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Short Communication

ENVIRONMENTALLY BENIGN ALUM CATALYZED EFFICIENT SYNTHESIS OF 2,3-DIHYDROQUINAZOLINE-4(1H)-ONES DERIVATIVES IN WATER

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ABSTRACT

Described 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 10% aqueous Alum ($K\ Al(SO_4)_2 \cdot 12H_2O$). Green impact of reaction significantly enhanced due to use of water as solvent and naturally occurring substance as catalyst. Good to excellent yield of products, simple working strategy and easy purification are the advantage of present methodology.

Keywords: Quinazoline, Alum catalysed, Water mediated, Green methodology.

1. 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 have attracted 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 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], antiinflammatory [9, 10], antitubercular [11], anti-hypertensive [12] and antidiabetics [13]. Such wide spectrum of quinazoline strongly demands possible derivatisation to test out for further pharmaceutical possibilities. Various methods have been proposed to obtain quinazoline analogues using catalysts like ammonium bromide [14], Zirconyl chloride [15] Heteropolyacids [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 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.

Readily accessible Potassium alum sulphate ($KAl(SO_4)_2 \cdot 12H_2O$) for the synthesis one pot quinazoline has not attempted. Such catalyst simplifies the reaction procedure and do not pass on unpleasant toxic residue to environment. Potash alum, perhaps most easily available substance and extensively used as support in reactions [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.

2. EXPERIMENTAL

The reagents and solvents were purchased from 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 analysed by FT-IR spectroscopy (JASCO FT/IR-460 plus spectrometer).

^{1}HNMR and ^{13}CNMR spectra of compounds were recorded on a Bruker DRX-400Avance instrument in DMSO-d_6.

2.1. General procedure

In a RBF containing 20 ml of 10% Potash alum, 2-aminobezamide (0.01mol; 1.36gm), and substituted aldehyde (0.01mol) were added with stirring. The reaction mixture was stirred at room temperature. Progress of reaction was monitored by thin layer chromatography (TLC) using Ethyl acetate-Hexane. After completion of reaction, reaction mixture was filtered off and filtrate was neutralized by saturated solution of sodium bicarbonate, brine and extracted with ethyl acetate. Organic layer was dried on anhydrous sodium sulphate and evaporated in reduced pressure to afford pure product after recrystallization from ethanol. Representative compounds were scanned for spectral data and found satisfactory agreement with reported. Facile methodology for synthesis of quinazoline derivatives is shown in fig. 1.

2.2. Spectral data of representative compounds

2-phenyl-2,3-dihydroquinazolin-4(1H)-one; (1) m.p., 219°C, ^{1}H-NMR (400 MHz, DMSO-d_6): 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}.

3. RESULTS AND DISCUSSION

Series of reactions were performed to optimize reaction condition including amount of catalyst with respect to yield of product. Room temperature and 'on' water was kept as fix reaction 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. Potash alum is water soluble naturally occurring substance and solubility was found excellent upto 15-16% w/v in water. 10% alum showed pH 3.0-3.2, and by considering this fact, we chose alum as catalyst.

It has been observed that nature of substituent present on aromatic aldehydes has affect on yield of reaction. This correlation was underlined by considering yield of product as shown in table 1. Electron donating functionality increases yield of product, whereas electron withdrawing functionaliy reduces it.

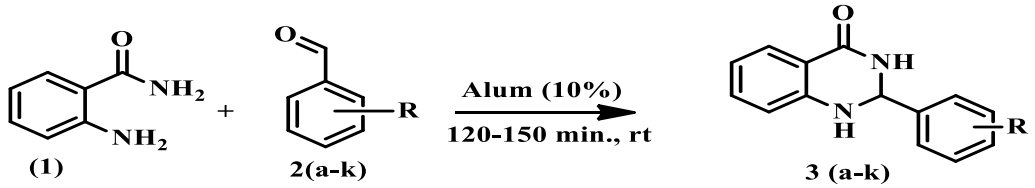

Fig. 1: Reaction Scheme for synthesis of 2, 3-dihydroquinazoline-4(1H)-ones

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

Sr. No.	-R	Comp.	Time in min.	Yield[a] %	M.P. (Lit.) in °C	Ref.
1.	-H	**3a**	120	77	219 (218-220)	[25]
2.	*p*-OMe	**3b**	120	86	184 (181-182)	[25]
3.	*p*-OH	**3c**	140	69	177 (183-185)	[25]
4.	*p*-Me	**3d**	120	88	224 (227-229)	[25]
5.	*p*-Br	**3e**	120	90	195 (197-198)	[25]
6.	*p*-Cl	**3f**	150	72	208 (206-208)	[25]
7.	*p*-NO_2	**3g**	150	55	212 (214-216)	[25]
8.	*p*-$N(Me)_2$	**3h**	140	80	224 (227-229)	[25]
9.	*m*-OMe	**3i**	120	90	151 (147-149)	[25]
10.	*m*-OH	**3j**	120	67	204 (209-210)	[25]
11.	*o*-Me	**3k**	120	75	190 (188-189)	[25]

[a]*Isolated yields; Reaction condition: 2-aminobenzamide (0.01 mol), p-methoxy benzaldehyde (0.01 mol), stirred in 10% Potash alum (20 ml) at rt.*

4. CONCLUSION

In conclusion, an efficient, green method for the synthesis of quinazoline analogues has been described using readily Potash alum as naturally occurring catalyst. The green reaction profile and mild reaction conditions are main advantage of this method. Reaction takes place at room temperature by simply stirring method, with operational simplicity offers excellent yields.

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