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## Recent advances in the catalytic exploitation of chitosan based catalysts in organic transformations

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### Abstract

Chitosan is obtained by the deacetylation of a naturally occurring biopolymer called chitin which is one of the key constituents of the shells of crustaceans. Chitosan has been exploited as a “green” catalyst in its native form as well as a solid support for carrying out various reactions. It offers several advantages like biodegradability, non-toxicity, biocompatibility, low cost, reusability etc. Advances in the exploitation of chitosan and its derivatives in various organic transformations are reported in this review.

**Keywords:** Chitosan, green catalysis, organic transformations, biopolymer

### Introduction

Even though the history of the development and applications of catalysis can be outlined as far back as the eighteenth century, then too catalyst research continues to be the most preferred fields in chemical research. In an effort to move towards ‘sustainable development’, organic synthesis is at the forefront of the development of energy efficient clean processes as well as products, making eco-efficiency and green chemistry as the new guiding principles of synthesis oriented research. Since catalysis is one of the most valuable principles out of twelve principles of Green Chemistry, a remarkable upsurge of interest has been observed in carrying out reactions using nontoxic, green and environmentally friendly catalysts in recent years. One of the emerging candidates, in this regard has been the use of natural biopolymers. The major advantages of employing such catalysts are that they are environmentally friendly, nontoxic, green and chiefly heterogeneous. One of the most promising catalyst in this category is chitosan that has gained considerable attention due to its exclusive features including biodegradability, non-toxicity, biocompatibility, low allergen city, low cost, reusability and its mucoadhesive properties <sup>[1]</sup>.

Chitosan is a natural polycationic linear polysaccharide, obtained by extensive deacetylation of isolated chitin under alkaline conditions and thus, is composed of  $\beta$ -(1-4)-linked d-glucosamine and *N*-acetyl-D-glucosamine units randomly distributed throughout the polymeric structure (Fig. 1). The composition of chitosan polymer is 44.11% carbon, 6.84%, hydrogen and 7.97% nitrogen. The amino groups present in the main backbone of chitosan impart positive charge to its surface in the acidic environment, in contrast to majority of polysaccharides which are generally neutral or negatively charged. This unique property of chitosan allows it to form electrostatic complexes and multi-layered structures with the other negatively charged polymers <sup>[2]</sup>. Chitosan has emerged to be a useful drug delivery carrier<sup>[3]</sup> and advantageous for various other biomedical applications <sup>[4]</sup> such as tissue engineering <sup>[5]</sup>, wound-healing <sup>[6]</sup> and obesity treatment <sup>[7]</sup> due to its polycationic nature, non-toxicity and biocompatibility. In addition, chitosan possess several biological properties, such as antitumor <sup>[8]</sup>, antioxidant <sup>[9]</sup> and antimicrobial <sup>[10]</sup> activities.

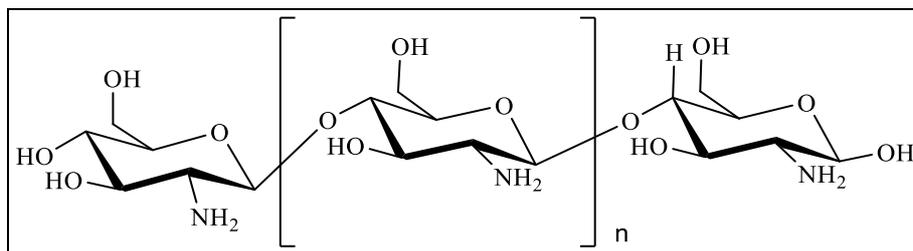


Fig 1: Structure of Chitosan

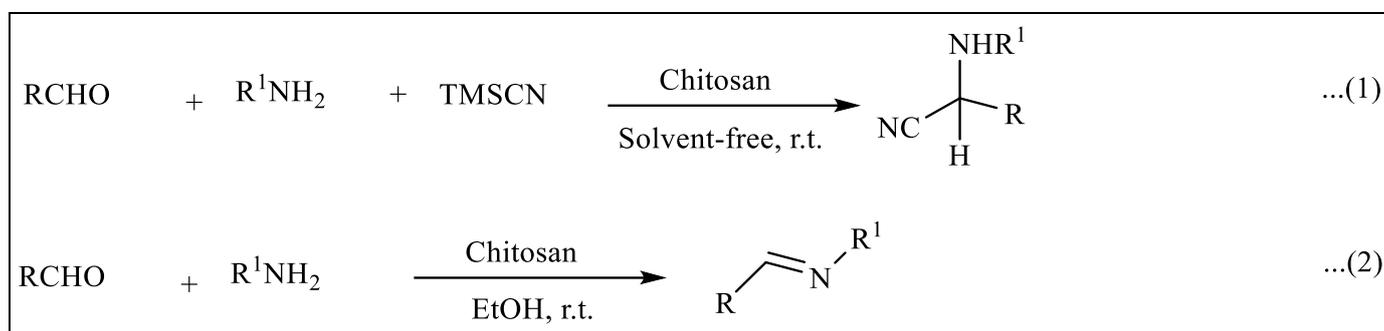
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Chitosan is derived from naturally occurring chitin, therefore, many of its physicochemical parameters such as degree of deacetylation, molar mass, crystallinity and viscosity depend upon the origin of the isolated chitin, the method for processing the biomass, and the extraction procedure [11,12]. These parameters greatly affect the various factors such as the processability, chemical reactivity, accessible surface area, surface polarity, and stability of chitosan [13]. Owing to its intrinsic properties such as hydrogen bonding, gel formation and self-assembly [1] chitosan provides a wide spectrum of opportunities for the preparation of chitosan-based nanomaterials such as nano and biomaterials [14, 15], microreactors [16], monoliths [17] and membranes [18]. Chitosan has been widely explored as a catalyst supporter to promote the efficiency of chemical reactions [19]. The presence of readily functionalizable hydroxyl and amino groups on the chitosan and its insolubility in organic solvents make it very attractive in the application [20]. The presence of various functional groups (e.g., amino and acetamido groups,

hydroxylic groups, and chiral centers) makes chitosan a versatile tool for the coordination of transition metals<sup>[21]</sup>, the stabilization of nanoparticles<sup>[22,23]</sup>, encapsulation of chemical drugs<sup>[24]</sup> and for supporting living organisms and enzymes<sup>[25]</sup>. This review attempts to highlight the progress achieved so far in the application of chitosan and its derivatives as catalyst in organic synthesis.

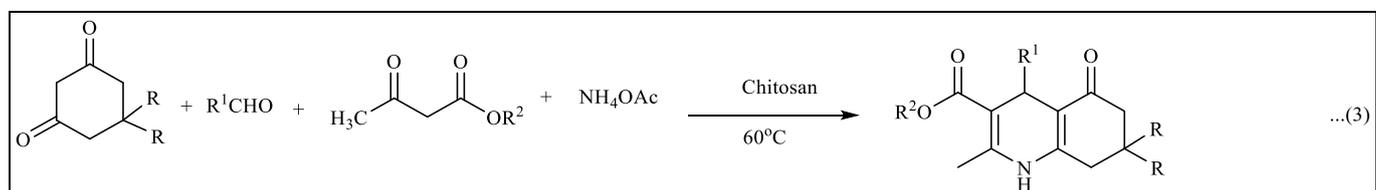
### Various Organic Transformations Catalyzed by Chitosan and its Derivatives

Solvent free Strecker synthesis of  $\alpha$ -aminonitriles has been described by reaction of amines, trimethyl silyl cyanide and aldehydes in presence of chitosan as catalyst at room temperature (eq. 1) by Dekamin *et al.* [26] They have also reported the chitosan catalysed synthesis of various imines *via* reaction of aldehydes and amines in ethanol at room temperature (eq. 2).



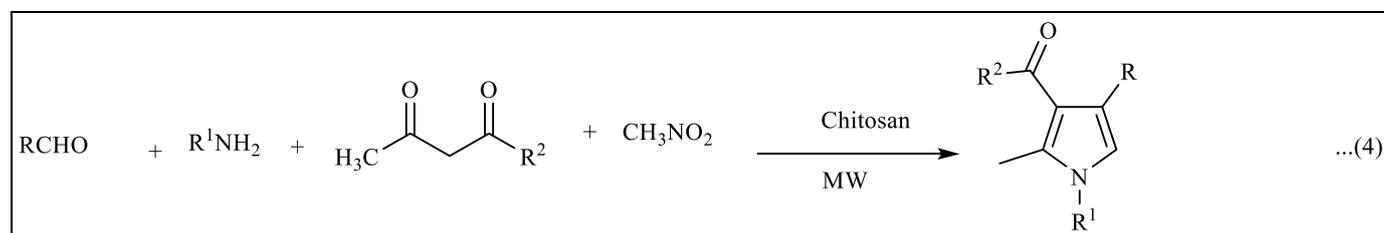
Zhalen *et al.* have described chitosan catalysed solvent free synthesis of 1,4-dihydropyridine derivatives *via* one-pot four-

component reaction of aldehydes, dimedone,  $\beta$ -ketoesters or acetoacetanilide and ammonium acetate at 60°C (eq. 3) [27].



The condensation of reaction of aldehydes, amines, 1,3-dicarbonyl compounds, and nitromethane afforded highly

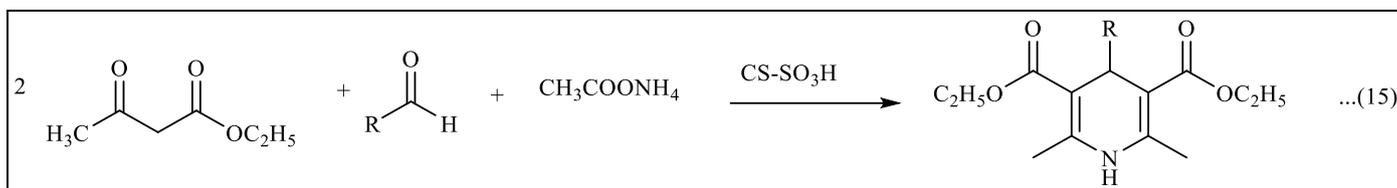
substituted pyrroles in presence of chitosan as catalyst under microwave irradiation (eq. 4) as reported by Hassani *et al.* [28].



Al-Matar and co-workers [29] have reported chitosan catalysed synthesis of 6-amino-5-cyano-2-methyl-4-phenyl-4*H*-pyran-3-carboxylic acid ethyl ester, 2-amino-4-phenyl-4*a*,5,6,7-tetrahydro-4*H*-naphthalene-1,3,3-tricarbonitrile, 2-amino-7-hydroxy-4-phenyl-4*H*-chromene-3-carbonitrile, 6-amino-3-methyl-4-phenyl-1,4-dihydro-pyrano[2,3-*c*]pyrazole-5-carbonitrile, 5-amino-2-(*Z*)-benzylidene-3-oxo-7-phenyl-2,3-dihydro-7*H*-thiazolo[3,2-*a*]pyridine-6,8-dicarbonitrile, 2-

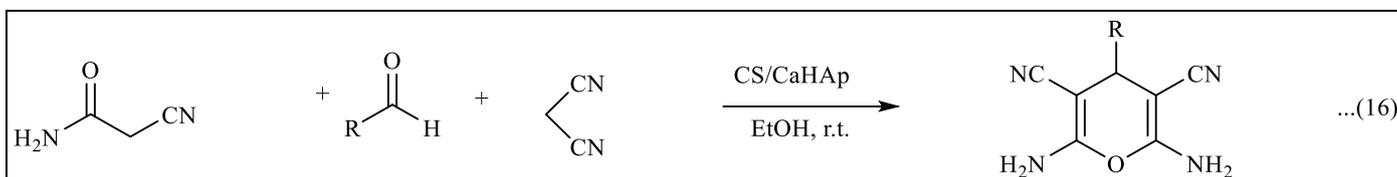
amino-4,6-diphenyl-benzene-1,3-dicarbonitrile, 2-amino-4-phenyl-4*H*-benzo[*h*]chromene-3-carbonitrile, 3-amino-1-phenyl-1*H*-benzo[*f*]chromene-2-carbonitrile *via* reaction of benzylidene-malononitrile with various active methylene compounds like ethyl acetoacetate, cyclohexanone, resorcinol, methylpyrazolone, 2-(1-phenylethylidene) malononitrile, thiazolylacetone, 1-naphthol, 2-naphthol respectively in ethanol under reflux conditions (eqs. 5-12).





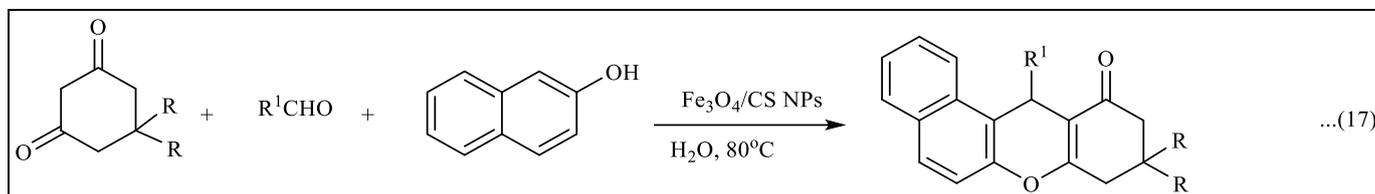
Chitosan-doped calcium hydroxyapatites (CS/CaHAPs) catalysed synthesis of 2,6-diamino-4-substituted phenyl-4H-pyran-3,5-dicarbonitrile derivatives has been reported by

three component condensation reaction of aldehyde, malononitrile and cyanoacetamide at room temperature in ethanol as solvent (eq. 16) [33].



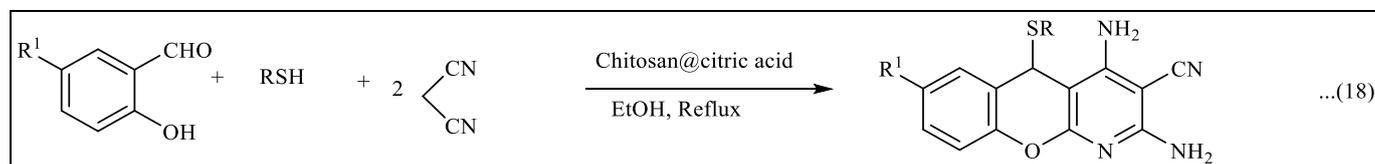
Tetrahydrobenzo [a]xanthene-11-ones were reported to be synthesized *via* one pot three component condensation of 2-naphthol with cyclohexane-1,3-dione derivatives and

aldehydes using chitosan-coated magnetic nanoparticles (Fe<sub>3</sub>O<sub>4</sub>/CS NPs) in water at 80°C (eq. 17) [34].



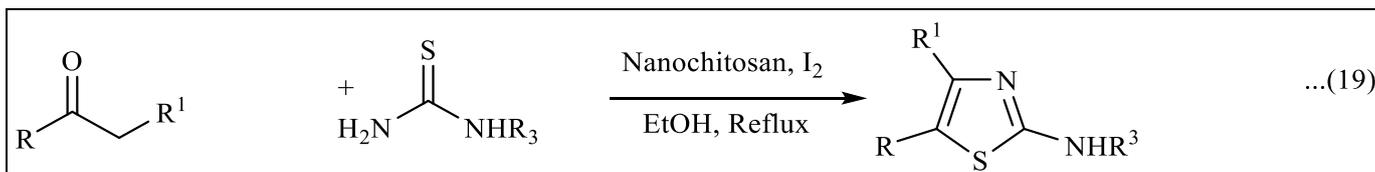
Chitosan functionalised by citric acid (CS@CA) has been employed as a catalyst for the synthesis of 2,4-diamino-5H-[1]benzopyrano[2,3b]pyridine-3-carbonitriles-5-(aryltio) or

5-[(arylmethylthio) substituted pyridines by one pot multicomponent reaction of salicylaldehydes, thiols and malononitrile in ethanol under reflux conditions (eq. 18) [35].



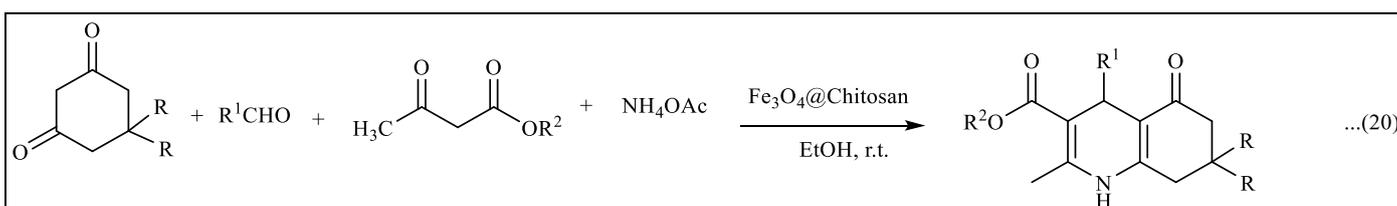
Synthesis of 2-aminothiazoles has been achieved by Safari *et al.* by one-pot reaction of ketone and thiourea in presence of

iodine and chitosan nanoparticle using ethanol as solvent under reflux conditions (eq. 19) [36].



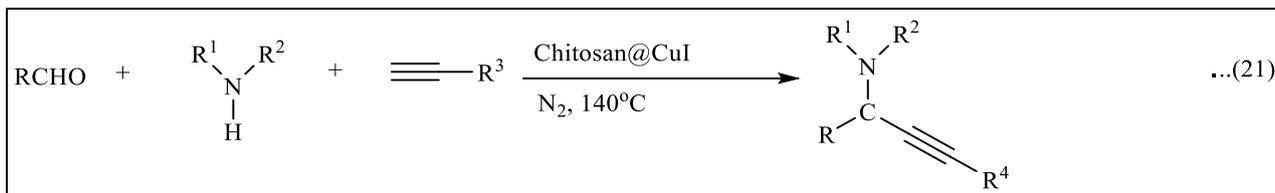
Maleki and co-workers [37] have reportedly synthesised 1,4-dihydropyridines by one pot four component reaction of several aldehyde, 1,3-cyclohexandione derivative, ethyl

acetoacetate or methyl acetoacetate and ammonium acetate catalyzed by magnetite/chitosan at room temperature (eq. 20).



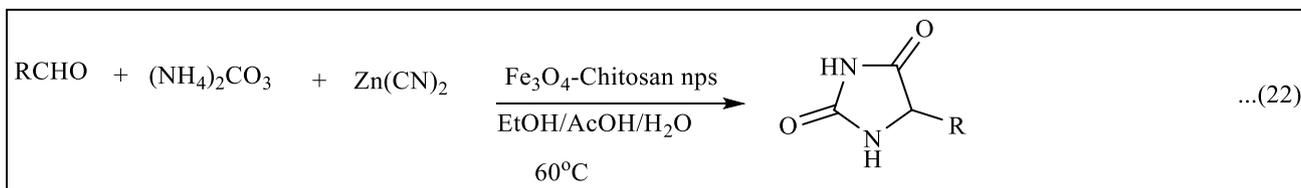
Chitosan supported copper catalyst (chit@CuI) has been reportedly used by Kaur and co-workers for the three

component coupling (A3-coupling) of aldehyde, amine and alkyne under solvent free conditions at 140°C (eq. 21) [38].



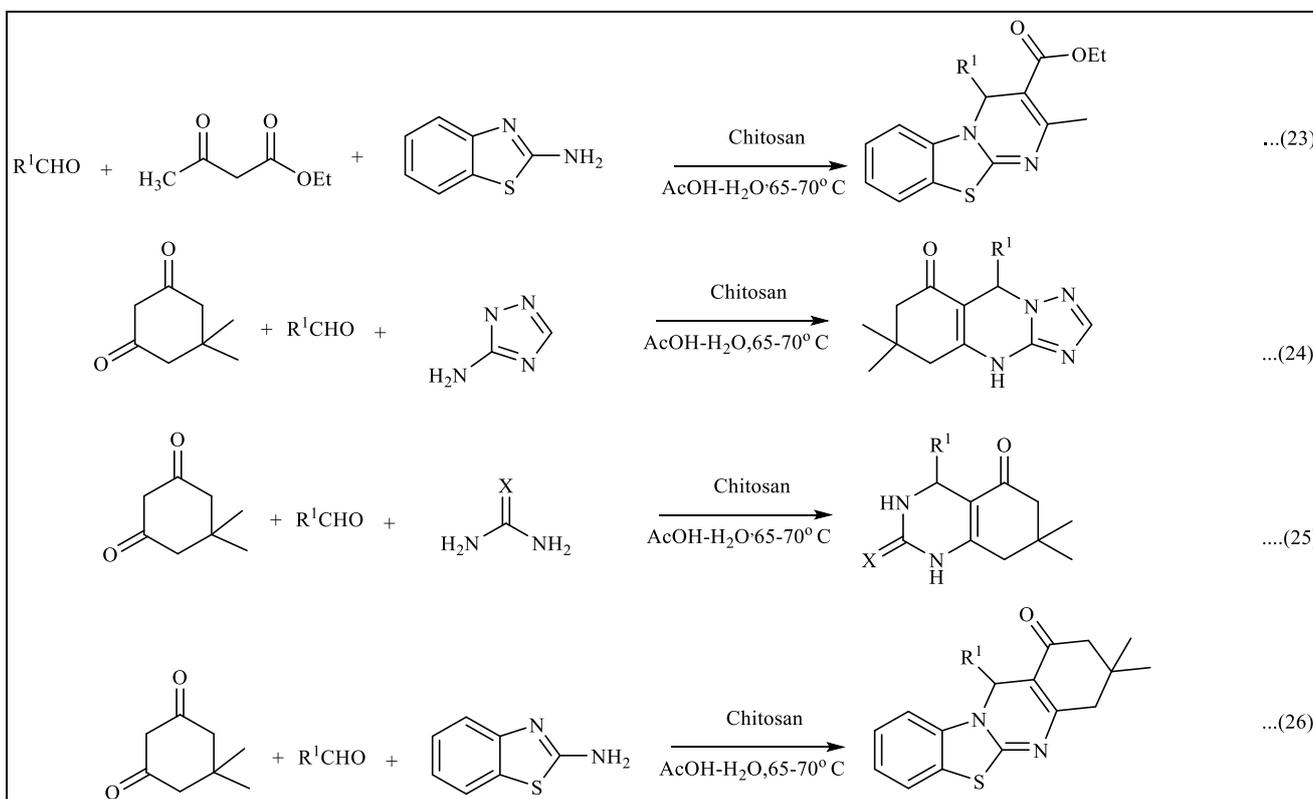
Synthesis of 5-substituted hydantoin can be accomplished by reaction of aldehydes, ammonium carbonate, zinc cyanide in presence of magnetic  $\text{Fe}_3\text{O}_4$ -Chitosan nanoparticles as in

ethanol:acetic acid: water system (1:1:1) (eq. 22) as reported by Safari *et al.* [39].



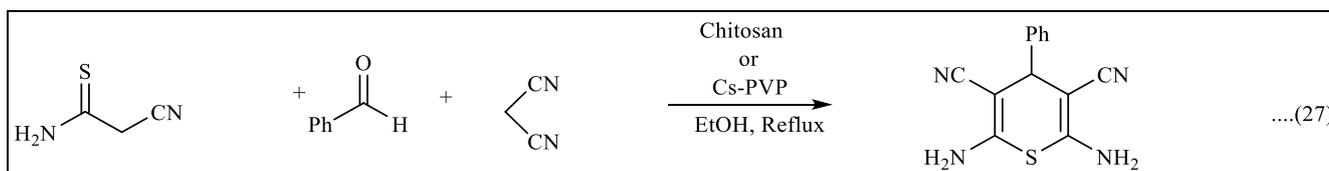
Sahu and co-workers [40] have described an efficient chitosan catalysed synthesis of 4*H*-Pyrimido [2,1-*b*] benzothiazole derivatives by reaction of ethyl acetoacetate, aldehydes and 2-aminobenzothiazole in acetic acid (2%) in aqueous media at 60–65 °C (eq. 23). They have also reported synthesis of 1,2,4-

triazoloquinazolines, octahydroquinazolinones, and fused thiazolo [2,3-*b*] quinazolinones by reaction of dimedone, aldehyde and 3-amino-1,2,4-triazole/ urea/thiourea respectively, under the same reaction conditions (eq. 24-26).



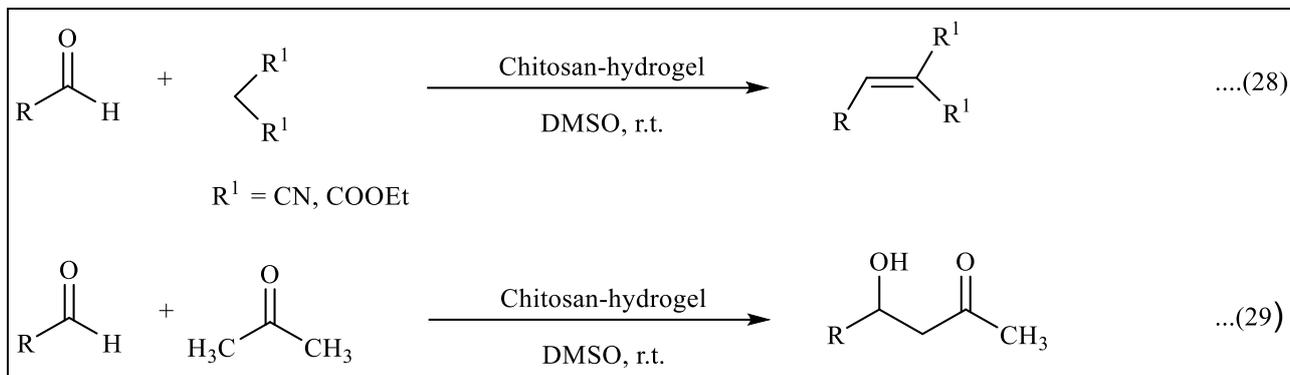
Chitosan as well as chitosan-grafted-poly(4-vinylpyridine) (Cs-PVP) copolymers were utilised as catalysts for the synthesis of thiopyran *via* one-pot condensation of

benzaldehyde, 2-cyanothioacetamide and malononitrile in ethanol under reflux conditions (eq. 27) [41].



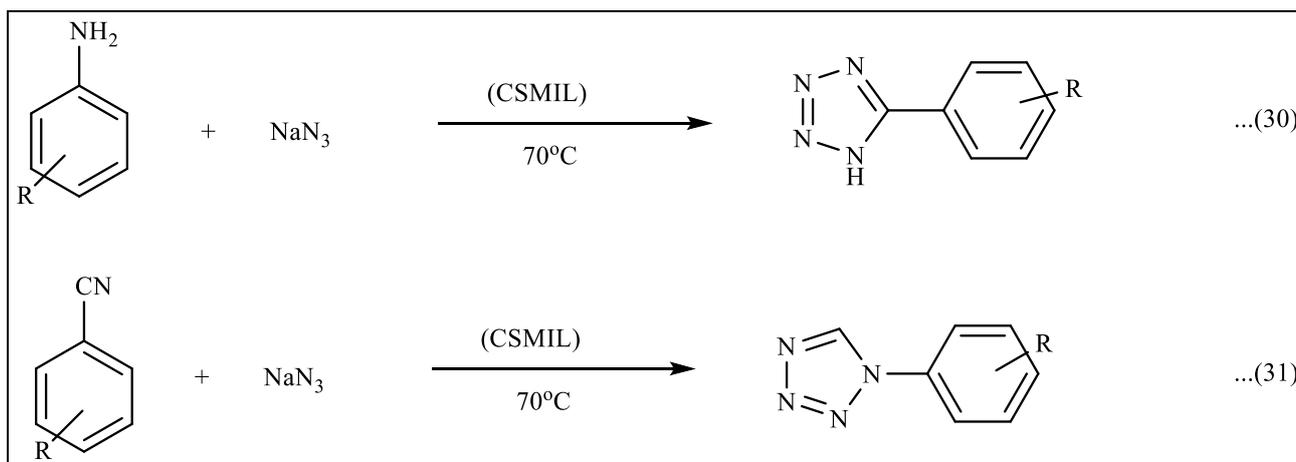
Chitosan hydrogel-catalyzed aldol reaction between acetone and aromatic aldehydes as well as Knoevenagel reactions

between aromatic aldehydes and active methylene compounds in DMSO (eq. 28-29) has been reported by Reddy *et al.* [42].



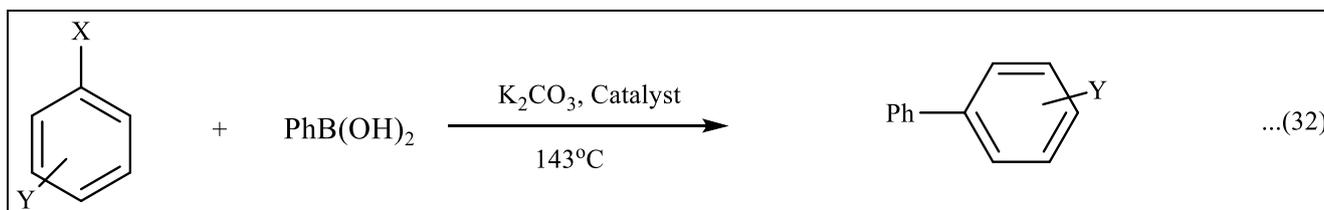
Chitosan supported magnetic ionic liquid nanoparticles (CSMIL) (which was prepared by reaction of chitosan and methyl imidazole with  $FeCl_3$ ) has been employed as catalyst

for the efficient synthesis of 1- and 5-substituted 1*H*-tetrazoles from nitriles and amines at 70°C under solvent-free conditions (eq. 30-31) [43].



Hardy and co-workers have utilised Chitosan-based Pd catalysts for Suzuki reaction, wherein reaction of substituted halobenzenes with phenyl boronic acid was carried out in

presence potassium carbonate and Chitosan-based Pd catalysts in xylene at 143°C [44].



## Conclusions

The present article intends to review the catalytic application of chitosan as an organocatalyst in its native form as well as modified chitosan in the field of organic synthesis. Chitosan, a biomaterial derived from the shells of crabs, lobsters, crayfish etc.. It offers the benefits of being renewable, biodegradable, non-toxicity, operational simplicity as well as low cost.

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