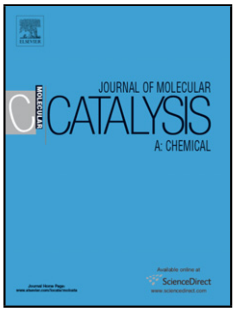

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Preparation and characterization of Lewis acid grafted sulfonated carbon@titania composites for the multicomponent synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles and benzoxanthenones under solvent-free conditions

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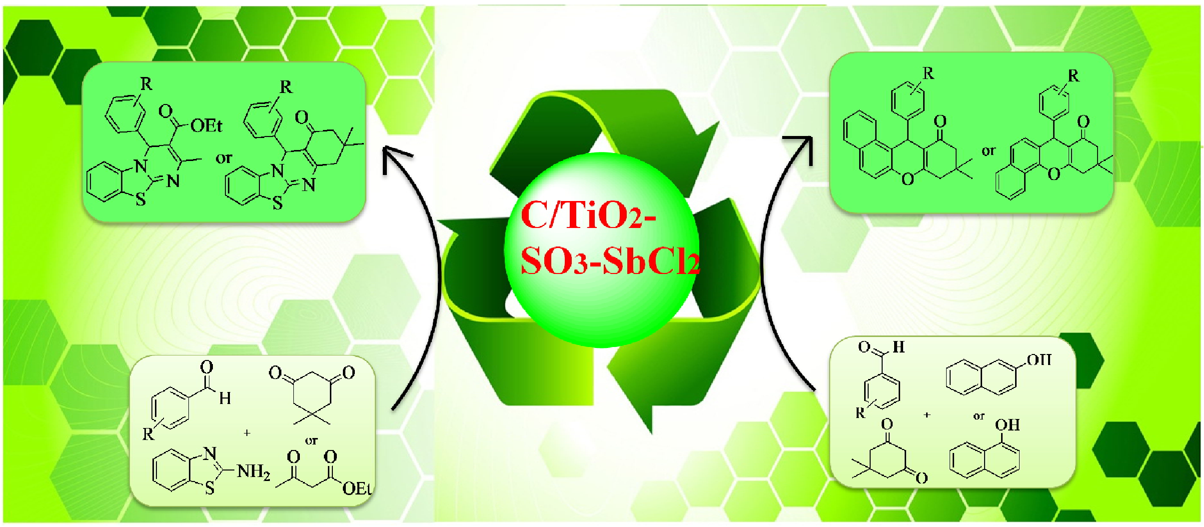
Graphical abstract

A series of Lewis acid covalently grafted over sulfonated carbon@titania composites have been designed and investigated as sustainable recyclable catalytic system for multicomponent synthesis.



Highlights

- Design, synthesis and characterization of C/TiO_2-SO_3M.
- 4*H*-Pyrimido[2,1-*b*]benzothiazoles and benzoxanthenones were synthesised.
- Multicomponent synthesis was effectively carried out under solvent-free conditions.
- The catalyst showed excellent recyclability with negligible leaching of Lewis acid.

Abstract

A series of novel and highly efficient Lewis acids covalently grafted over sulfonic acid functionalized carbon@titania composites were successfully synthesized via sulfonation of carbon@titania composites followed by treatment with different Lewis acids like $AlCl_3$, $FeCl_3$, $SbCl_3$, $SnCl_2$, $Cu(OAc)_2$ and$Bi(NO_3)_3$. The utility of the developed catalysts was explored for the synthesis of a diverse range of 4*H*-pyrimido[2,1-*b*]benzothiazoles and benzoxanthenones, and among various catalysts, C/TiO_2-SO_3-$SbCl_2$ was found to be the most active.We report here the synthesis of five novel compounds and the structure of one of the compounds has also been confirmed by single-crystal X-ray diffraction. All the five prepared composites were characterized by FTIR and ICP-AES analysis, whereas the most active one, C/TiO_2-SO_3-$SbCl_2$ was further characterized by XRD, EDX, CHNS, SEM, TEM, HRTEM and TGA. The catalyst can be recovered and reused for atleast five runs without any significant impact on catalytic activity and selectivity. The high catalytic activity, thermal stability, simple recovery and reusability, and eco-friendly nature of the catalyst makes the present method to be particularly attractive from the view point of green chemistry.

Keywords: Lewis acids, sulfonated carbon@titania composites, 4*H*-pyrimido[2,1-*b*]benzothiazoles, benzoxanthenones, solid acid catalyst, recylability.

1. Introduction

Lewis acid catalysts such as $AlCl_3$, BF_3, and transition metal halides find wide applications in the production of industrially important chemicals, including polymers and pharmaceuticals **[1]**. However, these homogeneous catalysts are highly toxic, moisture sensitive, show air intolerance and expensive. In addition, the recovery and reuse of homogeneous Lewis acid catalysts is an extremely formidable obstacle. Recently, the use of Lewis acids supported on ‘‘inert’’ carriers has received considerable importance **[2-5]**. The improved activity, greater selectivity, ease of handling, enhanced reaction rates, simple workup and recyclability are other common features that make the use of supported Lewis acids as attractive alternatives to conventional homogeneous reagents. For this purpose, biomass-derived porous carbons have been found to be potential supports for the preparation of carbon-supported catalysts with a wide range of catalytic applications. Such carbonaceous catalysts are environmentally benign and could provide a cost-competitive advantage as compared to existing heterogeneous catalysts. Excellent physical properties of carbon materials such as chemically inert nature, stability against various chemical environments, low cost, hydrophobicity and tunable surface properties make such catalytic systems compatible with diverse catalysis reactions **[6-9]**. Recently, carbon based materials have been dispersed over inorganic oxides like silica, titania etc. to develop hybrid composite materials that show synergistic effect of both the organic and inorganic support material on the catalytic performance of the final catalyst **[10-14]**. Such hybrid materials show enhanced chemical and thermal stability, higher catalytic activity and availability of active surface groups for the linkage of the active catalytic species.

Multicomponent reactions (MCRs) have become powerful tools in organic, combinatorial and medicinal chemistry, and have attracted much attention from synthetic organic chemists because they can build complex molecules with a diverse range of complexities from readily available starting materials **[15-18]**. 4*H*-Pyrimido[2,1-*b*]benzothiazole derivatives are an important class of fused heterocycles due to their broad range of potential biological activities, as well as their importance in the preparation of drug molecules and natural products **[19-23]**. Xanthenes and benzoxanthenones represent the most common structural motifs found in several natural products and synthetic bioactive compounds. Over the recent years, these have attracted considerable attention due to their diverse biological properties as well as their use as dyes and fluorescent materials **[24-27]**. Synthetic strategies mediated through the use of variable catalytic systems have been reported in literature for the synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles **[28-31]** and benzoxanthenones **[32-43]**. Many of these synthetic methods, however, have limitations such as harsh reaction conditions, long reaction time, expensive catalysts, and generation of noticeable amount of side products. Thus, there is an ample scope for the development of new greener synthetic protocols to assemble such scaffolds.

In this context, considering the broad applicability of carbon based organic-inorganic hybrid materials, we have designed and synthesized novel and sustainable catalytic system utilizing carbon@titania composites functionalized by sulfonic acid as the support material for the immobilization of different Lewis acids. The catalytic activity of the solid Lewis acid catalysts has been explored for the one-pot multicomponent synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles and benzoxanthenones under solvent-free conditions. The aim of this protocol is to highlight the synergistic effect of the combined use of multicomponent coupling reactions under solvent-free conditions and application of solid Lewis acid catalyst supported on carbon@titania composites for the development of new eco-friendly strategy for heterocyclic synthesis.

2. Experimental

2.1 Reagents and instrumentation

All starting materials were purchased from commercial sources and used without further purification. The ^{1}H and ^{13}C NMR data were recorded in $CDCl_3$ or DMSO-d_6 or $CDCl_3$+DMSO-d_6 on Bruker Avance III (400 MHz) spectrometer. The FTIR spectra were recorded on Thermo Nicolet, Avatar 370 spectrophotometer, XRD was recorded in 2θ range of 10-80° on Bruker AXS D8 Advance and mass spectral data on Bruker Esquires 3000 (ESI). CHNS analysis was recorded on ThermoFinnigan FLASH EA 1112 series. SEM images were recorded using JEOL Model JSM-6390LVScanning ElectronMicroscope, Transmission Electron Micrographs (TEM) were recorded on Philips CM-200. EDX analysis was carried out using JEOL Model JED-2300 and TGA was recorded on Perkin Elmer, Diamond TG/DTA.

2.2 Preparation and Characterization of Lewis acid grafted sulfonated carbon@titania composites

Initially, carbon@titania composites were prepared by the partial carbonization of starch in the presence of nano-titania leading to the formation of amorphous carbon@titania composites. Thereafter, the functionalization of the as prepared composites with sulfonic acid group was done using conc. sulfuric acid followed by treatment with different lewis acids viz $AlCl_3$, $FeCl_3$, $SbCl_3$, $SnCl_2$, $Cu(OAc)_2$, $Bi(NO_3)_3$,thereby forming respective Lewis acid grafted sulfonated carbon@titania composites [C/TiO_2-SO_3-$AlCl_2$, C/TiO_2-SO_3-$FeCl_2$, C/TiO_2-SO_3-$SbCl_2$, C/TiO_2-SO_3-SnCl, C/TiO_2-SO_3-Cu(OAc), C/TiO_2-SO_3-$Bi(NO_3)_2$]. Among the different inorganic oxides available, we have used titanium dioxide because of its unique surface properties. Besides, titanium dioxide has been shown to exhibit promising electrochemical properties, high photocatalytic activity, high chemical and thermal stability, easy commercial availability and non-toxicity**[44-45]**. Titania and its composites have usually been studied for their photocatalytic properties**[46-49]**, whereas in the present work titania based carbon composites have been studied for catalytic activity.

In a typical procedure, a mixture of starch and nano-titania (nanopowder, <100nm particle size (BET), >14.0 m^2/g; 10 g) in the ratio of 1: 1.2 was taken in a round-bottom flask and heated at 353 K for 10 h. The incomplete carbonization of resulting mixture was done by heating strongly at 673 K under N_2 atmosphere for 10 h leading to the formation of amorphous carbon@titania composites. Afterwards, the sulfonation of the as prepared composites was done by adding concentrated sulfuric acid (>96 wt%) and further heated at 423 K for 10 h under N_2 atmosphere. The sulfonated composite obtained was then washed repeatedly with hot distilled water (>353 K) until sulfate anions were no longer detected in the filtered water. Sulfonated carbon@titania composites were dried in an oven at 373 K for 2 h (7 g) and then converted into lewis acid grafted sulfonated carbon@titania composites through anion metathesis. The solid acid (2 g) was treated with different lewis acids (0.5 mmol) viz $AlCl_3$, $FeCl_3$, $SbCl_3$, $SnCl_2$, $Cu(OAc)_2$ or $Bi(NO_3)_3$ in acetonitrile (10 mL) at reflux temperature for 24 h. After cooling to room temperature, the mixture was filtered, washed with acetonitrile and dried under vacuum and finally kept at 90 ˚C overnight. The catalysts were conditioned by refluxing for 12 h each in xylene at 130 ˚C (2×2 h), ethanol at 78 ˚C (2×2 h) and acetonitrile at 80 ˚C (2×2 h) and finally dried in oven at 90 ˚C overnight.

The general procedure for the synthesis of Lewis acid grafted sulfonated carbon@titania composites has been shown in **Scheme 1**.All the solid Lewis acid catalysts were characterized by FTIR and ICP-AES analysis. The most active catalyst, C/TiO_2-SO_3-$SbCl_2$ was further characterized by XRD, CHNS, SEM, TEM, HRTEM and TGA.

FTIR

Successful functionalization and modification of the carbon @titania composites can be inferred from the FTIR analysis. The FTIR spectrum of Lewis acid grafted sulfonated carbon@titania composites shows the presence of a broad band in the range 3412-3472 cm^{-1} due to phenolic OH groups of the polycyclic aromatic carbon rings. The strong absorptions in the range 1700-1720 and 1606-1649 cm^{-1} were assigned to C=O and C=C stretching frequencies respectively. The C=O groups were produced by the oxidation of carbon by small amounts of sulfuric acid used for sulfonation.In addition, the presence of sulfonic acid group was confirmed by characteristic peaks at 1152-1180 and 1031-1137 cm^{-1} due to O=S=O asymmetric and symmetric stretching vibrations. The presence of a well defined band in the range 526-563 cm^{-1} is characteristic of TiO_2 attributable to Ti-O stretching frequency. It is also worth noting that there are no significant changes observed in the spectra of sulfonated carbon@titania composite and Lewis acid grafted sulfonated carbon@titania composites as the linkage of Lewis acid to SO_3H of the catalyst has only a slight decreasing effect on the S=O stretching frequency (**Fig. S1, ESI and Fig. 1**). Also there is no significant difference in the FTIR spectra of different Lewis acid catalysts as is clear from the **Table 1**.

ICP-AES

The amount of metal loaded onto the solid Lewis acid catalysts was determined by inductively coupled plasma atomic emission spectroscopy and it was found that 0.28 wt% Al, 0.58 wt% Fe, 1.26 wt% Sb, 1.23 wt% Sn, 0.60 wt% Cu and 2.17 wt% Bi were present in C/TiO_2-SO_3-$AlCl_2$, C/TiO_2-SO_3-$FeCl_2$, C/TiO_2-SO_3-$SbCl_2$, C/TiO_2-SO_3-SnCl, C/TiO_2-SO_3-Cu(OAc) and C/TiO_2-SO_3-$Bi(NO_3)_2$ respectively.

CHNS

The amount of sulfonic acid group grafted onto the surface ofC/TiO_2-SO_3-$SbCl_2$ was determined by elemental analysis. The loading of 1.5 wt% sulfur indicated that 0.32 mmole of -SO_3H groups were grafted per gram of C/TiO_2-SO_3-$SbCl_2$.

XRD

The XRD pattern of C/TiO_2-SO_3-$SbCl_2$exhibited diffraction peaks corresponding to combination of both rutile and anatase phase of TiO_2. The peaks at 25.1°, 41.0°, 48.2°, 54.1°and 68.8°correspond to the (101), (004), (200), (211) and (116) reflections of anatase TiO_2 whereas peaks at 27.2°, 35.8° and 56.4° correspond to the (110), (101) and (211) planes of rutile phase **[50-51]**. The observed diffraction peaks agree well with the tetragonal structure of TiO_2 (**Fig. 2**). This factindicates that the crystalline structure of titania nanoparticles is conserved even after the composite formation with carbon. The average crystallite size of titania nanoparticles was determined by Scherrer's equation and found to be 24 nm.

Energy dispersive X-ray analysis (EDX)

The elemental composition of C/TiO_2-SO_3-$SbCl_2$ was determined from energy dispersive X-Ray (EDX) analysis. The EDX spectrum, displayed in **Fig. 3**, clearly reveals the presence of all the expected main elements C, S, O, Ti, Sb and Cl in C/TiO_2-SO_3-$SbCl_2$.

Scanning electron microscopy (SEM)

The shape and surface morphology of the C/TiO_2-SO_3-$SbCl_2$ was investigated by scanning electron microscopy (**Fig. 4**). The SEM micrographs of the composite material exhibited irregular massivecongeries with relatively rough surface depicting the amorphous nature of the composite formed.

Transmission electron microscopy (TEM)

To provide more accurate information on the particle size and fine structure of the catalyst, transmission electron microscopy (TEM) was carried out. It can be seen from the TEM micrographs that the nanoparticles of TiO_2 with spherical morphology are partially agglomerated on the surface of the carbon material (Fig. 5a, b). The sulfonated carbonmaterial with immobilized antimony chloride appears as light grey spherical particles over which black coloured spots of titania can be visualised. The average size of titania nanoparticles as determined from TEM analysis was found to be 26 nm which is in accordance with the results obtained from XRD data (**Fig. 5c**). The TEM image of the C/TiO_2-SO_3-$SbCl_2$ does not show any significant change from the TEM micrographs of the sulfonated carbon@titania composites (C/TiO_2-SO_3H) depicting that the microstructure of the catalyst is preserved even after its modification by treatment with Lewis acid (**Fig. 5d**). The HRTEM image of the C/TiO_2-SO_3-$SbCl_2$ clearly shows the lattice fringes with d-spacing of 0.32 nm and 0.35 nm corresponding to (110) plane of rutile TiO_2 and (101) plane of anatase TiO_2 respectively (**Fig. 5e**), thereby confirming the presence of highly crystalline TiO_2 on the carbon material of the composite. In addition, the TEM micrographs were also taken for the recovered catalyst. Interestingly, it was observed that the shape and size of the particles remain unchanged which ultimately provides evidence that the morphology of the catalyst remains the same even after several catalytic runs.

Thermal gravimetric analysis (TGA)

The thermal stability of C/TiO_2-SO_3-$SbCl_2$ was investigated by carrying out the thermal analysis in the temperature range of 40-700 °C in a static atmosphere of nitrogen (**Fig. 6**).

The primary weight loss from the catalyst up to 100 °C is attributed to the elimination of the physically adsorbed solvent and chiefly surface adsorbed water, whereas weight loss at higher temperatures from 240-700 ^{o}Ccould be largely attributed to thermal decomposition of the organic moieties on the surface of the composite. Thus, from the TGA analysis, it can be concluded that the catalyst is thermally stable upto 240 °C, confirming that it could be safely used in organic reactions at 100 °C

2.3 General procedure for the C/TiO_2-SO_3-$SbCl_2$catalyzed synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles

To a mixture of ethylacetoacetate (1.0 mmol), aldehyde (1.0 mmol) and 2-aminobenzothiazole (1.0 mmol) in a round bottom flask (25 mL), C/TiO_2-SO_3H-$SbCl_2$ (0.1g) was added and the reaction mixture was heated at 90 ^{o}C for the appropriate time. On completion of the reaction (monitored by TLC), hot ethanol (2×10 mL) was added and the catalyst was separated by simple filteration. Removal of the solvent under reduced pressure afforded the product, which was further purified by crystallization from ethanol.

2.4 General procedure for the C/TiO_2-SO_3-$SbCl_2$ catalyzed synthesis of benzoxanthenones

A mixture of α- or β-naphthol (1.0 mmol), aldehyde (1.0 mmol), dimedone (1.0 mmol) and C/TiO_2-SO_3H-$SbCl_2$ (0.1g) was taken in a round bottom flask (25 mL) and heated at 100°C under solvent-free conditions for the appropriate time. After completion of the reaction as monitored by TLC, hot ethanol (2×10 mL) was added and catalyst was separated by simple filteration. The filtrate was concentrated to get the crude product, which was crystallized from ethanol. The catalyst was washed with double distilled water (3×10 mL) followed by CH_2Cl_2 (2×10 mL). It was dried at 90 ^{o}C for 2 h and reused for subsequent reactions.

All the products were characterized by ^{1}H, ^{13}C NMR and mass spectral data and comparison with authentic samples obtained commercially or prepared according to the literature methods. The structure of compound 5lwas also confirmed by single-crystal X-ray diffraction.

3. Results and Discussion

3.1Catalytic testing for the one-pot synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles

Initially, to select the most appropriate solid Lewis acid catalyst for the one-pot multicomponent synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles, the reaction of 2-aminobenzothiazole (1.0 mmol), 3-nitrobenzadehyde (1.0 mmol) and ethylacetoacetate (1.0 mmol) was investigated as the model reaction. It was found that C/TiO_2-SO_3-$SbCl_2$ was the most effective catalyst in terms of reaction time and yield among the different lewis acid catalysts screened (**Table 2, entry 3**). The high activity of C/TiO_2-SO_3-$SbCl_2$ may be due to the mild nature of the Lewis acid grafted on the sulfonated composite. Strong Lewis acids like $AlCl_3$ and $FeCl_3$ lead to undesirable side reactions and thus, reduces the desired product formation. Whereas, otherweak Lewis acids tend to be less active and thus need longer reaction time. Further, the effect of catalyst amount on the model reaction was also examined by varying the catalyst amount to 0.05 g (0.5 mol% Sb), 0.1 g (1 mol% Sb), 0.2 g (2 mol% Sb) and 0.3 g (3 mol% Sb). It was found that 0.1 g (1 mol% Sb) of C/TiO_2-SO_3-$SbCl_2$ was sufficient to get the optimum product yield and further increasing the catalyst amount did not increase the yields considerably (**Table 3, entry 5, 6, 9, 10**). To optimize the reaction conditions, the effect of different solvents and reaction temperature on the model reaction was studied. The model reaction was examined in different solvents such as water, ethanol, acetonitrile as well as under solvent-free conditions. It was found that higher product yields were obtained when the reaction was carried out under solvent-free conditions in comparison to liquid phase conditions (**Table 3**). The highest catalytic activity under solvent-free conditions may be due to the good dispersion of active reagent sites which facilitates better contact between reactant molecules and the catalyst **[53]**. Moreover, due to the absence of any solvent (as medium), there is no dilution effect and the heat needed for energy of activation is directly available to the reactant molecules. Further, to select the optimum reaction temperature, the model reaction was carried out under solvent-free conditions at 80, 90, 100 and 120 °C, and 90 °C was choosen to be the optimum reaction temperature considering the product yield and reaction time (**Table 3, entry 6**). Subsequently, with optimal conditions in hand, to study the scope and limitations of the present protocol, a wide range of substituted aldehydes were allowed to undergo three component condensation in the presence of C/TiO_2-SO_3-$SbCl_2$ under solvent-free conditions and the desired products were obtained in quantitative yields (**Table 4, products 5a-m**). The single crystal X-ray crystallography confirmed the formation of ethyl 2-methyl-4-(3-methoxyphenyl)-4*H*-pyrimido[2,1-*b*][1,3]benzothiazole-3-carboxylate (**Fig. 7, S3, ESI**). The scope of the reaction was further extended using dimedone as the 1,3-dicarbonyl compound for the multicomponent synthesis under the optimized conditions. The reaction using dimedone also proceeded smoothly with different aldehydes leading to the formation of fused thiazolo[2,3-*b*]quinazolinones in good to excellent yields (**Table 4, 6a-e**). Therefore, the present protocol has general applicability accommodating a variety of substitution patterns.

3.2 Catalytic testing for the one-pot synthesis of benzoxanthenones

The catalytic activity of different Lewis acid catalysts has been evaluated for the one-pot synthesis of benzoxanthenones using aldehyde (1 mmol), dimedone (1 mmol) and β-naphthol (1 mmol). C/TiO_2-SO_3-$SbCl_2$ was again found to be the most active catalyst for the one-pot multicomponent synthesis of benzoxanthenones among the different Lewis acid catalysts screened (**Table 2, entry 3**). To derive the optimal reaction parameters such as the amount of the catalyst required, reaction temperature, and the influence of the solvent for the C/TiO_2-SO_3-$SbCl_2$ catalyzed benzoxanthenone formation, the model reaction was performed under different variations of these parameters (**Table 3**). The optimum amount of catalyst for the model reaction was found to be 0.1 g (1 mol% Sb) in order to obtain the best results. The influence of the reaction medium was evaluated for the model reaction in protic and aprotic solvents as well as under solvent free conditions (**Table 3**) in the presence of catalytic amount of C/TiO_2-SO_3-$SbCl_2$ and again best results were obtained under solvent-free conditions (**Table 3 entry 7**). Further, the model reaction was carried out by varying the reaction temperature and the optimum reaction temperature was found to be 100 °C, as increase of the reaction temperature to 120 °C did not show a significant increase in the product yield (**Table 3, entry 8**), which however, decreased to 80% and 50% on lowering the reaction temperatures to 90 and 80 °C, respectively (**Table 3, entries 4 and 5**). Using the optimized conditions and to evaluate the scope of the developed method, the present reaction was further extended to a broader range of substituted aldehydes and found that the reaction works well for both electron-donating and electron-withdrawing groups (**Table 5, 11a-j**). In order to demonstrate generality and scope of this new efficient methodology, the optimized reaction conditions were investigated using 1-naphthol also and the results are summarized in **Table 5**. Again, almost quantitative yields were obtained with various substituted aldehydes for the desired products (**Table 5, 12a–j**) under the optimized conditions. Finally, the scope of the present protocol was further investigated using other 1,3-dicarbonyl compounds like ethylacetoacetate and acetylacetone instead of dimedone for quantitative preparation of benzoxanthenones. However, the three component reaction of aldehyde, 2-naphthol and etylacetoacetate/acetylacetone afforded aryl-14*H*-dibenzo[*a*,*j*]xanthenes (**13a-d**) instead of expected formation of benzoxanthenones. The higher reactivity of aldehydes with 2-naphthol in comparison to ethylacetoacetate and acetylacetone lead to the formation of benzoxanthenes instead of the expected product. Thereafter, the reaction was also tried with other substituted aldehydes and the products were obtained in almost quantitative yields (**Table 5, 13a-d**) under the optimized conditions.

To establish the catalytic performance of the present catalyst for the one-pot multicomponent synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles and benzoxanthenones, the test reaction in each case was carried out in the presence of nano-titania, amorphous carbon, non-sulfonated carbon@titania, sulfonated amorphous carbon, antimony chloride grafted sulfonated carbon, anhyd. $SbCl_3$ and without using any catalyst under the same reaction conditions (**Table 6**). As is clear from **Table 6**, the hybrid composite (C/TiO_2-SO_3-$SbCl_2$) showed an enhanced catalytic performance compared with nano-titania, amorphous carbon, non-sulfonated carbon@titania, sulfonated amorphous carbon and antimony chloride grafted sulfonated carbon catalyst. The amorphous carbon provided a large specific surface area with high density of catalytically active sites, allowing high loading of sulfonic acid functionality, and thus facilitating the linkage of Lewis acid. Whereas, the nano-titania in the composite provides good mechanical and thermal stability to the composite. In addition, nano-titania also provides large surface, on which biomaterial is well dispersed and carbonized without aggregation of the carbon particles. Hence, due to the synergistic effect of nano-titania and amorphous carbon, the composite material exhibited enhanced catalytic activity. It is noteworthy to mention that the use of homogeneous anhyd. $SbCl_3$ as catalyst gave the desired product in shorter reaction times in comparison to the heterogeneous C/TiO_2-SO_3-$SbCl_2$ catalyst, but the homogeneous Lewis acid catalyst get decomposed during the work-upprocedure whereas heterogeneous C/TiO_2-SO_3-$SbCl_2$ could be easily recovered and reused for several catalytic cycles and also gave higher conversion. Thus, C/TiO_2-SO_3-$SbCl_2$ was found to be superior and thus selected as the heterogeneous catalyst to carry out the present multicomponent synthesis.

Finally, to examine the efficiency of the present protocol for the synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles and benzoxanthenones, it has been compared with some of the previously reported methods. The results summarized in **Table 7**, show that the present protocol is indeed superior to several of the others in terms of high TOFs which clearly indicate the high catalytic activity of the present catalytic system with such low amounts of lewis acid loading onto the sulfonated composite material. Besides, high product yields, low, reaction time and elimination of solvent are other added advantages of the present protocol.

3.4 Recyclability

In case of solid Lewis acids, the study of catalytic activity is an important aspect. To investigate this, the catalyst was recovered from the reaction mixture by simple filtration, dried in vacuum oven at 100 ^{o}C and was reused as such for subsequent experiments under similar reaction conditions (**Table 4, 5i, Table 5, 11a**). The activity of the recovered catalyst did not decrease appreciably even after five consecutive runs, and no significant loss of conversion was observed, depicting the high stability of the catalyst under the reaction conditions (**Fig. 8**). In addition, no quantifiable amount of leached antimony was detected in the filtrate by ICP-AES analysis, hence it can be concluded that the catalytic process is truly heterogeneous.

Reaction conditions: 2-aminobenzothiazole (1mmol), 3-nitrobenzaldehyde (1mmol), ethylacetoacetate (1mmol), C/TiO_2-SO_3-$SbCl_2$ (0.1g, 1 mol% Sb) at 90 ^{o}C under solvent-free conditions (**Table 4, 5i**). Reaction conditions: 2-naphthol (1 mmol), benzaldehyde (1 mmol), dimedone (1mmol), C/TiO_2-SO_3-$SbCl_2$ (0.1 g, 1mol% Sb) at 100 ^{o}C under solvent-free conditions (**Table 5, 11a**)

4. Conclusion

In conclusion, the present work describes the synthesis and characterization of novel heterogeneous Lewis acid catalyst that exhibits excellent catalytic activity, high thermal and chemical stability, thus increasing the applicability of Lewis acids in different reaction conditions that are otherwise highly sensitive to moisture and air. The developed catalyst is air-stable, strongly acidic and showed high catalytic potential for the eco-friendly multicomponent synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles and benzoxanthenones. High TOFs, short reaction time, high product yield, mild reaction conditions, facile preparation and reusability of the catalyst are the noteworthy advantages of the present catalytic protocol.

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6. References

[1] D. Schinzer, Lewis acids and selectivity in organic synthesis, Kluwer AcademicPublishers, Dordrecht 1989.

[2] P. T. Anastas and M. M. Kirchhoff, Acc. Chem. Res. 35 (2002) 686–694.

[3]K. Nakajima, R. Noma, M. Kitano and M. Hara, J. Mol. Catal. A: Chem. 388-389 (2014) 100-105.

[4]A. Corma and H. Garcia, Chem. Rev. 103 (2003) 4307-4365.

[5] A. Corma and H. Garcia, Adv. Synth. Catal. 348 (2006) 1391-1412.

[6]E. B. Garcia, F. J. M. Hodar, A. F. P. Cadenas and F. C. Marin, Catalysts3 (2013) 853-877.

[7] K. Nakajima and M. Hara, ACS Catal. 2 (2012) 1296-1304.

[8] A. Takagaki, M. Toda, M. Okamura, J. N. Kondo, S. Hayashi, K. Domen and M. Hara, Catal. Today 116 (2006) 157-161.

[9] D. Yamaguchi and M. Hara, Solid State Sci. 12 (2010) 1018-1023.

[10] P. Zhang, Z. Mo, L. Han, Y. Wang, G. Zhao, C. Zhang and Z. Li,J. Mol. Catal. A: Chem. 402 (2015) 17–22.

[11] P. A. Russo, M. M. Antunes, P. Neves, P. V. Wiper, E. Fazio, F. Neri, F. Barreca, L. Mafra, M. Pillinger, N. Pinna and A. A. Valente, Green Chem. 16 (2014) 4292–4305.

[12] J. Zhu, M. Lu, M. Li, Mingshi, J. Zhu and Y. Shan, Chin. J. Chem. 29(2011) 655-660.

[13] D. Nandan, P. Sreenivasulu, S. K. Saxena and N. Viswanadham, Chem. Commun., 47 (2011) 11537-11539.

[14] J. Wang, C. Fan, Z. Ren, X. Fu, G. Qian, Z. Wang, Dalton Trans. 43 (2014)13783-13791.

[15] K. Kumaravel and G. Vasuki, Curr. Org. Chem., 13 (2009) 1820-1841.

[16] V. Nair, C. Rajesh, A. Vinod, U. S. Bindu, A. R. Streekenth, S. Mathen and L. Balagopal, Acc. Chem. Res. 36 (2003) 899-907.

[17] D. J. Ramon and M. Yus, Angew. Chem., Int. Ed., 44 (2005) 1602-1634.

[18] A. A. Domling, Chem. Rev., 106 (2006) 17-89.

[19] H. S. Hilal, M. S. A. Shtayeh, R. Arafat, T. A. Tel, W. Voelter and A. Barakat, Eur. J. Med. Chem. 41 (2006) 1017-1024.

[20] V. N. Bhosale, S. P. Vartale, V. K. Deshmukh and S. V. Kuberkar, J. Chem. Pharm. Res., 2 (2010) 51-58.

[21] P. K. Sharma, M. Kumar and V. Mohan, Res. Chem. Intermed. 36 (2010) 985-993.

[22] L. Racane, V. T. Kulenovic, S. K. Pavelic, I. Ratkaj, P. Peixoto, R. Nhili, S. Depauw, M. P. Hildebrand, M. H. D. Cordonnier, K. Pavelic and G. J. K. Zamola,J. Med. Chem. 53 (2010) 2418-2432.

[23] Q. Chao, K. G. Sprankle, R. M. Grotzfeld, A. G. Lai, T. A. Carter, A. M. Velasco, R. N. Gunawardane, M. D. Cramer, M. F. Gardner, J. James, P. P. Zarrinkar, H. K. Patel and S. S. Bhagwat, J. Med. Chem. 52 (2009) 7808-7816.

[24] J. P. Poupelin, G. S. Ruf, O. F. Blanpin, G. Narcisse, G. U. Ernouf and R. Lacroix, Eur. J. Med. Chem. 13(1978)67-71.

[25] H. N. Hafez, M. I. Hegab, I. S. A. Farag and A. B. A. E. Gazzar, Bioorg. Med. Chem. Lett. 18 (2008) 4538-4543.

[26] S. Chatterjee, M. Iqbal, J. C. Kauer, J. P. Mallamo, S. Senadhi, S. Mallya, D. B. Coyne and R. Siman, Bioorg. Med. Chem. Lett. 6 (1996) 1619-1622.

[27] C. G. Knight and V. Stephens, Biochem. J.258 (1989) 683-687.

[28] A. Shaabani, A. Rahmati and S. Naderi, Bioorg. Med. Chem. Lett. 15(2005) 5553-5557.

[29] L. Nagarapu, H. K. Gaikwad, J. D. Palem, R. Venkatesh, R. Bantu and B. Sridhar, Synth. Commun. 43 (2013) 93-104.

[30] A. B. Atar, Y. S. Jeong, Y. T. Jeong, Tetrahedron 70 (2014) 5207-5213.

[31] M. S. Chaitanya, G. Nagendrappa and V. P. Vaidya, J. Chem. Pharm. Res. 2(2010) 206-213.

[32] B. F. Mirjalili, A. Bamoniri and A. Akbari, Tetrahedron Lett. 49 (2008) 6454-6456.

[33] G. C. Nandi, S. Samai, R. Kumar and M. S. Singh, Tetrahedron 65 (2009) 7129-7134.

[34] J. M. Khurana and D. Magoo, Tetrahedron Lett. 50 (2009) 4777-4780.

[35] N. Foroughifar, A. Mobinikhaledi and H. Moghanian, Int. J. Green Nanotechnol. Phys. Chem. 1 (2009) 57-63.

[36] J. J. Li, W. Y. Tang, L. M. Lu and W .K. Su, Tetrahedron Lett., 49 (2008) 7117-7120.

[37] S. Gao, C. H. Tsai and C. F. Yao, Synlett (2009) 949-954.

[38] R. Z. Wang, L. F. Zhang and Z. S. Cui, Synth. Commun., 39 (2009) 2101-2017.

[39] M. M. Heravi, H. Alinejhad, K. Bakhtiari and H. A. Oskooie, Mol. Divers 14 (2010) 621-626.

[40] B. Das, K. Laxminarayana, M. Krishnaiah and Y. Srinivas, Synlett (2007) 3107-3112.

[41] N. Karimi, H. A. Oskooie, M. M. Heravi and L. Tahershamsi, Synth. Commun. 41 (2011) 307-312.

[42] Z. H. Zhang, P. Zhang, Y. Peng, S. H. Yang, H. J. Wang and J. J. Deng, Chem. Sci. 122 (2010) 427-432.

[43] J. Li, L. Lu and W. Su, Tetrahedron Lett. 51 (2010) 2434-2437.

[44] Z. Zhang, C. C. Wang, R. Zakaria and J. Y. Ying, J. Phys. Chem. B 102 (1998) 10871-10878.

[45] K. Fukushima and I Yamada, J. Appl. Phys. 65 (1989) 619-623.

[46] Y. Y. Xu, S. Q. Lua, Y. Z. Zheng, H. B. Fang, X. Tao and J. F. Chen, Catal. Commun. 69 (2015) 63-67.

[47] M. Bellardita, E. I. G. Lopez, G. Marci, B. Megna, F. R. Pomilla and L. Palmisano, RSC Adv. 5 (2015) 59037-59047.

[48] Z. Zhao Z, Y. Wang, J. Xu and Y. Wang, RSC Adv. 5 (2015) 59297-59305.

[49] P. Kumar, R. K. Chauhan, B. Sain and S. L. Jain, Dalton Trans. 44 (2015)4546-4543.

[50] S. Dai S, Y. Wu, T. Sakai, Z. Du Z, H. Sakai and M. Abe, Nanoscale Res. Lett. 5 (2010) 1829-1835.

[51] W. C. Oh, M. L. Chen, Bull. Korean Chem. Soc.,29 (2008)159-164.

[52] R S Varma, Green Chem. 1 (1999) 43-55.

[53] M. M. Heravi, E. Hashemi, Y. S. Beheshtiha, K. Kamjou, M. Toolabi andN. Hosseintash, J. Mol. Catal. A: Chem., 392 (2014) 173-180.

[54] P. K. Sahu, P. K. Sahu, Y. Sharma andD. D. Agarwal, J. Hetercycl Chem. 51 (2014) 1193-1198.

[55] V. Rama, K. Kanagaraj andK. Pitchumani, Tetrahedron Lett. 53 (2012) 1018-1024.

[56] P. Srihari, B. Ganganna, K. Rajendraprasad, D. C. Bhunia andJ. S. Jadhav,Indian J. Chem. 50B (2011) 1755-1761.

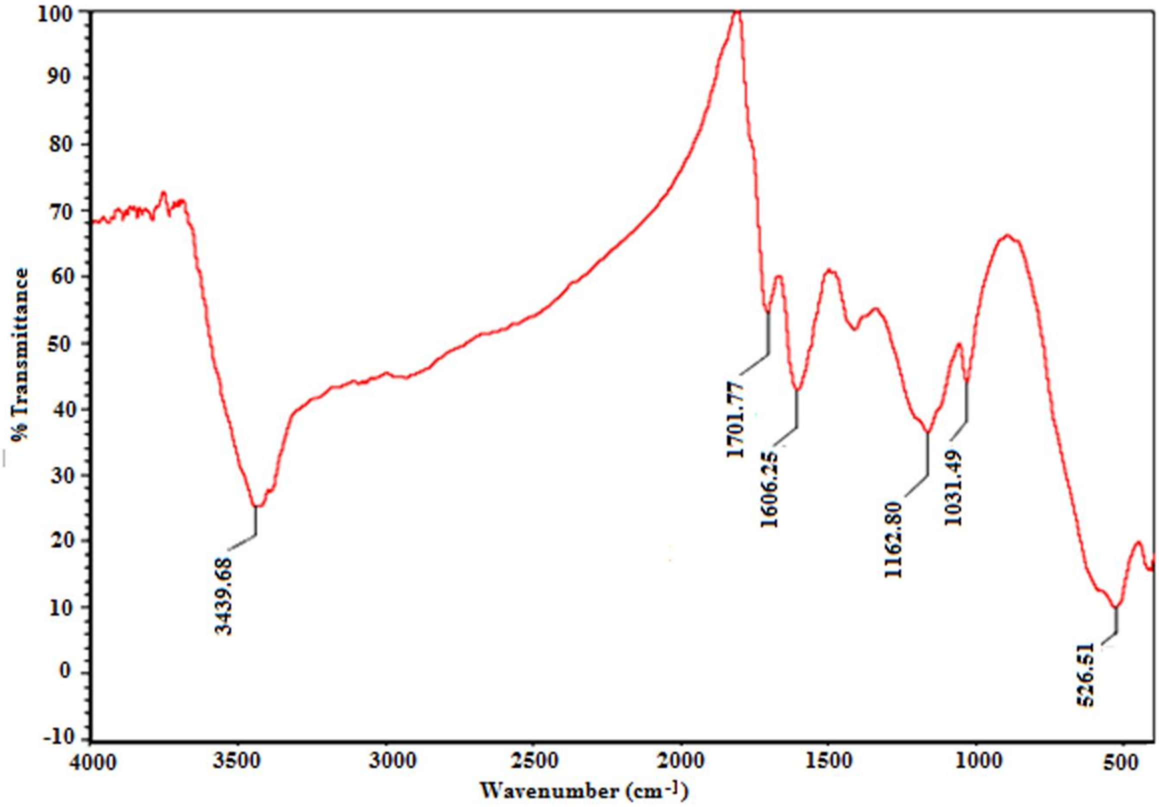


Fig. 1 FTIR spectra of C/TiO_2-SO_3-$SbCl_2$.

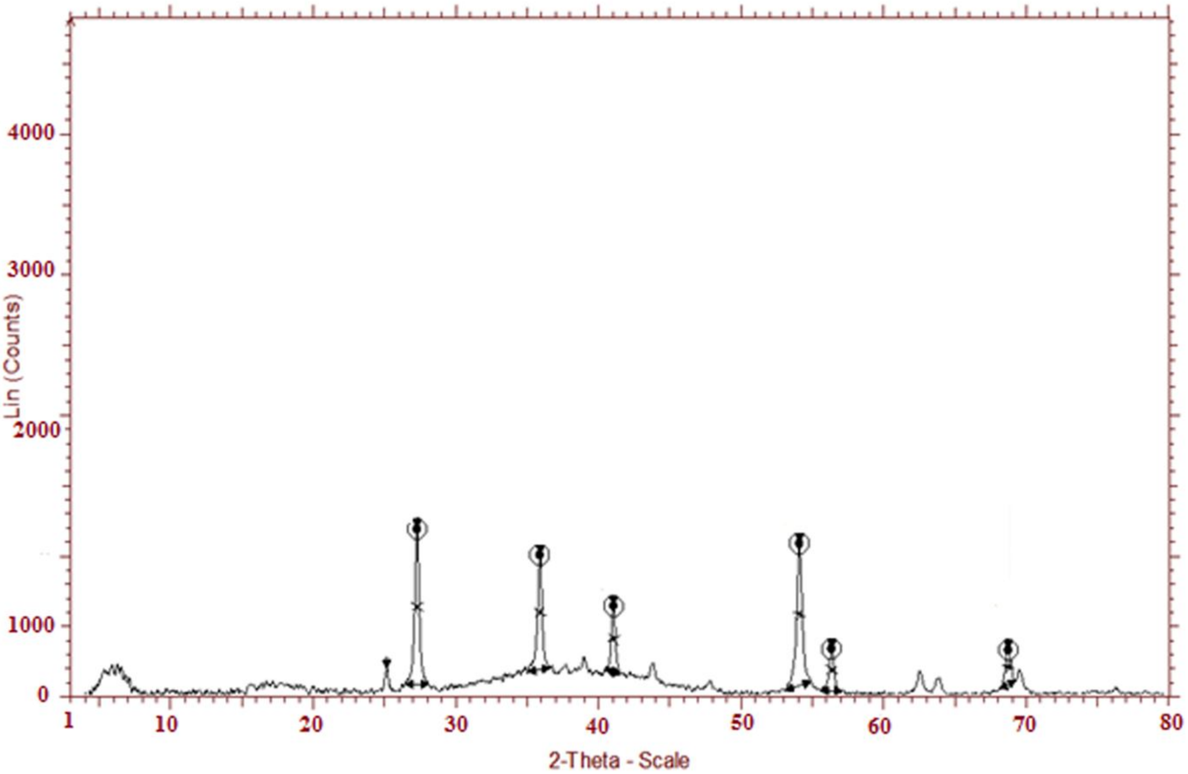


Fig. 2 XRD of C/TiO_2-SO_3-$SbCl_2$.

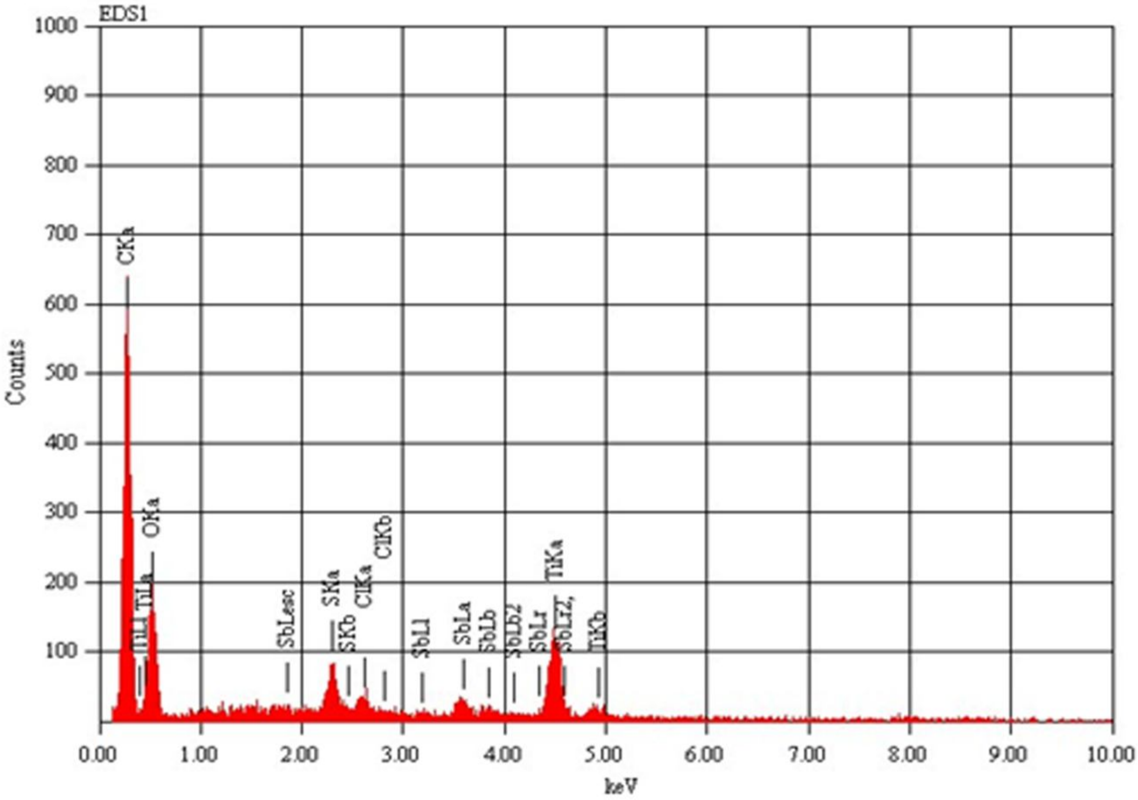


Fig. 3 EDX spectra of C/TiO_2-SO_3-$SbCl_2$.

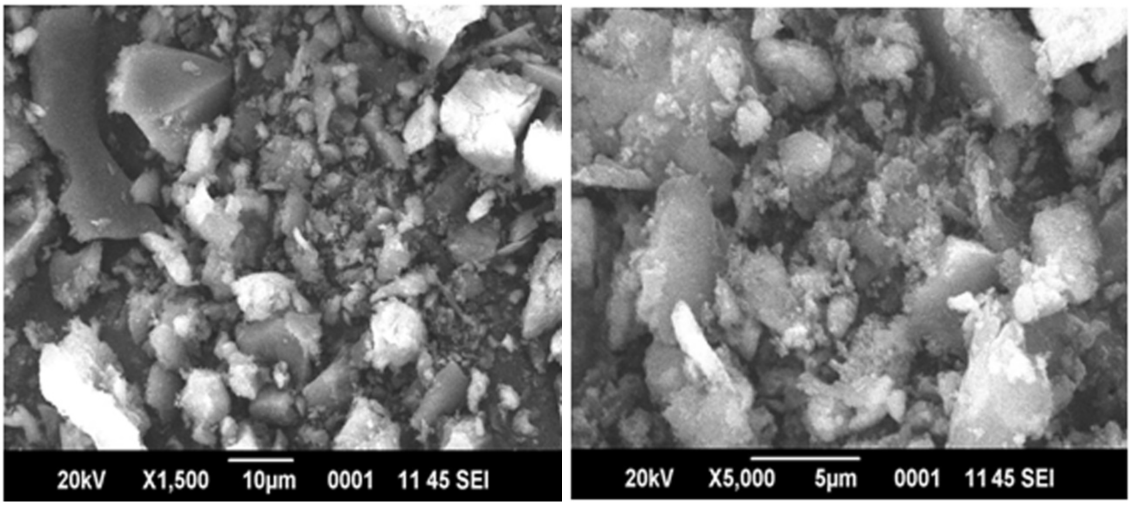


Fig. 4SEM images of C/TiO_2-SO_3-$SbCl_2$.

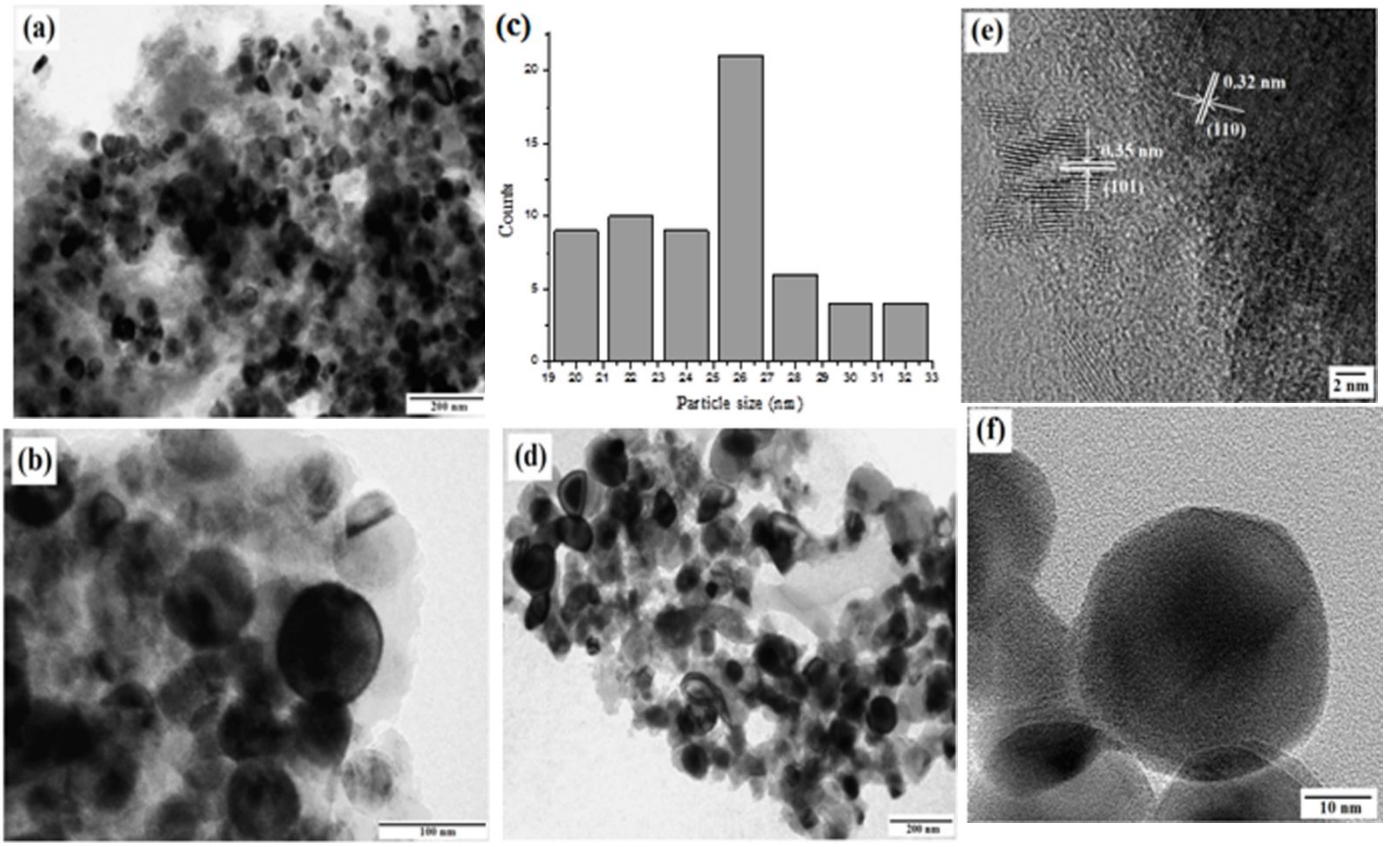


Fig. 5(a, b)TEM images of C/TiO_2-SO_3-$SbCl_2$; **(c)** Particle size histogram; **(d)**TEM image of C/TiO_2-SO_3H; **(e, f)**HRTEM images of C/TiO_2-SO_3-$SbCl_2$.

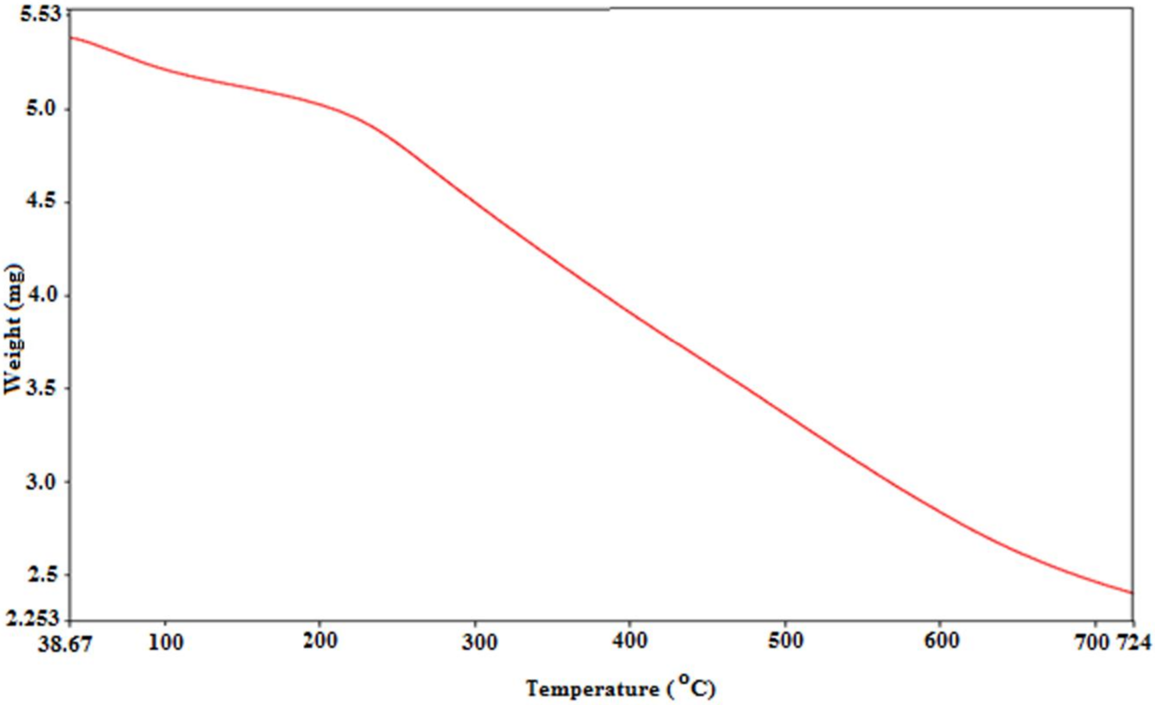


Fig. 6 TGA of C/TiO_2-SO_3-$SbCl_2$.

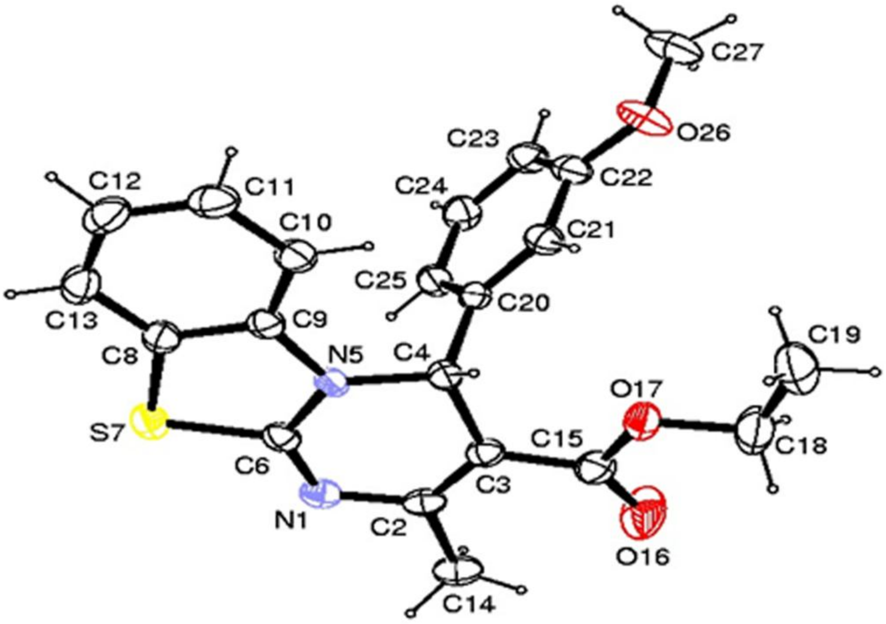


Fig. 7 ORTEP view of Ethyl 2-methyl-4-(3-methoxyphenyl)-4*H*-pyrimido[2,1-*b*][1,3]benzothiazole-3-carboxylate (CCDC No. 1409951).

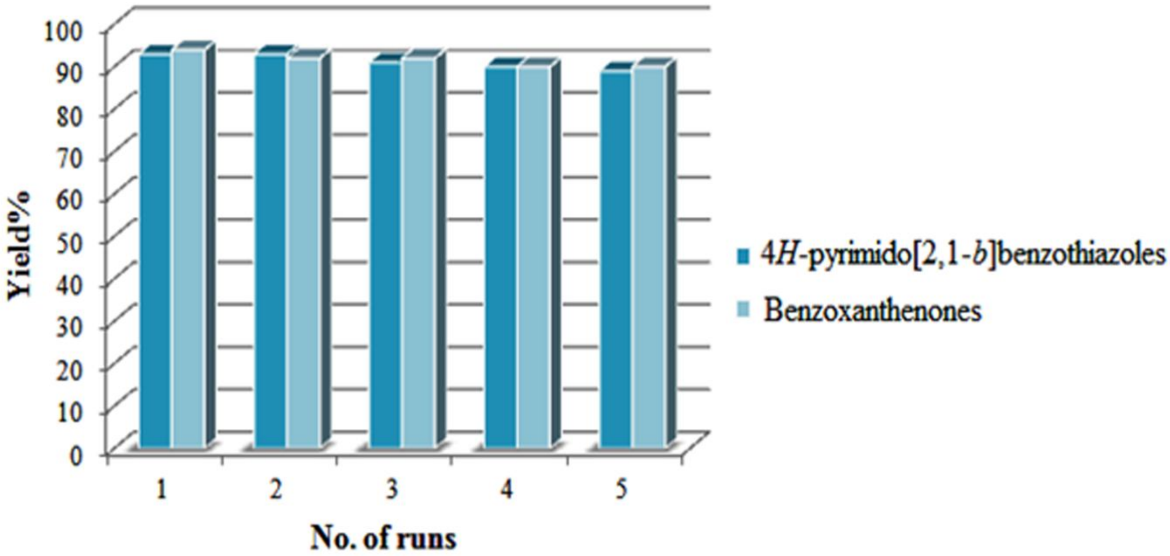
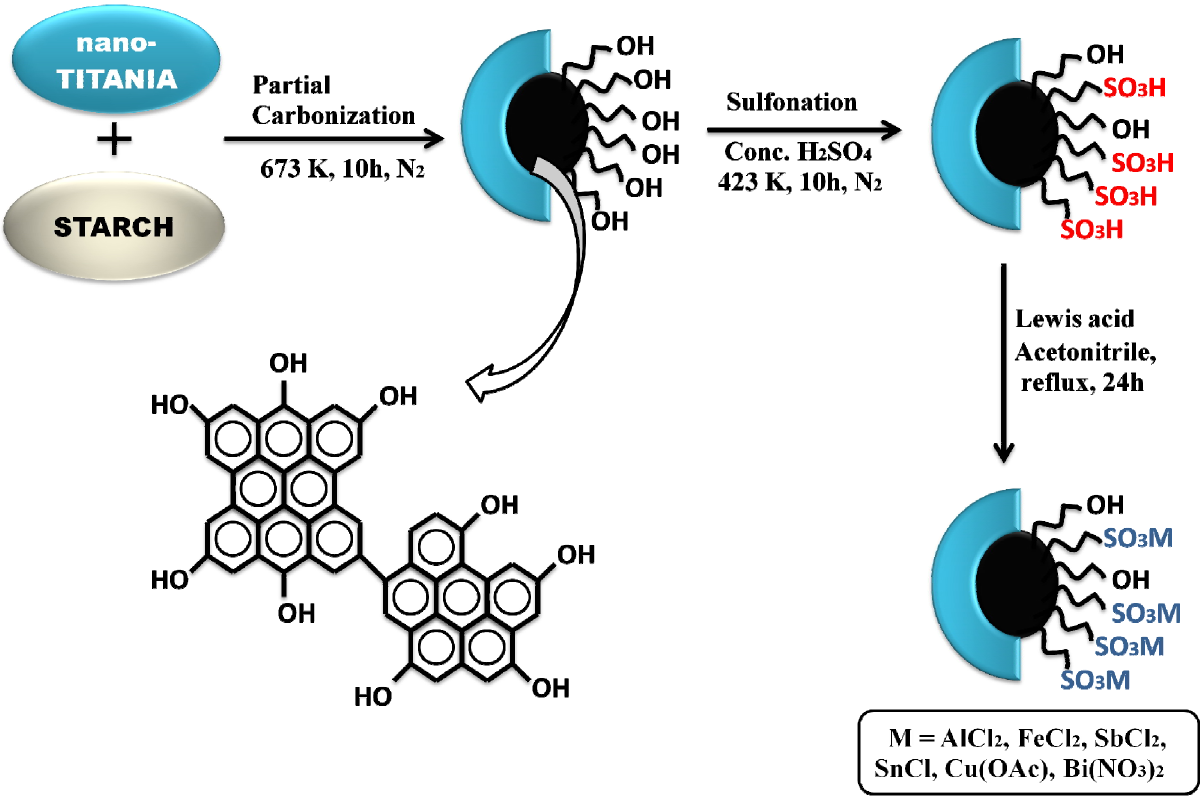


Fig. 8 Recyclability of C/TiO_2-SO_3-$SbCl_2$.



Scheme 1. General scheme for the synthesis of Lewis acid grafted sulfonated carbon@titania composites.

Table 1. Major absorption frequencies in FTIR (ν_{max} in cm^{-1})[a] of Lewis acid grafted sulfonated carbon@titania composites

				SO_2 stretch		
Entry	**Catalyst**	**Phenolic –OH**	**C=C**	**Asym.**	**Sym.**	**Ti-O**
1.	$C/TiO_2-SO_3-AlCl_2$	3462	1614	1157	1035	563
2.	$C/TiO_2-SO_3-FeCl_2$	3414	1645	1178	1033	551
3.	$C/TiO_2-SO_3-SbCl_2$	3439	1606	1162	1031	526
4.	C/TiO_2-SO_3-SnCl	3472	1641	1159	1037	544
5.	$C/TiO_2-SO_3-Cu(OAc)$	3422	1649	1180	1035	545
6.	$C/TiO_2-SO_3-Bi(NO_3)_2$	3412	1637	1152	1037	543

[a] FTIR was recorded on Perkin-Elmer FTIR spectrophotometer using KBr discs.

Table 2. Comparison of catalytic activities of different Lewis acid grafted sulfonated carbon@titania composites for the one-pot synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles and benzoxanthenones

		4*H*-pyrimido[2,1-*b*]benzothiazoles[a]		Benzoxanthenones[b]	
Entry	Lewis acid grafted sulfonated carbon@titania composites	Time (h)	Yield[c] (%)	Time (h)	Yield[c] (%)
1.	C/TiO_2-SO_3-$AlCl_2$	2.0	90	1.5	91
2.	C/TiO_2-SO_3-$FeCl_2$	2.5	92	2	92
3.	**C/TiO_2-SO_3-$SbCl_2$**	**1.25**	**93**	**0.75**	**94**
4.	C/TiO_2-SO_3-$SnCl$	3	88	3	89
5.	C/TiO_2-SO_3-$Cu(OAc)$	4	90	3	85
6.	C/TiO_2-SO_3-$Bi(NO_3)_2$	2.5	90	2	90

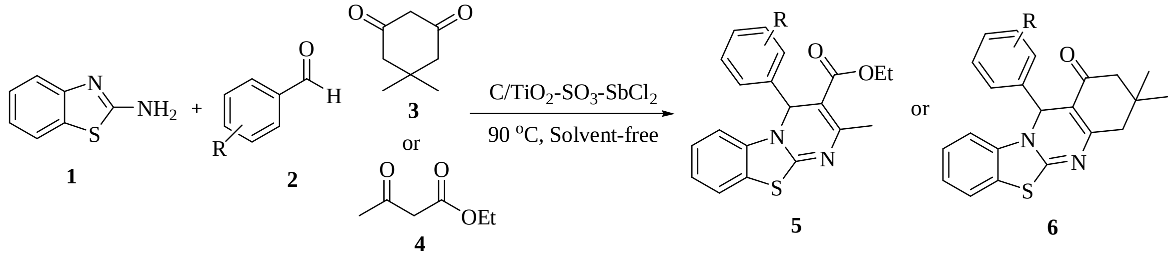
[a]Reaction conditions: 2-aminobenzothiazole (1mmol), 3-nitrobenzaldehyde (1mmol), ethylacetoacetate (1mmol), Lewis acid grafted sulfonated carbon@titania composites (1 mol% metal) at 90 °C under solvent-free conditions. [b]Reaction conditions: 2-naphthol (1 mmol), benzaldehyde (1 mmol), dimedone (1mmol), Lewis acid grafted sulfonated carbon@titania composites (1 mol% metal) at 100 °C under solvent-free conditions. [c]Isolated yields.

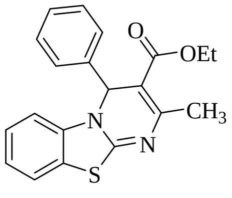
Table 3. Effect of different solvents, temperature and catalyst amount on C/TiO_2-SO_3-$SbCl_2$ catalyzed one-pot synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles and benzoxanthenones

Entry	Solvent	Temperature	Catalyst^{a} (g)	4*H*-pyrimido[2,1-*b*]benzothiazoles^{b}		Benzoxanthenones^{c}	
				Time (h)	Yield (%)^{d}	Time (h)	Yield (%)^{d}
1.	Ethanol	Reflux	0.1	1.25	45^{e}	3	Trace
2.	Acetonitrile	Reflux	0.1	1.25	40^{e}	3	Trace
3.	Water	Reflux	0.1	1.25	30^{e}	3	Trace
4.	Solvent-free	80 ^{o}C	0.1	1.5	80	1	50
5.	Solvent-free	90^{o} C	0.05	1.25	60	1	70
6.	**Solvent-free**	**90^{o} C**	**0.1**	**1.25**	**93**	1	80
7.	**Solvent-free**	**100^{o} C**	0.1	1.0	93	**0.75**	**94**
8.	Solvent-free	120^{o}C	0.1	1.0	94	0.8	95
9.	Solvent-free	90^{o} C	0.2	1	93	0.8	93
10.	Solvent-free	90^{o} C	0.3	0.8	94	0.75	94

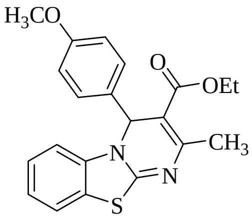
[a] Refers to antimony chloride grafted sulfonated carbon@titania composite. [b] Reaction conditions: 2-aminobenzothiazole (1mmol), 3-nitrobenzaldehyde (1mmol) and ethylacetoacetate (1mmol). [c] Reaction conditions: 2-naphthol (1 mmol), benzaldehyde (1 mmol) and dimedone (1mmol). [d] Isolated yields. [e] Column chromatographic yields.

Table 4. C/TiO$_2$-SO$_3$-SbCl$_2$ catalyzed one-pot multi-component synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles[a,b]

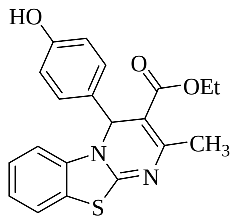




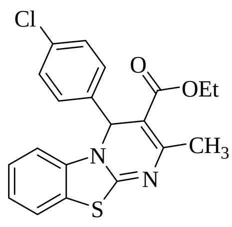
5a: .1.5 h, 92%



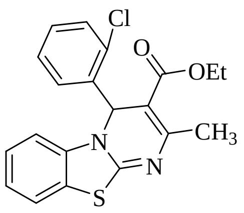
5b: 3 h, 90%



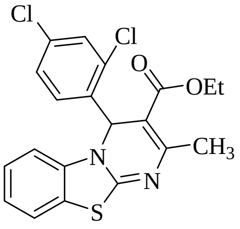
5c: 3 h, 93%



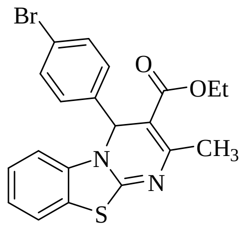
5d: 2 h, 89%



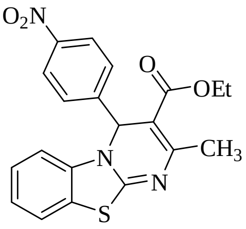
5e: 1 h, 88%



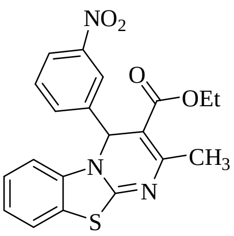
5f: 1 h, 94%



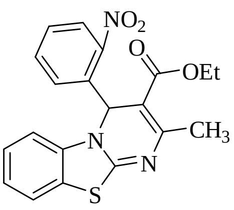
5g: 2 h, 92%



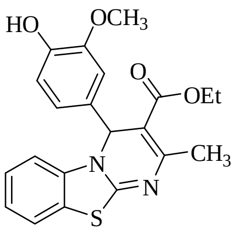
5h: 1.5 h, 88%



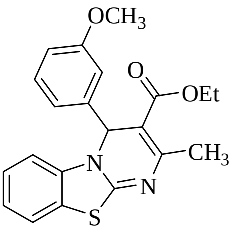
5i: 1.25 h, 93%



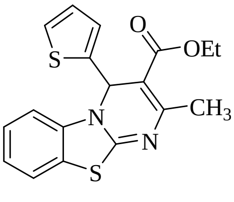
5j: 1 h, 93%



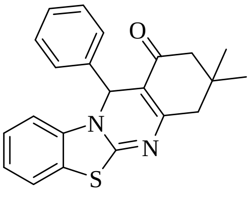
5k: 2.5 h, 85%



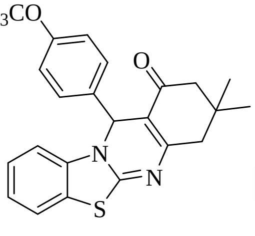
5l: 2 h, 92%



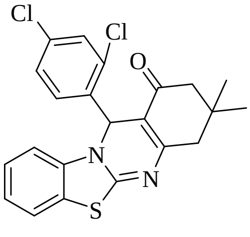
5m: 2 h, 90%



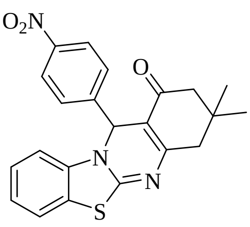
6a: 2 h, 92%



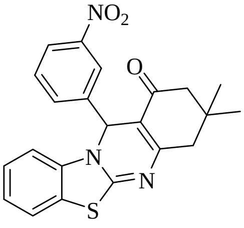
6b: 3 h, 88%



6c: 1.5 h, 93%



6d: 2 h, 85%



6e: 1.5 h, 91%

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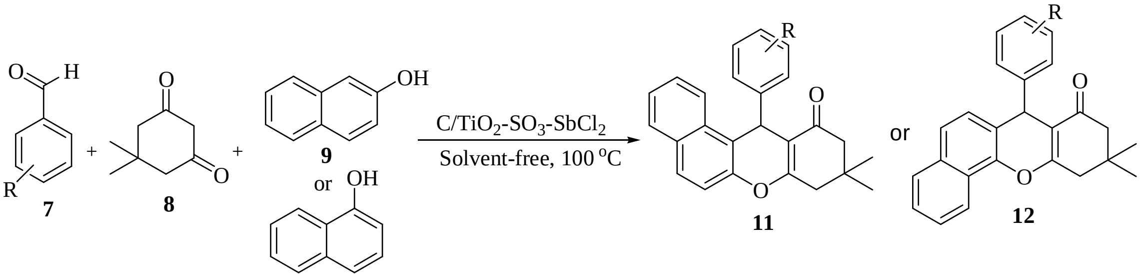
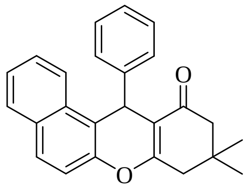
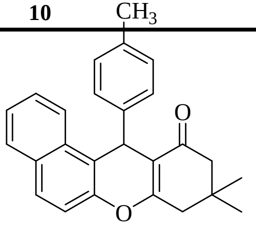
[a] Reaction conditions: 2-aminobenzothiazole (1mmol), aldehyde (1mmol) , ethylacetoacetate or dimedone (1mmol) and C/TiO_2-SO_3-$SbCl_2$ (0.1 g, 1 mol% Sb) at 90 °C under solvent-free conditions. [b] Isolated yields.

Table 5. C/TiO$_2$-SO$_3$-SbCl$_2$ catalyzed multi-component synthesis of benzoxanthenones[a,b]

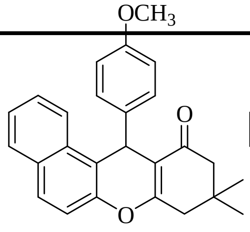




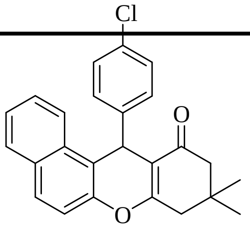
11a: 0.75 h, 94%



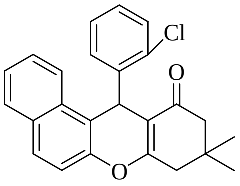
11b: 0.75 h, 92%



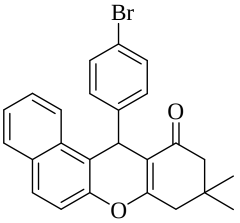
11c: 2 h, 90%



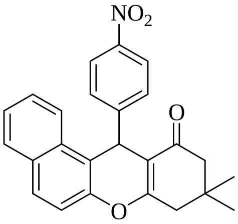
11d: 1h, 93%



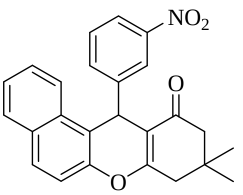
11e: 0.80 h, 93%



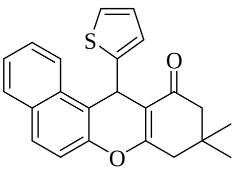
11f:1.25 h, 92%



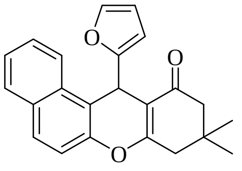
11g: 1.5 h, 90%



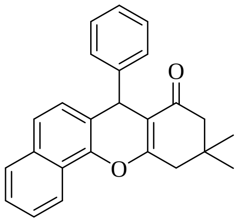
11h: 1.5 h, 90%



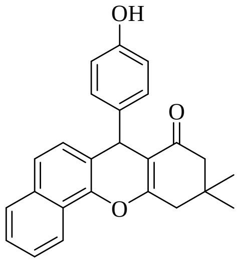
11i: 2 h, 91%



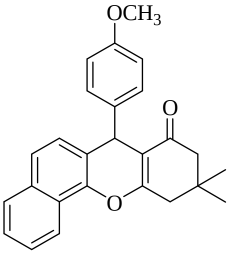
11j: 1.5 h, 90%



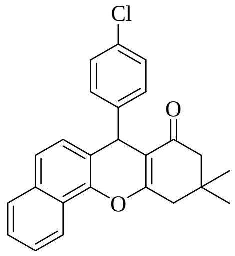
12a: 0.75 h, 92%



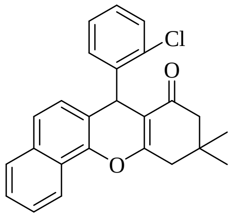
12b: 1 h, 94%



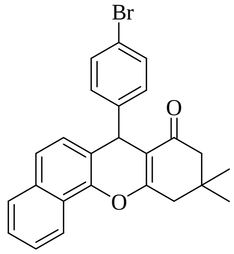
12c: 2.5 h, 90%



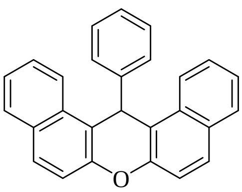
12d: 1 h, 92%



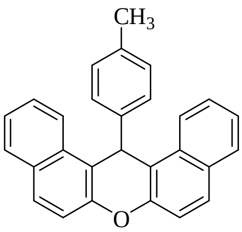
12e: 0.75 h, 94%



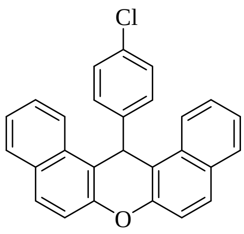
12f: 1.5 h, 91%



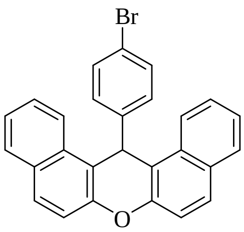
13a: 2 h, 90%



13b: 2 h, 94%



13c: 2.5 h, 92%



13d: 3h, 92%

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[a]Reaction conditions: naphthol (1 mmol), aldehyde (1 mmol), dimedone (1mmol) and C/TiO$_2$-SO$_3$-SbCl$_2$ (0.1g, 1 mol% Sb) at 100 °C under solvent-free conditions (11 a-j and 12a-j); 2-naphthol (2 mmol), aldehyde (1 mmol) and C/TiO$_2$-SO$_3$-SbCl$_2$ (0.1 g, 1 mol% Sb) under solvent-free conditions at 100 °C (13a-d). [b]Isolated yield.

Table 6. Comparison of catalytic activity of C/TiO$_2$-SO$_3$-SbCl$_2$ with nano-titania, amorphous carbon, non-sulfonated carbon@titania, sulfonated amorphous carbon and anhyd. SbCl$_3$ for the synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles and benzoxanthenones

Entry	Catalyst	4*H*-pyrimido[2,1-b]benzothiazoles[a]		Benzoxanthenones[b]	
		Time (h)	Yield (%)[c]	Time (h)	Yield (%)[c]
1.	No catalyst	8	10[d]	8	Trace
2.	Nano-titania	8	22[d]	8	20[d]
3.	Amorphous carbon	8	24[d]	8	25[d]
4.	Non-sulfonated carbon@titania	8	30[d]	8	28[d]
5.	Sulfonated amorphous carbon	1.25	45	1	60
6.	Antimony chloride grafted sulfonated carbon	4.5	85	6	80
7.	Anhyd. SbCl$_3$	1	88	.75	90
8.	**C/TiO$_2$-SO$_3$-SbCl$_2$**	**1.25**	**93**	**1**	**94**

[a]Reaction conditions: 2-aminobenzothiazole (1mmol), 3-nitrobenzaldehyde (1mmol), ethylacetoacetate (1mmol) and catalyst(0.1 g for entries 1-5, 1 mol% SbCl$_3$ for entry 7, 0.1 g, 1 mol% Sb for entry 6, 8) at 90 °C under solvent-free conditions. [b]Reaction conditions: 2-naphthol (1 mmol), benzaldehyde (1 mmol), dimedone (1mmol) and catalyst(0.1 g for entries 1-5, 1 mol% SbCl$_3$ for entry 7, 0.1 g, 1 mol% Sb for entry 6, 8) at 100 °C under solvent-free conditions.[c]Isolated yields.[d]Column chromatographic yields.

Table 7. Comparison of the catalytic activity of C/TiO$_2$-SO$_3$-SbCl$_2$ with reported catalytic systems for the one-pot multicomponent synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles and benzoxanthenones

Reaction	Catalyst	Catalyst loading	Reaction conditions	Time (h)	Yield[c] (%)	TOF[d] (h^{-1})
4*H*-pyrimido[2,1-*b*]benzothiazoles[a]	TBAHS **[29]**	30 mol%	Ethylene glycol, 120 °C	2	72	1.2
	SMI-SO$_3$H **[53]**	0.08g	Solvent-free, 100 °C	3	76	1.49
	Acetic acid **[54]**	20 mol%	Methanol, 60-65 °C	18	62	0.17
	FeF$_3$ **[30]**	10 mol%	Solvent-free, 80 °C	2	85	4.2
	C/TiO$_2$-SO$_3$-SbCl$_2$[e]	**1 mol%**	**Solvent-free, 90 °C**	**1.5**	**88**	**58.66**
Benzoxanthenones[b]	*p*-TSA **[34]**	10 mol%	Solvent-free, [bmim]BF$_4$, 80 °C	3	90	3
	HY Zeolite **[55]**	20 mg	Solvent-free, 80 °C	1	93	4.65
	SMI-SO$_3$H **[39]**	0.07g	Solvent-free, 80 °C	0.8	78	5.73
	Phosphomolybdic acid **[56]**	10 mol%	DCE, reflux	6	71	1.18
	C/TiO$_2$-SO$_3$-SbCl$_2$[e]	1 mol%	**Solvent-free, 100 °C**	**0.75**	**94**	**125.33**

[a] Reaction conditions: 2-aminobenzothiazole (1mmol), 4-nitrobenzaldehyde (1mmol), ethylacetoacetate (1mmol), C/TiO$_2$-SO$_3$-SbCl$_2$ (0.1 g, 1mol% Sb) at 90 °C under solvent-free conditions. [b] Reaction conditions: 2-naphthol (1 mmol), benzaldehyde (1 mmol), dimedone (1mmol), C/TiO$_2$-SO$_3$-SbCl$_2$ (0.1 g, 1mol% Sb) at 100 °C under solvent-free conditions. [c] Isolated yield; [d] Turn over frequency; [e] Our work