A series of α-(2-benzimidazolylthio) 4′-substituted acetophenones (II, X = OCH_3, C_6H_5, Cl, Br, NO_2) was prepared by condensation of 2-benzimidazolinethione with the suitably substituted 2-bromoacetophenone. The infrared spectra of the products in KBr disks, or in chloroform or methylene chloride solution, showed no absorption bands due to OH but did exhibit carbonyl stretching for an aryl ketone in the region of 1680–1695 cm^{-1}. As expected for structure IIb, the methylene protons appeared as a singlet in the nmr spectra (DMSO-d_6) at 5.06–5.28 ppm. In all cases, no quartet was observed for the methylene protons, as was reported for Ia and expected for IIa.

These results clearly show that a *para* substituent, whether strongly electron donating (II, X = OCH_3) or electron withdrawing (II, X = NO_2), has no effect on the position of the tautomeric equilibrium. The lack of substituent effects on the ring–chain tautomerism IIa ⇄ IIb contrasts with the report by Lutz and Moncure[2] that *para* substitution in the aroyl group of *cis*-β-aroylacrylic acids significantly affects the position of equilibrium with its lactone ring tautomer, electron-attracting groups assisting cyclization and electron-donating substituents favoring the open-chain form. In addition, Beke and coworkers[3] found that ring–chain tautomerism in cotarnine is appreciably influenced by substitution of the NCH_3 group by N-2,4-dinitrophenyl. Finally, Beke[4] has noted that the electron density on the carbinolamine carbon atom can be affected by the nature of the substituent on carbon.

Experimental Section

Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Elemental analyses were carried out by F. B. Strauss, Oxford, England. Infrared spectra were recorded on Perkin-Elmer 137 and 337 spectrophotometers. Nuclear magnetic resonance spectra were determined on a Varian A-60 spectrometer. Tetramethylsilane was used as internal standard.

α-(2-Benzimidazolylthio)-4′-methoxyacetophenone (II, X = OCH_3).—2-Benzimidazolinethione (2.10 g, 0.014 mol) and 2-bromo-4′-methoxyacetophenone (3.21 g, 0.014 mol) were suspended in 235 ml of 2-butanone and the mixture was refluxed for 6 hours. The reaction mixture was cooled and filtered to yield 4.65 g of α-(2-benzimidazolylthio)-4′-methoxyacetophenone hydrobromide, mp 248°. The hydrobromide was suspended in 50 ml of ethanol and the mixture was heated to reflux. Freshly distilled triethylamine was added dropwise until the salt had dissolved and the reaction mixture was then refluxed for 15 min and poured into 400 ml of water. The resulting white precipitate was filtered and dried, giving 3.48 g (84%) of II, X = OCH_3, mp 162.0–163.0°. Fluffy white needles, mp 163.0–163.5°, were obtained upon recrystallization from benzene.

Anal. Calcd for $C_{16}H_{14}N_2O_2S$: C, 64.41; H, 4.73; N, 9.39. Found: C, 64.49; H, 4.73; N, 9.09.

α-(2-Benzimidazolylthio)-4′-phenylacetophenone (II, X = C_6H_5).—2-Benzimidazolinethione and 2-bromo-4′-phenylacetophenone were allowed to react as above, giving α-(2-benzimidazolylthio)-4′-phenylacetophenone hydrobromide, mp 242.0–245.0°. Work-up as for II, X = OCH_3, gave II, X = C_6H_5, mp 201.0–203.0°, in 65% yield. Recrystallization from benzene–chloroform (3:1) gave an analytical sample, mp 200.5–202.0°.

Anal. Calcd for $C_{21}H_{16}N_2OS$: C, 73.23; H, 4.68; N, 8.13. Found: C, 72.91; H, 5.00; N, 8.36.

α-(2-Benzimidazolylthio)-4′-chloroacetophenone (II, X = Cl).—2-Benzimidazolinethione and 2-bromo-4′-chloroacetophenone were refluxed in 2-butanone for 1.5 hr, giving α-(2-benzimidazolylthio)-4′-chloroacetophenone hydrobromide, mp 247.0–248.0°. Work-up as above gave II, X = Cl, mp 181.0–183.0°, in 87% yield. Recrystallization from benzene–chloroform (7:3) gave II, X = Cl, as a very fine, white powder, mp 184.–185.0°.

Anal. Calcd for $C_{15}H_{11}ClN_2OS$: C, 59.50; H, 3.66; N, 9.29. Found: C, 59.75; H, 3.92; N, 9.52.

α-(2-Benzimidazolylthio)-4′-bromoacetophenone (II, X = Br).—2-Benzimidazolinethione and 2,4′-dibromoacetophenone were refluxed in 2-butanone for 3.5 hr, giving α-(2-benzimidazolylthio)-4′-bromoacetophenone hydrobromide, mp 240.0–243.0°. Work-up as above gave II, X = Br, mp 208.0–210.0°, in 40% yield. Recrystallization from chloroform–benzene (2:1) gave II, X = Br, as a white powder, mp 208.5–210.0°.

Anal. Calcd for $C_{15}H_{11}BrN_2OS$: C, 51.89; H, 3.19; N, 8.07. Found: C, 52.10; H, 3.02; N, 7.97.

α-(2-Benzimidazolylthio)-4′-nitroacetophenone (II, X = NO_2).—2-Benzimidazolinethione and 2-bromo-4′-nitroacetophenone were refluxed in 2-butanone for 4 hr, giving α-(2-benzimidazolylthio)-4′-nitroacetophenone hydrobromide, mp 245.0–248.0°. Work-up as above gave crude II, X = NO_2, mp 180.0–182.0°, in 68% yield. Recrystallization from chloroform–benzene (7:3) gave II, X = NO_2, as pale yellow needles, mp 195.0–197.0°, in 42% yield.

Anal. Calcd for $C_{15}H_{11}N_3O_3S$: C, 57.50; H, 3.54; N, 13.14. Found: C, 57.68; H, 3.48; N, 13.42.

Registry No.—IIb, X = OCH_3, 22794-86-1; IIb, X = OCH_3, hydrobromide, 22794-87-2; IIb, X = C_6H_5, 22794-88-3; IIb, X = C_6H_5, hydrobromide, 22866-47-3; IIb, X = Cl, 22794-89-4; IIb, X = Cl, hydrobromide, 22794-90-7; IIb, X = Br, 21547-82-0; IIb, X = Br, hydrobromide, 22866-48-4; IIb, X = NO_2, 22794-92-9; IIb, X = NO_2, hydrobromide, 22794-93-0.

(2) R. E. Lutz and H. Moncure, Jr., *J. Org. Chem.*, **26**, 746 (1961).

(3) D. Beke, C. Szantay, and M. Barczai-Beke, *Acta Chim. Acad., Sci. Hung.*, **21**, 153 (1959).

(4) D. Beke, *Advan. Heterocycl. Chem.*, **1**, 172 1963.

A Simple Synthesis of the Naphth[2,1-*b*]oxepin and Naphth[2,1-*b*]oxocin Systems[1]

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Acetals are known to readily form the stabilized α-alkoxy carbonium ion which, being an electrophilic species, reacts with a variety of nucleophilic reagents.[3] Protonation of vinyl ethers, too, gives rise to the α-alkoxy carbonium ion.[3] Semicyclic diacetals, *e.g.*, 2,5-dimethoxytetrahydrofuran (**1**), and cyclic vinyl ether acetals, *e.g.*, 2-ethoxy-2,3-dihydro-4H-pyran (**2**), can react with a nucleophilic reagent *via* the above-mentioned intermediate at both of the positions α to the ring oxygen. This has led us to an idea of forming new heterocyclic systems with suitable reagents, containing two nucleophilic sites.

We now wish to report a reaction of **1** and **2** with β-naphthol (**3**) and some transformations of the products obtained.

A solution of **3** in aqueous acetic acid with a small amount of hydrochloric acid reacted with **1** and **2** at

(1) Presented at the 3rd Symposium on the Chemistry of Heterocyclic Compounds, Brno, Czechoslovakia, Sept 1969.

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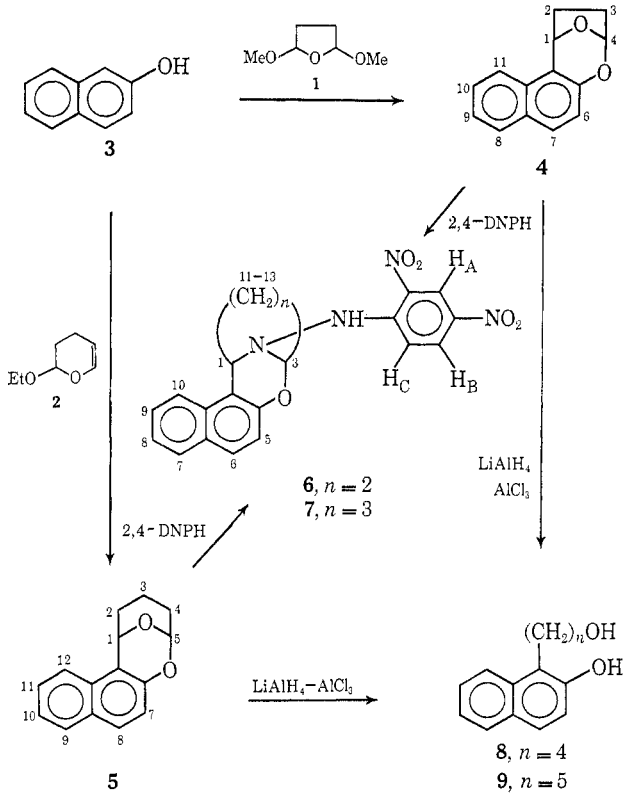
(3) E. Schmitz and I. Eichhorn in "The Chemistry of the Ether Linkage," S. Patai, Ed., Interscience Publishers, Inc., New York, N. Y., 1967, pp 310–351, and literature cited therein.

room temperature, yielding 1,4-epoxy-1,2,3,4-tetrahydronaphth[2,1-*b*]oxepin (**4**) and 1,5-epoxy-1,2,3,4-tetrahydro-5H-naphth[2,1-*b*]oxocin (**5**) (see Scheme I), respectively.

SCHEME I



Elemental analyses, mass spectrometric molecular weights, and infrared spectra of **4** and **5** are consistent with the assigned structures. Ultraviolet spectra of **4** and **5** are closely similar to that of 3-methyl-2,3-dihydro-1H-naphtho[2,1-*b*]pyran (2-methyl-5,6-benzochroman)[4] and, moreover, there is a complete agreement between the structures of **4** and **5** and their 60-MHz nmr spectra. Both of them showed expected signals of aromatic and methylene protons. One-proton multiplets [with **4** at τ 3.95 (H-4) and 4.20 (H-1), with **5** at τ 4.25 (H-5) and 4.40 (H-1)] are assigned both on the basis of their chemical shifts and decoupling experiments. With both **4** and **5**, irradiation of the multiplets of adjacent methylene protons caused only the lower field one-proton multiplets to collapse to singlets, whereas the higher field one-proton multiplets collapsed only partly, apparently owing to a long-range coupling to the aromatic hydrogens. With **5**, the upfield shift of H-1 and H-5 signals (compared with compound **4**) is approximately of the same magnitude as the shift between cyclopentane and cyclohexane protons.[5]

Treatment of **4** and **5** with 2,4-dinitrophenylhydrazine in acidified ethanol resulted in replacement of the epoxy bridges by the reagent and gave N-(2,4-dinitroanilino)-1,3-ethano-2,3-dihydro-1H-naphth[1,2-*e*]-1,3-oxazine (**6**) and N-(2,4-dinitroanilino)-1,3-propano-2,3-dihydro-1H-naphth[1,2-*e*]-1,3-oxazine (**7**), respectively. Their ultraviolet spectra showed no 2,4-dinitrophenylhydrazone bands at 365–385 mμ[6] and corresponded to the addition of the maxima of **4** or **5** and 2,4-dinitrophenylhydrazine. Again, their elemental analyses, mass spectrometric molecular weights, infrared spectra, and nmr spectra are in complete agreement with the assigned structures.

Additional chemical evidence for the structures of compounds **4** and **5** was obtained when the method of Eliel[7] for reduction of acetals and ketals by means of lithium aluminum hydride–aluminum chloride was applied to them. We carried out the reduction with the aim of selectively removing the epoxy bridges and thus arriving at the corresponding tetrahydronaphth-[2,1-*b*]oxepin[8] and tetrahydro-5H-naphth[2,1-*b*]oxocin. However, we were able to isolate only the corresponding 1-(4-hydroxybutyl)-2-hydroxynaphthalene (**8**) and 1-(5-hydroxypentyl)-2-hydroxynaphthalene (**9**), though in yields in excess of 80%.

Compound **8** was reported earlier by Chatterjea;[8] however, no constants were given. The similarity of ultraviolet spectra of **8** and **4** and **9** and **5** is striking; both **8** and **9** show hydroxyl bands in the infrared and alcoholic and phenolic protons in the nmr. With **9**, both the resonances of alcoholic and phenolic protons were obscured by the methylene resonances in deuteriochloroform. When the nmr spectrum was run in dimethyl sulfoxide,[9] both the alcoholic and phenolic protons were shifted downfield and gave separate singlets. Owing to the acidity of the phenolic hydrogen, no spin–spin splitting of the alcoholic proton was observed.

Experimental Section[10]

Oxepin (4).—Acetal **1** (4.95 g) was added to a solution of 5.4 g of **3** in 25 ml of acetic acid, 5 ml of water, and 1 ml of concentrated hydrochloric acid. The mixture was kept standing at room temperature for 24 hr and slowly diluted with 100 ml of water, and the precipitate of crude **4** was treated with 100 ml of 5% sodium hydroxide to remove unreacted **3**. The mixture was extracted three times with 100 ml of diethyl ether, and the combined extracts were dried ($MgSO_4$) and evaporated to dryness in *vacuo*. Crystallization of the residue from methanol afforded 6.9 g (83%) of white, crystalline **4**: mp 91–92°; ir (CCl_4) no OH and CO bands, 3028 cm^{-1} (aromatic CH); (Nujol) 1625, 1575, and 1470, 1250 and 1090 (=COC), 1194 (COC), 828 (two adjacent aromatic H), and 768[11] cm^{-1} (four adjacent aromatic H); uv λ_{max}^{MeOH} 226 mμ (log ϵ 4.43), 260 (sh, 3.52), 268 (3.71), 278 (3.82), 290 (3.70), 309 (sh, 3.11), 321 (3.43), 329 (sh, 3.40), and 335 (3.51); nmr τ 2.14–3.05 (m, 6, H-6–11), 3.95 (m, 1,H-4), 4.20 (m, 1, H-4), and 7.70 (m, 4, H-2,3); mass spectrum mol wt 212.

Anal. Calcd for $C_{14}H_{12}O_2$: C, 79.22; H, 5.69. Found: C, 79.44; H, 5.47.

(4) E. Wenkert, R. D. Youssefyeh, and R. G. Lewis, *J. Amer. Chem. Soc.*, **82**, 4679 (1960).

(5) R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds," John Wiley & Sons, Inc., New York, N. Y., 1967, p 136.

(6) F. Bohlmann, *Chem. Ber.*, **84**, 490 (1951).

(7) E. L. Eliel, V. G. Badding, and M. N. Rerick, *J. Amer. Chem. Soc.*, **84**, 2371 (1962).

(8) J. N. Chatterjea, *J. Indian Chem. Soc.*, **32**, 203 (1955).

(9) O. L. Chapman and R. W. King, *J. Amer. Chem. Soc.*, **86**, 1256 (1964).

(10) Microanalyses were performed by M-H-W Laboratories, Garden City, Mich. Melting points were determined on a Kofler micro hot stage. Melting and boiling points are uncorrected. Nmr spectra were obtained on a Varian A-60 spectrometer using tetramethylsilane as an internal reference in chloroform-*d* unless otherwise stated. Uv spectra were obtained in methanol on a Coleman–Hitachi Model 124 spectrophotometer. Ir spectra were obtained on a Perkin-Elmer Model 237B grating spectrophotometer. Mass spectra were taken on a Consolidated Electrodynamic Corp. Model 21-104 spectrometer.

(11) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1964, p 27.

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.

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

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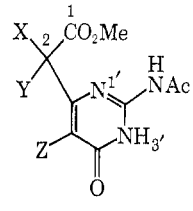
In connection with other synthetic studies underway in this laboratory, we required a convenient synthesis of pyrimidone **1** (Chart I). Utilizing the readily avail-

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.