Pyrano[4,3-*d*]pyrimidinium salts
2.* Reactions of 1,3-dimethyl-2,4-dioxopyrano[4,3-*d*]pyrimidinium salts with hydrazine

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Reactions of 5-aryl- and 5,7-diaryl-1,3-dimethyl-2,4-dioxopyrano[4,3-*d*]pyrimidinium salts with hydrazine were studied. In the former case, the reaction products were the 6-amino-1,3-dimethyl-2,4-dioxopyrido[4,3-*d*]pyrimidinium salts. 5,7-Diarylpyrano[4,3-*d*]pyrimidinium salts were transformed into either the corresponding pyridinium salts or 1*H*-pyrimido-[5,4-*d*][1,2]diazepine-2,4(3*H*,9*H*)-diones, depending on the hydrazine concentration and the reaction time.

Key words: pyrano[4,3-*d*]pyrimidinium salts, recyclization, 6-amino-2,4-dioxopyrido-[4,3-*d*]pyrimidinium salts, 1*H*-pyrimido[5,4-*d*][1,2]diazepine-2,4(3*H*,9*H*)-diones.

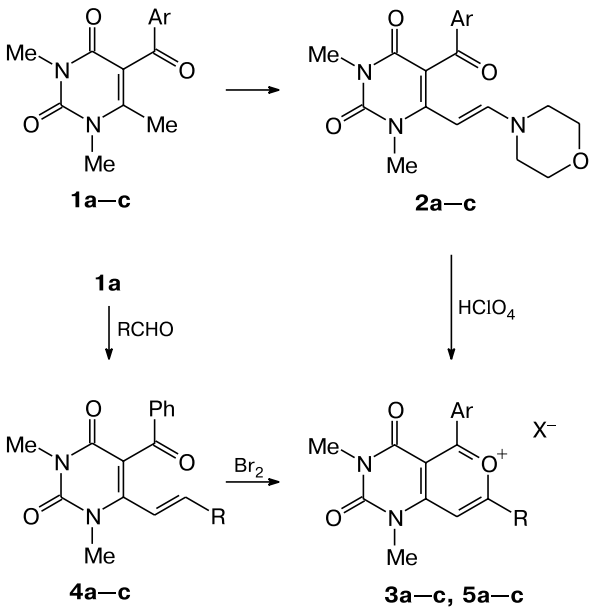
The nucleophilic substitution reaction at the O atom of the pyrylium ring is one of the most important properties of pyrylium cations. Recyclization of pyrylium and benzo[*c*]pyrylium salts into pyridines and isoquinolines, respectively, were reviewed.[2,3] Recently,[1] we have found that treatment of the pyrano[4,3-*d*]pyrimidinium salts with ammonia and primary amines gives, as in the case of benzo[*c*]pyrylium salts, the corresponding pyrido[4,3-*d*]-pyrimidines and pyrido[4,3-*d*]pyrimidinium salts. These reactions open up a simple route to novel fused systems containing the uracil ring, which is believed to impart biological activity to many relevant compounds.

Proceeding further in the investigation of the recyclization of pyrano[4,3-*d*]pyrimidinium salts under the action of nitrogen nucleophiles, we studied their reactions with hydrazine.

The pathway of the reactions of benzo[*c*]pyrylium salts with hydrazine is known to depend on the presence or the absence of a substituent in the pyrylium ring and on the substituent nature. 1,3-Dialkylbenzo[*c*]pyrylium perchlorates in the presence of hydrazine were transformed into *N*-aminoisoquinolinium cations[4], while reactions of 1-arylbenzo[*c*]pyrylium salts result in their recyclization into benzo-2,3-diazepines.[5] 3- and 4-Functionalized benzo[*c*]pyrylium cations behave in a more complicated way and the reaction outcome depends on both the substituent nature and the hydrazine concentration. For instance, heating of 3-ethoxy- and 4-cyanobenzo[*c*]-pyrylium perchlorates with an equimolar amount of hydrazine leads to *N*-aminoisoquinolinium derivatives, while the reaction with a great excess of the nucleophile gives benzo-2,3-diazepines.[6,7]

5-Aryl- and 5,7-diaryl-2,4-dioxopyrano[4,3-*d*]pyrimidinium salts were prepared according to earlier developed

Scheme 1



1—3: Ar = Ph (**a**), 4-BrC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**)
3: R = H; $X^- = ClO_4^-$
4, 5: R = Ar′ = Ph (**a**), 4-BrC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**);
5: Ar = Ph, $X^- = Br^-$

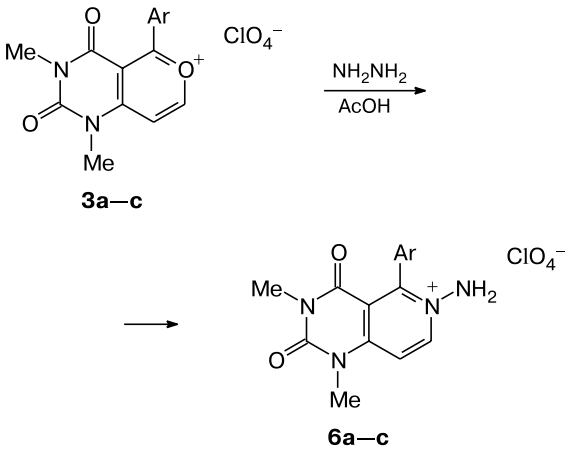
* For Part 1, see Ref. 1.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1720—1725, May, 2008.

procedures.[1] For instance, 5-aroyl-1,3,6-methyluracils **1a—c** were transformed into 5-aroyl-6-(2-morpholinoethenyl)pyrimidine-2,4(1*H*,3*H*)-diones **2a—c** and further, under the action of $HClO_4$, into the target 5-aryl-1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-pyrano[4,3-*d*]pyrimidinium perchlorates **3a—c**. Condensation of 5-benzoyl-1,3,6-trimethyluracil **1a** with aromatic aldehydes leads to 6-(2-arylethenyl)-5-phenylpyrimidine-2,4(1*H*,3*H*)-diones **4a—c**, which easily undergo cyclization into 7-aryl-1,3-dimethyl-2,4-dioxo-5-phenyl-1*H*,2*H*,3*H*,4*H*-pyrano[4,3-*d*]pyrimidinium bromides **5a—c** (Scheme 1).

We found that heating of 5-arylpyrano[4,3-*d*]pyrimidinium perchlorates **3a—c** with hydrazine results in their recyclization into 6-amino-5-aryl-1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-pyrido[4,3-*d*]pyrimidinium cations **6a—c**, regardless of the hydrazine concentration or the reaction time (Scheme 2).

Scheme 2



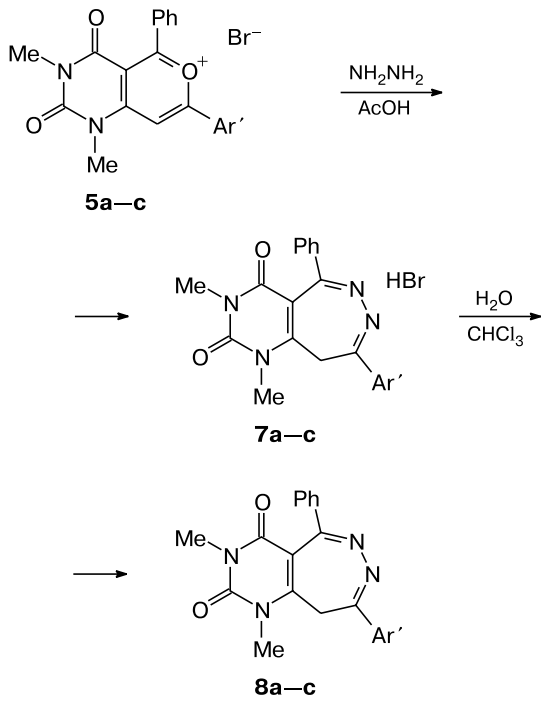
Ar = Ph (**a**), 4-BrC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**)

The structures of compounds **6a—c** were determined from their IR and ^{1}H NMR spectra. The IR spectra show absorption peaks of the amino group at 3245—3260 and 3325—3350 cm^{-1}. In the ^{1}H NMR spectra, the N-amino group is manifested as a broadened singlet (δ 7.16—7.19, 2 H) that disappears upon deuteration.

When heated for a short time with an equimolar amount of hydrazine, 5,7-diarylpyrano[4,3-*d*]pyrimidinium bromides **5a—c** undergo recyclization into 8-aryl-1,3-dimethyl-5-phenyl-1*H*-pyrimido[5,4-*d*][1,2]diazepine-2,4(3*H*,9*H*)-dione hydrobromides **7a—c**, which are transformed into free bases **8a—c** under the action of water (Scheme 3).

The presence of the diazepine ring is confirmed by doublets at δ 2.97—3.03 and 4.33—4.42 (J = 13.20—13.50 Hz) in the ^{1}H NMR spectra of compounds **8**, which persist upon deuteration. We assigned them to the signals for

Scheme 3



Ar′ = Ph (**a**), 4-BrC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**)

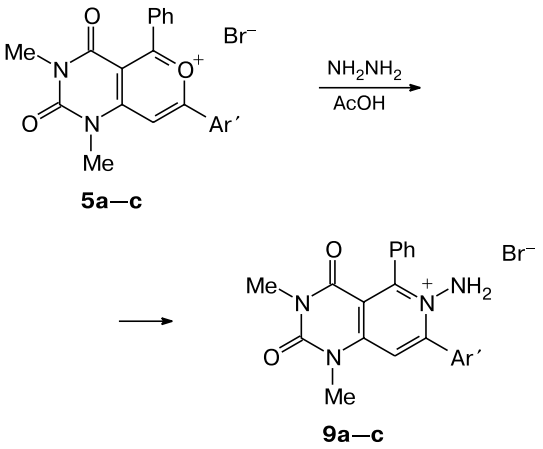
nonequivalent protons of the endocyclic CH_2 group. An analogous methylene group in diazepine hydrobromides **7** is manifested as doublets at δ 2.79—2.90 and 4.67—4.75 (J = 14.12—14.13 Hz). The nonequivalence of the methylene protons is probably due to the nonplanar structure of the diazepine ring in compounds **7** and **8** and to the high energy barrier to its conformational changes. The acid proton in hydrobromides **7** absorbs at 3375—3380 cm^{-1}.

Treatment of salts **5a—c** with excess hydrazine for 30 min gave 6-amino-7-aryl-1,3-dimethyl-2,4-dioxo-5-phenyl-1*H*,2*H*,3*H*,4*H*-pyrido[4,3-*d*]pyrimidinium bromides **9a—c** (Scheme 4).

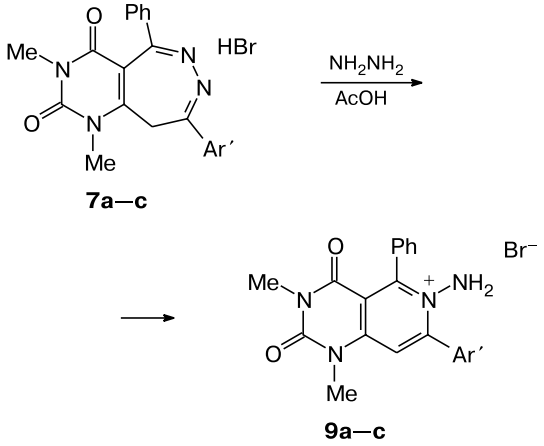
The *N*-amino group in 6-amino-5,7-diarylpyrido-[4,3-*d*]pyrimidinium salts **9** absorbs at 3250—3300 and 3285—3350 cm^{-1}. In the ^{1}H NMR spectra, its protons are manifested as singlets at δ 6.32—6.39, which disappear upon deuteration. The singlet at δ 7.92—7.99 relates to the H(8) proton.

By analyzing experimental data, we assumed that reactions of pyrano[4,3-*d*]pyrimidinium salts with hydrazine involve intermediate formation of a diazepine ring from the pyrylium one and recyclization of the former in the presence of excess hydrazine into an *N*-aminopyridinium ring. This assumption is confirmed by isolation of 6-aminopyrido[4,3-*d*]pyrimidinium bromides **9** in 70—80% yields upon heating of diazepine hydrobromides **7** with an equimolar amount of hydrazine for 30 min (Scheme 5).

Scheme 4



Scheme 5



Ar′ = Ph (**a**), 4-BrC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**)

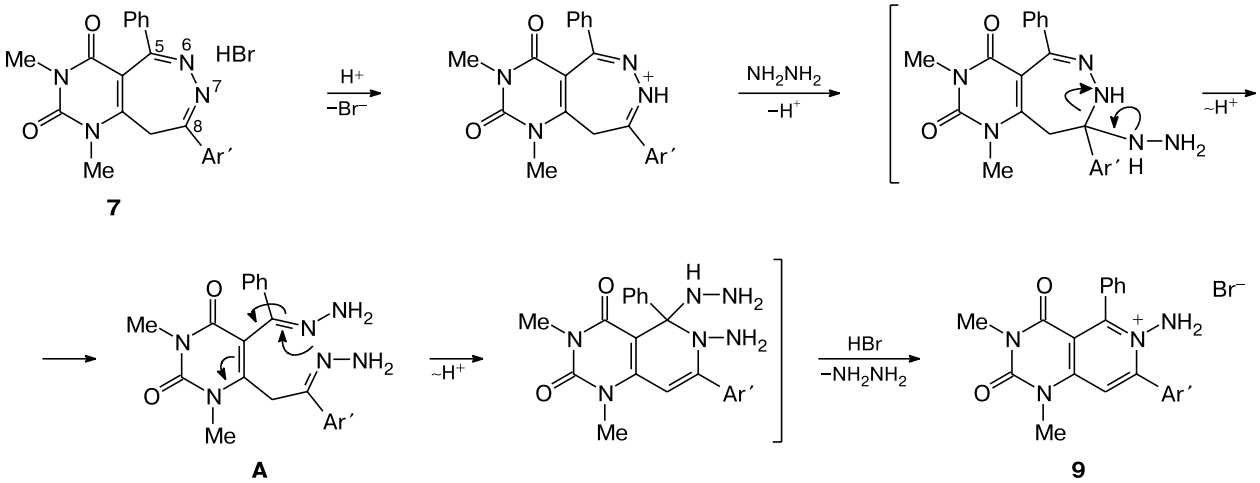
The transformation can be represented as recyclization in which hydrazine molecules serve as both nucleophiles and nucleofuges. Apparently, the reaction proceeds through the formation of intermediate dihydrazone **A**, which undergoes the closure of a pyridine ring upon elimination of the hydrazine molecule (Scheme 6).

In the proposed reaction scheme, the nucleophile may attack either the C(5) or C(8) atom because both pathways lead to intermediate **A**.

The driving force of the reaction is the formation of the aromatic pyridinium ion, which is more stable than diazepine. This was confirmed by HF/6-311G* calculations[8] of the total energies of pyrimido[5,4-*d*][1,2]-diazepine hydrobromide **7a** and 6-aminopyrido[4,3-*d*]-pyrimidinium bromide **9a**. Indeed, pyridinium cation in salt **9a** is more stable (by 18.3 kcal mol^{-1}) than the diazepinium cation in hydrobromide **7a**.

Thus, we studied reactions of 5-aryl- and 5,7-diarylpyrano[4,3-*d*]pyrimidinium salts with hydrazine. We found that 5-arylpyrano[4,3-*d*]pyrimidinium perchlorates yield 6-aminopyrido[4,3-*d*]pyrimidinium salts, regardless of the reaction conditions. At the same time, 5,7-diarylpyrano[4,3-*d*]pyrimidinium salts can yield both pyrimido-[5,4-*d*][1,2]diazepines and 6-aminopyrido[4,3-*d*]pyrimidinium salts, depending on the reaction time and the hydrazine concentration. The formation of 6-aminopyrido[4,3-*d*]pyrimidinium salts is preceded by recyclization of the 5,7-diarylpyrano[4,3-*d*]pyrimidinium salt into pyrimido[5,4-*d*][1,2]diazepinium salts.

Scheme 6



Experimental

IR spectra were recorded on a Specord IR-71 spectrophotometer (Nujol). ^{1}H NMR spectra were recorded on Bruker Avance DPX-250 and Varian Unity-300 instruments in $CDCl_3$, DMSO-d_6, and $CDCl_3$ + CF_3COOH with HMDS as the internal standard. Compounds **1a—c** were prepared as described earlier.[9]

5-Aroyl-1,3-dimethyl-6-(2-morpholinoethenyl)pyrimidine-2,4(1*H*,3*H*)-diones 2 (general procedure). A mixture of 5-aroyl-1,3,6-trimethylpyrimidine-2,4-dione **1** (0.02 mol), triethyl orthoformate (0.06 mol), and morpholine (0.06 mol) was refluxed for 2 h. On cooling to 80 °C, EtOH (15 mL) was added and the resulting suspension was refluxed for 3—5 min. The precipitate was filtered off, washed with EtOH, and dried at 80—100 °C.

5-Benzoyl-1,3-dimethyl-6-(2-morpholinoethenyl)pyrimidine-2,4(1*H*,3*H*)-dione (2a). Yield 4.12 g (58%), yellow crystals, m.p. 154—156 °C (EtOH). Found (%): C, 63.88; H, 5.83. $C_{19}H_{21}N_3O_4$. Calculated (%): C, 64.21; H, 5.96. ^{1}H NMR ($CDCl_3$), δ: 2.91 (t, 4 H, $N(CH_2)_2$, J = 4.9 Hz); 3.35 (s, 3 H, N(3)Me); 3.41 (s, 3 H, N(1)Me); 3.45 (t, 4 H, $O(CH_2)_2$, J = 4.9 Hz); 4.51 (d, 1 H, C(6)C<u>H</u>, J = 12.95 Hz); 6.45 (d, 1 H, C(6)CHC<u>H</u>, J = 12.95 Hz); 7.36 (t, 2 H, *m*-H_{Ph}, J = 7.07 Hz); 7.48 (t, 1 H, *p*-H_{Ph}, J = 7.27 Hz); 7.79 (d, 2 H, *o*-H_{Ph}, J = 6.95 Hz). IR, ν/cm^{-1}: 1605, 1660, 1695 (C=O).

5-(4-Bromobenzoyl)-1,3-dimethyl-6-(2-morpholinoethenyl)-pyrimidine-2,4(1*H*,3*H*)-dione (2b). Yield 7.82 g (90%), yellow crystals, m.p. 236—238 °C (EtOH). Found (%): C, 52.29; 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 = 5.0 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 = 5.0 Hz); 4.54 (d, 1 H, C(6)C<u>H</u>, J = 13.11 Hz); 6.44 (d, 1 H, C(6)CHC<u>H</u>, J = 13.11 Hz); 7.52 (d, 2 H, *o*-H_{Ar}, J = 8.48 Hz); 7.67 (d, 2 H, *m*-H_{Ar}, J = 8.48 Hz). IR, ν/cm^{-1}: 1620, 1670, 1705 (C=O).

5-(4-Methoxybenzoyl)-1,3-dimethyl-6-(2-morpholinoethenyl)pyrimidine-2,4(1*H*,3*H*)-dione (2c). Yield 5.93 g (77%), yellow crystals, m.p. 172—176 °C (EtOH). Found (%): C, 62.65; H, 5.80. $C_{20}H_{23}N_3O_5$. Calculated (%): C, 62.33; H, 6.02. ^{1}H NMR ($CDCl_3$), δ: 2.91 (t, 4 H, $N(CH_2)_2$, J = 4.9 Hz); 3.31 (s, 3 H, N(3)Me); 3.39 (s, 3 H, N(1)Me); 3.44 (t, 4 H, $O(CH_2)_2$, J = 4.9 Hz); 3.80 (s, 3 H, OMe); 4.54 (d, 1 H, C(6)C<u>H</u>, J = 13.14 Hz); 6.48 (d, 1 H, C(6)CHC<u>H</u>, J = 12.80 Hz); 6.84 (d, 2 H, *m*-H_{Ar}, J = 8.76 Hz); 7.78 (d, 2 H, *o*-H_{Ar}, J = 8.76 Hz). IR, ν/cm^{-1}: 1605, 1655, 1680 (C=O).

5-Aryl-1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-pyrano[4,3-*d*]pyrimidinium perchlorates 3 (general procedure). 70% Perchloric acid (0.06 mol) was added dropwise to a stirred suspension of enamine **2** (0.01 mol) in $HC(OEt)_3$ (30 mL). The resulting solution was refluxed for 5 min, cooled, and diluted with AcOEt (30 mL). The precipitate that formed was filtered off, washed with AcOEt, and dried at 80—100 °C.

1,3-Dimethyl-2,4-dioxo-5-phenyl-1*H*,2*H*,3*H*,4*H*-pyrano[4,3-*d*]pyrimidinium perchlorate (3a). Yield 3.21 g (87%), colorless crystals, m.p. 153—155 °C (AcOEt). Found (%): C, 48.64; H, 3.41; Cl, 9.42. $C_{15}H_{13}ClN_2O_7$. Calculated (%): C, 48.86; H, 3.55; Cl, 9.61. ^{1}H NMR ($CDCl_3$ + CF_3COOH), δ: 3.49 (s, 3 H, N(3)Me); 3.87 (s, 3 H, N(1)Me); 7.60 (t, 2 H, *m*-H_{Ph}, J = 7.7 Hz); 7.76—7.79 (d + t, 3 H, *o*-H_{Ph}, *p*-H_{Ph}); 7.83 (d, 1 H, C(8)H, J = 5.34 Hz); 8.96 (d, 1 H, C(7)H, J = 5.34 Hz). IR, ν/cm^{-1}: 1090 br (Cl—O); 1630, 1695 (C=O).

5-(4-Bromophenyl)-1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-pyrano[4,3-*d*]pyrimidinium perchlorate (3b). Yield 4.20 g (94%), colorless crystals, m.p. 238—240 °C (AcOEt). Found (%): C, 40.56; 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, *m*-H_{Ar}, J = 8.49 Hz); 7.76 (d, 2 H, *o*-H_{Ar}, J = 8.49 Hz); 7.84 (d, 1 H, C(8)H, J = 5.40 Hz); 8.95 (d, 1 H, C(7)H, J = 5.40 Hz). IR, ν/cm^{-1}: 1075, 1100 (Cl—O); 1630, 1690 (C=O).

5-(4-Methoxyphenyl)-1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-pyrano[4,3-*d*]pyrimidinium perchlorate (3c). Yield 2.59 g (65%), colorless crystals, m.p. 196—198 °C (AcOEt). Found (%): C, 48.42; H, 3.63; Cl, 8.60. $C_{16}H_{15}ClN_2O_8$. Calculated (%): C, 48.19; H, 3.79; Cl, 8.89. ^{1}H NMR ($CDCl_3$ + CF_3COOH), δ: 3.52 (s, 3 H, N(3)Me); 3.85 (s, 3 H, N(1)Me); 4.00 (s, 3 H, OMe); 7.11 (d, 2 H, *m*-H_{Ar}, J = 8.42 Hz); 7.71 (br.s, 1 H, C(8)H); 7.88 (d, 2 H, *o*-H_{Ar}, J = 8.68 Hz); 8.84 (br.s, 1 H, C(7)H). IR, ν/cm^{-1}: 1095 (Cl—O); 1620, 1690 (C=O).

6-(2-Arylethenyl)-5-benzoyl-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-diones 4 (general procedure). A solution of ketone **1a** (0.02 mol), an aromatic aldehyde (0.03 mol), and piperidine (0.01 mol) in EtOH (20 mL) was refluxed for 15 h. On cooling, the precipitate that formed was filtered off, washed with EtOH, and dried at 80—100 °C.

5-Benzoyl-1,3-dimethyl-6-(2-phenylethenyl)pyrimidine-2,4(1*H*,3*H*)-dione (4a). Yield 4.98 g (72%), yellow crystals, m.p. 149—151 °C (EtOH). Found (%): C, 72.49; H, 5.05. $C_{21}H_{18}N_2O_3$. Calculated (%): C, 72.82; H, 5.24. ^{1}H NMR ($CDCl_3$), δ: 3.38 (s, 3 H, N(3)Me); 3.46 (s, 3 H, N(1)Me); 6.51 (d, 1 H, C(6)C<u>H</u>, J = 16.43 Hz); 6.81 (d, 1 H, C(6)CHC<u>H</u>, J = 16.12 Hz); 7.14—7.22 (m, 2 H, *o*-$H_{Ar'}$); 7.23—7.29 (m, 3 H, *m*-$H_{Ar'}$, *p*-$H_{Ar'}$); 7.38 (t, 2 H, *m*-H_{Ph}, J = 7.43 Hz); 7.50 (t, 1 H, *p*-H_{Ph}, J = 7.43 Hz); 7.82 (d, 2 H, *o*-H_{Ph}, J = 6.95 Hz). IR, ν/cm^{-1}: 1630, 1655, 1700 (C=O).

5-Benzoyl-6-[2-(4-bromophenyl)ethenyl]-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (4b). Yield 5.95 g (70%), yellow crystals, m.p. 195—198 °C (EtOH). Found (%): C, 59.08; H, 4.30; Br, 18.52. $C_{21}H_{17}BrN_2O_3$. Calculated (%): C, 59.31; H, 4.03; Br, 18.79. ^{1}H NMR ($CDCl_3$), δ: 3.37 (s, 3 H, N(3)Me); 3.45 (s, 3 H, N(1)Me); 6.49 (d, 1 H, C(6)C<u>H</u>, J = 16.2 Hz); 6.74 (d, 1 H, C(6)CHC<u>H</u>, J = 16.2 Hz); 7.03 (d, 2 H, *o*-$H_{Ar'}$, J = 8.48 Hz); 7.33—7.41 (m, 4 H, *m*-$H_{Ar'}$, *m*-H_{Ph}); 7.49 (t, 1 H, *p*-H_{Ph}, J = 7.33 Hz); 7.79 (d, 2 H, *o*-H_{Ph}, J = 7.33 Hz). IR, ν/cm^{-1}: 1635, 1655, 1700 (C=O).

5-Benzoyl-6-[2-(4-methoxyphenyl)ethenyl]-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (4c). Yield 5.86 g (78%), yellow crystals, m.p. 178—181 °C (EtOH). Found (%): C, 70.47; H, 5.25. $C_{22}H_{20}N_2O_4$. Calculated (%): C, 70.20; H, 5.36. ^{1}H NMR ($CDCl_3$), δ: 3.37 (s, 3 H, N(3)Me); 3.45 (s, 3 H, N(1)Me); 3.74 (s, 3 H, OMe); 6.35 (d, 1 H, C(6)C<u>H</u>, J = 16.11 Hz); 6.75 (d + d, 3 H, C(6)CHC<u>H</u>, *m*-$H_{Ar'}$, J_{CH-CH} = 16.2 Hz, $J_{Ar'}$ = 9.16 Hz); 7.12 (d, 2 H, *o*-$H_{Ar'}$, J = 8.47 Hz); 7.36 (t, 2 H, *m*-H_{Ph}, J = 7.27 Hz); 7.48 (t, 1 H, *p*-H_{Ph}, J = 7.27 Hz); 7.80 (d, 2 H, *o*-H_{Ph}, J = 6.95 Hz). IR, ν/cm^{-1}: 1640, 1660, 1700 (C=O).

7-Aryl-1,3-dimethyl-2,4-dioxo-5-phenyl-1*H*,2*H*,3*H*,4*H*-pyrano[4,3-*d*]pyrimidinium bromides 5 (general procedure). A solution of Br_2 (0.01 mol) in $CHCl_3$ (10 mL) was added dropwise at 50—60 °C to a stirred solution of compound **4** (0.01 mol) in $CHCl_3$ (30 mL). The reaction mixture was refluxed for 30 min. The yellow precipitate that formed was filtered off, washed with $CHCl_3$ and AcOEt, and dried at 80—100 °C.

1,3-Dimethyl-2,4-dioxo-5,7-diphenyl-1*H*,2*H*,3*H*,4*H*-pyrano-[4,3-*d*]pyrimidinium bromide (5a). Yield 3.83 g (90%), yellow crystals, m.p. 248—251 °C ($CHCl_3$). Found (%): C, 59.12; H, 3.88; Br, 18.59. $C_{21}H_{17}BrN_2O_3$. Calculated (%): C, 59.31; H, 4.03; Br, 18.79. ^{1}H NMR ($CDCl_3$ + CF_3COOH), δ: 3.52 (s, 3 H, N(3)Me); 4.01 (s, 3 H, N(1)Me); 7.63—7.72 (m, 4 H, *m*-H_{Ph}, *m*-$H_{Ph'}$); 7.79—7.90 (m, 4 H, *o*-H_{Ph}, *p*-H_{Ph}, *p*-$H_{Ph'}$); 8.12 (s, 1 H, C(8)H); 8.19 (d, 2 H, *o*-$H_{Ph'}$, *J* = 7.53 Hz). IR, ν/cm^{-1}: 1620, 1695 (C=O).

7-(4-Bromophenyl)-1,3-dimethyl-2,4-dioxo-5-phenyl-1*H*,2*H*,3*H*,4*H*-pyrano[4,3-*d*]pyrimidinium bromide (5b). Yield 4.03 g (80%), yellow crystals, m.p. 273—277 °C ($CHCl_3$). Found (%): C, 50.35; H, 3.47; Br, 32.14. $C_{21}H_{16}Br_2N_2O_3$. Calculated (%): C, 50.03; H, 3.20; Br, 31.70. ^{1}H NMR ($CDCl_3$ + CF_3COOH), δ: 3.52 (s, 3 H, N(3)Me); 4.00 (s, 3 H, N(1)Me); 7.68 (t, 2 H, *m*-H_{Ph}, *J* = 7.70 Hz); 7.80—7.88 (m, 5 H, *o*-H_{Ph}, *p*-H_{Ph}, *m*-$H_{Ar'}$); 8.05 (d, 2 H, *o*-H_{Ph}, *J* = 8.48 Hz); 8.13 (s, 1 H, C(8)H). IR, ν/cm^{-1}: 1615, 1685 (C=O).

7-(4-Methoxyphenyl)-1,3-dimethyl-2,4-dioxo-5-phenyl-1*H*,2*H*,3*H*,4*H*-pyrano[4,3-*d*]pyrimidinium bromide (5c). Yield 3.78 g (83%), yellow crystals, m.p. 227—229 °C ($CHCl_3$). Found (%): C, 58.28; H, 4.10; Br, 17.73. $C_{22}H_{19}BrN_2O_4$. Calculated (%): C, 58.04; H, 4.21; Br, 17.55. ^{1}H NMR ($CDCl_3$ + CF_3COOH), δ: 3.51 (s, 3 H, N(3)Me); 3.96—4.01 (both s, 6 H, N(1)Me, OMe); 7.18 (d, 2 H, *m*-$H_{Ar'}$, *J* = 8.84 Hz); 7.66 (t, 2 H, *m*-H_{Ph}, *J* = 7.59 Hz); 7.78—7.87 (m, 3 H, *o*-H_{Ph}, *p*-H_{Ph}); 7.95 (s, 1 H, C(8)H); 8.21 (d, 2 H, *o*-$H_{Ar'}$, *J* = 8.85 Hz). IR, ν/cm^{-1}: 1605, 1680 (C=O).

6-Amino-5-aryl-1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-pyrido[4,3-*d*]pyrimidinium perchlorates 6 (general procedure). Hydrazine hydrate (0.55 mmol) was added to a stirred suspension of pyrano[4,3-*d*]pyrimidinium salt **3** (0.5 mmol) in AcOH (2 mL). The resulting bright red solution was refluxed for 5 min. On cooling, the precipitate that formed was filtered off, washed with AcOH, and dried at 80—100 °C.

6-Amino-1,3-dimethyl-2,4-dioxo-5-phenyl-1*H*,2*H*,3*H*,4*H*-pyrido[4,3-*d*]pyrimidinium perchlorate (6a). Yield 151 mg (79%), colorless crystals, m.p. 234—236 °C (AcOH). Found (%): C, 47.22; H, 3.76; Cl, 8.91. $C_{15}H_{15}ClN_4O_6$. Calculated (%): C, 47.07; H, 3.95; Cl, 9.26. ^{1}H NMR (DMSO-d_6), δ: 3.11 (s, 3 H, N(3)Me); 3.60 (s, 3 H, N(1)Me); 7.15 (br.s, 2 H, NH_2); 7.30—7.36 (m, 2 H, *m*-H_{Ph}); 7.50—7.56 (m, 3 H, *o*-H_{Ph}, *p*-H_{Ph}); 8.01 (d, 1 H, C(8)H, *J* = 7.54 Hz); 8.94 (d, 1 H, C(7)H, *J* = 7.54 Hz). IR, ν/cm^{-1}: 1070, 1090 (Cl—O); 1615, 1670 (C=O); 3245, 3350 (NH_2).

6-Amino-5-(4-bromophenyl)-1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-pyrido[4,3-*d*]pyrimidinium perchlorate (6b). Yield 196 mg (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, *m*-H_{Ar}, *J* = 8.4 Hz); 7.69 (d, 2 H, *o*-H_{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). IR, ν/cm^{-1}: 1100 br (Cl—O); 1630, 1685 (C=O); 3255, 3340 (NH_2).

6-Amino-5-(4-methoxyphenyl)-1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-pyrido[4,3-*d*]pyrimidinium perchlorate (6c). Yield 148 mg (72%), colorless crystals, m.p. 300—303 °C (AcOH). Found (%): C, 46.28; H, 4.03; Cl, 8.37. $C_{16}H_{17}ClN_4O_7$. Calculated (%): C, 46.56; H, 4.15; Cl, 8.59. ^{1}H NMR (DMSO-d_6), δ: 3.12 (s, 3 H, N(3)Me); 3.59 (s, 3 H, N(1)Me); 3.82 (s, 3 H, OMe); 7.09 (d, 2 H, *m*-H_{Ar}, *J* = 8.79 Hz); 7.17 (br.s, 2 H, NH_2); 7.29 (d, 2 H, *o*-H_{Ar}, *J* = 8.79 Hz); 7.97 (d, 1 H, C(8)H, *J* = 7.54 Hz); 8.91 (d, 1 H, C(7)H, *J* = 7.54 Hz). IR, ν/cm^{-1}: 1090 br (Cl—O); 1625, 1675 (C=O); 3260, 3325 (NH_2).

8-Aryl-1,3-dimethyl-5-phenyl-1*H*-pyrimido[5,4-*d*][1,2]-diazepine-2,4(3*H*,9*H*)-dione hydrobromides 7 (general procedure). Hydrazine hydrate (2.2 mmol) was added to a stirred suspension of pyrano[4,3-*d*]pyrimidinium salt **5** (2 mmol) in AcOH (10 mL). The resulting orange solution was refluxed for 1 min. On cooling, the precipitate that formed was filtered off, washed with AcOH, and dried at 80—100 °C.

1,3-Dimethyl-5,8-diphenyl-1*H*-pyrimido[5,4-*d*][1,2]-diazepine-2,4(3*H*,9*H*)-dione hydrobromide (7a). Yield 648 mg (74%), colorless crystals, m.p. 242—245 °C (AcOH). Found (%): C, 57.17; H, 4.16; Br, 17.84. $C_{21}H_{19}BrN_4O_2$. Calculated (%): C, 57.41; H, 4.36; Br, 18.19. ^{1}H NMR (DMSO-d_6), δ: 2.91 (d, 1 H, C(9)H, *J* = 14.13 Hz); 3.03 (s, 3 H, N(3)Me); 3.50 (s, 3 H, N(1)Me); 4.73 (d, 1 H, C(9)H, *J* = 14.13 Hz); 4.95—5.50 (br.s, H^+ + H_2O); 7.34—7.41 (m, 3 H, *m*-H_{Ph}, *p*-H_{Ph}); 7.44—7.51 (m, 3 H, *m*-$H_{Ph'}$, *p*-$H_{Ph'}$); 7.61—7.66 (m, 2 H, *o*-H_{Ph}); 7.93—8.02 (m, 2 H, *o*-$H_{Ph'}$). IR, ν/cm^{-1}: 1665, 1705 (C=O), 3380 br (NH).

8-(4-Bromophenyl)-1,3-dimethyl-5-phenyl-1*H*-pyrimido-[5,4-*d*][1,2]diazepine-2,4(3*H*,9*H*)-dione hydrobromide (7b). Yield 652 mg (63%), colorless crystals, m.p. 281—286 °C (AcOH). Found (%): C, 48.35; H, 3.38; Br, 30.56. $C_{21}H_{18}Br_2N_4O_2$. Calculated (%): C, 48.67; H, 3.50; Br, 30.84. ^{1}H NMR (DMSO-d_6), δ: 2.91 (d, 1 H, C(9)H, *J* = 14.13 Hz); 3.02 (s, 3 H, N(3)Me); 3.51 (s, 3 H, N(1)Me); 4.38—4.53 (br.s, H^+ + H_2O); 4.69 (d, 1 H, C(9)H, *J* = 14.13 Hz); 7.33—7.42 (m, 3 H, *m*-H_{Ph}, *p*-H_{Ph}); 7.60—7.71 (m, 4 H, *o*-H_{Ph}, *m*-$H_{Ar'}$); 7.92 (d, 2 H, *o*-$H_{Ar'}$, *J* = 8.47 Hz). IR, ν/cm^{-1}: 1670, 1710 (C=O), 3380 br (NH).

8-(4-Methoxyphenyl)-1,3-dimethyl-5-phenyl-1*H*-pyrimido-[5,4-*d*][1,2]diazepine-2,4(3*H*,9*H*)-dione hydrobromide (7c). Yield 748 mg (80%), colorless crystals, m.p. 259—261 °C (AcOH). Found (%): C, 56.43; H, 4.32; Br, 17.37. $C_{22}H_{21}BrN_4O_3$. Calculated (%): C, 56.30; H, 4.51; Br, 17.02. ^{1}H NMR (DMSO-d_6), δ: 2.89 (d, 1 H, C(9)H, *J* = 14.22 Hz); 3.06 (s, 3 H, N(3)Me); 3.56 (s, 3 H, N(1)Me); 3.83 (s, 3 H, OMe); 4.50—5.05 (br.s + d, H^+ + H_2O, C(9)H, *J* = 13.90 Hz); 7.05 (d, 2 H, *m*-$H_{Ar'}$, *J* = 8.85 Hz); 7.38—7.44 (m, 3 H, *m*-H_{Ph}, *p*-H_{Ph}); 7.63—7.69 (m, 2 H, *o*-H_{Ph}); 7.98 (d, 2 H, *o*-$H_{Ar'}$, *J* = 8.84 Hz). IR, ν/cm^{-1}: 1660, 1705 (C=O), 3375 br (NH).

8-Aryl-1,3-dimethyl-5-phenyl-1*H*-pyrimido[5,4-*d*][1,2]-diazepine-2,4(3*H*,9*H*)-diones 8 (general procedure). Diazepine bromide **7** (200 mg) was treated with a mixture of water (10 mL) and $CHCl_3$ (10 mL). The chloroform layer was separated and evaporated to dryness. The product was dried at 80—100 °C.

1,3-Dimethyl-5,8-diphenyl-1*H*-pyrimido[5,4-*d*][1,2]-diazepine-2,4(3*H*,9*H*)-dione (8a). Yield 146 mg (90%), colorless crystals, m.p. 255—258 °C ($CHCl_3$). Found (%): C, 70.04; H, 5.17. $C_{21}H_{18}N_4O_2$. Calculated (%): C, 70.38; H, 5.06. ^{1}H NMR ($CDCl_3$), δ: 3.02 (d, 1 H, C(9)H, *J* = 13.50 Hz); 3.26 (s, 3 H, N(3)Me); 3.62 (s, 3 H, N(1)Me); 4.41 (d, 1 H, C(9)H, *J* = 13.19 Hz); 7.39—7.50 (m, 6 H, *m*-H_{Ph}, *p*-H_{Ph}, *m*-$H_{Ph'}$, *p*-$H_{Ph'}$); 7.67—7.72 (m, 2 H, *o*-H_{Ph}); 7.83—7.90 (m, 2 H, *o*-$H_{Ph'}$). IR, ν/cm^{-1}: 1645, 1700 (C=O).

8-(4-Bromophenyl)-1,3-dimethyl-5-phenyl-1*H*-pyrimido-[5,4-*d*][1,2]diazepine-2,4(3*H*,9*H*)-dione (8b). Yield 128 mg (76%), colorless crystals, m.p. 283—287 °C ($CHCl_3$). Found (%): C, 57.85; H, 4.07; Br, 17.93. $C_{21}H_{17}BrN_4O_2$. Calculated (%): C, 57.68; H, 3.92; Br, 18.27. ^{1}H NMR ($CDCl_3$), δ: 3.00 (d,

1 H, C(9)H, J = 13.50 Hz); 3.26 (s, 3 H, N(3)Me); 3.60 (s, 3 H, N(1)Me); 4.33 (d, 1 H, C(9)H, J = 13.50 Hz); 7.39—7.45 (m, 3 H, *m*-H_{Ph}, *p*-H_{Ph}); 7.59 (d, 2 H, *m*-$H_{Ar'}$, J = 8.79 Hz); 7.66—7.70 (m, 2 H, *o*-H_{Ph}); 7.73 (d, 2 H, *o*-$H_{Ar'}$, J = 8.80 Hz). IR, ν/cm^{-1}: 1650, 1705 (C=O).

8-(4-Methoxyphenyl)-1,3-dimethyl-5-phenyl-1*H*-pyrimido-[5,4-*d*][1,2]diazepine-2,4(3*H*,9*H*)-dione (8c). Yield 149 mg (90%), colorless crystals, m.p. 266—268 °C ($CHCl_3$). Found (%): C, 67.74; H, 5.12. $C_{22}H_{20}N_4O_3$. Calculated (%): C, 68.03; H, 5.19. ^{1}H NMR ($CDCl_3$), δ: 2.97 (d, 1 H, C(9)H, J = 13.19 Hz); 3.26 (s, 3 H, N(3)Me); 3.61 (s, 3 H, N(1)Me); 3.85 (s, 3 H, OMe); 4.38 (d, 1 H, C(9)H, J = 13.50 Hz); 6.96 (d, 2 H, *m*-$H_{Ar'}$, J = 9.1 Hz); 7.38—7.43 (m, 3 H, *m*-H_{Ph}, *p*-H_{Ph}); 7.66—7.71 (m, 2 H, *o*-H_{Ph}); 7.82 (d, 2 H, *o*-$H_{Ar'}$, J = 9.1 Hz). IR, ν/cm^{-1}: 1650, 1700 (C=O).

6-Amino-7-aryl-1,3-dimethyl-2,4-dioxo-5-phenyl-1*H*,2*H*,3*H*,4*H*-pyrido[4,3-*d*]pyrimidinium bromides 9 (general procedure). ***Method A.*** Hydrazine hydrate (1.5 mmol) was added to a stirred suspension of pyrano[4,3-*d*]pyrimidinium salt **5** (0.5 mmol) in AcOH (2 mL). The reaction mixture was refluxed for 30 min, the original orange solution turning pale yellow. The solution was cooled and diluted with Et_2O (2 mL). The precipitate that formed was filtered off, washed with Et_2O and AcOH, and dried at 80—100 °C.

Method B. Hydrazine hydrate (0.55 mmol) was added to a stirred suspension of diazepine bromide **7** (0.5 mmol) in AcOH (2 mL). The reaction mixture was refluxed for 30 min, the original orange solution turning pale yellow. The solution was cooled and diluted with Et_2O (2 mL). The precipitate that formed was filtered off, washed with Et_2O and AcOH, and dried at 80—100 °C.

6-Amino-1,3-dimethyl-2,4-dioxo-5,7-diphenyl-1*H*,2*H*,3*H*,4*H*-pyrido[4,3-*d*]pyrimidinium bromide (9a). Yield 178 mg (81%) (method ***A***) or 158 mg (72%) (method ***B***), colorless crystals, m.p. 192—195 °C (AcOH). Found (%): C, 57.20; H, 4.21; Br, 17.98. $C_{21}H_{19}BrN_4O_2$. Calculated (%): C, 57.41; H, 4.36; Br, 18.19. ^{1}H NMR (DMSO-d_6), δ: 3.12 (s, 3 H, N(3)Me); 3.66 (s, 3 H, N(1)Me); 6.34 (s, 2 H, NH_2); 7.44—7.65 (m, 8 H, 4 *m*-H_{Ph} + 2 *p*-H_{Ph} + 2 *o*-H_{Ph}); 7.84—7.90 (m, 2 H, 2 *o*-H_{Ph}); 7.96 (s, 1 H, C(8)H). IR, ν/cm^{-1}: 1610, 1660 (C=O); 3250, 3350 (NH_2).

6-Amino-7-(4-bromophenyl)-1,3-dimethyl-2,4-dioxo-5-phenyl-1*H*,2*H*,3*H*,4*H*-pyrido[4,3-*d*]pyrimidinium bromide (9b). Yield 194 mg (75%) (method ***A***) or 181 mg (70%) (method ***B***), colorless crystals, m.p. 272—275 °C (AcOH). Found (%): C, 48.36; H, 3.35; Br, 31.09. $C_{21}H_{18}Br_2N_4O_2$. Calculated (%): C, 48.67; H, 3.50; Br, 30.84. ^{1}H NMR (DMSO-d_6), δ: 3.12 (s, 3 H, N(3)Me); 3.65 (s, 3 H, N(1)Me); 6.32 (s, 2 H, NH_2); 7.41—7.46 (m, 2 H, *m*-H_{Ph}); 7.51—7.58 (m, 3 H, *o*-H_{Ph} + *p*-H_{Ph}); 7.82 (d + d, 4 H, *o*-$H_{Ar'}$, *m*-$H_{Ar'}$, J = 9.1 Hz); 7.99 (s, 1 H, C(8)H). IR, ν/cm^{-1}: 1610, 1670 (C=O); 3300, 3330 (NH_2).

6-Amino-7-(4-methoxyphenyl)-1,3-dimethyl-2,4-dioxo-5-phenyl-1*H*,2*H*,3*H*,4*H*-pyrido[4,3-*d*]pyrimidinium bromide (9c). Yield 173 mg (74%) (method ***A***) or 185 mg (79%) (method ***B***), colorless crystals, m.p. 207—208 °C (AcOH). Found (%): C, 56.58; H, 4.42; Br, 16.67. $C_{22}H_{21}BrN_4O_3$. Calculated (%): C, 56.30; H, 4.51; Br, 17.03. ^{1}H NMR (DMSO-d_6), δ: 3.15 (s, 3 H, N(3)Me); 3.70 (s, 3 H, N(1)Me); 3.88 (s, 3 H, OMe); 6.39 (s, 2 H, NH_2); 7.19 (d, 2 H, *m*-$H_{Ar'}$, J = 8.66 Hz); 7.47—7.53 (m, 2 H, *m*-H_{Ph}); 7.54—7.60 (m, 3 H, *o*-H_{Ph}, *p*-H_{Ph}); 7.92 (d, 3 H, C(8)H, *o*-$H_{Ar'}$, J = 7.93 Hz). IR, ν/cm^{-1}: 1600, 1690 (C=O); 3250, 3285 (NH_2).

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Received January 10, 2008