Journal of Molecular Structure 1231 (2021) 129900

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstr

# Sodium alginate: Biopolymeric catalyst for the synthesis of 2-amino-4-arylthiazole derivatives in aqueous medium

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ARTICLE INFO

*Article history:*
Received 18 September 2020
Revised 3 December 2020
Accepted 29 December 2020
Available online 13 January 2021

*Keywords:*
2-amino-4-arylthiazol
Thiourea
Phenyl acetylene
Alginate/TBBDA

ABSTRACT

Regarded as a naturally occurring macromolecule and without any post-modification, sodium alginate which possesses a granular form was found to be an efficient and recoverable bifunctional heterogeneous organocatalyst for the synthesis of 2-amino-4-arylthiazole derivatives was carried out by the reaction of substituted phenyl acetylene and thiourea in an eco-friendly condition in the presence of TBBDA (tetrabromobenzene-1,3-disulfonamide (tetrabromobenzene-1,3-disulfonamide). Mild reaction conditions, simple reaction procedure, easy purification, high yields of products, eco-friendly catalyst usage and convenient reusability are the highlighted points of this protocol.



## 1. Introduction

Currently, noticing the environmental pollution and its effects on human life compels the researchers to develop procedures using eco-friendly materials and chemical methods. In this sense, chemical processes applying more eco-friendly catalysts, chemicals, solvents and atom-efficient processes would receive more and more attention [1,2]. Accordingly, heterogeneous catalysis – due to the products' higher purity the separation simplicity and recycling of the catalysts – has been regarded as a useful tool [3]. In this respect, a wide variety of heterogeneous catalysts has been developed by the immobilization of transition metals on the inorganic materials' surface, and synthetic organic polymers as support material [4-7]. Moreover, as alternative to synthetic organic polymers in heterogeneous catalytic systems, important attention has been paid to bioploymeric macromolecules. The biopolymers' popularity, i.e. starch, cellulose, chitosan, collagen, wool and alginates [8-10] would arise from their environmental sustainability. Nonetheless, macromolecules' use in pure form, as heterogeneous catalysts, has become basically significant due to the elimination of metals'toxicity, biodegradability and eco-friendly properties, cost-effectiveness and availability [11,12].

In this sense, it is worth mentioning that; sodium alginate plays a significant role as a natural and biodegradable polymer. Founded in the cell walls of brown algae, sodium alginate, which is the sodium salt of alginic acid, can be regarded as a natural anionic macromolecule.

Alginic acid is a polysaccharide distributed widely as a linear polysaccharide in the cell walls of the brown algae and as capsular polysaccharides in soil bacteria, In addition, it can be extracted from the main source in brown seaweeds of the class *Phaeophyceae*, such as *Ascophyllum nodosum*, *Laminariaspp*, etc. [13,14]. $\alpha$-(1→4)-L-guluronic acid (G) and $\beta$-(1→4)-D-mannuronic acid (M) were the monomers of alginate. Moreover, alginates can be regarded as true block copolymers, composed of homopolymeric regions of M and G blocks, interspersed with alternating MG blocks (Fig. 1).

Detailed investigations have shown that alginates have no regular repeating unit. The different proportions (M/G) depend on the source of the derived alginates [15]. Each of these has a different conformation and, therefore, physical behavior. Alginates have attracted considerable attention in the food, chemical and medicinal economies, paper, textile, agricultural industries and catalytic activity because of the abundant amounts and useful properties [16-21]. Simultaneously, one can find each monomeric unit of sodium alginate containing a carboxylate and two hydroxyl groups. Accordingly, the nucleophilic and electrophilic reaction constituents can be activated by carboxylate groups and hydrogen bonding as a bifunctional heterogeneous organocatalyst [22,23]. Due to their large surface area, biodegradable, and good biocompatibility, and alginate would basically receive great attention. Thus, alginate would greatly be applied; i.e. in drug delivery systems [24], tissue engineering [25], sensors [26] removal of pollution [27] and catalysts. Nowadays, sodium alginate – as a natural material – would be ap-

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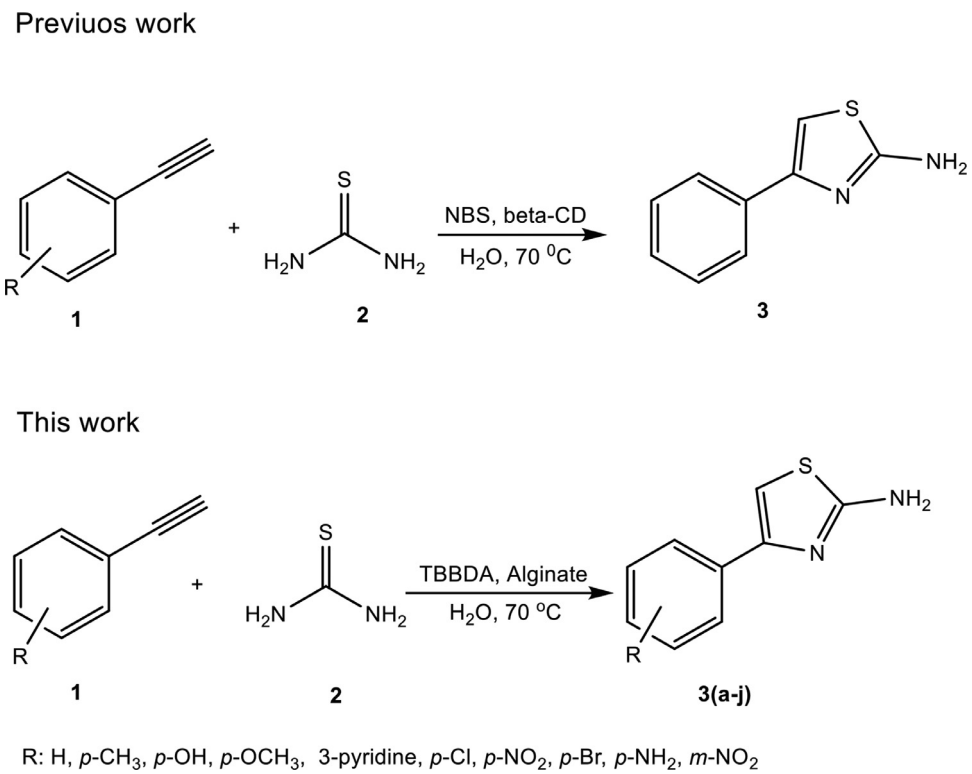
https://doi.org/10.1016/j.molstruc.2021.129900
0022-2860/




**Scheme 1.** Comparison of the previous method for the (A) synthesis of thiazole framework (B) with the present work.

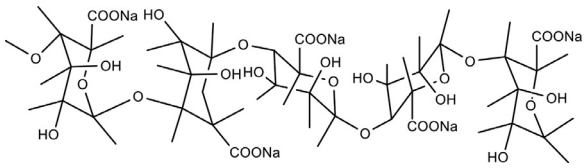


**Fig. 1.** Structure of Alginate.

plied as a solid catalyst in Suzuki cross-coupling [16], Mannich reaction [12], pyrimidone [28] and pyran synthesis [29].

Another point that should be considered is that solvent is an inseparable part of chemical reactions and, according to the rules of green chemistry, water is the best solvent because it is founds in nature and is environmentally friendly [30,31]**.** In recent years, organic reactions in water, due to the insolubility of materials and organic products in water, have been regarded as a big challenge. Accordingly, some natural biopolymers such as cellulose, chitosan, and alginates can be used for organic chemical reactions because of their green nature, environmental compatibility and absorbing water [29,32,33].

Moreover sodium alginate's capability in absorbing 200–300 times of its own weight [24] significantly indicates its catalytic activity. In this sense, it is so when the reaction's byproduct is water. These requirements are fully met in the multicomponent reaction (MCR) for the synthesis of 2-amino-4-aryl thiazole derivatives through condensation of different phenyl acethylene and thiourea.

Thiazole is one of the most important heterocyclic compounds and its role in many biologically active compounds and drug design is undeniable. Some examples containing thiazole are antineoplastic agents [34,35], anti-HIV drug [36], antifungal agent [37], antiparasitic agent [38], anti-inflammatory agents [39,40], antiulcer agent [41] and insecticide [42]. However, several protocols which have been reported for synthesis of thiazoles have been done using acetophenone [43-46] and phenacyl bromide [47,48]; but, there are few reports for the synthesis of thiazoles with substituted phenyl acetylene [49] and it can be introduced as a newer method than others. Moreover, phenacyl bromide as an intermediate has been produced *in-situ* with reaction between phenyl acetylene and TBBDA. In addition, the synthesis of these compounds under environmentally compatible conditions can be extremely important.

In continuous of our study on the preparation of thiazoles using TBBDA [43,50] and designing reactions according to green chemistry [51,52], herein, we report a mild and efficient procedure for the synthesis of thiazole derivatives in the presence of sodium alginate along with TBBDA in aqueous medium in order to reduce harmful effects of organic solvents (Scheme 1). Moreover, reaction time was reduced and different 2-amino-4-arylthiazole derivatives were synthesized. We believe that alginate can activate substrates or intermediates with carboxylate and hydroxyl group and act as a linear polymer support, making the related reaction at its surface easier. Considering these interpretations, this linear support is more suitable for larger molecules with more space than beta CD with a cyclic structure. As can participate more effectively in this chemical reaction, the number of active hydroxyl and carboxylate groups is more than betacyclodexterine.

## 2. Experimental

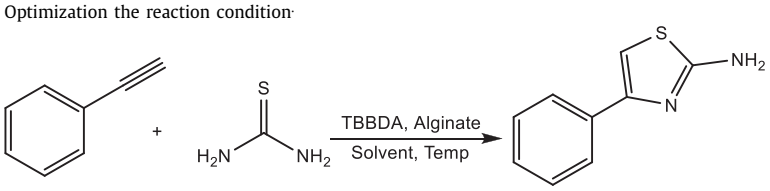
### 2.1. Chemicals

All commercial materials were purchased from Merck or Fluka companies and used without further purification. Sodium alginate (SA, low viscosity) was obtained from sigma-aldrich (China).

### 2.2. Apparatus

Nuclear magnetic resonance (NMR) spectra were recorded in DMSO–$d_6$ on Bruker Avance spectrometers of 250 MHz, 400 MHz and 500 MHz for 1H NMR and 62.5, 100 and 125 MHz for $^{13}$C

**Table 1**
Optimization the reaction condition[a]




1 2 3a

| Entry | Conditions | Time (h) | Yield (%)[b] |
|---|---|---|---|
| 1 | TBBDA (0.25 mmol), water, 70 °C, Alginate (0) | 8 | N.R |
| 2 | TBBDA (0.2 mmol), $H_2O$, 70 °C, Alginate (0.05 g) | 4 | 75 |
| **3** | **TBBDA (0.25 mmol), $H_2O$, 70 °C, Alginate (0.05 g)** | **2** | **87** |
| 4 | TBBDA (0.25 mmol), $H_2O$/EtOH, 70 °C, Alginate (0.05 g) | 2 | 72 |
| 5 | TBBDA (0.25 mmol), $H_2O$/MeCN, 70 °C, Alginate (0.05 g) | 2 | 63 |
| 6 | TBBDA (0.25 mmol), $H_2O$, RT, Alginate (0.05 g) | 4 | 44 |
| 7 | TBBDA (0.25 mmol), $H_2O$, Reflux, Alginate (0.05 g) | 2 | 87 |
| 8 | TBBDA (0.25 mmol), $H_2O$, 70 °C, Alginate (0.025 g) | 2 | 80 |
| 9 | TBBDA (0.25 mmol), $H_2O$, 70 °C, Alginate (0.1 g) | 2 | 88 |
| 10 | TBBDA (0.25 mmol), $H_2O$, 70 °C, Chitosan (0.1 g) | 5 | 40 |
| 11 | TBBDA (0.25 mmol), $H_2O$, 70 °C, Starch (0.1 g) | 24 | Trace |
| 12 | NBS (0.25 mmol), $H_2O$, 70 °C, Alginate (0.1 g) | 24 | 50 |
| 13 | HBr, $H_2O$, 70 °C, Alginate (0.1 g) | 24 | N.R |

[a]Reaction conditions: phenyl acetylene, TBBDA and thiourea in $H_2O$ (10 mL).
[b]Isolated yield.

NMR using TMS as an internal standard; chemical shifts were expressed in parts per million (ppm). Infrared (IR) spectroscopy was conducted on a Perkin Elmer GX FT-IR spectrometer. Mass spectra were recorded on a Shimadzu QP 1100 BX Mass Spectrometer. Melting points were determined on a Stuarf Scientific SMP3 apparatus. Energy dispersive X-ray (EDX) and Scanning electron microscopy (SEM) analysis of the prepared catalyst was fulfilled on a FESEM-SIGM (Germany) instrument.

### *2.3. General procedure for the synthesis of 2-amino-4-arylthiazoles*

In a round bottom flask (25 mL), a mixture of phenyl acetylene (1 mmol), TBBDA (0.25 mmol), thiourea (2 mmol) and sodium alginate (10 mol%) in $H_2O$ (10 mL) was stirred at 70 °C. The progress of the reaction was monitored by TLC (eluent: *n*-hexane–EtOAc, 6:1). Solvent was evaporated and, then, the crude product was dissolved in boiling water, extracted with ether (3 × 30 ml), and, finally adjusted to pH=10 with the amount of ammonia to gain the pure product. The products were characterized using physical and spectroscopic (IR, NMR, MS) data.

4-phenylthiazol-2-amine *(3a)*

Yellow solid, Yield: 87%, mp: 149–150 °C, [lit. mp: 148–150 °C] [56], IR (KBr): 3436, 3251, 1599 $cm^{-1}$.

$^1H$ NMR (250 MHz, DMSO–$d_6$): $\delta_H$ (ppm): 6.9 (s, 1H, thiazole H), 7.0 (s, 2H, $NH_2$), 7.24 (t, 1H, $J$ = 7.25 Hz, ArH), 7.36 (t, 2H, $J$ = 7 Hz, ArH), 7.7 (d, 2H, $J$ = 11.6 Hz, ArH).$^{13}C$ NMR (63 MHz, DMSO–$d_6$): 101.9, 125.9, 127.6, 128.9, 135.3, 150.3, 168.7 ppm. MS (*m/z*): 176.

4-p-Tolylthiazol-2-amine *(3b)*

Yellow solid, Yield: 85%, mp: 133–135 °C, [lit. mp: 130–132 °C] [56], IR (KBr): 3454, 3299, 1637$cm^{-1}$.

$^1H$ NMR (250 MHz, DMSO–$d_6$): $\delta_H$ (ppm): 2.2 (s, 3H, $CH_3$), 6.9 (s, 1H, thiazole H), 6.99 (s, 2H, $NH_2$), 7.15 (d, 2H, ArH, $J$ = 8.25 Hz), 7.67 (d, 2H, ArH, $J$ = 8.25 Hz), $^{13}C$ NMR (63 MHz, DMSO–$d_6$): $\delta_C$ 21.2, 101.0, 125.9, 129.4, 132.5, 136.88, 150.1, 168.6 ppm, MS (*m/z*): 190

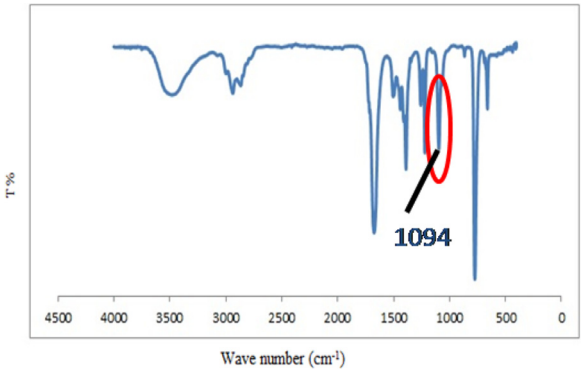



**Fig. 2.** IR spectrum of mixture in the middle of the reaction.

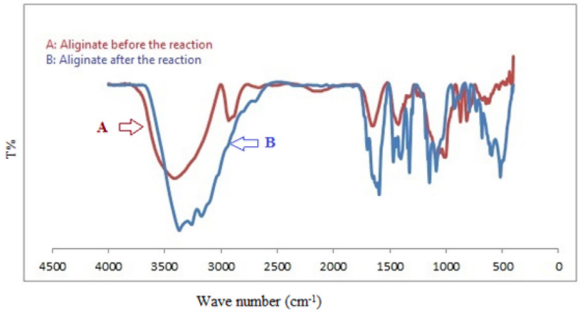


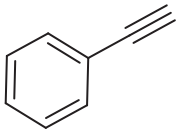
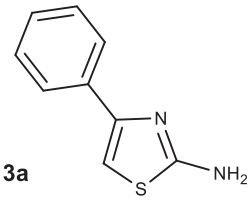
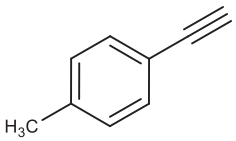
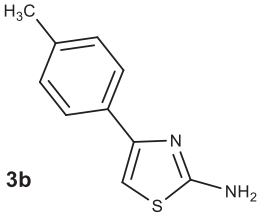
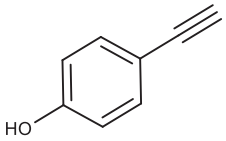
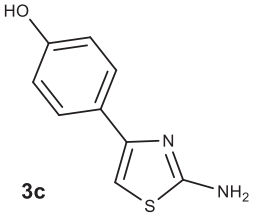
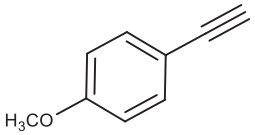
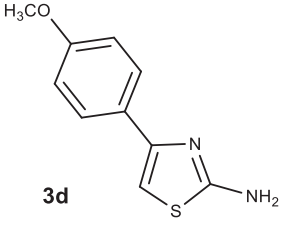
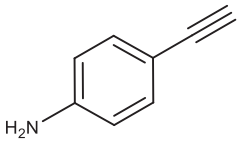
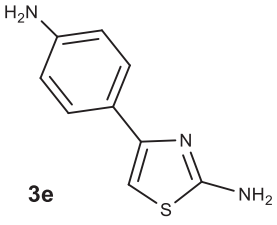
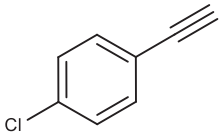
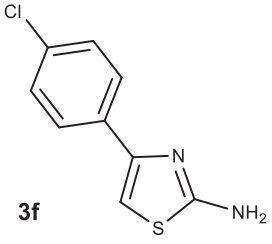
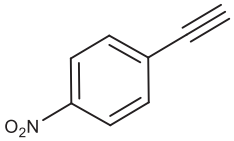
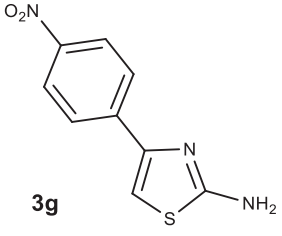

**Fig. 3.** IR spectrum for investigation of the recyclability of alginate as a catalyst.

4-(2-Aminothiazol-4-yl) phenol *(3c)*

Yellow solid, Yield: 74%, mp: 174–176 °C, [lit. mp: 175–177 °C] [56], IR (KBr): 3434, 3316, 1639 $cm^{-1}$.

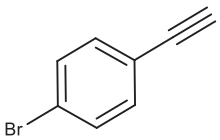
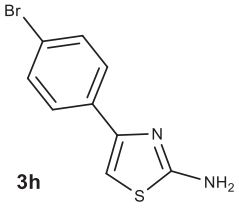
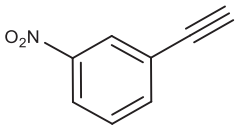
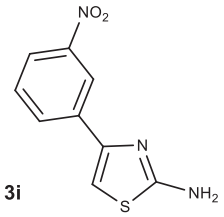
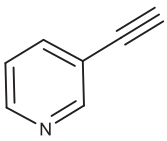
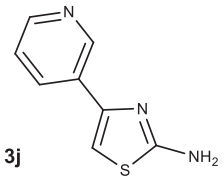
$^1H$ NMR (400 MHz, DMSO–$d_6$): $\delta_H$ (ppm) 6.71 (d, 2H, $J$ = 8.8 Hz, ArH), 6.83 (s, 1H, thiazole H), 7.37 (d, 2H, $J$ = 8.8 Hz, ArH), 8.62 (s, 1H, OH); $^{13}C$ NMR (100 MHz, DMSO–$d_6$): $\delta_C$ 99.8, 115.7, 119.7, 127.4, 139.3, 158.5, 170.1 ppm, MS (*m/z*): 192.

**Table 2**
Synthesis of 2-amino-4-arylthiazole **3(a-j)** using alginate/ TBBDA[a]

| Entry | Phenylacetylene | Time (h), Yield (%)[b] |
|---|---|---|
| 1 |  | (2 h, 87 %)  **3a** |
| 2 |  | (2 h, 85 %)  **3b** |
| 3 |  | (2 h, 74 %)  **3c** |
| 4 |  | (2 h, 80 %)  **3d** |
| 5 |  | (4 h, 80 %)  **3e** |
| 6 |  | (2 h, 92 %)  **3f** |
| 7 |  | (2 h, 94 %)  **3g** |

(*continued on next page*)

**Table 2** (*continued*)

| Entry | Phenylacetylene | Time (h), Yield (%)[b] |
|---|---|---|
| 8 |  | (2 h, 90 %)  **3h** |
| 9 |  | (3 h, 80 %)  **3i** |
| 10 |  | (4 h, 74 %)  **3j** |

[a]Reaction condition: phenylacetylene (1 mmol), thiourea (2 mmol), TBBDA (0.25 mmol) and sodium alginate (0.05 g) at 70 °C in $H_2O$ (10 mL).
[b]Isolated yield.

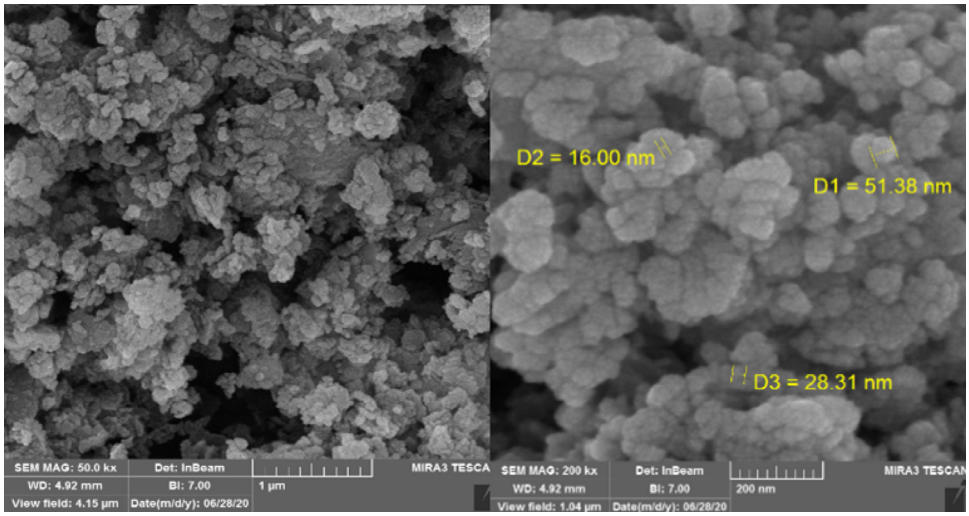



**Fig. 4.** SEM of sodium alginate.

4-(4-Methoxyphenyl) thiazol-2-amine *(3d)*

Yellow solid, Yield: 80%, mp: 200–202 °C, [lit. mp: 200–203 °C] [56], IR (KBr): 3439, 3284, 1634 $cm^{-1}$.

$^1H$ NMR (250 MHz, DMSO–$d_6$): $\delta_H$ (ppm): 3.76 (s, 3H, $OCH_3$), 6.81 (s, 1H, thiazole H), 6.91 (d, 2H, ArH, $J$ = 7.5 Hz), 6.95 (s, 2H, $NH_2$), 7.71 (d, 2H, ArH, $J$ = 7.5 Hz), $^{13}C$ NMR (63 MHz, DMSO–$d_6$): 55.5, 99.7, 114.2, 127.2, 129.3, 150.1, 158.9, 168.5 ppm, MS (*m/z*): 206.

4-(4-aminophenyl)thiazol-2-amine *(3e)*

Yellow solid, Yield: 80%, mp: 173–174 °C [lit. ref: 174–175 °C] [57].

4-(4-Chlorophenyl) thiazol-2-amine *(3f)*

White solid, Yield: 92%, mp: 205–207 °C, [lit. mp: 203–205 °C] [56], IR (KBr): 3439, 3284, 1634 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO–$d_6$): $\delta_H$ (ppm): 6.91 (1H, s, thiazole H), 6.95 (2H, s, $NH_2$), 7.26 (d, 2H, $J$ = 8.4 Hz, ArH), 7.6 (d, 2H, $J$ = 8.4 Hz, ArH), $^{13}C$ NMR (100 MHz, DMSO–$d_6$): 102.2, 127.1, 128.4, 131.4, 133.7, 148.5, 168.3 ppm, MS(*m/z*): 210.

4-(4-Nitrophenyl) thiazol-2-amine *(3g)*

White solid, Yield: 94%, mp: 284–286 °C, [lit. mp: 283–285 °C] [56], IR (KBr): 3398, 3302, 1641 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO–$d_6$): $\delta_H$ (ppm): 7.11 (2H, s, $NH_2$), 7.26 (1H, s, thiazole H), 7.9 (d, 2H, $J$ = 8.8 Hz, ArH) 8.08 (d, 2H,

$J$ = 8.8 Hz, ArH). $^{13}$C NMR (100 MHz, DMSO–$d_6$): 106.5, 123.9, 126.2, 140.7, 145.9, 147.6, 168.5 ppm, MS (*m/z*): 221.

4-(4-Bromophenyl) thiazol-2-amine *(3h)*

Yellow solid, Yield: 90%, mp: 228–230 °C, [lit. mp: 227–230 °C] [56], IR (KBr): 3388, 3283, 1634 cm$^{-1}$.
$^1$H NMR (250 MHz, DMSO–$d_6$): $\delta_H$ (ppm): 7.09 (s, 1H, thiazole H), 7.12 (s, 2H, $NH_2$), 7.54 (d, 2H, $J$ = 8 Hz), 7.73 (d, 2H, $J$ = 8 Hz), $^{13}$C NMR (62.5 MHz, DMSO–$d_6$): $\delta_c$: 102.8, 120.5, 128.0, 131.8, 134.5, 149.0, 168.8 ppm, MS (*m/z*): 255.

4-(3-Nitrophenyl) thiazol-2-amine *(3i)*

Yellow solid, Yield: 80%, mp: 285–286 °C, [lit. mp: 282–283 °C] [58], IR (KBr): 3431, 3296, 1634 cm$^{-1}$.
$^1$H NMR (500 MHz, DMSO–$d_6$): $\delta_H$ (ppm): 7.21 (s, 2H, $NH_2$), 7.32(s, 1H, thiazole H), 7.64 (t, 1H, $J$ = 8.15 Hz), 8.09 (d, 1H, $J$ = 8.15 Hz), 8.22 (d, 1H, $J$ = 8.15 Hz), 8.60 (s, 1H, ArH), $^{13}$C NMR (125 MHz, DMSO–$d_6$): $\delta_c$ 104.2, 119.8, 121.6, 130.0, 131.4, 136.3, 147.3, 148.2, 168.5 ppm, MS (*m/z*): 221.

4-(Pyridin-3-yl) thiazol-2-amine *(3j)*

Brown solid, Yield: 74%, mp: 198–200 °C, [lit. mp: 200 °C] [59], IR (KBr): 3320, 3149, 1676 cm$^{-1}$. $^1$H NMR (250 MHz, DMSO–$d_6$): $\delta_H$ (ppm) 6.98 (s, 1H, thiazole H), 7.21 (s, 2H, $NH_2$), 7.55 (t, 1H, $J$ = 6.25 Hz), 8.26 (d, 1H, $J$ = 7.25 Hz), 8.78 (d, 1H, $J$ = 5 Hz), 9.11 (s, 1H, ArH), $^{13}$C NMR (62.5 MHz, DMSO–$d_6$): $\delta_c$: 111.4, 122.1, 130.5, 132.2, 138.3, 147.8, 149.4, 168.5 ppm.

## 3. Results and discussion

Initial studies were carried out using phenyl acetylene, thiourea in the absence of sodium alginate and it found trace amount of product (Table 1, entry 1). Afterwards, the reaction was checked in the presence of alginate/TBBDA (Table 1, entries 2, 3) and, then, the amount of TBBDA was investigated. The data of Table 1 show that the best amount is 0.25 mmol (Table 1, entry 3). Because of hydrophilic structure of alginate, we tried some organic solvents with water (Table 1, entries 1–5); but, according to table 1, using $H_2O$ as solvent resulted in increased yields. Subsequently, the effect of temperature has been checked on the reaction (Table 1, entries 6, 7). The best result was observed at 70 °C (Table 1, entry 3). Sodium alginate plays a basic role in this reaction and it is considered as an advantage to accelerate this reaction. Based on results of entries 8 and 9, optimum amount of sodium alginate was chosen 0.05 g or 10 mol% (Table 1, entry 3). Due to the structural similarity of starch and chitosan with alginate, the progress of the reaction in the presence of starch and chitosan was examined; but, the corresponding product was obtained with low efficiency (Table 1, entries 10, 11). Finally, we examined the model reaction using NBS and HBr along with sodium alginate. As can be seen in Table 1, the TBBDA/alginate exhibited superior behavior in the synthesis of the product as compared to NBS or HBr (entries 12–13 vs 3).

In this sence, a wide range of substituted phenyl acetylene with both electron-withdrawing and electron-donating groups was used to synthesize 2-amino-4-arylthiazole derivatives by green conditions (Table 2). It was also observed that the substituted phenyl acetylene containing electron-donating groups (Table 2- entries 2–5 & 10), leads to decrease the yield of the corresponding products. The substituted phenyl acetylene containing electron-withdrawing groups (Table 2, entries 6–9) has better results. The excellent yields of 2-amino-4-arylthiazoles were obtained with *para*-substituted phenyl acetylene containing electron-withdrawing groups within the lowest reaction time, i.e. 4-(4-chlorophenyl)thiazol 2-amine **3f**, 4-(4-nitrophenyl)thiazol-2-amine **3g** and 4-(4-bromophenyl)thiazol 2-amine **3h**.

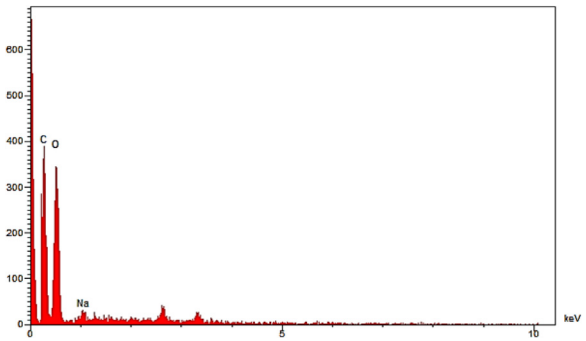



**Fig. 5.** EDS spectrum of sodium alginate.

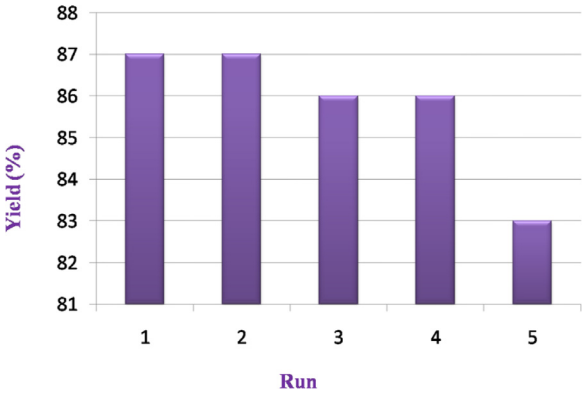



**Fig. 6.** Recycling of catalyst for synthesis of 4-phenylthiazol-2-amine.

Since alginate is known as linear polymer, it can be used as a support for the interaction of reactants. The interaction between alginate and phenyl acetylene was investigated and it was shown revealed that, in the absence of alginate, the reaction would take longer than when alginate reacted in the reaction media. This indicates that phenyl acetylene or TBBDA is activated by alginate. The role of alginate was illustrated by IR spectrum of mixture of the model reaction for 60 min (the reaction was completed in 120 min) (Fig. 2). It showed that the peak of $C = S$ bond in 1036 cm$^{-1}$ has been moved to 1094 cm$^{-1}$ indicating that thiourea is activated by alginate. The recyclability of alginate as a catalyst was investigated by reaction of phenyl acethylene (1 mmol), TBBDA (0.25 mmol), and thiourea (2 mmol) in $H_2O$ as a model. After 5 times, the structure of catalyst didn't make much difference (Fig. 3).

Chemical characterization of sodium alginate has been provided with SEM and EDX analysis. SEM was applied to obtain information on the surface morphology. In the SEM images, sodium alginate shows microspherical shape (Fig. 4).

The EDX peaks in Fig. 5 shows the peak of C, O and Na in the sodium alginate structure. The amount of percentage of weight and atomic is given in the Table 3.

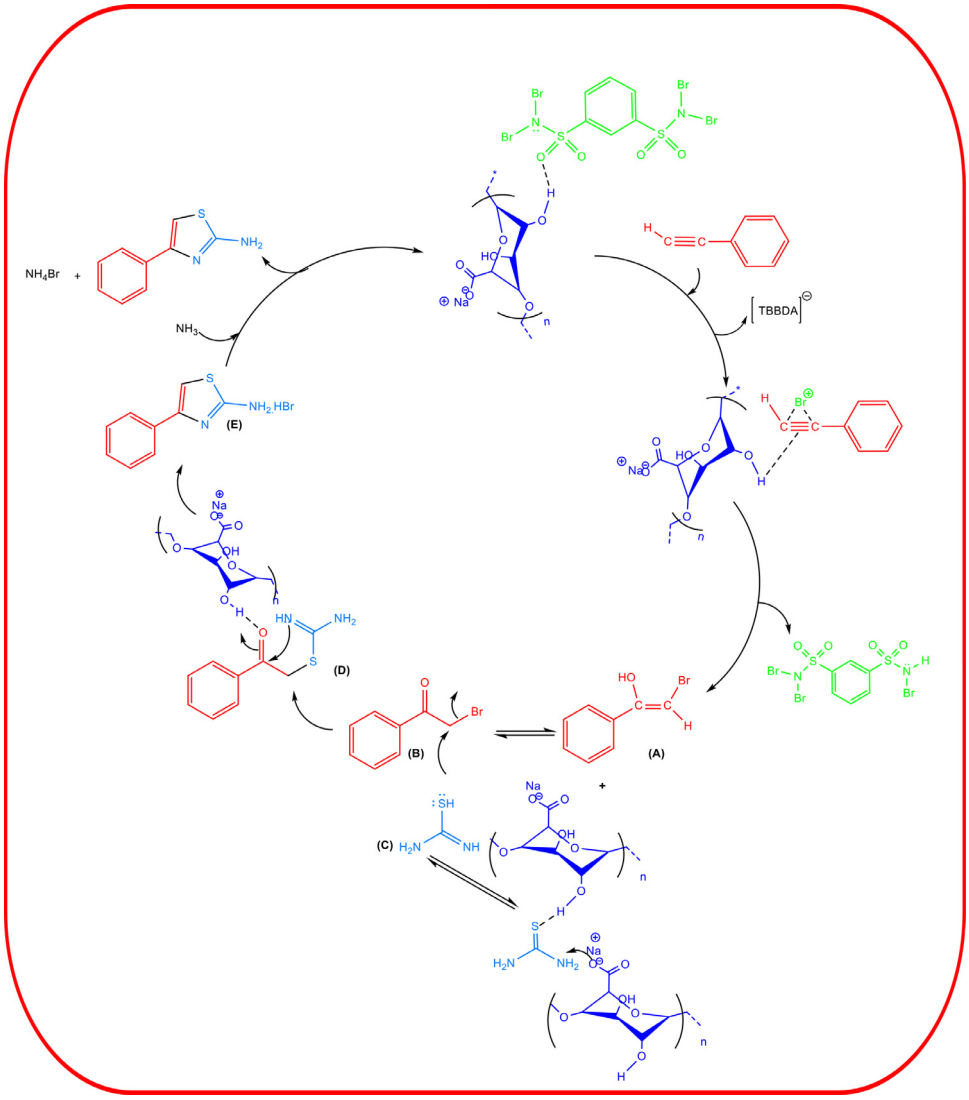
**Table 3**
Atomic composition of sodium alginate determined by EDX.

| Element | Weight (%) | Atomic (%) |
|---|---|---|
| C | 44.95 | 52.27 |
| O | 53.78 | 46.96 |
| Na | 1.27 | 0.77 |

**Table 4**
Comparison of the present methodology with the reported catalysts for the synthesis of 3a. [a].

| Entry | Catalyst | Temperature( °C) | Time (h) | Yield (%) |
|---|---|---|---|---|
| 1 | NBS/$\beta$-CD | 70 | 4 | 72 |
| 2 | TBBDA/Alginate | 70 | 2 | 87,86,86,83[this work] |

[a] Reaction condition: phenylacetylene (1 mmol), thiourea (2 mmol) at 70 °C in $H_2O$ (10 mL).




**Scheme 2.** Possible mechanism of synthesis of 2-amino-4-arylthiazoles over TBBDA/alginate.

After completion of the reaction, the catalyst was easily separated from the reaction medium by filtration. Recyclability of catalyst was investigated (Fig. 6). The catalyst was washed with acetone, ethanol and dried in air. The recovered catalyst can be reused for five rounds without any losing of catalytic properties (87, 87, 86, 86, 83).

As compared to the previous work [49] we did this protocol with better yield in shorter time, the use of alginate as an environmentally friendly material with its unique structure has highlighted our approach (Table 4, entry 2). This compound has a higher TOF than $\beta$-cyclodextrin and also has a high thermal stability. Furthermore TBBDA has more distinctive features than NBS such as high resistance, releasing more bromine than other resource and can happen easily. Morevever TBBDA is insoluble in $H_2O$ as it can be an advantage to purify the product [53–55].

The plausible mechanism for this reaction is shown in Scheme 2. The reaction starts when hydrogen bonding is formed between the–OH groups which exist on the alginate and the oxygen of sulfonyl group in TBBDA. Evidently the TBBDA would easily release $Br^+$. During the second step, phenyl acetylene was activated by sodium alginate through hydrogen bonding. Afterwards the reaction between TBBDA (0.25 mmol) and phenyl acetylene (1 mmol) produced phenacyl bromide **B**. In addition under basic conditions by sodium alginate, thiourea was converted to enol **C**. Significantly, the most important issue in the third step would be the hydrogen bonding between the–OH groups and carbonyl groups in $\alpha$–bromo ketones B. Accordingly, intermediate **D** would be afforded by the subsequent reaction of the **B** with thiourea **C**, resulting in an intramolecular nucleophilic addition/dehydration reaction to generate **E** in the presence of alginate. Finally, intermediate **E** undergoes neutralization reaction to furnish the de-

sired aminothiazole product. In this mechanism, alginate with hydroxyl and carboxylate groups played catalytic role *via* activating the thiourea, phenyl acetylene, intermediates and TBBDA with hydrogen bonding and the basic catalytic activity.

## 4. Conclusion

In conclusion, 2-amino-4-arylthiazole derivatives were synthesized with reactions of the substituted phenyl acetylene and thiourea in aqueous phase. Using the sodium alginate as an environmentally friendly, available and nontoxic catalyst is the point of interest of this protocol. Easy purification, reusability, high thermal and chemical stability of the catalyst, high selectivity with different electron-withdrawing and electron-donating groups, eco-friendly conditions and high efficiency are other benefits of our work.

## CRediT author statement

Samareh Gorji: Doing laboratory work, preparing data and writing. Ramin Ghorbani-Vaghei: Supervisor and presenter of research work and results analysis. Sedighe Alavinia: Editing

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

The authors wish to thank Bu-Ali Sina University, Center of Excellence Developmental of Environmentally Friendly Methods for Chemical Synthesis (CEDEFMCS).

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.molstruc.2021.129900.

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