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ORIGINAL PAPER

Nanostarch: a novel and green catalyst for synthesis of 2-aminothiazoles

Javad Safari[1] · **Masoud Sadeghi**[1]

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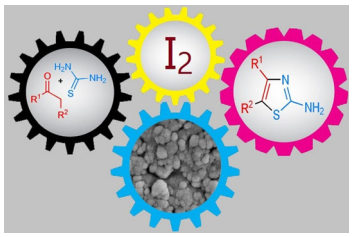
Abstract In this work, starch nanoparticles as a green and cheap catalyst were obtained based on the precipitation of amorphous starch in ethanol. It was found that starch nanoparticles are efficient catalyst for the synthesis of 2-aminothiazoles using methylcarbonyl compounds and thiourea as precursors. The use of green and biodegradable nanostarch makes this present methodology quite simple, shorter reaction times and milder conditions, and more convenient and economically viable compared to catalyzed methods reported in the literature.
Graphical abstract



Keywords Methylcarbonyl · 2-aminothiazoles · Nanostarch · Nanoparticle · Iodine

✉ Javad Safari
safari@kashanu.ac.ir;
safari_jav@yahoo.com

[1] Laboratory of Organic Chemistry Research, Department of Organic Chemistry, College of Chemistry and Biochemistry, University of Kashan, Kashan 87317-51167, Islamic Republic of Iran

Introduction

Starch like most natural polymers (such as chitin, chitosan, cellulose), is a natural, renewable, biocompatible, and biodegradable polymer that produced by many plants as a source of stored energy. Starch is the second most abundant natural polymer after cellulose. It has low cost and easily can be extracted from various plant parts, such as plant roots, stalks, seeds, and variety staple crops such as corn, potato, wheat, rice. Starch or amylum is a carbohydrate that consists of glucose monomer units that has two type arrangement, amylose and amylopectin. Amylose is a linear polymer of glucose units that are connected to each other through α-link (1–4). There are about 1.6 % of the glucose units connected by α-link (1–6) and they are attached to the main structure of amylose, which leads to the branched structure of amylose (Scheme 1). Amylopectin is a large and branched polysaccharide that the main structure of molecule is similar to amylose. In total, starch is formed from 20 to 30 % amylose and 70 to 80 % amylopectin [1–3].

The use of starch (or carbohydrates in general) as a catalyst has attracted much attention in recent years [4–6]. The main reasons for this attention are the cost, availability and biodegradability properties of carbohydrates.

Starch nanoparticles (NPs) have unique properties different from the bulk properties because of their nanometric size [7]. In recent year, new processes have been introduced to produce starch NPs, such as the precipitation of amorphous starch [8, 9], enzymatic hydrolysis and combining complex formation [10], microfluidization [11], ultrasonic irradiation [12], and ionic liquid [13]. There are a number of reports that have presented the use of functionalized starch NPs for organic reactions. However, to the best our knowledge, there are no similar applications for starch NPs as the catalyst in organic reactions [14–17].

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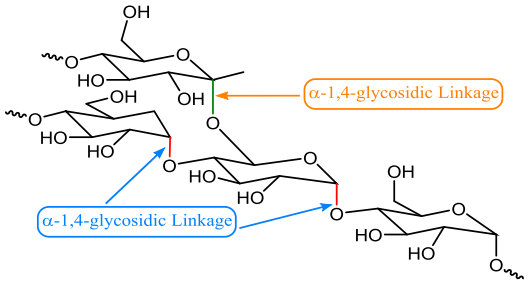
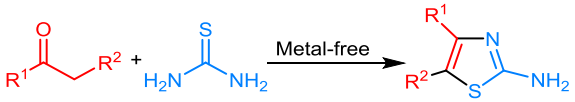
Scheme 1



Scheme 2



R^1= H, Ar, R, OR

R^2= H, -CH_2-COR

2-aminothiazoles have a special place in organic synthesis due to the medical and pharmaceutical applications [18, 19]. In the meantime, 2-aminothiazoles has been considered as a special case in recent years. There are various synthetic ways for preparation of 2-aminothiazoles [20–35]. The most straightforward and easy way for the synthesis of 2-aminothiazoles is the use of methylcarbonyl compounds and thiourea as the raw materials. The following protocols use acetophenone and thiourea as precursors for the synthesis of 2-aminothiazole: CuO/I_2 [36], $NaICl_2$ [37], O_2/KI/[Bmim]OTf [38], and CBr_4/Et_3N [39].

In recent paper, our group propose starch NPs for the synthesis of 2-aminothiazole in satisfied yield and fairly short time (Scheme 2).

Results and discussion

In the first of study, starch was modified to starch NPs by a precipitation process. The structural organization of starch NPs was investigated by FT-IR, SEM and XRD.

The FT-IR of starch and starch NPs were taken with KBr pellets and shown in Fig. 1. The characterization peaks in the starch spectrum are 3409 cm^{-1} (–OH stretching), 2926 cm^{-1} (C–H stretching) 1020 and 10158 cm^{-1} (C–O stretching). The characteristic absorption peaks in the FT-IR spectrum of starch NPs include 3427 cm^{-1} (–OH group), 2932, 1026 and 1155 cm^{-1} (C–O stretching). There is not much difference between two

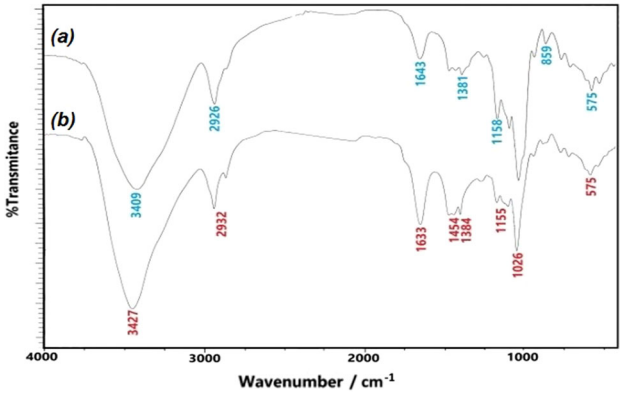


Fig. 1 **a** FT-IR spectra of starch (*blue*) and **b** starch NPs (*red*)

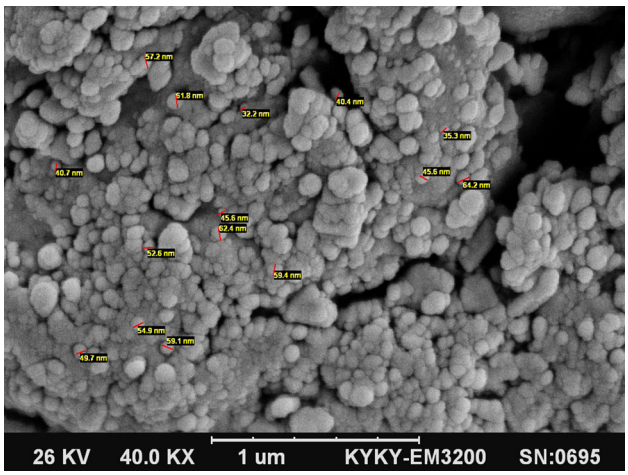


Fig. 2 SEM image of synthesized starch NPs

spectrums because of the chemical similarity of the two species. However, minor differences are visible due to the different particle size.

SEM image of synthesized starch NPs is shown in Fig. 2 the synthesized NPs have a good average diameter (70 nm).

The X-ray diffraction (XRD) patterns of the starch and starch NPs are shown in Fig. 3. The original starch gives three characteristic peaks at $2\theta = 11$ (weak diffraction peak), 14 (strong diffraction peak), and 27 (strong diffraction peak) indicating the high degree of crystallinity of starch. However, there are no similar peaks in the diffractograms of the starch NPs. The broad peaks in the X-ray diffraction of starch NPs are attributed to the increased amorphous nature of the starch NPs. The XRD of the starch NPs is characteristic of an amorphous polymer.

To investigate the feasibility of the synthetic method for the synthesis of 2-aminothiazoles, initial experiments were

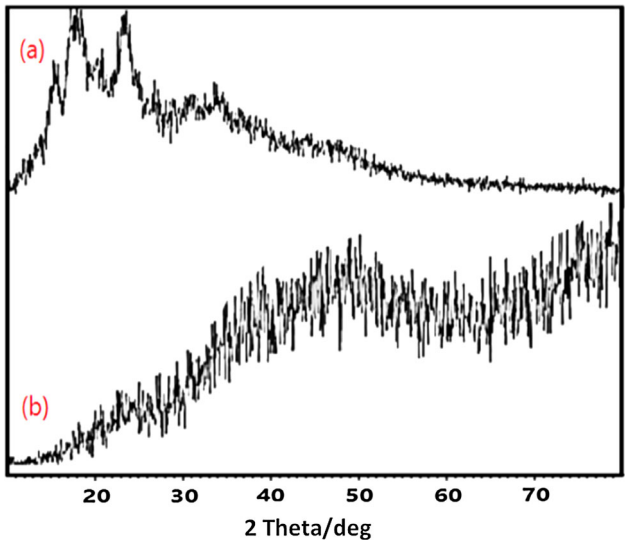
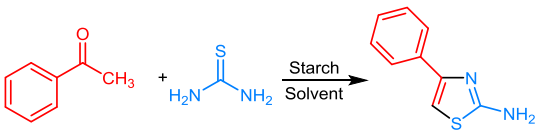


Fig. 3 X-ray diffraction patterns of the starch (**a**) and starch NPs (**b**)

performed using acetophenone, thiourea and iodine as reactants at 80 °C. A reaction model was carried out, to compare starch and starch NPs catalytic properties. The results were indicated, starch NPs have better efficiency than bulk case (Table 1, entry 3).

With regard to the Table 1, starch NPs was selected as the main catalyst and all reactions were carried out utilizing starch NPs. After that it was decided to search for the optimal conditions for the desired reaction. The various solvent and amounts of catalyst were used. In addition, the optimal temperature conditions were screened. The results indicate that DMSO is more efficient than other solvents such as EtOH, CH_3CN and EtOAc. The varying amounts of starch NPs were employed, and 10 mg was used as the best catalyst amount under the reaction conditions (Table 1, entry 10).

Table 1 Optimization of the reaction conditions



Entry	Nanocatalyst/mg	Solvent	Temperature/°C	Yield/%
1	–	–	80	65 [40]
2	50 (bulk starch)	EtOH	80	58
3	50	EtOH	80	65
4	50	**DMSO**	80	75
5	50	CH_3CN	80	55
6	50	EtOAc	80	60
7	40	DMSO	80	80
8	30	DMSO	80	75
9	20	DMSO	80	90
10	**10**	DMSO	80	**92**
11	5	DMSO	80	90
12	10	DMSO	70	85
13	10	DMSO	90	80

Reaction condition: acetophenone (1 eq), thiourea (1 eq), iodine (1 eq), and solvent stirred at 80 °C for 1 h

After determining the optimal conditions, we surveyed more substrates, and achieved the satisfactory results, which were prepared are summarized in Table 2.

Generally, α-hydrogen in aldehydes, β-ketoesters, and β-diketones has higher acid strength than ketones. The less pKa substrates, resulting in the more formation of the enol and more α-iodocarbonyl intermediate (Scheme 3). As expected, the methylcarbonyl substrates contain more acidic hydrogen (such as β-ketoesters entries 7, 8, and 9, β-diketone entry 10), showed better results than the cases containing less acidic hydrogen (such as entries 2–5).

The plausible mechanism for the formation of the 2-aminothiazoles is shown in Scheme 4. It is clear from the structure of starch that there are many hydroxyl groups (–OH) on the structure of starch. These hydroxyl groups can activate the methylcarbonyl substrates in the reaction by hydrogen bonding. The hydrogen bonding between the hydroxyl groups on the starch and the carbonyl group in the methylcarbonyl compounds is a key factor in the production of α-iodocarbonyl, nucleophilic attack of thiourea species at the α-position of α-iodocarbonyl, and the ring closure of thiazole. Studies showed that in the absence of a suitable catalyst, the α-iodocarbonyl species is not produced with a good yield [36].

In summary, we have demonstrated a simple and efficient protocol for the synthesis of 2-aminothiazoles using starch NPs as the catalyst. We have used methylcarbonyl compounds and thiourea as precursors. This method is very quick, and avoids the use of expensive reagents and high temperature.

Experimental

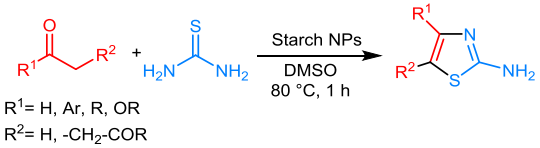
Materials

Chemicals were purchased from the Merck and Fluka chemical companies in high purity. All of the materials were of commercial reagent grade.

Apparatus

Melting points were determined using an Electrothermal 9100 apparatus and are uncorrected. FT-IR spectra were recorded as KBr pellets on a Shimadzu FT-IR-8400S spectrometer. ^{1}HNMR (400 MHz) and ^{13}CNMR spectra

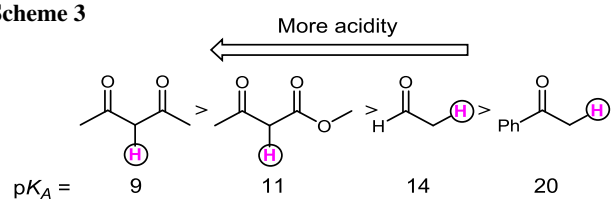
Table 2 Starch NPs catalyzed synthesis of 2-aminothiazoles



Entry	R^1	R^2	M.p. /°C	Lit. m.p. /°C	Yield /%
1	H	H	89–90	90–92 [29]	95
2	Ph	H	151–153	148–150 [35]	92
3	4-Cl-Ph	H	161–162	162–163 [35]	85
4	4-NO_2-Ph	H	285–286	286–287 [35]	96
5	3-Me-Ph	H	88–91	79–92 [29]	88
6	2-OH-Ph	H	138–139	139–140 [29]	84
7	4-OH-Ph	H	198–200	198–200 [35]	90
8	CH_3	COOEt	177–179	177–178 [29]	96
9	CH_3	COOMe	225–226	224–226 [29]	96
10	CH_3	$COOCH_2CH{=}CH_2$	148–149	148–150 [29]	97

Reaction condition: acetophenone (0.5 mmol), thiourea (0.5 mmol), iodine (0.5 mmol), starch NPs (10 mg) and DMSO (2 mL) stirred at 80 °C for 1 h

Scheme 3



were obtained using a Bruker DRX-400 AVANCE spectrometer. Analytical thin-layer chromatography (TLC) was accomplished on 0.2 mm precoated plates of silica gel 60 F-254 (Merck) or neutral alumina oxide gel 60F 254 (Merck). Morphological characteristics of the nanostructures were characterized using a scanning electron microscope (SEM, EVO LS 10, Zeiss, Carl Zeiss Inc., Germany) operating at an accelerating voltage of 20 kV under high vacuum.

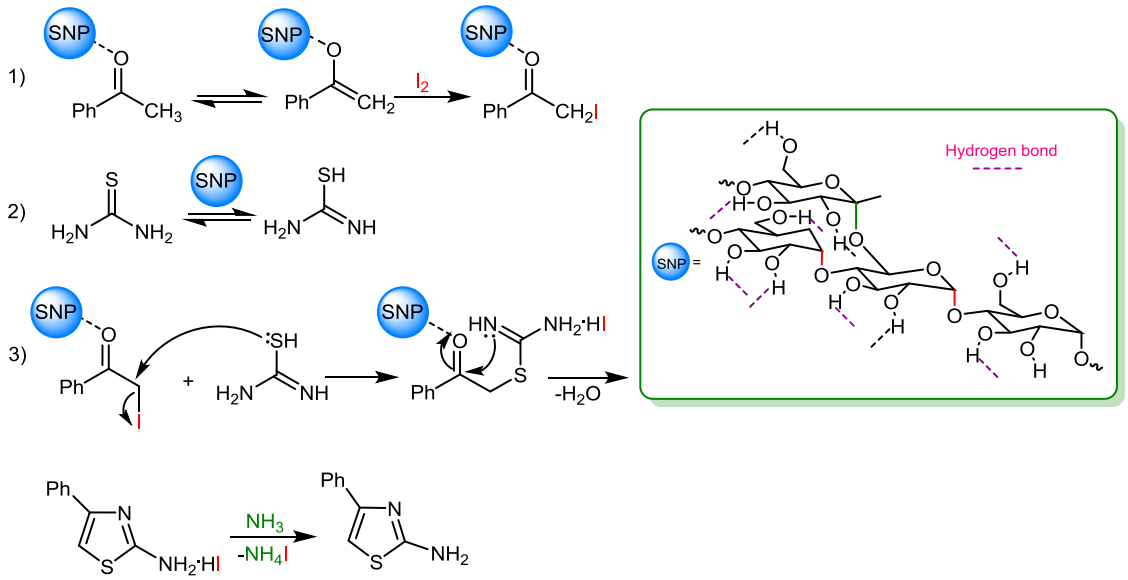
Procedure for preparation of starch NPs

Starch NPs were prepared using precipitation of amorphous starch. 8.2 g of starch was added into 35 mL of distilled water and then the mixture was heated at 90 °C. After constant stirring for 1 h to complete gelatinization of corn starch, 150 mL of absolute ethanol was added drop-wise to the previous solution with constant stirring. The resulting suspensions containing nanoparticle were cooled at the room temperature and another 35 mL of absolute ethanol was added drop-wise to the suspensions for 1 h with constant stirring. The suspensions were centrifuged and the prepared starch NPs were washed using absolute ethanol to remove the water. The starch NPs was dried at 50 °C to remove ethanol.

Procedure for preparation of 2-aminothiazole by starch NPs

A mixture of methylcarbonyl (0.5 mmol), thiourea (0.5 mmol), iodine (0.5 mmol), DMSO (2 mL) and 10 mg Starch NPs were stirred at 80 °C. After completion of the reaction (monitored by TLC, petroleum:ethyl acetate, 4:1), the reaction was quenched by the addition of 10 mL distilled water. The aqueous solution was extracted with EtOAc (3 × 10 mL) and the combined extract was dried with anhydrous Na_2SO_4. The solvent was vacuumed, and finally, the resulting precipitate was recrystallized by EtOH.

Scheme 4



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