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One-pot three-component synthesis of pyrimidine-5-carbonitrile derivatives in water using *p*-dodecylbenzenesulfonic acid as catalyst and evaluation of *in vitro* anti-inflammatory and anthelmintic activities.

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ABSTRACT

The present paper deals with the synthesis of Pyrimidine-5-carbonitriles by condensation of aromatic aldehydes, p-chlorobenzoylacetonitrile and substituted urea using Conc. H_2SO_4 in ethanol and DBSA (p-dodecylbenezenesulfonic acid) in water as catalyst. It was observed that use of DBSA as catalyst increased the rate of reaction. The products are formed in high yields under eco-friendly conditions. All newly synthesized compounds were characterized by IR, ^1H NMR and ^{13}C NMR spectral data. Compounds (4a-k) were screened for anthelmintic activity and anti-inflammatory.

Keywords: *p*-dodecylbenezenesulfonic acid (DBSA); Pyrimidine; Green Solvent; Anthelmintic activities and *In Vitro* anti-inflammatory.

INTRODUCTION

Helminths infection is a serious problem in humans especially in the children and domestic animals. Anthelmintic drugs are used to control these infections and it has selective toxic effects on these parasites. Intracellular microtubules in cell of worm are gradually lost by action of anthalmentic drugs. The gastro-intestinal helminthes becomes resistant to currently available anthelmintic drugs thus there is a primary problem in treatment of helminthes diseases.[1]

The increasing importance of pyrimidines and their derivatives as intermediates for the synthesis of biologically and industrially useful compounds prompted us to synthesize pyrimidinecarbonitrile derivatives. Literature survey revealed that pyrimidine derivatives have been identified as potent bactericidal and fungicidal agents,[2,3] analgesic,[4] anti-hypertensive[5] and anti-tumor agents.[6] Thiouracils are similarly used as for anti-inflammatory and virucidal agents.[7] Our initial efforts are to explore new activity of pyrimidines derivatives; we have synthesized some new pyrimidine-5-carbonitrile 4a-k derivatives. The new derivatives were characterized by IR, ^1H NMR spectroscopy and these compounds were tested for their anthelmintic and i*n vitro* anti-inflammatory activity.

Development of eco-friendly synthesis rout is always desirable as it protects our mother earth. The conventional methods impose adverse effect on eco-system and human health. Therefore it is demand of time to search alternative

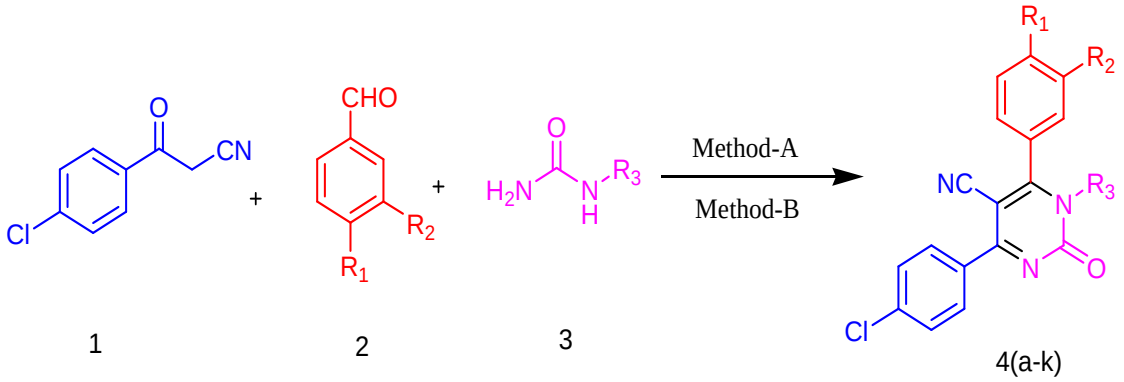
greener approaches to minimize pollution and related problem. The greener approach includes minimum waste generation, solvent free reactions, [8] eco-friendly catalyst,[9] water as solvent [10] etc. One step reaction involved three component condensation is famous in synthetic organic chemistry to yield target molecule. The first one step synthesis of DHPMS was reported by Biginelli in 1893. [11] Biginelli reaction [12] has some drawback due to several new methodology have been reported such as LiBr, [13] Cu (OTf) $_2$, [14] conc. HCl solid-support, [15] $SbCl_3$–Al2O3, [16] I_2-Al_2O_3, [17] and Zeolite. [18]

RESULTS AND DISCUSSION

Dodecylbenzenesulfonic acid (DBSA) is phase-transfer catalyst, can act as a combined Brønsted acid surfactant-catalyst. It performs the dual role of both an acid catalyst and a surfactant. [19] The use of DBSA [20,21] as catalyst in cyclisation prompted us to search for improved and more efficient catalytic condition for the pyrimidine synthesis. In water, DBSA has been

used efficiently for the synthesis of pyrimidine. We have successfully synthesized of 4-(4-chlorophenyl)-1,2-dihydro-6-aryl-2-oxo-1-aryl-pyrimidine-5-carbonitrile using Conc. H_2SO_4 in ethanol and *p*-dodecylbenzenesulfonic acid (DBSA) as the catalyst (10 mol %) in aqueous media. The model reaction of p-chloro-benzoylacetonitrile **1** (1 mmol), aldehyde **2** (1 mmol), substituted urea **3** (1 mmol) and DBSA (10 mol %) in water (20 ml) at room temperature afforded the product **4** with 90% yield as shown in Scheme 1.

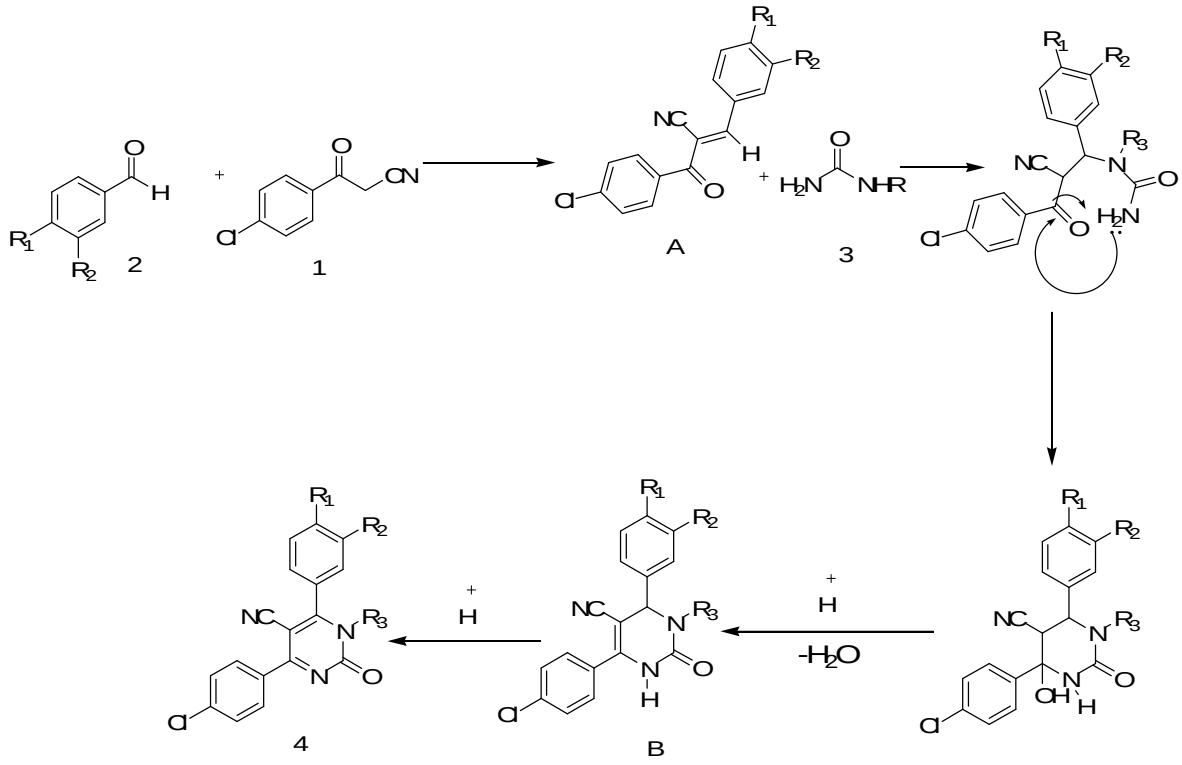
The method has advantages such as environmentally begin; short reaction time, high yield and simple work up. The results are summarized in Table 1. It is presumed that the reaction may proceed through the *insitu* benzylidenebenzoyle acetonitrile **A** intermediate containing an electron-poor C=C double bond is produced by rapid Knoevenagel condensation of p-chlorobenzoyle acetonitrile with the aromatic aldehyde, followed by Michael addition, cycloaddition, isomerization, aromatization to afford the pyrimidine-5-carbonitrile **4** (Scheme 2). Intermediate **B** is not stable and was not isolated from the reaction mixture. DBSA facilitate reaction perhaps by protonation.



Scheme1.
Reagents and Conditions:- ***(1) Method A:*** *DBSA (10 mol %) in water /RT*
(2) Method B: *Conc.H_2SO_4 in ethanol / RT*

TABLE 1 DBSA Catalyzed formation of pyrimidine-5-carbonitrile

	Product			Color and Physical Status	Method-A		Method-B	
	R_1	R_2	R_3	(Crystallization Solvent)	Time (h)	Yield (%)	Time(h)	Yield (%)
4a	OH	OCH_3	C_6H_5	Yellow (Ethyl Acetate)	0.30	77	3.10	52
4b	OH	OCH_3	4-$CH_3C_6H_4$	Orange (Ethanol)	0.30	80	2.30	54
4c	OH	OCH_3	4-ClC_6H_4	Orange (Ethanol)	0.45	85	3.30	58
4d	OH	OCH_3	4-BrC_6H_4	Orange (Ethanol)	0.50	75	1.40	85
4e	$N(CH_3)_2$	H	C_6H_5	Yellow (Ethyl Acetate)	0.50	70	1.30	59
4f	$N(CH_3)_2$	H	4-$CH_3C_6H_4$	Yellow (Ethyl Acetate)	0.30	79	2.30	60
4g	$N(CH_3)_2$	H	4-ClC_6H_4	Red (Ethanol)	0.45	86	1.50	64
4h	$N(CH_3)_2$	H	4-BrC_6H_4	Yellow (Ethanol)	0.40	90	1.30	61
4i	4-Cl	H	C_6H_5	Red (Ethanol)	0.15	88	1.45	51
4j	4-Cl	H	4-$CH_3C_6H_4$	Orange (Ethanol)	1.00	79	2.10	64
4k	OCH_3	OCH_3	C_6H_5	Orange (Ethanol)	0.30	88	2.22	80



Scheme 2

All the compounds showed moderate to potent anthelmintic activity. In vitro anthelmintic activity of synthesized compounds is summarized in Table 2. Compound 4-(4-chlorophenyl)-1,2-dihydro-6-(4-dimethylaminophenyl)-2-oxo-1-phenyl pyrimidine-5-carbonitril **4e** showed more potent paralyzing effect than the standard albendazole. In addition to these 0.2 and 0.5 % concentrations of compound **4e** exhibits less time for death than the standard. Other compounds exhibited moderate activity. This data revealed that pyrimidine-5-carbonitrile ring may be responsible for the anthelmintic activity and the compounds with additional hetero atom in the structure also may responsible to increase in the potency. Table 3 listed that compounds **4c** have promising anti-inflammatory activity compared with the reference *in vitro* anti-inflammatory drug, diclofenac sodium. This study can be extended to animal testing to explore anti-inflammatory potency in biological system.

MATERIALS AND METHODS

Melting points were determined on a Gallenkamp Melting Point Apparatus, Mod. MFB-595 in open capillary tubes. The ^{1}H NMR and ^{13}C-NMR spectra were recorded on a Varian XL-300 spectrometer (300 MHz). Chemical shifts are reported in ppm from internal tetramethylsilane standard and are given δ -units. The solvents for NMR spectra was duterio-chloroform unless otherwise stated. Infrared spectra were taken on Shimadzu IR - 408, a Shimadzu FTIR instrument in potassium bromide pellets unless otherwise stated .

3.1 General Procedure for the Synthesis of 4-(4-chlorophenyl)-1,2-dihydro-6-aryl-2-oxo-1-aryl-5-carbonitrile

Method A: A mixture of *p*-chloro-benzoylacetonitrile **1 (**1mmol), aldehyde **2** (1mmol), substituted urea **3** (1mmol), and DBSA (10 mol %) in water (20 ml) were stirred at room temperature for the corresponding time as mentioned in Table 1. After completion of the reaction, the reaction mixture was poured onto crushed ice (30g) containing (10 g) NaCl and stirred for 5-10min. The solid separated was filtered, washed with ice-cold water (50 mL) and then recrystallized to afford pure product.

Method B: A mixture of *p*-chloro-benzoylacetonitrile **1 (**1mmol), aldehyde **2** (1mmol), substituted urea **3** (1mmol), and two drop of 2N H_2SO_4 (2 N) in ethanol (20 ml) were stirred at room temperature for the corresponding time as

mentioned in Table 1. After completion of the reaction, solvent was removed under reduced pressure. The solid separated was recrystallized to afford pure product.

3.1.1.4-(4-chlorophenyl)-1,2-dihydro-6-(4-hydroxy-3-methoxyphenyl)-2-oxo-1-phenylpyrimidine-5-carbonitrile (4a)

IR (KBr) υ: [Cm^{-1}] 1595(C=C), 1668(C=O str of amide), 2139(-CN), 2926 (Aromatic C-H str), 3527(-OH); ^{1}H NMR ($CDCl_3$) δ: 4.09 (s, 3H, OCH_3), 6.29 (s, 1H, OH), 7.41 (dd, 1H, *J=7.9 Hz*, *J=2.6 Hz*, Ar-H), 7.48 (d, 2H, *J=8.6 Hz*, Ar-H), 7.49 (d, 1H, *J=7.9 Hz*, Ar-H), 7.52 (d, 2H, *J=8.6 Hz*, Ar-H), 7.82 (m, 5H, Ar-H), 7.92 (d, 1H, *J=2.6 Hz*, Ar-H). ^{13}C NMR($CDCl_3$) δ: 55.43, 61.83, 112.64, 115.85, 120.31, 121.40, 122.75, 124.92, 125.47, 128.32, 129.86, 130.20, 131.69, 133.51, 137.13, 138.55, 150.63, 153.11, 155.92, 163.15.

3.1.2. 4-(4-chlorophenyl)-1,2-dihydro-6-(4-hydroxy-3-methoxyphenyl)-2-oxo-1-(4-methylphenyl) pyrimidine-5-carbonitrile (4b)

IR (KBr) υ: [Cm^{-1}] 1626(C=C), 1663(C=O str of amide), 2238(-CN), 3053 (Aromatic C-H str), 3320 (-OH).; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.78 (s, 3H, CH_3), 4.01 (s, 3H, OCH_3), 6.31 (s, 1H, OH), 7.03 (d, 1H, *J=8.0 Hz*, Ar-H), 7.41 (dd, 1H, *J=8.0 Hz*, *J=2.2 Hz*, Ar-H), 7.48 (d, 2H, *J=7.6 Hz*, Ar-H), 7.52 (d, 2H, *J=7.9 Hz*, Ar-H), 7.57 (d, 2H, *J=7.6 Hz*, Ar-H), 7.83 (d, 2H, *J=7.9 Hz*, Ar-H), 7.93 (d, 1H, *J=2.2 Hz*, Ar-H). ^{13}C NMR($CDCl_3$): 29.34, 53.40, 60.83, 111.34, 114.75, 119.81, 120.91, 123.46, 124.90, 125.87, 127.12, 129.76, 130.60, 132.19, 133.81, 137.63, 139.17, 151.03, 153.31, 155.92, 160.25.

3.1.3. 4-(4-chlorophenyl)-1,2-dihydro-6-(4-hydroxy-3-methoxyphenyl)-2-oxo-1-(4-chlorophenyl)pyrimidine-5-carbonitrile (4c)

IR (KBr) υ: [Cm^{-1}] 1625(C=C), 1665(C=O str of amide), 2225(CN), 3054 (Aromatic C-H str), 3310 (-OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 84.09 (s, 3H, OCH_3), 6.41 (s, 1H, OH), 7.14 (d, 1H, *J=7.9 Hz*, Ar-H), 7.45 (dd, 1H, *J=7.9 Hz*, *J=2.4 Hz*, Ar-H), 7.49 (d, *J=7.6 Hz*, 2H, Ar-H), 7.51 (d, 2H, *J=8.6 Hz*, Ar-H), 7.50 (d, 2H, *J=8.6 Hz*, Ar-H), 7.80 (d, 2H, *J=7.6 Hz*, Ar-H), 7.91 (d, 1H, *J=2.4 Hz*, Ar-H); ^{13}C NMR($CDCl_3$): 56.41, 62.80, 112.14, 113.55, 118.81, 121.77, 123.76, 124.95, 125.89, 128.02, 129.66, 131.10, 132.39, 133.84, 138.73, 140.10, 150.43, 153.81, 156.22, 163.35.

3.1.4. 4-(4-chlorophenyl)-1,2-dihydro-6-(4-hydroxy-3-methoxyphenyl)-2-oxo-1-(4-Bromophenyl)pyrimidine-5-carbonitrile (4d)

IR (KBr) υ: [Cm^{-1}] 1627(C=C), 1661(C=O str of amide), 2220(CN), 3065 (Aromatic C-H str), 3300 (-OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.91 (s, 3H, OCH_3), 6.40 (s, 1H, OH), 7.24 (d, 1H, *J=8.8 Hz*, Ar-H), 7.43 (dd, 1H, *J=8.8 Hz*, *J=2.3 Hz*, Ar-H), 7.49 (d, 2H, *J=7.9 Hz*, Ar-H), 7.53 (d, 2H, *J=7.8 Hz*, Ar-H), 7.56 (d, 2H, *J=7.9 Hz*, Ar-H), 7.84 (d, 2H, *J=7.8 Hz*, Ar-H), 7.97 (d, 1H, *J=2.3 Hz*, Ar-H). ^{13}C NMR($CDCl_3$): 55.45, 59.89, 111.10, 113.95, 119.51, 121.07, 123.26, 124.05, 125.69, 127.12, 129.36, 131.10, 132.09, 134.64, 138.03, 141.45, 150.03, 153.80, 154.22, 160.15.

3.1.5.4-(4-chlorophenyl)-1,2-dihydro-6-(4-dimethylaminophenyl)-2-oxo-1-phenylpyrimidine-5-carbonitril (4e)

IR (KBr) υ: [Cm^{-1}] 1610(C=C), 1685(C=O str of amide), 2224(CN), 3033 (Aromatic C-H str); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.19 (s, 6H, $N(CH_3)_2$), 7.17 (d, 2H, Ar-H), 7.49 (d, 2H, Ar-H), 7.52 (d, 2H, Ar-H), 7.82 (m, 5H, Ar-H), 7.98 (d, 2H, Ar-H). ^{13}C NMR($CDCl_3$): 40.12, 77.83, 103.42, 112.83, 120.54, 123.49, 128.51, 131.74, 132.18, 133.87, 135.43, 137.92, 139.12, 140.79, 149.73, 155.02, 165.29, 166.51.

3.1.6. 4-(4-chlorophenyl)-1,2-dihydro-6-(4-dimethylaminophenyl)-2-oxo-1-(4-methylphenyl)pyrimidine-5-carbonitril (4f)

IR (KBr) υ: [Cm^{-1}] 3055 (Aromatic C-H str), 2247(CN), 1666(C=O str of amide), 1617(C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.25 (s, 3H, $-CH_3$), 3.19 (s, 6H, $-N(CH_3)_2$), 7.41 (s, 2H, *J=7.4 Hz*, Ar-H), 7.54 (d, 2H, *J=7.6 Hz*, Ar-H), 7.59(d, 2H, *J=7.4 Hz*, Ar-H), 7.72(d, 2H, *J=7.5 Hz*, Ar-H), 7.81 (s, 2H, *J=7.5 Hz*, Ar-H), 8.01 (s, 2H, *J=7.6 Hz*, Ar-H). ^{13}C NMR($CDCl_3$): 23.69, 43.18, 54.47, 112.51, 114.74, 118.42, 121.27, 122.37, 123.58, 125.83, 129.78, 131.29, 133.07, 135.68, 138.91, 148.92, 153.14, 163.60, 165.61.

3.1.7. 4-(4-chlorophenyl)-1,2-dihydro-6-(4-dimethylaminophenyl)-2-oxo-1-(4-Chlorophenyl) pyrimidine-5-carbonitril (4g)

IR (KBr) υ: [Cm^{-1}] 3055 (Aromatic C-H str), 2227(CN), 1670(C=O str of amide), 1619(C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.21 (s, 6H, $-N(CH_3)_2$), 7.47 δ (d, 2H, *J=7.0 Hz*, Ar-H), 7.56 (d, 2H, *J=7.0 Hz*, Ar-H), 7.61(d, 2H, *J=7.5 Hz*, Ar-H), 7.70(d, 2H, *J=7.2 Hz*, Ar-H), 7.80 (s, 2H, *J=7.5 Hz*, Ar-H), 8.11 (s, 2H, *J=7.2 Hz*, Ar-H). ^{13}C

NMR($CDCl_3$): 46.08, 57.47, 112.59, 115.71, 118.62, 120.57, 122.40, 123.78, 126.17, 129.48, 130.29, 133.67, 136.58, 138.90, 148.62, 154.24, 163.63, 166.41.

3.1.8. 4-(4-chlorophenyl)-1,2-dihydro-6-(4-dimethylaminophenyl)-2-oxo-1-(4-Bromophenyl) pyrimidine-5-carbonitril (4h)

IR (KBr) υ: [Cm^{-1}] 3110 (Aromatic C-H str), 2225(CN), 1688(C=O str of amide), 1620(C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.24 (s, 6H, -$N(CH_3)_2$), 7.41 (s, 2H, *J=7.1 Hz*, Ar-H), 7.57 (d, 2H, *J=7.0 Hz*, Ar-H), 7.66 (d, 2H, *J=6.9 Hz*, Ar-H), 7.70 (d, 2H, *J=7.1 Hz*, Ar-H), 7.82 (s, 2H, *J=6.9Hz*, Ar-H), 8.10 (s, 2H, *J=7.0 Hz*, Ar-H), ^{13}C NMR($CDCl_3$): 38.94, 59.42, 113.50, 115.74, 117.62, 120.00, 122.43, 123.65, 127.17, 129.03, 130.21, 134.15, 136.48, 137.94, 148.55, 154.66, 164.64, 166.96.

3.1.9. 4-(4-chlorophenyl)-1,2-dihydro-6-(4-chlorophenyl)-2-oxo-1-phenylpyrimidine-5-carbonitril (4i)

IR (KBr) υ: [Cm^{-1}] 3050 (Aromatic C-H str), 2234(CN), 1675(C=O str of amide), 1615(C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.15(d, 2H, *J=7.7 Hz*, Ar-H) 7.49 (d, 2H, *J=7.0 Hz*, Ar-H), 7.53 (d, 2H, *J=7.7 Hz*, Ar-H), 7.82 (m, 5H, Ar-H), 7.96 (d, 2H, *J=7.0 Hz*, Ar-H), ^{13}C NMR($CDCl_3$): 69.87, 115.48, 117.45, 120.29, 122.51, 124.49, 126.73, 128.56, 130.47, 131.84, 134.55, 136.61, 137.13, 139.37, 153.21, 166.37, 167.85.

3.1.10.4-(4-chlorophenyl)-1,2-dihydro-6-(4-chlorophenyl)-2-oxo-1-(4-methylphenyl) pyrimidine-5-carbonitrile (4j)

IR (KBr) υ: [Cm^{-1}] 3048 (Aromatic C-H str), 2260(CN), 1690(C=O str of amide), 1610(C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.35 (s, 3H, -CH_3), 7.41 (s, 2H, *J=7.4 Hz*, Ar-H), 7.53 (d, 2H, *J=7.5 Hz*, Ar-H), 7.59 (d, 2H, *J=7.4 Hz*, Ar-H), 7.73 (d, 2H, *J=7.5 Hz* Ar-H), 7.80(s, 2H, *J=7.5 Hz*, Ar-H), 8.01 (s, 2H, *J=7.5 Hz*, Ar-H), ^{13}C NMR($CDCl_3$): 35.12, 70.14, 117.29, 118.03, 120.86, 122.54, 128.17, 129.94, 131.41, 132.48, 133.23, 134.58, 137.69, 138.41, 140.34, 157.55, 164.30, 165.52.

3.1.11.4-(4-chlorophenyl)-1,2-dihydro-6-(3,4-dimethoxyphenyl)-2-oxo-1phenylpyrimidine-5-carbonitrile (IVk)

IR (KBr) υ: [Cm^{-1}] 3050 (Aromatic C-H str), 2240 (CN), 1670(C=O str of amide), 1615(C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.O1 (s, 2 x OCH_3), 6.99(s, 1H, Ar-H), 7.25 (s, 1H, Ar-H), 7.48 (d, 2H, Ar-H), 7.68 (s, 5H, Ar-H), 7.92 (d, 2H, Ar-H), 8.12(s, 1H, Ar-H). ^{13}C NMR($CDCl_3$): 55.43, 61.83, 65.03, 112.60, 115.75, 117.37, 120.41, 122.70, 124.92, 125.47, 127.31, 128.24, 130.77, 131.66, 134.50, 136.21, 138.45, 151.53, 153.01, 154.91, 161.10.

3.2 Pharmacological part

3.2.1. Anthelmintic activity: The synthesized compounds **4a-k** were screened for anthelmintic activity by using earthworms, Pheretima posthuma. [22] Five earthworms of nearly equal size were placed in standard drug solution and test compound's solutions at room temperature. Normal saline used as control. The standard drug and test compounds were dissolved in minimum quantity of dimethyl formamide (DMF) and adjusted the volume up to 15 ml with normal saline solution to get the concentration of 0.1 % , 0.2 % and 0.5% (m/V). Albendazole diluted with normal saline solution to obtain 1% (m/V) served as standard. The compounds were evaluated by the time taken for complete paralysis and death of earthworms. The mean lethal time for each test compound was recorded and compared with standard drug. The time taken by worms to become motionless was noted as paralysis time. To ascertain the death of the motionless worms were frequently applied with external stimuli, which stimulate and induce movement in the worms, if alive. The comparison results with standard drugs such as are listed in Table 2.

3.2.2. *In vitro* anti-inflammatory activity: The synthesized compounds are screened for anti-inflammatory activity by using inhibition of albumin denaturation technique which was studied according to Muzushima and Kabayashi. [23] The standard drug and test compounds were dissolved in minimum amount of dimethyl formamide (DMF) and diluted with phosphate buffer (0.2 M, pH 7.4). Final concentration of DMF in all solutions was less than 2.0%. Test solution (1 ml) containing different concentrations of drug was mixed with 1 ml of 1% mM albumin solution in phosphate buffer and incubated at 27 ° ±1 ° C in BOD incubator for 15 min. Denaturation was induced by keeping the reaction mixture at 60 ° ±1 ° C in water bath for 10 min. After cooling the turbidity was measured at 660 nm (UV-Visible Spectrophotometer SL-159, Elico India Ltd.). Percentage of inhibition of denaturation was calculated from control where no drug was added. Each experiment was done in triplicate and average was taken. The Diclofenac sodium was used as reference drug. [24,25] The percentage inhibition of denaturation was calculated by using following formula.

% of Inhibition = 100 X [Vt / Vc – 1]

Where,
Vt = Mean absorbence of test sample.
Vc = Mean absorbence of control.

The results are described in Table 3.

TABLE 2: Anthamintic activity

Compounds	Time (in minutes)					
	For paralysis % Concentration (m/v)			For death % Concentration (m/v)		
	0.1	0.2	0.5	0.1	0.2	0.5
Control	-	-	-	-	-	-
4a	75	55	60	120	113	95
4b	65	55	59	130	75	64
4c	77	37	75	100	58	51
4d	76	62	56	90	86	77
4e	42	49	33	112	87	65
4f	80	75	60	123	102	95
4g	52	50	69	100	82	62
4h	68	51	57	102	88	90
4i	67	59	51	110	101	86
4j	70	65	58	134	112	87
4k	73	58	60	112	99	80
Albendazole	50	45	40	70	63	55

TABLE 3. Anti-inflammatory activity of compounds

Compounds	Absorbance Value (Mean ± SEM)	Inhibition of Denaturation (in %)
Control	0.087±0.001	---
Diclofenac sodium	0.161±0.004	85.05
4a	0.111±0.002	27.58
4b	0.102±0.002	17.24
4c	**0.158±0.004**	**81.60**
4d	0.110±0.001	26.43
4e	0.106±0.003	21.83
4f	0.134±0.005	54.02
4g	0.132±0.001	51.72
4h	0.112±0.001	28.46
4i	0.108±0.002	24.13
4j	0.138±0.003	58.62
4k	0.136±0.001	55.04

CONCLUSION

We have developed an exceedingly simple, mild and clean synthetic procedure for the synthesis of several novel pyrimidine-5-carbonitrile derivatives (4a-k) using DBSA surfactant. Surfactants catalyze the reaction efficiently at room temperature with short reaction times without using any harmful organic reagents and solvents. Anthalmintic activity data have shown that **4e** derivative is potent activity against standard drug while **4c** have significant *in vitro* anti-inflammatory activity.

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REFERENCES

[1] S. Geert, P. Dorny, *Bulletin-des-Seances Academic-Royaledes-Sciencesd Dutre-Mer*, **1995**, 3, 401–423.
[2] H. H. Locher, H. Schlunegger, P.G. Hartman, P. Anghern, R. L. Then, *Antimicrob. Agents Chemother*, **1996**, 40, 1376–1381.

[3] A. Mai, D. Rotili, S. Massa, G. Brosch, G. Simonetti, C. Passariello, A. T. Palamara, *Bioorg. Med. Chem. Lett*. **2007**, 17**,** 1221–1225.
[4] G. Regnier, L. Canevar, R. J. Le, J. C. Douarec, S. Halstop, J. Daussy, *J. Med. Chem.* **1972**. 15, 295-299.
[5] C. A. Winter, E. A. Fisley, G. W. Nuss, *Proc. Soc. Exp. Biol. Med.* **1962**, 111, 544-547.
[6] K. Suguira, A. F. Schmid, M. M. Schmid, F. G. Brown, *Cancer Chemother. Rep*. **1973**. 1, 31-236.
[7] Mojtahedi M M, Saidi M R, Shirzi J S, Bolourtchian M, *Syn. Commun.* **2002**. 32, 851-855.
[8] I. Saxena, D. C. Borah, J. C. Sarma, *Tetrahedron Letters.* **2005**. 46**,** 1159-1160.
[9] M. B. Deshmukh, P.V. Anbhule, S. D. Jadhav, S. S. Jagtap, D. R. Patil, S. M. Salunkhe, S. A. Sankpal, *Indian Journal of Chem*. **2008**. 47B, 792-798.
[10] A. K. Bose, S. M. Maghar, S. M. Pednekar, . N. Ganguly, H. Dang, H. William, A. Mandadi, *Tetrahedron Letters*. **2005**, 46**,** 1901-1904.
[11] P. Biginelli, *Gazz. Chim. Ital*, **1893**, 23, 360–413.
[12] C. O. Kappe, W.M.F.Fabian, M. A. Semones, *Tetrahedron*, **1997**, 53, 2803–2816.
[13] G. Maiti, P. Kundu, C. Guin, *Tetrahedron Lett*, **2003**, 44, 2757-2758.
[14] A. S. Paraskar, G. K. Dewkar, A. Sudalai, *Tetrahedron Lett*, **2003**, 44, 3305-3308.
[15] C. Liu, J. Wang, Y. Li, *J. Mol. Catal. A: Chem*, **2006**, 258, 367-370.
[16] K. K. Kapoor,B. A. Ganai, S. Kumar,C. S. Andotra, *Can. J. Chem*, **2006**, 84**,** 433-437.
[17] A. Naseem, E. Johan, L. van, *Tetrahedron Letters*, **2007**. 48, 5407-5409.
[18] J. S. Yadav, B.V.S. Reddy,N. Lingaiah, P.S. Saiprasad, *Eur. J. Org. Chem*, **2004**, 2004**,** 552-557.
[19] J. J.Shrikhande, *Res J. Chem. Envir*, **2007**. 11, 82-85.
[20] M. A. Bigdeli, G. Gholami, E. Sheikhhosseini, *Chinese Chemical Lett*, **2011,** 22**,** 903-906.
[21] B. Das, J. Kashanna, R. A. Kumar, P. Jangili, *Monatshefte für Chemie*, **2013**, 144, 223-226.
[22] E. Jayachandran,K. Bhatia, L. V. Nargund, G. A. Roy, *Indian Drugs*, **2003**, 40, 408-410.
[23] Y. Muzushima, M. Kobayashi, *J. Pharm. Pharmacol*, **1968**, 20, 169-172.
[24] H. P.Rang, M. M. Dale, J. M. Ritter, P.K. Moore, *Pharmacology*, **2003**, third ed. Churchill Livingstone, New York,
[25] L. J. Robert, J. D. Morrow, Analgesic-antipyretic and anti-inflammatory agents and drug employed in the treatment of gout. in: Hardman J.G., Limbird L.E., Gilman A.G. (Eds.), Goodman and Gillman's, the Pharmacological Basis of Therapeutics, **2001,** tenth ed. Mc Graw-Hill Professional, New York, 687.