Pyrano[4,3-*d*]pyrimidinium salts
1. Reactions with N-nucleophiles

E. B. Tsupak, M. A. Shevchenko, V. V. Kostrub, and Yu. N. Tkachenko*

South Federal University, Department of Chemistry,
7 ul. Zorge, 344090 Rostov-on-Don, Russian Federation.
E-mail: dastr@yandex.ru

5-Aroyl-1,3,6-trimethyluracils were converted to pyrano[4,3-*d*]pyrimidinium salts. Reactions of the salts obtained with ammonia, primary amines, and hydrazine were studied.

Key words: 5-aroyl-1,3,6-trimethyluracils, 5-aroyl-6-[2-(4-methylphenyl)-2-oxoethyl]pyrimidine-2,4(1*H*,3*H*)-diones, 5-aroyl-6-(2-morpholinoethenyl)pyrimidine-2,4(1*H*,3*H*)-diones, 5-aroyl-6-(2-arylethenyl)pyrimidine-2,4(1*H*,3*H*)-diones, pyrano[4,3-*d*]pyrimidinium salts, recyclization, pyrido[4,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones, pyrido[4,3-*d*]pyrimidinium salts, 1*H*-pyrimido[5,4-*d*][1,2]diazepine-2,4(3*H*,9*H*)-diones.

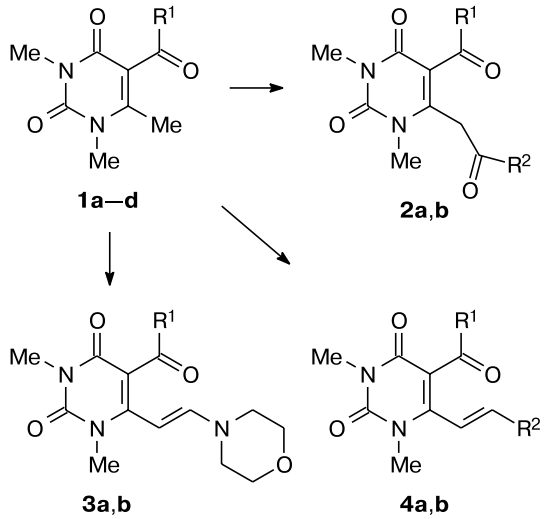
Pyrylium and benzopyrylium salts are important heterocyclic compounds. 2-Benzopyrylium salts, in contrast to isomeric 1-benzopyrylium ones, are capable of recyclization and substitution of oxygen atom, which allows one to use them for the preparation of various hetero- and carbocyclic systems. They are widely used in the synthesis of naphthalenes,[1] benz[*a*]anthracenes,[2] indenes,[3] chrysenes,[4] benzo[*b*]furans,[5] isoquinolines,[6] and isoquinolinium salts.[7] At the same time, uracil and many of its derivatives are widely spread in the nature and have versatile biological activity. Thus, it can be supposed that the fused heterocyclic cations, including uracil and pyrylium rings, are very interesting subjects to be studied. In particular, in the reactions with N-nucleophiles they might serve as the synthetic precursors of pyrido[4,3-*d*]pyrimidinium system, which lately is under the intensive research by medical chemistry.[8—11] Nevertheless, there is no information on pyrano[4,3-*d*]pyrimidinium salts and their properties in the available periodic literature.

In the present work, we report our results on the research of convenient ways for the synthesis of pyrano[4,3-*d*]pyrimidinium salt derivatives starting from 5-aroyl-1,3,6-trimethyluracils. We also studied the reactivity of the salts obtained toward N-nucleophiles: ammonia, primary amines, and hydrazine.

One of the methods often used for the synthesis of pyrylium and benzo[*c*]pyrylium cations is the cyclization of 1,5-dicarbonyl compounds in the presence of acids.[12] From this point of view, 5-aroyl-1,3,6-trimethyluracils[13] seem to be very prospective starting compounds for the preparation of pyrano[4,3-*d*]pyrimidinium salts. The 6-methyl group in these compounds has a noticeable CH-activity[14—16] and can be converted to phenacyl or enamine group,[17] as well as to styryl one, the presence of which can also serve as the basis for the pyran ring closure.[18]

5-Aroyl-1,3,6-trimethyluracils **1** have been converted to 5-aroyl-1,3-dimethyl-6-[2-(4-methylphenyl)-2-oxoethyl]pyrimidine-2,4(1*H*,3*H*)-diones **2a**,**b** by the reaction with aromatic acyl chlorides in the presence of aluminum chloride (Scheme 1). The condensation of ke-

Scheme 1



1: R^1 = 4-MeC_6H_4 (**a**), Ph (**b**), 4-BrC_6H_4 (**c**), 2,4-$Cl_2C_6H_3$ (**d**)
2: R^1 = R^2 = 4-MeC_6H_4 (**a**); R^1 = Ph, R^2 = 4-MeC_6H_4 (**b**)
3: R^1 = 4-BrC_6H_4 (**a**), 2,4-$Cl_2C_6H_3$ (**b**)
4: R^1 = Ph, R^2 = 4-MeC_6H_4 (**a**); R^1 = R^2 = 4-BrC_6H_4 (**b**)

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 11, pp. 2251—2257, November, 2007.

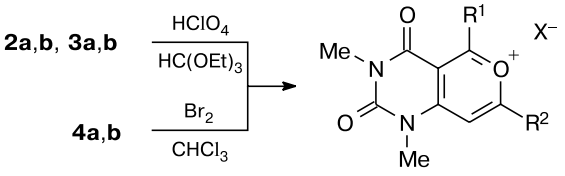
1066-5285/07/5611-2330

tones **1** with triethyl orthoformate and morpholine leads to 5-aroyl-1,3-dimethyl-6-(2-morpholinoethenyl)pyrimidine-2,4(1*H*,3*H*)-diones **3a**,**b**, whereas with aromatic aldehydes in the presence of piperidine, to 5-aroyl-6-(2-arylethenyl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-diones **4a**,**b**.

The formation of the target 1,5-diketones **2**, enamines **3**, and styryls **4** was confirmed by ^{1}H and IR spectroscopy and mass spectrometry data.

We have shown that diketones **2a**,**b** and enamines **3a**,**b** upon treatment with $HClO_4$ in triethyl orthoformate and styryls **4a**,**b** upon treatment with bromine in $CHCl_3$ were converted to 1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrano[4,3-*d*]pyrimidinium perchlorates and bromides **5a**—**f**, respectively (Scheme 2).

Scheme 2



5a—f

5	R^1	R^2	X
a	4-MeC_6H_4	4-MeC_6H_4	ClO_4
b	Ph	4-MeC_6H_4	ClO_4
c	4-BrC_6H_4	H	ClO_4
d	2,4-$Cl_2C_6H_3$	H	ClO_4
e	Ph	4-MeC_6H_4	Br
f	4-BrC_6H_4	4-BrC_6H_4	Br

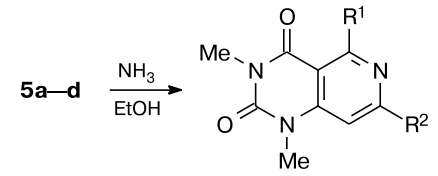
The structure of pyrano[4,3-*d*]pyrimidinium cations was ascribed to salts **5** as a result of the comparative analysis of the ^{1}H NMR spectra, in which, due to the cationic charge, a downfield shift of the signals of protons of the *N*-methyl groups, in comparison with the neutral starting compounds is observed. This difference in the chemical shift values of the N(1)Me groups is 0.4—0.6 ppm; the N(3)Me groups are more remote from the positively charged center and the downfield shift here is considerably smaller in value.

When the reactions of pyrano[4,3-*d*]pyrimidinium perchlorates **5a**—**d** with afore-mentioned N-nucleophiles were studied, we found that they undergo the recyclization to 1,3-dimethylpyrido[4,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **6a**—**d** upon treatment with ammonia (Scheme 3).

The structures of pyrido[4,3-*d*]pyrimidines **6c**,**d** were confirmed not only by ^{1}H NMR and IR spectroscopy data, but also by the synthesis of the authentic samples from enamines **3a**,**b** by the method described earlier[19] (Scheme 4).

The heating of pyrano[4,3-*d*]pyrimidinium perchlorates and bromides **5a**—**f** with primary amines in acetic

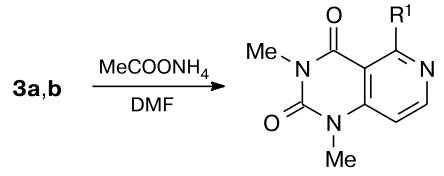
Scheme 3



6a—d

$R^1 = R^2$ = 4-MeC_6H_4 (**a**); R^1 = Ph, R^2 = 4-MeC_6H_4 (**b**); R^1 = 4-BrC_6H_4, R^2 = H (**c**); R^1 = 2,4-$Cl_2C_6H_3$, R^2 = H (**d**)

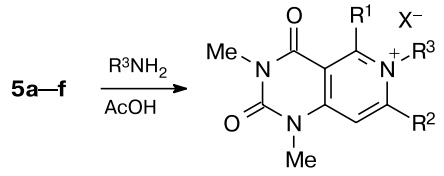
Scheme 4



6c,**d**

acid afforded 1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[4,3-*d*]pyrimidinium salts **7a**—**f** (Scheme 5).

Scheme 5



7a—f

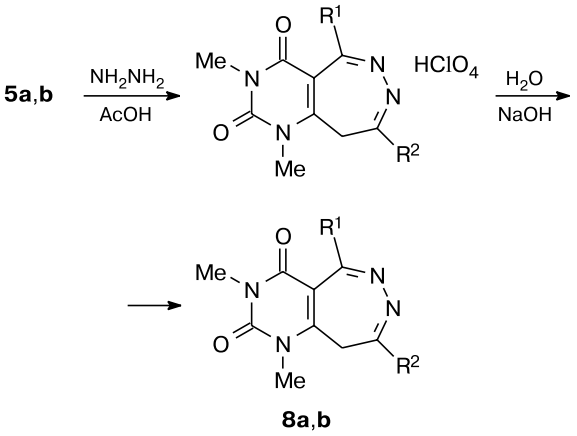
7	R^1	R^2	R^3	X
a	4-MeC_6H_4	4-MeC_6H_4	Ph	ClO_4
b	Ph	4-MeC_6H_4	4-BrC_6H_4	ClO_4
c	4-BrC_6H_4	H	3,5-$Me_2C_6H_3$	ClO_4
d	2,4-$Cl_2C_6H_3$	H	4-BrC_6H_4	ClO_4
e	Ph	4-MeC_6H_4	4-$MeOC_6H_4$	Br
f	4-BrC_6H_4	4-BrC_6H_4	3,4-$(MeO)_2C_6H_3(CH_2)_2$	Br

In the ^{1}H NMR spectra of pyrido[4,3-*d*]pyrimidinium cations **7**, chemical shifts of protons of the methyl groups in the uracil ring are downfield shifted relatively to those in the spectra of neutral pyridouracils **6** (by ~0.2 ppm).

The reaction of pyranopyrimidinium perchlorates **5a**—**d** with hydrazine proceeds readily, but is not straightforward as it is in the reaction with ammonia and arylamines: the structures of the reaction product depend on the presence or absence of a substituent at the C(7) atom. Perchlorates **5a**,**b**, containing aryl substituents in positions 5 and 7, react with the ring expansion and, after treatment with diluted alkaline solution, give the

neutral 1,3-dimethyl-1*H*-pyrimido[5,4-*d*][1,2]diazepine-2,4(3*H*,9*H*)-diones **8a**,**b** (Scheme 6), the structures of which were confirmed by spectroscopy methods. Thus, in the ^{1}H NMR spectra, the methylene group resonates as a pair of doublets in the interval δ 2.97—3.00 and 4.38—4.42 (J = 13.27—13.33 Hz). The nonequivalency of the methylene protons, obviously, is caused by the nonplanar structure of the seven-membered ring of diazepines **8a**,**b** and by the high energy barrier for its conformation to be changed. In the mass spectrum, there is a peak pointing out the $[M - N_2]^+$ fragmentation.

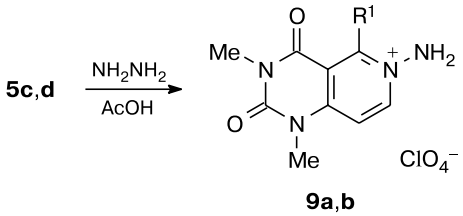
Scheme 6



R^1 = Ph, R^2 = 4-MeC_6H_4 (**a**); R^1 = R^2 = 4-MeC_6H_4 (**b**)

7-Unsubstituted salts **5c**,**d** upon treatment with hydrazine do not undergo the ring expansion, rather they undergo recyclization to 6-amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[4,3-*d*]pyrimidinium perchlorates **9a**,**b** (Scheme 7).

Scheme 7



R^1 = 4-BrC_6H_4 (**a**), 2,4-$Cl_2C_6H_3$ (**b**)

In the ^{1}H NMR spectra of 6-aminopyrido[4,3-*d*]pyrimidinium salts **9a**,**b**, signals of the methylene groups, characteristic of diazepines **8a**,**b**, are absent, however two doublets are contained in the intervals δ 8.03—8.08 and 8.94—8.99 (J = 7.4—7.5 Hz), which are assigned by us to the C(8)H and C(7)H protons of the pyridinium ring, respectively. A singlet of two protons of the amino group in the region δ 7.19—7.42 is also observed. In the mass spectrum, there is a peak pointing out the $[M - NH_2]^+$ fragmentation.

The nature of such an interesting behavior of pyrano[4,3-*d*]pyrimidinium salts **5** in the reactions with hydrazine requires further study.

In conclusion, the methods for the synthesis of pyrano[4,3-*d*]pyrimidinium salts, starting from 5-aroyl-1,3,6-trimethyluracils, were elaborated. The reactions of the salts obtained with ammonia, primary amines, and hydrazine, which lead to the formation of pyrido[4,3-*d*]pyrimidine, pyrido[4,3-*d*]pyrimidinium, and pyrimido[5,4-*d*][1,2]diazepine systems, were studied.

Experimental

IR spectra of compounds obtained were recorded on a Specord IR-71 spectrometer in Nujol. ^{1}H NMR spectra were recorded on a Bruker Avance DPX-250 and Varian Unity-300 spectrometers in $CDCl_3$, DMSO-d_6, and $CDCl_3$—CF_3COOH mixture; HMDS was used as the internal standard. Mass spectra were recorded on a Kratos instrument with direct inlet of the sample into the source of ions (EI, energy of ionization: 70 eV, operating voltage: 1.75 kV). Compounds **1a**—**d** were obtained according to the procedure described earlier.[13]

1,3-Dimethyl-5-(4-methylbenzoyl)-6-[2-(4-methylphenyl)-2-oxoethyl]pyrimidine-2,4(1*H*,3*H*)-dione (2a). A mixture of $AlCl_3$ (1 g, 7.49 mmol), 4-toluoyl chloride (1 mL, 1.17 g, 7.56 mmol), and 5-(4-methylbenzoyl)-1,3,6-trimethylpyrimidine-2,4(1*H*,3*H*)-dione (**1a**) (2 g, 7.35 mmol) was melted and heated for 1 h at 190—200 °C. The tar-like mixture obtained was refluxed with water (20 mL) for 15 min 3 times, water was decanted. The residue was recrystallized from EtOH and dried at 100 °C to obtain 0.94 g (33%) of compound **2a** as colorless crystals, m.p. 250—255 °C (EtOH). Found (%): C, 70.56; H, 5.61. $C_{23}H_{22}N_2O_4$. Calculated (%): C, 70.75; H, 5.68. ^{1}H NMR ($CDCl_3$), δ: 2.33—2.39 (2 s, 6 H, ArMe, Ar′Me); 3.36—3.37 (2 s, 6 H, N(3)Me, N(1)Me); 4.38 (s, 2 H, C(6)CH_2); 7.15—7.27 (m, 4 H, $H(3)_{Ar}$, $H(5)_{Ar}$, $H(3)_{Ar'}$, $H(5)_{Ar'}$); 7.67—7.78 (m, 4 H, $H(2)_{Ar}$, $H(6)_{Ar}$, $H(2)_{Ar'}$, $H(6)_{Ar'}$). MS, m/z: 390 $[M]^+$, 375 $[M - CH_3]^+$, 360 $[M - 2\ CH_3]^+$, 271 $[M - COC_7H_7]^+$, 119 $[COC_7H_7]^+$, 91 $[C_7H_7]^+$. IR, ν/cm^{-1}: 1635, 1660, 1675, 1705 (C=O).

5-Benzoyl-1,3-dimethyl-6-[2-(4-methylphenyl)-2-oxoethyl]pyrimidine-2,4(1*H*,3*H*)-dione (2b) was obtained similarly to compound **2a** from $AlCl_3$ (1 g, 7.49 mmol), 4-toluoyl chloride (1 mL, 1.17 g, 7.56 mmol), and ketone **1b** (1.88 g, 7.29 mmol). The yield was 1.18 g (43%), colorless crystals, m.p. 235—237 °C (EtOH). Found (%): C, 70.39; H, 5.43. $C_{22}H_{20}N_2O_4$. Calculated (%): C, 70.20; H, 5.36. ^{1}H NMR ($CDCl_3$), δ: 2.39 (s, 3 H, Ar′Me); 3.36—3.38 (2 s, 6 H, N(3)Me, N(1)Me); 4.40 (s, 2 H, C(6)CH_2); 7.24 (d, 2 H, $H(3)_{Ar'}$, $H(5)_{Ar'}$, J = 8.1 Hz); 7.38 (t, 1 H, $H(3)_{Ar}$, J = 7.32 Hz); 7.50 (br.t, 1 H, $H(4)_{Ar}$, J = 7.32 Hz); 7.72—7.83 (m, 4 H, $H(2)_{Ar}$, $H(6)_{Ar}$, $H(2)_{Ar'}$, $H(6)_{Ar'}$). MS, m/z: 376 $[M]^+$, 257 $[M - COC_7H_7]^+$, 119 $[COC_7H_7]^+$, 91 $[C_7H_7]^+$. IR, ν/cm^{-1}: 1650, 1655, 1670, 1700 (C=O).

5-(4-Bromobenzoyl)-1,3-dimethyl-6-(2-morpholinoethenyl)-pyrimidine-2,4(1*H*,3*H*)-dione (3a). A mixture of pyrimidinedione **1c** (3 g, 8.9 mmol), triethyl orthoformate (3.95 g, 4.44 mL, 26.7 mmol), and morpholine (2.32 g, 2.32 mL, 26.7 mmol) was refluxed for 2 h. The mixture was cooled to 80 °C and EtOH (10 mL) was added to it. The suspension obtained was refluxed for 3—5 min and cooled to ~20 °C. The precipitate was filtered off, washed with EtOH, and dried at 80—100 °C to obtain 3.47 g (90%) of compound **3a** as yellow crystals, m.p. 236—238 °C (from EtOH). Found (%): C, 52.19; H, 4.77; Br, 18.01. $C_{19}H_{20}BrN_3O_4$. Calculated (%): C, 52.55; H, 4.64; Br, 18.40. ^{1}H NMR ($CDCl_3$), δ: 2.96 (t, 4 H, $N(CH_2)_2$, J = 4.8 Hz); 3.34 (s, 3 H, N(3)Me); 3.41 (s, 3 H, N(1)Me); 3.51 (t, 4 H, $O(CH_2)_2$, J = 4.8 Hz); 4.54 (d, 1 H, C(6)CH, J = 13.11 Hz); 6.44 (d, 1 H, C(6)CHC<u>H</u>, J = 13.11 Hz); 7.51 (d, 2 H, $H(2)_{Ar}$, $H(6)_{Ar}$, J = 8.48 Hz); 7.67 (d, 2 H, $H(3)_{Ar}$, $H(5)_{Ar}$, J = 8.48 Hz). IR, ν/cm^{-1}: 1620, 1670, 1705 (C=O).

5-(2,4-Dichlorobenzoyl)-1,3-dimethyl-6-(2-morpholino-ethenyl)pyrimidine-2,4(1*H*,3*H*)-dione (3b) was obtained similarly to compound **3a** from ketone **1d** (2.91 g, 8.89 mmol), triethyl orthoformate (3.95 g, 4.44 mL, 26.7 mmol), and morpholine (2.32 g, 2.32 mL, 26.7 mmol). The yield was 2.42 g (64%), yellow crystals, m.p. 182—186 °C (EtOH). Found (%): C, 54.04; H, 4.40; Cl, 16.57. $C_{19}H_{19}Cl_2N_3O_4$. Calculated (%): C, 53.79; H, 4.51; Cl, 16.71. ^{1}H NMR ($CDCl_3$), δ: 3.09 (t, 4 H, $N(CH_2)_2$, J = 4.8 Hz); 3.33 (s, 3 H, N(3)Me); 3.41 (s, 3 H, N(1)Me); 3.62 (t, 4 H, $O(CH_2)_2$, J = 4.8 Hz); 4.67 (d, 1 H, C(6)CH, J = 12.34 Hz); 6.68 (d, 1 H, C(6)CHC<u>H</u>, J = 12.34 Hz); 7.21 (dd, 1 H, $H(5)_{Ar}$, J_o = 8.3 Hz, J_m = 1.93 Hz); 7.33 (d, 1 H, $H(3)_{Ar}$, J = 1.93 Hz); 7.44 (d, 2 H, $H(6)_{Ar}$, J = 8.48 Hz). IR, ν/cm^{-1}: 1615, 1665, 1700 (C=O).

5-Benzoyl-1,3-dimethyl-6-[2-(4-methylphenyl)ethenyl]pyrimidine-2,4(1*H*,3*H*)-dione (4a). A solution of ketone **1b** (5 g, 19.4 mmol), 4-tolualdehyde (4.5 mL, 4.6 g, 38.3 mmol), and piperidine (1 mL, 0.87 g, 10.2 mmol) in EtOH (20 mL) was refluxed for 10 h. After the reaction mixture was cooled, the precipitate of light yellow color that formed was filtered off, washed with EtOH, and dried at 110—120 °C to obtain 6.45 g (92%) of compound **4a** as yellow crystals, m.p. 207—211 °C (EtOH). Found (%): C, 73.52; H, 5.70. $C_{22}H_{20}N_2O_3$. Calculated (%): C, 73.32; H, 5.59. ^{1}H NMR ($CDCl_3$), δ: 2.27 (s, 3 H, Ar´Me); 3.37 (s, 3 H, N(3)Me); 3.44 (s, 3 H, N(1)Me); 6.46 (d, 1 H, C(6)CH, J = 16.2 Hz); 6.77 (d, 1 H, C(6)CHC<u>H</u>, J = 16.2 Hz); 7.06 (s, 4 H, Ar´); 7.31—7.39 (m, 2 H, $H(3)_{Ar}$, $H(5)_{Ar}$); 7.48 (t, 1 H, $H(4)_{Ar}$, J = 7.33 Hz); 7.81 (d, 2 H, $H(2)_{Ar}$, $H(6)_{Ar}$, J = 6.94 Hz). IR, ν/cm^{-1}: 1635, 1650, 1695 (C=O).

5-(4-Bromobenzoyl)-6-[2-(4-bromophenyl)ethenyl]-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (4b) was obtained similarly to compound **4a** from ketone **1c** (1.01 g, 3 mmol), 4-bromobenzaldehyde (0.72 g, 3.89 mmol), and piperidine (0.2 mL, 0.174 g, 2 mmol) in EtOH (10 mL). The yield was 1.25 g (83%), yellow crystals, m.p. 206—210 °C (EtOH). Found (%): C, 50.24; H, 3.31; Br, 31.22. $C_{21}H_{16}Br_2N_2O_3$. Calculated (%): C, 50.03; H, 3.20; Br, 31.70. ^{1}H NMR ($CDCl_3$), δ: 3.37 (s, 3 H, N(3)Me); 3.46 (s, 3 H, N(1)Me); 6.51 (d, 1 H, C(6)CH, J = 16.2 Hz); 6.73 (d, 1 H, C(6)CHC<u>H</u>, J = 16.2 Hz); 7.08 (d, 2 H, $H(2)_{Ar'}$, $H(6)_{Ar'}$, J = 8.49 Hz); 7.42 (d, 2 H, $H(3)_{Ar'}$, $H(5)_{Ar'}$, J = 8.48 Hz); 7.54 (d, 2 H, $H(3)_{Ar}$, $H(5)_{Ar}$, J = 8.48 Hz); 7.67 (t, 2 H, $H(2)_{Ar}$, $H(6)_{Ar}$, J = 8.48 Hz). IR, ν/cm^{-1}: 1630, 1650, 1700 (C=O).

1,3-Dimethyl-5,7-bis(4-methylphenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrano[4,3-*d*]pyrimidinium perchlorate (5a). Perchloric acid (1 mL of 70% aq. solution, 1.675 g, 11.7 mmol) in $HC(OEt)_3$ (20 mL) was added to diketone **2a** (2.07 g, 5.30 mmol). The solution formed was diluted with AcOEt (20 mL). The precipitate formed was filtered off, washed with AcOEt, and dried at 100 °C to obtain 1.38 g (55%) of perchlorate **5a** as colorless crystals, m.p. 295 °C (AcOEt). Found (%): C, 58.35; H, 4.31; Cl, 7.18. $C_{23}H_{21}ClN_2O_7$. Calculated (%): C, 58.42; H, 4.48; Cl, 7.50. ^{1}H NMR ($CDCl_3$—CF_3COOH), δ: 2.47—2.52 (2 s, 6 H, ArMe, Ar´Me); 3.48 (s, 3 H, N(3)Me); 3.92 (s, 3 H, N(1)Me); 7.41—7.49 (br.d, 4 H, $H(3)_{Ar}$, $H(5)_{Ar}$, $H(3)_{Ar'}$, $H(5)_{Ar'}$, J = 8.2 Hz); 7.75 (d, 2 H, $H(2)_{Ar'}$, $H(6)_{Ar'}$, J = 7.9 Hz); 7.92 (s, 1 H, C(8)H); 8.03 (d, 2 H, $H(2)_{Ar}$, $H(6)_{Ar}$, J = 8.21 Hz). MS, *m/z*: 373 $[M]^+$, 119 $[COC_7H_7]^+$, 91 $[C_7H_7]^+$. IR, ν/cm^{-1}: 1090, 1100 (Cl—O); 1610, 1695 (C=O).

1,3-Dimethyl-7-(4-methylphenyl)-2,4-dioxo-5-phenyl-1,2,3,4-tetrahydropyrano[4,3-*d*]pyrimidinium perchlorate (5b) was obtained similarly to compound **5a** from diketone **2b** (2 g, 5.31 mmol) and 70% aq. $HClO_4$ (1 mL, 1.675 g, 11.7 mmol) in $HC(OEt)_3$ (20 mL). The yield was 1.43 g (59%), colorless crystals, m.p. 295—298 °C (AcOEt). Found (%): C, 57.23; H, 4.05; Cl, 7.70. $C_{22}H_{19}ClN_2O_7$. Calculated (%): C, 57.59; H, 4.17; Cl, 7.73. ^{1}H NMR ($CDCl_3$—CF_3COOH), δ: 2.50 (s, 3 H, Ar´Me); 3.49 (s, 3 H, N(3)Me); 3.97 (s, 3 H, N(1)Me); 7.47 (d, 2 H, $H(3)_{Ar'}$, $H(5)_{Ar'}$, J = 8.1 Hz); 7.60—7.69 (m, 2 H, $H(3)_{Ar}$, $H(5)_{Ar}$); 7.76—7.88 (m, 3 H, $H(4)_{Ar}$, $H(2)_{Ar'}$, $H(6)_{Ar'}$); 8.02 (s, 1 H, C(8)H); 8.07 (d, 2 H, $H(2)_{Ar}$, $H(6)_{Ar}$, J = 8.1 Hz). MS, *m/z*: 359 $[M]^+$, 343 $[M - O]^+$, 119 $[COC_7H_7]^+$, 91 $[C_7H_7]^+$, 77 $[C_6H_5]^+$. IR, ν/cm^{-1}: 1075, 1100 (Cl—O); 1615, 1700 (C=O).

5-(4-Bromophenyl)-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrano[4,3-*d*]pyrimidinium perchlorate (5c). Perchloric acid (1.2 mL of 70% aq. solution, 2.01 g, 14 mmol) was added dropwise to a stirred suspension of enamine **3a** (1 g, 2.3 mmol) in $HC(OEt)_3$ (15 mL). The warming up of the reaction mixture and dissolution of the starting enamine were observed. The reaction mixture was refluxed for 5 min. The precipitate of light yellow color that formed was filtered off, washed with AcOEt, and dried at 100 °C to obtain 0.965 g (94%) of perchlorate **5c** as colorless crystals, m.p. 238—240 °C (AcOEt). Found (%): C, 40.65; H, 2.50; Br + Cl, 25.62. $C_{15}H_{12}BrClN_2O_7$. Calculated (%): C, 40.25; H, 2.70; Br + Cl, 25.77. ^{1}H NMR ($CDCl_3$—CF_3COOH), δ: 3.49 (s, 3 H, N(3)Me); 3.86 (s, 3 H, N(1)Me); 7.63 (d, 2 H, $H(3)_{Ar}$, $H(5)_{Ar}$, J = 8.49 Hz); 7.76 (d, 2 H, $H(2)_{Ar}$, $H(6)_{Ar}$, J = 8.49 Hz); 7.83 (d, 1 H, C(8)H, J = 5.40 Hz); 8.95 (d, 1 H, C(7)H, J = 5.40 Hz). MS, *m/z*: 349 $[M]^+$, 347 $[M]^+$, 185 $[COC_6H_4Br]^+$, 183 $[COC_6H_4Br]^+$, 157 $[C_6H_4Br]^+$, 155 $[C_6H_4Br]^+$, 81 $[Br]^+$, 79 $[Br]^+$. IR, ν/cm^{-1}: 1075, 1100 (Cl—O); 1630, 1690 (C=O).

5-(2,4-Dichlorophenyl)-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrano[4,3-*d*]pyrimidinium perchlorate (5d) was obtained similarly to compound **5c** from enamine **3a** (0.5 g, 1.18 mmol), $HC(OEt)_3$ (10 mL), and 70% aq. $HClO_4$ (0.61 mL, 1.02 g, 7.12 mmol). The yield was 0.496 g (96%), colorless crystals, m.p. 288—290 °C (AcOEt). Found (%): C, 40.82; H, 2.58; Cl, 24.09. $C_{15}H_{11}Cl_3N_2O_7$. Calculated (%): C, 41.17; H, 2.53; Cl, 24.30. ^{1}H NMR ($CDCl_3$—CF_3COOH), δ: 3.45 (s, 3 H, N(3)Me); 3.87 (s, 3 H, N(1)Me); 7.51 (s, 2 H, $H(3)_{Ar}$, $H(5)_{Ar}$); 7.62 (s, 1 H, $H(6)_{Ar}$); 7.95 (d, 1 H, C(8)H, J = 4.73 Hz); 9.03 (d, 1 H, C(7)H, J = 4.74 Hz). IR, ν/cm^{-1}: 1100 br. (Cl—O); 1630, 1700 (C=O).

1,3-Dimethyl-7-(4-methylphenyl)-2,4-dioxo-5-phenyl-1,2,3,4-tetrahydropyrano[4,3-*d*]pyrimidinium bromide (5e). A solution of Br_2 (0.141 mL, 0.445 g, 2.78 mmol) in $CHCl_3$ (1 mL) was added dropwise to a preheated to 50—60 °C and stirred solution of styryl **4a** (1 g, 2.77 mmol) in $CHCl_3$ (20 mL). The suspension obtained was refluxed for 30 min. The reaction mixture was cooled to 20 °C, the precipitate was filtered off, washed with AcOEt, and dried at 100 °C to obtain 1.08 g (88%) of salt **5e** as yellow crystals, m.p. 275—278 °C ($CHCl_3$). Found (%): C, 60.29; H, 4.71; Br, 17.93. $C_{22}H_{19}BrN_2O_3$. Calculated (%): C, 60.15; H, 4.36; Br, 18.19. ^{1}H NMR ($CDCl_3$—CF_3COOH), δ: 2.50 (s, 3 H, Ar′Me); 3.49 (s, 3 H, N(3)Me); 3.97 (s, 3 H, N(1)Me); 7.47 (d, 2 H, $H(3)_{Ar'}$, $H(5)_{Ar'}$, J = 8.1 Hz); 7.60—7.69 (t, 2 H, $H(3)_{Ar}$, $H(5)_{Ar}$, J = 7.3 Hz); 7.76—7.88 (m, 3 H, $H(4)_{Ar}$, $H(2)_{Ar'}$, $H(6)_{Ar'}$); 8.02 (s, 1 H, C(8)H); 8.07 (d, 2 H, $H(2)_{Ar}$, $H(6)_{Ar}$, J = 8.1 Hz). MS, *m/z*: 359 $[M]^+$, 343 $[M - O]^+$, 119 $[COC_7H_7]^+$, 91 $[C_7H_7]^+$, 79 $[Br]^+$. IR, ν/cm^{-1}: 1625, 1690 (C=O).

5,7-Bis(4-bromophenyl)-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrano[4,3-*d*]pyrimidinium bromide (5f) was obtained similarly to compound **5e** from styryl **4b** (0.25 g, 0.496 mmol) in $CHCl_3$, (4 mL) and Br_2 (0.025 mL, 0.08 g, 0.5 mmol) in $CHCl_3$ (1 mL). The yield was 0.234 g (81%), yellow crystals, m.p. 244—246 °C ($CHCl_3$). Found (%): C, 43.32; H, 2.68; Br, 41.30. $C_{21}H_{15}Br_3N_2O_3$. Calculated (%): C, 43.26; H, 2.59; Br, 41.11. ^{1}H NMR ($CDCl_3$—CF_3COOH), δ: 3.51 (s, 3 H, N(3)Me); 4.00 (s, 3 H, N(1)Me); 7.72 (d, 2 H, $H(3)_{Ar}$, $H(5)_{Ar}$, J = 8.48 Hz); 7.83 (d, 4 H, $H(2)_{Ar}$, $H(6)_{Ar}$, $H(3)_{Ar'}$, $H(5)_{Ar'}$); 8.03 (d, 2 H, $H(2)_{Ar'}$, $H(6)_{Ar'}$, J = 8.49 Hz); 8.13 (s, 1 H, C(8)H). MS, *m/z*: 505 $[M]^+$, 503 $[M]^+$, 501 $[M]^+$, 489 $[M - O]^+$, 487 $[M - O]^+$, 485 $[M - O]^+$, 185 $[COC_6H_4Br]^+$, 183 $[COC_6H_4Br]^+$, 157 $[C_6H_4Br]^+$, 155 $[C_6H_4Br]^+$, 81 $[Br]^+$, 79 $[Br]^+$. IR, ν/cm^{-1}: 1615, 1685 (C=O).

5-Aryl-1,3-dimethylpyrido[4,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones 6a—d (general procedure). Ammonia (0.5 mL of 22% aq. solution) was added to a stirred suspension of pyrano[4,3-*d*]pyrimidinium salt **5** (100 mg) in EtOH (1 mL). The solution was refluxed for 2 h. The precipitate, formed during cooling, was filtered off, washed with EtOH, and dried at 100—110 °C (Tables 1 and 2). In the IR spectra of compounds **6**, two strong absorption bands of carbonyl groups at 1665—1670 and 1705—1715 cm^{-1} were observed.

5,6-Diaryl-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[4,3-*d*]pyrimidinium salts 7a—f (general procedure). Amine (0.9 mmol) was added to a stirred suspension of salt **5** (0.3 mmol) in AcOH (1 mL). The solution was refluxed for 15 min, after cooling to ~20 °C, it was diluted with AcOEt (3 mL). After 1 h, the precipitate formed was filtered off, washed with AcOE, and dried at 100—110 °C (see Tables 1 and 2). In the IR spectra of compounds **7**, absorption maxima of carbonyl groups in the regions 1610—1630 and 1680—1700 cm^{-1} were observed. In the spectra of perchlorates **7a—d**, there is a characteristic maximum of absorption of perchlorate ion at 1095—1100 cm^{-1}.

1,3-Dimethyl-5,8-bis(4-methylphenyl)-1*H*-pyrimido[5,4-*d*]-[1,2]diazepine-2,4(3*H*,9*H*)-dione (8a). Salt **5a** (100 mg, 0.21 mmol) and 80% hydrazine hydrate (0.039 mL, 0.039 g,

Table 1. Yields, melting points, and elemental analysis data for pyrido[4,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **6a—d** and pyrido[4,3-*d*]pyrimidinium salts **7a—f**

Compound	Yield (%)	M.p./°C	Found / Calculated (%)			Molecular formula
			C	H	Hal	
6a	77	233—236	74.05 74.37	5.61 5.70	—	$C_{23}H_{21}N_3O_2$
6b	76	253—256	73.67 73.93	5.34 5.36	—	$C_{22}H_{19}N_3O_2$
6c	66	226—228	52.33 52.04	3.44 3.49	22.73 [a] 23.08	$C_{15}H_{12}BrN_3O_2$
6d	55	170—172	53.26 53.59	3.38 3.30	20.65 [b] 21.09	$C_{15}H_{11}Cl_2N_3O_2$
7a	81	290—295	63.43 63.56	4.62 4.78	6.52 [b] 6.47	$C_{29}H_{26}ClN_3O_6$
7b	91	214—216	54.69 54.88	3.88 3.78	18.50 [c] 18.82	$C_{28}H_{23}BrClN_3O_6$
7c	67	302—304	50.04 50.16	3.68 3.84	20.25 [c] 20.95	$C_{23}H_{21}BrClN_3O_6$
7d	63	256—260	42.45 42.63	2.49 2.56	31.08 [c] 31.49	$C_{21}H_{15}BrCl_3N_3O_6$
7e	48	205—207	64.26 63.98	4.93 4.81	14.35 [a] 14.68	$C_{29}H_{26}BrN_3O_3$
7f	83	190—192	49.62 49.89	3.65 3.78	31.77 [a] 32.12	$C_{31}H_{28}Br_3N_3O_4$

[a] Hal = Br.
[b] Hal = Cl.
[c] Hal = Br + Cl.

Table 2. ^{1}H NMR spectra of pyrido[4,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones **6a—d** (in $CDCl_3$) and pyrido[4,3-*d*]pyrimidinium salts **7a—f**

Compound	δ (*J*/Hz)					
	1-Me	3-Me	5-R^1	6-R^3	7-R^2	C(8)H
6a	3.68	3.25	2.43 (s, 3 H, ArMe); 7.25 (d, 2 H, *m*-H arom., *J* = 8.13); 8.11 (d, 2 H, *o*-H arom., *J* = 8.2)	—	2.41 (s, 3 H, ArMe); 7.17 (d, 2 H, *m*-H arom., *J* = 7.98); 7.33 (d, 2 H, *o*-H arom., *J* = 7.91)	7.66 (s)
6b	3.70	3.38	7.42—7.53 (m, 5 H, Ar)	—	2.42 (s, 3 H, ArMe); 7.28 (d, 2 H, *m*-H arom., *J* = 8.1); 7.99 (d, 2 H, *o*-H arom., *J* = 8.1)	7.40 (s)
6c	3.66	3.39	7.32 (d, 2 H, *m*-H arom., *J* = 8.5); 7.58 (d, 2 H, *o*-H arom., *J* = 8.5)	—	8.72 (d, 1 H, C(7)H, *J* = 5.90)	7.12 (d, *J* = 5.91)
6d	3.66	3.38	7.22 (d, 1 H, $H(6)_{Ar}$, *J* = 7.0); 7.36 (dd, 1 H, $H(5)_{Ar}$, J_o = 7.0, J_m = 2.05); 7.48 (d, 1 H, $H(3)_{Ar}$, *J* = 2.05)	—	8.77 (d, 1 H, C(7)H, *J* = 5.93)	7.18 (d, *J* = 5.93)
7a [a]	3.88	3.44	2.27 (s, 3 H, ArMe); 6.93—7.20 (m, 4 H, Ar)	6.93—7.20 (m, 5 H, Ar)	2.29 (s, 3 H, ArMe); 6.93—7.20 (m, 4 H, Ar)	7.86 (s)
7b [a]	3.84	3.39	7.08—7.39 (m, 5 H, Ar)	7.08—7.39 (m, 4 H, Ar)	2.32 (s, 3 H, ArMe); 6.85 (d, 2 H, *m*-H arom., *J* = 8.53); 7.08—7.39 (m, 2 H, *o*-H arom.)	7.83 (s)
7c [a]	3.87	3.43	7.01—7.08 (m, 2 H, *m*-H arom.); 7.49 (d, 2 H, *o*-H arom., *J* = 8.1)	2.26 (s, 6 H, 2 ArMe); 6.78 (s, 2 H, *o*-H arom.); 7.01—7.08 (m, 1 H, *p*-H arom.)	8.71 (d, 1 H, C(7)H, *J* = 7.14)	7.98 (d, *J* = 7.14)
7d [a]	3.85	3.42	7.15—7.34 (m, 2 H, $H(5)_{Ar}$, $H(6)_{Ar}$); 7.39 (d, 1 H, $H(3)_{Ar}$, *J* = 1.89)	7.15—7.34 (m, 2 H, *m*-H arom.); 7.56 (d, 2 H, *o*-H arom., *J* = 8.84)	8.71 (d, 1 H, C(7)H, *J* = 6.64)	8.02 (d, *J* = 7.27)
7e [b]	3.60	3.25	7.18—7.30 (m, 5 H, Ar)	3.79 (s, 3 H, OMe); 6.49 (d, 2 H, *m*-H arom., *J* = 8.8); 7.18—7.30 (m, 2 H, *o*-H arom.)	2.31 (s, 3 H, ArMe); 7.11 (d, 2 H, *m*-H arom., *J* = 8.06); 7.36 (d, 2 H, *o*-H arom., *J* = 8.1)	8.03 (s)
7f [b]	3.56	3.23	7.85 (s, 4 H, Ar)	2.48 (t, 2 H, $N(6)CH_2C\underline{H}_2$, *J* = 7.91); 3.67 (s, 3 H, 4-OMe); 3.71 (s, 3 H, 3-OMe); 4.13 (t, 2 H, $N(6)CH_2$, *J* = 7.91); 5.70 (s, 1 H, $H(2)_{Ar}$, *J* = 1.68); 5.92 (d, 1 H, $H(6)_{Ar}$, J_o = 8.13, J_m = 1.68); 6.59 (d, 1 H, $H(5)_{Ar}$, *J* = 8.21)	7.62 (d, 2 H, *m*-H arom., *J* = 8.43); 7.80 (s, 2 H, *o*-H arom., *J* = 8.50)	8.02 (s)

[a] In $CDCl_3$—CF_3COOH.
[b] In DMSO-d_6.

0.62 mmol) in AcOH (1 mL) were refluxed for 15 min. The precipitate, formed during cooling, was filtered off, washed with AcOH, hydrolyzed with a mixture of 1% aq. NaOH (5 mL) and $CHCl_3$ (5 mL). The chloroform extract was separated and concentrated. The product was dried at 100 °C to obtain 32 mg (39%) of compound **8a** as colorless crystals, m.p. 270—271 °C ($CHCl_3$). Found (%): C, 71.23; H, 5.58. $C_{23}H_{22}N_4O_2$. Calculated (%): C, 71.48; H, 5.74. ^{1}H NMR ($CDCl_3$), δ: 2.32—2.39 (2 s, 6 H, ArMe, Ar´Me); 2.97 (d, 1 H, C(9)H, *J* = 13.27 Hz); 3.27 (s, 3 H, N(3)Me); 3.62 (s, 3 H, N(1)Me); 4.38 (d, 1 H, C(9)H, *J* = 13.27 Hz); 7.19—7.28 (m, 4 H, $H(3)_{Ar}$, $H(5)_{Ar}$, $H(3)_{Ar'}$, $H(5)_{Ar'}$); 7.58 (d, 2 H, $H(2)_{Ar'}$, $H(6)_{Ar'}$, *J* = 8.21 Hz); 7.76 (d, 2 H, $H(2)_{Ar}$, $H(6)_{Ar}$, *J* = 8.43 Hz). IR, ν/cm^{-1}: 1660, 1700 (C=O).

1,3-Dimethyl-8-(4-methylphenyl)-5-phenyl-1*H*-pyrimido[5,4-*d*][1,2]diazepine-2,4(3*H*,9*H*)-dione (8b) was obtained similarly to compound **8a** from salt **5b** (300 mg, 0.654 mmol) and 80% hydrazine hydrate (0.104 mL, 0.104 g, 1.67 mmol) in AcOH (3 mL). The yield was 110 mg (45%), colorless crystals, m.p. 260—265 °C ($CHCl_3$). Found (%): C, 70.86; H, 5.30. $C_{22}H_{20}N_4O_2$. Calculated (%): C, 70.95; H, 5.41. ^{1}H NMR ($CDCl_3$), δ: 2.41 (s, 3 H, Ar´Me); 3.00 (d, 1 H, C(9)H,

J = 13.36 Hz); 3.28 (s, 3 H, N(3)Me); 3.64 (s, 3 H, N(1)Me); 4.42 (d, 1 H, C(9)H, J = 13.33 Hz); 7.28 (d, 2 H, $H(3)_{Ar'}$, $H(5)_{Ar'}$, J = 8.2 Hz); 7.42—7.45 (m, 3 H, $H(3)_{Ar}$, $H(4)_{Ar}$, $H(5)_{Ar}$); 7.70—7.73 (m, 2 H, $H(2)_{Ar}$, $H(6)_{Ar}$); 7.78 (d, 2 H, $H(2)_{Ar'}$, $H(6)_{Ar'}$, J = 8.2 Hz). MS, m/z: 372 $[M]^+$, 357 $[M - CH_3]^+$, 344 $[M - N_2]^+$, 287 $[M - N_2 - MeNCO]^+$, 269 $[M - C_6H_5CN]^+$, 255 $[M - MeC_6H_4CN]^+$, 91 $[C_7H_7]^+$. IR, ν/cm^{-1}: 1670, 1705 (C=O).

6-Amino-5-(4-bromophenyl)-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[4,3-*d*]pyrimidinium perchlorate (9a) was obtained similarly to salts **7a—f** from salt **5c** (0.16 g, 0.357 mmol) and 80% hydrazine hydrate (0.039 mL, 0.039 g, 0.62 mmol) in AcOH (2 mL). The yield was 0.14 g (85%), colorless crystals, m.p. 320—324 °C (AcOH). Found (%): C, 38.86; H, 3.05; Br + Cl, 24.65. $C_{15}H_{14}BrClN_4O_6$. Calculated (%): C, 39.03; H, 3.06; Br + Cl, 24.99. ^{1}H NMR (DMSO-d_6), δ: 3.18 (s, 3 H, N(3)Me); 3.66 (s, 3 H, N(1)Me); 7.19 (s, 2 H, NH_2); 7.31 (d, 2 H, $H(3)_{Ar}$, $H(5)_{Ar}$, J = 8.4 Hz); 7.69 (d, 2 H, $H(2)_{Ar}$, $H(6)_{Ar}$, J = 8.4 Hz); 8.03 (d, 1 H, C(8)H, J = 7.5 Hz); 8.94 (d, 1 H, C(7)H, J = 7.5 Hz). MS, m/z: 361 $[M]^+$, 345 $[M - NH_2]^+$, 155 $[C_6H_4Br]^+$, 79 $[Br]^+$. IR, ν/cm^{-1}: 1100 br (Cl—O); 1630, 1685 (C=O); 3255, 3340 (NH_2).

6-Amino-5-(2,4-dichlorophenyl)-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[4,3-*d*]pyrimidinium perchlorate (9b) was obtained similarly to salts **7a—f** from salt **5d** (0.1 g, 0.23 mmol) and 80% hydrazine hydrate (0.029 mL, 0.029 g, 0.46 mmol) in AcOH (1 mL). The yield was 55 mg (53%), colorless crystals, m.p. 248—250 °C (AcOH). Found (%): C, 39.71; H, 3.02; Cl, 23.24. $C_{15}H_{13}Cl_3N_4O_6$. Calculated (%): C, 39.89; H, 2.90; Cl, 23.55. ^{1}H NMR (DMSO-d_6), δ: 3.15 (s, 3 H, N(3)Me); 3.63 (s, 3 H, N(1)Me); 7.39 (d, 1 H, $H(6)_{Ar}$, J = 8.75 Hz); 7.42 (s, 2 H, NH_2); 7.65 (dd, 1 H, $H(5)_{Ar}$, J_o = 8.59 Hz, J_m = 2.02 Hz); 7.69 (d, 1 H, $H(3)_{Ar}$, J = 2.02 Hz); 8.08 (d, 1 H, C(8)H, J = 7.41 Hz); 8.99 (d, 1 H, C(7)H, J = 7.41 Hz). IR, ν/cm^{-1}: 1100 br (Cl—O); 1640, 1690 (C=O); 3200, 3315 (NH_2).

References

1. S. V. Verin, D. E. Tosunyan, E. V. Kuznetsov, and Yu. A. Zhdanov, *Khim. Geterotsikl. Soedin.*, 1990, 315 [*Chem. Heterocycl. Compd.*, 1990, **26**, 266 (Engl. Transl.)].
2. Yu. A. Zhdanov, S. V. Verin, I. V. Korobka, and E. V. Kuznetsov, *Khim. Geterotsikl. Soedin.*, 1988, 1185 [*Chem. Heterocycl. Compd.*, 1988, **24**, 974 (Engl. Transl.)].
3. Yu. A. Zhdanov, V. G. Brovchenko, N. A. Klyuev, and E. V. Kuznetsov, *Khim. Geterotsikl. Soedin.*, 1989, 454 [*Chem. Heterocycl. Compd.*, 1989, **25**, 375 (Engl. Transl.)].
4. I. V. Korobka, Yu. V. Revinskii, and E. V. Kuznetsov, *Khim. Geterotsikl. Soedin.*, 1985, 910 [*Chem. Heterocycl. Compd.*, 1985, **21**, 754 (Engl. Transl.)].
5. S. V. Verin and E. V. Kuznetsov, *Khim. Geterotsikl. Soedin.*, 1992, 169 [*Chem. Heterocycl. Compd.*, 1992, **28**, 135 (Engl. Transl.)].
6. I. V. Shcherbakova, V. G. Brovchenko, and E. V. Kuznetsov, *Khim. Prirodn. Soedin.*, 1985, 815 [*Chem. Nat. Compd.*, 1985, **21**, 774 (Engl. Transl.)].
7. K. Dimroth and H. Odenwälder, *Chem. Ber.*, 1971, **104**, 2984.
8. A. M. Thompson, A. J. Bridges, D. W. Fry, A. J. Kraker, and W. A. Denny, *J. Med. Chem.*, 1995, **38**, 3780.
9. G. W. Rewcastle, B. D. Palmer, A. M. Thompson, A. J. Bridges, D. R. Cody, H. Zhou, D. W. Fry, A. McMichael, and W. A. Denny, *J. Med. Chem.*, 1996, **39**, 1823.
10. A. M. Thompson, D. K. Murray, W. L. Elliott, D. W. Fry, J. A. Nelson, H. D. Hollis Showalter, B. J. Roberts, P. W. Vincent, and W. A. Denny, *J. Med. Chem.*, 1997, **40**, 915.
11. J. B. Smaill, B. D. Palmer, G. W. Rewcastle, W. A. Denny, D. J. McNamara, E. M. Dobrusin, A. J. Bridges, H. Zhou, H. D. Hollis Showalter, R. T. Winters, W. R. Leopold, D. W. Fry, J. M. Nelson, V. Slintak, W. L. Elliot, B. J. Roberts, P. W. Vincent, and S. J. Patmore, *J. Med. Chem.*, 1999, **42**, 1803.
12. E. V. Kuznetsov, I. V. Shcherbakova, and A. T. Balaban, *Adv. Heterocycl. Chem.*, 1990, **50**, 157.
13. E. B. Tsupak, M. A. Shevchenko, A. F. Pozharskii, and Yu. N. Tkachenko, *Khim. Geterotsikl. Soedin.*, 2003, 1096 [*Chem. Heterocycl. Compd.*, 2003, **39**, 953 (Engl. Transl.)].
14. S. Senda, T. Asao, I. Sugiyama, and K. Hirota, *Tetrahedron Lett.*, 1980, **21**, 531.
15. K. Hirota, T. Asao, I. Sugiyama, and S. Senda, *Heterocycles*, 1981, **15**, 289.
16. K. Singh, S. Singh, and A. Mahajan, *J. Org. Chem.*, 2005, **70**, 6114.
17. K. Hirota, T. Asao, S. Senda, Y. Kitade, and Y. Maki, *J. Heterocycl. Chem.*, 1988, **25**, 985.
18. A. G. Ismail and D. G. Wibberley, *J. Chem. Soc. C*, 1968, 2706.
19. K. Hirota, Y. Kitade, and H. Sajiki, *Heterocycles*, 1998, **47**, 871.

Received July 11, 2007;
in revised form September 27, 2007