



IONIC LIQUID MEDIATED ONE POT SYNTHESIS OF 3, 4-DIHYDROPYRIMIDINONES (DHPMs), USING MODIFIED BIGINELLI REACTION

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Abstract:-

The synthesis of 3,4-dihydropyrimidinones by modified Biginelli reaction by using aryl/heteryl aldehydes, dicarbonyls and urea / thiourea in N-methyl pyridinium tosylate as ionic liquid.

Keywords:- Aryl/ heteryl aldehydes, dicarbonyles and urea / thiourea and N-methyl pyridinium tosylate as ionic liquid.

Introduction:- 3,4-Dihydropyrimidinones (DHPM'S) denoted as Biginelli compounds and their derivatives are highly important heterocyclic units due to their therapeutic and pharmacological properties like antiviral, antitumor, antibacterial and anti-inflammatory, Ca⁺⁺ channel modulators, antihypertensive, and alpha/a antagonists activities.^[i-iii] Over recent decades there has been increasing focus on DHPMs as potential lead structures in drug discovery. A large number of DHPMs based scaffolds have already been developed for the drugs or lead compounds.

Some of the reported methods for the synthesis of DHPMS using various reagents are- One pot synthesis of DHPMS catalysed by using Lanthanide triflate^[iv], Cupric chloride and lithium chloride, Indium chloride^[v], Indium tribromide^[vi], Bronsted base -(t-BuOK) catalysed^[vii], Iodine catalysed^[viii] as catalysts. Because of some draw backs of these methods we tried to develop green method for synthesis of DHPMS.

Considering the therapeutic significance of dihydropyrimidinones several efforts are found to made to provide convenient and efficient one pot multicomponent condensation system catalyzed by heterogeneous /homogeneous catalysis in presence of inert media or under solvent free conditions.

Materials and Methods:- Chemicals used were of synthetic grade and made by S.D. fine or spectrochem and used without further purification. ¹H-NMR spectra were recorded on a

Bucker Advance II FT at 400MHz instrument and Mass spectra was recorded on a Jeol SX-102 instrument. Melting points were taken open capillaries and are uncorrected. IR spectra were recorded on Jasco FTIR using KBr disc.

Experimental section

In a typical reaction procedure an aldehyde (10 mmol), 1, 3-dicarbonyl (11 mmol) and urea/thiourea (13 mmol) were heated in a pre molten N-methyl pyridinium tosylate (2 g) with stirring at 120 C. after completion of reaction content was poured on ice cooled water to obtain solid product. Thus obtained product was filtered and crystallized from ethanol to obtain pure DHPMs (**Scheme I**). Characterization of product was made by physical constant and spectral technique.^[ix]

Result and Discussion

The synthesis of 3, 4-Dihydropyrimidinones (DHPM'S) carried by cyclocondensation, using ionic liquid N-methyl pyridinium tosylate as a catalyst.

We choose the reaction of 4-mehoxy benzaldehyde, ethyl acetoacetate and urea as a model reaction to find out suitable catalyst for synthesis of 3, 4-Dihydropyrimidinones (DHPM'S) derivatives. Same reaction is carried out by using catalyst such as H⁺/EtOH, NaHCO₃ in DMF, Yb(OTf)₃, Zn(NH₂SO₃)₂, Indium III Chloride, Bronsted base -(t-BuOK) etc. and were examine to obtained better yield, but it is our finding that all these catalyst took long time duration as compared to ionic liquid N-MPyTS. This catalyst is soluble in water and recyclable.

Conclusion

The significant features of this newly developed protocol are the time required for the completion of the cyclocondensation is markly reduced, needs moderate heating and the yields of the products are near to stoichiometric, clean reactions, as well as avoidance of column chromatographic purifications. We believe this novel method is a useful contribution to the existing methodologies. Hence, we claim that this route is rapid, economical, efficient and eco-friendly.

Acknowledgement:-Authors are thankful to Prof.D.B.Ingle for his valuable guidance and Sophisticated Analytical Instrumentation Facility, CDRI, Lucknow for spectral services.

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Data:-

Ethyl 1, 2, 3, 4-tetrahydro-6-methyl-2-oxo-4-(1,3-diphenyl-1H-pyrazol-4-yl)pyrimidine-5-carboxylate.(VI)

Mass: ESI⁺ (m/z, % Intensity), 403 (M⁺,¹⁰⁰), 401 (13.85) and 249 (7.7).

IR :(KBr, cm⁻¹) Characteristics absorptions:

3428(NH str), 3227(Ar-H str),3108(CH Olefinic str),1699 (C=O str), 1647 (C=N str) and 1600 (C=C str).

PMR (DMSO,δppm): 0.85 (t,3H,J =8Hz,CH₃), 2.29 (s, 3H, CH₃), 3.75 (q, 2H, J =8Hz, CH₂), 5.44 (s, 1H, CH), 7.28-7.96 (m,10H,ArH),8.39 (s,1H,pyrazoyl) and 9.22 (s, 2H, NH, exchangeable with D₂O).

¹³CMR (DMSO,δppm): 13.73, 17.80, 45.49, 58.92, 99.80, 118.28, 129.44, 133.13, 139.38, 148.08, 150.37, 151.98, 165.0 and 165.16

Table I. Physical characterization of DHPMs.

Sr. No.	Aldehyde	X	Yields (%)	M.P.(°C)
I	4-OCH ₃ C ₆ H ₅	O	80	200-201
II	4-Cl C ₆ H ₅	O	88	210-212
III	4-Me-C ₆ H ₅	O	84	215-216
IV	3,4-di OCH ₃ C ₆ H ₅	O	91	177-178
V	3-OH C ₆ H ₅	O	78	207-208

VI	1,3-diphenyl pyrazolyl	O	67	283-284
VII	1,3-diphenyl pyrazolyl	S	68	292-293
VIII	2-Cl-quinolinyl	S	72	242-243
IX	2-Cl-quinolinyl	O	73	260-261

Received on July 11, 2017.