Oxocin (5).—Compound **2**[12] (4.3 g) was added to a solution of 4.8 g of **3** in 32 ml of acetic acid, 4.5 ml of water, and 0.8 ml of concentrated hydrochloric acid. The mixture was kept standing at room temperature for 20 hr and evaporated *in vacuo*. The oily residue was thoroughly washed with saturated Na_2CO_3 solution and extracted four times with 50 ml of diethyl ether. The combined extracts were dried ($MgSO_4$), concentrated *in vacuo*, and distilled, yielding 6.3 g (83.5%) of **5**: bp 135–138° (0.4 mm); $n^{23}D$ 1.6296; ir (neat) no OH and CO bands, the overtone and combination pattern of aromatic CH at 2000–1600 cm^{-1} was the same as with 4,5-benzindan,[13] 1253 and 1025 (=COC), 1145 (COC), 822 (two adjacent aromatic H), and 757 cm^{-1} (four adjacent aromatic H); uv λ_{max}^{MeOH} 228 mμ (log ε 4.57), 259 (sh, 3.67), 266 (3.79), 277 (3.84), 288 (3.75), 309 (sh, 3.42), 320 (3.58), 331 (sh, 3.58), and 334 (3.64); nmr τ 2.0–3.0 (m, 6, H-7–12), 4.25 (m, 1, H-5), 4.40 (m, 1, H-1), 8.03 (m, 4, H-2, H-4), and 8.39 (m, 2, H-3); mass spectrum mol wt 226.

Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.65; H, 6.24. Found: C, 80.10; H, 6.45.

Oxazine (6).—A solution of 2.12 g of **4** in 50 ml of ethanol was added to a solution of 1.92 g of 2,4-dinitrophenylhydrazine in 200 ml of ethanol and 8 ml of concentrated sulfuric acid, and the mixture was kept at room temperature overnight. The yellow precipitate was filtered, washed with ethanol, and crystallized from 90% ethanol, yielding 3.54 g (90.5%) of **6**: mp 195–196°; ir ($CHCl_3$) 3315 cm^{-1} (NH), uv λ_{max}^{MeOH} 232 mμ (log ε 4.21), 258 (sh, 3.82), 265 (3.85), 278 (sh, 3.67), 290 (3.49), 320 (sh, 3.88), 334 (4.06), and 344 (sh, 4.02); nmr τ 0.58 (s, 1, lost on shaking with acidified D_2O, NH), 1.13 (d, 1, J_{AB} = 2.4 Hz, H-A), 1.80 (two d, 1, J_{BC} = 8.4 Hz, H-B), 2.80 (d, 1, J_{AC} = 0, H-C), 2.08–3.03 (m, 6, H-5–10), 4.78 (m, 1, H-3), 5.26 (m, 1, H-1), and 7.71 (m, 4, H-11, H-12); mass spectrum mol wt 392.

Anal. Calcd for $C_{20}H_{16}O_5N_4$: C, 61.22; H, 4.11; N, 14.27. Found: C, 61.03; H, 4.05; N, 14.14.

Oxazine (7).—A solution of 0.56 g of **5** in 10 ml of methanol was added to a solution of 0.50 g of 2,4-dinitrophenylhydrazine in 30 ml of methanol and 2 ml of concentrated sulfuric acid, and the mixture was refluxed for 30 min. After cooling, the orange precipitate was filtered, washed with methanol, and crystallized from methanol, yielding 0.91 g (90%) of **7**: mp 163–164°; ir ($CHCl_3$) 3315 cm^{-1} (NH); uv λ_{max}^{MeOH} 231 mμ (log ε 4.93), 255 (sh, 4.12), 265 (4.15), 274 (sh, 4.04), 288 (3.80), 319 (sh, 4.18), 334 (4.35), and 338 (sh, 4.33); nmr τ 0.64 (s, 1, lost on shaking with acidified D_2O, NH), 1.13 (d, 1, J_{AB} = 2.4 Hz, H-A), 1.64 (two d, 1, J_{BC} = 9.0 Hz H-B), 2.60 (d, 1, J_{AC} = 0, H-C), 2.0–2.87 (m, 6, H-5–10), 4.80 (m, 1, H-3), 5.26 (m, 1, H-1), 7.74 (m, 4, H-11, H-13), and 8.42 (m, 2, H-12); mass spectrum mol wt 406.

Anal. Calcd for $C_{21}H_{18}O_5N_4$: C, 62.06; H, 4.46; N, 13.78. Found: C, 61.94; H, 4.48; N, 13.79.

Naphthol (8).—The reduction of 10.6 g of **4** was carried out according to the procedure described by Eliel, *et al.*[7] The product was crystallized from benzene, affording 9.24 g (85.5%) of **8**: mp 84°; ir (Nujol) 3430 (OH), 820 (two adjacent aromatic H), and 754 cm^{-1} (four adjacent aromatic H); uv λ_{max}^{MeOH} 230 mμ (log ε 4.79), 271 (sh, 3.56), 280 (3.68), 291 (2.60), 327 (sh, 3.39), and 335 (3.44); nmr τ 1.87–2.87 (m, 6, aromatic H), 5.67 (br s, 2, lost on shaking with D_2O, OH), 6.14 (partially resolved t, 2, J = 7.0 Hz, OCH_2), 6.82 (partially resolved t, 2, J = 8.0 Hz, $ArCH_2$), and 8.22 (m, 4, CH_2).

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.74; H, 7.45. Found: C, 77.92; H, 7.37.

Naphthol (9).—The reduction was carried out as above. From 4.2 g of **5**, 3.78 g (86.5%) of **9** was obtained which was crystallized from benzene: mp 81–82°; ir (CCl_4) 3600 (sharp, OH), (br), and 2927 and 2858 cm^{-1} (CH_2); (Nujol) 860 (two adjacent aromatic H) and 770 cm^{-1} (four adjacent aromatic H); uv λ_{max}^{MeOH} 229 mμ (log ε 4.74), 269 (sh, 3.53), 280 (3.66), 291 (3.58), 273 (sh, 3.37), and 335 (3.41); nmr (Me_2SO) τ 0.50 (s, 1, lost on shaking with D_2O, ArOH), 5.55 (s, 1, lost on shaking with D_2O, ROH), 1.94–2.74 (m, 6, aromatic H), 6.40 (m, 2, OCH_2), 6.90 (m, 2, $ArCH_2$), and 8.40 (m, 6, CH_2).

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.25; H, 7.87. Found: C, 78.48; H, 7.72.

(12) We are indebted to Dr. H. Gross, Institute of Organic Chemistry, German Academy of Science, Berlin, for kindly supplying us with a sample of compound **2**.

(13) H. Dannenberg and A.-U. Rahman, *Chem. Ber.*, **88**, 1407 (1955).

Registry No.—**4**, 22794-75-8; **5**, 22794-76-9; **6**, 22794-77-0; **7**, 22794-78-1; **8**, 22794-79-2; **9**, 22794-80-5.

Acknowledgment.—The financial assistance of the National Research Council of Canada and the award of an Izaak Walton Killam Postdoctoral Scholarship to one of us (J. J.) are gratefully acknowledged.

Unusual Selectivity in the Halogenation of Methyl [2′-Acetamido-4′(3′H)-pyrimidon-6′-yl]-acetate with N-Halosuccinimides in N,N-Dimethylformamide

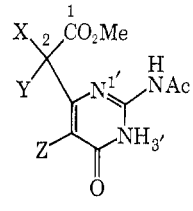
JOHN F. W. KEANA AND FRANKLIN P. MASON

Department of Chemistry, University of Oregon, Eugene, Oregon 97403

Received July 14, 1969

In connection with other synthetic studies underway in this laboratory, we required a convenient synthesis of pyrimidone **1** (Chart I). Utilizing the readily avail-

CHART I



1, X = Y = O; Z = H or Cl
2, X = Y = Z = H
3, X = H; Y = Z = Br
4, X = Y = Br; Z = H
5, X = Y = H; Z = Br
6, X = OAc; Y = H; Z = Br
7, X = Cl; Y = Z = H
8, X = Y = Cl; Z = H
9, X = H; Y = Z = Cl
10, X = Y = Z = Cl
11, X = Y = Cl; Z = Br
12, X = H; Y = Cl; Z = Br

able[1,2] methyl [2′-acetamido-4′(3′H)-pyrimidon-6′-yl]-acetate (**2**) as starting material, we became interested in the selective halogenation of this substance as a means of introducing a functional group at the α position of the side chain which might be later transformed into the desired carbonyl function. In the course of this work, a remarkable difference in selectivity of N-bromosuccinimide (NBS) and N-chlorosuccinimide (NCS) toward ester **2** was observed and constitutes the subject of this report.

While electrophilic reagents normally attack the 4(3H)-pyrimidone ring system at the 5 position,[3] it was thought that the carbomethoxy group of pyrimidone **2** might sufficiently activate the 2 position so that halo-

(1) Ester **2** was prepared by acetylation of the corresponding ester amine synthesized by the method of D. E. Worrall [*J. Amer. Chem. Soc.*, **65**, 2053 (1943)].

(2) It has not been established which double-bond tautomer involving the nitrogen atoms in the heterocyclic rings of compounds **2–12** is the preferred one.

(3) D. J. Brown and S. F. Mason, "The Pyrimidines," Interscience Publishers, Inc., New York, N. Y., 1962, pp 176–178.

genation would take place there in this substance. Bromination of ester **2** with 2 equiv of NBS in N,N-dimethylformamide (DMF) afforded 2,5′-dibromide **3** in 77% yield rather than the desired 2,2-dibromide **4**, as shown by the nmr spectrum (see Table I), which exhibited a one-proton singlet at δ 5.82[4] (C-2 proton). Dibromide **4** would have been expected to exhibit absorption at δ 6.2–6.8 (vinyl proton) (see nmr of **2**, **7**, and **8**). Treatment of ester **2** with 1 equiv of NBS led to monobromide **5** in 87% yield, as deduced from the nmr spectrum, which exhibited a two-proton singlet at δ 3.75 (C-2 protons). As expected, only one bromine atom of dibromide **3** could be replaced by acetate ion in acetic acid, affording bromodiacetate **6**. Probably owing to steric reasons, it was not possible to add an additional bromine atom to C-2 of dibromide **3** even under forcing conditions.

TABLE I

NMR (IN $CDCl_3$) CHEMICAL SHIFTS (δ) FROM TMS

Compd	C-2 proton(s) (integral)	C-5′ proton(s) (integral)
2	3.65 (2)	6.15 (1)
3	5.82 (1)	...
5	3.75 (2)	...
6	6.33 (1)	...
7	5.21 (1)	6.48 (1)
8	...	6.75 (1)
9	5.72 (1)	...
12	5.81 (1)	...

Results in contrast with those above were obtained when NCS was utilized as the halogenation agent in DMF. When ester **2** was treated with 1.33 equiv of NCS, a mixture was produced in which dichloride **8** (see below) predominated. However, column chromatography allowed separation of monochloride **7** in 37% yield. The chlorine atom in **7** was attached to the C-2 position rather than the usual[3] C-5′ position. Consistent with this view, the nmr spectrum of **7** displayed two one-proton singlets at δ 5.21 and 6.48 (C-2 and C-5′ protons, respectively).

The action of 2.00 equiv of NCS on ester **2** led to a 3:1 mixture (by nmr) of dichlorides **8** and **9**. Pure **8** could be readily obtained in 61% yield by fractional crystallization of the reaction mixture. It was not possible to separate pure **9** from **8** readily by crystallization or column chromatography. Pure **9** was eventually obtained in low yield by taking advantage of the observation that dichloride **8** added a third chlorine atom to give trichloride **10** at a much greater rate than did dichloride **9**. These last two substances were separable by column chromatography. Trichloride **10** was best prepared by treatment of ester **2** with excess NCS.

In order to interrelate the NBS- and NCS-derived products, the dichloride **8** was brominated utilizing NBS to afford bromo dichloride **11**. Unfortunately, attempts to produce this substance *via* chlorination of bromide **5** failed. The two series were interrelated through the bromo chloride **12**, which was prepared by bromination of chloride **7** with NBS and by monochlorination of bromide **5** with NCS.

(4) Complete spectral information for pertinent substances is to be found in the Experimental Section.

Experimental Section

Infrared spectra were recorded with a Beckman IR-5 spectrophotometer. The small letters in parentheses found after infrared maxima refer to the relative intensities of the peaks. Weak, moderate, and strong are referred to as w, m, and s, respectively. Nmr spectra were determined on a Varian Associates Model A-60 high-resolution spectrometer. Chemical shifts are recorded in parts per million downfield from internal TMS. Elemental analyses were performed by either Alfred Bernhard Laboratories, Mülheim, Germany, or Chemalytics, Inc., Tempe, Ariz. Mass spectra were determined on a CEC-110 spectrometer (70 eV) equipped with a direct inlet attachment. DMF was distilled prior to use. NCS was recrystallized from benzene. All reactions were run under a nitrogen atmosphere.

Methyl [2′-Acetamido-4′(3′H)-pyrimidon-6′-yl]acetate (2).—A mixture of 2.00 g of methyl [2′-amino-4′(3′H)-pyrimidon-6′-yl]acetate,[1] mp 194.5–195.5°, and 7.0 ml of acetic anhydride was heated at 130° with stirring for 10 min and cooled, and the excess solvent was removed at reduced pressure. The resulting light yellow solid was washed with ethanol and air dried, affording 2.07 g (84%), mp 184.5–186.5°. Four recrystallizations from ethanol afforded the analytical specimen as fine, white needles: mp 185–186°; nmr (DMSO-d_6) δ 2.21 (s, 3, N-acetate protons), 3.58 (s, 2, methylene protons), 3.69 (s, 3, methyl ester protons), 3.2–4.5 (s, 1, NH), and 6.13 (s, 1, vinyl proton); ir (KBr) 5.77 (m), 5.93 (m, sh), and 6.15 μ (s); uv max (EtOH) 235 mμ (ϵ 12,300) and 288 (8260).

Anal. Calcd for $C_9H_{11}N_3O_4$: C, 47.99; H, 4.92; N, 18.66. Found: C, 47.94; H, 5.01; N, 18.66.

Methyl Bromo[2′-acetamido-5′-bromo-4′(3′H)-pyrimidon-6′-yl]acetate (3).—A mixture of 2.00 g (8.88 mmol) of ester **2**, mp 184–186°, 3.49 g (2.2 × 8.88 mmol) of NBS, and 50 ml of DMF was heated for 17 hr at 60°. Removal of the solvent under reduced pressure and trituration of the resulting semisolid with water (two 20-ml portions) afforded, after drying, 3.30 g of a white solid, which was shown to be 6.5% succinimide by nmr (90% yield of dibromide **3**). Crystallization from ethyl acetate produced 2.61 g (77%) of a white powder, mp 215–222°, suitable for subsequent reactions. Three recrystallizations from ethyl acetate afforded the analytical specimen as a white, microcrystalline powder: mp 220–222°; nmr (DMSO-d_6) δ 2.18 (s, 3, N-acetate protons), 2.8–3.8 (s, 1, NH), 3.75 (s, 3, methyl ester protons), 6.12 (s, 1, methine proton), and 11.8–11.9 (s, 1, NH); ir (KBr) 5.71 (m), 6.04 (s,) 6.26 (s), and 6.50 μ (m); uv max (EtOH) 235 mμ (ϵ 12,400) and 307 (9000).

Anal. Calcd for $C_9H_9Br_2N_3O_4$: C, 28.22; H, 2.37; N, 10.97. Found: C, 28.37; H, 2.42; N, 11.02.

Methyl [2′-Acetamido-5′-bromo-4′(3′H)-pyrimidon-6′-yl]-acetate (5).—A mixture of 500 mg (2.22 mmol) of ester **2**, 406 mg (1.1 × 2.22 mmol) of NBS, and 4.0 ml of DMF was heated at 70° for 100 min. Removal of the solvent under reduced pressure yielded 1.03 g of a semisolid, which was placed in a sublimation apparatus. Heating at 100° under high vacuum overnight led to 630 mg (94%) of a light orange, solid residue, mp 180–190°. Crystallization from methanol–ethyl acetate gave 525 mg (78%) of light orange plates, mp 194–198°, together with a second crop, 61 mg (9%), mp 185–195°. Three recrystallizations from methanol afforded the analytical specimen as colorless needles: mp 198–201°; nmr (DMSO-d_6) δ 2.18 (s, 3, N-acetate protons), 3.71 (s, 3, methyl ester protons), and 3.82 (s, 2, methylene protons); ir ($CHCl_3$) 5.75 (m), 5.95 (s), 6.20 (s), and 6.43 μ (m); uv max (EtOH) 244 mμ (ϵ 11,100) and 297 (11,400).

Anal. Calcd for $C_9H_{10}BrN_3O_4$: C, 35.54; H, 3.31; N, 13.82; Br, 26.28. Found: C, 35.39; H, 3.27; N, 13.74; Br, 26.14.

Methyl Acetoxy[2′-acetamido-5′-bromo-4′(3′H)-pyrimidon-6′-yl]acetate (6).—A mixture of 1.00 g (2.62 mmol) of dibromide **3**, mp 215–222°, 430 mg (5.24 mmol) of sodium acetate, and 1.5 ml of acetic acid was heated with stirring at 110° for 40 min. Addition of 3 ml of water to the cooled mixture produced a white precipitate, which was collected and dried to yield 905 mg, mp 185–195° dec. The solid was boiled with 50 ml of ethyl acetate and filtered from 150 mg of an insoluble solid, mp 265°, and the mother liquor was evaporated at reduced pressure, affording 750 mg (79%) of a white powder, mp 199–201°. Three recrystallizations from ethyl acetate afforded the analytical specimen as a white, microcrystalline powder: mp 209–211°; nmr (DMSO-d_6)

δ 2.16 (s, 6, N- and O-acetate), 2.8–3.5 (s, 1, NH), 3.75 (s, 3, methyl ester protons), 6.37 (s, 1, methine proton), and 11.7–11.9 (s, 1, NH); ir (KBr) 5.64 (s), 5.70 (s), 6.01 (s), 6.21 (s), 6.46 (s), 7.26 (m), and 8.25 μ (s), uv max (EtOH) 240 mμ (ε 12,020) and 305 (11,210).

Anal. Calcd for $C_{11}H_{12}BrN_3O_6$: C, 36.48; H, 3.34; N, 11.60; Br, 22.07. Found: C, 36.64; H, 3.38; N, 11.47; Br, 22.26.

Methyl Chloro[2′-acetamido-4′(3′H)-pyrimidon-6′-yl]acetate (7).—A mixture of 1.800 g (8.00 mmol) of ester **2**, 1.44 g (1.33 × 8.00 mmol) of NCS, and 15 ml of DMF was heated at 65° for 1 hr. Removal of the solvent under reduced pressure afforded a semisolid, which was placed in a sublimation apparatus and heated at 100° under high vacuum for 48 hr. The residual oil was chromatographed over silica gel. Elution with 15% ethyl acetate in benzene yielded 602 mg of dichloride **8** (see below), mp 185–188°. Further elution with the same solvent mixture afforded 550 mg of a mixture composed of 65% **8** and 35% succinimide (by nmr). Continued elution with 20% ethyl acetate in benzene produced mixtures of succinimide, **7**, **8**, and **9**, and finally 780 mg (37%) of quite pure monochloride **7**, mp 136–138°. Four recrystallizations from ethyl acetate afforded the analytical specimen as colorless stars: mp 139–141°; nmr ($CDCl_3$) δ 2.32 (s, 3, N-acetate protons), 3.75 (s, 3, methyl ester protons), 5.28 (s, 1, methine proton), and 6.50 (s, 1, vinyl proton); ir ($CHCl_3$) 5.68 (s), 5.84 (m), 5.96 (s), 6.17 (s), 6.36 (s), 7.24 (m), and 7.99 μ (m); uv max (EtOH) 236 mμ (ε 12,600) and 290 (7830); mass spectrum *m/e* 261, 259 (parent ion), 225, 224, 219, 217, 183, and 182.

Anal. Calcd for $C_9H_{10}ClN_3O_4$: C, 41.62; H, 3.85. Found: C, 41.59; H, 3.91.

Methyl Dichloro[2′-acetamido-4′(3′H)-pyrimidon-6′-yl]acetate (8).—A mixture of 2.27 g (10.0 mmol) of ester **2**, 2.70 g (2.0 × 10.0 mmol) of NCS, and 20 ml of DMF was heated at 65° for 20 hr. The solvent was removed at reduced pressure and the residue was triturated with three 10-ml portions of warm water. The resulting solid was dried, affording 2.46 g which, by nmr analysis, was 8% succinimide, 22% 2,5′-dichloride **9**, and 70% 2,2-dichloride **8**. One recrystallization from ethyl acetate afforded 1.805 g (61%) of dichloride **8**, mp 181–184°. Two more recrystallizations from ethyl acetate afforded the analytical specimen as white stars: mp 189–190°; nmr ($CDCl_3$) δ 2.30 (s, 3, N-acetate protons), 3.86 (s, 3, methyl ester protons), 6.77 (s, 1, vinyl proton), 8.8–9.4 (s, 1, NH), and 14.6–15.2 (s, 1, NH); ir ($CHCl_3$) 5.67 (m), 5.93 (s), 6.18 (m), and 6.36 μ (m); uv max (EtOH) 234 mμ (ε 12,500) and 293 (6770); mass spectrum *m/e* 295, 293 (parent ion), 260, 258 (loss of Cl), 253, 251 (loss of ketene), 236, 234, 217, and 216.

Anal. Calcd for $C_9H_9Cl_2N_3O_4$: C, 36.76; H, 3.06; Cl, 24.12; N, 14.29. Found: C, 36.77; H, 3.04; Cl, 24.45; N, 14.29.

Methyl Chloro[2′-acetamido-5′-chloro-4′(3′H)-pyrimidon-6′-yl]acetate (9).—Dichlorination of 10.0 mmol of ester **2** as described in the previous experiment afforded, after removal of some 2,2-dichloride **8** by recrystallization, 747 mg of a semisolid, which by nmr analysis was 16% succinimide, 42% **8**, and 42% **9** (1.08 mmol of both **8** and **9**). To this mixture was added 2 ml of DMF and 160 mg (1.1 × 1.08 mmol) of NCS. The solution was heated at 65° for 90 min, the solvent was removed, and the residue was placed in a sublimation apparatus and heated at 100° at high vacuum for 18 hr. The residual oil, 750 mg, was chromatographed over silica gel. Elution with 10% ethyl acetate in benzene afforded in early fractions 240 mg (7% based on starting ester **2**) of trichloride **10**, mp 183–188°. Continued elution afforded a mixture of **10**, **9**, and succinimide. Finally, elution with 15% ethyl acetate in benzene produced 148 mg of nearly pure 2,5′-dichloride **9**. Recrystallization from ethyl acetate gave 75 mg (2.6%) of a white solid, mp 200–204°. Three additional recrystallizations from ethyl acetate afforded the analytical specimen as white strars: mp 202–206°; nmr ($CDCl_3$), δ 2.32 (s, 3, N-acetate protons), 3.80 (s, 3, methyl ester protons), and 5.78 (s, 1, vinyl proton); ir (KBr) 5.68 (m), 6.01 (s), 6.25 (s), 6.47 (s), 7.80 (m), and 8.08 μ (s); uv max (EtOH) 244 mμ (ε 10,800), and 301 (9000); mass spectrum *m/e* 295, 293 (parent ion), 253, 251 (loss of ketene), 219, 217, 218, 216, 194 and 192.

Anal. Calcd for $C_9H_9Cl_2N_3O_4$: C, 36.76; H, 3.06. Found: C, 36.69; H, 2.97.

Methyl Dichloro[2′-acetamido-5′-chloro-4′(3′H)-pyrimidon-6′-yl]acetate (10).—A mixture of 7.20 g (32.0 mmol) of ester **2**, 15.4 g (3.5 × 32.0 mmol) of NCS, and 100 ml of DMF was heated at 75° for 21 hr. Removal of the solvent under reduced pressure afforded a semisolid, which was placed in a sublimation apparatus and heated under high vacuum at 100° for 156 hr. The residue, 10.75 g, which proved to be 93% trichloride **10** (96% yield) by nmr analysis, was recrystallized from benzene to yield 6.13 g (58%) of light orange plates, mp 175–185°. Three additional recrystallizations from benzene afforded the analytical specimen as colorless needles: mp 188–190°; nmr ($CDCl_3$) δ 2.32 (s, 3, N-acetate protons), 3.82 (s, 3, methyl ester protons), 9.4–9.6 (s, 1, NH), and 11.7–12.7 (s, 1, NH); ir ($CHCl_3$) 5.65 (m), 5.92 (s), 6.23 (s), 6.45 (m), and 8.01 μ (m); uv max (EtOH) 243 mμ (ε 12,010) and 310 (8930); mass spectrum *m/e* 331, 329, 327 (parent ion), 294, 292 (loss of Cl), 289, 287, 285 (loss of ketene), 252, 251, 250, 249, 229, 227, 225, 201, 199, and 197.

Anal. Calcd for $C_9H_8Cl_3N_3O_4$: C, 32.87; H, 2.44. Found: C, 32.76; H, 2.29.

Methyl Dichloro[2′-acetamido-5′-bromo-4′(3′H)-pyrimidon-6′-yl]acetate (11).—A mixture of 293 mg (1.00 mmol) of dichloride **8**, mp 185–188°, 200 mg (1.10 mmol) of NBS, and 2.0 ml of DMF was heated at 65° for 50 min. Removal of the solvent under reduced pressure afforded a semisolid, which was placed in a sublimation apparatus and heated under high vacuum at 100° for 23 hr. The solid residue, 349 mg, mp 176–196°, was recrystallized from ethyl acetate to yield 285 mg (77%) of a white powder, mp 196–205°. Four further recrystallizations from ethyl acetate afforded the analytical specimen as fine, white needles: mp 204–208°; nmr ($CDCl_3$) δ 2.34 (s, 3, N-acetate protons) and 3.85 (s, 3, methyl ester protons); ir ($CHCl_3$) 5.64 (m), 5.95 (s), 6.22 (s), 6.96 (m), and 8.00 μ (m); uv max (EtOH) 244 mμ (ε 11,190) and 312 (9015); mass spectrum *m/e* 377, 375, 373, 371 (parent ion in the correct ratio for Cl_2Br), 340, 338, 336 (loss of Cl), 333, 331, 329 (loss of ketene), 296, 294, 292, 274, 272, and 270.

Anal. Calcd for $C_9H_8BrCl_2N_3O_4$: C, 28.98; H, 2.16. Found: C, 29.14; H, 2.13.

Methyl Chloro[2′-acetamido-5′-bromo-4′(3′H)-pyrimidon-6′-yl]acetate (12). A. From Monochloride 7.—A mixture of 260 mg (1.00 mmol) of chloride **7**, mp 133–138°, 200 mg (1.1 × 1.00 mmol) of NBS, and 2.0 ml of DMF was heated at 65° for 65 min. Removal of the solvent at reduced pressure yielded 515 mg of a semisolid, which was placed in a sublimation apparatus and heated under high vacuum at 100° for 18 hr. The solid residue, 326 mg, was recrystallized from ethyl acetate to yield 263 mg (78%) of an off-white solid, mp 220–223° dec. Two additional recrystallizations from ethyl acetate afforded the analytical specimen as white needles: mp 223–225.5°; nmr ($CDCl_3$) δ 2.29 (s, 3, N-acetate protons), 3.78 (s, 3, methyl ester protons), and 5.81 (s, 1, methine proton); ir (KBr) 5.70 (m), 6.06 (s), 6.26 (s), 6.50 (s), 7.80 (m), 8.11 (s), and 8.33 μ (s) uv max (EtOH) 245 mμ (ε 10,570) and 307 (9890); mass spectrum *m/e* 341, 339, 337 (parent ion), 299, 297, 295 (loss of ketene), 262, 260, and 258.

Anal. Calcd for $C_9H_9BrClN_3O_4$: C, 31.92; H, 2.68. Found: C, 31.59; H, 2.53.

B. From Monobromide 5.—A mixture of 304 mg (1.00 mmol) of bromide **5**, mp 193–198°, 148 mg (1.1 × 1.00 mmol) of NCS, and 3.0 ml of DMF was heated at 65° for 3 hr. Removal of the solvent at reduced pressure yielded 487 mg of a semisolid, which was placed in a sublimation apparatus and heated under high vacuum at 100° for 20 hr. A 100-mg portion of the residue, 320 mg, was recrystallized from ethyl acetate to yield 90 mg (80%) of an off-white solid, mp 218–224°. One additional recrystallization afforded 78 mg of a white, microcrystalline solid, mp 223–226°. This substance proved to be identical by nmr and mixture melting point with material prepared in part A above.

Registry No.—**2**, 22794-57-6; **3**, 22794-58-7; **5**, 22794-59-8; **6**, 22866-44-0; **7**, 22794-60-1; **8**, 22794-61-2; **9**, 22794-62-3; **10**, 22794-63-4; **11**, 22794-64-5; **12**, 22794-65-6.

Acknowledgments.—The authors wish to extend their thanks to the National Science Foundation (Grant GP 10736) and the National Institutes of Health (Grant 5-R01-NB07586-02) for support of this research. F. P. Mason thanks the National Science Foundation for an institutional training fellowship.