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SYNTHESIS OF BIOLOGICALLY ACTIVE HETEROCYCLIC COMPOUNDS BY USING EGG SHELL POWDER CATALYST

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ABSTRACT:
This review provides a glance report on the recent eggshell powder (ESP) applications that catalyzed organic transformations. ESP catalyst is derived from waste, water-insoluble, non-toxic, cheap, biodegradable and highly efficient catalyst useful for various multi-component reactions, C-C bond formation and synthesis of biologically active heterocycles. Since it comes from waste, it is environmentally beneficial and a green alternative for creating catalytic systems. It has been applicable for the Knoevenagel condensation, synthesis of dihydropyrano[2,3-c]pyrazole derivatives, pyrazole-phthalazine derivatives, substituted 2-aryl benzothiazoles, 7,8-dihydro-4H-chromen-5(6H)-ones, Synthesis of 2-amino-7-methyl-5-oxo-4-phenyl-4,5-dihydropyran[4,3-b]pyran-3-carbonitrile derivatives, Synthesis of dimethyl carbonate by transesterification, lactose isomerization to lactulose, Synthesis of 2-amino chromene, 1,8-dioxo-octa hydro xanthene and Schiff base formation. Interestingly, it has also been helpful for insolvent-free Sonogashira reactions, Suzuki-Miyaura reactions in the presence of Pd-eggshell-based catalysts, and azide-alkyne cycloaddition reactions**.**

KEYWORDS- Egg Shell Powder, Eco-friendly, Isomerisation, Waste-derived Catalyst

INTRODUCTION-

For the synthesis of organic compounds, the need for environmentally friendly conditions, green pathways, and low cost with short reaction times is increasing. Therefore, it is preferable to use the nature/ bio-derived biodegradable catalysts[i]. Due to the greater toxicity problem and cost-effectiveness of organic chemicals, it is necessary to reuse and recycle all the chemicals and catalysts as much as possible for a better and greener future. Considering the challenges of the upcoming future and the hazard level of toxic chemicals, researchers are developing catalysts or chemical intermediates with more sustainable and eco-friendlier alternatives[ii]. The significant role of the catalyst is to enhance the reaction rate without altering the thermodynamic equilibrium of a particular reaction[iii-vi]. Hence, the present needs to find an alternative catalyst system for an eco-friendly environment that is safer for human beings and has a lower toxicity level.

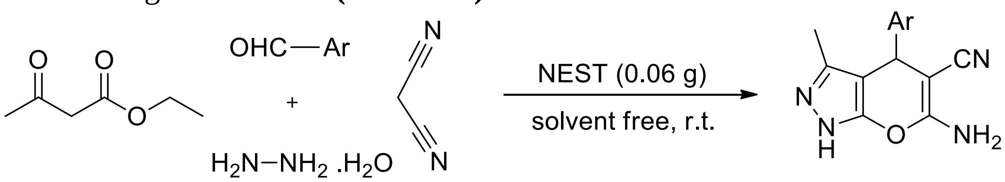
Homogeneous and heterogeneous are the major types of catalyst systems. At the same time, in this review, we will focus on heterogeneous catalysis and the eco-friendly and biologically derived eggshell powder[vii-viii] or calcined egg shell[ix]. Homogeneous catalysis is well recognized in synthetic organic chemistry with few disadvantages, such as difficult separation of the soluble complexes from the reaction mixture, non-recyclability, possibility of breakdown of the complexes, decreasing catalytic activity, etc.[x-xi] Compared to homogeneous, heterogeneous catalysts are easy to recover from the reaction mixture, which furnishes practical importance in both academics and the industrial sector. e.g., appropriate in flow reactors[xii-xiii]. Heterogeneous catalysts are less selective than homogeneous ones due to the presence of a large number of active sites present on it[xiv]. In recent years, the development of green heterogeneous catalytic systems has attained great significance for its implication in the chemical processes. It may cause benign environmental consequences with high selectivity of the desired molecules, great yield, and lesser side products [xv-xvi].

The eggshell is an important natural calcium feedstock in the form of calcium carbonate along with a small percentage of calcium phosphate[xviii-xix]. Literature reveals that eggshell contains approximately 95% CaCO3,2% Ca3(PO4)2, 2% MgCO3, and 1% of organic substances, mostly albuminous. In egg shells, the calcium content is 28.2–41.2%, and the phosphorus content is 0.102% **[xx-xxi]**. Due to the basic nature of ESP**[xxii]**, it could be widely used in synthetic organic processes where an external base is necessary for a reaction to precede the reaction rate without altering the thermodynamics.

The use of eggshell powder as a catalyst is still a promising area of research where researchers are engaged to explore newer opportunities for organic transformations. Synthesis of some biologically active heterocycles using the eggshell catalyst is given below.

Dehghani Tafti *et.al*. in 2021[xxiii]

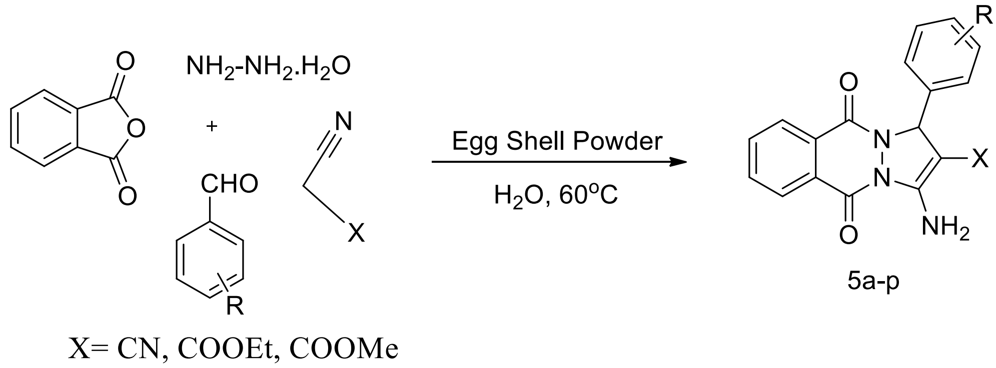
Nano-eggshell/Ti(IV) as a novel naturally based catalyst was prepared, characterized, and applied for the synthesis of dihydropyrano[2,3-c]pyrazole derivatives via a four-component reaction of aldehydes, ethyl acetoacetate, malononitrile, and hydrazine hydrate at room temperature under solvent-free conditions. The principal affairs of this procedure are mild conditions, short reaction times, easy work-up, high yields, reusability of the catalyst and the absence of toxic organic solvents **(Scheme 1)**



Scheme 1

Recently, Jonnalagadda S. B. *et. al*. in 2020[xxiv]

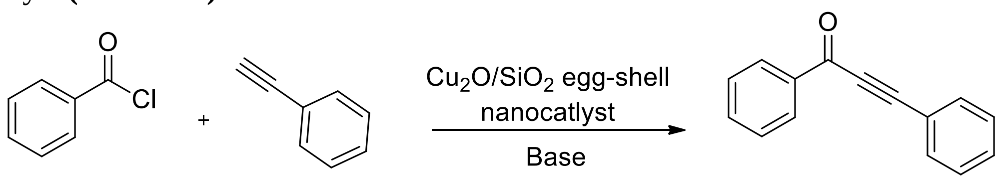
An eco-friendly and efficient green protocol for the synthesis of pyrazole-phthalazine derivatives (**5a–p**) using biodegradable eggshell powder (ESP) as a heterogeneous catalyst. The reaction is a four-component system employed via condensation of phthalic anhydride, hydrazine hydride with various compounds with active methylene group, and different substituted aryl aldehydes. The reaction contains water as a solvent and is carried out at 60^{o}C. This four-component, one-pot condensation reaction proceeded through the Knoevenagel–Michael reaction pathway. This reaction offers high yields with a short reaction time. The use of water as a solvent is an ecologically benign and economical alternative to organic solvents **(Scheme 2).**



Scheme 2

Kang Hyun Park *et al.* in 2018[xxv]

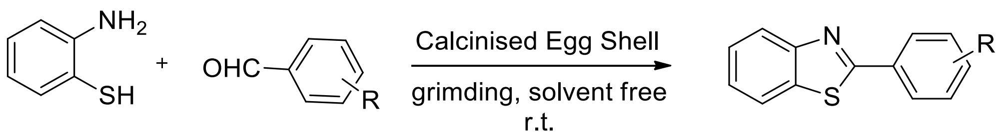
Kang Hyun Park et al. reported the **s**olvent-free Sonogashira reactions for synthesizing ynones from acyl chlorides and terminal alkynes catalyzed by Cu_2O/SiO_2 eggshell nanocatalyst.**(Scheme 3).**



Scheme 3

Borhade A. V. *et al.* in 2016[xxvi]

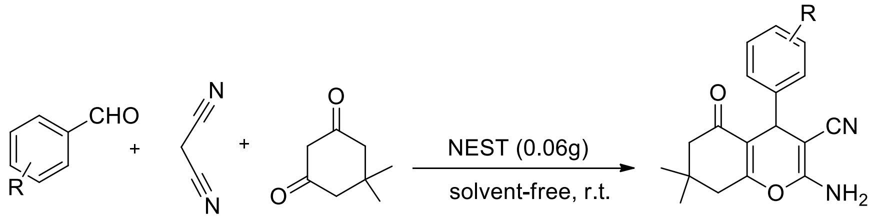
Borhade A. V. et al.prepared calcined eggshells as an efficient and green catalyst from chicken eggshell waste and is characterized by different analytical techniques such as FT-IR, XRD, TGA, SEM, and EDAX. The calcined eggshell is a safe, inexpensive,and green catalyst with high catalytic efficiency obtained from renewable resources here explores the catalytic activity to synthesize a series of substituted2-aryl benzothiazoles have been synthesized by reaction ofo-amino thiophenol and aromatic aldehydes under solvent-free conditions using a grinding method at room temperature. The reaction proceeds smoothly in excellent yields (86-97%), with a short reaction time (15-48 min) and an easy work-up procedure. The reuse of catalysts and purification of products by non-chromatographic methods are some additional features of the present protocol **(Scheme 4).**



Scheme 4

Mosaddegh, E. and Asadollah Hassankhani, A. in 2013[xxvii]

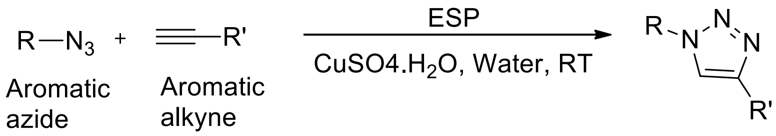
Mosaddegh, E. and Asadollah Hassankhani, A. has been developed an efficient and eco-friendly method for the synthesis of 7,8-dihydro-4H-chromen-5(6H)-ones by using eggshell as a natural and heterogeneous catalyst. This new and green methodology is of interest due to the use of a green, bioactive, and biodegradable catalyst, its short reaction time, high yields without further purification, and the ability to carry out large-scale reactions **(Scheme 5).**



Scheme 5

Sarma D. *et al*. in 2016[xxviii]

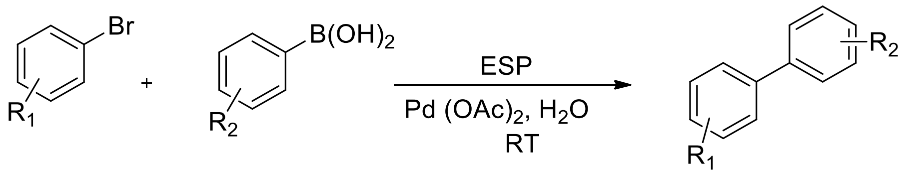
A highly economic and green protocol for azide-alkyne cycloaddition reactions in water has been developed. The protocol uses readily available, considered as waste material, (ESP) as an additive for CuAAC reaction in aqueous media **(Scheme 6).**



Scheme 6

Sarma, D. *et al*. in 2015[xxix]

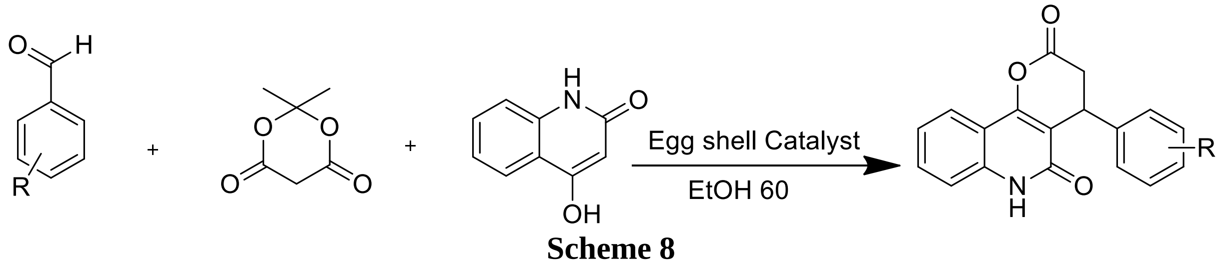
Sarma, D. et al. reported an eggshell-based heterogeneous catalyst and successfully carried out several reactions such as click or azide-alkyne cycloaddition, peptide coupling reaction, and palladium-catalyzed Suzuki–Miyaura reaction using ESP (**Scheme 7**).



Scheme 7

Youseftabar-Miri *et. al*. in 2014[xxx]

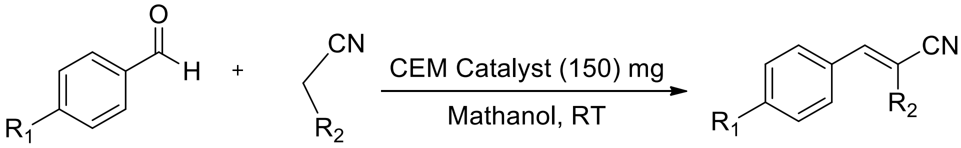
Youseftabar-Miri et al. carried out the organic transformations for the synthesis of pyrano[3,2-c]quinoline derivatives using eggshell as a heterogeneous catalyst at 60 °C and ethanol as a solvent and described that the eggshell catalyst could be recovered and reused for several times without losing its activity (**Scheme 8**).



Scheme 8

Yassine Riadii and coworkers in 2014[xxxi]

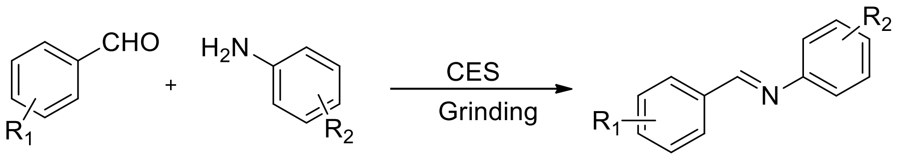
Yassine Riadii and coworkers synthesized a magnetically separable cobalt-iron nano-catalyst based on eggshell as a heterogeneous catalyst and a base alternative for the Knoevenagel condensation reaction (**Scheme 9**).



Scheme 9

Patil and coworkers in 2013[xxxii]

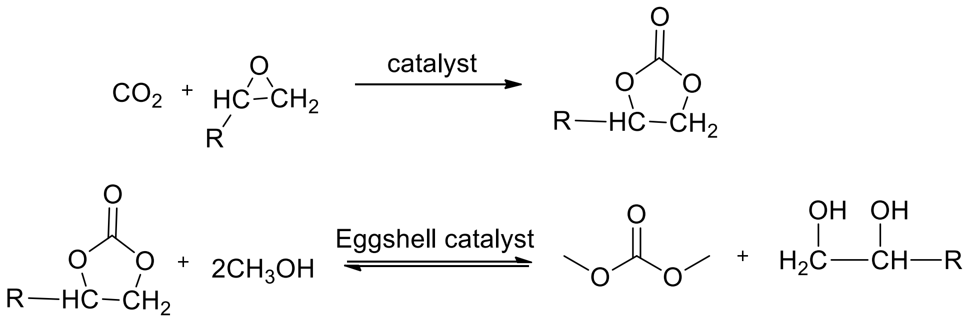
Patil and coworkers synthesized functionalized Schiff bases by using the natural catalyst (calcined eggshell or CES) under solvent-free conditions in which CES acts as a dehydrating agent (**Scheme 10**).



Scheme 10

Gao, *et al*. in 2012[xxxiii]

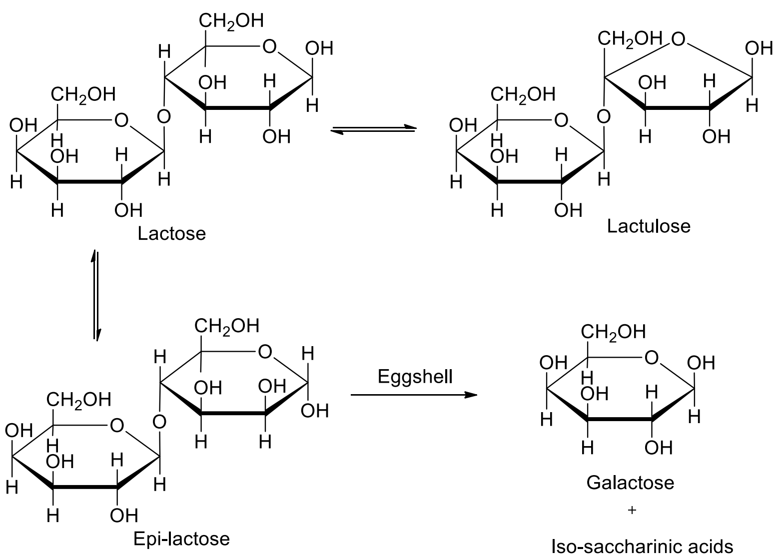
Gao, et. al. synthesized dimethyl carbonate (DMC) using waste eggshell as a heterogeneous catalyst by the treatment of propylene carbonate and methanol at 25 °C and 1 atm pressure (**Scheme 11**).



Scheme 11

Montilla, et. al. in 2005[xxxiv]

Montilla et al. developed a feasible way to produce lactulose from lactose by employing an egg shell as a catalyst (which accelerates the formation of lactulose) through ultra-filtrate, which is an alternative for consuming these industrial wastes. Here, the reaction was stirred and refluxed at 98 °C in glycerol for 60 min using 6 mg/ml of eggshell catalyst loading, giving the optimal lactulose production (**Scheme 12**).



Scheme 12

CONCLUSION:

Egg shell powder (ESP) as a biodegradable, highly efficient, environmentally benign, and reusable catalyst. Different advantages with the use of egg shell powder are overviewed. The requirement of a safe and eco-friendly future is partially fulfilled with the use of such a variety of catalytic systems. The eco-friendly catalyst with a green solvent system for synthesizing active intermediates is always part of appreciation among researchers. Eggshell powder as a catalyst will definitely be the most focused on meeting the bio-derived and eco-friendly nature challenge.

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