A Novel and Efficient One-Pot Synthesis of 2-Aminopyrimidinones and Their Self-Assembly

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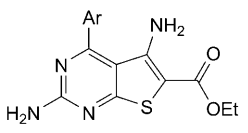
Dedicated to Prof. *Abdoljalil Mostashari* on the occasion of his 70th birthday

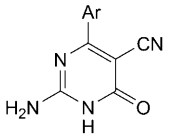
A three-component reaction of benzaldehyde derivatives, methyl cyanoacetate, and guanidinium carbonate affords 2-amino-4-aryl-1,6-dihydro-6-oxopyrimidine-5-carbonitriles and the four-component reaction of benzaldehyde derivatives, methyl cyanoacetate, and guanidinium hydrochloride in the presence of piperidine leads to piperidinium salts of pyrimidinones. X-ray crystallography data confirm self-assembly and H-bonding in these compounds.

Introduction. – The H-bond is one of the most important interactions for molecular recognition in supramolecular chemistry [1]. Designed supramolecular interactions continue to play a central role in the development of novel and functional nanoscale devices and materials. In this way, syntheses of molecules capable of forming defined H-bonding interactions have led to the creation of artificial self-assembling structures. Recently, studies on supramolecular noncovalent polymers which have potential applications in nanotechnology, crystal engineering, and particularly in organic media containing H-bonding are in progress [2]. In these molecules, H-bonding is considerably strong, and in the solid phase, X-ray diffraction provides visualization of H-bonded arrays. The synthesis and characterization of novel structures which are able to form additional H-bonds is of great importance [3][4].

2-Aminopyrimidinones have received significant attention, because of their diverse biological activities [5], such as inhibitors of GSK3β (glycogen synthase kinase 3β) [6]. Furthermore, compound **A** and its derivatives are inhibitors of HSP90 activity *in vitro* or *in vivo*, and are used, *inter alia,* in the treatment of cancer. The starting materials for the synthesis of derivatives of compound **A** are 2-amino-4-aryl-1,6-dihydro-6-oxopyrimidine-5-carbonitriles **B** [7].



A



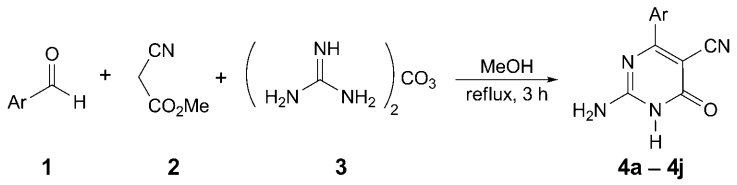
B

There are several reports on syntheses of 2-aminopyrimidinones, for example, *a*) by condensation reactions of 1,3-dicarbonyl compounds such as β-aldehyde esters, β-keto esters, and β-diesters with guanidinium hydrochloride [8], *b*) by condensation of arylmethylidene malononitriles with amidines and guanidinium carbonate [9], *c*) by reaction of cyanoacetamide and *N*-cyanoimidates [10], or *d*) by three-component condensation of aromatic aldehydes, methyl cyanoacetate, and guanidinium carbonate in the presence of a strong base [7].

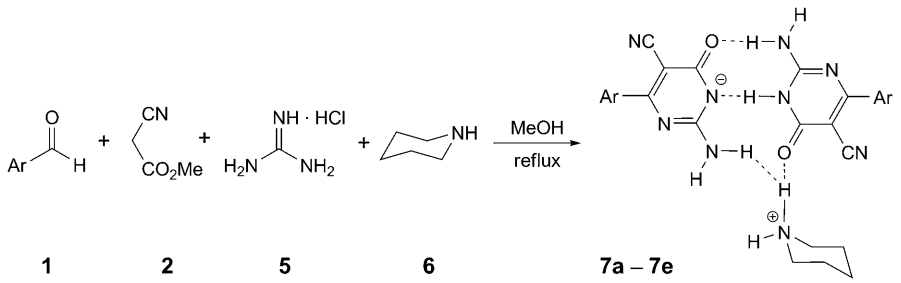
However, the syntheses of these compounds usually require lengthy routes with low yields and suffer from drawbacks such as laborious synthesis of starting materials, long reaction times, or use of highly basic catalysts.

Thus, the development of a method to synthesize 2-aminopyrimidinones in one step would be desirable. Herein, we report simple and efficient one-pot, three-, and four-component reactions for the synthesis of 2-aminopyrimidones (*Schemes 1* and *2*).

Scheme 1



Scheme 2



The one-pot three-component reaction of benzaldehyde derivatives **1**, methyl cyanoacetate (**2**), and guanidinium carbonate (**3**) gave 2-amino-4-aryl-1,6-dihydro-6-oxopyrimidine-5-carbonitriles (**4**) (*Scheme 1*).

The advantage of this synthetic method is that strongly basic conditions are not required in comparison with the reported method [7]. The results of the synthesis of 2-amino-4-aryl-1,6-dihydro-6-oxopyrimidine-5-carbonitriles (**4**) are summarized in *Table 1*.

The products were characterized on the basis of their NMR spectra and mass spectrometric data. For example, the ^{1}H-NMR spectrum of **4e** exhibited a signal at 11.90 ppm due to the lactam NH group. The H-decoupled ^{13}C-NMR spectrum of **4e** revealed two distinct resonances at 116.8 and 118.3 ppm for the two CN groups, whilst the signal of the CO group appeared at 170.0 ppm.

Table 1. *Synthesis of 2-Amino-4-aryl-1,6-dihydro-6-oxopyrimidine-5-carbonitriles* **4**

Product	Ar	Yield [%][a])
4a	C_6H_5	41
4b	4-Br–C_6H_4	52
4c	4-Cl–C_6H_4	48
4d	2,3-Cl_2–C_6H_3	36
4e	4-NC–C_6H_4	40
4f	4-Me–C_6H_4	42
4g	3-HO–C_6H_4	39
4h	4-HO–C_6H_4	62
4i	3-O_2N–C_6H_4	43
4j	4-O_2N–C_6H_4	54

[a]) Yields of isolated pyrimidinone.

We also attempted a one-pot, four-component condensation reaction of aromatic benzaldehydes (**1**), methyl cyanoacetate (**2**), guanidinium hydrochloride (**5**), and piperidine (**6**), in which the latter acts both as a base and reagent (*Scheme 2*). The results are summarized in *Table 2*. A ^{1}H-NMR experiment was performed in (D_6)DMSO, as a solvent which is known to disrupt H-bonds. However, in our experiment, the ^{1}H-NMR data indicated the formation of zwitterionic product structures **7a**–**7e**. The integral of the H-signals of the piperidinium ions in relation to the aromatic H-signals amounts to 1:2. The outcome of X-ray structural determinations on **7b** and **7c** confirms these results. According to the X-ray structure data, it is confirmed that the two pyrimidinonate skeletons contain one negative charge. The molecular structure of compound **7b** is shown in *Fig. 1*, which demonstrates the formation of the zwitterionic product and the essential role of piperidinium ions in the construction of the salt. Piperidinium pyrimidinonate **7c** was crystallized and characterized by X-ray diffraction as well. The structure is almost isomorphous with the structure of **7b** and thus verifies the formation of an analogous supramolecular structure. Therefore, only the structure of **7b** will be discussed in detail.

Table 2. *Synthesis of Piperidinium Pyrimidinonate* **7** via *One-Pot Four-Component Reaction*

Product	Ar	Yield [%][a])
7a	C_6H_5	48
7b	4-Br–C_6H_4	62
7c	4-Cl–C_6H_4	59
7d	4-Me–C_6H_4	53
7e	4-F_3C–C_6H_4	43

[a]) Yields of isolated **7**.

The X-ray structure clearly shows three H-bonds (N13 ··· O35: 2.91 Å, N14 ··· N34: 2.86 Å, N33 ··· O15: 2.82 Å) connecting a pair of molecules (*Fig. 1*). The role of the piperidinium ion in the molecular association is crucial. Two of them act as tethers to

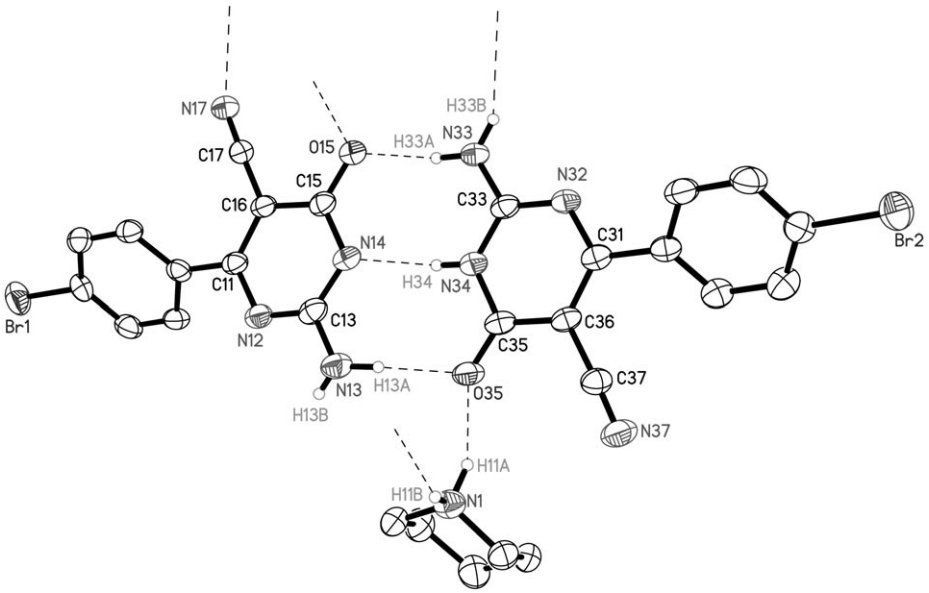


Fig. 1. *Thermal ellipsoid plot of the triple H-bridged motif observed for compound* **7b**. The dashed lines with open ends indicate other H-bridges to neighboring molecules as described in the text.

connect *via* H-bridges two pairs of molecules piled upon each other. These H-bridges are N1 ··· O35 with 2.87 Å and N1 ··· O15′ with 2.82 Å (see *Figs. 1* and *2*).

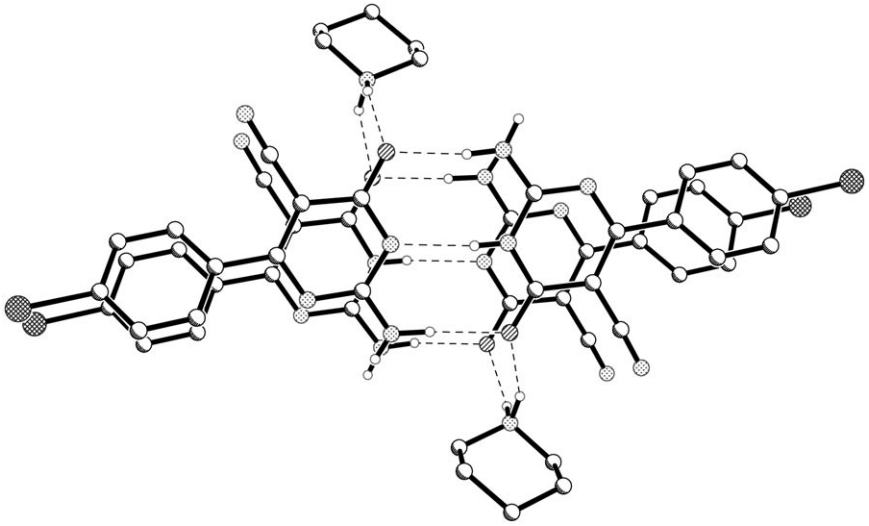


Fig. 2. *In the crystal structure of compound* **7b**, *the H-bonding and the tetrameric unit is recognizable*

As can be concluded from the structures, piperidine mediates the association by making three complementary H-bonds possible. The formation of the piperidinium salt

generates the AAD face and provides a DDA-AAD pairing interaction. The piled molecular pairs show $\pi-\pi$ interactions between the stacked heterocycles. The distances of the overlapping atoms to the opposite ring planes amount to only 3.375 Å (C35′), 3.455 Å (C36′), 3.392 Å (N12′), and 3.319 Å (C13′).

In addition to X-ray crystallography data, other techniques were used for the confirmation of the molecular association, such as ^{1}H-NMR spectroscopy and high-resolution mass spectrometry. The ratio of the signals for the H-atoms of the piperidine ring and also of the aromatic H-atoms in the ^{1}H-NMR spectra was used for determining the piperidinium/pyrimidinonate ratio. HR-MS data for compound **7a** confirmed molecular association with an *m*/*z* value of 510.2326 ($C_{27}H_{28}N_9O_2$) and showed the ratio piperidinium/pyrimidinonate to be 1:2.

In summary, we have described efficient one-pot three- and four-component reactions for the synthesis of 2-amino-4-aryl-1,6-dihydro-6-oxopyrimidine-5-carbonitriles and their piperidinium salts. X-Ray crystallography data of the piperidinium salts of **7b** and **7c** confirmed self-assembly of these compounds *via* H-bonding. The use of the simple and available starting materials, the high bond forming efficiency, and the atom economy are advantages of this method.

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Experimental Part

General. All commercially available materials were used without further purification. All reactions were followed by TLC (silica gel *60* F_{254}; Merck). The detection was performed with UV light. Column chromatography (CC): silica gel *60* (200–300 mesh; *Merck*). M.p.: *Electrothermal 9100* apparatus; uncorrected. IR Spectra: *ABB* FT-IR (*FTLA 2000*) spectrometer; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR: *Bruker DRX-300 Avance* in (D_6)DMSO at 300 and 75 MHz, resp.; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. HR-MS: *Jeol JMS-700* (HR-EI), (HR-FAB) and ESI-POS (*Bruker Apex Qe-FT-ICR* instrument) spectrometer; in *m*/*z* (rel. %).

General Procedure for the Synthesis of 2-Amino-4-aryl-1,6-dihydro-6-oxopyrimidine-5-carbonitriles **4a**–**4j**. A soln. of aromatic aldehyde **1** (2 mmol), **2** (2.1 mmol, 0.20 g), and **3** (1.1 mmol, 0.20 g) in MeOH (25 ml) was heated at reflux. The progress of the reaction was monitored by TLC (hexane/AcOEt 3:1). On completion, HCl (2M) was added to neutralize the mixture. The precipitated solid was filtered, washed with cold CH_2Cl_2 and H_2O. The products were obtained in yields of 36–62%.

2-Amino-1,6-dihydro-6-oxo-4-phenylpyrimidine-5-carbonitrile (**4a**). Yield: 87 mg (41%). M.p. 344–346° (dec.). IR (KBr): 3392, 3138, 2223, 1638. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.00 (br. *s*, NH_2); 7.45–7.59 (*m*, 3 arom. H); 7.68–7.71 (*m*, 2 arom. H); 11.79 (br. *s*, NH). ^{13}C-NMR (75 MHz, (D_6)DMSO): 84.8; 117.3; 128.2; 130.9; 136.6; 156.4; 161.7; 171.6. EI-HR-MS: 212.0700 ($C_{11}H_8N_4O^+$; calc. 212.0698).

2-Amino-4-(4-bromophenyl)-1,6-dihydro-6-oxopyrimidine-5-carbonitrile (**4b**). Yield: 152 mg (52%). M.p. 284–286° (dec.). IR (KBr): 3392, 3153, 2215, 1669. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.10 (br. *s*, NH_2); 7.70 (br. *s*, 4 arom. H); 12.00 (br. *s*, NH). ^{13}C-NMR (75 MHz, (D_6)DMSO): 84.3; 117.7; 124.3; 130.3; 131.3; 136.0; 158.0; 164.2; 170.1. EI-HR-MS: 291.9796 ($C_{11}H_7{}^{81}BrN_4O^+$; calc. 291.9783), 289.9810 ($C_{11}H_7{}^{79}BrN_4O^+$; calc. 289.9804).

2-Amino-4-(4-chlorophenyl)-1,6-dihydro-6-oxopyrimidine-5-carbonitrile (**4c**). Yield: 120 mg (48%). M.p. 346–348° (dec.). IR (KBr): 3400, 3138, 2215, 1638. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.00 (br. *s*, NH_2); 7.60 (*d*, $J=8.0$, 2 arom. H); 7.80 (*d*, $J=8.0$, 2 arom. H); 11.80 (br. *s*, NH). ^{13}C-NMR (75 MHz, (D_6)DMSO): 84.9; 117.1; 128.4; 130.1; 135.3; 135.7; 156.5; 161.7; 170.3. EI-HR-MS: 248.0249 ($C_{11}H_7{}^{37}ClN_4O^+$; calc. 248.0227), 246.0310 ($C_{11}H_7{}^{35}ClN_4O^+$; calc. 246.0308).

2-Amino-4-(2,3-dichlorophenyl)-1,6-dihydro-6-oxopyrimidine-5-carbonitrile (**4d**). Yield: 101 mg (36%). M.p. 322–323° (dec.). IR (KBr): 3330, 3123, 2223, 1648. ^{1}H-NMR (300 MHz, (D$_6$)DMSO): 7.10 (br. *s*, NH); 7.46–7.51 (*m*, 2 arom. H); 7.79–7.81 (*m*, 1 arom. H); 8.40 (br. *s*, NH); 11.90 (br. *s*, NH). ^{13}C-NMR (75 MHz, (D$_6$)DMSO): 87.5; 115.7; 128.2; 128.6; 131.5; 132.1; 138.5; 157.0; 160.6; 170.9. EI-HR-MS: 283.9860 ($C_{11}H_6{}^{37}Cl_2N_4O^+$; calc. 283.9860), 281.9900 ($C_{11}H_6{}^{37}Cl^{35}ClN_4O^+$; calc. 281.9911), 279.9918 ($C_{11}H_6{}^{35}Cl_2N_4O^+$; calc. 279.9919).

2-Amino-4-(4-cyanophenyl)-1,6-dihydro-6-oxopyrimidine-5-carbonitrile (**4e**). Yield: 95 mg (40%). M.p. 360–361° (dec.). IR (KBr): 3392, 3146, 2215, 1654. ^{1}H-NMR (300 MHz, (D$_6$)DMSO): 7.10 (br. *s*, NH); 7.90 (*d*, *J* = 8.3, 2 arom. H); 8.00 (*d*, *J* = 8.3, 2 arom. H); 8.40 (br. *s*, NH); 11.90 (br. *s*, NH). ^{13}C-NMR (75 MHz, (D$_6$)DMSO): 85.5; 113.2; 116.8; 118.3; 129.1; 132.3; 140.9; 156.7; 161.5; 170.0. EI-HR-MS: 237.0625 ($C_{12}H_7N_5O^+$; calc. 237.0650).

2-Amino-1,6-dihydro-4-(4-methylphenyl)-6-oxopyrimidine-5-carbonitrile (**4f**). Yield: 95 mg (42%). M.p. 329–330° (dec.). IR (KBr): 3330, 3100, 2230, 1670. ^{1}H-NMR (300 MHz, (D$_6$)DMSO): 2.40 (*s*, Me); 7.10 (br. *s*, NH); 7.30 (*d*, *J* = 8.6, 2 arom. H); 7.70 (*d*, *J* = 8.6, 2 arom. H); 8.30 (br. *s*, NH); 11.90 (br. *s*, NH). ^{13}C-NMR (75 MHz, (D$_6$)DMSO): 21.0; 85.0; 117.4; 128.3; 128.8; 133.7; 140.0; 156.4; 161.7; 170.5. EI-HR-MS: 226.0840 ($C_{12}H_{10}N_4O^+$; calc. 226.0854).

2-Amino-1,6-dihydro-4-(3-hydroxyphenyl)-6-oxopyrimidine-5-carbonitrile (**4g**). Yield: 90 mg (39%). M.p. 330–332° (dec.). IR (KBr): 3407, 3138, 2215, 1661. H-NMR (300 MHz, (D$_6$)DMSO): 6.80 (br. *s*, NH); 6.90 (*d*, *J* = 7.5, 1 arom. H); 7.18–7.29 (*m*, 2 arom. H); 7.30 (*t*, *J* = 7.5, 1 arom. H); 8.20 (br. *s*, NH); 9.80 (br. *s*, OH); 11.70 (br. *s*, NH). ^{13}C-NMR (75 MHz, (D$_6$)DMSO): 84.7; 115.0; 117.2; 117.9; 119.0; 129.3; 137.8; 156.4; 157.1; 161.8; 71.7. EI-HR-MS: 228.0649 ($C_{11}H_8N_4O_2^+$; calc. 228.0648).

2-Amino-1,6-dihydro-4-(4-hydroxyphenyl)-6-oxopyrimidine-5-carbonitrile (**4h**). Yield: 141 mg (62%). M.p. 320–322° (dec.). IR (KBr): 3369, 3100, 2223, 1676. ^{1}H-NMR (300 MHz, (D$_6$)DMSO): 6.80 (br. *s*, NH$_2$); 6.90 (*d*, *J* = 8.5, 2 arom. H); 7.80 (*d*, *J* = 8.5, 2 arom. H); 10.20 (br. *s*, OH); 11.60 (br. *s*, NH). ^{13}C-NMR (75 MHz, (D$_6$)DMSO): 83.3; 117.8; 127.0; 129.0; 130.4; 156.1; 160.3; 162.1; 170.7. EI-HR-MS: 228.0649 ($C_{11}H_8N_4O_2^+$; calc. 228.0648).

2-Amino-1,6-dihydro-4-(3-nitrophenyl)-6-oxopyrimidine-5-carbonitrile (**4i**). Yield: 103 mg (43%). M.p. 310–312° (dec.). IR (KBr): 3400, 3153, 2215, 1653. ^{1}H-NMR (300 MHz, (D$_6$)DMSO): 7.10 (br. *s*, NH$_2$); 7.80 (*t*, *J* = 8.2, 1 arom. H); 8.20 (*d*, *J* = 8.2, 1 arom. H); 8.40 (*d*, *J* = 8.2, 1 arom. H); 8.60 (br. *s*, 1 arom. H); 11.80 (br. *s*, NH). ^{13}C-NMR (75 MHz, (D$_6$)DMSO): 85.3; 116.8; 123.0; 125.5; 130.1; 134.5; 137.9; 147.6; 156.7; 161.5; 168.9. EI-HR-MS: 257.0569 ($C_{11}H_7N_5O_3^+$; calc. 257.0549).

2-Amino-1,6-dihydro-4-(4-nitrophenyl)-6-oxopyrimidine-5-carbonitrile (**4j**). Yield: 139 mg (54%). M.p. 320–323° (dec.). IR (KBr): 3392, 3138, 2215, 1661, 1530, 1361. ^{1}H-NMR (300 MHz, (D$_6$)DMSO): 7.10 (br. *s*, NH); 8.00 (*d*, *J* = 10.5, 2 arom. H); 8.30 (*d*, *J* = 10.5, 2 arom. H); 11.90 (br. *s*, NH). ^{13}C-NMR (75 MHz, (D$_6$)DMSO): 85.7; 116.7; 123.5; 129.7; 142.6; 148.7; 156.7; 161.4; 169.7. EI-MS (70 eV): 257.1 (100, M^+), 215 (50), 169 (20), 141 (17).

*General Procedure for the Synthesis of Piperidinium 2-Amino-6-aryl-5-cyano-4-oxo-4*H*-pyrimidin-3-ide – 2-Amino-4-aryl-1,6-dihydro-6-oxopyrimidine-5-carbonitriles* **7a**–**7e**. A soln. of aromatic aldehyde **1** (2 mmol), **2** (2.1 mmol, 0.20 g), **5** (2.2 mmol, 0.20 g), and **6** (0.34 g, 4 mmol) in MeOH (50 ml) was heated at reflux. The progress of the reaction was monitored by TLC (hexane/AcOEt 3:1). The solvent was removed under reduced pressure, and MeCN was added to the mixture. The precipitated solid was filtered and further purified by crystallization from EtOH. The yields of the products were 43–62%.

*Piperidinium 2-Amino-5-cyano-4-oxo-6-phenyl-4*H*-pyrimidin-3-ide – 2-Amino-1,6-dihydro-6-oxo-4-phenylpyrimidine-5-carbonitrile (1:1)* (**7a**). Yield: 244 mg (48%). M.p. 290–292° (dec.). IR (KBr): 3430, 3323, 2946, 2208, 1676, 1523. ^{1}H-NMR (300 MHz, (D$_6$)DMSO): 1.50–1.77 (*m*, 3 CH$_2$); 2.90–3.00 (*m*, 2 CH$_2$N); 4.00 (br. *s*, 7 NH); 7.40–7.62 (*m*, 6 arom. H); 7.75–7.90 (*m*, 4 arom. H). ^{13}C-NMR (75 MHz, (D$_6$)DMSO): 21.8; 22.5; 43.9; 83.5; 118.8; 128.0; 128.1; 130.2; 137.4; 160.4; 168.4; 170.7. FAB-HR-MS (pos.): 510.2326 ($[M+1]^+$, $C_{27}H_{28}N_9O_2^+$; calc. 510.2366), 298.1669 ($C_{16}H_{20}N_5O^+$; calc. 298.1668), 213.0780 ($C_{11}H_9N_4O^+$; calc. 213.0776).

*Piperidinium 2-Amino-6-(4-bromophenyl)-5-cyano-4-oxo-4*H*-pyrimidin-3-ide – 2-Amino-4-(4-bromophenyl)-1,6-dihydro-6-oxopyrimidine-5-carbonitrile (1:1)* (**7b**). Yield: 368 mg (62%). M.p. 250–252° (dec.). IR (KBr): 3407, 3350, 3207, 2948, 2207, 1676, 1523. ^{1}H-NMR (300 MHz, (D$_6$)DMSO): 1.50–1.75 (*m*, 3 CH$_2$); 2.95–3.10 (*m*, 2 CH$_2$N); 3.60 (br. *s*, 7 NH); 7.70 (*dd*, *J* = 8.0, 8 arom. H). ^{13}C-NMR (75 MHz,

(D_6)DMSO): 21.8; 22.4; 43.8; 83.4; 118.7; 123.8; 130.3; 131.2; 136.6; 160.6; 168.6; 169.4. ESI-MS: 378.3 ($[M - C_{11}H_{87}{}^{81}BrN_4O + 1]^+$), 376.3 ($[M - C_{11}H_7{}^{79}BrN_4O + 1]^+$), 293.2 ($C_{11}H_8{}^{81}BrN_4O^+$), 291.2 ($C_{11}H_8{}^{79}BrN_4O^+$).

*Piperidinium 2-Amino-6-(4-chlorophenyl)-5-cyano-4-oxo-4*H*-pyrimidin-3-ide – 2-Amino-4-(4-chlorophenyl)-1,6-dihydro-6-oxopyrimidine-5-carbonitrile (1:1)* (**7c**). Yield: 343 mg (59%). M.p. 294–295° (dec.). IR (KBr): 3400, 3100, 2207, 1661, 1530. ^{1}H-NMR (300 MHz, (D_6)DMSO): 1.50–1.70 (*m*, 3 CH_2); 3.00 (*t*, *J* = 5.5, 2 CH_2N); 4.00 (br. *s*, 7 NH); 7.55 (*d*, *J* = 8.5, 4 arom. H); 7.80 (*d*, *J* = 8.5, 4 arom. H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 21.8; 22.4; 43.9; 83.5; 118.6; 128.2; 130.0; 135.0; 136.2; 160.5; 168.4; 169.3. FAB-HR-MS (pos.): 334.1282 ($[M - C_{11}H_7{}^{37}ClN_4O + 1]^+$, $C_{16}H_{19}{}^{37}ClN_5O^+$; calc. 334.1248),

Table 3. *Crystallographic Data for Compounds* **7b** *and* **7c**

	7b	**7c**
Chemical formula	$C_{27}H_{25}Br_2N_9O_2$	$C_{27}H_{25}Cl_2N_9O_2$
M_r	667.38	578.46
Crystal system	Triclinic	Triclinic
Space group	$P\bar{1}$	$P\bar{1}$
a [Å]	9.447(3)	9.322(1)
b [Å]	10.888(4)	10.932(2)
c [Å]	15.047(5)	14.682(2)
α [°]	103.24(1)	102.16(1)
β [°]	102.66(1)	102.42(1)
γ [°]	92.45(1)	92.61(1)
V [Å^3]	1462.8(9)	1421.9(4)
Z	2	2
Calc. density D_x [Mg m^{-3}]	1.515	1.35
Radiation type	MoK_α	MoK_α
Wavelength (λ)	0.71073	0.71073
θ_{range} [°]	1.4–27.5	1.9–27.5
μ [mm^{-1}]	2.81	0.271
Temperature [K]	200(2)	200(2)
Crystal shape	polyhedron	polyhedron
Crystal size [mm^3]	0.22 × 0.18 × 0.10	0.24 × 0.22 × 0.2
Crystal color	yellow	yellow
Diffractometer	*Bruker Smart CCD*	*Bruker Smart CCD*
Data collection method	0.3° ω-scans	0.3° ω-scans
No. of measured reflexions	15282	14901
No. of independent reflexions	6670	6469
No. of observed reflexions	4890	4547
Criterion of observed reflexions	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.0266	0.0299
θ_{max} [°]	27	27
R	0.037	0.042
wR	0.089	0.112
No. of parameters	407	407
h_{min}/h_{max}	−12/12	−12/12
k_{min}/k_{max}	−14/14	−14/14
l_{min}/l_{max}	−19/19	−19/18
Goodness-of-fit on F^2	1.01	1.04
$\Delta\rho_{max}$	0.61	0.43
$\Delta\rho_{min}$	−0.51	−0.32

332.1300 ($[M - C_{11}H_7{}^{35}ClN_4O]^+$, $C_{16}H_{19}{}^{35}ClN_5O^+$; calc. 332.1278), 249.0374 ($C_{11}H_8{}^{37}ClN_4O^+$; calc. 249.0359), 247.0413 ($C_{11}H_8{}^{35}ClN_4O^+$; calc. 247.0387).

*Piperidinium 2-Amino-6-(4-methylphenyl)-5-cyano-4-oxo-4*H*-pyrimidin-3-ide – 2-Amino-1,6-dihydro-4-(4-methylphenyl)-6-oxopyrimidine-5-carbonitrile (1:1)* (**7d**). Yield: 286 mg (53%). M.p. 280–281° (dec.). IR (KBr): 3500, 3400, 3332, 2200, 1669. ^{1}H-NMR (300 MHz, (D_6)DMSO): 1.40–1.65 (*m*, 3 CH_2); 2.35 (*s*, 2 Me); 2.80 (*t*, J = 5.5, 2 CH_2N); 4.2 (br. *s*, 7 NH_2); 7.35 (*d*, J = 8.0, 4 arom. H); 7.70 (*d*, J = 8.0, 4 arom. H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 21.0; 21.9; 22.5; 43.8; 83.2; 119.0; 128.2; 128.6; 134.6; 140.1; 160.4; 168.6; 170.5. ESI-MS: 312.3 ($[M - C_{12}H_{10}N_4O + 1]^+$), 227.3 ($C_{12}H_{11}N_4O^+$).

*Piperidinium 2-Amino-5-cyano-4-oxo-6-[4-(trifluoromethyl)phenyl]-4*H*-pyrimidin-3-ide-2-Amino-1,6-dihydro-6-oxo-4-[4-(trifluoromethyl)phenyl]pyrimidine-5-carbonitrile (1:1)* (**7e**). Yield: 278 mg (43%). M.p. > 310° (dec.). IR (KBr): 3476, 3315, 3192, 2207, 1684. ^{1}H-NMR (300 MHz, (D_6)DMSO): 1.55–1.70 (*m*, 3 CH_2); 2.99 (*t*, J = 5.5, 2 CH_2N); 4.4 (br. *s*, 7 NH); 7.85 (*d*, J = 8.2, 4 arom. H); 7.96 (*d*, J = 8.2, 4 arom. H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 21.8; 22.4; 43.8; 84.0; 118.5; 122.3; 125.1; 125.2; 125.3; 125.9; 129.1; 130.1; 130.5; 141.4; 160.8; 168.5; 169.4. ESI-MS: 366.3 ($[M - C_{12}H_7F_3N_4O]^+$), 281.4 ($C_{12}H_8F_3N_4O^+$).

X-Ray Structure Determination of Compounds **7b** *and* **7c**. The crystallographic data are presented in *Table 3*. Intensities were corrected for *Lorentz* and polarization effects, an empirical absorption correction was applied using SADABS [11] based on the *Laue* symmetry of the reciprocal space, μ = 0.27 mm^{-1}, structure solved by direct methods and refined against F^2 with a full-matrix least-squares algorithm using the SHELXTL-PLUS (5.10) software package [12]. H-atoms were treated using appropriate riding models except for the H-atoms bonded to N-atoms, which were refined isotropically, goodness-of-fit = 1.01 for **7b** and 1.04 for **7c**. Further details of crystal structures of compounds **7b** and **7c** can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (e-mail: deposit@ccdc.cm.ac.uk), quoting the deposition numbers CCDC-734321 and -734322, resp.

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