Shri. Yogeshwari Education Society's

YOGESHWARI MAHAVIDYALAYA, AMBAJOGAI

Tq. Ambajogai - 431 517, Dist. Beed (M.S.)

Estd. 29th June 1956

NAAC Re-Accredited Grade 'B'

Dr. U.D. JOSHI

Principal & Professor

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Affiliated to Dr. B.A.M. University, A'bad

Ref.No. : YMA/Jr-Sr/20 -20

Date 01/07/2019

To

The Principal,

Dnyanopasak College,

Parbhani-431401, MS, India

Subject: Collaboration

Respected Sir

With reference to the above subject, our institution is willing to collaborate with your institution for the purpose of;

1) Student Exchange

2) Teacher Exchange

3) Academic Activities

4) Research activities

This collaboration will be for one year. Kindly convey your acceptance.

Principal
Yogeshwari Mahavidyalaya
Ambajogai

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Ref.No. : YMA/Jr-Sr/20 -20

Date 11 / 07 /2019

To

The Principal,

Dnyanopasak College,

Parbhani-431401, MS, India

Subject: Collaborating Activity

Respected Sir

As per the collaboration, I am giving consent to following faculty for joint publication of research article under the Research Activity.

Name of the faculty: Dr. V. R. Choudhari, (Department of Chemistry)

Principal
Yogeshwari Mahavidyalaya
Ambajogai

ejpmr, 2020,7(4), 420-424

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article
ISSN 2394-3211
EJPMR

SYNTHESIS OF OCTAHYDROQUINAZOLINONE DERIVATIVES AND ITS ANTICANCER ACTIVITY EVALUATION

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Article Received on 27/01/2020 **Article Revised on 17/02/2020** **Article Accepted on 07/03/2020**

ABSTRACT
A convenient method was expanded for the synthesis of octahydroquinazolinones by one-pot reaction of a different salicylaldehyde, dimedone and urea/thiourea using $[Hmim]HSO_4$ in catalytic amount. The synthesized derivatives were tested for inhibition of cancer cell. The primary analysis showed that number of synthesized molecules exhibited considerably admirable inhibition activities against MCF-7 human breast cancer cell.

KEYWORDS: Anticancer activity, one-pot synthesis, salicylaldehyde, $[Hmim]HSO_4$, Octahydroquinazolinones.

INTRODUCTION

One-pot synthesis is very considerable for the formation of numerous heterocyclic molecules[1] and this approach has been employed successfully in construction of many bioactive moieties and natural products.[2] The octahydroquinazolinone synthesis has attracted the awareness of chemists due to their highly useful anti-bacterial activity against many kinds of bacteria including *Esherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*.[3] Exceptionally quinazoline derivatives has been employed as an anti-cancer drugs,[4-6] analgesic,[7] anti-inflammatory,[8] anti-bacterial,[9] anti-convulsant,[10] anti-mycobacterial agents[11] and anti-fungal.[12]

A range of protocols have been reported for octahydroquinazolinone synthesis by the reaction of aldehydes with dimedone and urea or thiourea involving the use of catalysts such as thiamine hydrochloride,[13] NH_4VO_3,[14] TMSCl,[15] Nafion-H,[16] conc. H_2SO_4,[17] conc. HCl,[18] heteropolyacid,[19] bakers' yeast[20] and ionic liquids.[21-22] Among these, a number of protocols experiences the few drawbacks such as extended reaction time, reduced product yield and unsafe and costly catalysts with partial reusability.

Here in we describe an useful methodology for the synthesis of octahydroquinazolinones by using ionic liquid $[Hmim]HSO_4$ catalyst at room temperature (**Scheme 1**). All prepared molecules were evaluated for the inhibition of Breast cancer cell.

MATERIALS AND METHODS

The column chromatography was performed over silica gel (80-120 mesh). Melting points of synthesized derivatives were carried out in open glass capillary tube and were uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker 300 MHz spectrometer in $CDCl_3$ solvent with TMS as an internal standard. Mass spectra were carried out on Polaris-Q Thermo scientific GC-MS spectrometer.

2.1 Typical procedure for the synthesis of octahydroquinazolinones: In 50 ml round bottom flask, A mixture of dimedone (1 mmol), urea/thiourea (1.2 mmol), $[Hmim]HSO_4$ (10 mol %) and acetonitrile (10 ml) was added. The mixture was stirred at room temperature for half an hour. The substituted salicylaldehyde (1 mmol) was then added and stirring was continued for suitable time (Table 2). After the completion of reaction indicated by TLC, the reaction mixture was diluted with water (15 mL) and extracted with diethylether (3 x 4-5mL). The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The obtained crude product was purified by column chromatography (silica gel, pet ether-EtOAc) to get analytically pure product.

4-(5-Bromo-2-hydroxyphenyl)-3,4,7,8-tetrahydro-7,7-dimethylquinazoline-2,5(1H,6H)-dione(4d): ^1H NMR (300 MHz, $CDCl_3$): δ 9.61 (s, 2H, 2 x NH), 7.10-7.12 (m, 2H), 6.80(d, 1H, J = 4.5Hz), 5.82 (s, 1H), 5.28 (s, 1H, OH), 3.21(s, 2H), 3.05(s, 2H, CH_2), 1.92 (s, 6H, 2 x CH_3); ^{13}C NMR (300 MHz, $CDCl_3$): δ 30.2, 33.2, 38.6, 46.5, 58.2, 108.2, 118.0, 121.0, 126.5, 130.8, 134.4, 140.2, 148.6, 170.8, 191.2; GC-MS, m/z: 364 (M^+).

1,2,3,4,7,8-Hexahydro-4-(2-hydroxy-5-iodophenyl)-7,7-dimethyl-2-thioxoquinazolin-5(6H)-one (4i): ^1H NMR (300 MHz, $CDCl_3$): δ 10.24 (s, 2H, 2 x NH), 7.22-7.26

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