrument equipped with a JMA-DA-5000 data processor.

**General Reaction Procedure for Bromine-Substituted Compounds with Sodium Methoxide and 2-Nitropropane (Method A)** A mixture of sodium

methoxide and 2-nitropropane in methanol was added to a solution of a bromo-substituted compound in methanol. The mixture was stirred at room temperature for 3 h. After removal of the solvent *in vacuo*, a small amount of water was added to the residue and the mixture was extracted with $CHCl_3$ (3 times). The combined extract was dried over $MgSO_4$ and filtered. The filtrate was concentrated to dryness. The product was purified by recrystallization from a suitable solvent.

**General Reaction Procedure for 6-Pyrimidinylmethyl Nitrate with Sodium Methoxide (Method B)** A solution of sodium methoxide and 6-pyrimidinylmethyl nitrate in methanol was stirred at room temperature for 3 h. The reaction mixture was treated as described in method A as above.

**General Reaction Procedure and Computation of the Products Ratio (Tables I, II, and III)** A solution of starting material (1 eq means 2.0 mmol) and sodium methoxide (2.0 mM/ml in methanol) in methanol (entire volume, 30 ml) was stirred at room temperature for 3 h. The solvent was removed *in vacuo* at room temperature. The residue was dissolved in water (20 ml) and the mixture was extracted with $CHCl_3$ (3 times). The combined extract was dried over $MgSO_4$ and filtered. The filtrate was passed through a short silica gel column (Wako-gel C-200, 5 g, inner diameter 17 mm) eluted with a mixture of $CHCl_3$–$CH_3CN$ (gradient from 9 : 1 to 8 : 2). The eluent was concentrated to dryness *in vacuo*. The residue was subjected to determination of the products ratio by the following methods.

Computation by NMR (Table I): A part of the residue was dissolved in $CDCl_3$ and the NMR spectrum was recorded. Integration intensities of characteristic peaks [C(6)-C<u>H</u>$_2$– for **1a**, C(6)-C<u>H</u>O for **2** and **5a**, and C(6)-<u>H</u> for **3** and **6a**] were computed and the meanvalues from three experiments are shown.

Computation by IATROSCAN (Tables II and III): The residue was dissolved in $CHCl_3$ (20 ml). The solution was placed on a Chromatrod-S III (silica gel rod, 5 rods were used for each measurement) and developed with a mixture of $CHCl_3$–$CH_3CN$ (20 : 1). The rods were measured using an IATROSCAN MK-5 (Iatron Laboratories, Inc.) equipped with a Chromatopack CR-6A (Shimadzu). Each reaction was carried out twice under the same reaction conditions and the product ratio was computed.

**(5-Bromo-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)-methyl Nitrate (1b)** A solution of $AgNO_3$ (2.72 g, 16.0 mmol) in $CH_3CN$ (30 ml) was added to a solution of **1a** (4.99 g, 13.0 mmol) in $CH_3CN$ (70 ml). The mixture was heated at 90—95 °C for 2 h. The resulting crystalline mass was filtered off and the filtrate was washed with brine. The separated white mass was filtered off and the filtrate was dried over $MgSO_4$. After removal of the solvent *in vacuo*, the residue was recrystallized from $CH_3OH$ to give colorless prisms (4.23 g, 90%), mp 104—105 °C. *Anal.* Calcd for $C_7H_8BrN_3O_5$: C, 28.59; H, 2.74; Br, 27.17; N, 14.29. Found: C, 28.84; H, 2.67; Br, 26.92; N, 14.49. IR (KBr): 1708, 1670 (C=O), 1608, 1360, 1280 ($ONO_2$) $cm^{-1}$. UV $\lambda_{max}$ nm (log $\varepsilon$): 292 (3.95). $^1$H-NMR (90 MHz) $\delta$: 3.39 (3H, s, N–$CH_3$), 3.52 (3H, s, N–$CH_3$), 5.67 (2H, s, C(6)-$CH_2$). EI-MS *m/z* (relative intensity in %): 295 ($M^+$ for $^{81}$Br, 85.0), 293 ($M^+$ for $^{79}$Br, 85.0), 162 (100).

**5-Bromo-6-formyl-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (2)** This compound had a melting point of 84—86 °C; yield 78% (Table II), colorless plates (*n*-hexane–ether). *Anal.* Calcd for $C_7H_7BrN_2O_3$: C, 34.03; H, 2.86; Br, 32.34; N, 11.34. Found: C, 34.02; H, 2.77; Br, 32.11; N, 11.40. IR (KBr): 1702, 1650 (C=O) $cm^{-1}$. UV $\lambda_{max}$ nm (log $\varepsilon$): 211 (3.98), 285 (3.94). $^1$H-NMR (90 MHz) $\delta$: 3.46 and 3.55 (each 3H, s, N–$CH_3$), 10.18 (1H, s, C(6)-CHO). EI-MS *m/z* (relative intensity in %): 248 ($M^+$ for $^{81}$Br, 77.6), 246 ($M^+$ for $^{79}$Br, 77.5).

**5-Bromo-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (3)** This compound had a melting point of 184—185 °C; yield 80% (Table II), colorless needles ($CH_3OH$) [lit.[8]) mp 181—182 °C ($H_2O$)]. $^1$H-NMR (90 MHz) $\delta$: 3.39 and 3.41 (each 3H, s, N–$CH_3$), 7.51 (1H, s, C(6)-H). EI-MS *m/z* (relative intensity in %): 220 ($M^+$ for $^{81}$Br, 80.0), 218 ($M^+$ for $^{79}$Br, 80.6).

**5-Bromo-1-(3-bromopropyl)-6-formyl-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (5a)** This compound was obtained as a viscous oil, yield 45%. IR (neat): 1707, 1658 br (C=O) $cm^{-1}$. UV $\lambda_{max}$ nm (log $\varepsilon$): 210 (3.95), 283 (3.91). $^1$H-NMR (90 MHz) $\delta$: 2.28 (2H, m, –$CH_2$–), 3.44 (2H, t, $J$=6.6 Hz, Br-$CH_2$), 3.45 (3H, s, N–$CH_3$), 4.17 (2H, t, $J$=6.6 Hz, N–$CH_2$), 10.19 (1H, s, CHO). EI-MS *m/z* (relative intensity in %): 356 ($M^+$ for 2 × $^{81}$Br, 11.7), 354 ($M^+$ for $^{81}$Br and $^{79}$Br, 23.2), 352 ($M^+$ for 2 × $^{79}$Br, 12.1). HR-MS Calcd for $C_9H_{10}Br_2N_2O_3$ *m/z*: 355.9017 (for 2 × $^{81}$Br), 353.9038 (for $^{79}$Br and $^{81}$Br), 351.9058 (for 2 × $^{79}$Br). Found: 355.9006, 353.9045, 351.9048.

**3-(5-Bromo-6-formyl-3-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)propyl Nitrate (5b)** This compound had a melting point of 87—89 °C; yield 82% (Table II), yellow needles (hexane–$CH_2Cl_2$). *Anal.* Calcd for $C_9H_{10}BrN_3O_6$: C, 32.17; H, 3.00; Br, 23.78; N, 12.50. Found: C, 32.13; H, 2.87; Br, 23.48; N, 12.54. IR (KBr): 1717, 1660 (C=O), 1623, 1355, 1277 ($ONO_2$) $cm^{-1}$. UV $\lambda_{max}$ nm (log $\varepsilon$): 207 (4.00), 281 (3.95). $^1$H-NMR (90 MHz) $\delta$: 2.17 (2H, m, –$CH_2$–), 3.45 (3H, s, N–$CH_3$), 4.16 (2H, t, $J$=7.1 Hz, N–$CH_2$), 4.56 (2H, t, $J$=6.1 Hz, $O_2NO$–$CH_2$), 10.20 (1H, s, CHO). EI-MS *m/z* (relative intensity in %): 337 ($M^+$ for $^{81}$Br, 80.9), 335 ($M^+$ for $^{79}$Br, 83.6).

**5-Bromo-1-(3-bromopropyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinedione (6a)** This compound had a melting point of 74—75 °C; yield 85% (Table I), colorless needles (ether). *Anal.* Calcd for $C_8H_{10}Br_2N_2O_2$: C, 29.47; H, 3.09; Br, 49.02; N, 8.59. Found: C, 29.51; H, 3.03; Br, 48.79; N, 8.59. IR (KBr): 1713, 1660 (C=O) $cm^{-1}$. UV $\lambda_{max}$ nm (log $\varepsilon$): 212 (3.97), 283 (3.97). $^1$H-NMR (90 MHz) $\delta$: 2.28 (2H, m, –$CH_2$–), 3.40 (3H, s, N–$CH_3$), 3.45 (2H, t, $J$=6.2 Hz, Br-$CH_2$), 3.96 (2H, t, $J$=6.7 Hz, N–$CH_2$), 7.61 (1H, s, C(6)-H). EI-MS *m/z* (relative intensity in %): 327 ($M^+$ for 2 × $^{81}$Br, 49.2), 325 ($M^+$ for $^{81}$Br and $^{79}$Br, 100.0), 323 ($M^+$ for 2 × $^{79}$Br, 52.5).

**3-(5-Bromo-3-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)propyl Nitrate (6b)** This compound had a melting point of 88—90 °C; yield 78% (Table II), colorless needles (MeOH). *Anal.* Calcd for $C_8H_{10}BrN_3O_5$: C, 31.19; H, 3.27; Br, 25.94; N, 13.64. Found: C, 31.23; H, 3.14; Br, 25.68; N, 13.70. IR (KBr): 1705, 1677, 1660 (C=O), 1605, 1340, 1275 ($ONO_2$) $cm^{-1}$. UV $\lambda_{max}$ nm (log $\varepsilon$): 207 (3.98), 280 (3.93). $^1$H-NMR (90 MHz) $\delta$: 2.18 (2H, m, –$CH_2$–), 3.40 (3H, s, N–$CH_3$), 3.91 (2H, t, $J$=7.0 Hz, N–$CH_2$), 4.54 (2H, t, $J$=5.9 Hz, $O_2NO$–$CH_2$), 7.54 (1H, s, C(6)-H). EI-MS *m/z* (relative intensity in %): 309 ($M^+$ for $^{81}$Br, 36.7), 307 ($M^+$ for $^{79}$Br, 36.6).

**2-(5-Bromo-6-formyl-3-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)ethyl Nitrate (8)** This compound had a melting point of 87—88 °C; yield 67% (Table III), pale yellow needles (ether). *Anal.* Calcd for $C_8H_8BrN_3O_6$: C, 29.83; H, 2.50; Br, 24.81; N, 13.05. Found: C, 30.01; H, 2.48; Br, 24.64; N, 13.12. IR (KBr): 1705, 1660 (C=O), 1618, 1440, 1288 ($ONO_2$) $cm^{-1}$. UV $\lambda_{max}$ nm (log $\varepsilon$): 206 (4.00), 281 (3.94). $^1$H-NMR (90 MHz) $\delta$: 3.46 (3H, s, N–$CH_3$), 4.55 (2H, m, $O_2NO$–$CH_2$), 4.69 (2H, m, N–$CH_2$), 10.17 (1H, s, CHO). EI-MS *m/z* (relative intensity in %): 323 ($M^+$ for $^{81}$Br, 26.7), 321 ($M^+$ for $^{79}$Br, 26.6).

**2-(5-Bromo-3-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-1-yl)ethyl Nitrate (10)** A mixture of **7** (1.0 g, 2.7 mmol) and tetraethylammonium chloride (45 mg, 0.27 mmol) in 40% NaOH (aq., 1.1 ml) and $CHCl_3$ (10 ml) was stirred at room temperature for 5.5 h. After completion of the reaction, the mixture was separated and the aqueous layer was extracted with $CHCl_3$ (3 times). The combined extract was dried over $MgSO_4$ and filtered. The solvent was removed from the filtrate and the crystalline residue was recrystallized from benzene to give 0.72 g (91%) of colorless prisms, mp 130—131 °C. *Anal.* Calcd for $C_7H_8BrN_3O_5$: C, 28.59; H, 2.74; Br, 27.17; N, 14.29. Found: C, 28.73; H, 2.78; Br, 27.03; N, 14.13. IR (KBr): 1715, 1665, 1640 (C=O), 1280 (O–$NO_2$) $cm^{-1}$. UV $\lambda_{max}$ nm (log $\varepsilon$): 206 (4.02), 278 (3.93). $^1$H-NMR (90 MHz) $\delta$: 3.41 (3H, s, N–$CH_3$), 4.10 (2H, dd, $J$=4.0, 5.3 Hz, N–$CH_2$), 4.73 (2H, dd, $J$=4.0, 5.3 Hz, $O_2NO$–$CH_2$), 7.49 (1H, s, C(6)-H). EI-MS *m/z* (relative intensity in %): 295 ($M^+$ for $^{81}$Br, 22.5), 293 ($M^+$ for $^{79}$Br, 22.8), 219 ($(M-CH_2ONO_2)^+$ for $^{81}$Br, 47.7), 217 ($(M-CH_2ONO_2)^+$ for $^{79}$Br, 48.8), 162 ((219 and 217 − $CH_2NCO)^+$ for $^{81}$Br, 99.3), 160 ((219 and 217 − $CH_2NCO)^+$ for $^{79}$Br, 100.0).

## References


1) T. Kinoshita, Y. Watanabe, Y. Takaishi, T. Okunaka, S. Nakao, S. Furukawa, *Chem. Pharm. Bull.*, **41**, 1485 (1993).
2) *a*) N. Kornblum, "The Chemistry of Functional Groups," Part 1, ed. by S. Patai, John Wiley and Sons, 1982, pp. 361—393; *b*) H. B. Hass, M. L. Bender, *J. Am. Chem. Soc.*, **71**, 1767 (1949).
3) T. Kinoshita, M. Uga, Y. Tanimoto, K. Ohishi, S. Furukawa, *Chem. Pharm. Bull.*, **40**, 2668 (1992).
4) T. Kinoshita, Y. Takaishi, T. Okunaka, T. Ohwada, S. Furukawa, *J. Heterocycl. Chem.*, **29**, 741 (1992).
5) T. Kinoshita, T. Okunaka, T. Ohwada, H. Kawanaka, S. Furukawa, *J. Heterocycl. Chem.*, **28**, 1901 (1991).
6) *a*) N. Kornblum, H. W. Frazir, *J. Am. Chem. Soc.*, **88**, 865 (1966); *b*) A. J. Boulton, A. McKillop, "Comprehensive Heterocyclic Chemistry," ed. by A. R. Katritzky, C. W. Rees, Vol. 2, ed. by A. J. Boulton, A. McKillop, Pergamon Press, Oxford, 1984, pp. 52—53; B. C. Uff, *ibid.*, Vol. 2, pp. 339—340; *c*) D. J. Brown, *ibid.*, Vol. 3, ed. by A. J. Boulton, A. McKillop, 1984, pp. 80—82.
7) K. Hirota, Y. Yamada, Y. Kitada, S. Senda, *J. Chem. Soc., Perkin Trans. 1*, **1981**, 2943.
8) "Beilsteins Handbuch der Organischen Chemie, Hauptwerk," Vol. 24, 1936, p. 319.