An Efficient One-Pot Synthesis of 6-Aryl-5-cyano-2-thiopyrimidinone Derivatives and Their Piperidinium Ionic Forms, X-ray Crystal Structures

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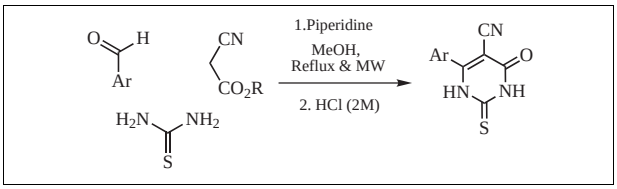

Three-component condensation of benzaldehyde derivatives, alkyl cyanoacetates and thiourea in the presence of piperidine in reflux condition provides a direct route to piperidinium 6-aryl-5-cyano 2-thiopyrimidonate salts in good yields. These reactions were also carried out under microwave irradiation. The yields of products under the microwave condition were better as compared to the reflux media. The acidification of these ionic forms resulted in the formation of 6-aryl-5-cyano-2-thiopyrimidone derivatives. The X-ray structures of the ionic forms (**4, 5,** and **7)** show that there are anionic thiopyrimidinone skeletons hydrogen bridged with piperidinium cations.

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Introduction.

Various analogues of thiopyrimidones have effective antibacterial, antifungal, antiviral, fungicidal, insecticidal, miticidal [1-3] and antileishmania activities [4]. They are also starting materials for the production of some uracil derivatives and nucleosides [5-7]. The versatile biological activities of thiopyrimidones prompted us to undertake the synthesis of these novel derivatives.

There are several methods for the synthesis of these compounds [8]. 6-Aryl-5-cyano-2-thiopyrimidone derivatives could be obtained from the condensation of aldehydes, alkyl cyanoacetate and thiourea in the presence of potassium carbonate [9]; the reaction of benzylidene cyanoacetate with thiourea in the presence of sodium alkoxides [10] and also the reaction of 3-aryl-3-chloro-2-cyano propenoates with symmetrically substituted thioureas [11]. The major drawbacks of the reported methods lie in a considerably low yield, long reaction time and the presence of strong bases such as sodium alkoxides. Therefore, the search for milder, more convenient and efficient methods for the preparation of thiopyrimidones continued to attract our attention. We wish to report here a facile and improved one-pot three-component condensation of benzaldehyde derivatives, alkyl cyanoacetates and thiourea in the presence of piperidine as a base under reflux and microwave irradiation conditions (Scheme 1). The reaction is completed after 6 h of reflux and 4-6 min under microwave irradiation.

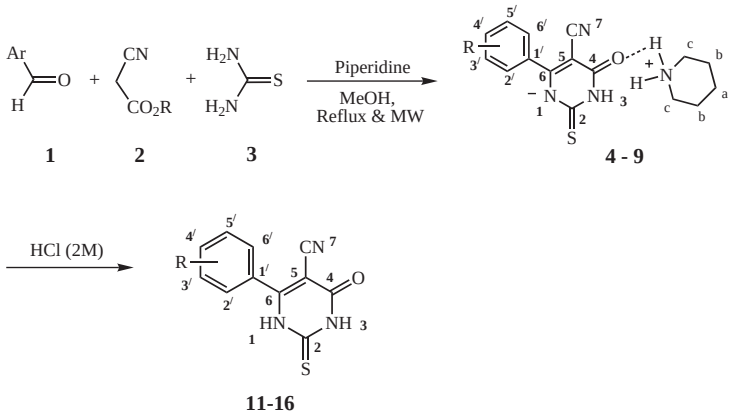
Results and Discussion.

By the end of the reaction, piperidinium 2-thiopyrimidonate salts were formed as a yellow precipitate. In all cases, by using piperidine as a base, we could obtain the piperidinium thiopyrimidinate ionic form directly as precipitate; from the mixture which itself facilitates the work-up. Moreover, by following acidification of the ionic form, 2-thiopyrimidinone is obtained in a greater yield as compared to the yield of the previously described procedure. These salts are stable and could be stored for a long time. Since these compounds are starting materials for the synthesis of some biologically active ingredients, they may be used directly for other reactions without the need for further purification or addition of any base. Pyrrolidine was also used as the base for this reaction. Although the yields were almost similar, piperidine could form better ionic crystal in comparison to pyrrolidine and piperidinium ionic form was purer than pyrrolidinium.

Moreove, microwave-assisted rapid organic reactions constitute an emerging technology that makes experimentally and industrially important organic syntheses more effective and more eco-friendly than conventional reactions [12].

Hence, microwaves have been applied to accelerate reaction rates in a variety of chemical transformations and to improve the yields of products in most cases. When a mixture of thiourea, benzaldehyde derivative, alkyl cyanoacetates and piperidine in MeOH was heated under the reflux condition or microwave irradiation (100%

Scheme 1



1 **2** **3** **4 - 9**

11-16

Table 1

Synthesis of 2-Thiopyrimidinate Piperidinium Ionic Forms (**4-9**)

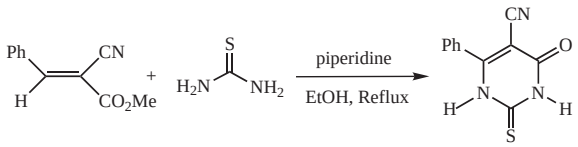
Entry	Ar	R	Yield† Reflux	Yield† M.W	Product
a	C_6H_5	Me	43*	47*	4
b	C_6H_5	Et	45*	48*	4
c	p- Br-C_6H_4	Me	45	53	5
d	p- Br-C_6H_4	Et	47	54	5
e	m-Cl-C_6H_4	Me	37	40	6
f	m-Cl- C_6H_4	Et	39	42	6
g	p- Cl- C_6H_4	Me	50	56	7
h	p- Cl- C_6H_4	Et	53	57	7
i	p-CN-C_6H_4	Me	43	50	8
j	p-CN-C_6H_4	Et	44	52	8
k	m-NO_2-C_6H_4	Me	47	53	9
l	m-NO_2-C_6H_4	Et	48	55	9

* In all reactions, the reflux and MW irradiation times are 6 hours and 4 minutes respectively, except for the reactions a, b, which are 8 hours and 6 minutes. † In all cases, the yields are measured in pure forms.

power, 850 W), piperidinium thiopyrimidone derivatives (**4-9**) were precipitated in the flask. The yield is related to the pure form of the products. Piperidine acts as a reactant and also as a catalyst for this cyclocondensation.

The structures of products (**4-9**) were identified according to their Mass spectra, ^{1}H and ^{13}C-NMR data and also X-ray structures. The ionic forms (**4-9**) were dissolved in hot water and then neutralized by the addition of 2 *M* HCl. The precipitate was a 6-aryl-5-cyano-2-thiopyrimidone derivative. We carried out these reactions on the surface of basic and neutral alumina in the presence of piperidine as the base, but the results were not satisfactory. We supposed that this reaction was a combination of Knoevenagel and Michael addition (Tandem reaction), but the reaction of 2-cyano-3-phenyl-2-propenoic acid methyl ester (**10**) with thiourea in the presence of piperidine resulted in the same product with lower yield (Scheme 2). So, it seems that the one-pot character of the reaction is very effective and plays a key role in the progress of the reaction. Considering the shown results in Table 1 indicates that the withdrawing character of substituted groups accelerates the rate of reaction. The obtained results with electron donating-substituted benzaldehydes confirm our assumption. Reactions of benzaldehyde derivatives with electron donating groups reduce the activity of alkenes and the yields of the reactions are low.

Scheme 2



10 **4**

^{1}H-NMR spectra of these salts show the peaks of piperidine hydrogens. ^{13}C-NMR spectra of piperidinium salts of thiopyrimidones (**4-9**) exhibited the carbonyl groups at δ 183-194 ppm and the carbon atom of carbonyl

groups in thiopyrimidinones **(11-16)** resonate at δ 176-178 ppm. Deshilding of carbonyl groups in piperidinium salts can confirm the intermolecular hydrogen bonding between piperidinium ion and carbonyl group in thiopyrimidinate skeletons.

The X-ray structure of the salts **4**, **5**, and **7** shows a proton abstraction from the 2-thiopyrimidone skeletons. It is shown that the former N2-H is more acidic. This can be ascribed to the mesomeric effect of the cyano group and thus the better delocalization possibilities for the negative charge. The abstracted proton is transferred to a piperidine N-atom [13]. The resulting piperidinium cations are linked to the anions by NH···O, NH···N, or NH···S hydrogen bonds.

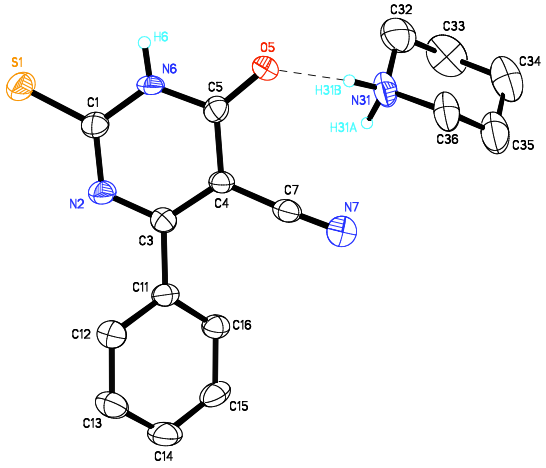


Figure 1. X-ray crystal structure of **4**.

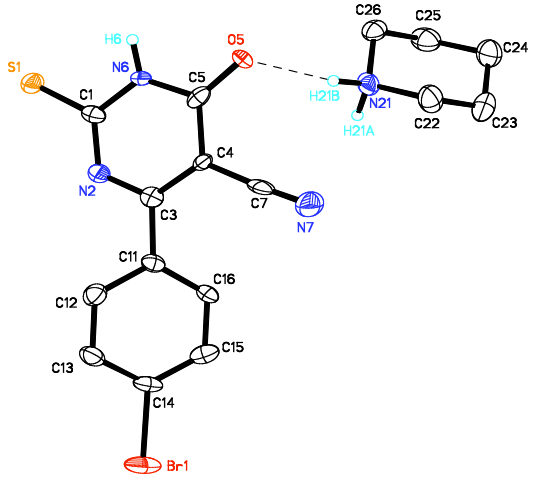


Figure 2. X-ray crystal structure of **5**.

The comparison of the C1-N bond lengths in the ring shows a shorter bond to N2 (anionic, next to the phenyl group) than to N6 (NH-group next to the carbonyl group)

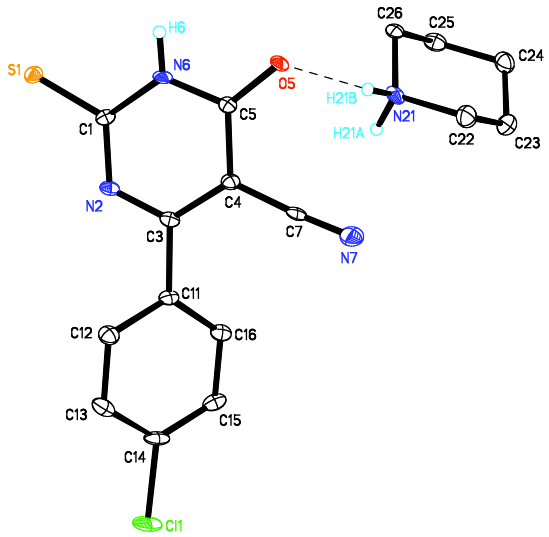


Figure 3. X-ray crystal structure of **7**

in all the structures. This is a consequence of the delocalization of the negative charge, for which a resonance form can be drawn with a C=N double bond and the negative charge at the sulfur atom. The same observation can be made for the other N-C bond lengths: N2-C3 is shorter than N6-C5 due to possible resonance forms that show delocalization of the negative charge to the cyano or the carbonyl group. Investigating the bond angles shows that the molecule is plane.

Table 2

Most Relevant Distances [Å] for Products **4, 5** and **7**

Bond length	**4**	**5**	**7**
C_1-N_2	1.341(4)	1.348 (6)	1.348 (3)
C_1-N_6	1.374 (4)	1.366 (6)	1.374 (4)
C_5-N_6	1.374 (4)	1.374(6)	1.371(4)
C_3-N_2	1.353 (4)	1.352(6)	1.341(4)
C_5-O_5	1.252(3)	1.250 (5)	1.251 (3)
S_1-C_1	1.687 (3)	1.691 (5)	1.692(3)
C_3-C_4	1.396(4)	1.394(6)	1.398(4)
C_4-C_5	1.425(4)	!.434(6)	1.431(4)

The thiopyrimidinate structure could be stabilized with piperidinium ionic form with different types of hydrogen bonding such as N-H…O, N-H…S or N-H…N. Figure 4 shows how the other hydrogen bridges (N-H···S and N-H···N2) form a dimmer of two cations and two anions in the solid state. The same situation can also be found for the compounds **5** and **7**, but in all cases the hydrogen bond N-H···O5 is by far the shortest, followed by N-H···S.

In conclusion, we were able to synthesize 6-aryl-5-cyano-2–thiopyrimidones and their piperidinium thio-pyrimidonate using an efficient one-pot three-component

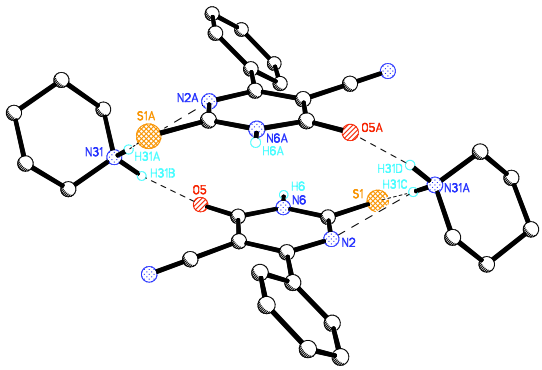


Figure 4. Different kinds of hydrogen bonding existed in piperidinium thiopyrimidonate 4 including (N-H…N), (N-H…S), (N-H…O).

condensation under reflux and microwave irradiation conditions. Good yields of products compared to the previously reported yield, short reaction times in the case of microwave irradiation and also mild reactioin conditions make this protocol complementary to the existing methods. Piperidinium thiopyrimidinate ionic forms are stable and could be used for further transformation.

EXPERIMENTAL

Melting points are uncorrected and were recorded on an Electrothermal 9100 and BÜCHI Melting point B-545 apparatuses. IR spectra were run on a Shimadzu IR-408 spectrometer or FTIR Mattson 1000 Unicam in Cm^{-1} (KBr). ^{1}H and ^{13}C NMR spectra were recorded at 90 and 22.5 MHz, respectively with JEOL 90 in DMSO-d_6 solution. EI+ (70 eV) Mass spectra were recorded on a VC Zab-2F- Mass spectrometer and HP 59970 CD GC/MS-MSD- (HP-5, 30m, He). High-resolution Mass spectra were obtained on the instrument using peak-matching techniques at EPSRC. All the crystallographic calculations were performed using the SHELXTL Software.

X-ray Diffraction Analyses: Data were collected with a Bruker Smart CCD at 200K (4 and 5) and a Bruker APEX diffractometer at 100 K (7) with Mo-Kα radiation for all structures; 1800 0.3 deg omega-scans were made, covering a whole sphere in reciprocal space; intensities were corrected for Lorentz and polarization effects, and an empirical absorption correction was applied using SADABS [13] based on the Laue symmetry of the reciprocal space; the structures were solved by direct methods and refined against F2 with a full-matrix least-squares algorithm using the SHELXTL-PLUS (5.10) software package [14]; hydrogen atoms were treated using appropriate riding models except of the hydrogen atoms of the nitrogen atoms which were refined isotropically. CCDC 257034 (4), 257037 (5), and 257038 (7) contain the supplementary crystallographic data for this structure.

These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk)

General Procedure for the Synthesis of 6-Aryl-5-cyano-2-thiopyrimidone Piperidinium Salts in Reflux Condition (**4-9**).

Piperidine (2 mmol) was added to a solution of the aromatic aldehyde (2 mmol), thiourea (3 mmol, 225 mg) and alkyl cyanoacetates (2.4 mmol) in 40 ml MeOH, the mixture was stirred for 4-6 h in the reflux condition. After completion of the reaction (monitored by TLC), the mixture was filtered and the precipitate was washed with a little water. Further purification was done by crystallization in MeOH; products were salts **4-9**.

General Procedure for the Synthesis of 6-Aryl-5-cyano-2-thiopyrimidone Piperidinium Salts (**4-9**) Under Microwave Irradiation.

A solution of benzaldehyde derivative (2 mmol), thiourea (3 mmol, 150 mg), alkyl cyanoacetate (2.4 mmol) and piperidine (2 mmol) in 5 ml MeOH in Teflon vessel was subjected to microwave irradiation (domestic microwave oven operated at 2450 MHz, power, 850 W) for 4-6 min. After filtration, the precipitate was washed with a little water. The resulting residue was crystallized using MeOH. The products were salts **4-9**. The salts (1 mmol) were dissolved in water (10 ml) and the solutions were neutralized by the slow addition of 2 *M* HCl, which resulted in the crystallization of the pure compounds.

Piperidinium 5-Cyano-6-phenyl-4-oxo-2-thioxo-1,2,3,4-tetra-hydropyrimidinate Salt (**4**).

M.p. 241˚C IR (KBr, cm^{-1}) 3040, 2952, 2212, 1626, 1513, 1474, 1251; ^{1}H-NMR (δ, DMSO-d_6) 1.57 (m, 6H, $3CH_2$, a, b piperidine protons), 3.0 (m, 4H, $2CH_2N$, c piperidine protons), 7.5 (m, 3H, Ar), 7.7ppm (m, 2H, Ar); ^{13}C-NMR (δ, DMSO-d_6) 21.5(a), 22.1(b), 43.8(c), 85.6(C-5), 119.1(C-7, CN), 128.4(C-3', 5'), 128.5(C-2', 6'), 130.5(C-4'), 138.1(C-1'), 163.0 (C-6), 168.0(C=S, C-2), 183.6(C=O, C-4) ppm. HRMS (EI) $^{+}$: Calcd. ($C_{11}H_7N_3OS$) 229.0310 Found 229.0296 (100%, mmu= -1.4).

Piperidinium 5-Cyano-6-(4-bromophenyl)-4-oxo-2-thioxo-1,2,3,4-tetrahydro-pyrimidinate Salt (**5**).

M.p. 260˚C, IR (KBr, cm^{-1}) 3030, 2947, 2211, 1620, 1572, 1516, 1469, 1252; ^{1}H-NMR (δ, DMSO-d_6) 1.60 (m, 6H, 3CH2, a, b piperidine protons), 3.0 (m, 4H, 2CH2N, c, piperidine protons), 7.75ppm (brs, 4H, Ar), 9.40(brs, 1H, NH); ^{13}C-NMR (δ, DMSO-d_6) 21.8 (a), 22.4(b), 44.1(c), 85.9(C-5), 119.2(C-7, CN), 124.4(C-1'), 131.0(C-3', 5'), 131.8(C-2', 6'), 137.5(C-4'), 163.2(C-6), 167.3(C=S, C-2), 184.0 (C=O, C-4), HRMS(EI)+: Calcd. ($C_{11}H_6{}^{81}Br\ N_3OS$) 308.9394, Found 308.9420(100%, mmu=+2.6); Calcd. ($C_{11}H_6{}^{79}Br\ N_3OS$) 306.9427 Found 306.9434 (94.9%, mmu=+0.7)

Piperidinium 5-Cyano-6-(3-chlorophenyl)-4-oxo-2-thioxo-1,2,3,4-tetrahydro-pyrimidinate Salt (**6**).

M.p. 213˚C; IR (KBr,cm^{-1}) 3050, 2949, 2213, 1615, 1569, 1513, 1248, 1120; ^{1}HNMR (δ, DMSO-d_6) 1.6 (m, 6H, $3CH_2$, a, b piperidine protons), 3.0 (m, 4H, $2CH_2N$, c , piperidine protons), 7.40 –7.90 (m, 4H, Ar), 9.30 (brs, 1H, NH); ^{13}CNMR (δ, DMSO-d6) 21.4(a), 22.1(b), 43.8(c), 85.6(C-5), 118.8 (C-7, CN), 127.1(C-6'), 128.2(C-2'), 130.3(C-5'), 130.5(C-4'), 133.3(C-3'), 140.0(C-1'), 162.8(C-6), 166.3(C=S, C-2), 183.8(C=O, C-4); HRMS(EI)+: Calcd: ($C_{11}H_6{}^{37}ClN_3OS$)

264.9891, Found 264.9875(17.4%, mmu=-1.6); Calcd. ($C_{11}H_6{}^{35}Cl$ N3OS) 262.9920 Found 262.9913 (44.2%, mmu=0.7).

Piperidinium 5-Cyano-6-(4-chlorophenyl)-4-oxo-2-thioxo-1,2,3,4-tetrahydro-pyrimidinate Salt (**7**).

M.p. 267˚C; IR (KBr cm^{-1}) 3030, 2948, 2212, 1621, 1572, 1516, 1470, 1252; ^{1}H-NMR (δ, DMSO-d_6) 1.6 (m, 6H, $3CH_2$, a, b piperidine protons), 3.0 (m, 4H, $2CH_2N$, c, piperidine protons), 7.55(d, 2H, J=9Hz, Ar), 7.75 (d, 2H, J=9Hz, Ar), 8.50(brs, 1H, NH); ^{13}C-NMR (δ, DMSO-d_6) 21.5(a), 22.1(b), 43.7(c), 85.4(C-5), 119.0(C-7, CN), 128.5(C-3', 5'), 130.45(C-2', 6'), 135.3(C-1'), 136.8(C-4'), 162.9(C-6), 166.7(C=S, C-2), 183.6(C=O, C-4); HRMS(EI)$^+$: Calcd.($C_{11}H_6{}^{37}ClN_3OS$) 264.9891, Found 264.9888(39.3%, mmu=-0.3); Calcd. ($C_{11}H_6{}^{35}ClN_3OS$) 262.9920 Found 262.9929(+0.9)**.**

Piperidinium 5-Cyano-6-(4-cyanophenyl)-4-oxo-2-thioxo-1,2,3,4-tetra-hydropyrimidinate Salt (**8**).

M.p. 251˚C; IR (KBr, cm^{-1}) 3200, 3100, 2940, 2227, 2214, 1622, 1502, and 1248; ^{1}H-NMR (δ, DMS-d_6) 1.6 (m, 6H, $3CH_2$, a, b piperidine protons), 3.0 (m, 4H, $2CH_2N$, c, piperidine protons), 7.9 (m, 4H, Ar), 9.30 (brs, 1H, NH); ^{13}C-NMR (δ, DMSO-d_6) 21.5(a), 22.1(b), 43.7(c), 86.0(C-5), 112.7(CN), 119.0(C-7,CN), 121.0(C-4'), 129.5(C-2',6'), 132.6(C-3',5'), 142.5(C-1'), 162.7(C-6), 166.4(C=S, C-2), 185.0(C=O, C-4); HRMS(EI)$^+$: Calcd. ($C_{12}H_6N_4OS$) 254.0262 Found 254.0297(100%, mmu=+3.5).

Piperidinium 5-Cyano-6-(3-nithrophenyl)-4-oxo-2-thioxo-1,2,3,4-tetrahydro-pyrimidinate Salt (**9**).

M.p. 225˚C; IR (KBr, cm^{-1}) 3042, 2209, 1642, 1536, 1515, 1351, 1255; ^{1}H-NMR (δ, DMSO-d_6) 1.6 (m, 6H, $3CH_2$, a, b piperidine protons), 3.0 (m, 4H, $2CH_2N$, c piperidine protons) 7.8 (t, 1H, J=9Hz), 8.15-8.60 (m, 3H, Ar); ^{13}C-NMR (δ, DMSO-d_6) 21.5(a), 22.1(b), 43.8(c), 85.8(C-5), 118.8 (C-7, CN), 123.4 (C-4'), 125.2 (C-1'), 130.4 (C-5'), 135.1 (C-6'), 139.5(C-2'), 148.1(C-3'), 162.8(C-6), 165.3 (C=S, C-2), 184.1(C=O, C-4) HRMS(EI)$^+$: Calcd.($C_{11}H_6N_4O_3S$) 274.0161 Found 274.0175(100%, mmu=+1.4).

5-Cyano-6-phenyl-2-thiopyrimidone (**11**).

M.p.299˚C (lit [9] M.p. 298-300ºC), IR (KBr, cm^{-1}) 3400, 3184, 2230, 1692, 1546, 1230; ^{1}H-NMR (δ, DMSO-d_6), 7.60-7.90 (brs, 5H, Ar), 13.20 (brs, 2H, NH_2); ^{13}C-NMR (δ, DMSO-d_6), 91.1 (C-5), 115.1 (C-7, CN), 129.0 (C-3',5'), 129.2 (C-2', 6'), 129.7 (C-4'), 132.7 (C-1') , 158.0 (C-6), 161.5 (C=S, C-2), 178.0 (C=O, C-4).

5-Cyano-6- (4-bromophenyl)-2-thiopyrimidone (**12**).

M.p. 284ºC, IR (KBr, cm^{-1}) 3500, 3215, 2230, 1707, 1569, 1230; ^{1}H-NMR (δ, DMSO-d_6), 7.62 (d, 2H, J= 9 Hz, Ar), 7.80 (d, 2H, J=9 Hz, Ar), 13.20 (brs, 2H, NH_2); ^{13}C-NMR (δ, DMSO-d_6), 91.3 (C-5), 114.9 (C-7, CN), 126.3 (C-1), 128.9 (C-3',5'), 131.4 (C-2',6'), 132.1 (C-4'), 158.9 (C-6), 160.5 (C=S, C-2), 176.7 (C=O, C-4).

Table 3

Crystal Data and Structure Refinement for Compounds **4**, **5** and **7**

	4	**5**	**7**
Empirical formula	$C_{16}H_{18}N_4OS$	$C_{16}H_{17}BrN_4OS$	$C_{16}H_{17}ClN_4OS$
Formula weight	314.40	393.31	348.85
Temperature	200(2)K	200(2)K	100(2)K
Wavelength	0.71073 Å	0.71073 Å	0.71073 Å
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/n$	$P2_1/c$	$P2_1/c$
Z	4	4	4
Unit cell dimensions	a= 12.0665(2) Å α = 90°	a= 7.3109(4) Å α = 90°	a= 7.282(3) Å α = 90°
	b=7.2437(3) Å β = 92.109(2)°	b= 11.7834(7) Å β = 92.054(2)°	b= 11.648(4) Å β = 93.087(2)°
	c= 18.6266(7) Å γ = 90°	c= 19.7507(11) Å γ = 90°	c= 19.448(7) Å γ = 90°
Volume	1626.98(9) $Å^3$	1700.38(17) $Å^3$	1647.1(10) $Å^3$
Density (calculated)	1.284 g/cm^3	1.54 g/cm^3	1.41 g/cm^3
Absorption Coefficient	0.21 mm^{-1}	2.55 mm^{-1}	0.37 mm^{-1}
Crystal shape	Polyhedron	polyhedron	polyhedron
Crystal size	0.29 x 0.03 x 0.03 mm^3	0.30 x 0.02 x 0.02 mm^3	0.33 x 0.05 x 0.05 mm^3
Theta range for data Collection	2.0 to 24.1 °	2.0 to 21.5 °	2.04 to 28.39 °
Index ranges	-13≤ h ≤13, -8 ≤ k ≤ 8, -21≤ l ≤ 21	-7≤ h ≤ 7, -12 ≤ k ≤ 12, -20 ≤ l ≤ 20	-9 ≤ h ≤ 9, -15 ≤ k ≤ 15, -25 ≤ l ≤ 25
Reflections collected	11560	9453	16405
Independent reflections	2580 (R(int) = 0.0987)	1959 (R(int) = 0.0834)	4087 (R(int) = 0.0589)
Observed reflections	1463 (I >2 σ (I))	1270 (I >2 σ (I))	3499 (I >2 σ (I))
Absorption correction	Semi-empirical from equivalents	Semi-empirical from equivalents	Semi-empirical from equivalents
Max. and min. Transmission	0.99 and 0.94	0.95 and 0.52	0.98 and 0.89
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	2580 / 0 / 211	1959 / 0 / 218	4087 / 0 / 218
Goodness-of-fit on F^2	0.97	0.99	1.27
Final R indices (I>2σ (I))	R1 = 0.048, wR2 = 0.100	R1 = 0.036, wR2 = 0.063	R1 = 0.076, wR2 = 0.159
Largest diff. peak and hole	0.31 and -0.23 $eÅ^{-3}$	0.32 and -0.43 $eÅ^{-3}$	0.73 and -0.43 $eÅ^{-3}$

5-Cyano-6-(3-chlorophenyl)-2-thiopyrimidone (**13**).

M.p. 229ºC, IR (KBr, cm^{-1}) 3369, 3184, 2230, 1707, 1553, 1223; ^{1}H-NMR (δ, DMSO-d_6), 7.62-7.85 (m, 4H, Ar), 13.30 (brs, 2H, NH_2); ^{13}C-NMR (δ, DMSO-d_6), 91.5 (C-5), 114.8 (CN, C-7), 127.9 (C-6'), 129.1(C-2'), 130.9 (C-5'), 131.6 (C-4'), 132.3 (C-3'), 133.4 (C-1'), 158.8 (C-6), 160.0 (C=S, C-2), 176.8 (C=O, C-4).

5-Cyano-6- (4-chlorophenyl)-2-thiopyrimidone (**14**).

M.p. 270.2ºC (lit [9] m.p. 270-271ºC), IR (KBr, cm^{-1}) 3461, 3120, 2230, 1661, 1545, 1461, 1230; ^{1}H-NMR (δ, DMSO-d_6) 7.65-7.75 (brs, 4H, Ar), 13.30 (brs, 2H, NH_2); ^{13}C-NMR (δ, DMSO-d_6), 91.4(C-5), 115.0(C-7, CN), 128.5(C-3', 5'), 129.1(C-2', 6'), 131.3(C-1'), 137.4 (C-4'), 159.0(C-6), 160.5(C=S, C-2), 176.8(C=O, C-4).

5-Cyano-6- (4-cyanophenyl)-2-thiopyrimidone (**15**).

M.p. 310ºC (decomposed), IR (KBr, Cm^{-1}) 3430, 3100, 2227, 2214, 1677, 1569, 1407, 1231; ^{1}H-NMR (δ, DMSO-d_6), 7.9 (d, 2H, J=9Hz, Ar), 8.05 (d, 2H, J=9Hz, Ar), 13.30 (brs, 2H, NH_2), ^{13}C-NMR (δ, DMSO-d_6): 85.5 (C-5), 112.4(C-4'), 118.3(CN), 118.5(C-7, CN), 129.0(C-2', 6'), 132.1(C-3', 5'), 142.0(C-1'), 162.2(C-6), 165.7(C=S, C-2), 183.3(C=O, C-4) ppm.

5-Cyano-6-(3-nitrophenyl)-2-thiopyrimidone (**16**).

M.p.264ºC, IR (KBr, cm^{-1}) 3453, 3092, 2230, 1676, 1546, 1353, 1230; ^{1}H-NMR (δ, DMSO-d_6), 7.9-8.3 (m, 2H, Ar), 8.40-8.70 (m, 2H, Ar) 13.5 (brs, 2H, NH_2); ^{13}C-NMR (δ, DMSO-d_6), 92.3(C-5), 115.1 (CN, C-7), 125.0(C-4'), 127.5(C-5'), 131.2(C-6'), 131.43(C-1'), 136.2(C-2'), 148.2(C-3'), 159.1(C-6),159.7(C=S, C-2), 177.0(C=O, C-4).

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