19TH ELECTRONIC CONFERENCES ON SYNTHETIC ORGANIC CHEMISTRY PAPER PRESENTED IN MICROWAVE SECTION ENTITLED ON

Calcium Bromide is an Efficient Catalyst for Synthesis of Dihydropyrimidones Under Microwave Condition

By

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Importance of Dihydropyrimidinones

- Dihydropyrimidinones shows following important biological activity
- Calcium channel blockers
- Antihypertensive
- Anticancer agents
- Antidiabetic activity
- Antithrombotic agent
- Carbonic anhydrase inhibitor
- α_{1a}-adrenergic antagonists
- Neuropeptide Y (NPY) antagonists
- Antileishmanial

The Biginelli reaction

- The synthesis of these compounds firstly reported by the Biginelli in 1893.
- The Biginelli reaction, is a direct and simple approach for the synthesis of 3,4-dihydropyrimidinones by one-pot cyclocondensation of ethyl acetoacetate, benzaldehyde and urea in the presence of strong acid.
- Shortcomings of this method is low yield, strongly acidic reaction condition.

Modifications of Biginelli Reaction

- $ZnCl_2$/TBAB
- LiBr
- $Cu(OTf)_2$
- $FeCl_3.6H_2O$, $NiCl_2.6H_2O$
- $Zr(H_2PO_4)_2$
- Sodium Selenate
- Lanthanide Triflate
- Indium (III) Chloride
- $CdCl_2$

- Silica sulphuric acid
- Mesoporous silica MCM-41
- *t*-BuOK
- $Y(NO_3)_3.6H_2O$
- Iron (III) trifluoroacetate and trifluoromethanesulfonate
- CaF_2
- PEG-embedded thiourea dioxide
- 12-Molybdophosphoric acid

- Chlorosulfonic acid
- Nafion-H
- Cobalt nitrate
- Silica-gel
- Silica-bonded *S*-Sulfonic acid [
- $NaIO_4$
- Aluminatesulfonic acid nanoparticles [
- Trichloroisocyanuric acid
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- 1,3-Dichloro-5,5-dimethylhydantoin
- Nano-$TiCl_4.SiO_2$
- $FePO_4.2H_2O$
- $LaCl_3/ClCH_2COOH$
- Other methods, for synthesis of dihydropyrimidiones are ionic liquid microwave irradiatio and ultrasound

Calcium Bromide is new catalyst in organic synthesis

- Calcium bromide is the calcium salt of hydrobromic acid. Calcium bromide is obtained by the interaction of bromine and milk of the lime in the presence of ammonia. It is readily soluble in water and absolute ethanol .
- It is thermally and chemically stable.
- Use of calcium bromide in organic synthesis is very rare

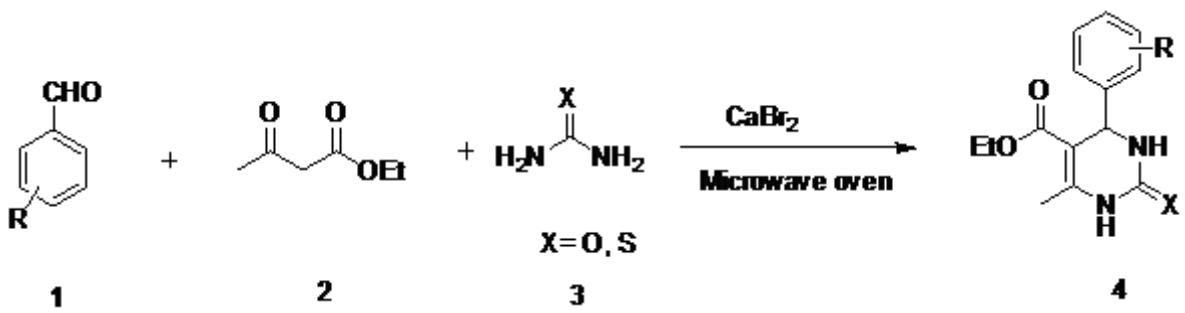
Results and Disscussion

- Calcium bromide is polar covalent molecules due to high electronegative difference between calcium and bromine. The binding electron pair in calcium and bromine is pulled towards bromine atom, forming a diploe within the molecule.
- Due to this dipole calcium bromide absorbs microwave energy and converts into heat. This generated heat used to bring reaction between urea, benzaldehyde and ethyl acetoacetaete.

- To lead off the reaction conditions for the calcium bromide catalyzed Biginelli condensation under microwaves, the reaction of benzaldehyde with ethyl acetoacetate and urea was taken as a model reaction .
- I tested to optimize the reaction conditions by changing the quantities of calcium bromide from 0 mole% - 20 mole%. It was noted that the condensation reaction can be efficiently carried out by taking 2mol% of the catalyst at 400w, in a short time span of only 1.5 to 3 minutes, which is much lesser and yield is high as compared to other catalysts using more than 5 to 20mol%. A further increase in the catalyst amount does not show any noticeable increase in the product yield (Table 1).

- Table 1. Optimising amount of catalysts for synthesis of dihydropyrimidiones

Entry	Amount of catalyst in mol%	Time in Minutes	% Yield[b]
1	0	15	25
2	0.5	10	41
3	1	5	52
4	2	2	94
5	5	2	95
6	10	1.5	95
7	15	1.5	95
8	20	1.5	94



21 examples with electron withdrawing as well as electron donating substituent's on benzaldehyde, yield in the range from 72 % to 94 %

Notably, this protocol is compatible with a wide range of functional groups such as methoxy, halides, nitro, hydroxyl, *N, N*-dimethyl-, and acid sensitive compound like cinnamaldehyde, furfural aldehyde could afford the corresponding products in excellent yield as well.

Conclusion

- In summary, here I reported an efficient synthesis of dihydropyrimidinones and dihydropyrimidinthiones using calcium bromide as a catalyst under microwave condition.
- The mild reaction conditions, rapid formation of product, high yields, inexpensive and easily available catalyst, are some notable merits of this method.

- Moreover, compatibility with the environment, more efficiency and easy separation of catalyst after synthesis are considered as another merit of this method.
- Most importantly, absence of organic solvents and use of microwave irradiation as an alternative energy source which obey principles number two and five out of the twelve principles of green chemistry, due to this, method contributes it to the development of green technology.

THANK YOU