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

Haritma Chopra, Ankita Chaudhary and Ritu Gaba

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 field 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 [1].

Chitosan is a natural polycationic linear polysaccharide, obtained by extensive deacetylation of isolated chitin under alkaline conditions and thus, is composed of β-(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 [2]. Chitosan has emerged to be a useful drug delivery carrier [3] and advantageous for various other biomedical applications [4] such as tissue engineering [5], wound-healing [6] and obesity treatment [7] due to its polycationic nature, non-toxicity and biocompatibility. In addition, chitosan possess several biological properties, such as antitumor [8], antioxidant [9] and antimicrobial [10] activities.

![Fig 1: Structure of Chitosan](image-url)
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. These parameters greatly affect the various factors such as the processability, chemical reactivity, accessible surface area, surface polarity, and stability of chitosan. Owing to its intrinsic properties such as hydrogen bonding, gel formation and self-assembly, chitosan provides a wide spectrum of opportunities for the preparation of chitosan-based nanomaterials such as nano and biomaterials, microreactors, monoliths and membranes. Chitosan has been widely explored as a catalyst supporter to promote the efficiency of chemical reactions. The condensation of reaction of aldehydes, amines, 1,3-dicarbonyl compounds, and nitromethane afforded highly active 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 α-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. They have also reported the chitosan catalysed synthesis of various imines (via reaction of aldehydes and amines in ethanol at room temperature (eq. 2).

![Image](image-url)

Zhalen et al. have described chitosan catalysed solvent free synthesis of 1,4-dihydropyridine derivatives via one-pot four-component reaction of aldehydes, dimedone, β-ketoesters or acetoacanilide and ammonium acetate at 60°C (eq. 3).

![Image](image-url)

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.

![Image](image-url)

Al-Matar and co-workers have reported chitosan catalysed synthesis of 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylic acid ethyl ester, 2-amino-4-phenyl-4α,5,6,7-tetrahydro-4H-naphthalene-1,3,3-tricarbonitrile, 2-amino-7-hydroxy-4-phenyl-4H-chromene-3-carbonitrile, 6-amino-3-methyl-4-phenyl-1,4-dihydro-pyran[2,3-c]pyrazole-5-carbonitrile, 5-amino-2-(Z)-benzylidene-3-oxo-7-phenyl-2,3-dihydro-7H-thiazolo[3,2-a]pyridine-6,8-dicarbonitrile, 2-amino-4,6-diphenyl-benzene-1,3-dicarbonitrile, 2-amino-4-phenyl-4H-benzof[1]chromene-3-carbonitrile, 3-amino-1-phenyl-1H-benzof[1]chromene-2-carbonitrile via reaction of benzylidene-malononitrile with various active methylene compounds like ethyl acetooacetate, cyclohexanone, resorcinol, methylpyrazolone, 2-(1-phenylethylidene) malononitrile, thiazolylacetanilide, 1-naphthol, 2-naphthol respectively in ethanol under reflux conditions (eqs. 5-12).
Solvent free synthesis of benzopyranopyridine derivatives by Friedlander reaction of 4-amino-3-formylcoumarin with various active methylene compounds like ethyl acetoacetate, acetyl acetone, 1,3-dimethyl barbituric acid, 1,3-dimethyl thiobarbituric acid, malononitrile, Meldrum’s acid, 3,3-dimethyl cyclohex-1,3-dione, 4-hydroxy coumarin, indane-1,3-dione etc. in the presence of chitosan at 80°C (eq.13) [30].

Chitosan catalysed efficient synthesis of curcumin 3,4-dihydropyrimidinone derivatives has been described by Lal and co-workers via Biginelli condensation which involves one-pot condensation reaction of curcumin, aldehydes and urea/thiourea in 2% acetic acid in water as reaction media at 60 °C (eq. 14) [31].

Sulfonic acid functionalized chitosan (CS-SO$_3$H) was employed as a catalyst in the synthesis of 1,4-dihydropyridines (1,4DHPs) via the condensation reaction of aldehydes, ethyl acetoacetate and ammonium acetate (eq. 15) [32].
Chitosan-doped calcium hydroxyapatites (CS/CaHaps) catalysed synthesis of 2,6-diamino-4-substituted phenyl-4H-pyran-3,5-dicarbonitrile derivatives has been reportedly 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 (Fe₃O₄/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-[(arylthio) 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 1,4dihydropyridines 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 hydantoins can be accomplished by reaction of aldehydes, ammonium carbonate, zinc cyanide in presence of magnetic Fe₃O₄-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 4H-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, octahydroquinolinones, 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-cyanothiocetamide 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 FeCl₃) has been employed as catalyst for the efficient synthesis of 1- and 5-substituted 1H-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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