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Nano-kaolin-$TiCl_4$ as a new, green and effective nano catalyst for one-pot synthesis of tetrahydrobenzo[*B*]pyrans

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Nano-kaolin-$TiCl_4$ as a new and mild solid acid catalyst is applied to the synthesis of biologically important tetrahydrobenzo[b]pyrans. The reaction involves the use of an aromatic aldehyde, malononitrile and dimedone. The procedure is very simple and the products are isolated with an easy workup in good-to-excellent yields. The morphology of nanocatalyst (nano-kaolin-$TiCl_4$) was observed using a scanning electron microscopy (SEM). Also, the vibrational spectrum analysis (FT-IR) of the catalyst has been performed.

Keywords: nano-kaolin-$TiCl_4$, dimedone, aldehydes, malononitrile, multicomponent reaction, tetrahydrobenzo[b]pyrans

INTRODUCTION

Multi-component reactions, by virtue of their convergence are widely applied in pharmaceutical chemistry in order to producing different structures and combinatorial libraries for drug discovery [1]. Tetrahydrobenzo[*b*]pyrans are some examples of multi-component reactions. Pyran derivatives belong to an important class of heterocyclic compounds having important biological properties such as insecticidal, antiviral, antileishmanial and antimicrobial activities [2-5].

Realizing the importance of 4*H*-pyran derivatives, in recent decades various methods has been reported for the tetrahydrobenzo[*b*]pyrans with the aim of obtaining more biologically potent heterocyclic systems using different catalysts via three-component condensations including the use of 2,2,2-trifluoroethanol [6], $BF_3.OEt_2$ [7], 4-Amino-1-(2,3-dihydroxy propyl) pyridinium hydroxide [8], triethylenetetraammonium trifluoro acetate [9], $PhB(OH)_2$ [10], $NH_4Al(SO_4)_2.12H_2O$ [11], (S)-proline [12], potassium phthalimide [13], thiamine hydrochloride [14], choline hydroxide [15], and NPs SiO_2-H_2SO_4 [16], etc.

In addition, heterogeneous solid acids have advantages such as simplicity in handling, economic regulations, easy recovery and frequent use without loss of their efficiency over in comparison with conventional homogeneous acid catalysts.

In this study, the kaolin has been used as an adsorbent for the preparation of nano-kaolin-$TiCl_4$ which has average small size and is well distributed.

We have now used nano-kaolin-$TiCl_4$ as a new rapid method affording excellent yield and using solid phase acidic green nano catalyst for the synthesis of tetrahydrobenzo[*b*]pyran derivatives at reflux.

EXPERIMENTAL

The chemicals for this work were purchased from Fluka (Buchs, Switzerland) and were used without further purification. The known products were identified by comparison of their melting points and spectral data with those reported in the literature. Melting points were recorded on an Electrothermal 9100 apparatus in open capillary tubes. IR spectra were recorded on a Shimadzu IR-470 spectrometer. The ^{1}H NMR spectra were recorded on Bruker DRX-400 Avance spectrometer at solution in DMSO-d_6 using TMS as the internal standard. The IR spectrum of the catalyst was recorded using a model Bruker Tensor 27 FT-IR operating within the range of 400-4000 cm^{-1}. The morphologies of the nanoparticles were observed using FESEM of a MIRA3 TESCAN microscope with an accelerating voltage of 15 kV.

Synthesis of nano-kaolin-$TiCl_4$

The reagent was prepared by stirring a mixture of $TiCl_4$ (0.5 ml) and 1 g of kaolin powder in 5 ml of n-hexan for 2 h at room temperature. The slurry was filtered and washed with *n*-hexan. The obtained solid (nano-kaolin-$TiCl_4$) was dried in an oven at 60°C for 4h and then pulverized at the mortar. The size of particles was obtained below 50 nm using SEM.

General procedure for the preparation of compounds 4a-j

A mixture of aromatic aldehyde (1 mmol), malononitrile (1.2 mmol) and dimedone (1 mmol) in 5 mL of EtOH was refluxed for the appropriate time in the presence of nano-kaolin-$TiCl_4$ (0.008g). After completion of reaction, as indicated by TLC (*n*-hexane:ethyl acetate 3:1), the reaction mixture

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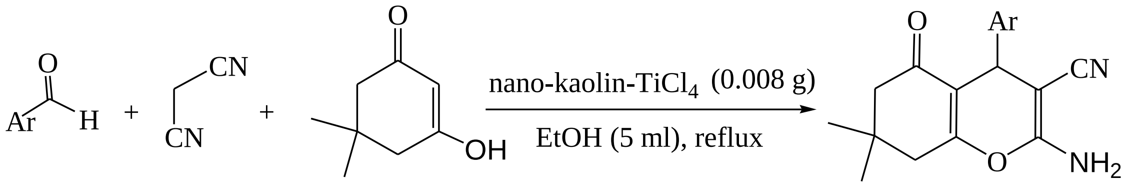
was filtered to remove the catalyst. After evaporation of the solvent, the crude product was re-crystallized from hot ethanol to obtain the pure compound.

RESULTS AND DISCUSSION

In continuation of our previous research on the use of nano solid acids in organic synthesis [16-24], nano-kaolin-TiCl$_4$, as a new nano catalyst, has been applied for the synthesis of tetrahydrobenzo[*b*]pyran derivatives.

The catalytic activity of nanoparticles was investigated for synthesis of tetrahydrobenzo[*b*]pyrans, by the condensation of an aldehyde **1a-j**, malononitrile **2** and dimedone **3** (Scheme (1).



1 **2** **3** **4**

Scheme 1. Synthesis of tetrahydrobenzo[*b*]pyran derivatives in the presence of nano-kaolin-TiCl$_4$ as catalyst.

The FT-IR spectrum of nano-kaolin-TiCl$_4$ shows a broad band at 3397 cm^{-1} which corresponds to the stretching vibrations of OH groups. The absorption bands around 1035 and 1116 cm^{-1} display the stretching vibrations of the Si-O bonds. For nano-kaolin-TiCl$_4$, kaolin absorptions appear in addition to the stretching vibrations of Si-O-Ti at 914 cm^{-1}; indicating that titanium chloride is supported on kaolin

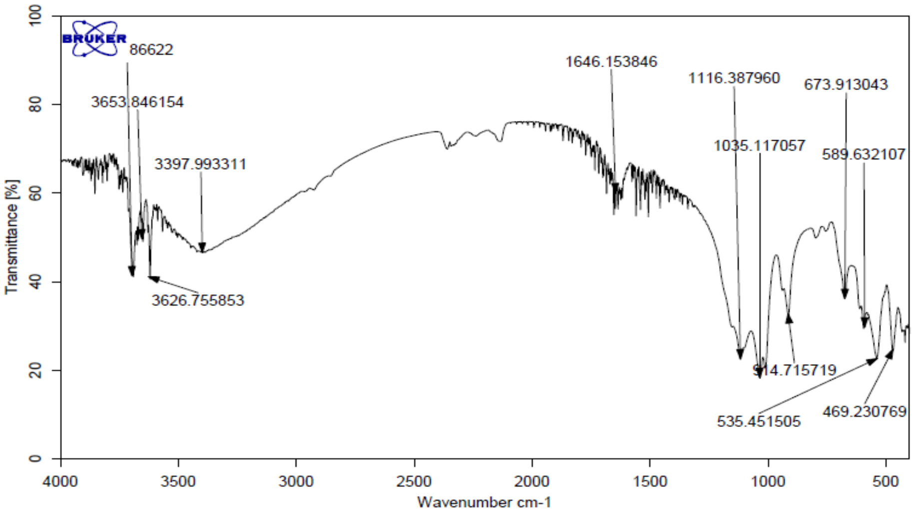


Fig. 1. FT IR spectrum of nano-kaolin-TiCl$_4$ catalyst

The morphology and size of nano-kaolin-TiCl$_4$ (Fig. 2) was observed by SEM images. As shown in Figure 2, the size of nano-kaolin-TiCl$_4$ is below 50 nm and homogeneous nano sheet surface was revealed. In order to determine the optimum quantity of nano-kaolin-TiCl$_4$, the reaction of dimedone, malononitrile and benzaldehyde was carried out under reflux in ethanol using different quantities of nano-kaolin-TiCl$_4$. As shown in Table 1, 0.008g of nano-kaolin-TiCl$_4$ gives an excellent yield in 15 min.

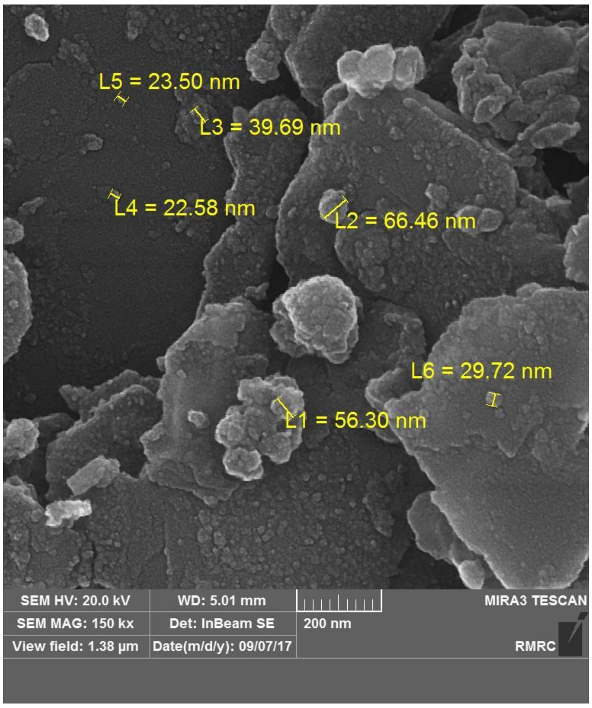


Fig. 2. SEM micrograph of nano-kaolin-TiCl$_4$

Table 1. Optimization of the reaction conditions for synthesis of 4a

Entry	Catalyst (amount)	Solvent/Condition	Time(min)	Yield
1	Nano-kaolin-TiCl$_4$ (0.008 g)	CH_2Cl_2/Reflux	15	32
2	Nano-kaolin-TiCl$_4$ (0.008 g)	EtOH/Reflux	15	94
3	Nano-kaolin-TiCl$_4$ (0.008 g)	CH_3CN/Reflux	15	45
4	Nano-kaolin-TiCl$_4$ (0.008 g)	MeOH/Reflux	15	57
5	Nano-kaolin-TiCl$_4$ (0.008 g)	H_2O/Reflux	15	83
6	Nano-kaolin-TiCl$_4$ (0.006 g)	EtOH/Reflux	15	68
7	Nano-kaolin-TiCl$_4$ (0.01 g)	EtOH/Reflux	15	95
8	Nano-kaolin-TiCl$_4$ (0.008 g) 2nd run	EtOH/Reflux	15	89
9	Nano-kaolin-TiCl$_4$ (0.008 g) 3rd run	EtOH/Reflux	15	86
10	kaolin (0.01 g)	EtOH/Reflux	20	Trace

To study the scope of the reaction, a series of aldehydes with dimedone and malononitrile were examined by nano-kaolin-TiCl$_4$ as catalyst. The results are shown in Table 2. In all cases, aromatic aldehyde substituted with either electron-donating or electron-withdrawing groups underwent the reaction smoothly and formed products in approving yields.

Table 2. Synthesis of tetrahydrobenzo[*b*]pyrans [a]

Entry	Ar	Product[b]	Time(min)	Yield[c]	M.P.(˚C) [Ref.]
1	C_6H_5	4a	15	94	231-233 [8]
2	4-ClC_6H_4	4b	15	86	214-216 [6]
3	4-$MeOC_6H_4$	4c	15	89	200-202 [16]
4	2-FC_6H_4	4d	15	87	230-232 [16]
5	4-$NO_2C_6H_4$	4e	15	91	180-181 [6]
6	2-$NO_2C_6H_4$	4f	15	90	225-227 [13]
7	4-FC_6H_4	4g	15	89	208-210 [15]
8	4-$Me_2NC_6H_4$	4h	15	90	214-215 [13]
9	4-HOC_6H_4	4i	15	91	217-219 [13]
10	1-naphthyl	4j	15	85	216-218 [16]

[a]Ratio of aldehyde (mmol): dimedone (mmol): malononitrile (mmol): catalyst (g) is 1:1:1.2: 0.008. [b]All products are known and were identified by their melting points, IR and ^{1}H NMR spectra. [c]Isolated yield

In order to establish better catalytic activity of nano-kaolin-TiCl$_4$, the synthesis of tetrahydrobenzo[*b*]pyran derivatives was compared with other catalysts reported in literature. As shown in Table 3, synthesis of these compounds catalyzed by nano-kaolin-TiCl$_4$ in EtOH offers production of the corresponding products in shorter time, much efficient yield and milder condition is done, while other methods require more amount of catalyst and longer reaction time for synthesis of tetrahydrobenzo[*b*]pyrans.

Table 3. Comparison of nano-kaolin-TiCl$_4$ and various catalysts in the synthesis of tetrahydrobenzo[*b*]pyrans

Entry	Catalyst	Conditions	Time	Yield	Ref.
1	2,2,2-Trifluoroethanol	Reflux	5 h	90	6
2	$BF_3.OEt_2$	EtOH, Reflux	2 h	85-90	7
3	[ADPPY][OH][a]	EtOH, 60°C	48 h	87	8
4	Triethylenetetraammonium trifluoro acetate	EtOH, Reflux	10 min	57-90	9
5	$PhB(OH)_2$	H_2O/EtOH, Reflux	10-60 min	42-95	10
6	Thiamine hydrochloride	EtOH, Reflux	10-60 min	87-96	14
7	$NH_4Al(SO_4)_2.12H_2O$	EtOH, 80°C	120-130 min	85-95	11
8	potassium phthalimide	H_2O, Reflux	10-25 min	90-98	13
9	NPs SiO_2-H_2SO_4	EtOH, Reflux	10 min	80-96	15
10	[Ch][OH][b]	H_2O, 80°C	10-300 min	79-98	16
11	Nano- kaolin-TiCl$_4$	EtOH, Reflux	15 min	85-94	This work

[a] 4-Amino-1-(2,3-dihydroxy propyl) pyridinium hydroxide; [b] Choline hydroxide

CONCLUSION

The present investigation shows that nano-kaolin-TiCl$_4$ a capable nanocatalyst to be used for tetrahydrobenzo[*b*]pyran synthesis via one-pot reaction of aldehydes, malononitrile and dimedone. Nano-kaolin-TiCl$_4$ was successfully prepared and characterized using FTIR and SEM. Prominent among the advantages of this method are such as shorter reaction times, simple work-up, affords excellent yield, and re-usable for a number of times without appreciable loss of activity. The present method does not involve any hazardous organic solvent. Therefore, this procedure could be classified as green chemistry.

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