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NOTE

Three-Component One-Pot Synthesis of 4,6-Diarylpyrimidin-2(1*H*)-ones Catalyzed by 1-Methyl-3-[2-(sulfooxy)ethyl]-1*H*-imidazol-3-ium Chloride

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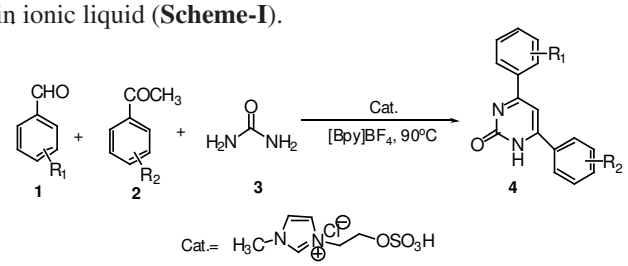
An efficient, one-pot, three-component cyclocondensation reaction of aromatic aldehydes, aromatic ketone and urea catalyzed by 1-methyl-3-[2-(sulfooxy)ethyl]-1*H*-imidazol-3-ium chloride is developed to give 4,6-diarylpyrimidin-2(1*H*)-ones.

Key Words: Synthesis, 4,6-Diarylpyrimidin-2(1*H*)-ones, 1-Methyl-3-[2-(sulfooxy)ethyl]-1*H*-imidazol-3-ium chloride.

Pyrimidinones is an important class of heterocycles due to their relevance to various biological, pharmaceutical and therapeutic activities[1], such as anticancer, anti HIV, antibacterial, antimalarial, antihypertensive, sedative, anticonvulsant, antithyroid, antihistaminic activities[2-4]. They are mostly used as calcium channel blockers[5,6], α-antagonista[7] and neuropeptide-antagonists[8].

Biginelli[9] first reported the one-step synthesis of 3,4-dihydropyrimidin-2(1*H*)-one in alcohol using strong mineral acid. Soon afterwards, various methods were reported concerning the synthesis of pyrimidine derivatives. Few one-pot syntheses have been published using different catalysts such as chlorotrimethylsilane[10], $H_3PMo_{12}O_{40}$[11], $H_6P_2W_{18}O_{62}\cdot 18H_2O$[12], sulfamic acid[13], $Bi(TFA)_3$ immobilized in [nbpy]$FeCl_4$[14], 2,4,6-trichloro-1,3,5-triazine[15], *etc*.

Herein, a novel catalyst synthesized in our lab, 1-methyl-3-(2-(sulfooxy)ethyl)-1*H*-imidazol-3-ium chloride (**I**) was firstly used to promote the simple preparation of 4,6-diarylethenes pyrimidin-2(1*H*)-ones *via* an efficient one-step three-component reaction of aromatic aldehyde, aromatic ketone and urea in ionic liquid (**Scheme-I**).



Scheme-I: Synthesis of 4,6-diarylpyrimidin-2(1*H*)-ones

All melting points are uncorrected and were measured on XT5 melting point apparatus. The ^1H and ^{13}C NMR spectra were run on a Bruker Advance DMX 400 spectrometer in $CDCl_3$ using TMS as internal standard. Mass spectra were obtained on a Bruker MicroTOF-QII instrument. The IR spectra were obtained in potassium bromide pellets with a Bruker 27FTIR-Tensor using KBr optics.

Synthesis of 4,6-diarylpyrimidin-2(1*H*)-ones[16]: The mixture of aromatic aldehyde (1 mmol), aryl ketone (1 mmol) urea (4 mmol), ionic liquid (2 mL) and **I** (0.4 mol %) were stirred at 90 ºC for the given time. After the completation (monitored by TLC), the mixture was diluted with water. The crude solid was filtered and washed with 95 % EtOH and then recrystallized with 95 % EtOH/DMF (1/4) to provide the pure product **4** (**Scheme-I**).

Initially, to optimize the reaction condition, the effects of solvents, reaction time and temperature on the yield of **4b** were evaluated and the results were summarized in Table-1. It was found that ionic liquid afforded better yield than other solvents. [Bpy]BF_4 was better than [Bmim]BF_4 may be due to its more suitable polarity and acidity to dissolve the reactants. The appreciable amount of catalyst was 0.4 mol %. However, the increasing of catalytic loading could not enhance the yield of the product (Table-1, entry 7). Subsequently, the best temperature was investigated. The results in Table-2 indicated the optimal temperature was 90 ºC.

To explore the application of this method, the scope of the substrates was evaluated with a variety of aromatic aldehydes and aromatic ketone (Table-3).

TABLE-1
SYNTHESIS OF **4b** UNDER DIFFERENT CONDITIONS[a]

Entry	Solvent	Catalyst (mol %)	Time (h)	Isolated yield (%)
1	CH_3COCH_3	0.4	12	Nr[b]
2	EtOH	0.4	12	NP[c]
3	DMF	0.4	12	Nr[b]
4	CH_3CN	0.4	12	NP[c]
5	THF	0.4	12	Nr[b]
6	$[Bmim]BF_4$	0.4	6	79
7	$[Bpy]BF_4$	0.4	6	88
8	$[Bpy]BF_4$	0.6	6	87
9	$[Bpy]BF_4$	0.5	6	88
10	$[Bpy]BF_4$	0.3	6	74
11	$[Bpy]BF_4$	0.2	6	62
12	$[Bpy]BF_4$	0.1	6	53

[a]Reaction condition: 3,4-dimethoxybenzaldehyde (1 mmol), 4-nitroacetophenone (1 mmol), and urea (4 mol) in 2 mL of different solvents at 90 ºC using 0.4 mol % 0.4 mol % of I as catalyst. [b]No reaction. [c]No desired products.

TABLE-2
SYNTHESIS OF **4b** AT DIFFERENT TEMPERATURE[a]

Entry	T (ºC)	Isolated yield (%)
1	r.t	Nr[b]
2	60	Nr[b]
3	80	64
4	90	88
5	100	88
6	110	86

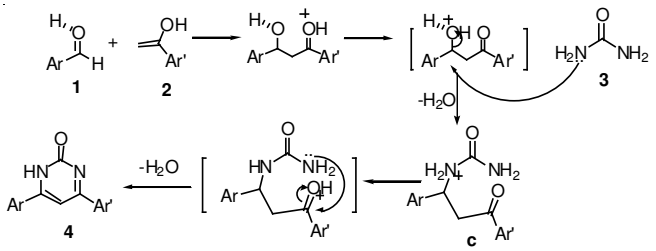
[a]Reaction condition: 4-nitroacetophenone (1 mmol), 3,4-dimethoxybenzaldehyde (1 mmol) and urea (4 mmol) in $[Bpy]BF_4$ at different temperature for 6 h catalyzed by 0.4 mol % of **I**. [b]No reaction.

TABLE-3
SYNTHESIS OF **4**[a]

Comp.	R_1	R_2	Time (h)	Isolated yield (%)
4a	2-OCH_3	4-NO_2	6	85
4b	3,4-$(OCH_3)_2$	4-NO_2	6	88
4c	4-OCH_3	4-NO_2	5	86
4d	3-Br	4-NO_2	6	87
4e	3-NO_2	4-NO_2	7	85
4f	3,4,5-$(CH_3O)_3C_6H_2$	4-NO_2	6	86
4g	4-OH	4-NO_2	6	84
4h	4-Br	4-Cl	6	85
4i	4-I	4-Cl	6	86
4j	3,4,5-$(CH_3O)_3C_6H_2$	4-Cl	7	87
4k	3,4-$(OCH_3)_2$	3-OH	6	86
4l	4-I	3-OH	6	87
4m	4-Cl	H	6	85
4n	4-OCH_3	H	7	83

[a]Reaction condition: aromatic aldehydes (1 mmol), aromatic ketone (1 mmol) and urea (4 mmol) in 2 mL of $[Bpy]BF_4$ at 90 ºC catalyzed by 0.4 mol % of **I**.

The possible reaction mechanism was proposed in **Scheme-II**. It is presumed that the reaction proceeds *via* initial Aldol addition of aromatic aldehyde with aryl ketone to give a chalcone, which addition with urea to give intermediate C. The cyclization and dehydration of C give products **4**.



Scheme-II

In summary, we report here a high yield one-pot synthesis of 4,6-diarylpyrimidin-2(1*H*)-ones, from readily available aromatic aldehydes, aromatic ketones and urea catalyzed by 1-methyl-3-[2-(sulfooxy)ethyl]-1*H*-imidazol-3-ium chloride. This new protocol provides an environmentally benign route along with the associated advantages of simplicity of operation and higher atomic efficiency.

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