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Nano-$TiCl_2$/cellulose: an eco-friendly bio-based catalyst for one-pot synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazole derivatives

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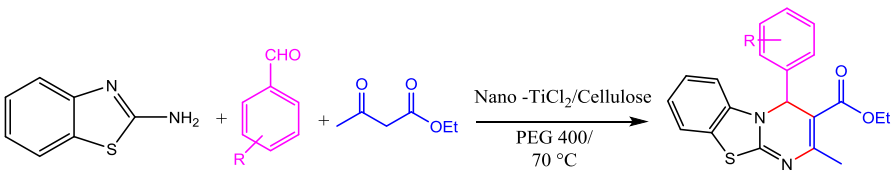
Abstract Cellulose is among the most abundant natural carbon-based biopolymers containing free OH groups with nucleophilic character for bonding to Lewis acids such as $TiCl_4$. Nano-$TiCl_2$/cellulose as a bio-based and eco-friendly Lewis acid catalyst was prepared via reaction of nano-cellulose and $TiCl_4$ in dichloromethane as solvent under room temperature conditions. This catalyst has been characterized by Fourier transform infrared spectroscopy, field emission scanning electron microscopy, powder X-ray diffraction, energy dispersive X-ray spectroscopy, X-ray fluorescence techniques, and transmission electron microscopy. Nano-$TiCl_2$/cellulose has been shown to effectively promote multi-component synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazole derivatives by reaction of aldehydes, β-ketoester, and 2-amino benzothiazole under thermal conditions in polyethylene glycol 400 as solvent. Simple methodology,an eco-friendly catalyst, a clean procedure, easy work-up, and excellent yields are some of the important advantages of this protocol.

Graphical Abstract



R=H, 4-NO_2, 4-Cl, 4-Br, 4-OH, 2-NO_2, 2-Cl, 2-EtO, 3-NO_2, 3-OH, 2,4-$(Cl)_2$, 2,4-$(MeO)_2$, 3,4-$(OH)_2$

13 examples
68-97% yeild

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Keywords 4*H*-pyrimido[2,1-*b*]benzothiazole · Nano-$TiCl_2$/cellulose · Solid acid · Supported Lewis acid · Nano-cellulose · Bio-based catalyst

Introduction

Benzothiazoles and their condensed system make a broader class of nitrogen and sulfur-containing compounds with a wide range of biological activities [1–11]. Among condensed benzothiazoles, pyrimido[2,1-*b*]benzothiazoles have attracted considerable interest because of their potent and significant pharmacological activities. A survey of the literature revealed that pyrimido[2,1-*b*]benzothiazoles display various biological activities like anti-tumor [12, 13], anti-allergic [14], anti-inflammatory [15], anticonvulsant [16], antiproliferative [17], and antimicrobial activities [18–20].

In view of the importance of pyrimido[2,1-*b*]benzothiazoles, the development of effective strategies for the synthesis of these fused heterocyclic compounds will be interesting in both organic synthesis and medicinal chemistry. A common synthetic approach to pyrimido[2,1-*b*]benzothiazole derivatives involves three-component condensation of 2-amino benzothiazole, aldehydes, and *β*-ketoesters [21–24]. Previously, this protocol has been catalyzed by acetic acid [13], 1,1,3,3-*N*,*N*,*N*′,*N*′-tetramethylguanidinium trifluoroacetate (TMGT) [22], tetrabutylammonium hydrogen sulfate (TBAHS) [23], *N*-sulfonic acid modified poly(styrene-maleic anhydride) (SMI-SO_3H) [26], Chitosan [24] and aluminum chloride [27]. Some of these catalysts suffer from drawbacks such as long reaction times [21, 25], high working temperature [23] and low yield [22, 25]. Therefore, development of new solid acids with numerous advantages such as cost-effectiveness, environmentally benign, easy workup and good stability for the synthesis of pyrimido[2,1-*b*]benzothiazole derivatives is of prime importance. Hence, we aim to develop inexpensive and available solid acid bio-based catalysts for this transformation.

Considering the new trends of science and technology towards using natural materials such as cellulose, the research efforts on green and eco-friendly methods have become popular and desirable. Cellulose is one of the most abundant natural carbon-based biopolymers containing free OH groups with nucleophilic character. It has been used for synthesis of some compounds used in enantioselective chromatography [28], protein immobilization [29], antibodies [30] and retarded drug release [31]. Cellulose is a potentially biodegradable material that can also be used as an efficient support for bonding several functional groups to produce clean and impressive biopolymer-based catalysts [32]. Cotton is a natural, cheap, and readily available source of cellulose. In this study, we have investigated the preparation of nano-cellulose by sulfuric acid hydrolysis (65 wt% H_2SO_4,10 mL/g cellulose, 45 °C) of pure cellulose isolated from cotton and synthesis of nano-$TiCl_2$/cellulose by bonding $TiCl_4$ to OH groups of D-glucose units in nano-cellulose. We intend to report herein nano-$TiCl_2$/cellulose as a new, biodegradable, inexpensive and eco-friendly bio-based catalyst for one-pot synthesis of pyrimido[2,1-*b*]benzothiazoles via three-component reaction of aldehydes, ethyl acetoacetate and 2-amino benzothiazole under thermal conditions.

Materials and methods

General remarks

All compounds were purchased from Merck, Aldrich, and Fluka chemical companies and used without any additional purification. A refrigerated centrifuge (Appendorf Centrifuge 5417R) was used for preparation of nano-cellulose. FT-IR spectra were run on a Bruker, Equinox 55 spectrometer. A Bruker (DRX-400 Avanes) NMR was used to record the ^{1}H-NMR and ^{13}C-NMR spectra. Melting points were determined by a Buchi melting point B-540 B. V. CHI apparatus and were uncorrected. X-ray diffraction (XRD) patterns were obtained by a Philips Xpert MPD diffractometer equipped with a Cu Ka anode (k = 1.54 Å) in the 2θ range from 10° to 80°. Field emission scanning electron microscopy (FESEM) was obtained on a Mira 3-XMU. Transmission electron microscopy (TEM) was obtained using a Philips CM120 with a LaB6 cathode and accelerating voltage of 120 kV. Quantitative elemental information (EDS) of nano-$TiCl_2$/cellulose was measured by an EDS instrument and Phenom pro X. XRF analysis was done using a Bruker, S4 Explorer instrument.

Preparation of nano-cellulose from cotton

Cotton fibers were washed with distilled water several times and dried in an air-circulated oven at 100 ± 2 °C until constant weight. Then, they were chopped to an approximate length of 5–10 mm. The fibers were then treated with a 17.5 w/v NaOH solution at 100 °C for 12 h under mechanical stirring. This treatment allowed purifying cellulose by removing other constituents like lignin, hemicellulose, wax, organic acids and so on present in the fibers. Subsequently, fibers were filtered and washed with distilled water until the alkali was completely eliminated. It was then bleached with 100 mL of 1:1 aqueous dilution of 3.5 % w/v sodium hypochlorite at 80 °C for 3 h under mechanical stirring. The resulting alpha cellulose was partially hydrolyzed using 65 % sulfuric acid aqueous solution with a cotton-to-acid weight ratio of 1–10 at 45 °C. After 1 h, the obtained suspension was diluted with water fivefold to stop the hydrolysis reaction. The suspension was centrifuged at 12,000 rpm to separate the nano-cellulose from acid solution. The washing with water and centrifuging was repeated four to five times to remove any remaining free acid.

Preparation of nano-$TiCl_2$/cellulose

In a well-ventilated system, $TiCl_4$ (5 mL) was added dropwise to the mixture of nano-cellulose (5 g) in chloroform (20 mL). The mixture was stirred for 1 h at room temperature. The resulted suspension was filtered, washed with chloroform and dried at room temperature.

FT-IR spectrum of nano-$TiCl_2$/cellulose (*KBr*). 3335, 1111, 1056, 1032, 828 cm^{-1}.

General procedure for synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazole derivatives

A mixture of 2-aminobenzothiazole I (1 mmol), aldehyde II (1 mmol), ethyl acetoacetate III (1 mmol), and PEG-400 (0.5 mL) was heated at 70 °C in the presence of nano-$TiCl_2$/cellulose (0.03 g). After completion of the reaction (monitored by TLC), hot ethanol (10 mL) was added to the mixture and filtered off for separation of catalyst. By adding water to filtrate, the product appeared as a pure solid in high yields.

Spectroscopic data of Ethyl-2-methyl-4-(4-nitrophenyl)-4H-pyrimido[2,1-*b*] [1,3] *benzothiazole-3-carboxylate* (Table 4, IV_b). Yellow solid.^{1}H NMR (Acetone-d_6, 400 MHz): δ 8.18 (d, $J = 8.8$ Hz, 2H), 7.80 (d, $J = 8$ Hz, 2H), 7.72 (d, $J = 8$ Hz, 1H), 7.41 (d, $J = 8$ Hz, 1H), 7.32 (t, $J = 8$ Hz, 1H), 7.22 (t, $J = 7.2$ Hz, 1H), 6.69 (s, 1H), 4.09–4.16 (m, 2H), 2.37 (s, 3H), 1.25 (t, $J = 7.2$ Hz, 3H). IR (KBr): 3074, 2981, 1700, 1670, 1585, 1501, 1347, 1272, 1242, 1202, 745 cm^{-1}. mp: 171–173 °C.

Spectroscopic data of Ethyl-2-methyl-4-(2-ethoxyphenyl)-4H-pyrimido[2,1-*b*] [1,3] *benzothiazole-3-carboxylate* (Table 4, IV_h). Yellow solid.^{1}H NMR (Acetone-d_6, 400 MHz): δ 7.63 (d, $J = 8$ Hz, 1H), 7.53 (dd, $J = 7.6$, 1.6 Hz, 1H), 7.47 (d, $J = 8$ Hz, 1H), 7.29 (m, 1H), 7.15–7.18 (m, 2H), 6.88–6.92 (m, 2H), 6.75 (s, 1H), 4.10–4.14 (m, 2H), 4.03 (q, $J = 7.2$ Hz, 2H), 2.37 (s, 3H), 1.50–1.54 (m, 3H), 1.16–1.20 (m, 3H). IR (KBr): 2980, 1692, 1600, 1511, 1493, 1242, 1201, 1075, 1040, 752 cm^{-1}. mp: 171–175 °C.

Spectroscopic data of Ethyl-2-methyl-4-(2,4-dimethoxyphenyl)-4H-pyrimido[2,1-*b*] [1,3] *benzothiazole-3-carboxylate* (Table 4, IV_l). Yellow solid.^{1}H NMR (Acetone-d_6, 400 MHz): δ 7.62 (d, $J = 7.6$ Hz, 1H), 7.45 (d, $J = 8$ Hz, 1H), 7.37 (d, $J = 8.4$ Hz, 1H), 7.30 (td, $J = 8$, 1.2 Hz, 1H), 7.15 (td, $J = 7.6$, 1.2 Hz, 1H), 6.68 (s, 1H), 6.44–6.48 (m, 2H), 4.05 (q, $J = 6.8$ Hz, 2H), 3.93 (s, 3H), 3.71 (s, 3H), 2.36 (s, 3H), 1.19 (t, $J = 6.8$ Hz, 3H). IR (KBr): 1694, 1583, 1497, 1271, 1239, 1203, 1075, 836, 739 cm^{-1}. mp: 164–166 °C.

Results and discussion

Catalyst characterization

The particle sizes of nano-cellulose and nano-$TiCl_2$/cellulose were investigated by field emission scanning electron microscopy (FESEM) and transmission electron microscopy (TEM) in which the achieved dimensions of catalyst were below 50 nm (Fig. 1).

Comparison of nano-$TiCl_2$/cellulose with nano-cellulose was achieved by FT-IR (ATR) spectra (Fig. 2). The FT-IR spectrum of nano-cellulose shows a broad band at 3337 $cm^{-1,}$ which corresponds to the stretching vibrations of OH groups. The absorption bands around 1055 and 1108 cm^{-1} display the stretching vibrations of the C–O bonds. For nano-$TiCl_2$/cellulose, cellulose absorptions appear in addition to the stretching vibrations of C–O–Ti at 828 cm^{-1}; indicating that titanium chloride is supported on nano-cellulose.

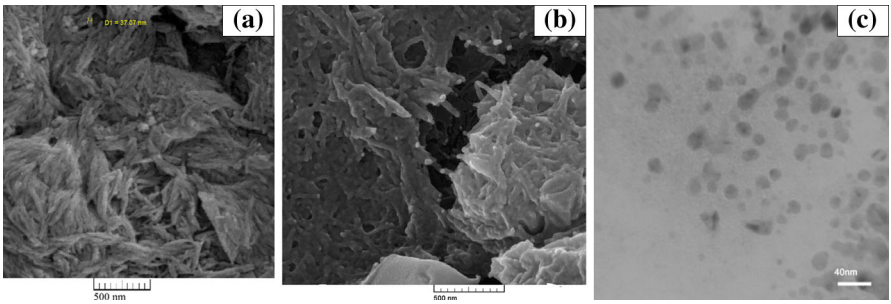


Fig. 1 **a** FESEM image of nano-cellulose, **b** FESEM of nano-$TiCl_2$/cellulose and **c** TEM of nano-$TiCl_2$/cellulose

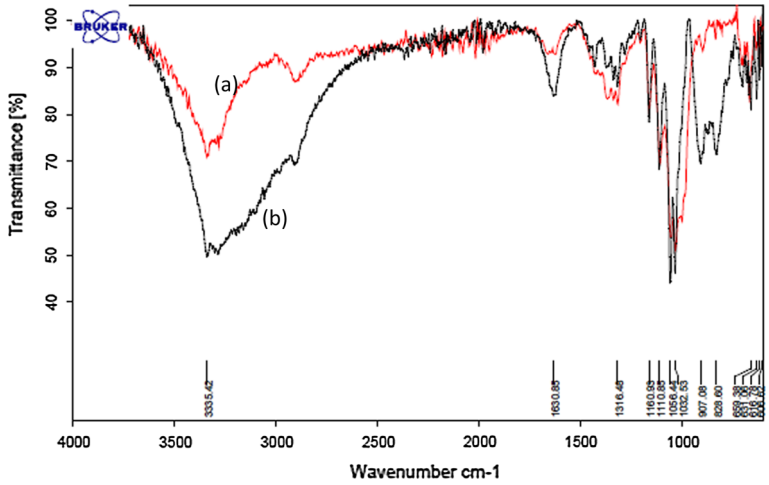


Fig. 2 FT-IR spectra of (*a*) nano-cellulose, (*b*) nano-$TiCl_2$/cellulose

Existence of Ti and Cl in catalyst was confirmed by EDS analysis data (Fig. 3). The percentages of Ti and Cl in $TiCl_4$ are 25.24 and 74.76, respectively. Thus, the amounts of Ti and Cl in EDS data (Ti: 20.3 %, Cl: 14.9 %) revealed the absence of any unreacted $TiCl_4$ in catalyst. Hence, XRF analysis of nano-$TiCl_2$/cellulose was performed to determine its elemental component (Table 1; Fig. 4).

To obtain the Ti:Cl ratio in nano-$TiCl_2$/cellulose using XRF analysis, Killo Counts Per Seconds (KCPS) of elements in catalyst were compared with KCPS of the same elements in pure samples, NaCl and TiO_2. By this comparison, the obtained amount of Ti and Cl was 12.02 g (0.25 mol) and 14.3 g (0.4 mol), respectively. Thus, the ratio of Ti:Cl in catalyst is approximately 1:2.

The X-ray diffraction (XRD) pattern of nano-$TiCl_2$/cellulose is depicted in Fig. 5. The values of 2θ and FWHM are shown in Table 2. According to the XRD pattern, the three signals in 2Θ equal to 15.13, 16.74, and 22.93 with FWHM equal to 0.472, 0.944, and 0.472, respectively, show the existence of cellulose. Other signals in 2Θ equal to 20.55, 28.56, 34.63, and 41.84 prove the bonding of Ti to the cellulose backbone.

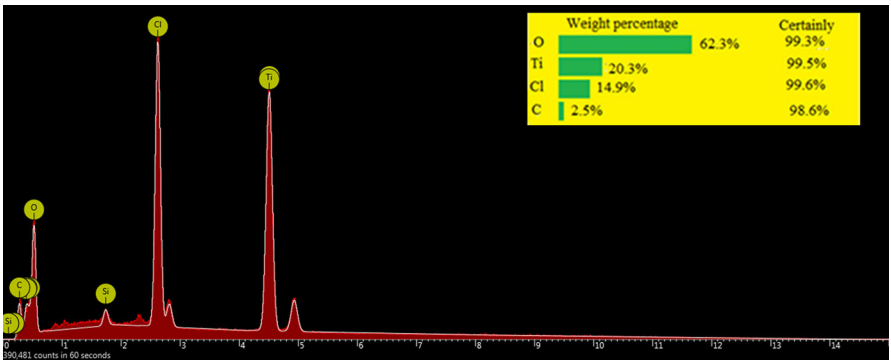


Fig. 3 EDS (EDX) spectra of nano-$TiCl_2$/cellulose

Table 1 Results of XRF analysis of nano-$TiCl_2$/cellulose and pure samples NaCl and TiO_2

Elemental component	$TiCl_2$/nano-cellulose		NaCl		TiO_2	
	KCPS	wt%	KCPS	wt%	KCPS	wt%
Cl	123.5	6.8	516.5	62.4		
TiO_2	464.3	22.2			2318.4	99.1
CO_2	1.6	67.1				
CaO	37.6	1.9				
SiO_2	7.1	1.43				
Al_2O_3	2.3	0.558				
SO_3	5.3	0.504				
MgO	1.9	0.374				
Total		100.86				

According to the above-mentioned data, we have proposed a structure for nano-$TiCl_2$/cellulose (Fig. 6). This catalyst does not need special precautions for preparation, handling or storage, and it can be stored at an ambient temperature for months without losing its catalytic activity.

Catalyst testing for synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazole derivatives

The catalytic activity of nano-$TiCl_2$/cellulose was investigated for the synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazole derivatives via three-component reactions of 2-aminobenzothiazole, aldehydes and ethyl acetoacetate. In order to optimize the reaction conditions, including solvent, temperature and catalyst loading, the model reaction of 2-aminobenzothiazole, 4-nitrobenzaldehyde and ethyl acetoacetate was initially carried out under different conditions in the presence of nano-$TiCl_2$/cellulose (Table 3). Different solvents including THF, H_2O, CH_3CN, C_2H_5OH, MeOH, PEG-200, and PEG-400 were screened (Table 3, Entries 3–10); condensation of

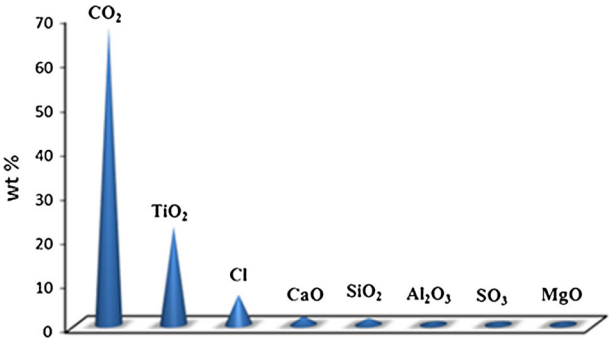


Fig. 4 XRF analysis of nano-$TiCl_2$/cellulose

Fig. 5 XRD pattern of nano-$TiCl_2$/cellulose

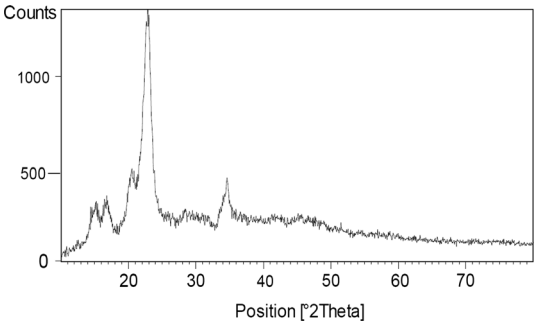


Table 2 Nano-$TiCl_2$/cellulose reflexes in XRD diffractogram

No	1	2	3	4	5	6	7
Pos. [°2θ]	15.130	16.748	20.553	22.935	28.563	34.634	41.846
FWHM [°2θ]	0.472	0.944	0.472	0.472	0.708	0.295	1.728

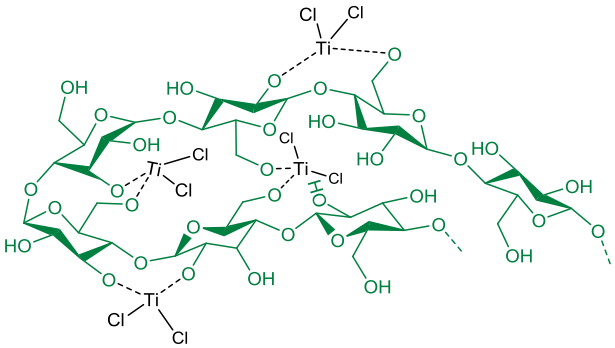
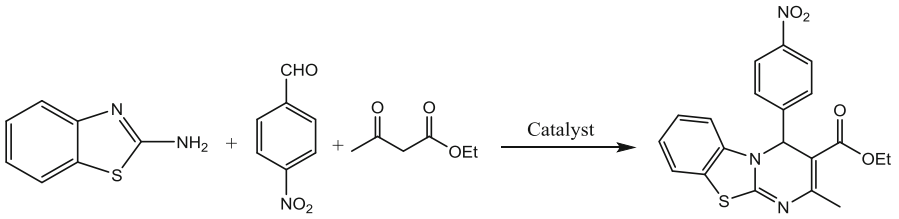


Fig. 6 Proposed structure of nano-$TiCl_2$/cellulose

Table 3 The reaction of 2-aminobenzothiazole, 4-nitrobenzaldehyde, and ethyl acetoacetate in the presence of nano-$TiCl_2$/cellulose under various conditions



Entry	Solvent	Catalyst (g)	Condition	Time (h)	Yield (%)[a]
1	–	Catalyst (0.05)[b]	R. T	6	30
2	–	Catalyst (0.05)[b]	70 °C	6	70
3	THF	Catalyst (0.05)[b]	Reflux	7	41
4	H_2O	Catalyst (0.05)[b]	Reflux	7	53
5	CH_3CN	Catalyst (0.05)[b]	Reflux	6	59
6	C_2H_5OH	Catalyst (0.05)[b]	Reflux	6	60
7	C_2H_5OH	Catalyst (0.05)[b]	R. T	7	37
8	MeOH	Catalyst (0.05)[b]	Reflux	5	50
9	PEG-200	Catalyst (0.05)[b]	70	4	75
10	PEG-400	Catalyst (0.05)[b]	70	1	92
11	PEG-400	Catalyst (0.05)[b]	100	1	80
12	PEG-400	Catalyst (0.05)[b]	50	2	65
13	PEG-400	Catalyst (0.05)[b]	R. T	4	40
14	PEG-400	Catalyst (0.04)[b]	70	1	85
15	PEG-400	Catalyst (0.03)[b]	70	1	96
16	PEG-400	Catalyst (0.02)[b]	70	3	78
17	PEG-200	Catalyst (0.03)[b]	70	4	70
18	PEG-400	–	R.T	7	–
19	PEG-400	–	70	7	30
20	PEG-400	Catalyst (0.03), second run[b]	70	1	92
21	PEG-400	Catalyst (0.03), third run[b]	70	1	88
22	PEG-400	Catalyst (0.03), forth run[b]	70	1	85
23	PEG-400	Catalyst (0.03), fifth run[b]	70	1	82
24	PEG-400	Catalyst (0.03), sixth run[b]	70	1	80

The amount ratios of 2-aminobenzothiazole (mmol), 4-nitrobenzaldehyde (mmol) and ethyl acetoacetate (mmol) are equal to 1:1:1

[a] Isolated yield

[b] nano-$TiCl_2$/cellulose

2-aminobenzothiazole, 4-nitrobenzaldehyde and ethyl acetoacetate was easier and gave the highest yield in the presence of PEG-400 as solvent (Table 3, Entry 10). The effect of reaction temperature was also examined (Table 3, Entry 10–13), and the reaction was found to proceed smoothly at 70 °C (Table 3, Entry 10). To

Table 4 Comparative study of the present method and some other reported methods for synthesis of4*H*-pyrimido[2,1-*b*]benzothiazole derivatives

Entry	Solvent	Catalyst	Temperature (°C)	Time (h)	Yield (%)[a]
1	MeOH	Acetic acid (20 mol%)	65	18	62 [13]
2	Ethylene glycol	TBAHS (30 mol%)[b]	120	2	72 [11]
3	–	TMGT (0.080 g)[c]	100	5	53 [10]
4	Acetic acid (2 %)	Chitosan (0.080 g)	70	1.6	93 [12]
5	PEG-400	Nano-$TiCl_2$/cellulose (0.03 g)	70	1	97 This work

[a] Isolated yield

[b] Tetrabutylammonium hydrogen sulfate

[c] 1,1,3,3-*N*,*N*,*N*′,*N*′-tetramethylguanidinium trifluoroacetat

optimize the catalyst amount, the model reaction was performed in the presence of various amounts of the catalyst and according to the obtained results (Table 3, Entries 14–16) 0.03 g of the catalyst was chosen as the best catalyst amount (Table 3, Entry 15). In conclusion, the best reaction condition for this transformation is the use of 0.03 g of the catalyst in the presence of PEG-400 as solvent at 70 °C (Table 3, Entry 15).

Moreover, reusability of the catalyst was investigated. After the reaction was completed, followed by the filtration, the filtered catalyst was washed with acetone and dried for 3 h at 70 °C, and then saved for the next reaction. The reusability of the catalyst was tested at least five times, and the desired product was isolated in each run (Table 3, Entries 20–24). It was found that the reactivity of the catalyst decreases slightly for the next run.

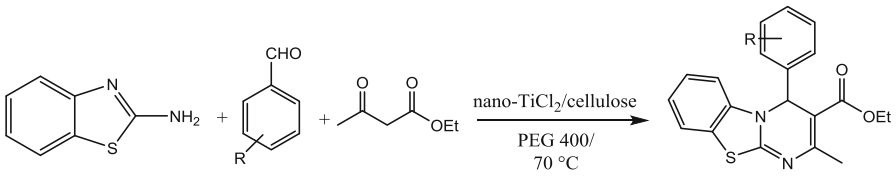
Comparison of the results of the nano-$TiCl_2$/cellulose-catalyzed reaction of 4-nitrobenzaldehyde (1 mmol), 2-aminobenzothiazole (1 mmol) and ethylacetoacetate (1 mmol) with previously reported methods shows the merit of the present protocol (Table 4).

Based on the optimized reaction conditions, a range of 4*H*-pyrimido[2,1-*b*]benzothiazole derivatives were synthesized by the reaction of 2-aminobenzothiazole (I, 1 mmol), aldehydes (II, 1 mmol) and ethyl acetoacetate (III, 1 mmol) (Table 5). Electronic effects and the nature of substituents on the aldehyde showed a significant effect in terms of the yield and reaction time under the optimized reaction conditions. The electron-withdrawing groups increased reactivity and afforded higher yields compared to the electron-donating groups.

The suggested mechanism for the synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazole (IV) is displayed in Scheme 1 in which supported titanium chloride could act as a Lewis acid to activate the carbonyl groups. It seems benzaldehyde (II) as an electrophile and *β*-ketosters (III) as active methylene compounds take part through an in situ Knoevenagel reaction and an alkene is primarily formed.

Afterwards, during the Michael addition reaction, 2-aminbenzothiazole, as a Michael donor, attacks alkene during nucleophilic reaction, so an iminium ion is

Table 5 Synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazole derivatives (IV_{a-m}) in the presence of nano-$TiCl_2$/cellulose at 70 °C



I **II** **III** **IV**

Entry	R (II_{a-j})	Product (V_{a-j})	Time (h)	Yield (%)[a]	M.P. [Ref]
1	H (II_a)	IV_a	1.5	80	178–180 [14]
2	4-NO_2-(II_b)	IV_b	1	96	171–173 [15]
3	4-Cl-(II_c)	IV_c	1	97	87–89 [14]
4	4-Br (II_d)	IV_d	1	95	110–114 [10]
5	4-OH-(II_e)	IV_e	2	79	210–212 [15]
6	2-NO_2-(II_f)	IV_f	1.5	85	122–125
7	2-Cl-(II_g)	IV_g	1	97	124–126 [11]
8	2-EtO-(II_h)	IV_h	2	75	171–175
9	3-NO_2-(II_i)	IV_i	1.5	90	222–224 [14]
10	3-OH-(IIj)	IV_j	2	80	260–263
11	2,4-$(Cl)_2$-(II_k)	IV_k	1	91	133–135 [11]
12	2,4-$(MeO)_2$-(II_l)	IV_l	2.5	74	164–166
13	3,4-$(OH)_2$-(II_m)	IV_m	2.5	68	225–227

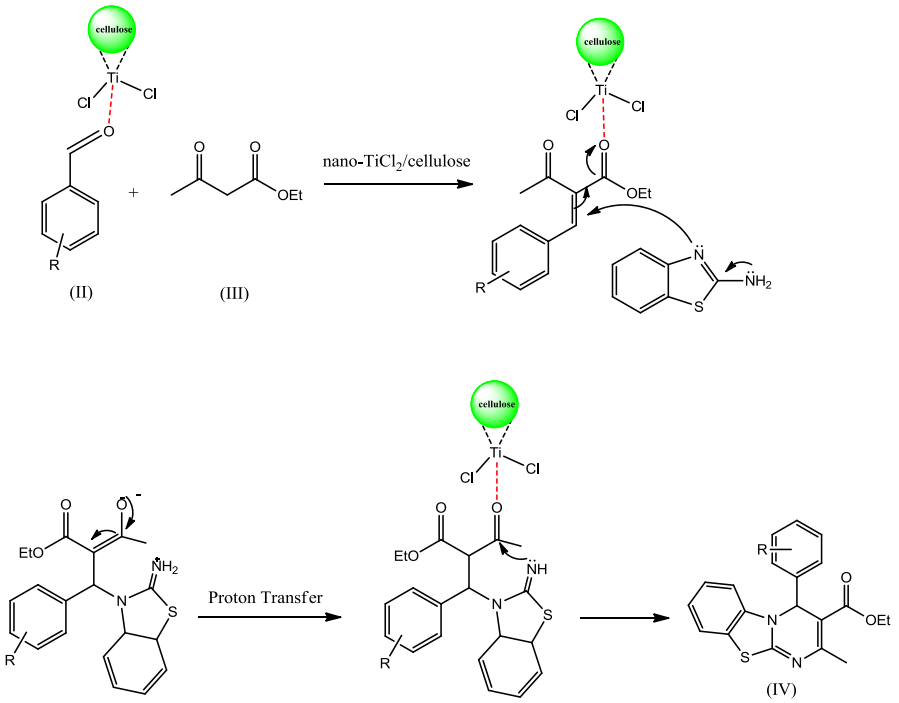
I (mmol): II (mmol): III (mmol): nano-$TiCl_2$/cellulose (g) is equal to 1:1:1:0.03

[a] Isolated yield

formed. Subsequently, with a proton transformation and an intramolecular cyclization, products IV_{a-m} are produced. The structure of the products IV_{a-m} was deduced from its mp, IR and ^{1}H NMR spectra. In the FTIR spectra, the ester C=O stretching frequency appeared around 1650 cm^{-1} due to conjugation. ^{1}H NMR spectra of products IV_{a-m} exhibited a singlet at about $\delta = 5.54$–6.33 ppm for H-4.

Hot filtration test

A hot filtration test was conducted to confirm that the nano-catalyst was indeed heterogeneous. In this test, a mixture of 2-aminobenzothiazole I (1 mmol), aldehyde II (1 mmol), ethyl acetoacetate III (1 mmol), and PEG-400 (0.5 mL) was heated at 70 °C in the presence of nano-$TiCl_2$/cellulose (0.03 g) for 30 min. The nano-$TiCl_2$/cellulose was then filtered off from the hot reaction mixture, and the reaction in the filtrate was still monitored. No increase in conversion was observed in the filtrate.



Scheme 1 Proposed mechanism for the synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazole derivatives IV_{a-m}

Leaching test

AAS (Atomic Absorption Spectroscopy) technique was employed to be sure that no leaching of Ti took place after the catalytic reaction. After the completion of reaction, chloroform was added to the mixture and filtered off for separation of catalyst. The filtrate (reaction mixture) was analyzed using AAS with a hollow cathode lamp at a wavelength of 346 nm using a C2H2/N2O flame, which indicates that no Ti species was detected in the filtrate solution.

Conclusion

In conclusion, nano-$TiCl_2$/cellulose can be described as a green, cheap, natural, biodegradable, and readily available biopolymer solid acid catalyst. The catalytic activity of the prepared catalyst was investigated in the synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazole derivatives through one-pot three-component reaction of aldehydes, ethyl acetoacetate, and 2-aminobenzothiazole in the presence of PEG-400 as solvent at 70 °C. Environmentally benign conditions, clean synthesis, easy work-up, and high yields are among the advantages of this novel methodology.

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