NaY Zeolite Functionalized by Sulfamic Acid/Cu(OAc)₂ as a Novel and Reusable Heterogeneous Hybrid Catalyst in Efficient Synthesis of Bis, Tris, and Tetrakis(indolyl) methanes, 3,4-Dihydropyrimidin-2(1*H*)-ones, and 2-Aryl-1*H*-benzothiazoles

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An efficient acid-catalyzed synthesis of some bis, tris, and tetrakis(indolyl)methanes, 3,4-dihydropyrimidin-2(1*H*)-ones, and 2-aryl-1*H*-benzothiazoles is reported using NaY zeolite functionalized by sulfamic acid/Cu(OAc)₂ (NaY zeolite-NHSO₃H/Cu(OAc)₂) in excellent yield. The heterogeneous catalyst has a simple work-up procedure and could be recycled and reused for six reaction cycles.

Keywords: Bis(indolyl)methane; Tris(indolyl)methane; Tetrakis(indolyl)methane; Heterogeneous catalyst; 3,4-Dihydropyrimidin-2(1*H*)-ones; 2-Aryl-1*H*-benzothiazoles; NaY zeolite functionalized by sulfamic acid/Cu(OAc)₂.

INTRODUCTION

Owing to the unique pharmacological properties of indole derivatives,¹ there is always a growing need for new synthetic methods in this field. Vibrindole A, which is a naturally occurring bisindolylmethane, exhibits important biological activity.² Bis(indolyl)methane and tris(indolyl)methane scaffolds, which are mostly present in natural products,³ exhibit a broad range of biological activities including prevention of bladder cancer growth,⁴ renal cell carcinoma growth,⁵ colon cancer,⁶ and breast cancer.⁷ Also, the oxidized forms of bis(indolyl)methane and tris(indolyl)methane are applied as dyes⁸ and calorimetric sensors.⁹ These various notable uses of bis(indolyl)methane and tris(indolyl) methane have encouraged researchers to find efficient methods for the synthesis of indole derivatives. The general method for the synthesis of bis(indolyl)methane includes the reaction of aldehydes or ketones with indoles in the presence of protic¹⁰ or Lewis acids,¹¹ which is analogous to the acid-catalyzed Ehrich test.¹² Numerous catalysts such as Montmorillonite K-10, ZrCl₄, ion-exchange resin, TBBDA, Ph₃CCl,¹³ iodine,¹⁴ zeolites,¹⁵ and silica sulfuric acid (SSA)¹⁶ have been found to promote these reactions.

Dihydropyrimidinones and their derivatives are of remarkable biological and pharmacological importance as

anti-inflammatory, antitumor, antiviral, and antifungal agents.¹⁷ In the last few decades, these compounds have also found applications as calcium channel blockers, antihypertensive agents, α_{1a} -antagonists, and neuropeptide Y (NDY) antagonists used for the treatment of prostatic hyperplasia.^{17,18} The synthesis of 3.4-dihydropyrimidin-2 (1H)-ones was first reported by Biginelli (1893) by a simple one-pot condensation of a β -keto ester, an aldehyde, and urea under strongly acidic conditions. However, this protocol often suffers from low yields of the more demanding products in the case of aliphatic and certain substituted aromatic aldehydes. Owing to the extensive biological and pharmacological applications of 3,4-dihydropyrimidin-2(1H)-ones, many improved routes have been continuously reported for the synthesis of these compounds either by the classical one-pot Biginelli approach¹⁹ or through the development of novel multistep procedures.²⁰ In recent years, a variety of catalytic methods for promoting the Biginelli reaction have been developed employing various metal salts as Lewis acid catalysts including LiBr,^{21a} NiCl₂· $6H_2O$,^{21b} FeCl₃· $6H_2O$,^{21b} CuCl₂· $2H_2O$,^{21c} CeCl₃· $7H_2O$,^{21d} Mn(OAc)₃· $2H_2O$,^{21e} ZrCl₄,^{21f} InCl₃,^{21g} InBr₃,^{21h} ZnCl₂,²¹ⁱ CdCl₂,^{21j} LiClO₄^{21k}, and Bi(NO₃)3.²¹¹

Compounds containing benzothiazoles rings have been widely used in the pharmaceutical industry.^{17,22}

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Benzothiazole derivatives are broadly established in bioorganic and medicinal chemistry and have applications in drug discovery and development. They have been applied for the treatment of autoimmune and inflammatory diseases²³ and in the prevention of epilepsy,²⁴ amyotrophic lateral sclerosis,²⁵ analgesim,²⁶ tuberculosis,²⁷ viral infections,²⁸ and cancer.²⁹ Also, benzothiazole derivatives are employed in industrial chemistry as antioxidants³⁰ and vulcanization acceletors.³¹ Therefore, due to the importance of these heterocyclic compounds for the synthesis of benzothiazoles, various methodologies have been described.^{29,32} From the various reports, the most popular method usually involves the oxidative condensation of 2-aminothio phenols with carboxylic acids^{28,33} or aldehydes.³⁴ Unfortunately, most of the previously reported procedures have many disadvantages and limitations such as high reaction temperature, severe reaction requirements, long reactions times, requirement for excess of reagents, tedious work-up procedures, low yields, use of costly toxic or air-sensitive catalysts, and so on.³⁵ Consequently, there is still a need to develop simple, mild, rapid, and inexpensive procedures for the synthesis of these heterocycles.

Recently, significant factors such as reusability. yield of products, simple recovery, cost of catalysts, short reaction times, and green chemistry have led to the use solid acid catalysts. Furthermore, applying heterogeneous catalysts such as zeolites have some benefits such as nontoxicity and environmental friendliness, suitable acidity, thermal stability, and shape selectivity, which affect the efficiency of reactions, work-up, and purity of the products.^{36–38} So, with the aim of developing a more efficient synthetic process, we now report the synthesis of some bis(indolyl)methane, tris(indolyl) methane, and tetrakis(indolyl)methane derivatives using NaY zeolite functionalized by sulfamic acid/Cu(OAc)₂ (NaY zeolite-NHSO₃H/Cu(OAc)₂) as a heterogeneous catalyst under mild conditions (Schemes 1 and 2). Also, this heterogeneous catalyst was used successfully for catalyzing the Biginelii reaction (Scheme 3). Finally,



several 2-aryl-1*H*-benzothiazoles were synthesized in high yields at room temperature in the presence of this catalyst (Scheme 4).

RESULTS AND DISCUSSION

Characterization of NaY zeolite-NHSO₃H/Cu(OAc)₂

The NaY zeolite-NHSO₃H/Cu(OAc)₂ catalyst was characterized by Fourier transform infrared (FT-IR) spectroscopy, scanning electron microscopy (SEM), energy-dispersive X-ray (EDX), thermogravimetric analysis (TGA), and X-ray diffraction (XRD). The FT-IR spectra of NaY zeolite, NaY zeolite-NH₂, NaY zeolite-NHSO₃H, and NaY zeolite-NHSO₃H/Cu(OAc)₂ are shown in Figure 1(a)–(d), respectively. The FT-IR spectra of all hybrid materials indicate an intense band at ~1049 cm⁻¹ attributable to the asymmetric stretching of the Al–O–Si chain of the zeolite. The symmetric stretching and bending frequency bands of the Al–O–Si



Scheme 4. Synthesis of 2-aryl-1H-benzothiazoles.



Fig. 1. FT-IR spectra of NaY zeolite (a), NaY zeolite-NH₂ (b), NaY zeolite-NHSO₃H (c), and NaY zeolite-NHSO₃H/Cu(OAc)₂ (d).

framework of the zeolite appear at 765 and 455 cm⁻¹, respectively.³⁹ The out-of-plane bending and stretching of the O–H group appear at 785 and 3400–3500 cm⁻¹, respectively. The peak appearing at 1150 is assigned to the S = O stretching vibration, which confirms the presence of the SO₃H group (Figure 1(c) and (d)). The symmetric and asymmetric stretching vibration modes of amine group are observed at 3200–3400 cm⁻¹ (Figure 1 (b)–(d)). The weak band at 2900 cm⁻¹ can be attributed to the C–H stretching vibration (Figure 1(d)).

The microstructure of the catalyst was investigated using SEM. The SEM image of NaY zeolite-NHSO₃H/ $Cu(OAc)_2$ in Figure 2(b) shows particles with a mean diameter of ~300 nm and nearly spherical shape, which indicates no change in the particle's size and shape when compared to those for NaY zeolite-NHSO₃H in Figure 2(a).



Fig. 2. SEM images of NaY zeolite-NHSO₃H (a) and NaY zeolite-NHSO₃H/Cu (OAc)₂ (b).





The EDX analysis of NaY zeolite-NHSO₃H/Cu $(OAc)_2$ clearly reveals the presence of Cu as well as other expected main elements including N, Al, Si, O, C, Na, and S (Figure 3(b)). The lower intensity of Na in comparison with that for NaY zeolite-NHSO₃H (Figure 3(a)) demonstrates the exchange of Na⁺ as a monovalent cation by the divalent cation Cu²⁺ in zeolite's pores without any change in the zeolite structure.

Thermal analysis was used to monitor the decomposition profile of NaY zeolite-NHSO₃H/Cu(OAc)₂ (Figure 4). It shows a weight loss of 12% up to 350° C in first stage due to the adsorbed water in the catalyst. The second-stage weight loss of 11% was observed in the temperature range of ~350–430°C, which is due to the organic moiety. The weight loss above 450°C is attributed to zeolite decomposition.



Figure 5 illustrates the XRD pattern of NaY zeolite-NHSO₃H (Figure 5(a)) and NaY zeolite-NHSO₃H/Cu(OAc)₂ (Figure 5(b)), which indicate no changes in the general structure and morphology of NaY zeolite during the immobilization procedures.

Synthesis of bis, tris, and tetrakis(indolyl)methanes using NaY zeolite-NHSO₃H/Cu(OAc)₂

To evaluate the synthetic potential of this method, the condensation of indole (2 mmol, 0.234 g) with benzaldehyde (1 mmol, 0.1 mL) in the presence of different amounts of NaY zeolite-NHSO₃H/Cu(OAc)₂ and in several solvents was studied as a model reaction. Considering the obtained results in terms of yields and reaction times (Table 1), MeCN was found to be the best solvent, and the optimal amount of the catalyst was 0.02 g (Table 1, entry 3). It is notable that NaY zeolite-NHSO₃H had lower catalytic effect than NaY/Cu



electron-withdrawing groups drive the reaction faster

(OAc)₂; therefore, bis(indolyl)methane was obtained in

lower yield and over longer reaction times (Table 1,

entry 13). To prove the generality of this protocol, the

reaction was then extended to a variety of aldehydes

and ketones with indole, whose results are summarized

in Table 2. As the results show, both electron-

withdrawing (Table 2, entries 5, 6, 10, 11, and 12) and

electron-releasing groups (Table 2, entries 2, 3, 4, 8,

and 9) tolerate this condensation. In regard to the sug-

gested mechanism in Scheme 5, in the first condensation

of indole, the activity of aldehyde for nucleophilic

attack is important. As is known, the electronwithdrawing substituents accelerate this step. So, the

than electron-releasing substituents (Table 2, entries 5, 6, 10, 1,1 and 12). Also, it was observed that ortho substituents (Table 2, entries 4, 5, 9, and 10) make the reaction slower than para substituents (Table 2, entries 3, 6, 8, and 12) probably due to steric effects. Also, glutaraldehyde as an aliphatic dialdehyde, terphetaldehyde, and isophthalaldehyde were converted to the corresponding tetrakis(indolyl)methanes in notable vields (Table 2, entries 13-15). In addition, the efficiency of the catalyst was tested for the condensation of indole with some α , β -unsaturated ketones, and it was observed that NaY zeolite-NHSO₃H/Cu(OAc)₂ was also effective and usable for the one-pot condensation of 3 mol of indole with α , β -unsaturated ketones (Table 2, entries 16-18). As expected from the suggested mechanism in Scheme 6, the reaction times for α , β -unsaturated ketones are quite long because of the low activity caused by conjugation. In this case, the reaction could be accelerated by electron-withdrawing groups in the alkene section of the molecule. Additionally, some ketones including cyclic aliphatic ketone, acyclic aliphatic ketone, and acethophenone as an aromatic ketone proceeded the reaction to provide the corresponding products following this methodology. Generally, it was found that ketones reacted very slowly and resulted in lower yields than aldehydes (Table 2, entries 19-22). Finally, isatin reacted to afford the corresponding bis(indolyl)methane only in one carbonyl.

Finally, in order to demonstrate the efficiency of this technique, it was compared with some reported methods (Table 3). As this table shows, the proposed method clearly gives improved yields and shorter reaction times. Also, the reusability of the catalyst makes Table 1. Optimization of the reaction parameters for synthesis of 3,3'-(phenylmethylene)bis(1H-indole)



Entry ^a	Catalyst	Amount of catalyst (g)	Solvent	Time (min)	Yield (%) ^b
1	No catalyst		MeCN	24 (h)	Trace
2	NaY zeolite	0.02	MeCN	200	30
3	NaY zeolite-NHSO ₃ H/Cu(OAc) ₂	0.02	MeCN	40	98
4	NaY zeolite-NHSO ₃ H/Cu(OAc) ₂	0.02	DMF	60	85
5	NaY zeolite-NHSO ₃ H/Cu(OAc) ₂	0.02	CHCl ₃	240	40
6	NaY zeolite-NHSO ₃ H/Cu(OAc) ₂	0.02	Ethyl acetate	100	70
7	NaY zeolite-NHSO ₃ H/Cu(OAc) ₂	0.02	Toluene	300	35
8	NaY zeolite-NHSO ₃ H/Cu(OAc) ₂	0.02	EtOH	60	85
9	NaY zeolite-NHSO ₃ H/Cu(OAc) ₂	0.02	H ₂ O	200	15
10	NaY zeolite-NHSO ₃ H/Cu(OAc) ₂	0.01	MeCN	100	50
11	NaY zeolite-NHSO ₃ H/Cu(OAc) ₂	0.025	MeCN	35	94
12	NaY zeolite-NHSO ₃ H/Cu(OAc) ₂	0.03	MeCN	35	88
13	NaY zeolite-NHSO ₃ H	0.02	MeCN	200	65

^a Conditions: indole (2 mmol), benzaldehyde (1 mmol), solvent 4 mL, room temperature. ^b Isolated yields.

Isolated yields.

the protocol less contaminative and nearly green. In addition, since the catalyst is heterogeneous, the workup procedure is easy, and chromatography or other complex purification methods are not necessary. According to the obtained results, it seems that NaY zeolite also helps the catalytic effect of sulfonic acid group and accelerates the reaction.

Synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones using NaY zeolite-NHSO₃H/Cu(OAc)₂

In order to study the efficiency of NaY zeolite-NHSO₃H/Cu(OAc)₂ in the condensation reactions, several 3,4-dihydropyrimidin-2(1*H*)-ones were prepared in the presence of NaY zeolite-NHSO₃H/Cu(OAc)₂ as the heterogeneous catalyst. For optimization of the reaction conditions, the reaction of benzaldehyde with ethylacetoacetate and urea as the model reaction was examined by employing solvent-free conditions under various catalyst molar ratios and reaction times. The experimental results indicated that the highest yield of the reaction product (97%) was obtained when NaY zeolite-NHSO₃H/Cu(OAc)₂ (0.01 g/mol) was employed under solvent-free conditions at 60° C heating. On the basis of the above results, to investigate the scope and generality of this method, the process was extended to other aliphatic (Table 4, entries 10, 11, and 13), aromatic (Table 4, entries 1–9), and heteroaromatic (Table 4, entry 12) aldehydes that tolerate both electron-withdrawing and electron-donating substituents. It was observed that although the aliphatic aldehydes generally reacted more slowly than aromatic aldehydes, the catalyst was effective for all aldehydes. The mechanism for the Biginelli reaction in acidic conditions has been proposed by Kappe.¹⁸

In order to show the merit of the present work in comparison with some reported procedures, we compare the results of the synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones (Table 4, entry1) in the presence of NaY zeolite-NHSO₃H/Cu(OAc)₂ with some other conditions (Table 5).

Synthesis of 2-aryl-1*H*-benzothiazoles using NaY zeolite-NHSO₃H/Cu(OAc)₂

The catalytic effect of NaY zeolite-NHSO₃H/Cu $(OAc)_2$ was also established by catalyzing the synthesis of deferent benzothiazoles via one-pot cyclocondensation of 2-aminothiophenoles with aromatic aldehydes

Entry ^a	Substrate	Product	Time (min)	Yield (%) ^b	Refs
1	PhCHO		40	98	40
2	4-Me-PhCHO		45	95	40
3	4-MeO-PhCHO		90	94	16
4	2-MeO-PhCHO		110	90	40
5	2-Cl-PhCHO		50	91	41
6	4-Cl-PhCHO		40	97	16
7	2,4-diCl-PhCHO		80	91	40
8	4-OH-PhCHO	но-Су	80	92	40
9	2-OH-PhCHO	OH In	90	90	16
10	2-NO ₂ -PhCHO	NO ₂ In	32	92	40
11	3-NO ₂ -PhCHO	NO ₂ In	35	93	40
12	4-NO ₂ -PhCHO	NO ₂ -	25	96	40
13 ^c	0		400	89	New
14 ^c	онс—Сно		50	95	42
15 ^c	онс		60	94	43
16 ^d			300	91	New
17 ^d			240	94	New
18 ^d		O2N	360	90	New
19	Met .		360	64	43
20			300	90	43

Entry ^a	Substrate	Product	Time (min)	Yield (%) ^b	Refs
21			300	92	43
22			360	75	43
23			50	96	43
		N H			

Table 2.	Continued
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^a Conditions: indole (2 mmol, 0.234 g), aldehyde (1 mmol), catalyst (0.02 g), MeCN (4 mL), rt.

^b Isolated yields.

^c Conditions: indole (4 mmol, 0.468 g), aldehyde (1 mmol), catalyst (0.04 g), MeCN (4 mL), rt.

^d Conditions: indole (3 mmol, 0.351 g), chalcone (1 mmol), catalyst (0.03 g), MeCN (4 mL), rt.



NaY zeolite-SO₃H/Cu(OAc)₂

Scheme 5. Suggested mechanism for synthesis of bis(indolyl)methane.

(Scheme 4). At first, reaction conditions were optimized for the condensation of 2-aminothiophenole and benzaldehyde as the model reaction. The best yields and reaction times were obtained under solvent-free condigood purity (Table 6). The possible mechanism for this condensation in the presence of Lewis $acid^{35a}$ and zeolite^{35b} has been reported previously.



NaY zeolite-NHSO₃H/Cu(OAc)₂

Scheme 6. Suggested mechanism for the synthesis of tris(indolyl)methane.

tions using 0.01 g/mol of catalyst at 40°C. Aldehydes with both electron-withdrawing and electron-releasing groups participated in this reaction, and 2-aryl-1*H*-benzothiazoles were obtained in excellent yields and

Catalyst recovery

To check the reusability of the catalyst, after the completion of the reaction of indole with benzaldehyde under the optimal reaction conditions, the filtered

Entry	Catalyst	Conditions	Time (min)	Yield (%)	Refs
1	NaY zeolite-NHSO ₃ H/Cu(OAc) ₂	rt	40	98	This work
2	Secondary amine/ionic liquids	M. W	5	95	40
3	Silica sulfuric acid	rt	42	92	16
4	Prolinium Triflate	rt	300	92	41
5	Nano-SiO ₂	80°C/Ultrasonic	60	93	44
6	1,3-Dibromo-5,5-dimethylhydantoin	50°C	57	90	45
7	n-Dodecylbenzene sulfonic acid	40°C	60	91	46

Table 3. Comparing this method with some reported methodologies for the synthesis of 3,3'-(phenylmethylene)bis(1H-indole)

Table 4. Preparation of 3,4-dihydropyrimidin-2(1H)-ones^a

					Mp (°C)
Entry	R	Reaction time (min)	Yield (%) ^b	Found	Reported (Ref)
1	C ₆ H ₅	15	97	205-207	204–206 ^{47a}
2	$4-F-C_6H_4$	12	94	181-182	182–184 ^{47a}
3	$3 - NO_{2} - C_{6}H_{4}$	17	91	223-225	227–229 ^{47a}
4	$2-Cl-C_6H_4$	20	90	220-223	222–224 ^{47a}
5	4-MeO-C ₆ H ₄	25	92	201-203	$205 - 207^{47a}$
6	$4-HO-C_6H_4$	35	88	225-228	$227 - 229^{47a}$
7	$2,4-Cl_2-C_6H_3$	60	93	249-251	249-250 ^{21b}
8	4-Me-C ₆ H ₄	20	98	211-213	215-216 ^{47b}
9	1-Naphthyl	55	89	250-252	247-248 ^{21k}
10	PhCH ₂ CH ₂	70	92	182–184	182–184 ^{47c}
11	$n-C_7H_{15}$	75	91	120-123	120–123 ^{47c}
12	Thiophen-2-yl	40	85	219-221	215-217 ^{21g}
13	C_2H_5	100	60	181–183	180–181 ^{47b}

^a Conditions : ethylacetoactate (1.5 mmol), aldehyde (1 mmol), urea (1 mmol), catalyst (0.01 g), solvent-free, 60°C. ^b Isolated yield.

Table 5. Comparison of different methods for the synthesis of ethyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5carboxylate

Entry	Catalyst	Time (min)	Solvent	Yield (%)	Temperature (°C)	Refs
1	NaY zeolite-NHSO3H/Cu(OAc)2	15	None	97	60	This work
2	CuCl ₂ .2H ₂ O	60	None	96	100	17f
3	$LaCl_3 \cdot 7H_2O:HCl$	300	EtOH	95	Reflux	21b
4	HC1	1080	EtOH	78	Reflux	21b
5	Concentrated HCl	4320	MeOH	79	rt	18a
6	LiBr	180	CH ₃ CN	92	Reflux	21a
7	Mn(OAc) ₃ .2H ₂ O	120	CH ₃ CN	96	Reflux	21e
8	ZrCl4	240	EtOH	90	Reflux	21f
9	InBr ₃	420	EtOH	98	Reflux	21g
10	InCl ₃ .4H ₂ O	420	EtOH	94	Reflux	21g
11	BiONO ₃	90	CH ₃ CN	96	40–50	211
12	$H_{3}PMo_{12}O_{40}$	300	AcOH	80	reflux	47d
13	<i>p</i> -TsOH	150	EtOH	91	reflux	47e
14	Silica sulfuric acid	360	EtOH	91	Reflux	47a
15	Ersorb-4	480	EtOH	93	80	47f
16	KSF	2880	None	82	130	47g

Synthesis of Some Heterocycles by a Novel Catalyst

				Mp (°C)		
Product	Ar	Time (min)	Yield (%) ^b	Found	Reported (Refs)	
1	C ₆ H ₅	20	95	113–115	112–114 ⁴⁸	
2	$4-NO_2C_6H_4$	18	97	230-232	232-235 ^{35b}	
3	$2,4-Cl_2C_6H_4$	30	92	156-158	154–158 ^{35b}	
4	4-MeOC ₆ H ₄	30	88	123-126	$120 - 122^{48}$	
5	$4-(CH_3)_2NC_6H_4$	35	87	170-172	169–172 ^{35b}	
6	$2-ClC_6H_4$	25	90	85-87	84–86 ⁴⁸	
7	$4-ClC_6H_4$	19	94	118-120	$118 - 119^{48}$	
8	$3-NO_2C_6H_4$	90	88	181-182	$182 - 184^{48}$	

Table 6. Preparation 2-aryl-1H-benzothiazoles under optimized conditions^a

^a Conditions: 2-aminothiophenol (1 mmol), aldehyde (1 mmol), catalyst (0.01 g), solvent-free, 40°C. ^b Isolated vield.

catalyst was washed with chloroform, dried at 60°C for 1 h, and reused for the model reaction (Table 2, entry 1). It was found that catalyst could be recycled for at least six reaction cycles without notable changes in its catalytic activity (Figure 6). Also after six runs, the FT-IR spectrum of the recovered catalyst displayed no obvious change in its structure in comparison to that of the fresh catalyst (Figure 7).

Conclusion

In conclusion, NaY zeolite-NHSO₃H/Cu(OAc)₂ was found to be a mild, efficient, and reusable solid acid catalyst for the reaction of indoles with aldehydes to furnish bis(indolyl)methanes, tris(indolyl)methanes, and tetrakis(indolyl)methanes at room temperature. Also, the syntheses of 3,4-dihydropyrimidin-2(1*H*)-ones and 2-aryl-1*H*-benzothiazoles were carried out successfully in the presence of NaY zeolite-NHSO₃H/Cu (OAc)₂. The reusability of this heterogeneous organic/







Fig. 7. FT-IR spectra of fresh catalyst and the six times reused catalyst.

inorganic hybrid catalyst makes this method nearly green and environmentally friendly. High yields, rather short reaction times, mild conditions, easy work-up, good purity, and low-cost procedure are advantages of this method.

EXPERIMENTAL

All chemicals used were purchased from Merck and Fluka. Melting points were determined on an electro-thermal digital melting point apparatus. The catalyst was characterized by an atomic absorption instrument (Varian SpectrAA 200), an X-Ray diffractometer (Philips 8440) at room temperature using Cu K α radiation, an FT-IR spectrometer (Galaxy series FT-IR 5000), and a TGA-DSC apparatus (Rheometric scientific STA-1500). NMR spectra were recorded on a Bruker (300 MHz) spectrometer, and the chemical shifts (ppm) were referenced to the internal standard

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tetramethylsilane (TMS). Microanalyses were performed by an elemental analyzer (Elemental, Vario EL III) at Arak University. The Microanalyses results agreed favorably with the calculated values. Reactions were monitored by thin-layer chromatography using silica gel-coated aluminum sheets F254 (Merck).

General procedure for the synthesis of NaY zeolite-NHSO₃H/Cu(OAc)₂ catalyst

To a mixture of NaY zeolite in toluene (20 mL), trimethoxysilvl propylamine (2 mL) was added and stirred for 24 h under reflux conditions. Then zeolite was separated by filtration and dried at 60°C. For sulfonation, chlorosulfonic acid (2 mL) and triethylamine (0.2 mL) were added to a mixture of functionalized zeolite (1 g) in toluene (20 mL) and stirred under reflux conditions for 24 h. Finally, the precipitate was filtrated, washed with water, and dried at 60°C as the NaY-SA compound. A pH analysis of NaY-SA for loading of SO₃H showed 1 mmol/g. In the next step, NaY-SA (1 g) was reacted with 100 mL of a 0.001 M solution of Cu(OAc)₂ in toluene for 24 h at room temperature. After sonication $(2 \times 3 \text{ min})$, the NaY zeolite-NHSO₃H/Cu(OAc)₂ product was filtered and dried at 60°C (Scheme 7). Then the loading of copper in NaY zeolite-NHSO₃H/Cu(OAc)₂ was determined to be 2% by atomic absorption spectroscopy.

General procedure for the synthesis of bis(indolyl) methanes

To a mixture of indole (2 mmol, 0.234 g) and aldehyde (1 mmol) in acetonitrile (4 mL), NaY zeolite-NHSO₃H/Cu(OAc)₂ (0.02 g) was added and stirred for an appropriate time at room temperature. After completion of the reaction as monitored by TLC (*n*-hexane/ EtOAc; 8:2), the NaY zeolite-NHSO₃H/Cu(OAc)₂ catalyst was filtered and the organic layer evaporated under reduced pressure to give the pure product.

General procedure for the synthesis of tris(indolyl) methanes

To a mixture of indole (3 mmol, 0.351 g) and α,β -unsaturated ketone (1 mmol) in 1,4-dioxane (4 mL), NaY zeolite-NHSO₃H/Cu(OAc)₂ (0.03 g) was added and stirred for an appropriate time at room temperature. The work-up stage was similar to that reported for the preparation of bis(indolyl)methanes.

Spectral data for the new compounds are as follows:

1,1,5,5-Tetra(1*H*-indol-3-yl)pentane (**13**, Table 2): Mp: 115–117°C. IR (cm⁻¹): 3410, 3053, 2924, 2852, 1616, 1456, 1415, 1336, 1276, 1244, 1091, 1010, 744, 491, 424. ¹HNMR (δ (ppm), CDCl₃): 0.92 (m, 2 H), 1.36 (m, 4 H), 4.68 (m, 2 H), 6.58–8.20 (m, 25 H). ¹³C NMR (δ (ppm), CDCl₃):25.50, 32.90, 36.01, 102.60, 110.37, 111.05, 111.26, 111.49, 114.88, 117.63, 118.12, 119.10, 119.53, 119.81, 120.73, 121.70, 121.98, 122.42, 123.69, 124.17, 126.11, 126.56, 127.83, 135.75, 136.53, 137.17, 138.79, 140.08. Elemental analysis: Calculated: C, 83.43; H, 6.06; N: 10.52. Obtained: C, 84.05; H, 6.23; N, 9.72.

3,3'-(3-(1*H*-Indol-2-yl)-1,3-diphenylpropane-1,1diyl)bis(1*H*-indole) (**16**, Table 2): Mp: 140–142°C. IR (cm⁻¹): 3408, 3053, 2928, 2850, 1608, 1508, 1454, 1415, 1336, 1217, 1167, 1093, 1008, 744, 459, 422. ¹H NMR (δ (ppm), CDCl₃): 2.90–2.97 (d, 2 H), 4.29 (m, 1 H), 6.57–8.05 (m, 28 H). ¹³C NMR (δ (ppm), CDCl₃): 29.67, 38.84, 42.22, 98.61, 119.25, 111.05, 121.61, 121.87, 122.12, 123.14, 125.16, 127.60, 128.11, 128.61, 128.96, 129.53, 131.58, 132.15, 135.45, 135.78, 139.16, 14.12, 145.50. Elemental analysis: Calculated: C, 86.47; H, 5.77; N, 7.76. Obtained: C, 87.11; H, 5.67; N: 7.22.

3,3'-(3-(1*H*-Indol-2-yl)-3-(4-nitrophenyl)-1-phenylpropane-1,1-diyl)bis(1*H*-indole) (**17**, Table 2): Mp: 127–129°C. IR (cm⁻¹): 3327, 3053, 2924, 2854, 1662,

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1595, 1514, 1454, 1415, 1338, 1215, 1095, 1012, 846, 742, 686, 422, 223; ¹H NMR (δ (ppm), CDCl₃): 2.02 (m, 2 H), 4.17–4.26 (d, 1 H), 6.96–8.32 (m, 27 H); ¹³C NMR (δ (ppm), CDCl₃): 31.10, 40.26, 63.34, 109.42, 111.64, 116.70, 117.95, 120.51, 123.36, 123.99, 125.27, 127.17, 127.78, 130.98, 133.53, 134.47, 140.49, 141.13, 142.37, 144.93, 161.43, 165.20. Elemental analysis: Calculated: C, 79.84; H, 5.15; N, 9.55. Obtained: C, 78.56; H, 5.31; N, 9.87.

3,3'-(3-(1*H*-Indol-2-yl)-3-(4-methoxyphenyl)-1-phenylpropane-1,1-diyl)bis(1*H*-indole) (**18**, Table 2): Mp: 114–116°C. IR (Cm⁻¹): 3404, 3059, 2920, 2850, 1656, 1595, 1510, 1456, 1421, 1338, 1294, 1251, 1217, , 1172, 1020, 829, 744, 692, 532, 422, 277. ¹H NMR (δ (ppm), CDCl₃): 1.27 (m, 2 H), 3.76 (m, 1 H), 3.88 (s, 3 H), 6.79–8.04 (m, 27 H). ¹³C NMR (δ (ppm), CDCl₃): 29.72, 47.99, 55.19, 55.44, 111.12, 113.79, 114.44, 119.14119.78,119.78, 121.32, 121.86, 122.23, 125.14, 127.60, 12813, 128.44, 128.59, 128.76, 130.27, 132.61, 133.02, 135.99, 136.33, 138.50, 140.18, 140.78, 144.79, 161.70; Elemental analysis: Calculated: C, 84.03; H, 5.82; N, 7.35; Obtained: C, 84.89; H, 5.91; N: 7.47.

General procedure for the synthesis of 3,4dihydropyrimidin-2(1*H*)-ones

A solution of β -keto ester 1 (1.5 mmol), the appropriate aldehyde 2 (1 mmol), urea 3 (1.2 mmol), and NaY zeolite-NHSO₃H/Cu(OAc)₂ (0.01 g) was heated at 60°C for an appropriate time (Table 4). The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was filtrated and cooled and poured onto 50 g of crushed ice and stirring was continued for few minutes. The solid products were filtered, washed with cold water (2 × 10 mL), and recrystallized from ethanol. All the products were characterized by their IR, ¹H, and ¹³C NMR spectral data, and their melting points were compared with the literature values (Table 4).^{21g,k,47a-c}

General procedure for the synthesis of 2-aryl-1*H*-benzothiazoles

To a mixture of 2-aminothiophenol (1 mmol) and aldehydes (1 mmol) was added NaY zeolite-NHSO₃H/ $Cu(OAc)_2$ (0.01 g) and heated at 40°C for an appropriate time (Table 6). Progress of the reaction was followed by TLC. After completion of the reaction, the catalyst was filtrated and the organic layer evaporated

under reduced pressure to give the pure product. For further purification, the products were recrystallized from ethanol 96%. All the products were characterized by their IR, ¹H, and ¹³C NMR spectral data, and their melting points were compared with literature values (Table 6).^{35b,48}

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