Environmentally benign EPZ-10 catalyzed preparation of 2,3-dihydroquinazoline-4(1H)-ones derivatives

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Abstract: ***Describe method consist of eco-friendly procedure for the preparation of 2,3-dihydroquinazoline-4(1H)-ones from equimolar 2-aminobenzamide and substituted aromatic aldehydes in presence of EPZ-10. Green impact of reaction significantly enhanced due to use of alcohol as solvent and naturally occurring clay substance as solid catalyst. Good to excellent yield of products, simple working strategy and easy purification are the advantage of present methodology***

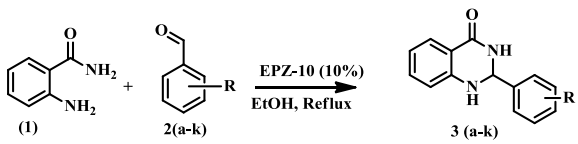
Keywords: green methodology, EPZ-10, quinazoline

I.INTRODUCTION

Search of expeditious and cost-effective methodologies to replace tedious, low productive traditional methodologies gains its own importance. Now a day's green methodologies has attract significant attention and environmentally benign, recyclable, chap solid catalysts get ultimate reputation. Such methodology offers to obtained complex pharmaceutically important molecules or intermediate by possibly viable ways. Such methodologies shine with imminent light when water incorporates as solvent, due to its non-toxic, green, cheap nature and biochemical consequence. [1, 2]

Quinazoline has been occupied distinct position in nitrogen containing heterocycles due to its spectacular wide spectrum of pharmaceutical properties. Various reports of quinazoline underline its widely biopharmaceutical activity like, anticancer [3-5], antibacterial [6]-[8], anti-inflammation [9],[10], anti-tuberculosis [11], anti-hypertension [12] and anti-diabetics [13]. Such wide spectrum of quinazoline strongly demands possible derivatisation to test out for further pharmaceutical possibilities. Various methods have been proposed to obtained quinazoline analogues using catalysts like ammonium bromide [14], Zirconyl chloride [15] Heteropoly acids [16], Gallium (III) triflate [17], Titanium oxide nano-particles [18], Starch solution [19], cyanuric chloride [20] and Cyclodextrin sulphonic acid [21]. Most of these methodologies are suffers from long reaction time, high temperature, use of expensive catalyst and tedious work procedures. 'On water' reports [22] of quinazoline synthesis by using expensive catalyst increase cost of reaction.

EPZ-10 is naturally occurring clay catalyst and used successfully to develop various methodologies to achieve green reaction profile. Such catalyst simplifies the reaction procedure and do not pass on unpleasant toxic residue to environment. EPZ-10 is well known and cost effective environmental friendly catalyst [23]. In continuation of our previous research work [24] to develop fast, naturally benign, productive methodology for small and fused heterocyclic compounds, we intended to developed facile, efficient, cost-effective and easy workup method for the synthesis of quinazoline derivatives. Here, introduce facile methodology as shown in scheme 1 for syntheses of quinazoline derivatives.



Scheme 1

II.EXPERIMENTAL

The reagents and solvents were purchased from Alfa aesar and Aldrich Chemical companies and used without further purification. All compounds obtained were describe for open head capillary tube for their melting point and are uncorrected. The samples were analyzed by FT-IRspectroscopy (JASCO FT/IR-460 plus spectrometer). 1HNMR and 13CNMR spectra of compounds were recorded on a Bruker DRX-400Avance instrument in DMSO-d6.

III.GENERAL PROCEDURE

In a RBF containing 20 ml of ethanol was added 2-aminobezamide (0.01mol; 1.36gm), substituted aldehyde (0.01mol) with stirring. To this EPZ-10 (10 mol%) was added on single lot. The reaction mixture

was reflux for appropriate time. Progress of reaction was monitor by thin layer chromatography (TLC) using Ethyl acetate-Hexane. After completion of reaction, reaction mixture was filter off to ice cold water. Obtained solid was recrystallized from suitable solvent. Representative compounds were scan for spectral data and found satisfactory agreement with reported.

Spectral data of representative compounds

2-phenyl-2,3-dihydroquinazolin-4(1H)-one;(1) m.p.= 219°C,1HNMR (400 MHz,DMSO-*d6*): δ= 8.27 (s, 1H), 7.61 (d, 1H), 7.50 (d, 2H), 7.31-7.41 (m, 3H), 7.22 (t, 1H), 7.06 (s,1H), 6.72 (d, 1H), 6.69 (t, 1H,), 5.75 (s, 1H) ppm;IR (KBr): 3310,3014, 1671, 1630, 1523 cm^{-1}.

Table 1.Quinazoline derivatisation with respect to yield of reaction, time and physical constant of obtained products.

Sr.	-R	Com.	Time (min.)	Yield[a] %	M.P. in °C
1.	-H	3a	30	77	219
2.	*p*-OMe	3b	30	86	184
3.	*p*-OH	3c	30	69	177
4.	*p*-Me	3d	30	88	224
5.	*p*-Br	3e	30	90	195
6.	*p*-Cl	3f	60	72	208
7.	*p*-NO_2	3g	60	55	212
8.	*p*-$N(Me)_2$	3h	30	80	224
9.	*m*-OMe	3i	30	90	151
10.	*m*-OH	3j	30	67	204
11.	*o*-Me	3k	30	75	190

[a]Isolated yields; Reaction condition: 2-aminobenzamide (0.01 mol), p-methoxy benzaldehyde (0.01 mol), reflux in ethanol with 10mol% of EPZ-10 as catalyst.

IV.RESULTS AND DISCUSSIONS

Series of reactions were performed to optimized reaction condition including the mole percent amount of catalyst with respect to yield of product. Reflux condition and reaction workup process was kept as fix parameters. 2-aminobenzamide and p-methoxy benzaldehyde were taken for model reaction and various reaction condition were applied. In continuation with our previous research work [25] silica chloride were successively used as reusable catalyst for the preparation of dihydroquinazoline, using thionyl chloride cause serious environmental damage and hence we are eager to replace silica-chloride with green and naturally occurring catalyst. EPZ-10 is naturally occurring substance and found excellent in alcohol.

It has been observed that nature of substituent present on aromatic aldehydes has effect on yield of reaction. This correlation was underline by considering yield of product as shown in Table 1. Electron donating functionality increase amount of yield of product, whereas withdrawing reduces it.

V.CONCLUSION

In conclusion, an efficient, green method for the synthesis of quinazoline analogues has been described using EPZ-10 as naturally occurring catalyst. The green reaction profile and mild reaction conditions are main advantage of this method. Reaction profile is overall environmentally benign and simple operational technique.

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