Development of sulfonic acids from renewable resources as heterogeneous acid catalysts in organic synthesis

PROJECT REPORT

SUBMITTED TO

THE UNIVERSITY GRANTS COMMISSION

BAHADUR SHAH ZAFAR MARG

NEW DELHI

By

Dr. SATYA PAUL

(Principal Investigator)

DEPARTMENT OF CHEMISTRY

UNIVERSITY OF JAMMU

JAMMU-180006

(J&K)

Project Report

"Development of sulfonic acids from renewable resources as heterogeneous acid catalysts in organic synthesis"

- UGC File No.: 41-281/2012(SR)
- Year of Commencement: 16-07-2012
- Name of the research Personnel appointed: Manmeet Kour
- Name of the Principal Investigator: Dr. Satya Paul
- Address: Department of Chemistry, University of Jammu, Jammu-180006

Annexure - III

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
NEW DELHI – 110 002

STATEMENT OF EXPENDITURE IN RESPECT OF MAJOR RESEARCH PROJECT

1. Name of Principal Investigator: Dr. Satya Paul

2. Dept. of Principal Investigator: P. G. Department of Chemistry

University/College: University of Jammu

3. UGC approval Letter No. and Date: F.No.41-281/2012(SR) dated 16.07.2012

4. Title of the Research Project : Developmet of sulfonic acids from renewable resources as heterogeneous acid catalysts in organic synthesis

5. Effective date of starting the project: 01.07.2012

6. a. Period of Expenditure: 01 July 2012 to 31 December 2015

b. Details of Expenditure

S. No.	Name of the item	Amount Approved (Rs.)	Expenditure incurred (Rs.)
	Books &Journals	-	-
	Equipment	3,50,000/-	39,920/-
	Contingency	50,000/-	23,674/-
	Field Work/Travel	20,000/-	6110/-
	Hiring Services	-	-
	Chemicals/Glassware	1,00,000/-	47,407/-
	Overhead	67,800/-	67,800/-
	Total	5,87,800/-	1,84,911/-

c. Staff: Ms. Manmeet Kour

Date of appointment: 27/11/2012

S.No	Items	From	To	Amount Approved (Rs.)	Grant released in First installment (Rs.)	Total Grant (Rs.)	Expenditure incurred (Rs.)
1.	Honorarium to PI (Retired Teachers) @ Rs. 18,000/-p.m.						
2.	**Project fellow:** i) **NET/GATE qualified**-Rs. 16,000/- p.m. for initial 2 years and Rs. 18,000/- p.m. for the third year. ii) **Non-GATE/Non-NET**- Rs. 14,000/- p.m. for initial 2 years and Rs. 16,000/- p.m. for the third year.	27/11/ 2012	31/05/ 2014	5,28,000/-	2,64,000/-	2,64,000/-	2,53,865/-

1. It is certified that the appointment have been made in accordance with the terms and conditions laid down by the commission.
2. If as a result of check or audit objection some irregularity is noticed at later date, action will be taken to refund, adjust or regularize the objected amounts
3. Payment @ revised rates shall be made with arrears on the availability of additional funds.
4. It is certified that the grant of **Rs. 7,66,800/- (Rs. Seven lakh sixty six thousand and eight hudred rupees only)** received from the University Grants Commission under the scheme of support for Major Research Project entitled **"Development of sulfonic acids from renewable resources as heterogeneous acid catalysts in organic synthesis"** vide UGC letter No. **F. 41-281/2012(SR)** dated **16-07-2012** and the expenditure amount of **Rs. 4,38,776 (Rs. Four lakh thirty eight thousand seven hundred seventy six rupees only)** has been utilized for the purpose for which it was sanctioned and in accordance with the terms and conditions laid down by the University Grants Commission. The unspent balance of **Rs 3,28,024/- (Three lakh twenty eight thousand and twenty four rupees only)** is refunded vide instrument No. JAKA416293038128 dated 19/10/2016.

Signature of the Principal Investigator

Dr. Sa[illegible]
Principal Investig[illegible]
UGC Project No. F41-2[illegible]012 (SR)
Department of Chemistry
University of Jammu, Jammu-06

Registrar
University of Jammu

Registrar

9/12

9/12/16

Annexure - IV

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
NEW DELHI – 110 002

STATEMENT OF EXPENDITURE INCURRED ON FIELD WORK

Name of the Principal Investigator: Dr. Satya Paul

S. No.	Name of the Place visited	Duration of the Visit		Mode of Journey	Expenditure Incurred (Rs.)
		From	To		
1.	UNIVERSITY GRANTS COMMISSION BAHADUR SHAH ZAFAR MARG NEW DELHI – 110 002	1 day (08/02/2014) Jammu to New Delhi New Delhi to Jammu		Train-2A By Air	6110/-
Total					6,110/-

Certified that the above expenditure is in accordance with the UGC norms for Major Research Projects.

PRINCIPAL INVESTIGATOR

Dr. Satya Paul
Principal Investigator
UGC Project No. F41-281/2012
Department of Chemistry
University of [illegible] Jammu-0

Registrar
University of Jammu

REGISTRAR/PRINCIPAL

9/12

9/12/16

Annexure - V

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
NEW DELHI – 110 002

Utilization Certificate

Certified that the grant of **Rs. 7,66,800/- (Rs. Seven lakh sixty six thousand and eight hudred rupees only)** received from the University Grants Commission under the scheme of support for Major Research Project entitled **"Development of sulfonic acids from renewable resources as heterogeneous acid catalysts in organic synthesis"** vide UGC letter No. **F. 41-281/2012(SR)** dated **16-07-2012** and the expenditure amount of **Rs. 4,38,776 (Rs. Four lakh thirty eight thousand seven hundred seventy six rupees only)** has been utilized for the purpose for which it was sanctioned and in accordance with the terms and conditions laid down by the University Grants Commission. The unspent balance of **Rs 3,28,024/- (Three lakh twenty eight thousand and twenty four rupees only)** is refunded vide instrument No. JAKA416293038128 dated 19/10/2016.

Principal Investigator

Dr. Satya Paul
Principal Investigator
UGC Project No F41-281/2012 (SR)
Department of Chemistry
University of Jammu, Jammu-06

SBL
9/12

9/12/16

Registrar
... of Jammu

Registrar

Statutory Auditor

M-No 504307

C. Gupta & Co.
Chartered Accountants
Jammu

ANNEXURE-VI

PROFORMA FOR SUPPLYING THE INFORMATION IN RESPECT OF THE STAFF APPOINTED UNDER THE SCHEME OF MAJOR RESEARCH PROJECT

UGC File No F. 41-281/2012(SR) **Year of Commencement** 01/07/2012

TITLE OF THE PROJECT: Development of sulfonic acids from renewable resources as heterogeneous acid catalysts in organic synthesis.

1.	**Name of the Principal Investigator**	Dr. Satya Paul
2.	**Name of the University**	University of Jammu, Jammu.
3.	**Name of the Research Personnel appointed**	Ms. Manmeet Kour
4.	**Academic Qualification**	M. Sc., M. Phil.
5.	**Date of joining**	27/11/2012
6.	**Date of Birth of Research Personnel**	27/03/1988
7.	**Amount of HRA, if Drawn**	Not drawn
8.	**No. of Candidates applied for the post**	09

CERTIFICATE

THIS IS TO CERTIFY THAT ALL THE RULES AND REGULATIONS OF UGC MAJOR RESEARCH PROJECT OUTLINED IN THE GUIDELINES HAVE BEEN FOLLOWED. ANY LAPSE ON THE PART OF THE UNIVERSITY WILL LIABLE TO TERMINATION OF SAID UGC PROJECT.

18.05.2017

PRINCIPAL INVESTIGATOR

Dr. Satya Paul
Principal Investigator
UGC Project No. F41-281/2012 (SR)
Department of Chemistry
University of Jammu, Jammu-06

Head
HEAD OF THE DEPTT.
Department of Chemistry,
University of Jammu, Jammu

Registrar
University of Jammu

REGISTRAR

19/5/17

18/05/17

Annexure -VIII

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
NEW DELHI-110 002.

Annual/Final Report of the work done on the Major Research Project.
(Report to be submitted within 6 weeks after completion of each year)

1. Project report No. 1st /2nd /3rd/Final FINAL

2. UGC Reference No.F. 41-281/2012 (SR); dated 16 July 2012

3. Period of report: from 01-07-2012 to 31-12-2015

4. Title of research project Development of sulfonic acids from renewable resources as heterogeneous acid catalysts in organic synthesis

5. (a) Name of the Principal Investigator Dr. Satya Paul

(b) Deptt. Chemistry

(c) University/College where work has progressed University of Jammu, Jammu

6. Effective date of starting of the project 01/07/2012

7. Grant approved and expenditure incurred during the period of the report:

a. Total amount approved Rs. 7,66,800/-

b. Total expenditure Rs. 4,38,776/-

c. Report of the work done: (Report attached)

18-05-2017
SIGNATURE OF THE PRINCIPAL INVESTIGATOR

Dr. Satya Paul
Principal Investigator
UGC Project No. F41-281/2012 (SR)
Department of Chemistry
University of Jammu, Jammu-06

~~Registrar~~
University of Jammu

REGISTRAR/PRINCIPAL

19/5/17

18/05/17

Annexure - IX

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
NEW DELHI – 110 002

PROFORMA FOR SUBMISSION OF INFORMATION AT THE TIME OF SENDING THE FINAL REPORT OF THE WORK DONE ON THE PROJECT

1	TITLE OF THE PROJECT	Development of sulfonic acids from renewable resources as heterogeneous acid catalysts in organic synthesis
2	NAME AND ADDRESS OF THE PRINCIPAL INVESTIGATOR	Dr. Satya Paul P.G. Department of Chemistry, University of Jammu
3	NAME AND ADDRESS OF THE INSTITUTION	P.G. Department of Chemistry, University of Jammu
4	UGC APPROVAL LETTER NO. AND DATE	F.No. 41-281/2012(SR) dated 16 July 2012
5	DATE OF IMPLEMENTATION	01 July 2012
6	TENURE OF THE PROJECT	01 July 2012 to 31 December 2015
7	TOTAL GRANT ALLOCATED	11,15,800/-
8	TOTAL GRANT RECEIVED	7,66,800/-
9	FINAL EXPENDITURE	4,38,776/-
10	OBJECTIVES OF THE PROJECT	Annexure A
11	WHETHER OBJECTIVES WERE ACHIEVED (GIVE DETAILS)	Yes (Annexure C)
12	ACHIEVEMENTS FROM THE PROJECT	Annexure D
13	SUMMARY OF THE FINDINGS (IN 500 WORDS)	Annexure E
14	CONTRIBUTION TO THE SOCIETY (GIVE DETAILS)	Annexure F
15	WHETHER ANY PH.D. ENROLLED/PRODUCED OUT OF THE PROJECT	Yes (01)
16	NO. OF PUBLICATIONS OUT OF THE PROJECT (PLEASE ATTACH)	06

18.05.2017

PRINCIPAL INVESTIGATOR

Dr. Satya Paul
Principal Investigator
UGC Project No. F41-281/2012 (SR)
Department of Chemistry
University of Jammu, Jammu-06

Registrar
University of Jammu

REGISTRAR/PRINCIPAL

19/5/17

18/05/17

ANNEXURE- A

OBJECTIVES

1. To prepare high surface area amorphous carbon/silica composites using natural organic materials (carbohydrates-glucose, starch, chitosan, cellulose etc.) and commercially available silica and MCM silicas by partial carbonization.

2. To introduce sulfonic acid groups onto amorphous carbon/silica composites by sulfonation with sulfuric acid so as to prepare high density sulfonic acid functionalized amorphous carbon/silica (commercial and MCM) composites.

3. To prepare sulfonated (SO_3H, SO_3LA) carbon/silica composites coated with hydrophobic ionic liquids.

4. To characterize sulfonated carbon/silica composites by XRD, FTIR, TEM, SEM, TGA, elemental analysis etc.

5. To perform acid catalyzed industrially important reactions like hydrolysis of polysaccharides to monosaccharides, regioselective Friedel-Craft's acylation of aromatic substrates, Fries rearrangement, Knoevenagel condensations, Michael reactions, Aldol reactions etc. and applications of these reactions for building up medicinally important molecules.

6. To perform acid catalyzed cyclizations leading to the formation of biologically important heterocyclic compounds like furan pyrrole, triazoles etc.

7. Different sulfonic acid functionalized amorphous carbon/silica composites would be prepared from different natural organic compounds so as to select the most active and selective solid acid.

8. Alternatively, above transformations could be effected using microwave synthesizer (**CEM monomode oven**).

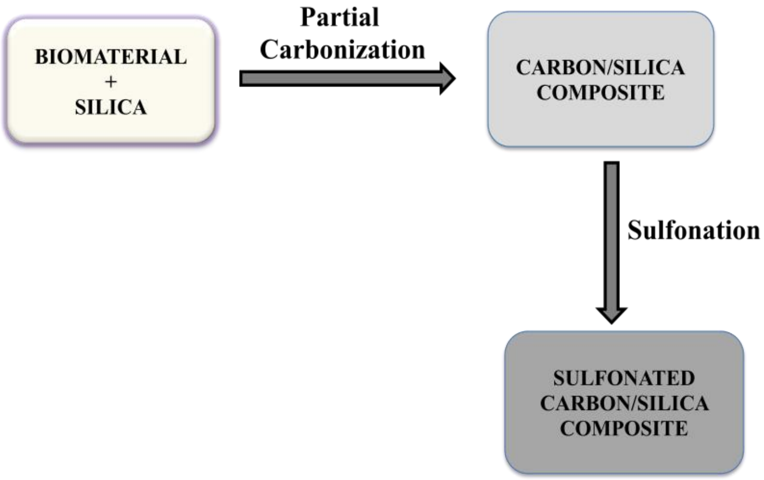
ANNEXURE– B

WORK DONE SO FAR AND RESULTS ACHEIVED AND PUBLICATIONS

Preparation and applications of sulfonated amorphous carbon/silica composites

Sulfonated amorphous carbon/silica composites were prepared by the partial carbonization of different natural organic materials like cellulose, glucose, maltose, starch, chitosan in presence of silica followed by sulfonation using sulfuric acid.

The preparation of the catalyst is presented with the help of scheme given below:

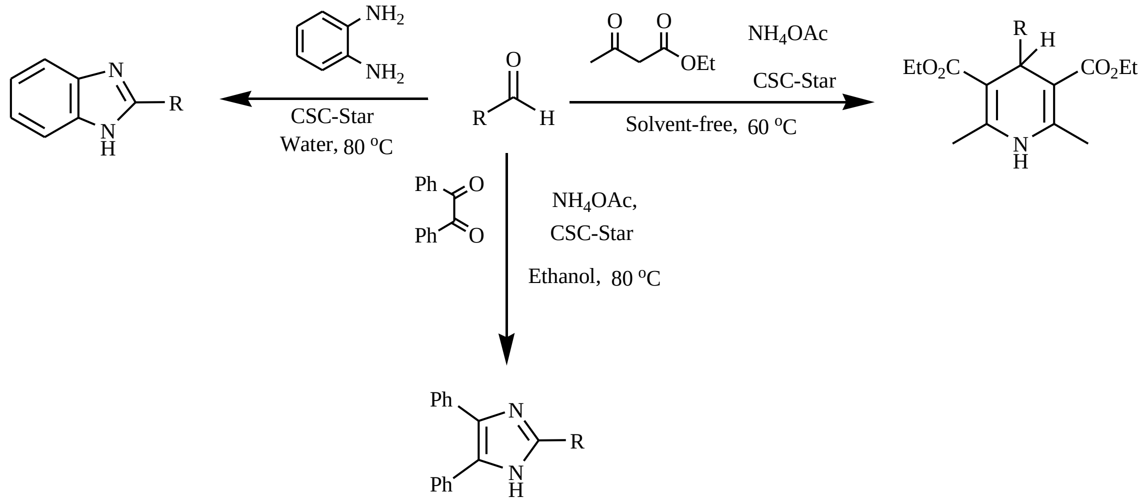


Scheme 1 Preparation of sulfonated carbon/silica composite.

The prepared solid acid catalysts were characterized by different spectroscopic techniques like FTIR, TGA, AAS, XRD, SEM, TEM and elemental analysis.

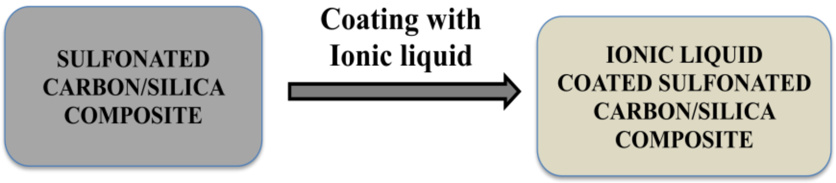
In our previous publication (Green Chem., **2011**, *13*, 2365), sulfonated carbon/silica composites prepared using starch as biomaterial (CSC-Star-SO_3H) was found to be most active for the chemoselective protection of aldehydes as 1,1-diacetates and for *N*-, *O*- and *S*-acylations. The application of the sulfonated carbon/silica composites prepared using starch as biomaterial was tested for the synthesis of 1,4-DHP's, 2,4,5-trisubstituted imidazoles and 2-arylbenzimidazoles (**Scheme 2**). The products isolated were characterized by ^1H and ^{13}C NMR, IR and Mass spectral studies (*Curr. Catal*. **2014,** *3*, 53-64, Reprint attached).

Scheme 2



Preparation and applications of ionic liquid coated sulfonated carbon/silica composites

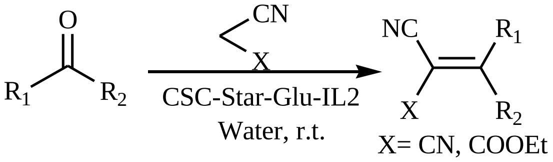
Sulfonated carbon/silica composites were prepared by using mixture of starch and cellulose in three different ratios-1:1, 3:1 and 1:3 respectively. The prepared sulfonated carbon/silica composites were then coated with ionic liquid, 1-butyl-3-methylimidazoliumbromide, [Bmim][Br] to get CSC-Star-Glu-IL1 [prepared from starch : glucose (1 : 1)], CSC-Star-Glu-IL2 [prepared from starch : glucose (3 : 1)] and CSC-Star-Glu-IL3 [prepared from starch : glucose (1 : 3)]. The preparation procedure is represented below:



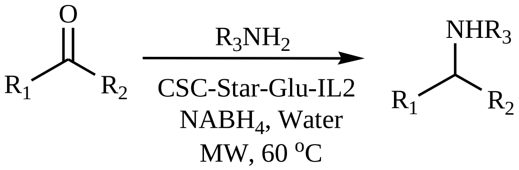
Scheme 3 Preparation of ionic liquid coated sulfonated carbon/silica composite.

The characterization of the ionic liquid coated sulfonated carbon/silica composites, CSC-Star-Glu-ILs viz. CSC-Star-Glu-IL1, CSC-Star-Glu-IL2 and CSC-Star-Glu-IL3 was carried out using FTIR, TGA and elemental analysis. The most active catalyst CSC-Star-Glu-IL2 was also characterized by XRD, SEM and TEM. The catalytic activity of CSC-Star-Glu-IL2 was evaluated for Knoevenagel condensation (**Scheme 4**), reductive amination of aldehydes and ketones (**Scheme 5**) and for Michael addition of indoles to *α,β*-unsaturated ketones in aqueous medium (**Scheme 6**). The characterization of the products was done by ^{1}H and ^{13}C NMR, IR and Mass spectroscopy (*RSC Adv.*, **2014**, *4*, 7461-7470, Reprint attached).

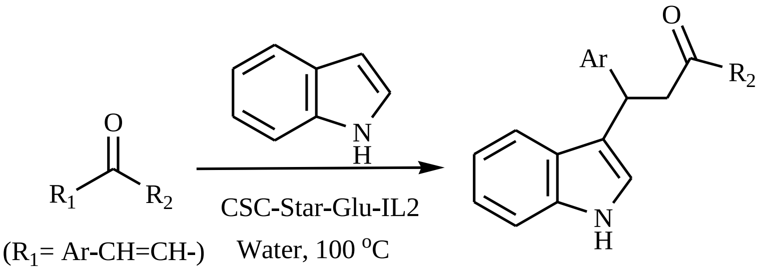
Scheme 4



Scheme 5

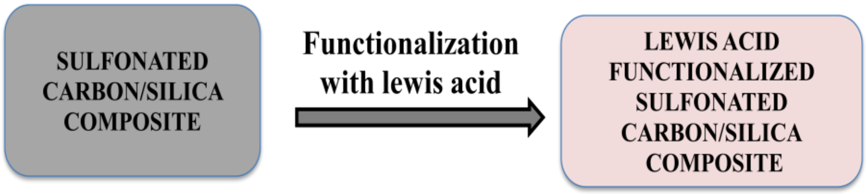


Scheme 6



Preparation and applications of Lewis acid functionalized sulfonated carbon/silica composites

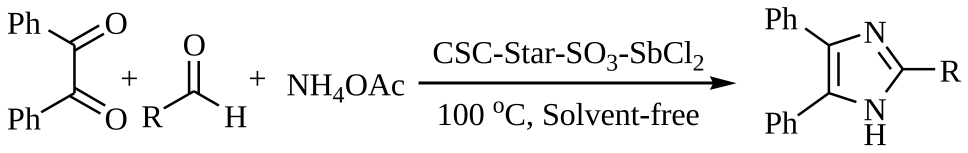
Sulfonated carbon/silica composites were treated with various Lewis acids like $FeCl_3$, $Bi(NO_3)_3$, $ZnCl_2$, $AlCl_3$, $SbCl_3$ to get the Lewis acid functionalized sulfonated carbon/silica composites (CSC-Star-SO_3-$FeCl_2$, CSC-Star-SO_3-$Bi(NO_3)_2$, CSC-Star-SO_3-ZnCl, CSC-Star-SO_3-$AlCl_2$ and CSC-Star-SO_3-$SbCl_2$). The preparation procedure is represented below:



Scheme 7. Preparation of Lewis acid functionalized sulfonated carbon/silica composite.

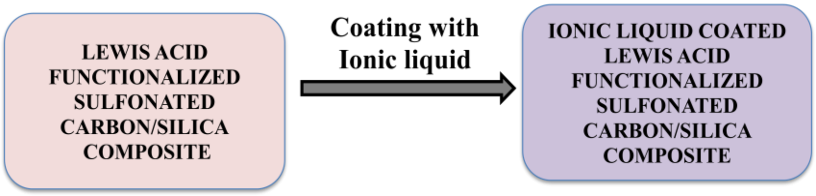
Lewis acid functionalized sulfonated carbon/silica composites were characterized by FTIR, TGA and AAS. The most active catalyst, CSC-Star-SO_3-$SbCl_2$ was also characterised by XRD, SEM and TEM. The catalytic activity of CSC-Star-SO_3-$SbCl_2$ was evaluated for the synthesis of 2,4,5-trisubstituted imidazoles (**Scheme 8**). The products isolated were characterized by ^{1}H and ^{13}C NMR, IR and Mass spectral studies.

Scheme 8



<u>Preparation and applications of ionic liquid coated Lewis acid functionalized sulfonated carbon/silica composites</u>

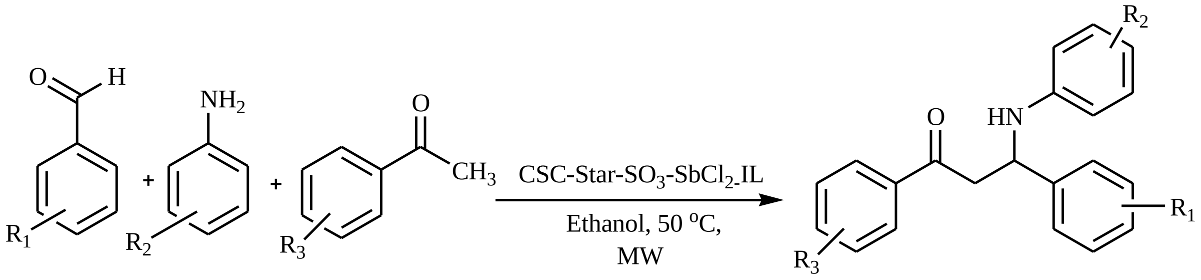
Lewis acid functionalized sulfonated carbon/silica composites (CSC-Star-SO_3-$FeCl_2$, CSC-Star-SO_3-$Bi(NO_3)_2$, CSC-Star-SO_3-ZnCl, CSC-Star-SO_3-$AlCl_2$ and CSC-Star-SO_3-$SbCl_2$) were then coated with ionic liquid, 1-butyl-3-methylimidazoliumbromide, [Bmim][Br] to get ionic liquid coated Lewis acid functionalized sulfonated carbon/silica composites CSC-Star-SO_3-$FeCl_2$-IL, CSC-Star-SO_3-$Bi(NO_3)_2$-IL, CSC-Star-SO_3-ZnCl-IL, CSC-Star-SO_3-$AlCl_2$-IL and CSC-Star-SO_3-$SbCl_2$-IL. The preparation procedure is shown below:



Scheme 9 Preparation of ionic liquid coated Lewis acid functionalized sulfonated carbon/silica composites.

Ionic liquid coated Lewis acid functionalized sulfonated carbon/silica composites were characterized by FTIR, TGA and AAS. The most active catalyst, CSC-Star-SO_3-$SbCl_2$-IL was also characterised by XRD, SEM and TEM. The application of the CSC-Star-SO_3-$SbCl_2$-IL was tested for Mannich reaction (**Scheme 10**). The products isolated were characterized by ^{1}H and ^{13}C NMR, IR and Mass spectral studies.

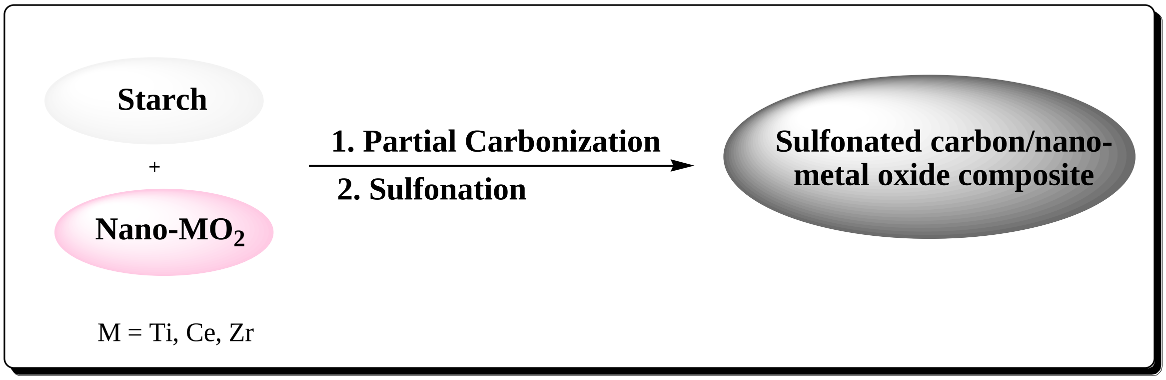
Scheme 10



Preparation and applications of sulfonated carbon/nano-metal oxide composites

Sulfonated carbon/nano-metal oxide composites were prepared by the incomplete carbonization of starch in the presence of different inorganic supports like nano-titania, nano-ceria and nano-zirconia to form carbon/nano-titania (C/TiO_2), carbon/nano-ceria (C/CeO_2) and carbon/nano-zirconia (C/ZrO_2) composites respectively, which on sulfonation with conc. sulfuric acid gave the corresponding sulfonated carbon/nano-metal oxide composites.

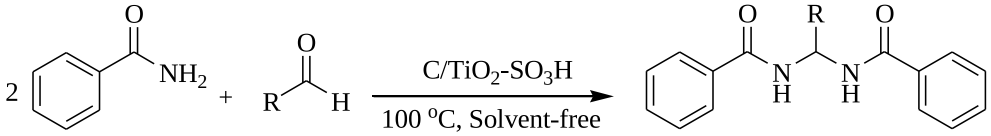
The preparation of the catalyst is presented with the help of scheme given below:



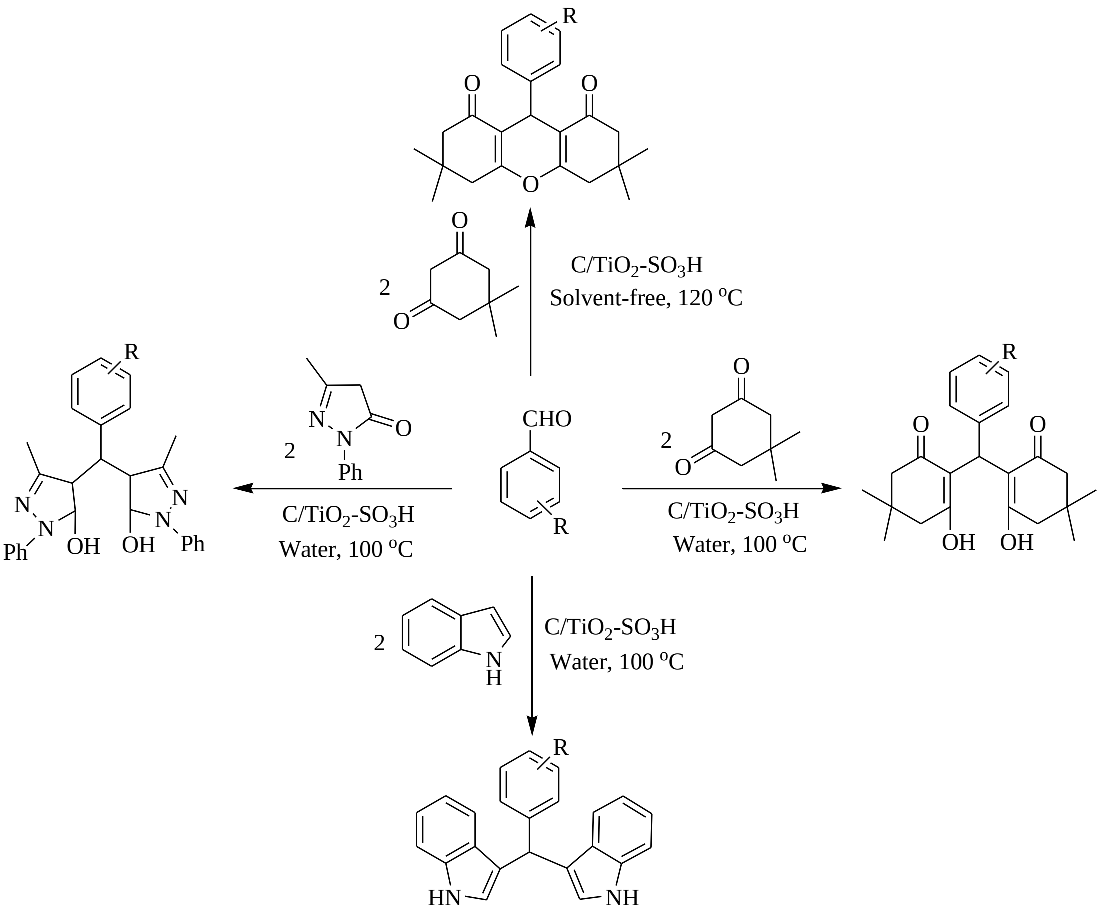
Scheme 11. Preparation of sulfonated carbon/nano-metal oxide composite.

The characterization of the sulfonated carbon/nano-metal oxide composites thus prepared (C/TiO_2-SO_3H, C/CeO_2-SO_3H and C/ZrO_2-SO_3H) was carried out with FTIR and CHNS analysis. The most active catalyst C/TiO_2-SO_3H was further characterized by XRD, SEM, TEM, HRTEM, EDX and TGA. The applicability of sulfonated carbon/nano-metal oxide composites was studied for the one-pot synthesis of *gem*-bisamides (**Scheme 12**), bis(heterocyclyl)methanes (**Scheme 13**) and *β*-aminocarbonyl compounds (**Scheme 14**). The products isolated were characterized by FTIR, ^1H NMR, ^{13}C NMR and mass spectral studies (*New. J. Chem.*, **2015**, *39*, 6338-6350)

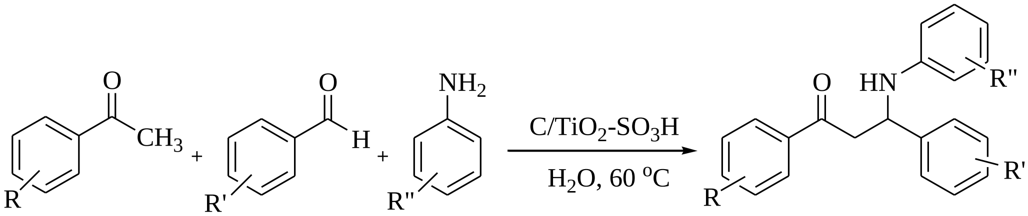
Scheme 12



Scheme 13



Scheme 14

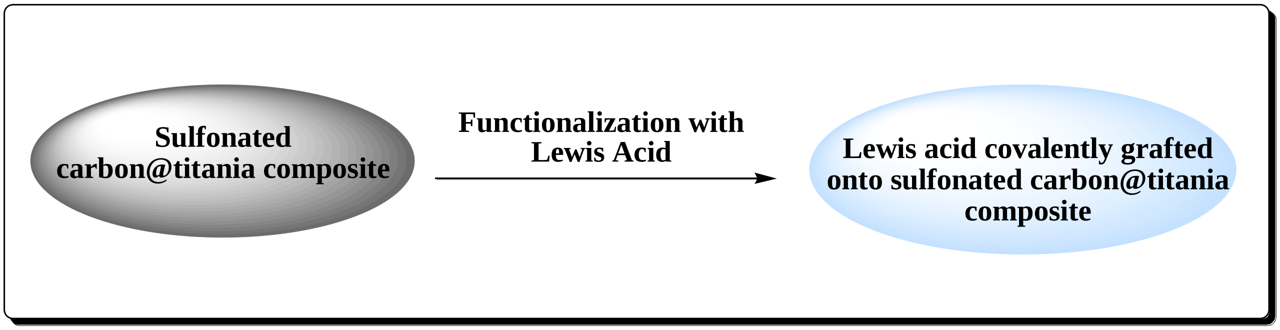


Preparation and applications of Lewis acid covalently grafted onto sulfonated carbon@titania composites

Lewis acid covalently grafted onto sulfonated carbon@titania composites were prepared by the treatment of sulfonated carbon@titania composites 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 covalently grafted onto 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-$Bi(NO_3)_2$].

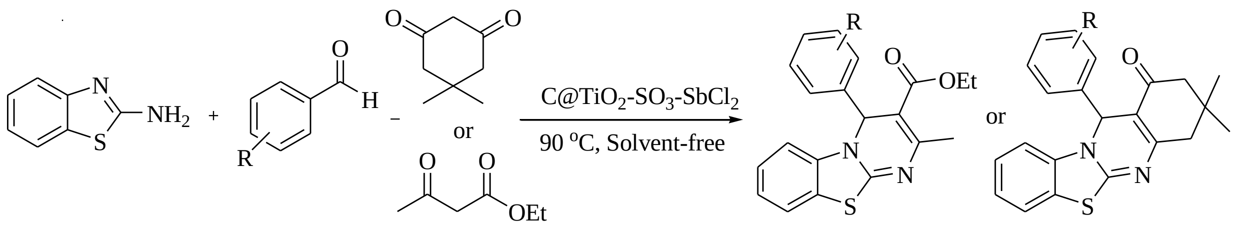
The general procedure for the synthesis of Lewis acid covalently grafted onto sulfonated carbon@titania composites is shown in **Scheme 15**.



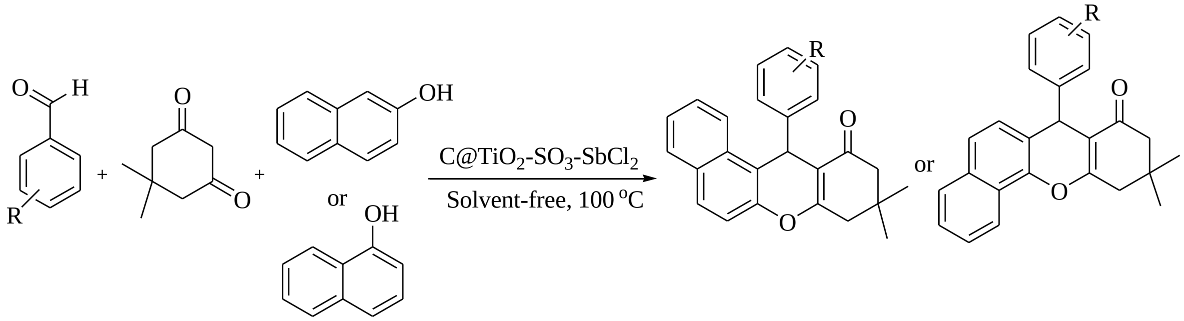
Scheme 15 General scheme for the synthesis of Lewis acid covalently grafted onto sulfonated carbon@titania composites.

All the prepared Lewis acid covalently grafted onto sulfonated carbon@titania composites 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. The catalytic activity of Lewis acid covalently grafted onto sulfonated carbon@titania composites was tested for the one-pot multicomponent synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles (**Scheme 16**) and benzoxanthenones (**Scheme 17**) as well as in Pechmann (**Scheme 18**) and aza-Michael reaction (**Scheme 19**). All the synthesized products were characterized by FTIR, ^{1}H NMR, ^{13}C NMR and mass spectral studies (*J. Mol. Catal. A: Chem.*, **2016**, 411, 299-310; *Monatsh Chem*. **2017**, 148, 327-337).

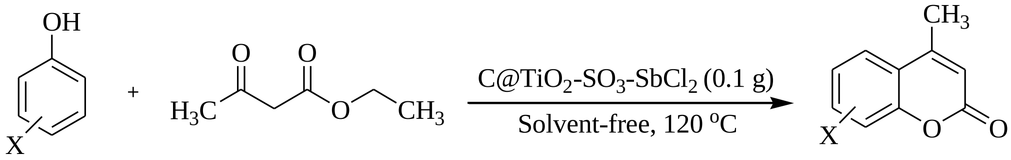
Scheme 16



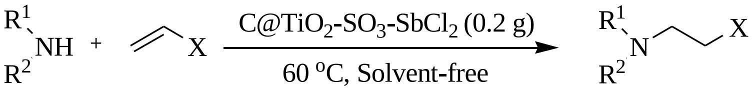
Scheme 17



Scheme 18

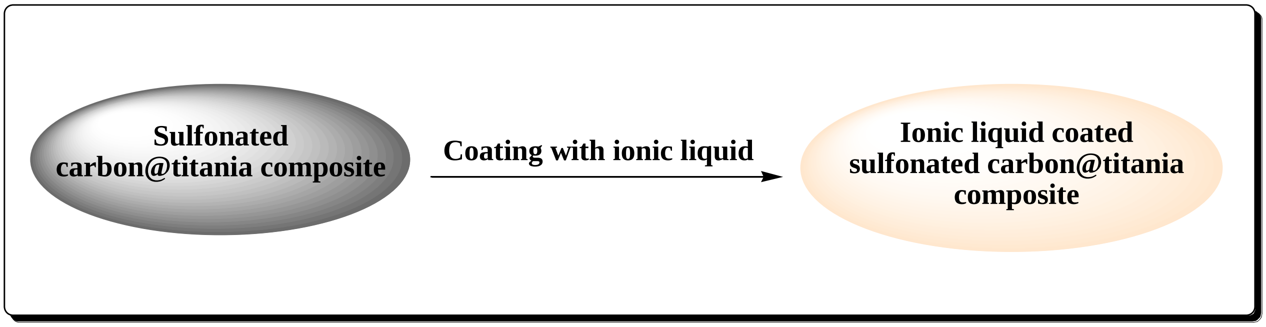


Scheme 19



Preparation and applications of ionic liquid coated sulfonated carbon@titania composites

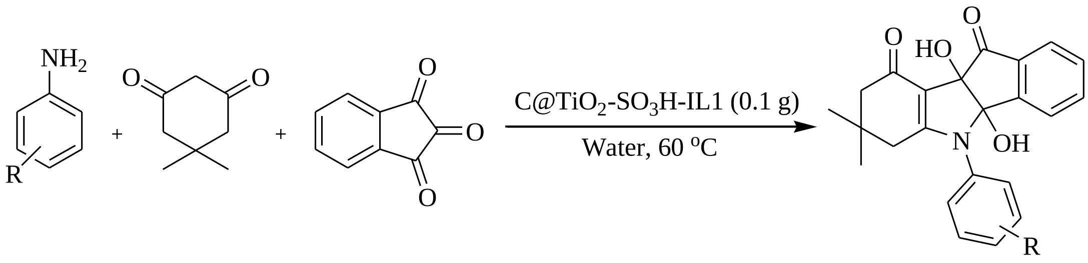
In the first step sulfonated carbon@titania composites were prepared by the partial carbonization of starch and nano-titania followed by sulfonation. These composites were then coated with ionic liquid, 1-decyl-3-methyl-imidazolium chloride [dmim][Cl] to get C@TiO_2-SO_3H-IL1 and 1-decyl-3-methyl-imidazolium tetrafluoroborate [dmim][BF_4] to get C@TiO_2-SO_3H-IL2. The general procedure for the synthesis of ionic liquid coated sulfonated carbon@titania composites has been represented in **Scheme 20**.



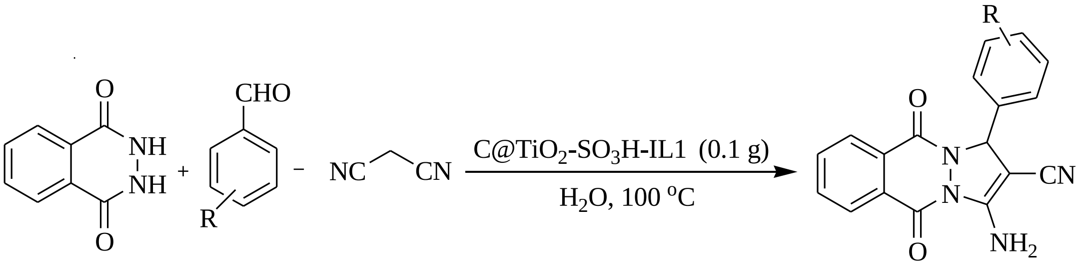
Scheme 20. General scheme for the synthesis of ionic liquid coated sulfonated carbon@titania composites.

Ionic liquid coated sulfonated carbon@titania composites ($C@TiO_2$-SO_3H-IL1 and $C@TiO_2$-SO_3H-IL2) were characterized by FTIR and TGA. The most active catalyst, $C@TiO_2$-SO_3H-IL1 was further characterized by XRD, CHNS, EDX, SEM and HRTEM. The applicability of $C@TiO_2$-SO_3H-IL1 was evaluated for the one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones (**Scheme 21**) and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones (**Scheme 22**). All the synthesized products were obtained in good to excellent yields and were characterized by FTIR, ^1H NMR, ^{13}C NMR and mass spectral studies (*New J. Chem*. **Submitted 2017**)

Scheme 21



Scheme 22



Publications

1. **1.** Manmeet Kour, Satya Paul, James H. Clark, Vivek K. Gupta, Rajni Kant, Preparation and characterization of Lewis acid grafted sulfonatedcarbon@titania composites for the multicomponent synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles and benzoxanthenones under solvent-free conditions., *J. Mol. Catal. A: Chem.*, **2016**, *411*, 299-310.
2. **2.** Manmeet Kour and Satya Paul, A green and convenient approach for the one-pot solvent-free synthesis of coumarins and *β*-amino carbonyl compounds using Lewis acid grafted sulfonated carbon@titania composite. *Monatsh Chem*, **2017**, 148, 327-337.
3. **3.** Manmeet Kour and Satya Paul, Sulfonated carbon/nano-metal oxide composites: a novel and recyclable solid acid catalyst for organic synthesis in benign reaction media. *New J. Chem.*, **2015***, 39*, 6338-6350.
4. **4.** Balbir Kumar, Manmeet Kour, Satya Paul, Rajni Kant and Vivek K. Gupta, Crystal structure of ethyl 4-(2-chlorophenyl)-2-methyl-4*H*-pyrimido[2,1-*b*][1,3]benzothiazole-3-carboxylate., *Acta Crystallography E*, **2015**, *E71*, 669.
5. **5.** Ionic liquid coated sulfonated carbon/silica composites: novel heterogeneous catalysts for organic syntheses in water.

   Princy Gupta, Manmeet Kour, Satya Paul and James H. Clark, *RSC Advances*, **2014**, *4*, 7461-7470.
6. **6.** Ionic liquid coated sulfonated carbon@titania composites: A novel and sustainable solid acid catalyst for the one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones in aqueous media

   Manmeet Kour, Madhvi Bhardwaj, Harsha Sharma, Satya Paul and James H. Clark, *New J. Chem.*, **2017** (Revised).

ANNEXURE- C

ACHIEVED OBJECTIVES

Most of the objectives mentioned in the Annexure A have been successfully achieved.

- Carbon/silica composites using natural organic materials have been prepared using commercially available silica.
- High density sulfonic acid functionalized amorphous carbon/silica composites have been prepared.
- Sulfonated carbon/silica composites coated with hydrophobic ionic liquids have been prepared.
- Characterization of the prepared sulfonated carbon/silica composites has been done using modern techniques.
- Important organic transformation mentioned in objective have been carried out using these solid acids under mild conditions.
- Some biologically important heterocycles like indeno[1,2-*b*]indole-9,10-diones and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones have been prepared under mild and green conditions.

ANNEXURE- D

ACHIEVEMENTS FROM THE PROJECT

We have successfully prepared a series of novel solid acids that have the potential of replacing conventional hazardous and polluting homogeneous acids, and these can be effectively utilized for carrying out industrially important acid catalyzed organic reactions. The characterization of the synthesized catalysts was done using modern spectroscopic techniques like FTIR, CHNS, ICP-AES, XRD, SEM, TEM, HRTEM and TGA. Further, their applicability was explored in key acid catalyzed reactions and in the multicomponent synthesis of heterocycles.

ANNEXURE- E

SUMMARY OF THE FINDINGS

We have developed a range of heterogeneous acid catalysts derived from inexpensive natural biomaterials including sulfonated amorphous carbon/silica composites, ionic liquid coated sulfonated carbon/silica composites, Lewis acid functionalized sulfonated carbon/silica composites, sulfonated carbon/nano-metal oxide composites, Lewis acid grafted sulfonated carbon@titania composites and ionic liquid coated sulfonated carbon@titania composites. The complete characterization of the prepared solid acid catalysts has been done using various spectroscopic techniques like FTIR, TGA, CHNS, SEM, TEM, HRTEM, XRD and ICP-AES. Subsequently, the catalytic activities of the developed catalysts have been evaluated for various synthetic organic transformations.

Five different sulfonated carbon/silica composites were prepared by the partial carbonization of different biomaterials in the presence of silica followed by sulfonation. The catalytic activity of the developed solid acids was tested for the synthesis of 1,4-DHP's, 2,4,5-trisubstituted imidazoles and 2-arylbenzimidazoles. Sulfonated carbon/silica composites prepared using starch as biomaterial (CSC-Star-SO_3H) was found to be most active among different catalysts screened. The reaction conditions were selected by the optimisation of different reaction parameters like solvent, temperature and catalyst amount. Thereafter, various substituted aldehydes were used under the optimized reaction conditions for the synthesis of diversely substituted 1,4-DHP's, 2,4,5-trisubstituted imidazoles and 2-arylbenzimidazoles.

Ionic liquid coated sulfonated carbon/silica composites, CSC-Star-Glu-ILs (CSC-Star-Glu-IL1, CSC-Star-Glu-IL2 and CSC-Star-Glu-IL3) were synthesized by using mixture of starch and cellulose in three different ratios viz. 1:1, 3:1 and 1:3 respectively. The catalytic activity of CSC-Star-Glu-ILs was evaluated for the one-pot Knoevenagel condensation, reductive amination of aldehydes and ketones, and for Michael addition of indoles to α,β-unsaturated ketones in aqueous medium.

Lewis acid functionalized sulfonated carbon/silica composites were prepared by treating sulfonated carbon/silica composites with various Lewis acids like $FeCl_3$, $Bi(NO_3)_3$, $ZnCl_2$, $AlCl_3$, $SbCl_3$ to get different Lewis acid functionalized sulfonated carbon/silica composites (CSC-Star-SO_3-$FeCl_2$, CSC-Star-SO_3-$Bi(NO_3)_2$, CSC-Star-SO_3-ZnCl, CSC-Star-SO_3-$AlCl_2$ and CSC-Star-

SO_3-$SbCl_2$). The catalytic activity of various solid Lewis acids was evaluated for the synthesis of 2,4,5-trisubstituted imidazoles under solvent-free conditions at 100 ^oC.

Three different sulfonated carbon/nano-metal oxide composites were synthesized by the partial carbonization of starch in the presence of different nano-metal oxides, nano-titania, nano-ceria and nano-zirconia followed by sulfonation, thereby forming C/TiO_2-SO_3H, C/CeO_2-SO_3H, and C/ZrO_2-SO_3H respectively. Sulfonated carbon/nano-titania composite (C/TiO_2-SO_3H) was found to be the most active amongst the three catalysts screened, giving higher yields of the desired products in shorter reaction times. Thereafter, various reaction parameters such as amount of catalyst, solvent and reaction temperature were optimised using C/TiO_2-SO_3H. After the optimisation of reaction conditions, the scope of the reaction was further extended for the synthesis of diversely substituted bisamides using various aldehydes having electron-donating and with-drawing groups. Further, the reusability of developed catalyst was tested for five reaction runs and it displayed excellent recyclability without significant drop in catalytic activity. Thereafter, various bis(heterocyclyl)methane derivatives were synthesized using different C-H activated compounds like dimedone, pyrazolone and indole in the presence of C/TiO_2-SO_3H in water at 100 °C. All the products were obtained in good yields and characterized by FTIR, ^1H NMR, ^{13}C NMR and mass spectral data. We have developed a mild and effective protocol for the one-pot three component synthesis of β-amino carbonyl compounds using C/TiO_2-SO_3H in the presence of water as benign reaction media at 60 °C. To explain the role of C/TiO_2-SO_3H as effective heterogeneous catalyst, its activity was compared to its precursors (nano-titania, amorphous carbon, non-sulfonated carbon nano/titania, sulfonated amorphous carbon) and sulfonated carbon/silica composite. C/TiO_2-SO_3H was found to be superior amongst all in terms of higher product yields. Moreover, the efficacy of the present protocol was also compared to some of the protocols reported in literature and the present catalytic system was found to be superior amongst others in terms of higher TOFs.

A series of novel and highly efficient Lewis acids covalently grafted onto sulfonic acid functionalized carbon@titania composites *via* sulfonation of carbon@titania composites followed by treatment with different Lewis acids *viz* $AlCl_3$, $FeCl_3$, $SbCl_3$, $SnCl_2$, $Cu(OAc)_2$, $Bi(NO_3)_3$ to get the respective solid Lewis acids 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-$Bi(NO_3)_2$. All the prepared Lewis acid covalently grafted onto sulfonated carbon@titania composites 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.

The catalytic activity of various solid Lewis acids was screened for the one-pot synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles under solvent-free conditions. It was observed that stronger Lewis acids gave undesirable side reactions, whereas the weak ones were less effective for the desired transformation. The milder Lewis acid, C@TiO_2-SO_3-$SbCl_2$ was found to be the most effective and gave higher yields of 4*H*-pyrimido[2,1-*b*]benzothiazoles amongst others. All the products were obtained in good to excellent yields and characterized by FTIR, ^{1}H NMR, ^{13}C NMR and mass spectral data. Further, the structure of one of the synthesized products has also been confirmed by single-crystal X-ray diffraction studies. C@TiO_2-SO_3-$SbCl_2$ has been used as an efficient reusable catalyst for the one-pot synthesis of benzoxanthenones by the condensation of 1 or 2-napthol, aldehyde and dimedone under solvent-free conditions at 100 °C. In addition to dimedone, the reaction was also carried out using other 1,3-dicarbonyl compounds such as ethyl acetoacetate and acetyl acetone giving the unexpected product dibenzoxanthenes. All the synthesized products were obtained in high yields. A sustainable protocol for the one-pot synthesis of coumarins *via* Pechmann reaction has been reported in the presence of C@TiO_2-SO_3-$SbCl_2$ under solvent-free conditions. The substrate scope of the reaction was studied by employing different substituted phenols under the optimised reaction conditions. Further, the catalytic activity of the present catalytic system was compared to its various precursors for the one-pot synthesis of coumarins. It was found that C@TiO_2-SO_3-$SbCl_2$ gave the desired product in higher yields and thus found to be superior than its precursors and also to its homogeneous counterpart. The catalytic activity of C@TiO_2-SO_3-$SbCl_2$ was also studied for the one-pot synthesis of β-amino carbonyl compounds by aza-Michael reaction. Different solid Lewis acids were screened for the aza-Michael addition of amine to acrylonitrile to select the most active one. C@TiO_2-SO_3-$SbCl_2$ was again found to be the most active solid Lewis acid catalyst to carry out the desired transformation. Variety of amines substituted with electron-donating and withdrawing groups were subjected to aza-Michael addition under the optimized reaction conditions giving good yields of the desired products.

Ionic liquid coated sulfonated carbon@titania composites were synthesized by coating sulfonated carbon@titania composites with ionic liquid, 1-decyl-3-methyl-imidazolium chloride [dmim][Cl] to get C@TiO_2-SO_3H-IL1 (1-decyl-3-methyl-imidazolium chloride coated sulfonated carbon@titania composite) and 1-decyl-3-methyl-imidazolium tetrafluoroborate [dmim][BF_4] to get C@TiO_2-SO_3H-IL2 (1-decyl-3-methyl-imidazolium tetrafluoroborate coated sulfonated carbon@titania composite). C@TiO_2-SO_3H-IL1 and C@TiO_2-SO_3H-IL2 were characterized by FTIR and TGA. The most active catalyst, C@TiO_2-SO_3H-IL1 was further characterized by XRD, CHNS, EDX, SEM and HRTEM. The catalytic activity of ionic liquid coated sulfonated carbon@titania composites was investigated for the one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones using water as solvent at 60 °C. Out of the two catalysts screened, C@TiO_2-SO_3H-IL1 gave the higher yields and thus found to be more active in comparison to C@TiO_2-SO_3H-IL2 for the desired reaction. Further, the effect of ionic liquid coating on the sulfonated composite was evaluated by carrying out the reaction in the presence of C/TiO_2-SO_3H also. It was found that C/TiO_2-SO_3H gave lower yields of the desired product, whereas coating of IL onto the sulfonated composite led to significant improvement in the product yields. All the products were obtained in good yields and characterized by FTIR, ^{1}H NMR, ^{13}C NMR and mass spectral data. The applicability of C@TiO_2-SO_3H-IL1 was further extended for the one-pot synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones in water at 100 °C. Various substituted aldehydes having electron-donating and withdrawing groups were successfully employed giving the desired product in good to excellent yields. In addition, the developed catalyst showed recyclability upto five consecutive runs without significant loss of activity.

ANNEXURE - F

CONTRIBUTION TO THE SOCIETY

The developed catalytic systems have ample scope to be utilized further towards the development of green methodologies. These developed solid acids replace the existing mineral acids like HCl, H_2SO_4 etc. which poses serious threat to the environment. These solid acids are easy to handle, non-toxic, recyclable under the reaction conditions. In industrial manufacturing, these solid acids have proved to be highly efficient.

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Ionic liquid coated sulfonated carbon/silica composites: novel heterogeneous catalysts for organic syntheses in water†

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Ionic liquid coated sulfonic acid functionalized amorphous carbon/silica composites derived from a starch–glucose mixture were developed and their catalytic activities were evaluated for Knoevenagel condensation, reductive amination of aldehydes and ketones, and for Michael addition of indole to α,β-unsaturated ketones in aqueous medium. The catalyst prepared from starch–glucose mixture (3 : 1) [CSC-Star-Glu-IL2] showed the highest activity in water. The catalysts were characterized by FTIR, TGA, elemental analysis, and the most active was further characterized by XRD, SEM and TEM.

Introduction

Reactions in water are now of great interest in organic syntheses.[1] In addition to scientific interest in aqueous media, social and legislative pressures to find environmentally benign alternatives to current organic chemical processes have made these reactions attractive from industrial and ecological points of view.[2] Many common organic solvents are likely to be banned or at least restricted in use as a consequence of REACH and similar multinational, national and regional regulations. These issues are beginning to present enormous challenges to the chemical, pharmaceutical and some other industries. Reactions in water offer significant environmental advantages and have attracted a great deal of interest since water is a desirable solvent due to its: low cost, safety, and environmentally benign nature. Although many reactions work well in water, some reactions proceed very slowly because the solubility of most organic molecules in pure water is limited. Because solubility is generally a great advantage for reactivity, a variety of strategies expanding the scope of water-based organic syntheses have been investigated. The concept of ionic liquid coating for solid acid catalysts was first reported by Valkenberg[3a] and co-workers. They have reported ionic liquid coated iron chloride catalyzed Friedel–Crafts acylation of aromatic compounds. Palladium acetate supported on amorphous silica with the aid of an ionic liquid, [bmim]PF_6 was reported for Mizoroki–Heck reaction by Hagiwara[3b] and co-workers. Kobayashi and co-workers have developed silica supported metal catalysts with hydrophobic ionic liquids for organic reactions in water.[3c,d] The authors suggested that the ionic liquid creates a hydrophobic environment on the siliceous surface resulting in better diffusion of organic substrates to the catalytic sites. Gu and co-workers[4a] have reported that coating of silica supported sulfonic acid catalysts with hydrophobic ionic liquid leads to a significant improvement of catalyst selectivity in an aqueous medium. Hara[4b] and co-workers reported sulfonated carbon derived from sugar for the first time and used it for the production of biodiesel. Recently, we have reported amorphous carbon/silica composites bearing sulfonic acid as solid acid catalysts for the chemoselective protection of aldehydes as 1,1-diacetates and for *N*-, *O*- and *S*-acylations.[5] As an extension of this work, herein, we prepared ionic liquid coated sulfonated carbon/silica composites as heterogeneous catalysts for Knoevenagel condensation and reductive amination of aldehydes and ketones, and for Michael addition of indole to α,β-unsaturated ketones in aqueous medium.

In our previous study,[5] it was found that starch and glucose are the best choice of biomaterials for preparing sulfonated carbon/silica composites. So, here we have a selected mixture of starch and glucose for preparing ionic liquid coated sulfonated carbon/silica composites. While ionic liquids themselves have had very limited success as alternative solvents (due to their high cost and difficulties in separations and reuse), their use in an immobilized state overcomes many of these difficulties while taking advantage of their useful properties (high solubilities of many compounds and high stabilization of polar reaction intermediates).

Due to the widespread synthetic utility of Knoevenagel condensation, a large number of methodologies have been developed for this reaction. In recent years, a wide range of catalysts, including Lewis acids,[6] zeolites,[7] solid bases,[8] heterogeneous catalysts[9] and amines immobilized on

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polymers,[10a] Yb(OTf)$_3$[10b] have been employed, each affording variable yields of products in solution or under solvent-free conditions. Al-Omran F. *et al.*[10c] have reported stereochemical Knoevenagel condensation of 2-(benzothiazol-2-ylthio) acetonitrile with furan-2-carbaldehyde and thiophene-2-carbaldehydes. Recently, a number of basic catalysts such as lithium hydroxide,[11] silica supported ammonium acetate,[12] L-proline,[13] chitosan hydrogel,[14] silica immobilized piperazine,[15] titanium isopropoxide/pyridine,[16] fly ash supported calcium oxide,[17] amine functionalized mesoporous silica,[18] thiourea,[19] mesoporous Mg–Fe bimetal oxides,[20] lipase,[21] and tertiary amine functionalized polyacrylonitrile[22] have been used to catalyze Knoevenagel condensation. However, basic catalysts cannot be applied to the substrates possessing base sensitive groups. To overcome these problems, number of acid catalyzed[23–26a] Knoevenagel condensation protocols have been developed. Moreover, many Knoevenagel condensations catalyzed by ionic liquids[26b–f] have also been reported. But, there is still scope for the development of new environment-friendly procedure using novel solid catalyst for Knoevenagel condensation. Herewith we have reported a novel ionic liquid coated sulfonated carbon/silica composites as a heterogeneous catalyst for the Knoevenagel condensation of aldehydes and ketones.

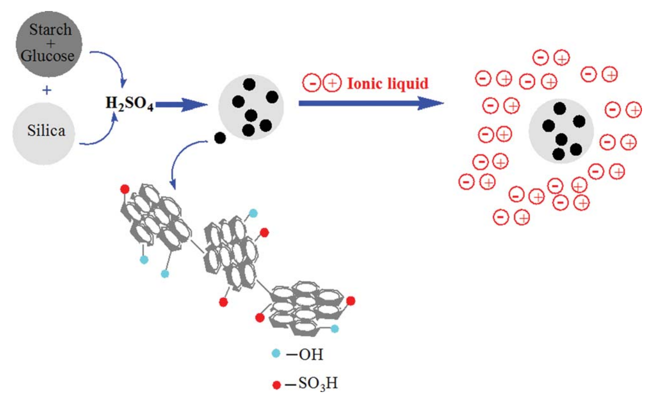
Reductive amination of aldehydes and ketones is a convenient method for the synthesis of functionalized amines which are important organic intermediates and have found wide applications in synthetic and combinatorial chemistry.[27] A number of reagents such as NaBH$_4$–silica phosphoric acid,[28] zinc borohydride *N*-methyl pyrrolidine,[29] NaBH$_4$–silica gel supported sulfuric acid,[30] NaBH$_4$–Amberlyst-15,[31] NaBH$_4$–silica chloride,[32] hydrido-iridium (III) complex,[33] fluorous organocatalyst,[34] NaBH$_4$–cellulose sulfuric acid[35] and NaBH$_4$ using carbon based solid acid catalyst[36] for reductive amination of aldehydes and ketones have been developed. However, most of the methods have limitations such as functional group tolerance, side reactions and harsh reaction conditions. So, there is a demand for an efficient and environment-friendly protocol for the reductive amination of aldehydes and ketones.

Michael reaction of indoles to α,β-unsaturated carbonyl compounds provides easy access to 3-substituted indoles, which are important building blocks for the synthesis of important biologically active compounds and natural products.[37–39] Recently, catalysts such as polyvinyl sulfonic acid,[40] metal halide hydrates,[41] task-specific ionic liquids,[42] bimetallic iron–palladium catalysts,[43a] and iron salts[43b] have been reported for the Michael addition of indole to α,β-unsaturated ketones. However, the acid-catalyzed conjugate addition of indoles requires careful control of acidity to prevent side reactions such as dimerization or polymerization. Further, many of these procedures involve strongly acidic conditions, expensive reagents, longer reaction time, give low yields of products due to the dimerization of indoles or polymerization of vinyl ketones and cumbersome product isolation. Keeping all these facts in view, we have developed a new environment-friendly procedure for Michael addition of indole to α,β-unsaturated ketones.

Results and discussion

Preparation and characterization of ionic liquid coated sulfonated carbon/silica composites

Firstly, sulfonated carbon/silica composites were prepared according to the method already reported,[5] except that instead of using different biomaterials, a mixture of starch and glucose in three different ratios 1 : 1, 3 : 1 and 1 : 3 respectively was taken. The sulfonated carbon/silica composites (CSC-Star-Glu) prepared were then coated with ionic liquid, 1-butyl-3-methylimidazolium bromide, [Bmim][Br] to get CSC-Star-Glu-IL1 [(prepared from starch : glucose (1 : 1))], CSC-Star-Glu-IL2 [(prepared from starch : glucose (3 : 1))] and CSC-Star-Glu-IL3 [(prepared from starch : glucose (1 : 3))]. The preparation procedure is represented in Scheme 1. The characterization of the ionic liquid coated sulfonated carbon/silica composites CSC-Star-Glu-ILs *viz.* CSC-Star-Glu-IL1, CSC-Star-Glu-IL2 and CSC-Star-Glu-IL3 was carried out with FTIR, TGA, and elemental analysis. The most active catalyst CSC-Star-Glu-IL2 was also characterized by XRD, SEM and TEM. The FTIR spectra of CSC-Star-Glu-ILs showed bands from 1625–1629 cm^{-1} which were assigned to aromatic C═C stretching modes in polyaromatic rings. The bands from 2930–2934 cm^{-1} in CSC-Star-Glu-ILs were due to the phenolic –OH groups. CSC-Star-Glu-ILs also showed absorption bands from 1455–1466 cm^{-1} (due to asymmetric stretching of SO$_2$) and from 1102–1110 cm^{-1} (due to symmetric stretching of SO$_2$), which indicated the presence of –SO$_3$H groups. CSC-Star-Glu-ILs showed bands from 3100–3110 and 3146–3152 cm^{-1} due to imidazolium ring –CH stretching. The bands from 2873–2875 and 2960–2962 cm^{-1} were due to aliphatic –CH stretching modes of methyl and butyl groups. The bands from 1570–1574 were assigned to stretching modes of imidazole ring and from 1160–1170 cm^{-1} were assigned to imidazole H–C–N bending modes. Further, the bands from 803–810, 750–753 and 651–655 cm^{-1} were due to in-plane imidazole ring bending, out of plane –CH bending and imidazole C$_2$–N$_1$–C$_5$ bending modes respectively. The presence of these bands showed the coating of ionic liquid on the surface of the catalyst. The major absorption frequencies are presented in Table 1. The FTIR spectra of CSC-Star-Glu-IL2 is shown in Fig. S1 (see ESI†). The stability of CSC-Star-Glu-ILs was



Scheme 1 Synthesis of CSC-Star-Glu-ILs.

Table 1 Major absorption frequencies in FTIR (ν_{max} in cm^{-1})[a] of sulfonated carbon/silica composites coated with 1-butyl-3-methylimidazolium bromide

			SO_2 stretch		Imidazole ring					
Catalyst	C=C	Phenolic-OH	Asym.	Sym.	(C–H) stretch	H–C–N bending	C_2–N_1–C_5 bending	In plane bending	Out of plane C–H bending	Aliphatic C–H stretch
CSC-Star-Glu-IL1	1628	2930	1455	1106	3146, 3100	1160	653	807	750	2872, 2960
CSC-Star-Glu-IL2	1625	2934	1466	1102	3152, 3106	1166	651	803	753	2875, 2962
CSC-Star-Glu-IL3	1629	2933	1460	1110	3150, 3110	1170	655	810	752	2873, 2960

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

determined by thermogravimetric analysis. The TGA curves showed almost negligible weight losses upto 240 °C, and then significant weight losses are observed after 247 °C. Thus, the catalysts are stable upto 240 °C and hence it is safe to carry out the reaction at room temperature, 60 and 100 °C. The weight losses of CSC-Star-Glu-IL1, CSC-Star-Glu-IL2 and CSC-Star-Glu-IL3 are represented in Table 2. The TGA of CSC-Star-Glu-IL2 is represented in Fig. S2 (see ESI†). The $-SO_3H$ loading in the CSC-Star-Glu-ILs was determined by elemental analysis. The CSC-Star-Glu-IL1, CSC-Star-Glu-IL2 and CSC-Star-Glu-IL3 were found to contain 0.55, 0.60 and 0.52 mmol of SO_3H per gram of catalysts respectively. The most active catalyst CSC-Star-Glu-IL2 was also characterized by XRD, SEM and TEM. XRD patterns of CSC-Star-Glu-IL2 (Fig. S3, see ESI†) showed a broad diffraction peak from $2\theta = 15$–$30°$, C(002), attributed to amorphous carbon sheets oriented in a considerable random fashion. SEM images (Fig. S4, see ESI†) showed the morphology of the catalyst and indicated that the catalyst possesses broad rod like shapes. TEM micrographs (Fig. S5, see ESI†) showed that the sulfonated carbon/silica composite is spherical in shape with ionic liquid coated on the surface of the catalyst (shown by dots on spheres in Fig. S5†).

In order to optimize the ionic liquid used for the preparation of catalysts, we firstly prepare CSC-Star-Glu [(prepared from starch : glucose (3 : 1))] and then coated it with different ionic liquids *viz.* 1-methyl-3-methylimidazolium bromide, [Mmim][Br], 1-ethyl-3-methylimidazolium bromide, [Emim][Br], 1-propyl-3-methylimidazolium bromide, [Pmim][Br], 1-butyl-3-methylimidazolium bromide, [Bmim][Br] and 1-pentyl-3-methylimidazolium bromide, [Pentmim][Br] to prepare different ionic liquid coated catalysts. Then we carried out Knoevenagel condensation taking 4-methoxybenzaldehyde and malononitrile as the test substrates and the results are presented in Table 3, which indicated that out of various ionic liquids, [Bmim][Br] exhibited highest activity. So, we chose [Bmim][Br] for coating sulfonated carbon/silica composites.

Catalyst testing for Knoevenagel condensation of aldehydes and ketones

Knoevenagel condensation was carried out by stirring a mixture of aldehyde or ketone, active methylene compound in the presence of CSC-Star-Glu-IL in water at room temperature (for aldehydes) or 60 °C (for ketones) (Scheme 2). To select the appropriate CSC-Star-Glu-IL, 4-methoxybenzaldehyde and malononitrile were selected as the test substrates and the reaction was carried using CSC-Star-Glu-IL1, CSC-Star-Glu-IL2 and CSC-Star-Glu-IL3 using water as the reaction medium. The results are presented in Table 4, which indicated that out of various catalysts, CSC-Star-Glu-IL2 exhibited highest activity.

This is because, out of these three catalysts, CSC-Star-Glu-IL2 contains 3 equivalent of starch and one equivalent of glucose. Since this catalyst contains maximum amount of amylopectin which will lead to the formation of more number of small polycyclic aromatic rings, providing more anchoring sites for SO_3H groups.[5,43c] Hence, more the number of SO_3H groups, more is the activity of the catalyst. The molar ratio of test substrates was also optimized after carrying out series of reactions. It was found that for 1 mmol of carbonyl compound, 1 mmol of active methylene compound was required. To select the appropriate amount of CSC-Star-Glu-IL2, the reaction with test substrates was carried using different amounts of the catalyst *i.e.* 0.050 g (3 mol% SO_3H), 0.10 g (6 mol% SO_3H), 0.15 g

Table 2 Thermogravimetric analysis[a] representing major weight losses in CSC-Star-Glu-ILs

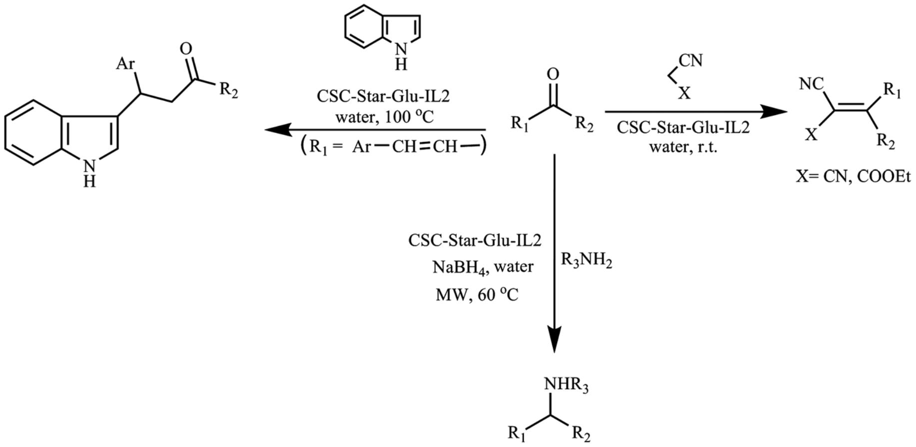
Entry	Catalyst	Loss of organic functionality (°C)
1	CSC-Star-Glu-IL1	245
2	CSC-Star-Glu-IL2	247
3	CSC-Star-Glu-IL3	240

[a] Thermal analysis was carried out on DTG-60 Shimadzu make thermal analyzer at the rate of 10 °C min^{-1}.

Table 3 Effect of coating of different ionic liquids on CSC-Star-Glu (3 : 1) on Knoevenagel condensation[a] in water

Entry	Ionic liquid	Yield[b] (%)
1	[Mmim][Br]	63
2	[Emim][Br]	68
3	[Pmim][Br]	70
4	[Bmim][Br]	95
5	[Pentmim][Br]	95

[a] *Reaction conditions*: 4-methoxybenzaldehyde (1 mmol), malononitrile (1 mmol) and catalyst (0.2 g) at room temperature in water (5 mL) for 0.5 h. [b] Isolated yields.



Scheme 2 CSC-Star-Glu-IL2 catalyzed Knoevenagel condensation of aldehydes and ketones with active methylene compounds, reductive amination of aldehydes and ketones, and Michael addition of indole to α,β-unsaturated ketones.

(9 mol% SO_3H) and 0.2 g (12 mol% SO_3H) and found that best results in terms of reaction time and yield were obtained with 0.2 g of CSC-Star-Glu-IL2. Further, to optimize the reaction temperature, we carried out the reaction with test substrates at room temperature, 60 and 80 °C and found that room temperature was the optimum reaction temperature for aldehydes and 60 °C for ketones (acetophenone as test substrate). Thus, the optimum conditions selected are: aldehyde or ketone (1 mmol), active methylene compound (1 mmol), CSC-Star-Glu-IL2 (0.2 g, 12 mol% SO_3H) and room temperature for aldehydes and 60 °C for ketones. The generality of the developed protocol was demonstrated by using various aldehydes and ketones possessing both electron-releasing and electon-withdrawing groups and excellent results were obtained (Table 5).

Catalyst testing for reductive amination of aldehydes and ketones

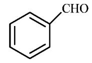
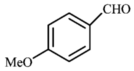
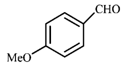
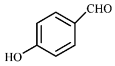
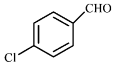
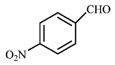
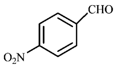
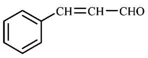
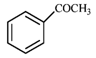
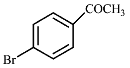
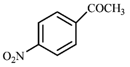
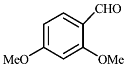
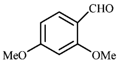
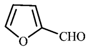
One-pot reductive amination of aldehydes and ketones was carried out by stirring a mixture of carbonyl compound, amine and $NaBH_4$ in the presence of CSC-Star-Glu-IL in water using microwave heating (Scheme 2). To select the appropriate CSC-Star-Glu-IL for reductive amination, 4-methoxybenzaldehyde and aniline were selected as the test substrates and the reaction was carried using CSC-Star-Glu-IL1, CSC-Star-Glu-IL2 and CSC-Star-Glu-IL3 in water. The results are presented in Table 4, which indicated that out of various catalysts, CSC-Star-Glu-IL2 exhibited highest activity. The test reaction was carried out under different set of conditions to select the optimum reaction conditions. First of all, molar ratio of test substrates was optimized. It was found that for 1 mmol of each of 4-methoxybenzaldehyde and aniline, 1.5 mmol of $NaBH_4$ was required. To select the optimum reaction temperature, we carried out the test reaction at different temperatures 60, 80 and 100 °C under stirring on a magnetic stirrer but the reaction did not go to completion even after 20 h at either of these temperatures. Then the reaction with test substrates was carried out in a microwave synthesizer at 60 °C and to our surprise, complete conversion of test substrates took place in just 10 min giving *N*-(4-methoxybenzyl)aniline in 90% isolated yield. To select the appropriate amount of catalyst, the reaction was carried out using different amounts of CSC-Star-Glu-IL2 *i.e.* 0.050 g (3 mol% SO_3H), 0.10 g (6 mol% SO_3H), 0.15 g (9 mol% SO_3H) and 0.2 g (12 mol% SO_3H) and found that best results in terms of reaction time and yield were obtained with 0.2 g of CSC-Star-Glu-IL2. Thus, the optimum conditions selected for the reductive

Table 4 Effect of CSC-Star-Glu-ILs[a] on Knoevenagel condensation[b], reductive amination[c] and Michael addition[d] in water

		Knoevenagel condensation		Reductive amination		Michael addition	
Entry	Catalyst	Time (h)	Yield[e] (%)	Time (min)	Yield[f] (%)	Time (h)	Yield[f] (%)
1	CSC-Star-Glu-IL1	0.5	90	10	85	13	78
2	CSC-Star-Glu-IL2	0.5	95	10	90	13	85
3	CSC-Star-Glu-IL3	0.5	88	10	80	13	75

[a] CSC-Star-Glu-IL1: catalyst prepared using 1 : 1 ratio of starch and glucose; CSC-Star-Glu-IL2: catalyst prepared using 3 : 1 ratio of starch and glucose; CSC-Star-Glu-IL3: catalyst prepared using 1 : 3 ratio of starch and glucose. [b] *Reaction conditions*: 4-methoxybenzaldehyde (1 mmol), malononitrile (1 mmol) and CSC-Star-Glu-IL (0.2 g)at room temperature in water (5 mL) for 0.5 h. [c] *Reaction conditions*: aldehyde or ketone (1 mmol), primary amine (1 mmol), CSC-Star-Glu-IL (0.2 g) in water (5 mL) at 60 °C in microwave synthesizer. [d] *Reaction conditions*: α,β-unsaturated ketone (1 mmol), indole (1.2 mmol), CSC-Star-Glu-IL (0.2 g) at 100 °C in water (7 mL). [e] Isolated yields. [f] Column chromatographic yields.

Table 5 CSC-Star-Glu-IL2 catalyzed Knoevenagel condensation of aldehydes and ketones in water[a]

Entry	Aldehyde/ketone	X	Time (h)	Yield[b] (%)	m.p./lit. m.p. (°C)
1		CN	2	94	82–84/82–84 (ref. 12)
2		CN	0.5	95	112–114/113–114 (ref. 11)
3		COOEt	1	86 (*E* isomer)	82–84/85 (ref. 11)
4		CN	1	94	188–190/187–188 (ref. 12)
5		CN	1.5	88	158–160/161–163 (ref. 12)
6		CN	0.5	90	157–160/159–160 (ref. 12)
7		COOEt	1	88 (*E* isomer)	128–130/129–131 (ref. 12)
8		CN	1	93	124–126/126 (ref. 11)
9		CN	2	85	90–91/92 (ref. 12)
10		COOEt	5	84 (*E* isomer)	83–85/84 (ref. 12)
11		COOEt	4	85 (*E* isomer)	140–143/144 (ref. 12)
12		COOEt	2	88 (*E* isomer)	135–138/138–140 (ref. 11)
13		CN	1.5	90	132–135/134–136 (ref. 11)
14		COOEt	1	88 (*E* isomer)	82–83/82–83 (ref. 22)
15	C_3H_7CHO	COOEt	5	85 (*E* isomer)	108-110[c]/109–111 (ref. 47)

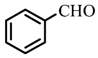
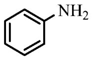
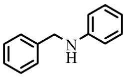
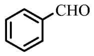
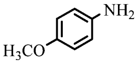
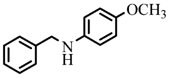
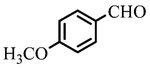
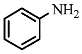
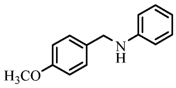
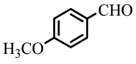
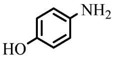
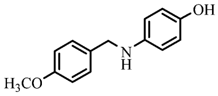
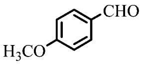
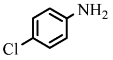
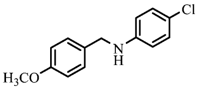
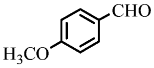
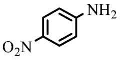
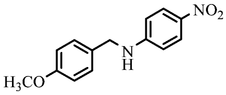
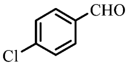
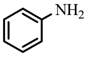
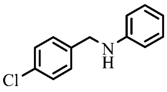
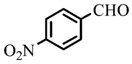
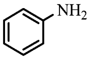
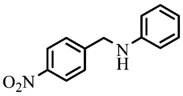
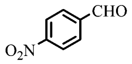
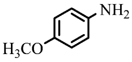
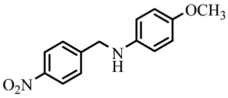
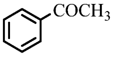
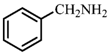
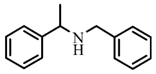
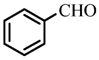
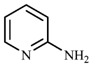
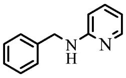
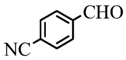
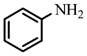
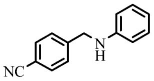
[a] *Reaction conditions*: aldehyde or ketone (1 mmol), active methylene compound (1 mmol), CSC-Star-Glu-IL2 (0.2 g, 12 mol% SO_3H) in water (5 mL) at room temperature for aldehydes and at 60 °C for ketones in water (5 mL). [b] Isolated yields. [c] Boiling point.

amination are: aldehyde (1 mmol), amine (1 mmol), $NaBH_4$ (1.5 mmol), CSC-Star-Glu-IL2 (0.2 g, 12 mol% SO_3H) in water (5 mL) under microwave heating at 60 °C. To demonstrate the generality of the developed protocol, various aldehydes and ketones possessing both electron-releasing and electron-withdrawing groups were chosen and excellent results were obtained (Table 6).

Catalyst testing for the Michael addition of indole to α,β-unsaturated ketones

Michael addition was carried out by stirring a mixture of α,β-unsaturated ketone and indole in the presence of CSC-Star-Glu-IL in water (Scheme 2). Again CSC-Star-Glu-IL2 was found to be the best catalyst for the Michael addition of indole (1.2 mmol) to 3-(4-methylphenyl)-1-phenylpropenone (1 mmol) (Table 4). Further, 0.2 g (12 mol% SO_3H) of CSC-Star-Glu-IL2 gave the best results in terms of reaction time and yield. To optimize the reaction temperature, the Michael addition was carried at 50, 80 and 100 °C using water as the reaction medium and found that 100 °C was the optimum reaction temperature. Thus, the optimum conditions selected are: α,β-unsaturated ketone (1 mmol), indole (1.2 mmol), CSC-Star-Glu-IL 0.2 g (12 mol% SO_3H), water (7 mL) and 100 °C was selected as the reaction temperature. To demonstrate the generality of the developed protocol, various α,β-unsaturated ketones possessing both electron-releasing and electron-withdrawing groups were chosen and excellent results were obtained (Table 7).

Table 6 CSC-Star-Glu-IL2 catalyzed reductive amination of aldehydes and ketones[a] in water using MW heating at 60 °C

Entry	Carbonyl compound	Amine	Product	Yield[b] (%)	m.p./lit. m.p. (°C)
1				96	36–37/35.5–37.8 (ref. 44)
2				86	47–48/48.6–48.9 (ref. 34)
3				90	47–48/48–49 (ref. 44)
4				88	100–101/102–103 (ref. 44)
5				90	76–77/78–81 (ref. 44)
6				86	140–141/140–141 (ref. 34)
7				93	209–211[c]/210–211 (ref. 44)
8				95	66–67/67–68 (ref. 44)
9				85	95–96/97.7–97.9 (ref. 34)
10				90	176–177[c]/179–181 (ref. 44)
11				85	Oil/oil (ref. 48)
12				90	Oil/oil (ref. 49)
13	C_3H_7CHO	$(C_2H_5)_2NH$	$C_3H_7CH_2N(C_2H_5)_2$	88	Oil/oil (ref. 49)

[a] *Reaction conditions*: aldehyde or ketone (1 mmol), primary amine (1 mmol), CSC-Star-Glu-IL2 (0.2 g, 12 mol% SO_3H) in water (5 mL) using MW heating at 60 °C for 10 min. [b] Column chromatographic yields. [c] Hydrochloride salt of amine.

Since the products are solids and insoluble in water, the effect of reaction time on yield of the products is required to be studied because the catalyst was also solid and exist with the product as the reaction progresses. To study this, the reaction mixture in case of entry 1 (Tables 5–7) was stirred under the reaction conditions for different periods of time *i.e.* upto 2 h for Knoevenagel condensation, 10 min for reductive amination and 16 h for Michael addition. In Knoevenagel condensation, initially, there was a sharp increase in yield up to 0.5 h *i.e.* 45%, then yield goes to 85% in 1.5 h until the reaction goes to completion in 2 h (Fig. 1a). In case of reductive amination, again sharp increase in yield was observed up to 2 min *i.e.* 40%, then up to 8 min yield goes to 88% till the reaction goes to completion in 10 min (Fig. 1b). In case of Michael addition, from 4 to 12 h (Fig. 1b) there is again sharp increase in yield and at 12 h, the yield of product reached its maximum level *i.e.* 83% and no further enhancement in yield was observed if the reaction was allowed to occur for longer reaction time.

Table 7 CSC-Star-Glu-IL2 catalyzed Michael addition of indole to α,β-unsaturated ketones at 100 °C in water[a]

Entry	Ar	R_2	Time (h)	Yield[b] (%)	m.p./lit. m.p. (°C)
1	C_6H_5	C_6H_5	12	83	126–127/127–128 (ref. 46)
2	$4\text{-}(OCH_3)C_6H_4$	C_6H_5	12.5	80	122–123/124–125 (ref. 45)
3	$4\text{-}(CH_3)C_6H_4$	C_6H_5	13	85	129–130/130–131 (ref. 46)
4	$4\text{-}(CH_3)C_6H_4$	$4\text{-}ClC_6H_4$	13	78	146–147/146–149 (ref. 46)
5	$4\text{-}ClC_6H_4$	C_6H_5	13.5	75	126–127/127–128 (ref. 46)

[a] *Reaction conditions*: α,β-unsaturated ketone (1 mmol), indole (1.2 mmol), CSC-Star-Glu-IL2 (0.2 g, 12 mol% SO_3H) at 100 °C in water (7 mL). [b] Column chromatographic yields.

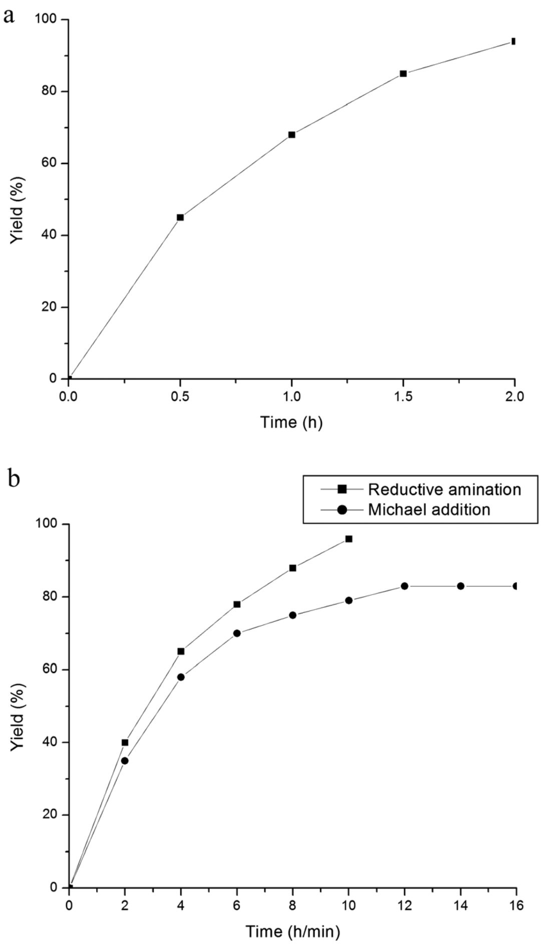


Fig. 1 (a) Effect of reaction time on the yield of products for Knoevenagel condensation (entry 1, Table 4). (b) Effect of reaction time on the yield of products for reductive amination and Michael addition (entry 1, Table 5 and Table 6).

Comparison of activity of CSC-Star-Glu-IL2 with CSC-Star-Glu (3 : 1) in water

We carried out Knoevenagel condensation (using 4-methoxybenzaldehyde and malononitrile as test substrates), reductive amination (4-methoxybenzaldehyde and aniline as test substrates) and Michael addition (indole and 3-(4-methylphenyl)-1-phenylpropenone as test substrates) with CSC-Star-Glu (3 : 1) in different solvents and found that lower yields of products were obtained in case of water as a solvent. To our surprise, a great improvement on the yield of products were obtained when CSC-Star-Glu (3 : 1) coated with ionic liquid *i.e.* CSC-Star-Glu-IL2 was used as catalyst to carry out the similar reactions in water. The results are presented in Fig. 2.

Finally, to examine the effect of ionic liquid loading on CSC-Star-Glu (3 : 1), we prepared catalysts with different loadings of ionic liquid and found that excellent yields in case of test substrates for Knoevenagel condensation, reductive amination and Michael addition were obtained when 50 wt% of ionic liquid was loaded on CSC-Star-Glu (3 : 1). The results are presented in Fig. 3.

Recyclability

Recyclability of CSC-Star-Glu-IL2 was investigated in case of entry 2 (Table 5), entry 5 (Table 6) and entry 3 (Table 7). The catalyst was separated by filtration after completion of the reaction and again used for subsequent reactions after adding fresh substrates under similar conditions for five consecutive runs (Fig. 4). It was found that catalyst could be recycled for five consecutive runs without loss of significant activity. The elemental analysis and FTIR of the CSC-Star-Glu-IL2 after 5th run indicated negligible change in the sulfur content and coating of ionic liquid respectively. The slight loss of activity may be due to the microscopic changes on the surface of the catalyst.

Heterogeneity

In order to rule out the possibility of leaching of ionic liquid film from the surface of the catalyst, we carried out the hot

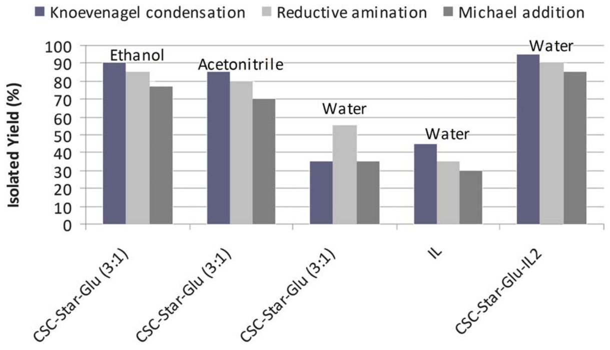


Fig. 2 Comparison of activity of CSC-Star-Glu-IL2 with CSC-Star-Glu for Knoevenagel condensation (Table 4, entry 2), reductive amination of aldehydes and ketones (Table 5, entry 3) and for Michael addition of indole to α,β-unsaturated ketones (Table 6, entry 3) in different solvents.

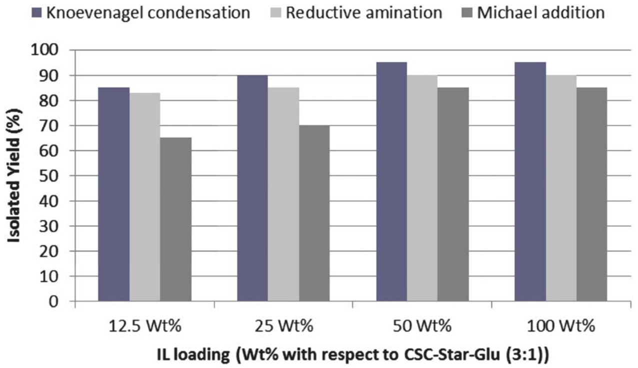


Fig. 3 Effect of ionic liquid loading on the activity of CSC-Star-Glu-IL2 for Knoevenagel condensation (Table 4, entry 2), reductive amination of aldehydes and ketones (Table 5, entry 3) and Michael addition of indole to α,β-unsaturated ketones (Table 6, entry 3) in water.

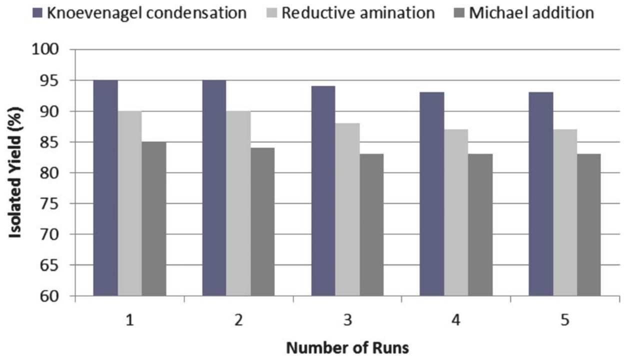


Fig. 4 Recyclability of CSC-Star-Glu-IL2 for Knoevenagel condensation (Table 4, entry 2), reductive amination of aldehydes and ketones (Table 5, entry 3) and Michael addition of indole to α,β-unsaturated ketones (Table 6, entry 3) in water.

filtration test. The reaction in case of entry 1 (Table 5) has been carried out in the presence of CSC-Star-Glu-IL2, until the conversion was 45% (0.5 h) and at that point, CSC-Star-Glu-IL2 was filtered off at the reaction temperature. The liquid phase was then transferred to another flask and allowed to react, but no further significant conversion was observed. Moreover, the elemental analysis and FTIR of the used CSC-Star-Glu-IL2 indicated negligible change in the sulfur content and coating of ionic liquid respectively. So, we conclude that there is no significant leaching of ionic liquid from the surface of the catalyst.

Experimental section

General remarks

The chemicals used were purchased from Aldrich chemical company and Merck. The products were characterized by their spectral data and comparison of their physical data with those of known samples. The ^{1}H NMR data were recorded in $CDCl_3$ or $CDCl_3$+DMSO-d_6 on Bruker DPX 200 (200 MHz) spectrometer using TMS as an internal standard. The FTIR spectra were recorded on Perkin-Elmer FTIR spectrophotometer using KBr windows and mass spectral data were recorded on Bruker Esquires 3000 (ESI). XRD diffraction patterns were determined on Bruker AXSD8 X-ray diffraction spectrometer and SEM using Jeol make T-300 Scanning electron Microscope. Transmission Electron Micrographs (TEM) were recorded on H7500 Hitachi. The amount of sulfur in composites was determined by elemental analysis on Elementar Analysensyteme GmbH Vari-oEL. Thermal analysis was carried out on DTG-60 Shimadzu make thermal analyzer. Microwave synthesizer manufactured by CEM (DISCOVER SYSTEM) was used for carrying out the reductive amination of aldehydes and ketones.

General procedure for the synthesis of CSC-Star-Glu-ILs

Sulfonated carbon/silica composites were prepared according to the method already reported,[5] except that instead of taking natural organic compounds, a mixture of starch and glucose in three different ratios 1 : 1, 3 : 1 and 1 : 3 respectively was taken. In the second step, the CSC-Star-Glu composite (1 g) was added to a solution of 1-butyl-3-methyl imidazolium bromide (0.5 g) in acetonitrile (8 mL) in a round bottom flask (25 mL). The solution was then stirred at room temperature for 30 minutes followed by removal of acetonitrile in a rotary evaporator at 50 °C. Finally, the solid obtained was dried under vacuum for 30 minutes to get a free flowing white powder (50 wt% of IL was loaded on CSC-Star-Glu).

General procedure for Knoevenagel condensation of aldehydes and ketones

To a mixture of aldehyde or ketone (1 mmol), active methylene compound (1 mmol) in a round-bottom flask (25 mL), CSC-Star-Glu-IL2 (0.2 g, 12 mol% SO_3H) was added and the reaction mixture was stirred at room temperature (for aldehydes) or 60 °C (for ketones) in water (5 mL) for an appropriate time (Table 5). After completion of the reaction (monitored by TLC), the reaction mixture was extracted with hot EtOAc (2 × 5 mL). The product was obtained after removal of the solvent under reduced pressure.

The geometry of Knoevenagel products may be *E* or *Z*. It is well known that the *E* and *Z* isomers can be distinguished by ^{1}H NMR spectral characteristics. When ethyl cyanoacetate was used as the active methylene compound, the reaction is highly stereoselective with only formation of *E*-isomer (Table 5). The assignment of stereochemistry of the isomer formed was made on the basis of chemical shift of vinylic (CH=C) protons which migrated to lower field (higher δ values) for the *E* isomers (when CH=C protons are *cis* to the ester group).[11,22,43d–43f] Thus, from the ^{1}H NMR data which is in coincidence with the data already reported,[11,22,43d–43f] it is confirmed that the products obtained are *E*-isomers, when ethyl cyanoacetate was used as the active methylene compound.

General procedure for reductive amination of aldehydes and ketones

To a mixture of aldehyde or ketone (1 mmol), amine (1 mmol), $NaBH_4$ (1.5 mmol) and CSC-Star-Glu-IL2 (0.2 g, 12 mol% SO_3H)

in a round-bottom flask (25 mL), water (5 mL) was added and reaction mixture was stirred at 60 °C in a microwave synthesizer for 10 min (Table 6). After completion of the reaction (monitored by TLC), the reaction mixture was extracted with hot ethyl acetate (2 × 5 mL). The organic layer was washed with water and dried over anhyd. Na_2SO_4. The product was obtained after removing the solvent under reduced pressure followed by passing through column of silica gel and elution with EtOAc : pet. ether (2 : 1).

General procedure for Michael addition of indole to α,β-unsaturated ketone

To a mixture of indole (1.2 mmol), α,β-unsaturated ketone (1 mmol) in a round-bottom flask (25 mL) and CSC-Star-Glu-IL2 (0.2 g, 12 mol% SO_3H), water (7 mL) was added and reaction mixture was stirred at 100 °C for an appropriate time (Table 7). After completion of the reaction (monitored by TLC), the reaction mixture was extracted with hot ethyl acetate (2 × 5 mL). The organic layer was washed with water and dried over anhyd. Na_2SO_4. Finally, the product was obtained after removal of the solvent under reduced pressure followed by passing through column of silica gel and elution with EtOAc : pet. ether (1 : 6).

The catalyst was dried in a vacuum desiccator for 1 h and reused in the next run.

The structures of the products were confirmed by IR, ^{1}H NMR, mass spectral data and comparison with authentic samples available commercially or prepared according to the literature methods.

Spectroscopic data of some selected compounds

Ethyl-(*E*)-2-cyano-3-(4′-methoxyphenyl)prop-2-enoate (Table 5, entry 3). IR (υ_{max} in cm^{-1}, KBr): 2227 (str.), 1595 (C=C str.) ^{1}H NMR ($CDCl_3$): δ 1.40 (t, J = 7 Hz, 3H, CH_2CH_3), 3.88 (s, 3H, OCH_3), 4.23–4.47 (q, J = 7 Hz, 2H, CH_2CH_3), 7.05 (d, J = 7 Hz, 2H, Ar-H), 7.94 (d, J = 7 Hz, 2H, Ar-H), 8.31 (s, 1H, CH). MS (ESI): 243 (M$^+$), 266 (M$^+$ + 23).

Ethyl-(*E*)-2-cyano-3-(2′,4′-dimethoxyphenyl)prop-2-enoate (Table 5, entry 12). IR (υ_{max} in cm^{-1}, KBr): 2221 (str.), 1540 (C=C str.) ^{1}H NMR ($CDCl_3$): δ 1.35–1.39 (t, J = 8 Hz, 3H, CH_2CH_3), 3.91 (s, 3H, OCH_3), 4.32–4.37 (q, J = 8 Hz, 2H, CH_2CH_3), 6.47 (s, 1H, Ar-H), 6.70 (d, J = 8 Hz, 2H, Ar-H), 8.43 (d, J = 8 Hz, 2H, Ar-H), 8.71 (s, 1H, CH). MS (ESI): 261.9 (M$^+$).

***N*-(4-Methoxybenzyl)aniline (Table 6, entry 3).** IR (υ_{max} in cm^{-1}, KBr): 3410 (N–H str.), 1597 (C=C str.). ^{1}H NMR ($CDCl_3$): δ 3.82 (s, 3H, OCH_3), 4.23 (bs, 1H, NH), 4.25 (s, 2H, CH_2), 6.15–7.30 (m, 9H, Ar-H). MS (ESI): 213 (M$^+$), 192.

***N*-(4-Methoxybenzyl)-4-chloroaniline (Table 6, entry 5).** IR (υ_{max} in cm^{-1}, KBr): 3409 (N–H str.), 1602 (C=C str.) ^{1}H NMR ($CDCl_3$): δ 3.87 (s, 3H, OCH_3), 3.94 (bs, 1H, NH), 4.22 (s, 2H, CH_2), 6.55 (d, J = 9.06 Hz, 2H, Ar-H), 6.84 (d, J = 9.06 Hz, 2H, Ar-H), 7.06 (d, J = 9.06 Hz, 2H, Ar-H), 7.27 (d, J = 8.30 Hz, 2H, Ar-H). MS (ESI): 247 (M$^+$), 249 (M$^+$ + 2).

3-(3-Indolyl)-1-(4-chlorophenyl)-3-(4-methylphenyl)propan-1-one (Table 7, entry 4). IR (υ_{max} in cm^{-1}, KBr): 3280 (N–H str.), 1720 (C=O str.). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.25 (s, 3H, CH_3), 3.79 (d, J = 7.6 Hz, 2H, CH_2), 4.95 (t, J = 7.6 Hz, 1H, CH), 6.84–8.0 (m, 13H, Ar-H), 8.10 (bs, 1H, NH). MS (ESI): 373 (M$^+$).

Conclusions

We have developed a novel catalytic system derived from amorphous carbon/silica composites and ionic liquid for carrying out Knoevenagel condensation, reductive amination and Michael addition in water. The catalyst allows reactions to be carried out in the most benign of reaction media and avoids most of the problems normally associated with the use of ionic liquids. The catalyst can be easily recycled without loss of activity. Simplicity of operation and the environmentally benign and legislatively robust nature of reaction conditions are the main advantages of the developed protocols.

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Sulfonated carbon/nano-metal oxide composites: a novel and recyclable solid acid catalyst for organic synthesis in benign reaction media†

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Novel sulfonated carbon/nano-metal oxide composites were successfully synthesized by the partial carbonization of starch in the presence of different nano-metal oxides (nano-titania, nano-ceria and nano-zirconia) followed by sulfonation. The catalytic activity of the prepared catalysts was evaluated for the one-pot synthesis of gem-bisamides, bis(heterocyclyl)methanes and for the one-pot three component synthesis of β-aminocarbonyl compounds *via* Mannich reaction. Different nano-metal oxides have been investigated as support materials, with a view to select the most active solid acid catalyst. Among the various catalysts, sulfonated carbon/nano-titania composite (C/TiO_2–SO_3H) was found to be the most active and selective, and could be recycled several times without significant loss of activity. All the catalysts were characterized by FTIR and CHNS analysis, and the most active catalyst was further characterized by XRD, SEM, TEM, HRTEM, EDX and TGA.

Introduction

Homogeneous acid catalysts such as Lewis and Bronsted acids represent an important class of catalysts that are commonly employed in the large-scale synthesis of industrial bulk chemicals as well as in the production of fine chemicals.[1] The electrophilic activation of a substrate by means of a Bronsted acid is, undoubtedly, the most straightforward and a common approach used to promote a chemical reaction, so Bronsted acids have been widely utilized as efficient catalysts for numerous organic transformations.[2] However, a restriction on the use of these homogeneous catalysts in industry is their difficulty in separation, high volatility, toxicity, waste generation and limited solubility/phase contact with the starting materials. Using the eco-friendly reusable heterogeneous solid acids instead of conventional, toxic and polluting homogeneous acid catalysts, is thus strongly recommended from the view point of "Green chemistry".[3] To successfully obtain a highly active heterogeneous catalyst, a rational choice is immobilization of homogeneous catalyst on a suitable insoluble support material. Recently, carbon based materials have been attracting attention as potential supports in heterogeneous catalysis.[4] Their high surface area ensures a high density of catalytic active sites when used as catalysts and catalyst supports. Because of their unique properties, such as resistance to acidic and basic conditions, good electric conductivity, tunability of surface chemistry, stability against various chemical environments and low cost, carbon based catalysts find wide applications in organic syntheses and in industrial manufacturing of materials.[5–12] Recently, it was found that carbon materials when dispersed over inorganic supports leads to organic/inorganic hybrid composites with more stability, activity and selectivity.[13,14] Among the various sulfonated carbon/inorganic support composites prepared so far, silica derived composites have been extensively studied, whereas composites derived from other inorganic support materials especially metal oxides like titania, ceria, zirconia *etc.* have been poorly explored.[15] Metal oxides are of high importance as catalyst supports in heterogeneous catalysis because of their interesting acid–base and redox properties, high chemical stability and being commercially available and non-toxic.[16] In this context, metal oxides can be efficiently utilized for the development of novel sulfonated organic/inorganic hybrid materials, thereby showing the synergistic effect of the composite on catalytic performance of the novel solid acid catalyst.

Amide and bisamide functionalized moieties represent important biological and medicinal scaffolds. Further, symmetrical and unsymmetrical *N*,*N*′-alkylidene bisamides and their derivatives are found as key structural subunits for the construction of peptidomimetic frameworks.[17] The preparation of symmetrical *N*,*N*′-alkylidene bisamides is an important organic transformation and several methods have been reported in literature for their synthesis.[18–21]

Bis(heterocyclyl)methanes represent an important class of compounds that constitute the building blocks of natural and

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† Electronic supplementary information (ESI) available: FTIR, XRD, particle size histograms, EDX, TGA, spectral details of all the products listed in Tables 5–7 and copies of spectras of ^1H, D_2O, ^{13}C and DEPT of selected products. See DOI: 10.1039/c5nj00607d

unnatural porphyrins.[22] These occur widely in various natural products and show versatile biological and pharmacological activities.[23–25] Synthetic strategies mediated through protic acids[26] and Lewis acids,[27] ionic liquids,[28] ion exchange resins[29] and rare earth metals[30] have been reported in the literature for the preparation of bis(heterocyclyl)methanes.

Mannich reaction, one of the most important carbon–carbon bond forming reactions has been enormously used for the preparation of secondary and tertiary amine derivatives.[31] These reactions provide synthetically and biologically important β-amino carbonyl compounds, which are important intermediates for the construction of various nitrogen-containing natural products and pharmaceuticals.[32] Mannich reaction of aromatic ketones, aromatic aldehydes and aromatic amines has been reported to be catalyzed by various Lewis and Bronsted acid catalysts.[33–44]

Most of the methods reported for the synthesis of gem-bisamides, bis(heterocyclyl)methanes and β-aminocarbonyl compounds suffer from drawbacks such as the use of corrosive reagent, expensive and large amount of catalyst, long reaction time, harmful reaction media, and low yields. Therefore, there is still a demand for the development of greener synthetic protocol for the synthesis of gem-bisamides, bis(heterocyclyl)-methanes and β-amino carbonyl compounds under mild conditions using inexpensive catalysts.

In the present work, we report the synthesis of novel sulfonated carbon/nano-metal oxide composites derived from inexpensive and renewable biomaterial, starch as carbon source and commercially available, non-toxic nano-metal oxides as inorganic support. The carbon material used provides high surface area for sulfonation and the inorganic support used provides thermal and mechanical stability to the composites formed. The catalytic activity of sulfonated carbon/nano-metal oxide composites was evaluated for the one-pot synthesis of gem-bisamides, bis(heterocyclyl)methanes and for one-pot three component Mannich reaction.

Results and discussion

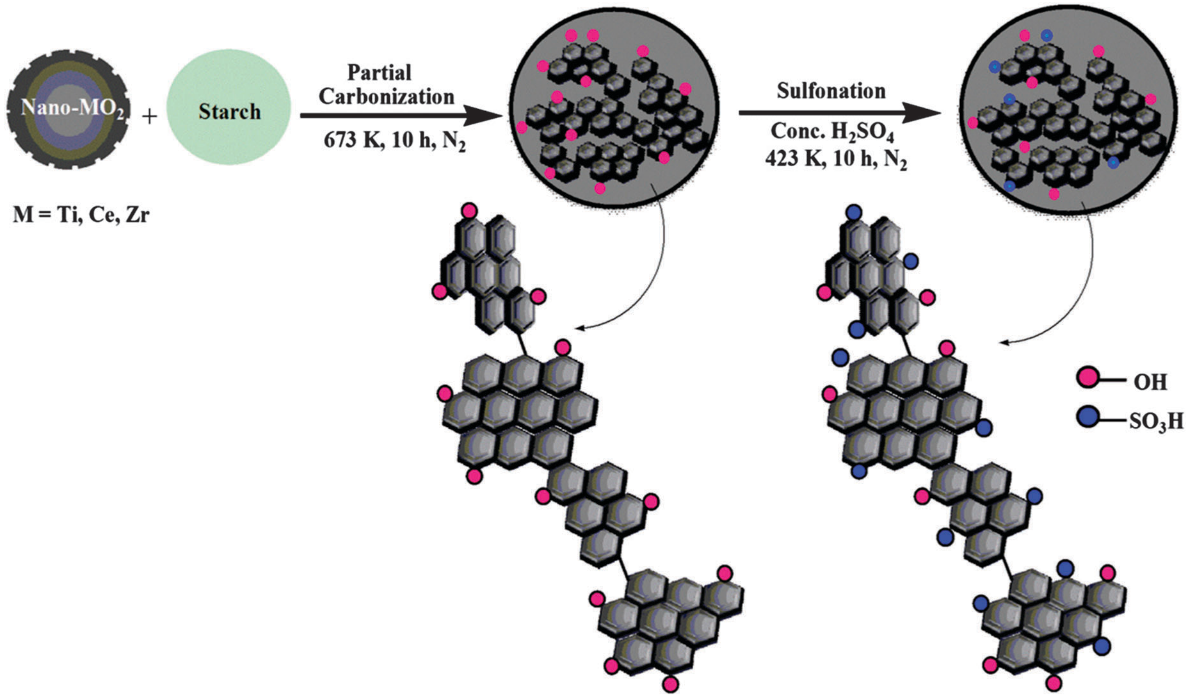
Characterization of sulfonated carbon/nano-metal oxide composites

Sulfonated carbon/nano-metal oxide composites have been prepared by the incomplete carbonization of starch in the presence of different inorganic supports like nano-titania, nano-ceria and nano-zirconia to form carbon/nano-titania (C/TiO_2), carbon/nano-ceria (C/CeO_2) and carbon/nano-zirconia (C/ZrO_2) composites respectively, which on sulfonation with conc. sulfuric acid gave corresponding sulfonated carbon/nano-metal oxide composites. We have used starch as a cheaper and green carbon precursor alternative to the commonly used high cost resins,[45] ionic surfactants[46] and triblock co-polymers.[47] Starch molecule has more hydroxyl groups and the amount of amylopectin ratio present in starch is important for the formation of small polycyclic aromatic rings that provide anchoring sites for $-SO_3H$ groups. It has been reported that the carbonization temperature has great effect on the catalytic activity of final sulfonic acid catalyst due to the pore structure and surface acid groups.[48] The carbon catalysts prepared under lower temperature carbonization process show better catalytic performance due to the smaller size of carbon sheets and hence availability of more surface active sites for the grafting of sulfonic groups. Whereas with increasing carbonization temperature, carbon materials become harder and the flexibility of the polycyclic aromatic carbon decreases through plane growth and carbon sheet stacking.[49] In consideration with these facts, the partial carbonization has been done at 673 K to get higher sulfonic acid densities in the final catalyst.

The partial carbonization of starch leads to pyrolysis followed by dehydration and dissociation of C–O–C linkages thereby leading to the formation of polycyclic aromatic carbon rings with surface hydroxyl groups. The presence of these groups provide anchoring sites to sulfonic acid groups during the sulfonation step. The general procedure for the synthesis of sulfonated carbon/nano-metal oxide composites is represented in Scheme 1. The characterization of the sulfonated carbon/nano-metal oxide composites thus prepared ($C/TiO_2–SO_3H$, $C/CeO_2–SO_3H$ and $C/ZrO_2–SO_3H$) was carried out with FTIR and CHNS analysis. The most active catalyst $C/TiO_2–SO_3H$ was further characterized by XRD, SEM, TEM, HRTEM, EDX and TGA.

The FTIR spectra of the sulfonated carbon/nano-metal oxide composites exhibited a strong and broad band in the range 3100–3400 cm^{-1} attributed to phenolic –OH groups present in the polycyclic aromatic rings. Further, bands in the range 1700–1720 cm^{-1} and 1580–1620 cm^{-1} were assigned to C=O groups and aromatic C=C stretching modes respectively. The C=O groups were produced by the oxidation of carbon by small amounts of sulfuric acid used for sulfonation. The absorption bands in the range 1210–1230 cm^{-1} and 1030–1040 cm^{-1} were due to asymmetric and symmetric stretching modes of SO_2 group indicating the successful incorporation of SO_3H groups into the carbon framework. The presence of a well defined band at 654 cm^{-1} in the spectra of $C/TiO_2–SO_3H$ is attributed to Ti–O stretching frequency characteristic of TiO_2 (ESI,† Fig. S1). The characteristic absorption bands of different composites prepared are presented in Table 1.

The sulfur content of different composites was determined by CHNS analysis and it was found that $C/TiO_2–SO_3H$ contained 1.2 wt%, $C/CeO_2–SO_3H$ contained 0.58 wt% and $C/ZrO_2–SO_3H$ contained 0.89 wt% of sulfur, equivalent to SO_3H loading of 0.32, 0.18, 0.28 mmol per g of the catalyst. The acid densities and the amount of C, H and S present in all the three catalysts is presented in Table 2 as determined by elemental analysis. Among the three solid acids, $C/TiO_2–SO_3H$ exhibited the highest SO_3H density. The most active sulfonated carbon/nano-titania composite ($C/TiO_2–SO_3H$) was further characterized by XRD, SEM, TEM, HRTEM, EDX and TGA. The presence of titania nanoparticles in the sulfonated carbon/nano-titania composites was confirmed by XRD data (ESI,† Fig. S2). The XRD pattern exhibited well defined sharp peaks that can be indexed to the presence of crystalline titania nanoparticles in anatase phase.[50] The diffraction peaks at 25.5°, 36.3°, 48.2° and 54.4° could be ascribed to characteristic reflections from (101), (004), (200)



Scheme 1 General procedure for the synthesis of sulfonated carbon/nano-metal oxide composites.

Table 1 Major absorption frequencies in FTIR[a] (ν_{max} in cm^{-1}) of sulfonated carbon/nano-metal oxide composites

				SO$_2$ stretch		
Entry	Catalyst	Phenolic–OH	C=C	Asym.	Sym.	M–O
1	C/TiO$_2$–SO$_3$H	3394	1614	1224	1035	654
2	C/CeO$_2$–SO$_3$H	3161	1587	1211	1037	693
3	C/ZrO$_2$–SO$_3$H	3240	1620	1230	1030	750

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

Table 2 Acid densities and amount of C, H and S present in sulfonated carbon/nano-metal oxide composites

Entry	Catalyst	–SO$_3$H[a] (mmol g^{-1})	S[a] (wt%)	C[a] (wt%)	H[a] (wt%)
1	C/TiO$_2$–SO$_3$H	0.32	1.2	19.6	1.5
2	C/CeO$_2$–SO$_3$H	0.18	0.58	20.1	1.7
3	C/ZrO$_2$–SO$_3$H	0.28	0.89	18.2	1.2

[a] Determined by elemental analysis.

and (211) planes of tetragonal TiO$_2$ respectively. An additional broad peak between 2θ = 20–30° attributed to the presence of amorphous carbon was also observed.[51] The average crystallite size of nano-titania as determined by the Debye Scherrer equation, was found to be 17 nm. The surface morphology of the catalyst was studied using the SEM analysis. The SEM micrographs showed the presence of aggregates of particles with somewhat spherical morphology.

A marked tendency to form large clusters was observed along with a slight roughening of the catalyst surface depicting the amorphous nature of composite material formed. A typical SEM image of the prepared catalyst is shown in Fig. 1a and b. The morphology and fine structure of sulfonated carbon/nano-titania composites was examined by TEM (Fig. 1c and d) and HRTEM analysis (Fig. 1e and f). The TEM image of the catalyst exhibited the presence of spherical particles as were observed in SEM micrographs also. The amorphous carbon appears as semitransparent background and the dark spots overlapping it represent the titania nano-particles, thereby the spherical particles as a whole depict the presence of composites. The TEM image provided the average size of composites as the titania nano-particles are not well resolved in the micrographs. A high resolution TEM image however, provided a clear idea about average particle size of titania nanoparticles. The average size of the composites as determined from TEM was found to be 60–65 nm (ESI,† Fig. S3 for particle size distribution histogram) and those of titania nanoparticles from HRTEM was found to be 25–27 nm (ESI,† Fig. S4 for particle size distribution histogram) which is somehow greater than that obtained from XRD data. It might be due to the agglomeration of one or more crystallites leading to an increase in particle size as determined from HRTEM. The HRTEM image showed clear lattice fringes with interplanar spacing of 3.3 Å corresponding to the (101) plane of anatase TiO$_2$.[50] The reused catalyst was further examined after 5th run by TEM analysis and as is clear from the TEM images, there is insignificant change in the structure of the catalyst, thereby showing the stability of the catalyst even after subsequent reaction cycles (ESI,† Fig. S5). The components of C/TiO$_2$–SO$_3$H were also analysed by using energy dispersive spectroscopy (EDX) which confirmed the presence of Ti in addition to C, O and S in the catalyst (ESI,† Fig. S6). To examine the thermal stability of C/TiO$_2$–SO$_3$H, thermal gravimetric analysis

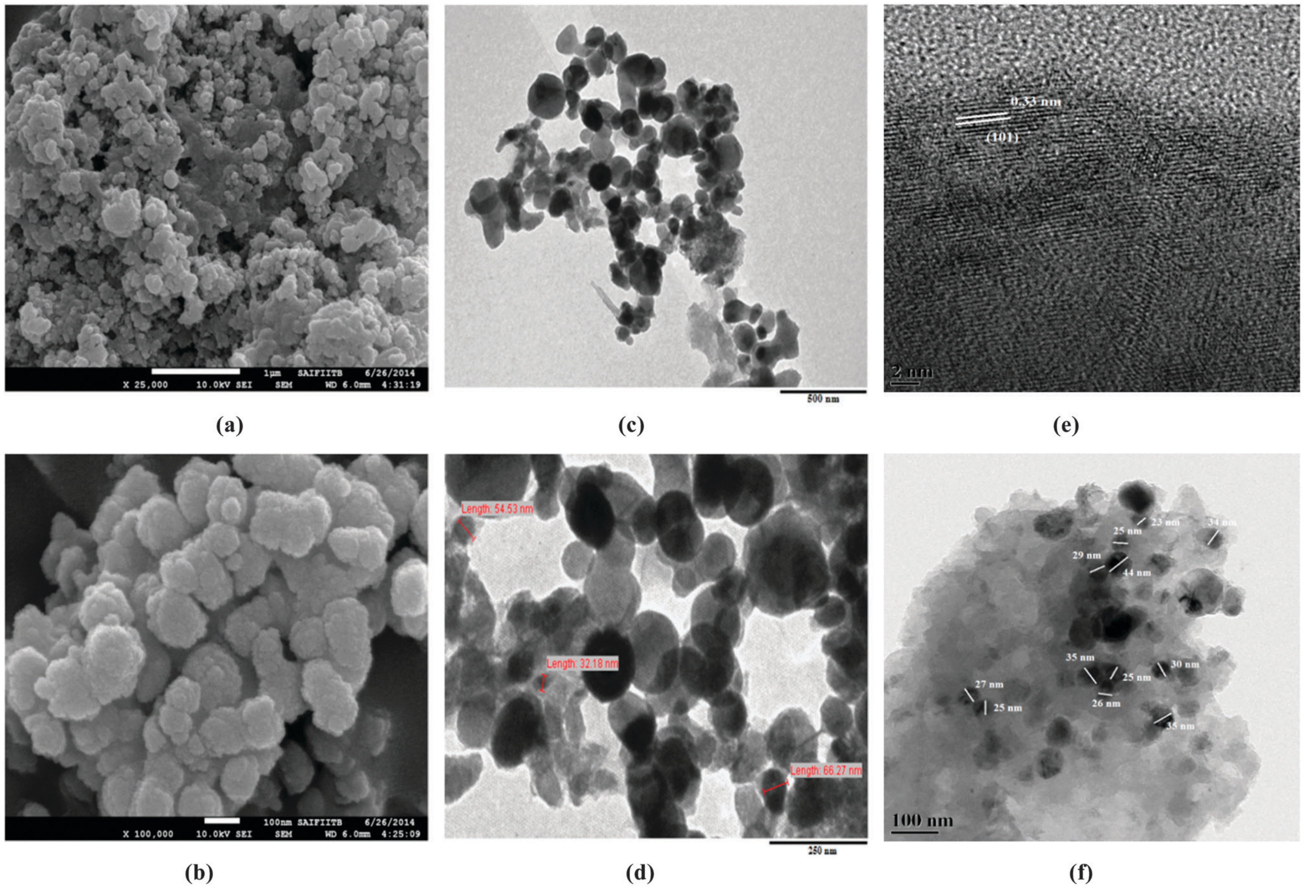


Fig. 1 SEM (a and b), TEM (c and d) and HRTEM (e and f) images of sulfonated carbon/nano-titania composite (C/TiO_2–SO_3H).

was carried out in the temperature range of 40–700 °C in a static atmosphere of nitrogen (ESI,† Fig. S7). The TGA analysis of C/TiO_2–SO_3H showed a weight loss below 100 °C that was attributable to the loss of adsorbed solvent or trapped water from the catalyst.

Further weight loss from 240–700 °C was due to the loss of organic functionality. Thus, from the TGA analysis, it can be concluded that the catalyst is stable upto 240 °C, confirming that it could be safely used in organic reactions below 240 °C.

Catalytic testing for the one-pot synthesis of symmetrical gem-bisamides

Our initial efforts were focused on finding the most effective catalyst among the various sulfonated carbon/nano-metal oxide composites. In order to screen the catalysts, the reaction of benzamide and 4-methylbenzaldehyde was taken as a model reaction under solvent-free conditions at 100 °C. It was found that among various composites, sulfonated carbon/nano-titania composites (C/TiO_2–SO_3H) efficiently catalyzed the synthesis of symmetrical gem-bisamides both in terms of reaction time and yield. The results are summarized in Table 3. Further, in order to optimize the amount of catalyst, we analyzed the reaction by varying the amount to 0.05 (1.6 mol% SO_3H), 0.1 (3.2 mol% SO_3H), 0.15 (4.8 mol% SO_3H), 0.2 (6.4 mol% SO_3H) and 0.3 g (9.6 mol% SO_3H) of C/TiO_2–SO_3H, and the optimum amount of catalyst turns out to be 0.2 g (6.4 mol% SO_3H) in order to obtain the best results. To study the solvent effect on the reaction of benzamide and 4-methylbenzaldehyde in presence of C/TiO_2–SO_3H, we carried out the reaction in different solvents such as ethanol, acetonitrile, water and toluene. When the reaction was performed in ethanol, acetonitrile and water only trace amount of product formation was observed (Table 4, entries 1 and 2 and 6), whereas in toluene appreciable amount of product formation take place (Table 4, entry 7), but reaction did not proceed to completion even when run for longer reaction times or with an increased amount of catalyst. Surprisingly, when the reaction was carried out under solvent-free conditions at 100 °C, both the yield and reaction time were significantly improved.

Further increase in reaction temperature had no significant effect on the amount of product formation. Thus, the optimum conditions selected are: benzamide (2 mmol), aldehyde (1 mmol), C/TiO_2–SO_3H (0.2 g, 6.4 mol% SO_3H) under solvent-free conditions at 100 °C. In order to explore the scope and limitations of this novel catalytic method, we investigated various aromatic aldehydes containing either electron-withdrawing or electron-donating groups under the optimized reaction conditions and excellent results were obtained (Table 5, products **3a–o**). The reaction is also compatible with various aliphatic aldehydes (Table 5, products **3n**, **3o**).

Table 3 Comparison of catalytic activities of different sulfonated carbon/nano-metal oxide composites for the one-pot synthesis of symmetrical gem-bisamides, bis(heterocyclyl)methanes and β-aminocarbonyl compounds

Entry	Sulfonated carbon/nano-metal oxide composites[a]	Bisamides[b]		Bis(heterocyclyl)methanes[c]		Mannich[d]	
		Time (h)	Yield[e] (%)	Time (h)	Yield[e] (%)	Time (h)	Yield[e] (%)
1	$C/TiO_2–SO_3H$	2	90	0.5	92	3	94
2	$C/CeO_2–SO_3H$	6	85	0.75	80	7	86
3	$C/ZrO_2–SO_3H$	2	70	0.75	82	5	85

[a] $C/TiO_2–SO_3H$: sulfonated carbon/nano-titania composite; $C/CeO_2–SO_3H$: sulfonated carbon/nano-ceria composite; $C/ZrO_2–SO_3H$: sulfonated carbon/nano-zirconia composite. [b] Reaction conditions: 4-methylbenzaldehyde (1 mmol), benzamide (2 mmol), sulfonated carbon/nano-metal oxide composite (0.2 g) at 100 °C under solvent-free conditions. [c] Reaction conditions: 4-methylbenzaldehyde (1 mmol), dimedone (2 mmol), sulfonated carbon/nano-metal oxide composite (0.2 g) at 100 °C in water (5 mL). [d] Reaction conditions: 4-bromobenzaldehyde (1 mmol), acetophenone (1 mmol), aniline (1 mmol), sulfonated carbon/nano-metal oxide composite (0.1 g) at 60 °C in water (5 mL). [e] Isolated yield.

Table 4 Effect of different solvents on $C/TiO_2–SO_3H$ catalyzed one-pot synthesis of symmetrical gem-bisamides, bis(heterocyclyl) methanes and β-aminocarbonyl compounds

Entry	Solvent	Temperature	Bisamides[a]		Bis(heterocyclyl)methanes[b]		Mannich[c]	
			Time (h)	Yield[e] (%)	Time (h)	Yield[e] (%)	Time (h)	Yield[e] (%)
1	Ethanol	Reflux	6	30[f]	1	80	5.5	90
2	Acetonitrile	Reflux	6	26[f]	2	72	6	89
3	Water	Rt	—	—	6	70	—	—
4	**Water**	**60 °C**	—	—	1.5	82	**3**	**94**
5	Water	80 °C	—	—	1	85	2.5	92
6	**Water**	**Reflux**	6	Trace	**0.5**	**92**	2.25	94
7	Toluene	Reflux	12	60[f]	—	—	—	—
8	Solvent-free	80 °C	6	76	1.5	87	4.5	85
9	**Solvent-free**	**100 °C**	**2**	**90**	1	90	4	88
10	Solvent-free	120 °C	2	91	0.25	94[d]	—	—

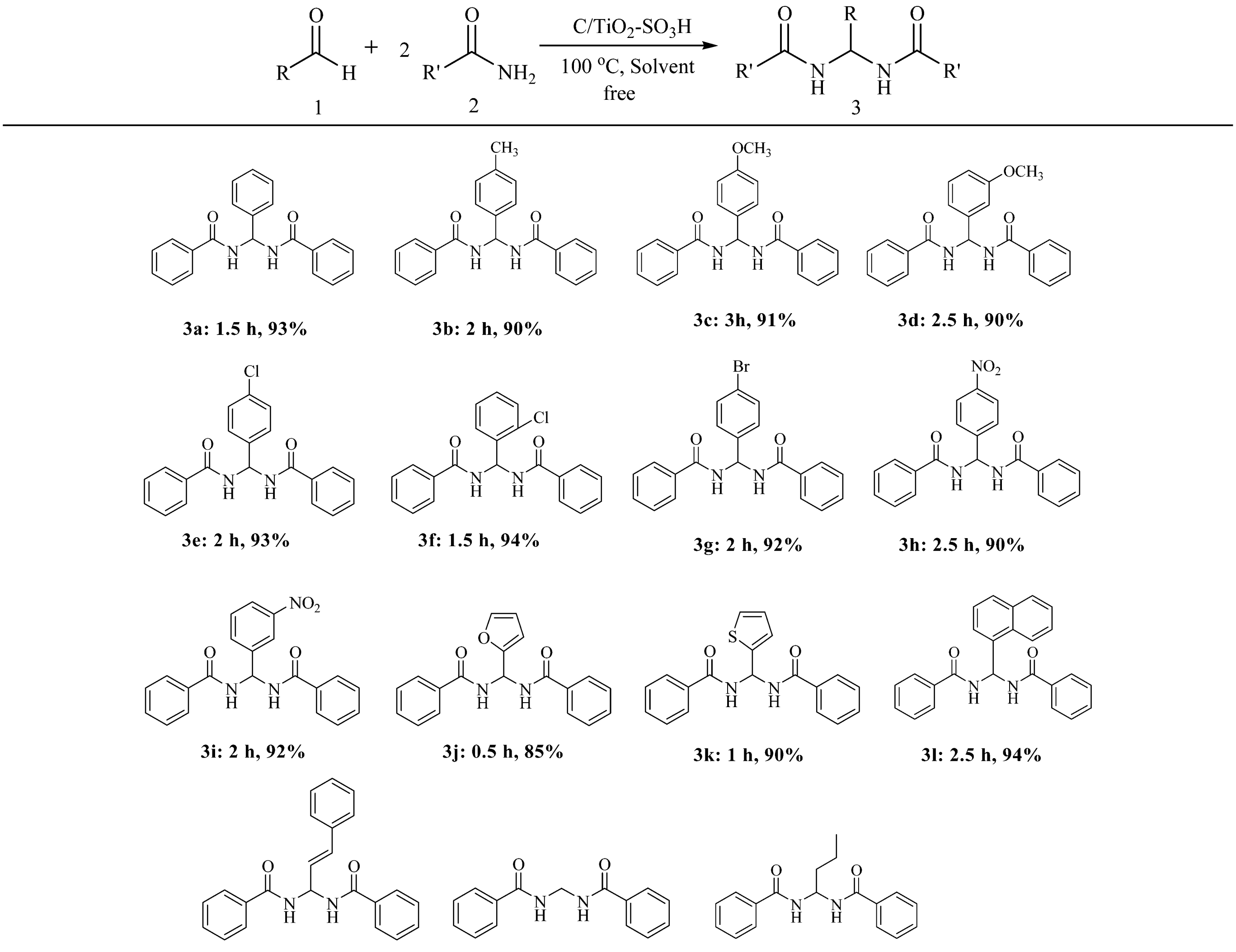
[a] Reaction conditions: 4-methylbenzaldehyde (1 mmol), benzamide (2 mmol) and $C/TiO_2–SO_3H$ (0.2 g, 6.4 mol% SO_3H). [b] Reaction conditions: 4-methylbenzaldehyde (1 mmol), dimedone (2 mmol) and $C/TiO_2–SO_3H$ (0.2 g, 6.4 mol% SO_3H). [c] Reaction conditions: 4-bromobenzaldehyde (1 mmol), acetophenone (1 mmol), aniline (1 mmol) and $C/TiO_2–SO_3H$ (0.1 g, 3.2 mol% SO_3H). [d] Refers to the yield of 1.8-dioxooctahydroxanthenes. [e] Isolated yield. [f] Column chromatographic yield.

Catalytic testing for the synthesis of bis(heterocyclyl)methanes

Initial attempts to optimize the reaction conditions for the synthesis of bis(heterocyclyl)methanes was done using dimedone as the C–H activated compound. To select the appropriate carbon/nano-metal oxide composite, 4-methylbenzaldehyde was selected as the test substrate and the reaction was carried out with different sulfonated composites at 100 °C. It was found that $C/TiO_2–SO_3H$ again turned out to be the most active catalyst for the synthesis of 2,2′-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cycloxene-1-one) (Table 3, entry 1). Further, 0.2 g (6.4 mol% SO_3H) of $C/TiO_2–SO_3H$ gave the best results in terms of reaction time and yield. The effect of different solvents on the reaction rate was also examined by carrying out the reaction in a variety of protic and aprotic solvents (Table 4), and the best results were obtained using water as solvent (Table 4, entry 6). Since the reaction in water at 100 °C was completed in 30 min. in the case of test substrate, so we thought that the reaction may be successful at room temperature. Then the test reaction was also carried out at room temperature, and found that 2,2′-(4-methylphenylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cycloxene-1-one) was formed in 70% yield in 6 h (Table 4, entry 3). These observations clearly indicate the significant effect of temperature on the reaction time and yield, so the reaction with rest of the substrates was carried out in water at 100 °C (Table 6, products **5a–j**).

Ilangovan *et al.* have reported that the reaction of dimedone and aromatic aldehydes leads to the formation of two different products under different set of conditions.[52] The open chain products, 2,2′-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cycloxene-1-ones) were formed when the reaction was carried out in aqueous media, whereas the formation of cyclized products, 1,8-dioxooctahydroxanthenes took place under solvent-free conditions. To examine the possibility of the cyclized product with our catalytic system, the reaction with test substrate was carried out under solvent-free conditions at 80, 100 and 120 °C. The formation of open chain product, 2,2′-(4-methylphenylmethylene)bis-(3-hydroxy-5,5-dimethyl-2-cycloxene-1-one) was observed at 80 and 100 °C (Table 4, entries 8 and 9), whereas, an increase in the reaction temperature to 120 °C, led to the formation of cyclized product, 3,3,6,6-tetramethyl-9-(4-tolyl)-1,8-dioxo-octahydroxanthene in excellent yields (Table 4, entry 10). Based on these results, it was concluded that $C/TiO_2–SO_3H$ in water at 100 °C gave the open chain products, 2,2′-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cycloxene-1-ones), whereas, $C/TiO_2–SO_3H$ under solvent-free conditions at 120 °C gave 1,8-dioxooctahydroxanthenes. In order to examine the substrate scope, various aromatic and heteroaromatic aldehydes with different substituents were chosen and excellent results were obtained (Table 6, products **5a–j**, **6a–j**). With these encouraging results, we turn to explore the scope of the reaction using other C–H activated compounds,

Table 5 C/TiO_2–SO_3H catalyzed one-pot synthesis of symmetrical gem-bisamides[a,b]



3a: 1.5 h, 93% **3b: 2 h, 90%** **3c: 3h, 91%** **3d: 2.5 h, 90%**

3e: 2 h, 93% **3f: 1.5 h, 94%** **3g: 2 h, 92%** **3h: 2.5 h, 90%**

3i: 2 h, 92% **3j: 0.5 h, 85%** **3k: 1 h, 90%** **3l: 2.5 h, 94%**

3m: 2 h, 85% **3n: 1.5 h, 82%** **3o: 2 h, 80%**

[a] Reaction conditions: aldehyde (1 mmol), benzamide (2 mmol), C/TiO_2–SO_3H (0.2 g, 6.4 mol% SO_3H) at 100 °C under solvent-free conditions. [b] Isolated yield.

pyrazolone and indole and the reaction was carried out using aromatic aldehydes in aqueous media at 100 °C as well as under solvent-free conditions at 120 °C.

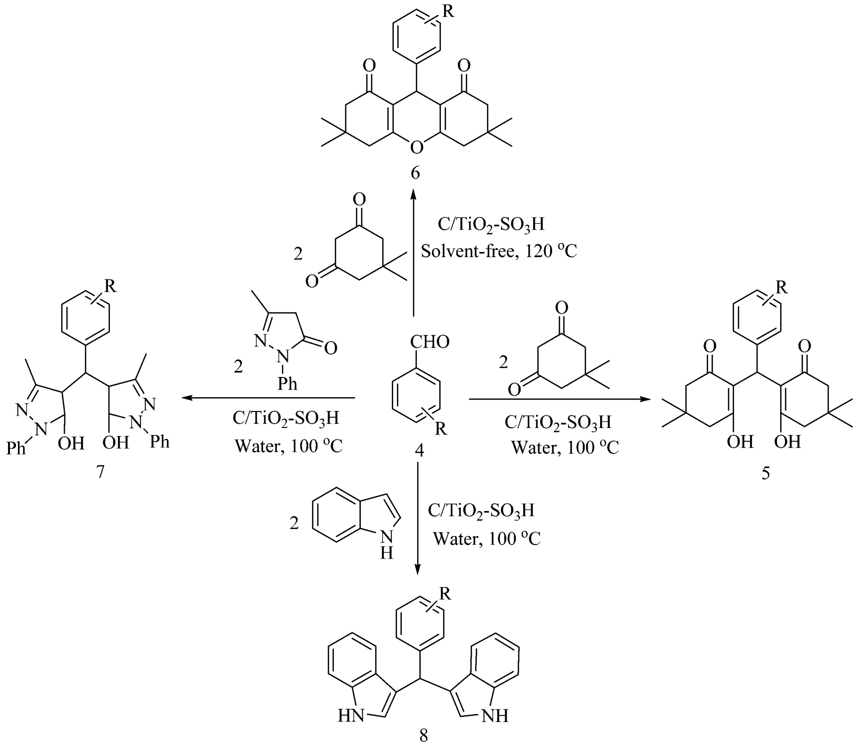
In case of both indole and pyrazolone, no cyclized product was formed, and 4,4′-arylmethylene bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) in case of pyrazolone and bis(indolyl)methanes in case of indole were obtained as the sole products. The milder conditions employing water at 100 °C were selected as the optimum reaction conditions. Further, a series of 4,4′-arylmethylene bis(3-methyl-1-phenyl-1H-pyrazol-5-ols) and bis(indolyl)methanes were synthesized in excellent yields using different aromatic aldehydes with electron-donating and electron-withdrawing groups (Table 6, products **7a–j**, **8a–j**).

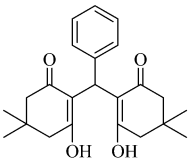
Catalyst testing for the one-pot three component Mannich reaction

Mannich reaction was carried out by stirring a mixture of aromatic aldehyde, ketone and amine in the presence of sulfonated carbon/nano-metal oxide composites in water.

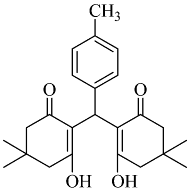
To select the appropriate sulfonated composite, the reaction of 4-bromobenzaldehyde, acetophenone and aniline was selected as the model reaction. Again C/TiO_2–SO_3H was found to be the best catalyst for the one-pot three component synthesis of β-amino carbonyl compounds both in terms of reaction time and yield (Table 3, entry 1). In order to optimize the amount of C/TiO_2–SO_3H, we carried out the model reaction with varying amounts 0.05 (1.6 mol% SO_3H), 0.1 (3.2 mol% SO_3H), 0.15 (4.8 mol% SO_3H), 0.2 (6.4 mol% SO_3H) and 0.3 g (9.6 mol% SO_3H) of C/TiO_2–SO_3H. The optimum amount of C/TiO_2–SO_3H was found to be 0.1 g (3.2 mol% SO_3H) in order to obtain the best results. Further, the efficiencies of several organic solvents as reaction media and solvent-free system were investigated for the synthesis of β-amino-carbonyl compounds. Polar solvents such as ethanol and acetonitrile were found to be the better solvents, however, a significant improvement was observed in aqueous media. To optimize the reaction temperature, the Mannich reaction was

Table 6 C/TiO$_2$–SO$_3$H catalyzed one-pot synthesis of bis(heterocyclyl)methanes[a,b,c]

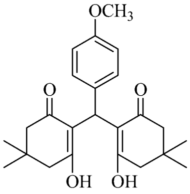




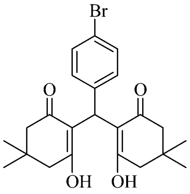
5a: 0.25h , 92%



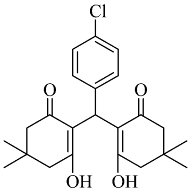
5b: 0.5h, 92%



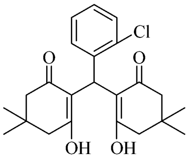
5c: 3h, 94%



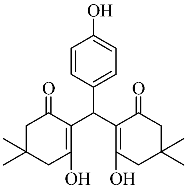
5d: 0.25h, 93%



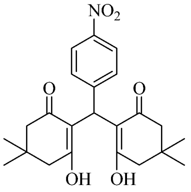
5e: 0.25 h, 94%



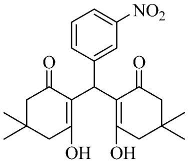
5f: 0.5h, 90%



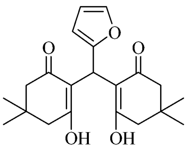
5g: 3h: 90%



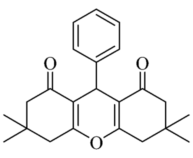
5h: 3h, 91%



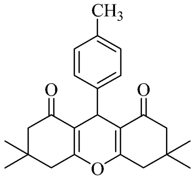
5i: 1.5h, 92%



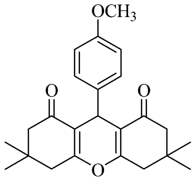
5j: 0.5h, 88%



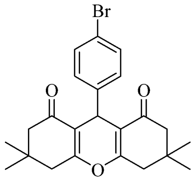
6a: 0.25h, 94%



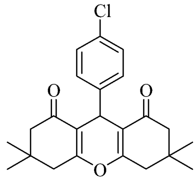
6b: 0.5h, 92%



6c: 1.5h, 90%

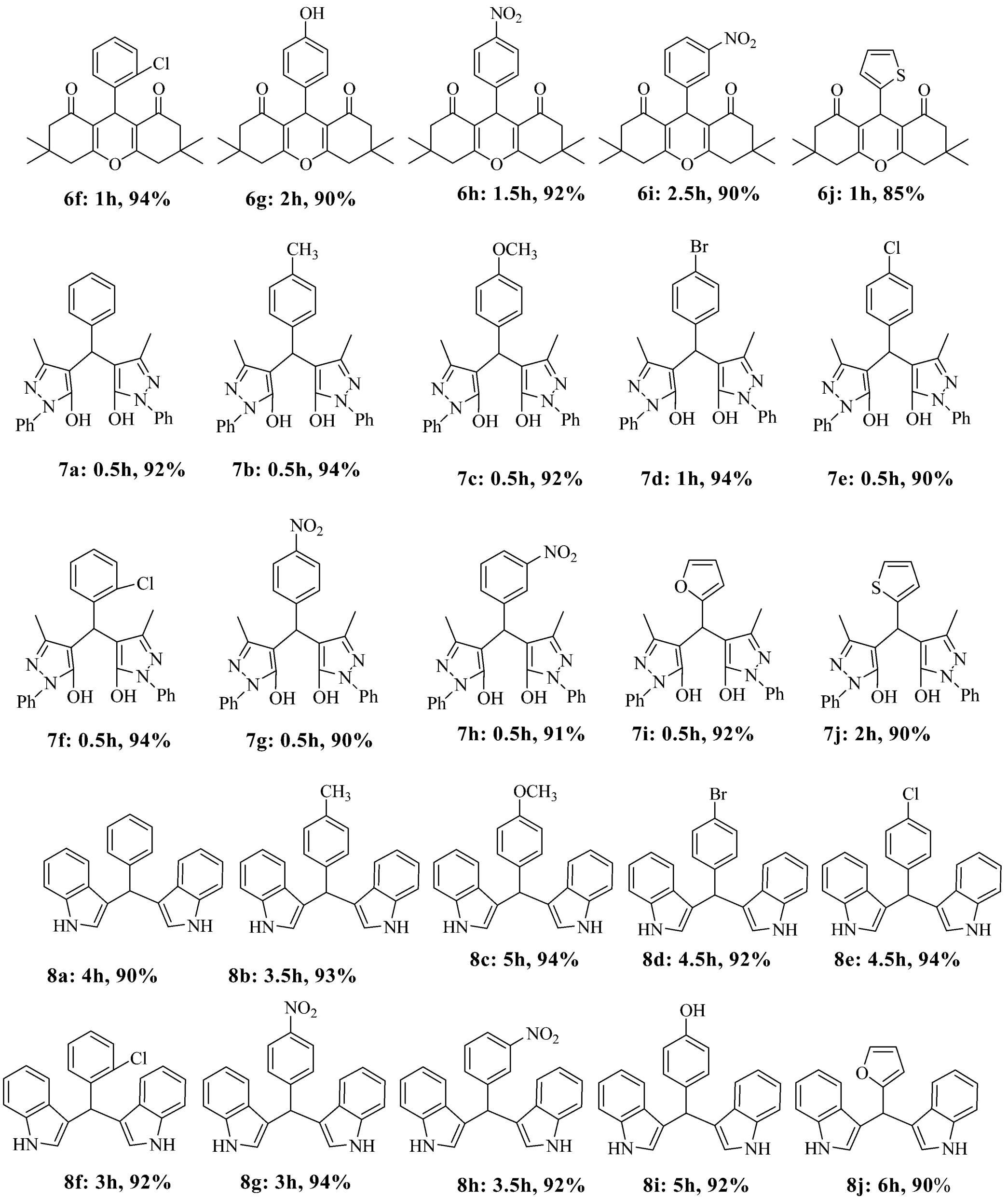


6d: 1h, 90%



6e: 0.5h, 94%

Table 6 (*continued*)



6f: 1h, 94% **6g: 2h, 90%** **6h: 1.5h, 92%** **6i: 2.5h, 90%** **6j: 1h, 85%**

7a: 0.5h, 92% **7b: 0.5h, 94%** **7c: 0.5h, 92%** **7d: 1h, 94%** **7e: 0.5h, 90%**

7f: 0.5h, 94% **7g: 0.5h, 90%** **7h: 0.5h, 91%** **7i: 0.5h, 92%** **7j: 2h, 90%**

8a: 4h, 90% **8b: 3.5h, 93%** **8c: 5h, 94%** **8d: 4.5h, 92%** **8e: 4.5h, 94%**

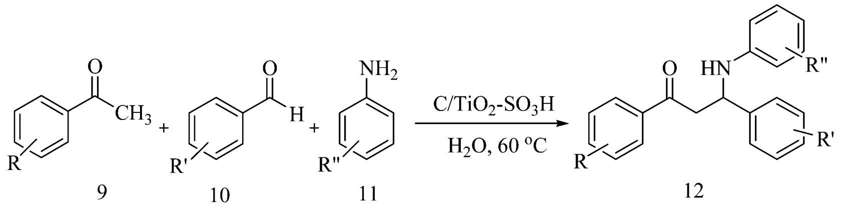
8f: 3h, 92% **8g: 3h, 94%** **8h: 3.5h, 92%** **8i: 5h, 92%** **8j: 6h, 90%**

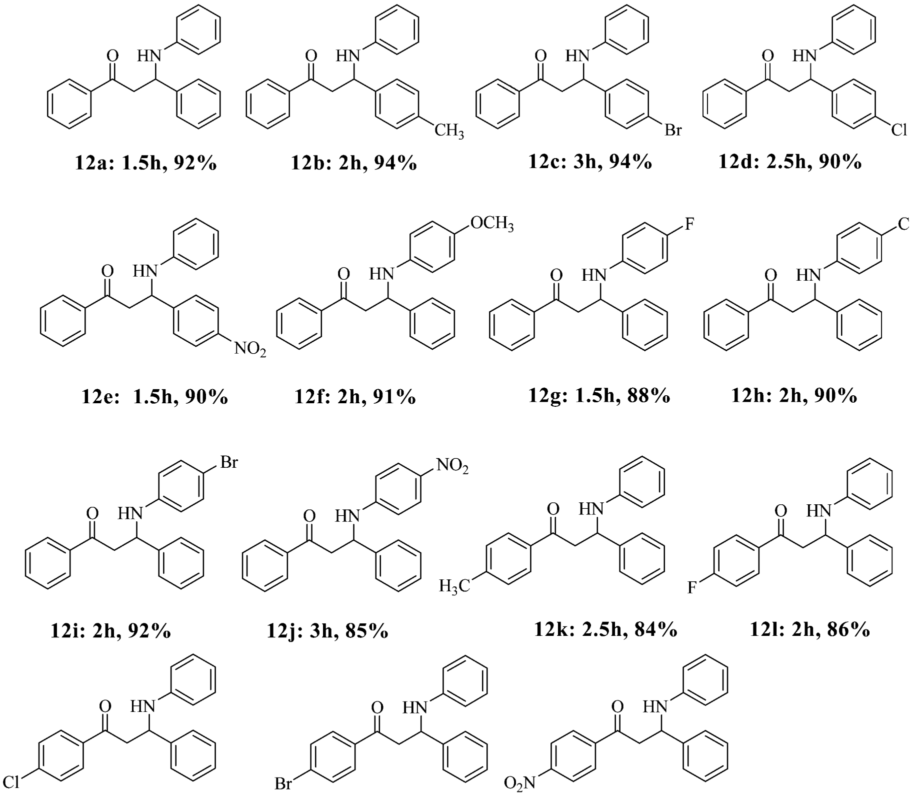
[a] Reaction conditions: aldehyde (1 mmol), dimedone or pyrazolone or indole (2 mmol), C/TiO_2–SO_3H (0.2 g, 6.4 mol% SO_3H) at 100 °C in water (5 mL) for products **5a–j**, **7a–j**, **8a–j**. [b] Reaction conditions: aldehyde (1 mmol), dimedone (2 mmol), C/TiO_2–SO_3H (0.2 g, 6.4 mol% SO_3H) at 120 °C under solvent-free conditions for products **6a–j**. [c] Isolated yield.

carried at 60, 80 and 100 °C using water as the reaction medium and found that 60 °C was the optimum reaction temperature (Table 4, entry 4). Thus the optimum conditions selected are: aromatic aldehyde (1 mmol), aromatic ketone (1 mmol), aromatic amine (1 mmol), C/TiO_2–SO_3H (0.1 g, 3.2 mol% SO_3H), water (5 mL) and 60 °C as the reaction temperature. To determine the scope of the designed protocol, a number of commercially available aromatic aldehydes, aromatic ketones and aromatic amines were chosen for the one-pot synthesis of β-aminocarbonyl compounds and the results are summarized in Table 7. The reaction proceeded smoothly with substrates having either electron-donating or with-drawing groups affording products in good to excellent yields.

In order to find out the role of C/TiO_2–SO_3H as heterogeneous catalyst for the one-pot synthesis of gem-bisamides, bis(heterocyclyl)methanes and β-aminocarbonyl compounds *via* Mannich reaction, the test reaction in each case was carried out in the presence of nano-titania, amorphous carbon, non-sulfonated carbon/nano-titania, sulfonated amorphous carbon, sulfonated carbon/silica composite and without using any catalyst. The results summarized in Table 8 clearly demonstrate the higher catalytic activity of sulfonated carbon/nano-titania composite

Table 7 $C/TiO_2–SO_3H$ catalyzed one-pot three component synthesis of β-aminocarbonyl compounds[a,b]




12a: 1.5h, 92% **12b: 2h, 94%** **12c: 3h, 94%** **12d: 2.5h, 90%**

12e: 1.5h, 90% **12f: 2h, 91%** **12g: 1.5h, 88%** **12h: 2h, 90%**

12i: 2h, 92% **12j: 3h, 85%** **12k: 2.5h, 84%** **12l: 2h, 86%**

12m: 3h, 90% **12n: 2h, 92%** **12o: 2.5h, 85%**

[a] Reaction conditions: ketone (1 mmol), aromatic aldehyde (1 mmol), aromatic amine (1 mmol), $C/TiO_2–SO_3H$ (0.1 g, 3.2 mol% SO_3H) at 60 °C in water. [b] Isolated yield.

in comparison to other solid acid catalysts both in terms of reaction time and product yield. Thus, $C/TiO_2–SO_3H$ was selected as the heterogeneous catalyst to carry out the desired organic transformation. Further, to study the merits of the current protocol for the synthesis of gem-bisamides, bis-(heterocyclyl)methanes and β-aminocarbonyl compounds, a comparison of the efficacy of $C/TiO_2–SO_3H$ with some of the reported catalytic systems in the literature was done. The results presented in Table 9 clearly depict the superiority of the present catalytic system in terms of higher value of TOF compared to others reported in literature. In addition, the present method comparatively affords a truly green process using benign reaction media along with higher product yields in shorter reaction time (Table 9, bold entries).

Recyclability and heterogeneity

For practical applicability of a heterogeneous catalyst, recyclability is a very important factor. Therefore, we investigated the efficiency of $C/TiO_2–SO_3H$ in repeated cycles of reaction (Table 5, **3b**, Table 6, **5b**, Table 7, **12c**). After completion of the reaction, the catalyst could be easily separated by simple filteration, washed with distilled water, dried and could be reused for subsequent runs. The results shown in Fig. 2 clearly demonstrate that the catalyst is recyclable upto 5th run without significant loss of activity. Furthermore, the amount of SO_3H in the used catalyst after 5th run was determined by elemental analysis, and found that 0.28 mmol g^{-1} of SO_3H was still grafted onto the surface of the catalyst compared to 0.32 mmol g^{-1} in fresh catalyst. These results indicate the high stability and activity of the catalyst after subsequent reaction cycles.

The heterogeneity of $C/TiO_2–SO_3H$ was tested by the hot filtration test to check any possibility of leaching of sulfonic acid groups from the catalyst surface. The reaction in case of product **12c**, Table 7 has been carried out in the presence of $C/TiO_2–SO_3H$, until the conversion was 40% (1 h) after which the catalyst was filtered off at the reaction temperature.

Table 8 Comparison of activity of C/TiO_2-SO_3H with nano-titania, amorphous carbon, non-sulfonated carbon/nano-titania, sulfonated amorphous carbon, sulfonated carbon/silica composite for the synthesis of gem-bisamides, bis(heterocyclyl) methanes and β-aminocarbonyl compounds

		Bisamides[a]		Bis(heterocyclyl)methanes[b]		Mannich[c]	
Entry	Catalyst	Time (h)	Yield (%)	Time (h)	Yield (%)	Time (h)	Yield (%)
1	No catalyst	10	NR[f]	5	20[d]	10	10[d]
2	Nano-Titania	10	18[d]	5	25[d]	10	12[d]
3	Amorphous carbon	10	20[d]	5	28[d]	10	15[d]
4	Non-sulfonated carbon/nano-titania	10	25[d]	5	30[d]	10	20[d]
5	Sulfonated amorphous carbon	2	45[d]	0.25	65[d]	3	50[d]
6	Sulfonated carbon/silica composite	2	70[e]	0.25	80[e]	3	78[d]
7	Sulfonated carbon/nano-titania composite	2	90[e]	0.25	94[e]	3	94[e]

[a] Reaction conditions: 4-methylbenzaldehyde (1 mmol), benzamide (2 mmol), catalyst (0.2 g) at 100 °C under solvent-free conditions. [b] Reaction conditions: 4-methylbenzaldehyde (1 mmol), dimedone (2 mmol), catalyst (0.2 g) at 120 °C under solvent-free conditions for the synthesis of 1,8-dioxooctahydroxanthenes. [c] Reaction conditions: 4-bromobenzaldehyde (1 mmol), acetophenone (1 mmol), aniline (1 mmol), catalyst (0.1 g) at 60 °C in water. [d] Column chromatographic yields. [e] Isolated yields. [f] NR: no reaction.

Table 9 Comparison of the catalytic activity of C/TiO_2-SO_3H with reported catalytic systems for the one-pot synthesis of symmetrical gem-bisamides, bis(heterocyclyl) methanes and β-aminocarbonyl compounds *via* Mannich reaction

Reaction	Catalyst	Reaction conditions	Yield[d] (%)	Time (h)	TOF[e] (min^{-1})
Bisamides[a]	Phosphotungstic acid[53]	Toluene, 110 °C, catalyst (0.3 mmol), 18 h	85	18	0.0026
	Boric acid[54]	Toluene, 120 °C, catalyst (0.3 mmole)	80	60	0.0006
	SBSSANPs[55]	Toluene,120 °C, catalyst (0.08 g)	91	6	0.0263
	Silica sulfuric acid[56]	EtOAc, 90 °C, silica sulfuric acid (25 mol%)	85	0.58	0.097
	C/TiO_2-SO_3H[f]	**Solvent-free, 100 °C, C/TiO_2-SO_3H (0.2 g)**	**90**	**2**	**0.117**
Bis(heterocyclyl)methanes[b]					
	TBAHS[26b]	1,4-Dioxane/water, reflux, TBAHS (10 mol%)	91	3.5	0.043
	VSA NRs[57]	Solvent-free, 80 °C, VSA NRs (10 mol%)	90	0.5	0.3
	Silica-bonded *N*-propyl sulfamic acid[58]	Ethanol, 80 °C, catalyst (0.03 g)	92	4	0.37
	PPA-SiO_2[59]	Solvent-free, 140 °C, PPA-SiO_2 (10 mol%)	83	0.5	0.27
	C/TiO_2-SO_3H[f]	**Solvent-free, 120 °C, C/TiO_2-SO_3H (0.2 g)**	**94**	**0.25**	**0.979**
Mannich[c]	$SiO_2-OAlCl_2$[37]	Ethanol, rt, $SiO_2-OAlCl_2$ (0.05 g, 20 mol% Al)	91	6	0.012
	CSA[60]	Solvent-free, rt, CSA (5 mol%)	83	8	0.034
	CBSA[5c]	Ethanol, rt, CBSA (0.1 g)	88	7	0.007
	$HClO_4$-SiO_2[61]	Ethanol, rt, $HClO_4$-SiO_2 (4 mol%)	75	17	0.0183
	C/TiO_2-SO_3H[f]	**Water, 60 °C, C/TiO_2-SO_3H (0.1 g)**	**94**	**3**	**0.163**

[a] Reaction conditions: 4-methylbenzaldehyde and benzamide. [b] Reaction conditions: 4-methylbenzaldehyde and dimedone for the synthesis of 1,8-dioxooctahydroxanthenes. [c] Reaction conditions: 4-bromobenzaldehyde, acetophenone and aniline. [d] Isolated yield. [e] Turn over frequency. [f] Our work.

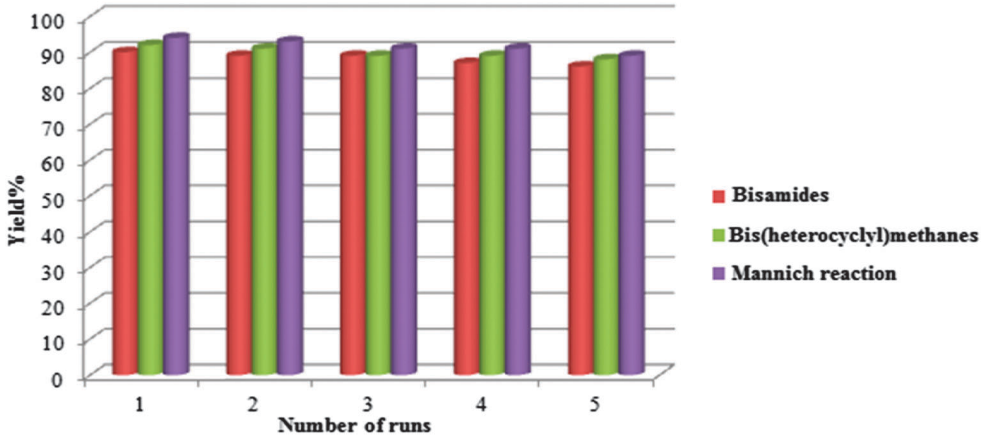


Fig. 2 Recyclability of C/TiO_2-SO_3H. Reaction conditions: 4-methylbenzaldehyde (1 mmol), benzamide (2 mmol), C/TiO_2-SO_3H (0.2 g, 6.4 mol% SO_3H) at 100 °C under solvent-free conditions for 2 h [bisamides]; 4-methylbenzaldehyde (1 mmol), dimedone (2 mmol), C/TiO_2-SO_3H (0.2 g, 6.4 mol% SO_3H) at 100 °C in water (5 mL) for 0.5 h [bis(heterocyclyl)methanes]; 4-bromobenzaldehyde (1 mmol), acetophenone (1 mmol), aniline (1 mmol), C/TiO_2-SO_3H (0.1 g, 3.2 mol% SO_3H) at 60 °C in water (5 mL) for 3 h [Mannich reaction].

The reaction was then continued further under same set of conditions without the catalyst and found that no significant conversion was observed. Thus, it can be concluded that the catalyst is heterogeneous in nature and no significant leaching of sulfonic acid groups takes place from the catalyst surface.

Conclusion

In conclusion, we have developed a green, sustainable and economic protocol for the one-pot synthesis of symmetrical gem-bisamides, bis(heterocyclyl)methanes and β-amino carbonyl compounds using novel sulfonated carbon/nano-metal oxide composites as solid acid catalyst. The highly active, stable solid acid catalyst was prepared from inexpensive, natural biomaterial starch and commercially available nano-metal oxides. The highlights of the developed protocol are novelity, operational simplicity, environmental friendliness, excellent yields and recyclability.

Experimental

General

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 Perkin-Elmer FTIR spectrophotometer and mass spectral data on Bruker Esquires 3000 (ESI). CHNS analysis was recorded on ThermoFinnigan FLASH EA 1112 series. SEM images were recorded using FEG SEM JSM-7600F Scanning Electron Microscope, Transmission Electron Micrographs (TEM) were recorded on Philips CM-200. EDX analysis was carried out using OXFORD X-MAX JSM-7600 and TGA was recorded on Perkin Elmer, Diamond TG/DTA. X-ray diffractograms (XRD) was recorded in 2 theta range of 10–80° on a Bruker AXSDB X-ray diffractometer using Cu Kα radiations.

General procedure for the synthesis of sulfonated carbon/nano-metal oxide composites

The mixture of starch and nano-metal oxides (10 g) in the ratio of 1 : 1.2 taken in a round-bottom flask, was heated at 353 K for 10 h. The mixture was then subjected to incomplete carbonization by heating at 673 K under nitrogen atmosphere for 10 h. The carbonization step leads to the dehydration and dissociation of C–O–C linkages present in the starch, thereby forming amorphous carbon/nano-metal oxide composites. The resulting mixture was then sulfonated by heating in concentrated sulfuric acid (15 mL, $>$96 wt%) at 423 K for 10 h under N_2 atmosphere. The composite material obtained was then washed repeatedly with hot distilled water ($>$353 K) until sulfate anions were no longer detected in the filtered water. Sulfonated carbon/nano-metal oxide composites were finally dried in an oven at 373 K for 2 h (7 g).

General procedure for the synthesis of symmetrical gem-bisamides (3a–o)

To a mixture of aldehyde (1 mmol) and amide (2 mmol) in a round bottom flask (25 mL), C/TiO_2–SO_3H (0.2 g, 6.4 mol% SO_3H) was added and the reaction mixture was heated at 100 °C under solvent-free conditions for an appropriate time. On completion of the reaction (monitored by TLC), hot ethanol (5 × 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.

General procedure for the synthesis of bis(heterocyclyl)methanes (5a–j, 6a–j, 7a–j, 8a–j)

To a mixture of aldehyde (1 mmol) and C–H activated compound (dimedone or indole or pyrazolone, 2 mmol) and C/TiO_2–SO_3H (0.2 g, 6.4 mol% SO_3H) in a round bottom flask (25 mL), water (5 mL) was added and the reaction mixture was stirred at 100 °C in case of synthesis of 2,2′-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cycloxene-1-ones), 4,4′-arylmethylene bis(3-methyl-1-phenyl-1H-pyrazol-5-ols) and bis(indolyl)methanes or 120 °C under solvent-free conditions in case of synthesis of 1,8-dioxo-octahydroxanthenes for an appropriate time. After completion of the reaction (monitored by TLC), the reaction mixture was extracted with hot EtOAc (5 × 10 mL) and filtered. The organic layer was washed with water and dried over anhyd. Na_2SO_4. Finally, the product was obtained after removal of the solvent under reduced pressure followed by crystallization with EtOAc: pet ether.

General procedure for the one-pot three component synthesis of β-amino carbonyl compounds *via* Mannich reaction (12a–o)

To a mixture of aromatic ketone (1 mmol), aromatic aldehyde (1 mmol), aromatic amine (1 mmol) and C/TiO_2–SO_3H (0.1 g, 3.2 mol% SO_3H) in a round-bottom flask (25 mL), water (5 mL) was added and the reaction mixture was stirred at 60 °C for an appropriate time. After completion of the reaction (as monitored by TLC), the reaction mixture was diluted with ethyl acetate (5 × 10 mL) and filtered. The organic layer was washed with water (100 mL) and dried over anhyd. Na_2SO_4. Finally, the product was obtained after removal of the solvent under reduced pressure and purified by crystallization with EtOAc: pet ether.

The catalyst was washed with double distilled water followed by CH_2Cl_2 (3 × 10 mL). It was dried at 90 °C for 2 h and reused for subsequent reactions. The structures of the products were confirmed by ^{1}H and ^{13}C NMR, mass spectral data and comparison with authentic samples obtained commercially or prepared according to the literature methods.

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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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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.

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 benzox-

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anthenones 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.

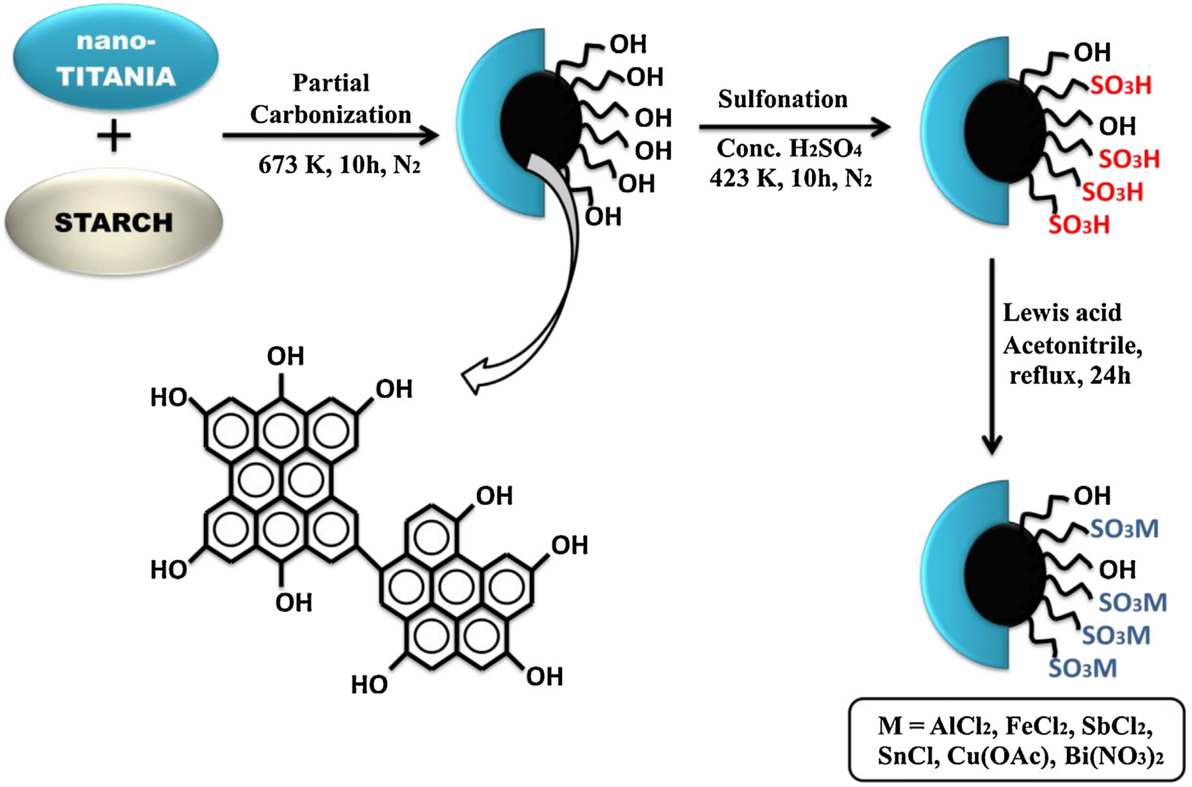
2. Experimental

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-6390LV Scanning Electron Microscope, 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 PerkinElmer, 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.



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

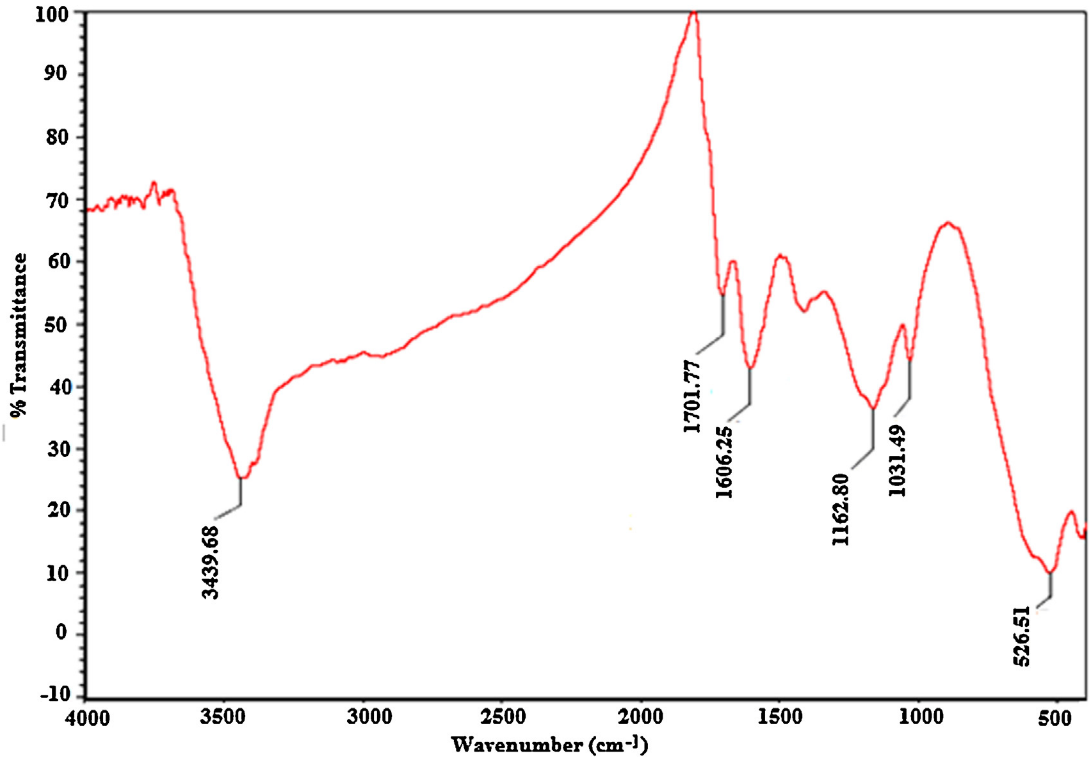


Fig. 1. FTIR spectra of C/TiO_2–SO_3–$SbCl_2$.

In a typical procedure, a mixture of starch and nano-titania (nanopowder, <100 nm 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.

2.3. 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.

2.4. 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,

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

Entry	Catalyst	Phenolic —OH	C=C	SO_2 Stretch Asym.	SO_2 Stretch 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 PerkinElmer FTIR spectrophotometer using KBr discs.

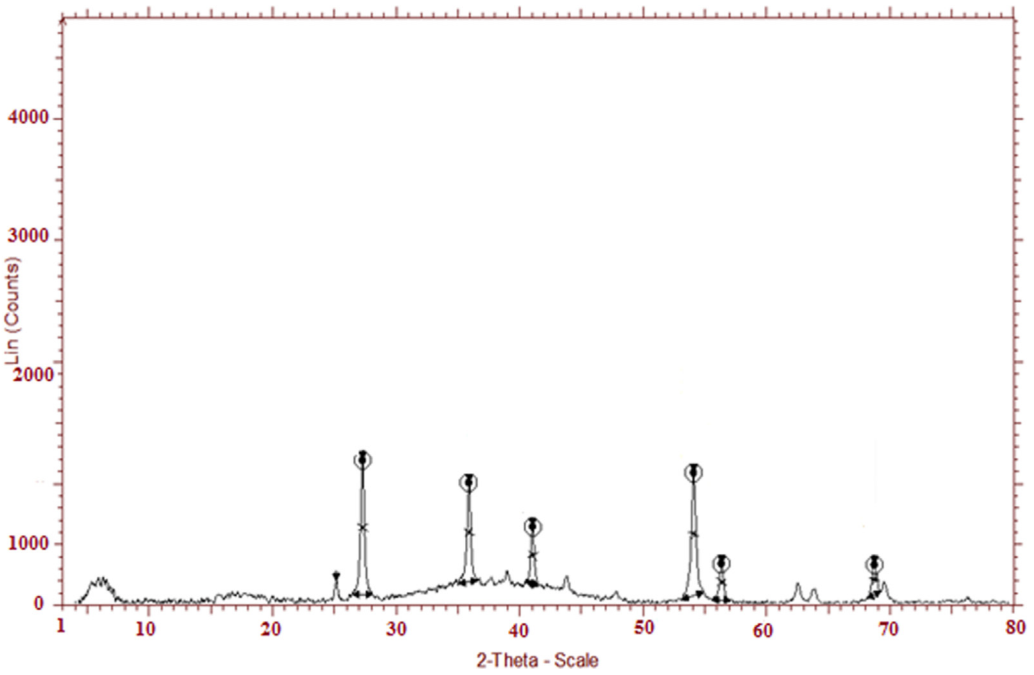


Fig. 2. XRD of $C/TiO_2–SO_3–SbCl_2$.

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.

2.5. CHNS

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

2.6. 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 (1 0 1), (0 0 4), (2 0 0), (2 1 1) and (1 1 6) reflections of anatase TiO_2 whereas peaks at 27.2°, 35.8° and 56.4°

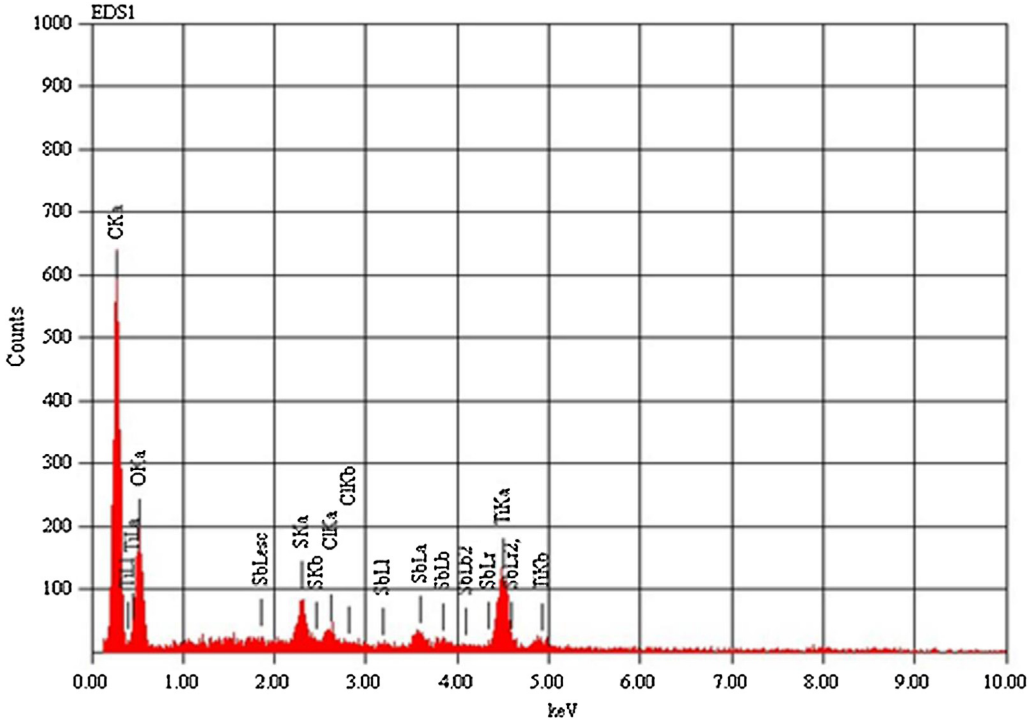


Fig. 3. EDX spectra of $C/TiO_2–SO_3–SbCl_2$.

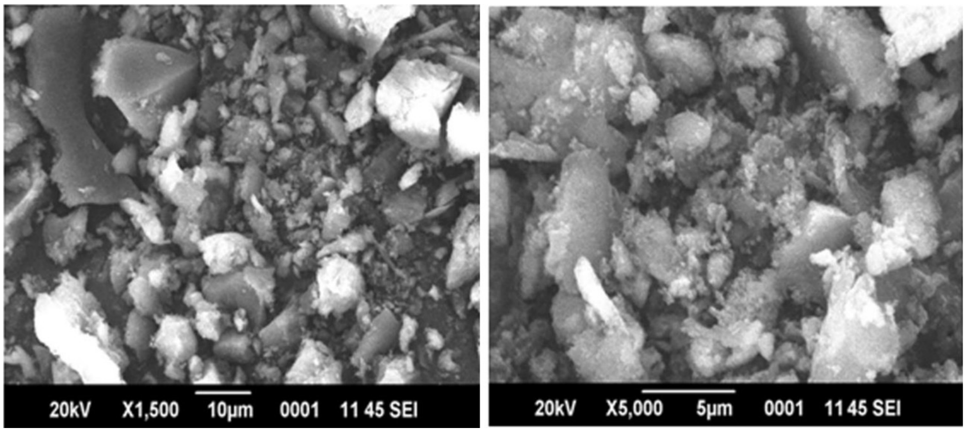


Fig. 4. SEM images of C/TiO_2–SO_3–$SbCl_2$.

correspond to the (1 1 0), (1 0 1) and (2 1 1) planes of rutile phase [50–51]. The observed diffraction peaks agree well with the tetragonal structure of TiO_2 (Fig. 2). This fact indicates 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.

2.7. *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–$SbCl_2$.

2.8. *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 massive congeries with relatively rough surface depicting the amorphous nature of the composite formed.

2.9. *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 carbon material 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

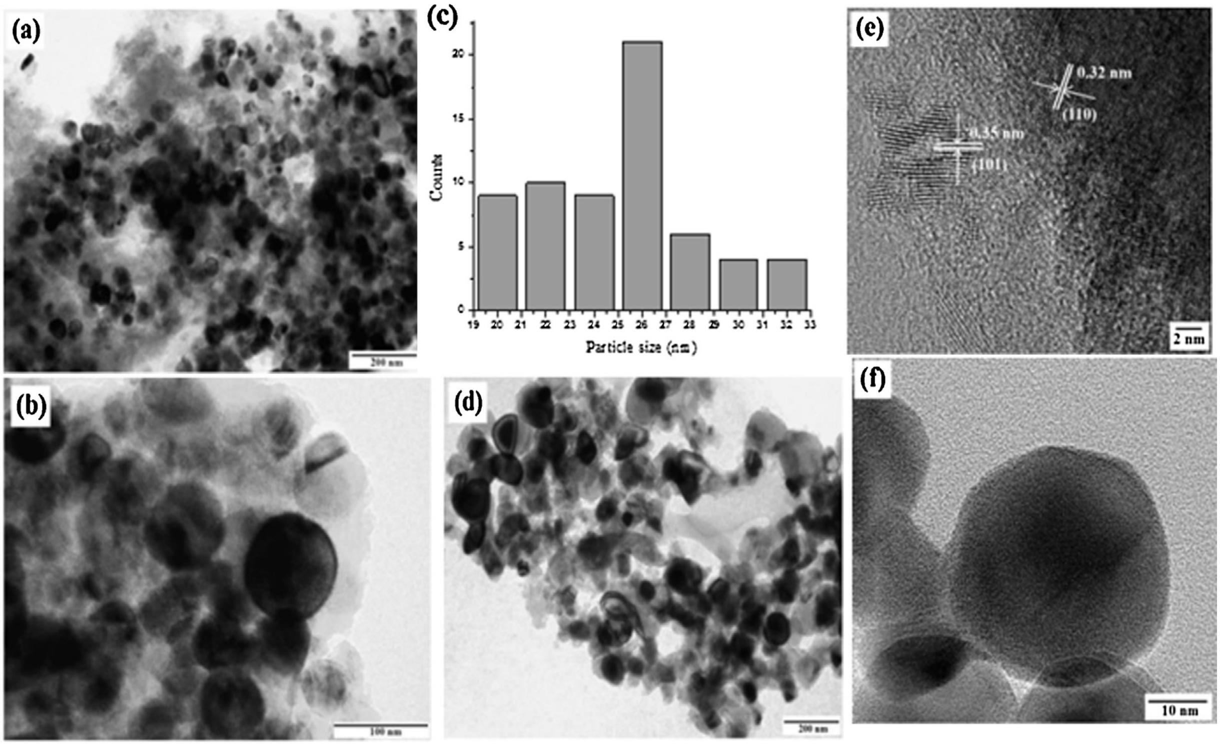


Fig. 5. (a, b) TEM images of C/TiO_2–SO_3–$SbCl_2$; (c) Particle size histogram; (d) TEM image of C/TiO_2–SO_3H; (e, f) HRTEM images of C/TiO_2–SO_3–$SbCl_2$.

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 (1 1 0) plane of rutile TiO_2 and (1 0 1) 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.

2.10. 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 to 700 °C could 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.

*2.11. 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), $C/TiO_2–SO_3H–SbCl_2$ (0.1 g) was added and the reaction mixture was heated at 90 °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.

2.12. 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 $C/TiO_2–SO_3H–SbCl_2$ (0.1 g) 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 °C for 2 h and reused for subsequent reactions.

All the products were characterized by ^1H, ^{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 5l was also confirmed by single-crystal X-ray diffraction.

3. Results and discussion

*3.1. Catalytic 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, other weak 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 [52]. 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

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.

Entry	Lewis acid grafted sulfonated carbon@titania composites	4*H*-pyrimido[2,1-*b*]benzothiazoles[a]		Benzoxanthenones[b]	
		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

The bold values represent the selected reaction conditions.

[a] Reaction conditions: 2-aminobenzothiazole (1 mmol), 3-nitrobenzaldehyde (1 mmol), ethylacetoacetate (1 mmol), 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 (1 mmol), 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 °C	0.1	1.5	80	1	50
5.	Solvent-free	90 °C	0.05	1.25	60	1	70
6.	**Solvent-free**	**90 °C**	**0.1**	**1.25**	**93**	1	80
7.	**Solvent-free**	**100 °C**	**0.1**	1.0	93	**0.75**	**94**
8.	Solvent-free	120 °C	0.1	1.0	94	0.8	95
9.	Solvent-free	90 °C	0.2	1	93	0.8	93
10.	Solvent-free	90 °C	0.3	0.8	94	0.75	94

The bold values represent the selected reaction conditions.

[a] Refers to antimony chloride grafted sulfonated carbon@titania composite.

[b] Reaction conditions: 2-aminobenzothiazole (1 mmol), 3-nitrobenzaldehyde (1 mmol) and ethylacetoacetate (1 mmol).

[c] Reaction conditions: 2-naphthol (1 mmol), benzaldehyde (1 mmol) and dimedone (1 mmol).

[d] Isolated yields.

[e] Column chromatographic yields.

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, respec-

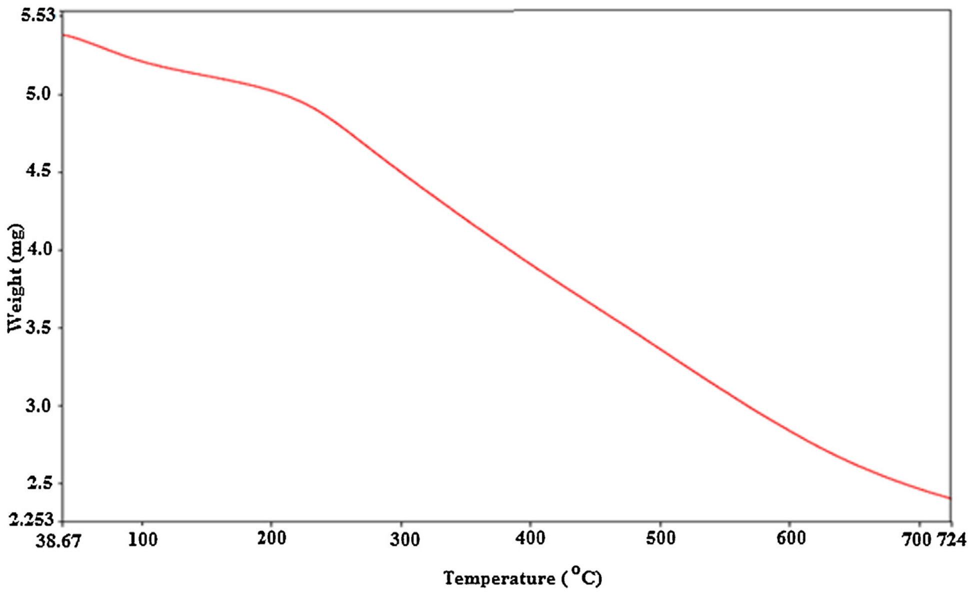
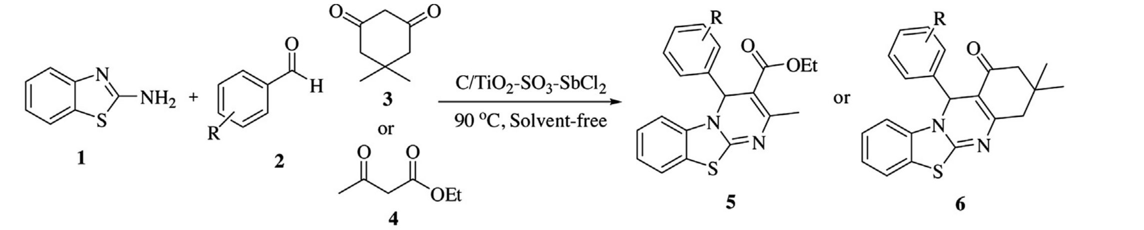
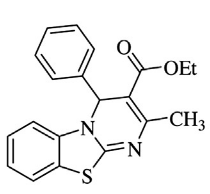


Fig. 6. TGA of $C/TiO_2{-}SO_3{-}SbCl_2$.

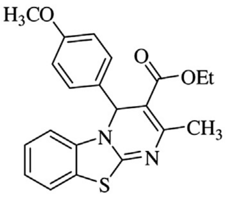
Table 4

C/TiO_2–SO_3–$SbCl_2$ catalyzed one-pot multi-component synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazoles[a,b].

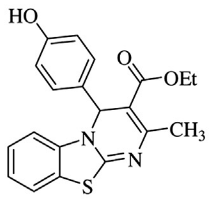




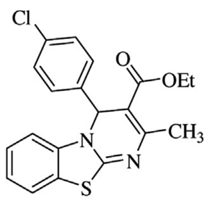
5a: .1.5 h, 92%



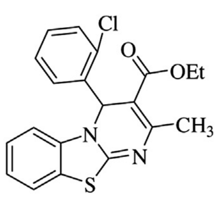
5b: 3 h, 90%



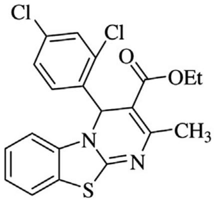
5c: 3 h, 93%



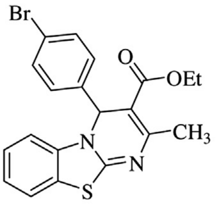
5d: 2 h, 89%



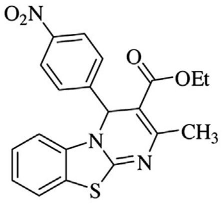
5e: 1 h, 88%



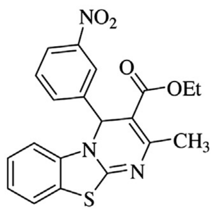
5f: 1 h, 94%



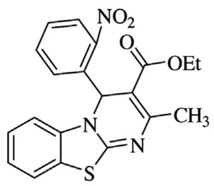
5g: 2 h, 92%



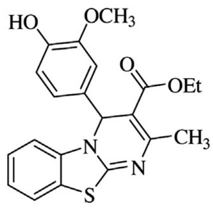
5h: 1.5 h, 88%



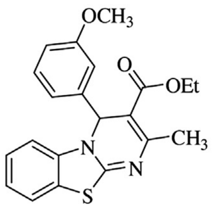
5i: 1.25 h, 93%



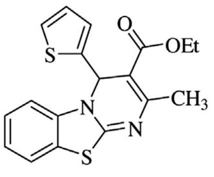
5j: 1 h, 93%



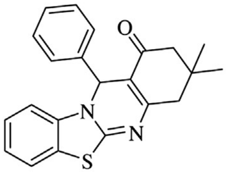
5k: 2.5 h, 85%



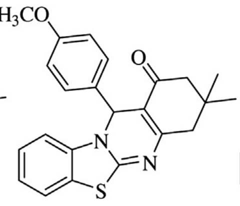
5l: 2 h, 92%



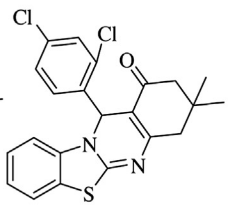
5m: 2 h, 90%



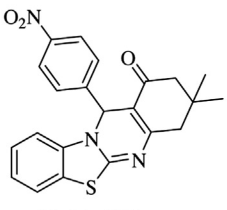
6a: 2 h, 92%



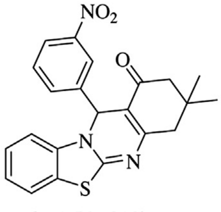
6b: 3 h, 88%



6c: 1.5 h, 93%



6d: 2 h, 85%



6e: 1.5 h, 91%

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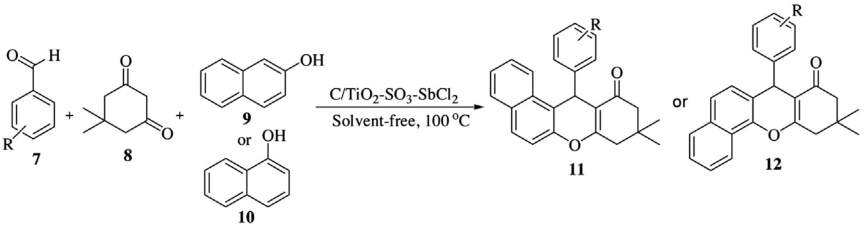
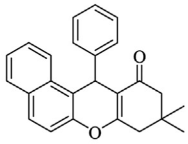
[a] Reaction conditions: 2-aminobenzothiazole (1 mmol), aldehyde (1 mmol), ethylacetoacetate or dimedone (1 mmol) and C/TiO_2–SO_3–$SbCl_2$ (0.1 g, 1 mol% Sb) at 90 °C under solvent-free conditions.

[b] Isolated yields.

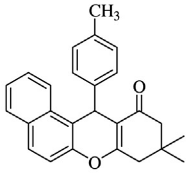
Table 5

C/TiO_2–SO_3–$SbCl_2$ catalyzed multi-component synthesis of benzoxanthenones[a,b].

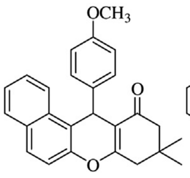




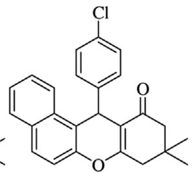
11a: 0.75 h, 94%



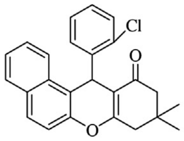
11b: 0.75 h, 92%



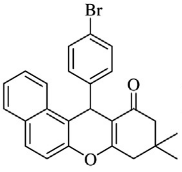
11c: 2 h, 90%



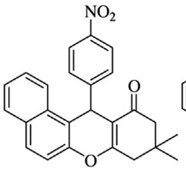
11d: 1h, 93%



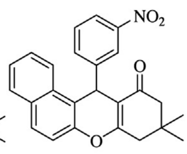
11e: 0.80 h, 93%



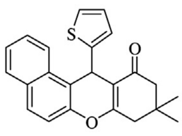
11f:1.25 h, 92%



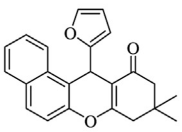
11g: 1.5 h, 90%



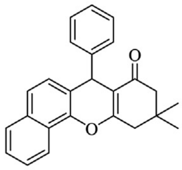
11h: 1.5 h, 90%



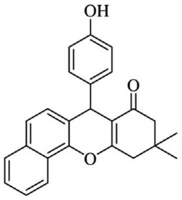
11i: 2 h, 91%



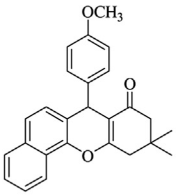
11j: 1.5 h, 90%



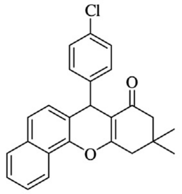
12a: 0.75 h, 92%



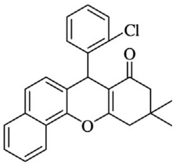
12b: 1 h, 94%



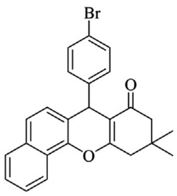
12c: 2.5 h, 90%



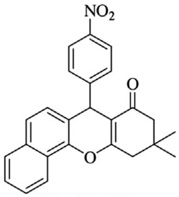
12d: 1 h, 92%



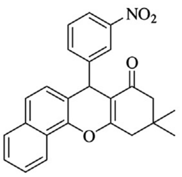
12e: 0.75 h, 94%



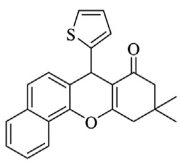
12f: 1.5 h, 91%



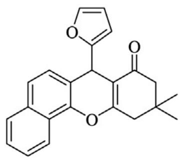
12g: 1 h, 90%



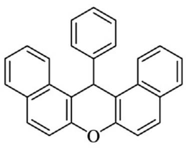
12h: 1.5 h, 93%



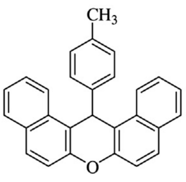
12i: 1 h, 90%



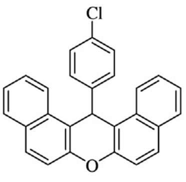
12j: 1 h, 88%



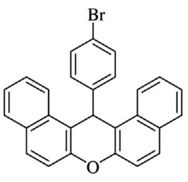
13a: 2 h, 90%



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 (1 mmol) and C/TiO_2–SO_3–$SbCl_2$ (0.1 g, 1 mol% Sb) at 100 °C under solvent-free conditions (11a–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 yields.

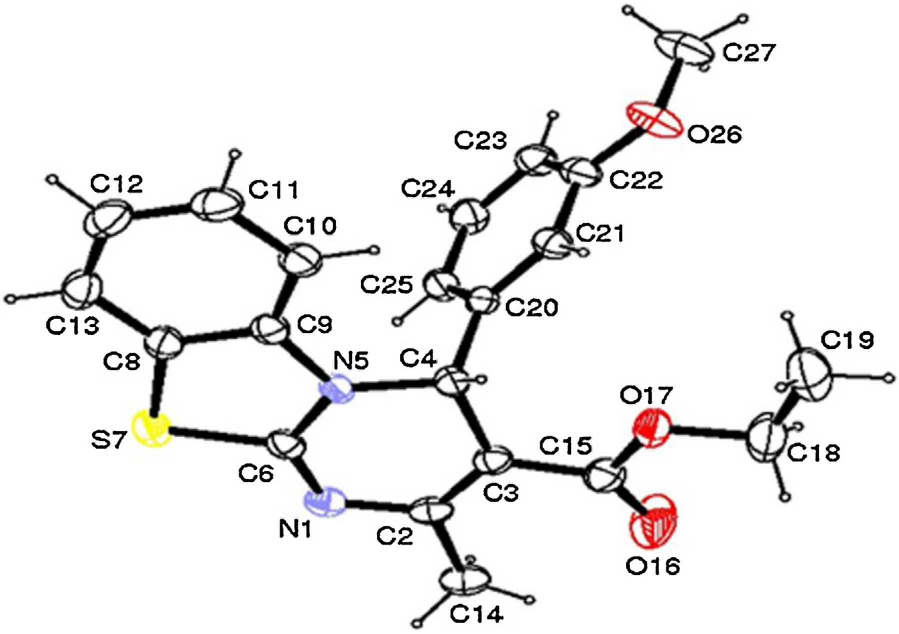

Fig. 7. ORTEP view of Ethyl 2-methyl-4-(3-methoxyphenyl)-4*H*-pyrimido[2,1-*b*][1,3]benzothiazole-3-carboxylate (CCDC No. 1409951).

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, antimony chloride grafted sulfonated 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**

The bold values represent the selected reaction conditions.

[a] Reaction conditions: 2-aminobenzothiazole (1 mmol), 3-nitrobenzaldehyde (1 mmol), ethylacetoacetate (1 mmol) and catalyst (0.1 g for entries 2–5, 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 (1 mmol) and catalyst (0.1 g for entries 2–5, 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_3H [53]	0.08 g	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_3H [39]	0.07 g	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**

The bold values represent the selected reaction conditions.

[a] Reaction conditions: 2-aminobenzothiazole (1 mmol), 4-nitrobenzaldehyde (1 mmol), ethylacetoacetate (1 mmol), C/TiO_2–SO_3–$SbCl_2$ (0.1 g, 1 mol% Sb) at 90 °C under solvent-free conditions.

[b] Reaction conditions: 2-naphthol (1 mmol), benzaldehyde (1 mmol), dimedone (1 mmol), C/TiO_2–SO_3–$SbCl_2$ (0.1 g, 1 mol% Sb) at 100 °C under solvent-free conditions.

[c] Isolated yield.

[d] Turn over frequency.

[e] Our work.

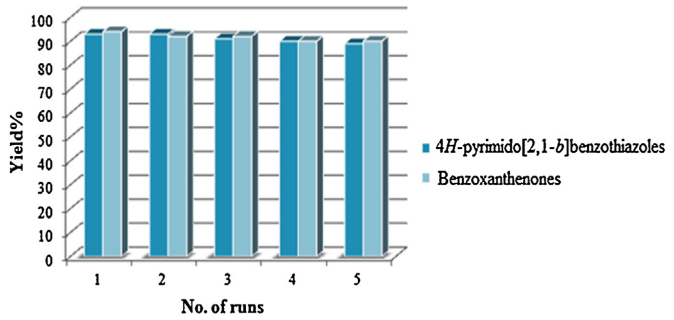

Fig. 8. Recyclability of $C/TiO_2–SO_3–SbCl_2$.
Reaction conditions: 2-aminobenzothiazole (1 mmol), 3-nitrobenzaldehyde (1 mmol), ethylacetoacetate (1 mmol), $C/TiO_2–SO_3–SbCl_2$ (0.1 g, 1 mol% Sb) at 90 °C under solvent-free conditions (Table 4, 5i). Reaction conditions: 2-naphthol (1 mmol), benzaldehyde (1 mmol), dimedone (1 mmol), $C/TiO_2–SO_3–SbCl_2$ (0.1 g, 1 mol% Sb) at 100 °C under solvent-free conditions (Table 5, 11a).

tively (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-up procedure 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.

3.3. *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 °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.

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.

Acknowledgements

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.molcata.2015.11.001.

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ORIGINAL PAPER

A green and convenient approach for the one-pot solvent-free synthesis of coumarins and β-amino carbonyl compounds using Lewis acid grafted sulfonated carbon@titania composite

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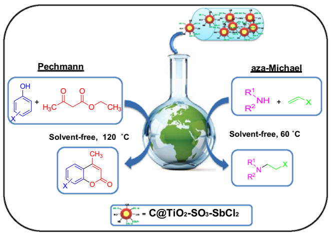
Abstract This paper reports an efficient protocol for the synthesis of coumarins via Pechmann reaction, and β-amino carbonyl compounds via aza-Michael reaction using catalytic amount of solid Lewis acid catalyst, C@TiO$_2$–SO$_3$–SbCl$_2$. Six different catalysts were prepared by covalent immobilization of homogeneous Lewis acids onto sulfonated carbon@titania composite derived from amorphous carbon and nano-titania. Among various catalysts tested, C@TiO$_2$–SO$_3$–SbCl$_2$ showed superior catalytic activity. The catalyst could be recycled without significant loss of its catalytic activity and demonstrated versatile catalysis for a wide range of substrates.

Graphical abstract



Keywords Green chemistry · Heterogeneous catalysis · Lewis acid · One-pot synthesis · Recyclability

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Electronic supplementary material The online version of this article (doi:10.1007/s00706-016-1752-4) contains supplementary material, which is available to authorized users.

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Introduction

Nowadays, organic synthesis has been oriented towards the development of new environmentally benign procedures so as to achieve the goals of "green chemistry" [1, 2]. Catalysis has been known to be an important contributor to enhance the synthetic efficiency in addition to the reduction of chemical waste generation. Lewis acids represent an important class of catalysts that show remarkable catalytic activity in several important organic transformations [3, 4]. The use of conventional Lewis acids, however, requires the presence of strictly anhydrous conditions as the Lewis acids get decomposed or completely deactivated even in the presence of trace amounts of water and are also accompanied with the production of corrosive acid waste that requires additional neutralization step [5]. In comparison with homogeneous analogues, heterogeneous Lewis acid catalysts have several advantages for the development of more sustainable protocols in terms of easy catalyst recovery from reaction media and recyclability up to several catalytic runs.

Coumarins have been known to occupy an important place in the sphere of natural products and synthetic organic chemistry. Natural and synthetic derivatives of coumarins have been shown to possess significant array of pharmacological properties [6–10] including antimicrobial, anticancer, antioxidant, anticoagulant, and anti-inflammatory. Typically, several reactions like Pechmann, Perkin, Knoevenagel, Reformatsky, Wittig, C–C coupling, and cycloaddition reactions have been applied for the synthesis of the coumarin skeleton [7–17]. However, acid catalyzed Pechmann reaction is the simple and most commonly used method for the synthesis of coumarins from activated phenols and β-ketoesters. The aza-Michael addition reaction constitutes an important methodology for the synthesis of β-amino carbonyl compounds that are biologically essential products and also used as key intermediates for the preparation of various β-amino alcohols, chiral auxiliaries, antibiotics, β-amino acids and other nitrogen-containing compounds [18, 19]. Various Bronsted and Lewis acid catalysts have been reported in literature for Pechmann and aza-Michael reaction [20–44] however, such methods suffer from one or more disadvantages like high cost, long reaction times, the requirement of excess reagents or catalysts, harsh reaction conditions, and the use of noxious solvents. Thus, the development of simple, recyclable, and environmentally friendly approach that can be performed under mild conditions for Pechmann and aza-Michael reaction is still desirable.

As part of our ongoing efforts to explore the synthesis and applicability of solid Lewis acids for various organic transformations [45], we have investigated the utility of $C@TiO_2–SO_3–SbCl_2$ for the efficient one-pot synthesis of coumarins via Pechmann reaction and β-amino carbonyl compounds via aza-Michael addition of amines to α,β-unsaturated carbonyl compounds and nitriles.

Results and discussion

Characterization of Lewis acid grafted sulfonated carbon@titania composites

TiO_2, being one of the potential semiconductor photocatalysts, is widely used for the degradation of organic pollutants due to several advantages, like low cost, non-toxicity, and stability [46–48]. Besides, it also finds broad applicability as heterogeneous catalyst support due to its high chemical and thermal stability and large specific surface area. It is known to enhance the activity in many cases due to the strong interaction between the active phase and the support [49]. Titania has been reported to form hybrid composite with carbon materials exhibiting enhanced catalytic activity [50–53]. The carbon material possesses high surface area due to porous structure and thus the resulting composite material can combine the properties of macroporous carbon and titania nanoparticles for applicability as efficient catalyst support for grafting Lewis acids. The detailed characterization of various Lewis acid grafted sulfonated carbon@titania composites has been reported in our previous publication [45]. The surface functionalization and elemental composition has been determined by FT-IR and CHNS analysis. ICP-AES and EDX analysis were used to determine the amount of metal loaded on the composite material. The phase and crystallinity of nano-titania was determined by powder X-ray diffraction (XRD) studies. Scanning electron micrographs and high resolution transmission electron micrographs were used to study the morphological changes and fine structure of $C@TiO_2–SO_3–SbCl_2$. The thermal stability of $C@TiO_2–SO_3–SbCl_2$ was analysed in the temperature range of 40–700 °C by thermal gravimetric analysis (see Supporting information for FTIR, SEM, TEM, HRTEM, EDX, XRD, and TGA). The TGA of $C@TiO_2–SO_3–SbCl_2$ shows the initial weight loss of 2.7 % due to the release of physisorbed water and solvent trapped onto the surface of $C@TiO_2–SO_3–SbCl_2$. Further, a major weight loss of 39 % was observed in the temperature range of 320–600 °C, which can be attributed to the decomposition of Lewis acid and organic moieties (Fig. S6). Thus, it is concluded that $C@TiO_2–SO_3–SbCl_2$ can be used safely below 300 °C.

Catalytic testing for the one-pot synthesis of coumarins via Pechmann reaction

Initially, we examined the catalytic activity of various solid Lewis acids on the model reaction of resorcinol and ethyl acetoacetate for the synthesis of corresponding coumarin derivative. As is clear from the results presented in Table 1, the catalytic performance of different solid Lewis acids screened follows the order: $C@TiO_2–SO_3–SbCl_2 > C@TiO_2–SO_3–FeCl_2 > C@TiO_2–SO_3–AlCl_2 > C@TiO_2–SO_3–BiNO_3 > C@TiO_2–SO_3–SnCl_2 > C@TiO_2–SO_3–Cu(OAc)$. The above order can be accounted for considering the difference in Lewis acid strength of various Lewis acids grafted on the sulfonated carbon@titania composites. The stronger Lewis acids lead to undesirable side reactions whereas the weak ones were less effective, thereby the mild Lewis acid, $SbCl_3$ was found to be most effective in the present case. Thus, $C@TiO_2–SO_3–SbCl_2$ was selected to carry out the Pechmann reaction for the synthesis of coumarin derivatives. Further, to establish the optimized reaction conditions, the model reaction was carried out in the presence of various amounts of catalyst and a range of temperature and solvents for appropriate times to give corresponding coumarin derivative. To study the effect of catalyst amount, the model reaction was performed in the presence of variable catalyst amounts. It was found that with 0.05 g catalyst (0.5 mol% Sb), the reaction yield was only 60 % which increased considerably to 94 % on increasing the catalyst amount to 0.1 g (1 mol% Sb). On further increasing the amount of catalyst, only a marginal increase in the reaction yield was observed (Table 2, entries 1–3). Therefore, 0.1 g $C@TiO_2–SO_3–SbCl_2$ (1 mol% Sb) was identified to be optimum for carrying out the Pechmann condensation. Next we investigated the effect of solvents, by carrying out the reaction using a range of protic/aprotic solvents including ethanol, toluene, acetonitrile, water and also under solvent-free conditions. As is clear from the results shown in Table 3, the best results were achieved under solvent-

Table 1 Comparison of catalytic activities of different Lewis acid grafted sulfonated carbon@titania composites for the one-pot synthesis of coumarins and β-amino carbonyl compounds

Entry	Catalyst	Pechmann reaction[a]		Aza-Michael reaction[b]	
		Time/h	Yield[c]/%	Time/h	Yield[d]/%
1	$C@TiO_2–SO_3–AlCl_2$	2	90	6	90
2	$C@TiO_2–SO_3–FeCl_2$	1	92	5	92
3	$C@TiO_2–SO_3–SbCl_2$	0.75	94	3	93
4	$C@TiO_2–SO_3–SnCl$	3	85	8	90
5	$C@TiO_2–SO_3–Cu(OAc)$	3	80	8	88
6	$C@TiO_2–SO_3–Bi(NO_3)_2$	2	90	6	90

[a] Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1 mmol), Lewis acid grafted sulfonated carbon@titania composites (1 mol% metal) at 120 °C under solvent-free conditions

[b] Reaction conditions: aniline (1 mmol), acrylonitrile (1 mmol), Lewis acid grafted sulfonated carbon@titania composites (1 mol% metal) at 60 °C under solvent-free conditions

[c] Isolated yields

[d] Column chromatography yields

Table 2 Effect of catalyst amount on Pechmann and aza-Michael reaction

Entry	Catalyst[a]/mol%	Pechmann reaction[b]		Aza-Michael reaction[c]	
		Time/min	Yield[d]/%	Time/h	Yield[e]/%
1	0.5	45	60	10	90
2	1	45	94	5	92
3	2	45	95	3	93
4	3	35	95	3	94

[a] Refers to antimony chloride grafted sulfonated carbon@titania composite

[b] Reaction conditions: resorcinol (1 mmol) and ethyl acetoacetate (1 mmol) at 120 °C under solvent-free conditions

[c] Reaction conditions: aniline (1 mmol) and acrylonitrile (1 mmol) at 60 °C under solvent-free conditions

[d] Isolated yields

[e] Column chromatography yields

free conditions. Further, it was observed that the conversion of phenol to corresponding coumarin increased considerably on increasing the reaction temperature from 60 to 120 °C (Table 3, entries 11–14) under solvent-free conditions and any further increase in reaction temperature did not affected the product yield appreciably. Thus, 120 °C was selected as the optimum reaction temperature. We then investigated substrate generality of substituted phenols and ethyl acetoacetate under optimized reaction conditions (Table 4). Pyrogallol, phloroglucinol, and resorcinol afforded excellent yields in shorter reaction times. In general, compared to unsubstituted phenol, substrates with electron-donating groups *para* to the site of electrophilic substitution afforded good yields of corresponding coumarin derivatives, whereas no product formation was observed in case of phenols possessing electron-withdrawing groups. Longer reaction time was needed in case of 1-naphthol and phenol probably due to the presence of another phenyl ring in case of 1-naphthol and unactivated ring in case of phenol.

Catalytic testing for the one-pot synthesis of β-amino carbonyl compounds via aza-Michael reaction

To explore the catalytic activity of different Lewis acid catalysts, the model reaction of aniline and acrylonitrile was investigated for the synthesis of corresponding β-amino carbonyl compound. As can be seen from the results summarised in Table 1, $C@TiO_2–SO_3–SbCl_2$ again displayed higher catalytic activity compared to other Lewis acid catalysts. Further, to determine the effect of catalyst loading, the model reaction was carried out in the presence of different amounts of catalyst and it was observed that the variation of $C@TiO_2–SO_3–SbCl_2$ amount had an effective influence on the reaction. We

Table 3 Effect of different solvents and reaction temperature on C@TiO_2–SO_3–$SbCl_2$ catalyzed Pechmann condensation and aza-Michael reaction

Entry	Solvent	Temp/°C	Pechmann reaction[a]		Aza-Michael reaction[b]	
			Time/h	Yield[c]/%	Time/h	Yield[d]/%
1	Ethanol	60	–	–	3	82
2	Ethanol	Reflux	4	64	–	–
3	Acetonitrile	60	–	–	3	86
4	Acetonitrile	Reflux	4	52	–	–
5	Toluene	Reflux	2	80	–	–
6	DCM	60	–	–	3	70
7	Water	60	–	–	3	79
8	Water	Reflux	24	Trace	–	–
9	Solvent-free	rt	10	Trace	8	45
10	Solvent-free	50	–	–	3	88
11	Solvent free	60	3	40	3	93
12	Solvent-free	90	3	84	–	–
13	Solvent-free	100	2	90	–	–
14	Solvent-free	120	0.75	94	–	–
15	Solvent-free	130	0.66	95	–	–

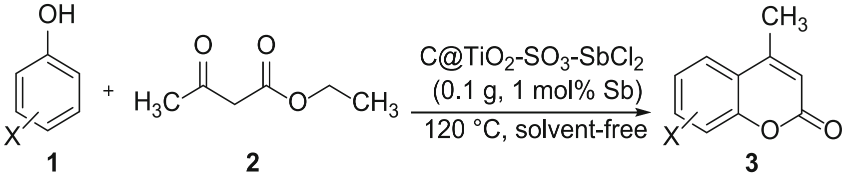
[a] Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1 mmol), and 0.1 g C@TiO_2–SO_3–$SbCl_2$ (1 mol% Sb)

[b] Reaction conditions: aniline (1 mmol), acrylonitrile (1 mmol), and 0.2 g C@TiO_2–SO_3–$SbCl_2$ (2 mol% Sb)

[c] Isolated yields

[d] Column chromatography yields

Table 4 C@TiO_2–SO_3–$SbCl_2$ catalyzed one-pot synthesis of coumarins



Entry	X (Product **3**)	Time/h	Yield[a]/%
1	7-OH	0.75	94
2	8-OH	1	88
3	7,8-$(OH)_2$	0.75	90
4	5,7-$(OH)_2$	0.75	92
5	6-CH_3	1.5	93
6	7-CH_3	1.5	90
7	7-OCH_3	1.5	91
8	6-OH	1	92
9	7,8-Benzo	2.5	88
10	H	3.5	85

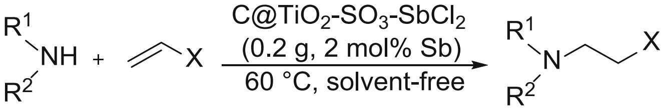
Reaction conditions: amine (1 mmol), alkene (1 mmol), and C@TiO_2–SO_3–$SbCl_2$ (0.2 g, 2 mol% Sb) at 60 °C under solvent-free conditions

[a] Isolated yield

observed that 0.2 g of the catalyst could catalyze the aza-Michael reaction efficiently affording the desired product in 93 % yield (Table 2, entry 3); increasing or decreasing the amount of the catalyst did not lead to any improvement in the yields. The model reaction was then carried out in several solvents such as EtOH, CH_3CN, DCM, H_2O and under solvent-free conditions (Table 3, entries 1, 3, 6, 7 and 9–11) to investigate the efficiency of the catalyst. In this study, it was found that conventional heating at 60 °C under solvent-free conditions is more efficient than using organic solvents, with respect to reaction time and yield of the desired *β*-amino carbonyl compound. Using the optimized reaction conditions, several structurally varied amines with electron-donating and electron-withdrawing groups were coupled with α,*β*-unsaturated carbonyl compounds and nitriles, and the results are summarized in Table 5. Both aromatic and aliphatic amines gave the corresponding *β*-amino carbonyl compounds in good yields. Aliphatic amines due to their high nucleophilicity in comparison to aromatic amines underwent the aza-Michael addition in shorter reaction times. In addition, the aza-Michael reaction of various substituted amines with ethyl acrylate was found to be faster in comparison to acrylonitrile due to high reactivity of ethyl acrylate in comparison to acrylonitrile.

In order to compare the catalytic activity of C@TiO_2–SO_3–$SbCl_2$, catalytic experiments were conducted using various homogeneous and heterogeneous acid catalysts under the same reaction conditions as well as in the absence of any catalyst. As expected, the condensation did not proceed without catalyst (Table 6, entry 1). It can be seen that homogeneous catalysts such as H_2SO_4 and *p*-toluenesulfonic acid (Table 6, entries 2, 3) are less efficient. Further, it was also observed that poor yields of the corresponding coumarin derivative and aza-Michael product were obtained when nano-titania, amorphous carbon, and carbon@titania were employed as catalysts (Table 6, entries 4, 5, and 6). The homogeneous $SbCl_3$ showed marked catalytic activity but suffers from the hazards associated with the use of conventional homogeneous Lewis acids, such as requirement of more than stoichiometric amount of Lewis acid, decomposition during work-up, non-recovery, and reusability of the catalyst. Remarkably, it can be seen that C@TiO_2–SO_3–$SbCl_2$ with lower catalyst loading exhibits high activity in Pechmann reaction and aza-Michael reaction under the same reaction conditions along with the added advantages of catalyst recovery and reusability (Table 6, entry 9). Further, to study the merits of the current protocol for the synthesis of coumarins and *β*-amino carbonyl compounds, a

Table 5 C@TiO_2–SO_3–$SbCl_2$ catalyzed one-pot synthesis of *β*-amino carbonyl compounds via aza-Michael reaction



Entry	Amine	*X* (Alkene)	Time/h	Yield[a]/%
1	Aniline	CN	3	93
2	4-Methylaniline	CN	3	90
3	4-Methoxyaniline	CN	3.5	89
4	4-Chloroaniline	CN	3.5	95
5	4-Fluoroaniline	CN	3	92
6	4-Bromoaniline	CN	3.5	90
7	Morpholine	CN	1.5	88
8	Piperidine	CN	1.5	89
9	Aniline	COOEt	1	92
10	4-Methoxyaniline	COOEt	2	90
11	4-Chloroaniline	COOEt	2	93
12	4-Bromoaniline	COOEt	2	90
13	Morpholine	COOEt	2	85
14	Piperidine	COOEt	2.5	87

Reaction conditions: amine (1 mmol), alkene (1 mmol), and C@TiO_2–SO_3–$SbCl_2$ (0.2 g, 2 mol% Sb) at 60 °C under solvent-free conditions

[a] Column chromatography yield

Table 6 Comparison of catalytic activity of C@TiO$_2$–SO$_3$–SbCl$_2$ with various homogeneous and heterogeneous catalysts for Pechmann and aza-Michael reaction

Entry	Catalyst	Pechmann reaction[a]		Aza-Michael reaction[b]	
		Time/h	Yield[c]/%	Time/h	Yield[d]/%
1	None	3	NR	7	Trace
2	H_2SO_4	2	30	–	–
3	p-TSOH	2	40	–	–
4	Nano-titania	2	10	5	15
5	Amorphous carbon	2	10	5	12
6	Non-sulfonated carbon@titania	2	20	5	20
7	Sulfonated amorphous carbon	2	35	5	60
8	Anhyd. $SbCl_3$	0.5	93	3	88
9	C@TiO$_2$–SO$_3$–SbCl$_2$	0.75	94	3	93

[a] Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1 mmol), and catalyst (1 mol% for entries 2 and 3, 0.1 g for entries 4–7, 9, 1 mol% $SbCl_3$ for entry 8) at 120 °C under solvent-free conditions

[b] Reaction conditions: aniline (1 mmol), acrylonitrile (1 mmol), and catalyst (1 mol% for entries 2 and 3, 0.1 g for entries 4–7, 9, 1 mol% $SbCl_3$ for entry 8) at 60 °C under solvent-free conditions

[c] Isolated yields

[d] Column chromatography yields

comparison of the efficacy of C@TiO$_2$–SO$_3$–SbCl$_2$ with some of the reported catalytic systems in the literature was done. As is clear from the results presented in Table 7, the present catalytic system affords high product yield in shorter reaction times with low loading amounts of the Lewis acid catalyst in comparison to others reported in literature (Table 7). In addition, the present protocol comparatively affords a truly green process using benign reaction media and heterogeneous Lewis acid catalyst.

Effect of pH on the stability and activity of C@TiO$_2$–SO$_3$–SbCl$_2$

The effect of pH on the stability of C@TiO$_2$–SO$_3$–SbCl$_2$ was examined by dispersing 50 mg of the catalyst in four different solutions having pH 3, 6, 8, and 10. These suspensions were allowed to remain as such for 24 h and afterwards magnetically stirred and filtered to separate the catalyst. The supernatant was examined by ICP-AES analysis to

Table 7 Comparison of the catalytic activity of C@TiO$_2$–SO$_3$–SbCl$_2$ with reported catalytic systems for the Pechmann and aza-Michael reaction

Reaction	Catalyst	Reaction conditions	Yield[c]/%	Time/h
Pechmann reaction[a]	Zeolite BEA [54]	$PhNO_2$, 130 °C, catalyst (0.2 g)	85	4
	ZAF-16 [55]	Toluene, 120 °C, catalyst (1.0 g)	65.1	4
	SO_4^{2-}/SnO_2 [56]	Solvent-free, 120 °C, catalyst (1.0 g)	78.3	2
	PANF-PAMSA [57]	Toluene, 110 °C	95	4
	C@TiO$_2$–SO$_3$–SbCl$_2$[e]	Solvent-free, 120 °C, C/TiO$_2$–SO$_3$H (0.1 g, 1 mol% Sb)	94	0.75
Aza-Michael reaction[b]	$FeCl_3$/mont. K10 [58]	Solvent-free, 60 °C, catalyst (10 wt%)	85[d]	5
	$SbCl_3$-HAP [59]	CH_3CN, N_2, 50 °C, 1.6 mol% catalyst	NR	10
	[DPPA] [HSO_4] [60]	H_2O, rt, catalyst (1 mmol)	90[d]	4
	TMSCl [61]	Solvent-free, 60 °C, TMSCl (10 mol%)	80[d]	3
	C@TiO$_2$–SO$_3$–SbCl$_2$[e]	Solvent-free, 60 °C, C/TiO$_2$–SO$_3$H (0.2 g, 2 mol% Sb)	94[d]	0.25

[a] Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1 mmol), and 0.1 g C@TiO$_2$–SO$_3$–SbCl$_2$ (1 mol% Sb) at 120 °C under solvent-free conditions

[b] Reaction conditions: aniline (1 mmol), acrylonitrile (1 mmol), and 0.2 g C@TiO$_2$–SO$_3$–SbCl$_2$ (2 mol% Sb) at 60 °C under solvent-free conditions

[c] Isolated yields

[d] Column chromatography yields

[e] Our work

determine any possibility of leaching of the Lewis acid. It was observed that no significant leaching was detected for solutions with pH 3, 6, and 8, whereas only a small amount of leached antimony was detected for solution with pH 10. These observations indicate that catalyst is stable in acidic and weakly basic conditions, whereas its stability is affected in the presence of strongly basic conditions. Further, to evaluate the effect of pH on catalytic activity of C/TiO_2–SO_3–$SbCl_2$, the test reaction in case of Pechmann reaction and aza-Michael addition (Table 4, entry 1; Table 5, entry 1) was carried out under the optimized conditions in the presence of C@TiO_2–SO_3–$SbCl_2$ separated from the respective suspensions (Table 8). The results indicated that there is no significant effect on the catalytic activity of C@TiO_2–SO_3–$SbCl_2$ in acidic and weakly basic conditions. Whereas, in strongly basic condition, the reaction time was enhanced as well as the yield of the products in both the reactions was also decreased (Table 8, entry 4). Thus, it can be concluded that in strongly basic conditions the catalytic stability and activity is affected to a small extent, whereas in acidic and weakly basic conditions, the catalyst maintains its activity and stability.

Recyclability

The stability and sustained catalytic activity of a catalyst is an important aspect to be considered from economic point of view. The catalyst reusability contributes to reduce the cost of the practical application processes. The reusability of the catalyst was thus investigated in the Pechmann and aza-Michael reaction. The catalyst was easily recovered after the reaction by simple filtration and washed with distilled water, followed by drying and then reused for further reactions (Table 4, entry 1; Table 5, entry 1). To our delight, the catalytic activity of the catalyst had only a slight change after five catalytic runs (Fig. 1), suggesting

Table 8 Effect of pH on the catalytic activity of C@TiO_2–SO_3–$SbCl_2$ for the Pechmann and aza-Michael reaction

Entry	pH	Pechmann[a]		Aza-Michael[b]	
		Time/h	Yield[c]/%	Time/h	Yield[d]/%
1	3	0.75	93	3	94
2	6	0.75	94	3	94
3	8	0.75	92	3	92
4	10	1.25	88	4	85

[a] Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1 mmol), and 0.1 g C@TiO_2–SO_3–$SbCl_2$ (1 mol% Sb) at 120 °C under solvent-free conditions

[b] Reaction conditions: aniline (1 mmol), acrylonitrile (1 mmol), and 0.2 g C@TiO_2–SO_3–$SbCl_2$ (2 mol% Sb) at 60 °C under solvent-free conditions

[c] Isolated yields

[d] Column chromatography yields

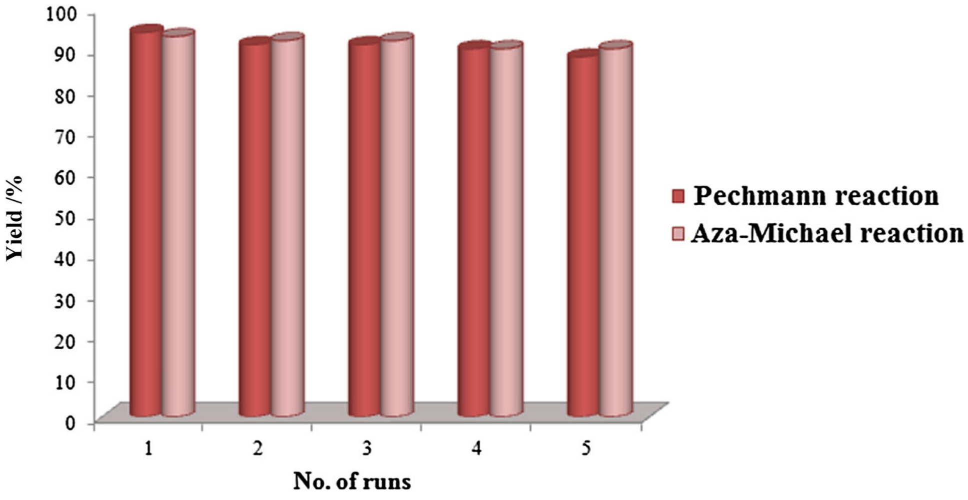


Fig. 1 Recyclability of C@TiO_2-SO_3-$SbCl_2$. Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1 mmol), 0.1 g C@TiO_2-SO_3-$SbCl_2$ (1 mol% Sb) at 120 °C under solvent-free conditions; aniline (1 mmol), acrylonitrile (1 mmol), 0.2 g C@TiO_2-SO_3-$SbCl_2$ (2 mol% Sb) at 60 °C under solvent-free conditions

the high chemical stability of the heterogeneous Lewis acid catalyst.

Further, the thermal stability of the catalyst after five reaction cycles was determined by carrying out the TG analysis. It was observed that the reused catalyst exhibited almost the same TG curve as the fresh one (Fig. 2) depicting that the present heterogeneous system shows high thermal stability after successive reaction cycles. Meanwhile, there was no significant decrease in the amount of metal after five cycles as determined from ICP analysis of heterogeneous Lewis acid catalyst.

Conclusion

To sum up, we have introduced an efficient and clean procedure for the excellent one-pot synthesis of coumarins via Pechmann reaction, and β-amino carbonyl compounds via aza-Michael reaction using C@TiO$_2$–SO$_3$–SbCl$_2$ as the heterogeneous Lewis acid catalyst. Low catalyst loading (1 mol%), quantitative yields of products, short reaction times, recyclability up to five consecutive runs without significant loss of activity, and easy separation are salient features of this catalytic system. The applicability of the

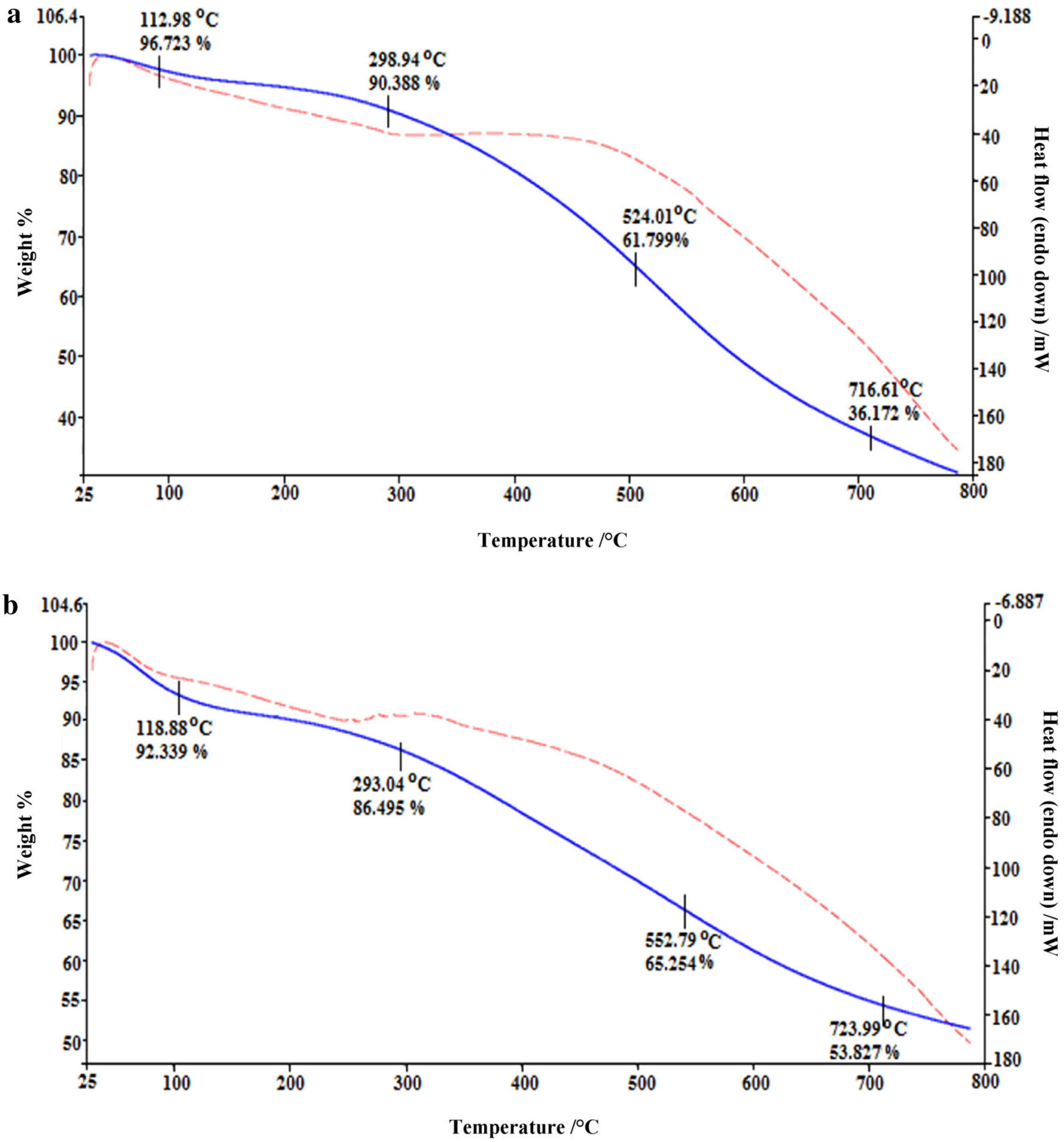


Fig. 2 TGA of **a** fresh C@TiO$_2$-SO$_3$-SbCl$_2$; **b** C@TiO$_2$-SO$_3$-SbCl$_2$ after five catalytic runs

present catalytic system is being extended to other acid catalyzed organic reactions.

Experimental

The chemicals used were purchased from Aldrich chemical company and Merck, and used without further purification. The products were characterized by their spectral data and comparison of their physical data with those of known samples. The ^{1}H and ^{13}C NMR data were recorded in $CDCl_3$ or DMSO-d_6 or $CDCl_3$ + DMSO-d_6 or CD_3COCD_3 on Bruker Avance III (400 MHz) spectrometer. The FT-IR 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 Esquire 3000 (ESI). CHNS analysis was recorded on ThermoFinnigan FLASH EA 1112 series. SEM images were recorded using JEOL Model JSM-6390LV Scanning Electron Microscope, 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.

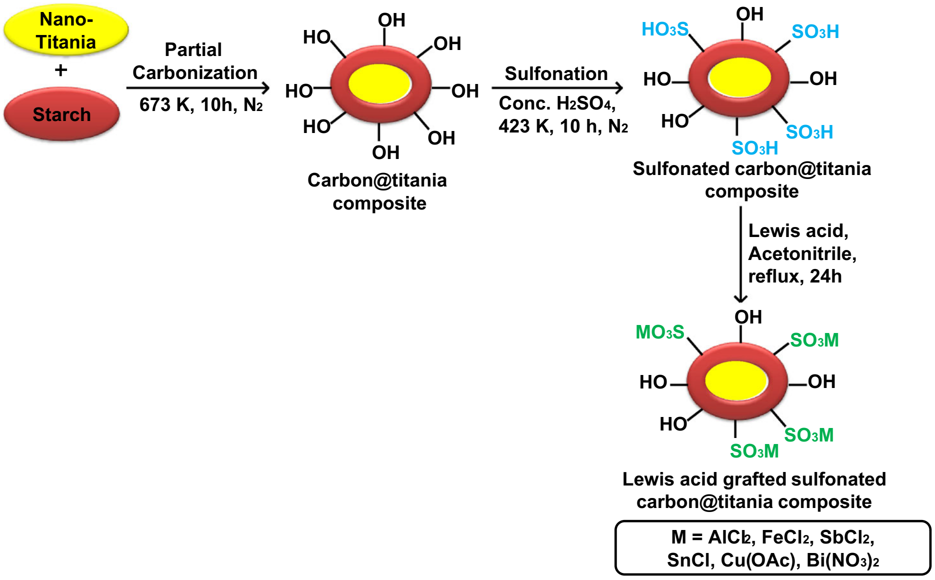
General procedure for the synthesis of Lewis acid grafted sulfonated carbon@titania composites

The general procedure for the synthesis of Lewis acid grafted sulfonated carbon@titania composites is represented in Scheme 1. Initially carbon@titania composites were prepared by taking 10 g of a mixture of starch and nano-titania in the ratio of 1:1.2 in a round-bottom flask and then heating the mixture at 353 K for 10 h. Afterwards, the incomplete carbonization of resulting mixture was done by heating it strongly at 673 K under N_2 atmosphere for 10 h leading to the formation of amorphous carbon@titania composites. The sulfonation of the as prepared composite was done by adding concentrated sulfuric acid (>96 wt%) and further heating it at 423 K for 10 h under N_2 atmosphere. The sulfonated composite thus 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 composite was 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 10 cm^3 acetonitrile 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.

General procedure for the $C@TiO_2–SO_3–SbCl_2$ catalyzed synthesis of coumarins via Pechmann reaction

In a 25 cm^3 round bottom flask, 0.1 g $C@TiO_2–SO_3–SbCl_2$ (1 mol% Sb) was added to the mixture of phenolic

Scheme 1



compound (1 mmol) and ethyl acetoacetate (1 mmol) and the reaction mixture was stirred for the appropriate time at 120 °C under solvent-free conditions. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was diluted with 30 cm^3 hot ethanol and the catalyst was separated by simple filtration to obtain the crude product. Compounds with purity below 95 % were further purified using column chromatography on silica gel and then recrystallized from hot ethanol to afford the pure coumarin derivatives.

General procedure for the C@TiO_2–SO_3–$SbCl_2$ catalyzed synthesis of *β*-amino carbonyl compounds via aza-Michael reaction

A mixture of amine (1 mmol), α,*β*-unsaturated compound (acrylonitrile or ethyl acrylate, 1 mmol) and 0.2 g C@TiO_2–SO_3–$SbCl_2$ (2 mol% Sb) was taken in a 25 cm^3 round bottom flask and stirred at 60 °C under solvent-free conditions for the appropriate time. After completion of the reaction (as monitored by TLC), the reaction mixture was diluted with 30 cm^3 ethyl acetate and filtered. The organic layer was washed with 100 cm^3 water and dried over anhydrous Na_2SO_4. The combined organic layer was concentrated in vacuum to give the crude product which was purified by column chromatography.

The products were characterized by comparison of their ^1H and ^{13}C NMR, mass spectral data, and elemental analysis with those of authentic samples obtained commercially or prepared according to the literature methods.

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Ionic liquid coated sulfonated carbon@titania composites for the one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones in aqueous media

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Abstract

A highly active and stable ionic liquid based novel solid Bronsted acid catalysts (C@TiO_2-SO_3H-ILs) have been prepared by coating a long chain ionic liquid onto sulfonated carbon@titania composites. The ionic liquid coating resulted in efficient stability and activity of C@TiO_2-SO_3H-ILs in aqueous conditions by creating hydrophobic environment on the catalyst surface. The catalytic activity of the newly designed catalysts was tested in the one-pot multicomponent synthesis of indeno[1,2-*b*]indole-9,10-diones and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones in aqueous media. The structure of most active catalyst, C@TiO_2-SO_3H-IL1 before and after the coating with ionic liquid was investigated by FTIR, TGA, XRD, CHNS, EDX, SEM and HRTEM. The catalyst allows easy recovery and excellent reusability upto five catalytic runs without considerable loss of activity.

Keywords

Ionic liquid coated solid acid, indeno[1,2-*b*]indolones-9,10-diones, 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones, recyclability, aqueous conditions

1. Introduction

In recent times, the prime focus of every synthetic process in industrial manufacture or laboratory synthesis is the minimization of environmental pollution. However, large volumes of toxic and polluting solvents are being released in the surroundings after every synthetic step, thereby causing negative impact on the environment. Thus, carrying out the organic

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reactions in benign reaction media like water can be of great help in reducing the toxic effects of the commonly used organic solvents. Water is considered as the most benign solvent and organic reactions involving water as solvent are very significant from a green chemistry perspective. The unique properties of water including high dielectric constant and cohesive energy density[1] accelerate several reactions and moreover, it is readily available, inexpensive, non-flammable, environmentally benign, neutral, and non-toxic. In addition, it is also known to promote selectivity in various organic transformations owing to its strong hydrogen bonding ability[2,3]. In spite of several potential advantages, one major drawback associated with the use of water as solvent is that most organic compounds do not dissolve in water to a significant extent, and solubility is generally considered a pre-requisite for reactivity. Thus, synthetic strategies promoting water based organic transformations have been widely explored to broaden the scope of water as an effective reaction media.

Another major concern relating to environmental protection is limiting the use of corrosive and often toxic homogeneous mineral acids, and developing novel heterogeneous catalysts that can overcome their drawbacks. Use of solid acid catalysts is an attractive solution to this problem because of their easy separation and facile recycling.

Thus, it is desirable to synthesize new heterogeneous acid catalysts that show high stability and activity in aqueous conditions. In this regard, ionic liquid based catalytic systems are being investigated, and have been reported to enhance both the catalytic activity and selectivity of some organic reactions in aqueous media. Valkenberg and co-workers introduced the idea of ionic liquid coated solid acids and reported the immobilization of chloroaluminate(III) and chloroferrate(III) ionic liquids onto different solid supports[4-6]. Later, Mehnert *et al*. and Fehrmann *et al.* developed supported ionic liquid phase (SILP) catalysts by the immobilization of monophosphine ligands dissolved in ionic liquid onto a modified silica support, thereby combining the advantages of the solid support and solution

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chemistry[7,8]. Further, Gu *et al*. reported that coating of ionic liquid onto the catalyst surface creates a hydrophobic environment on the catalytic surface in water, thereby resulting in better diffusion of organic substrates to the catalytically active sites. Due to the insolubility of the ionic liquid in water, it remains bonded to the catalyst surface leading to minimal leaching, thus enhancing the stability of the catalyst in aqueous reaction media[9-11]. In addition, it has been reported that the solid acids are rapidly deactivated in aqueous media[12]. A coating of ionic liquid layer in such cases surrounds the acidic groups and prevents its deactivation. The ionic liquid coating thus retains the activity of acidic groups in water, and hence the catalyst could be recycled and reused for further reaction cycles without appreciable loss of activity. Further, the ionic liquid coating creates an efficient hydrophobic environment on the catalyst surface that provides protection against the hydrolysis of the support material[9]. Therefore, ionic liquid based catalytic systems can be explored further for the development of novel solid acid catalysts that show enhanced stability in aqueous conditions.

Indeno[1,2-*b*]indoles represent a system of annulated 6-5-5-6-membered rings that form important class of heterocyclic compounds due to their potential biological applications. Indeno[1,2-*b*]indole moiety serves as ATP/GTP-competitive inhibitors of CK2 and act as DNA-intercalators and inhibitors of topoisomerase II with considerable cytotoxic activity towards cancer cells[13]. Despite their immense pharmacological importance, only a few reports are available in the literature concerning their synthesis[14] and most of them suffer from limitations such as low product yield, high reaction time, multistep syntheses and less substrate scope. Pyrazolo[1,2-*b*]phthalazine-diones are an important class of biologically active heterocyclic compounds that are present in the structures of a number of compounds showing anti-inflammatory, anti-allergic, analgesic, antihypoxic, anti-convulsant, cardiotonic, vasorelaxant, antipyretic anti-hyperglycemic, anti-bacterial, and anti-viral activities[15-17].

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These have also found diverse pharmaceutical applications as anti-cancer[18] and anti-diabetic agents[18]. Due to the interesting properties of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones, several novel catalysts have been developed and employed to allow facile access to this heterocyclic scaffold[20-23]. However, many of the reported methodologies suffer from the use of homogeneous acids, creating hazards for the operator, reactor corrosion and downstream waste problems. Thus, there is ample scope for the development of new sustainable protocols for the multicomponent synthesis of indeno[1,2-*b*]indole-9,10-diones and 1*H*- pyrazolo[1,2-*b*]phthalazine-5,10-diones.

In the present work, we report the synthesis of a novel solid acid catalyst that has high stability and activity in aqueous media. For this purpose, firstly we prepared a solid Bronsted acid catalyst (C@TiO_2-SO_3H) derived by the partial carbonization of starch in presence of nano-titania followed by sulfonation. Hara et al. reported for the first time the use of amorphous carbon bearing sulfonic acid groups as an efficient solid acid catalyst[24]. C@TiO_2-SO_3H was thereafter coated with imidazolium based ionic liquid having a long hydrophobic chain in its cation to get C@TiO_2-SO_3H-ILs. The catalytic activity of the synthesized catalyst was investigated for the one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones in water.

2. Results and Discussion

2.1 Synthesis and characterization of ionic liquid coated sulfonated carbon@titania composites

Sulfonated carbon@titania composites were prepared by the partial carbonization of starch and nano-titania followed by sulfonation using sulfuric acid. The composites were then coated with ionic liquid, 1-decyl-3-methyl-imidazolium chloride [dmim][Cl] to get C@TiO_2-SO_3H-IL1 (1-decyl-3-methyl-imidazolium chloride coated sulfonated carbon@titania composite) and 1-decyl-3-methyl-imidazolium tetrafluoroborate [dmim][BF_4] to get

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C@TiO_2-SO_3H-IL2 (1-decyl-3-methyl-imidazolium tetrafluoroborate coated sulfonated carbon@titania composite). The general procedure for the synthesis of ionic liquid coated sulfonated carbon@titania composites is represented in **Scheme 1**. Since, the hydrophobicity of ionic liquid is influenced by its cation and an increase in the alkyl chain length results in an increase in hydrophobicity of the corresponding ionic liquid[24], we have selected imidazolium based ionic liquid having a decyl carbon chain in its cation for the synthesis of C@TiO_2-SO_3H-ILs. The ionic liquid (IL) is bounded to the sulfonated composite (C@TiO_2-SO_3H) by electrostatic interactions, and the cohesion between the catalyst and IL is ensured by the hydrophobic nature of IL which is responsible for the insolubility of IL in water. As a result of this insolubility, the IL remains adsorbed onto the catalyst surface during the reaction and hence, no leaching of IL occurs. Ionic liquid coated sulfonated carbon@titania composites (C@TiO_2-SO_3H-IL1 and C@TiO_2-SO_3H-IL2) were characterized by FTIR and TGA. The most active catalyst, C@TiO_2-SO_3H-IL1 was further characterized by XRD, CHNS, EDX, SEM and HRTEM.

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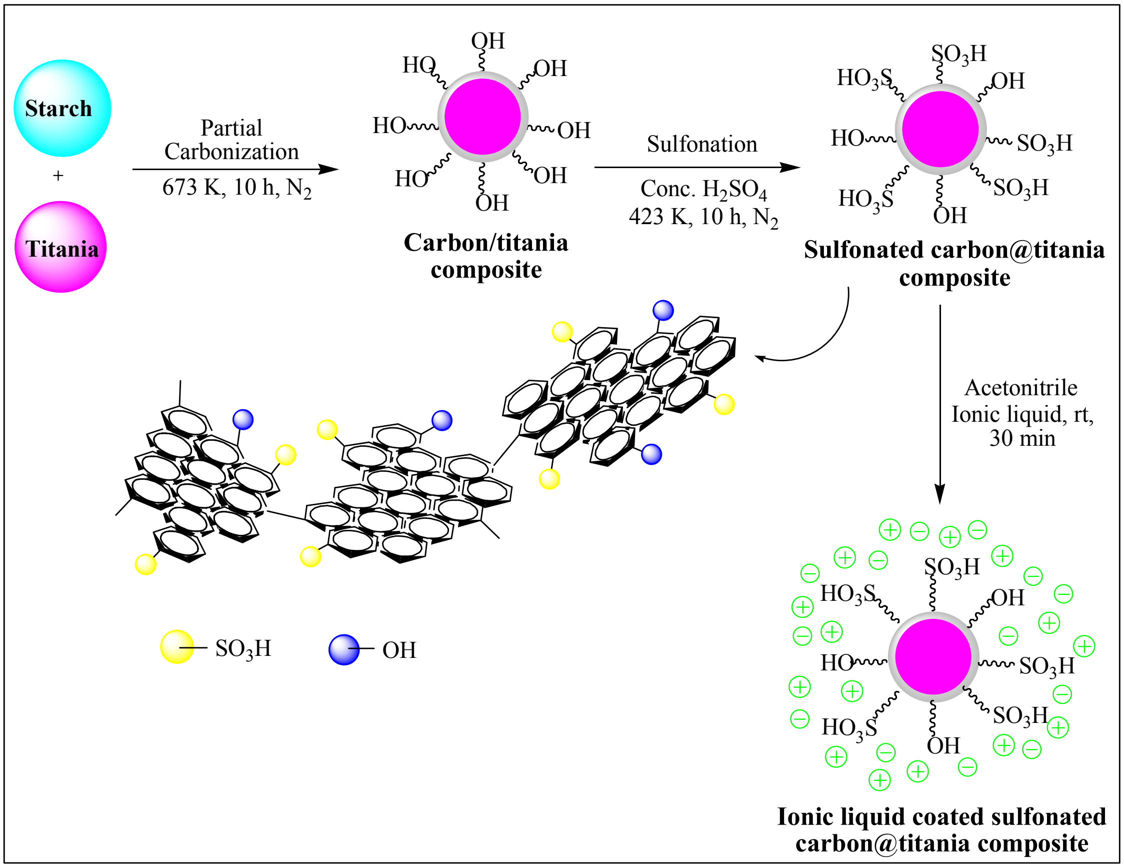

Scheme 1. General scheme for the synthesis of ionic liquid coated sulfonated carbon@titania composites.

FTIR

The detailed investigation of the functionalization of C@TiO_2-SO_3H-ILs was done by FTIR spectroscopy. The FTIR spectra of C@TiO_2-SO_3H-IL1, C@TiO_2-SO_3H-IL2 as well as C@TiO_2-SO_3H are shown in **Fig. 1**. The broad peaks appeared around 3500 cm^{-1} in all the three samples are due to phenolic -OH groups of the polyaromatic carbon rings. **Fig. 1b,c** shows the presence of bands in the range 3140-3150 and 3080-3095 cm^{-1} corresponding to imidazolium -CH stretching, and 2890-2950 and 2830-2850 cm^{-1} due to asymmetric stretching of $-CH_3$, $-CH_2$ and symmetrical stretching of $-CH_2$ groups respectively. These bands correspond to the presence of alkyl chains, indicating the successful coating of ionic

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liquid in C@TiO_2-SO_3H-ILs. Similar bands are absent in the spectra of parent material, C@TiO_2-SO_3H. Further, the peaks in the range 1710-1720 and 1570-1585 cm^{-1} in all the samples can be attributed to C=O and aromatic C=C stretching vibration modes. The C=O groups are produced by the oxidation of carbon with the sulfuric acid used for sulfonation. The spectra of C@TiO_2-SO_3H-IL1 and C@TiO_2-SO_3H-IL2 also shows the presence of additional bands in the range 1420-1430, 1275-1280 and 1220-1230 cm^{-1} attributable to C=N stretching, C-H in-plane and N-H in-plane-bending modes of the imidazole ring. Moreover, bands in the region 705-715 and 684-670 cm^{-1} corresponding to the out of plane -CH bending and C_2-N_1-C_5 bending modes of imidazole ring respectively are also observed. The presence of –SO_3H groups in all the samples is confirmed by the bands at 1160-1170 and 1035-1040 cm^{-1} due to characteristic asymmetric and symmetric stretching modes of SO_2 group respectively. The bands at 620-630 cm^{-1} in all the samples are characteristic of Ti-O stretching frequency, attributable to TiO_2[26].

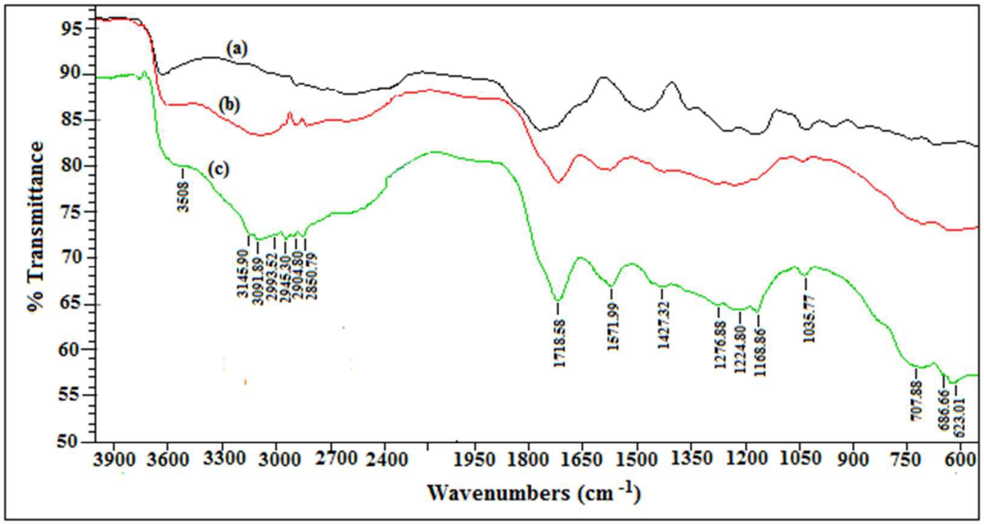

Fig. 1 FTIR spectra of **(a)** C@TiO_2-SO_3H; **(b)** C@TiO_2-SO_3H-IL2; and **(c)** C@TiO_2-SO_3H-IL1

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TGA

The thermal stability of C@TiO_2-SO_3H-ILs was determined by thermogravimetric analysis (**Fig. S1, ESI**). The initial weight loss of 3.9% in C@TiO_2-SO_3H-IL1 and 6.4% in C@TiO_2-SO_3H-IL2 upto 95 °C resulted from the release of adsorbed water and solvent trapped on the surface of ionic liquid coated sulfonated carbon@titania composites. The organic moieties of C@TiO_2-SO_3H-ILs were decomposed in the temperature range of 260-700 °C. As seen in **Fig. S1**, the decomposition of organic compounds takes place in two steps. The major weight loss in the temperature range of 260-420 °C is attributed to the decomposition of ionic liquid coated on the surface of C@TiO_2-SO_3H-ILs. It corresponds to ionic liquid loading of 16.2 wt% on C@TiO_2-SO_3H-IL1 and 13.8 wt% on C@TiO_2-SO_3H-IL2. The other major weight loss in the temperature range of 420-700 °C resulted from the complete decomposition of the residual organic moieties. Thus, from the thermal analysis, it is clear that C@TiO_2-SO_3H-IL1 is thermally stable upto 290 °C, C@TiO_2-SO_3H-IL2 is thermally stable upto 260 °C and these can be safely used for carrying out organic reactions at 100 °C. The major weight losses of C@TiO_2-SO_3H-IL1 and C@TiO_2-SO_3H-IL2 are represented in **Table 1**.

Table 1. Thermogravimetric analysis representing major weight losses in C@TiO_2-SO_3H-IL1 and C@TiO_2-SO_3H-IL2

Entry	**Catalyst**	**Loss of water and residual solvent (°C)**	**Loss of ionic liquid (°C)**	**Loss of residual organic functionality (°C)**
1	C@TiO_2-SO_3H-IL1	95	290-420	420-700
2	C@TiO_2-SO_3H-IL2	90	260-410	410-700

CHNS

The loading of sulfur onto C@TiO_2-SO_3H-ILs was determined by elemental analysis and found to be 8.7 wt% equivalent to 0.27 mmole of S present per gram of C@TiO_2-SO_3H-ILs. The amount of sulfur loaded corresponds to sulfonic acid density of 2.32 mmole g^{-1} of the

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C@TiO_2-SO_3H-ILs. The loading of IL obtained from TGA was found to be in good agreement with elemental analysis. The nitrogen content as determined from elemental analysis depicted that 16 wt% IL equivalent to 0.62 mmole g^{-1} was coated onto C@TiO_2-SO_3H-IL1.

EDX

The chemical purity of C@TiO_2-SO_3H-IL1 as well as its stoichiometry was analysed by EDX studies. The energy dispersive X-ray (EDX) spectrum of C@TiO_2-SO_3H-IL1 (**Fig. S2, ESI**) showed the presence of Cl in addition to C, S, O and Ti, which revealed the successful grafting of ionic liquid on the surface of sulfonated carbon@titania composites.

XRD

The crystallinity of the titania nano-particles in C@TiO_2-SO_3H-IL1 was analyzed by XRD (**Fig. S3, ESI**). The XRD pattern exhibited well defined sharp peaks at 2θ values of 25.4°, 41.4°, 48.2°, 54.4° and 62.8°, those can be ascribed to the typical (101), (004), (200), (211) and (204) diffractions of anatase TiO_2. In addition, peaks at $2\theta = 27.4°$, 36.1°, 56.6° agreeing well with the (110), (101) and (211) diffractions of rutile TiO_2 were also observed[15]. A broad diffraction peak in the range $2\theta = 20\text{-}30°$ can also be seen, which can be attributed to the presence of amorphous carbon in C@TiO_2-SO_3H-IL1[27]. The average crystallite size of titania nano-particles was determined using Debye-Scherrer equation and was found to be 56.2 nm. On comparison of the XRD pattern of C@TiO_2-SO_3H and C@TiO_2-SO_3H-IL1, it was found that the coating of ionic liquid, [dmim][Cl] on the surface of sulfonated composites did not significantly affect the structure of titania nanoparticles and they both match well with the data for standard tetragonal TiO_2 sample.

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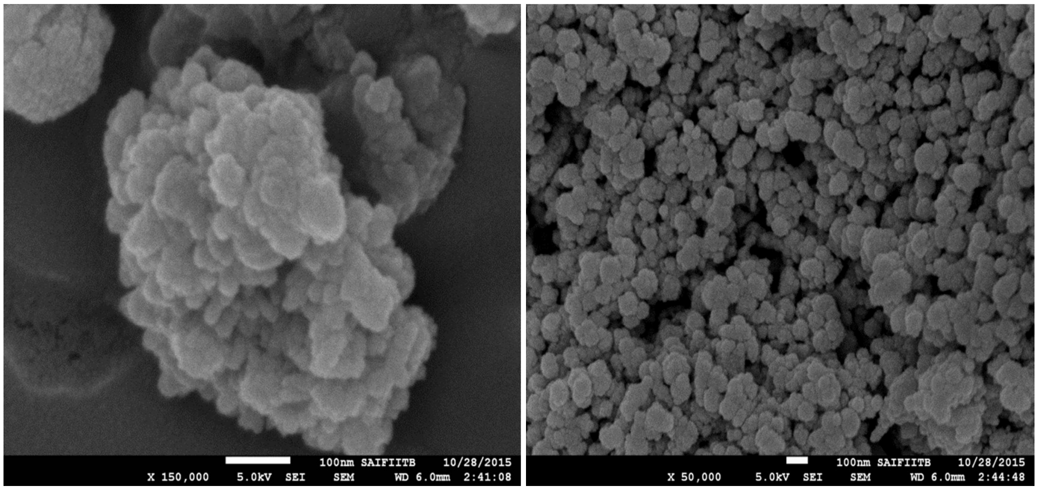
SEM

The SEM images of C@TiO_2-SO_3H-IL1 exhibited the presence of clusters of particles having quasi-spherical morphology (**Fig. 2**). A comparison of the SEM image of C@TiO_2-SO_3H and C@TiO_2-SO_3H-IL1 revealed that the surface morphology of two samples is somewhat similar. However, C@TiO_2-SO_3H-IL1 showed slightly more aggregation of particles and additional roughening of the surface, which may be due to the coating of the ionic liquid[28]. The coating of IL2 [dmim][BF_4], onto C@TiO_2-SO_3H (in case of C@TiO_2-SO_3H-IL2) may also cause aggregation as in the case of C@TiO_2-SO_3H-IL1 as the two ionic liquids used in the preparation of C@TiO_2-SO_3H-IL1 and C@TiO_2-SO_3H-IL2 are almost similar and differ only in their anions.



(a) **(b)**

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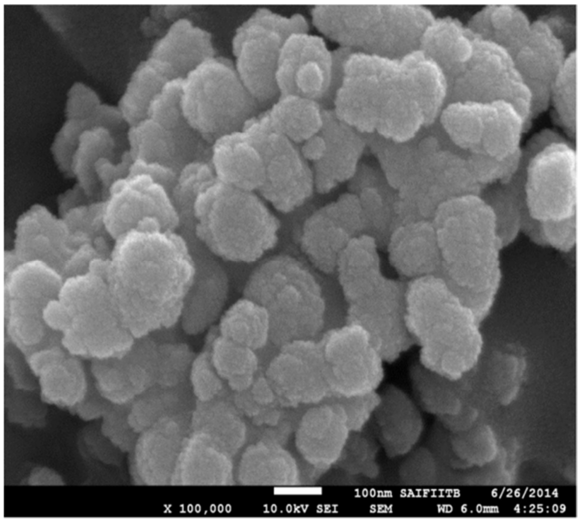

(c)

Fig. 2 SEM images of **(a, b)** C@TiO_2-SO_3H-IL1 **(c)** C@TiO_2-SO_3H.

HRTEM

The high resolution TEM images were used to obtain information on the particle size and fine microstructure of the prepared catalyst. The HRTEM images of C@TiO_2-SO_3H-IL1 also depicted the presence of semi-spherical aggregated particles with average size of 57.7 nm, which is in good agreement with the results obtained from XRD data (56.2 nm). The spherical particles represent the sulfonated composite material that are surrounded by a translucent lamellar type layer. The sulfonated carbon particles gets embedded in the pores of nano-titania during the carbonization process and hence the individual components of the composite material cannot be distinguished in the HRTEM images. A comparison of HRTEM images of C@TiO_2-SO_3H (**Fig. 3d**) and C@TiO_2-SO_3H-IL1 (**Fig. 3a**) reveals that the translucent layer surrounding the composites is present only in the HRTEM image of C@TiO_2-SO_3H-IL1, indicating that it might be the ionic liquid coating. When the sulfonated composites were coated with ionic liquid, the composites show a little aggregation in comparison to sulfonated carbon@titania composites as can be seen from the HRTEM images. The aggregation of composites might be due to the interaction of the surrounding

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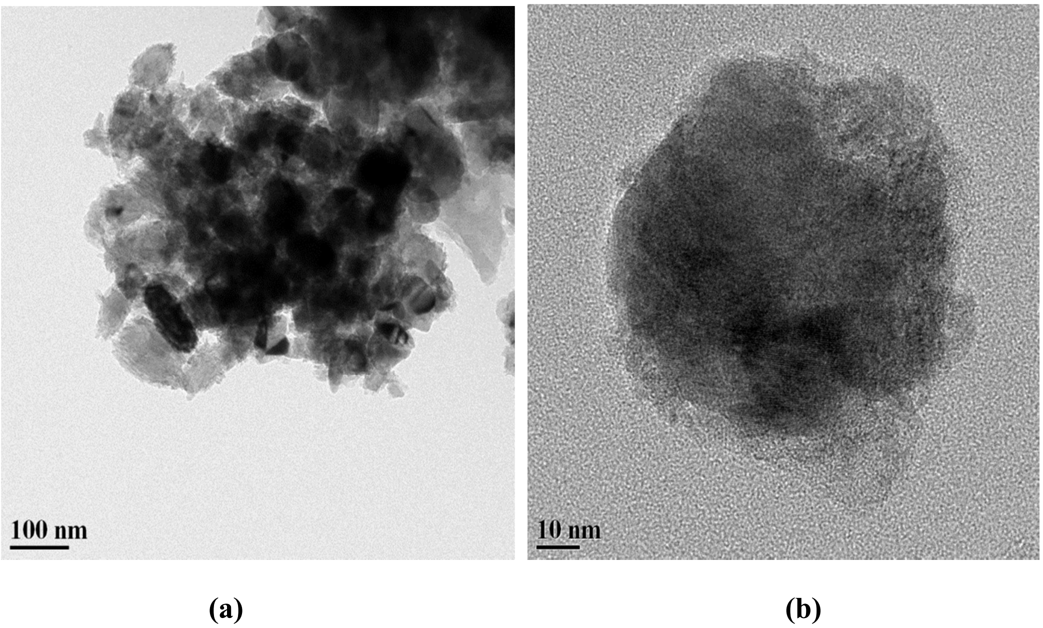
layers of ionic liquid with each other. The HRTEM images of C@TiO_2-SO_3H-IL1 also show clear lattice fringes with d-spacing of 0.36 nm, corresponding to (101) plane of anatase titania[29]. The HRTEM micrographs thus confirm the presence of highly crystalline titania-nanoparticles and amorphous carbon in the C@TiO_2-SO_3H-IL1.



(a) **(b)**

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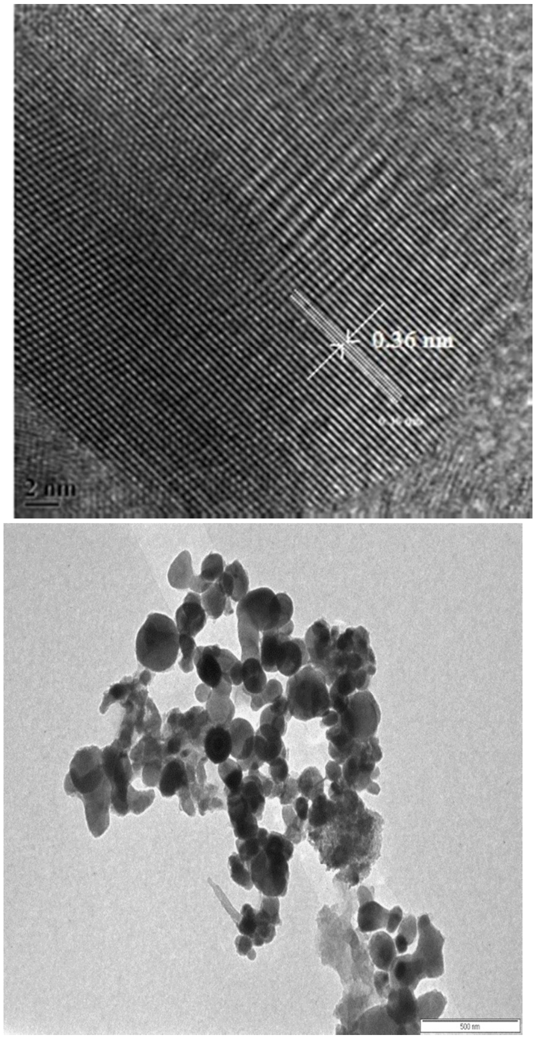

(c)

(d)

Fig. 3 HRTEM images of **(a-c)** C@TiO$_2$-SO$_3$H-IL1; **(d)** C@TiO$_2$-SO$_3$H.

2.2 Investigation of the catalytic activity of C@TiO$_2$-SO$_3$H-IL1 for the one-pot synthesis of indeno[1,2-b]indole-9,10-diones

To explore the catalytic activity of ionic liquid coated sulfonated carbon@titania composites, the model reaction of aniline, dimedone and ninhydrin was investigated in water at 60 °C using C@TiO$_2$-SO$_3$H-ILs. It was found that of the two catalysts screened, C@TiO$_2$-SO$_3$H-IL1 gave higher yields of the desired product and thus exhibited high catalytic activity in comparison to C@TiO$_2$-SO$_3$H-IL2 (**entry 2, Table 2**). Thus, C@TiO$_2$-SO$_3$H-IL1 was

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selected as the solid acid catalyst for further optimization of the reaction conditions. Further, the catalytic efficiency of C@TiO_2-SO_3H-IL1 for the preparation of indeno[1,2-*b*]indole-9,10-diones was studied by varying the catalyst amount to 0.05 g (1.35 mol% SO_3H), 0.1 g (2.7 mol% SO_3H), 0.15 g (4.05 mol% SO_3H) and 0.2 g (5.4 mol% SO_3H) for the model reaction. It was found that 0.1 g (2.7 mol% SO_3H) of C@TiO_2-SO_3H-IL1 was optimum to carry out the desired transformation. Lowering the catalyst amount to 0.05 g (1.35 mol% SO_3H) decreased the product yield to 54% (**entry 1, Table 3**), whereas an increase in catalyst amount did not significantly affect the yield. Thereafter, different solvents were screened to test the efficiency of the catalyst in different reaction medium and the results are presented in **Table 4**. Polar solvents afforded higher yields than the non-polar ones and water showed superiority among the different polar solvents investigated. Further, the effect of temperature on the test reaction was investigated by carrying out the reaction at rt, 60, 80 and 100 °C in water (**entries 5-8, Table 4**). It was observed that at temperature lower than 60 °C, the reaction did not proceed efficiently and at higher temperatures, only a marginal increase in product yield was observed. Thus, 60 °C was chosen as the optimum reaction temperature for the synthesis of indeno[1,2-*b*]indole-9,10-diones (**entry 6, Table 4**). In order to study the effect of ionic liquid coating on the catalytic activity of C@TiO_2-SO_3H-IL1 and to determine its role as a suitable solid acid catalyst in water, we carried out the test reaction using nano-titania, amorphous carbon, non-sulfonated carbon@titania, sulfonated carbon, [dmim][Cl] coated sulfonated carbon, mixture of nano-TiO_2 and [dmim][Cl] coated sulfonated carbon, [dmim][Cl] and C@TiO_2-SO_3H, under the optimized reaction conditions. The results summarized in **Table 5** clearly reveal that [dmim][Cl] gave poor yields of the desired product under the optimized reaction conditions, depicting that the ionic liquid alone is inefficient to catalyze the reaction efficiently. In addition, it was found that the coating of [dmim][Cl] onto C@TiO_2-SO_3H significantly reduced the reaction time along with increased product yield,

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thereby showing the appreciable role of ionic liquid coating in enhancing the catalyst stability. Further, to depict the synergistic effect of the organic/inorganic hybrid support on the activity of C@TiO_2-SO_3H-IL1, a comparison of the present catalyst has been done with simply a mixture of nano-titania and IL coated sulfonated carbon (entry 8, Table 5). It was found that the hybrid composite showed superior activity over mixture of nano-titania and IL coated sulfonated carbon, thereby depicting that the synergism of the two components of support material i.e. carbon and nano-titania has a significant effect on the catalytic activity of the catalyst. Thereafter, the effect of amount of ionic liquid loading onto C@TiO_2-SO_3H was also investigated in the one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones. It was found that an ionic liquid loading of 16 wt% gave the best results under the selected reaction conditions in terms of higher yields and further increase in loading amount to 32 wt% showed only marginal increase in product yield (**Fig 4**). After the optimization of the various reaction parameters, the developed catalytic system was employed to synthesize indeno[1,2-*b*]indole-9,10-dione derivatives using various amines substituted with electron-donating and electron-withdrawing groups. Aromatic amines with electron-donating groups showed superior reactivity in comparison to unsubstituted amine and those with electron-withdrawing groups (**Table 6**).

Table 2. Comparison of catalytic activity of ionic liquid coated sulfonated carbon@titania composites for the one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones

Entry	**Catalyst**	**Indeno[1,2-*b*]indole-9,10-diones**[a]		**1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones**[b]	
		Time (h)	**Yield**[c] **%**	**Time (min)**	**Yield**[c] **%**
1	**C@TiO_2-SO_3H-IL1**	**1**	**92**	**20**	**95**
2	C@TiO_2-SO_3H-IL2	1	85	20	90

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[a]Reaction conditions: aniline (1 mmol), dimedone (1 mmol), ninhydrin (1 mmol) and ionic liquid coated sulfonated carbon@titania composites (0.1 g) at 60 °C in water (5 mL). [b]Reaction conditions: phthalhydrazide (1 mmol), benzaldehyde (1 mmol), malononitrile (1 mmol) and ionic liquid coated sulfonated carbon@titania composites (0.1 g) at 100 °C in water (5 mL). [c]Isolated yield.

Table 3. Effect of catalyst amount on the C@TiO_2-SO_3H-IL1 catalyzed one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones

Entry	C@TiO_2-SO_3H-IL1 (g)	Indeno[1,2-*b*]indole-9,10-diones[a]		1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones[b]	
		Time (h)	Yield[c] (%)	Time (min)	Yield[c] (%)
1	0.05	1	54	45	88
2	**0.1**	**1**	**92**	**20**	**95**
3	0.15	1	93	15	95
4	0.2	0.75	93	15	96

[a]Reaction conditions: aniline (1 mmol), dimedone (1 mmol), ninhydrin (1 mmol) and C@TiO_2-SO_3H-IL1 at 60 °C in water (5 mL). [b]Reaction conditions: phthalhydrazide (1 mmol), benzaldehyde (1 mmol), malononitrile (1 mmol) and C@TiO_2-SO_3H-IL1 at 100 °C in water (5 mL). [c]Isolated yield.

Table 4. Effect of different solvents on the C@TiO_2-SO_3H-IL1 catalyzed one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones

Entry	Solvent	Temperature (°C)	Indeno[1,2-*b*]indole-9,10-diones[a]		1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones[b]	
			Time (h)	Yield[c] (%)	Time (min)	Yield[c] (%)
1	Acetonitrile	60	1	40[d]	-	-
2	Toluene	60	1	25[d]	-	-
3	Ethanol	60	1	65	-	-
4	Dioxane	60	1	20[d]	-	-

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5	Water	Rt	3	22[d]	120	Trace
6	**Water**	**60**	**1**	**92**	15	56
7	Water	80	1	93	15	70
8	**Water**	100	0.75	94	**20**	**95**
9	Water	110	-	-	15	95

[a] Reaction conditions: aniline (1 mmol), dimedone (1 mmol), ninhydrin (1 mmol), solvent (5 mL) and C@TiO_2-SO_3H-IL1 (0.1 g, 2.7 mol% SO_3H). [b] Reaction conditions: phthalhydrazide (1 mmol), benzaldehyde (1 mmol), malononitrile (1 mmol) and C@TiO_2-SO_3H-IL1 (0.1 g, 2.7 mol% SO_3H) in water (5 mL). [c] Isolated yield. [d] Column chromatography yield.

Table 5. Comparison of activity of nano-titania, amorphous carbon, non-sulfonated carbon@titania, sulfonated carbon, C@TiO_2-SO_3H, [dmim][Cl] and C@TiO_2-SO_3H-IL1 for the one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones

	Catalyst	**Indeno[1,2-*b*]indole-9,10-diones[a]**		**1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones[b]**	
		Time(h)	**Yield[c] (%)**	**Time (min)**	**Yield[c] (%)**
1	No catalyst	20	Trace	180	NR

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DOI: 10.1039/C7NJ00361G

2	Nano-titania	5	15[d]	180	Trace
3	Amorphous carbon	5	20[d]	180	NR
4	Non-sulfonated carbon@titania	5	25[d]	180	Trace
5	Sulfonated carbon	1	40[d]	15	34[d]
6	C@TiO$_2$-SO$_3$H	1	60	15	56
7	[dmim][Cl] coated sulfonated carbon	1	70	15	65
8	Mixture of nano-TiO$_2$ and [dmim][Cl] coated sulfonated carbon	1	73	15	70
9	[dmim][Cl]	1	45	15	40
10	**C@TiO$_2$-SO$_3$H-IL1**	**1**	**92**	**15**	**95**

---

[a] Reaction conditions: aniline (1 mmol), dimedone (1 mmol), ninhydrin (1 mmol) and catalyst (0.1g for entries 2-8) in water (5 mL) at 60 ˚C. [b] Reaction conditions: phthalhydrazide (1 mmol), benzaldehyde (1 mmol), malononitrile (1 mmol) and catalyst (0.1g for entries 2-8) in water (5 mL) at 100 ˚C. [c] Isolated yields. [d] Column chromatography yields.

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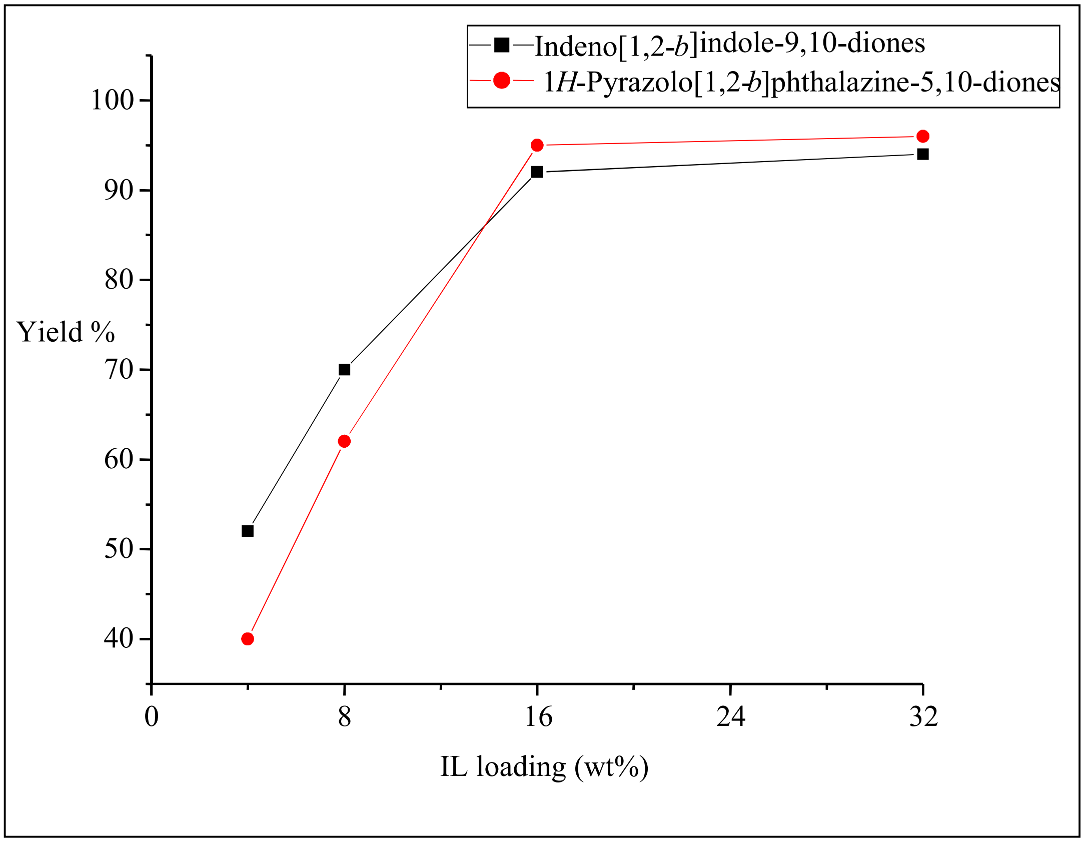

Fig. 4 Effect of ionic liquid loading on C@TiO_2-SO_3H-IL1 catalyzed one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones (**entry 1, Table 6**; **entry 1, Table 7**).

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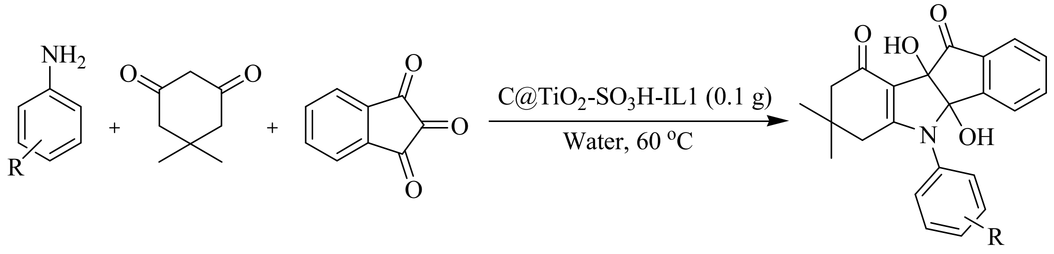
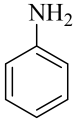
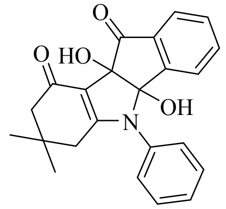
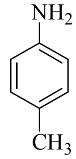
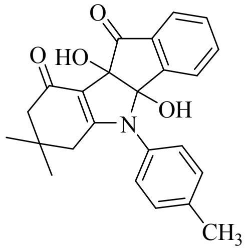
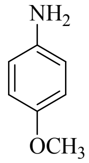
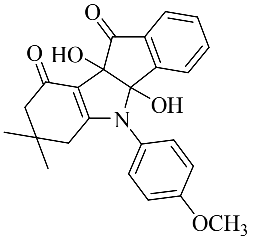
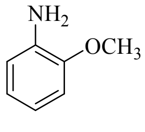
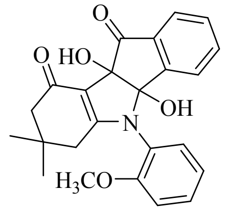
Table 6. C@TiO_2-SO_3H-IL1 catalyzed one-pot multicomponent synthesis of indeno[1,2-*b*]indole-9,10-diones[a]



Entry	Amine	Product	Time (h)	Yield[b] (%)	m.p./lit. m.p. (°C)
1			1	92	209-210/210-212[30]
2			1	93	217-218/214-216[30]
3			0.75	93	225-226/224-225[30]
4			1	90	169-170/170-172[14b]

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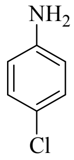
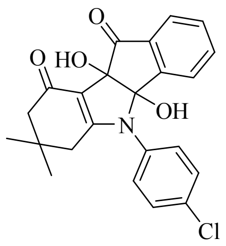
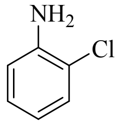
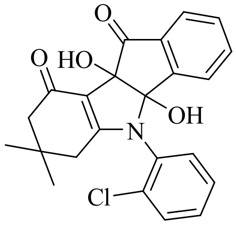
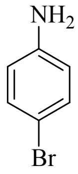
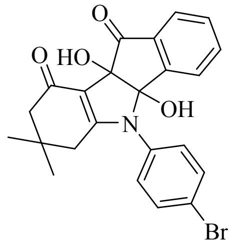
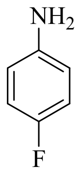
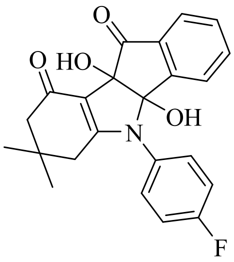
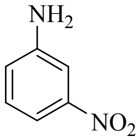
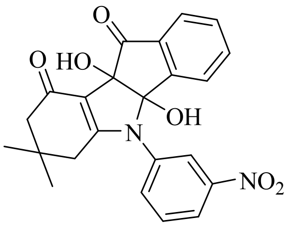
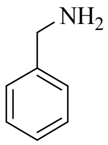
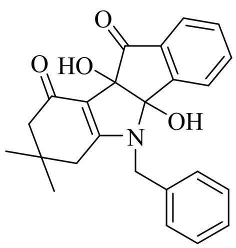
5			2	91	235-236/238-240[30]
6			1	88	230-231
7			2	91	161-162/160-162[30]
8			1.5	93	159-160
9			2	90	171-173/170-172[30]
10			1.5	94	191-192/188-190[30]

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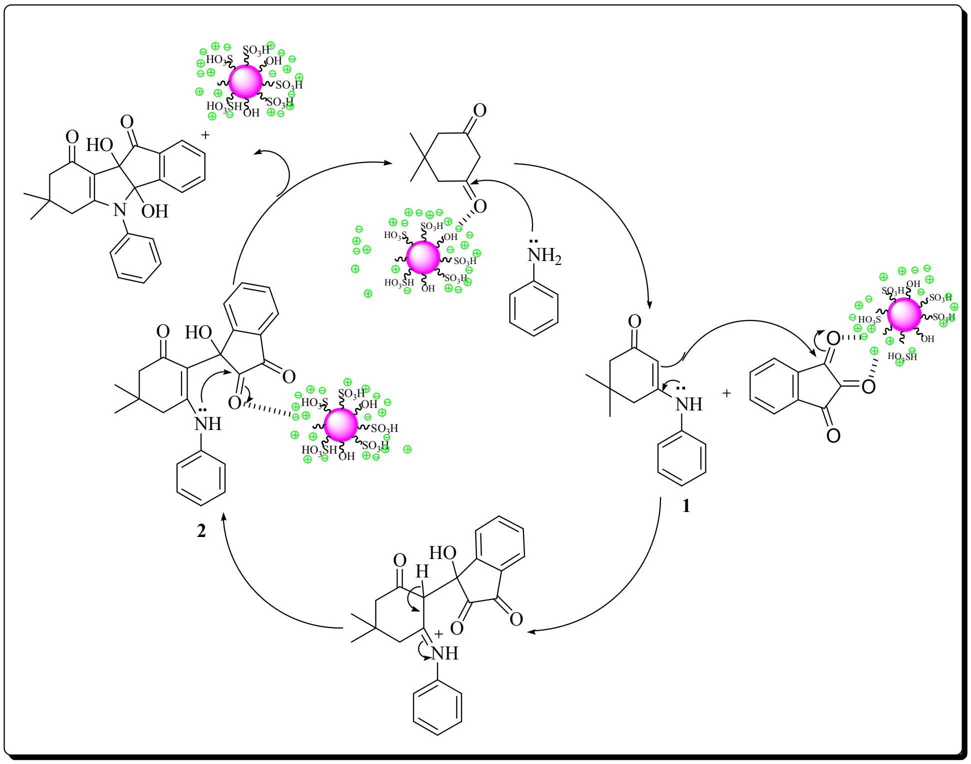
[a]Reaction conditions: aniline (1 mmol), dimedone (1 mmol), ninhydrin (1 mmol) and C@TiO_2-SO_3H-IL1 (0.1g, 2.7 mol% SO_3H) in water (5 mL) at 60 °C. [b]Isolated yield.

The probable mechanism for the one-pot multicomponent synthesis of indeno[1,2-*b*]indolones has been outlined in **Scheme 2.** The first step involves the formation of enaminone intermediate **1** *via* C@TiO_2-SO_3H-IL1 catalyzed condensation of dimedone and amine. The -SO_3H group enhances the electrophilicity of the carbonyl carbon of dimedone, thus promoting the condensation reaction. The ionic liquid layer helps in the diffusion of organic substrates to the catalytically active sulfonic groups, which are otherwise insoluble in the reaction medium. In the second step, Michael addition between intermediate **1** and ninhydrin is facilitated by C@TiO_2-SO_3H-IL1 to form intermediate **2**. Finally C@TiO_2-SO_3H-IL1 interacts with intermediate **2**, thus promoting the intramolecular cyclization with the formation of five membered ring to give the final product along with the regeneration of catalyst.



Scheme 2. Probable mechanism for the C@TiO_2-SO_3H-IL1 catalyzed one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones.

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2.3 Investigation of the catalytic activity of C@TiO_2-SO_3H-ILs for the one-pot synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones

1*H*-Pyrazolo[1,2-*b*]phthalazine-5,10-diones were synthesized *via* three component condensation of phthalhydrazide, aromatic aldehydes and malononitrile in aqueous medium at 100 °C. To investigate the catalytic activity of C@TiO_2-SO_3H-ILs in the one-pot multicomponent synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones, we focussed on systematic evaluation of various reaction parameters for the model reaction of phthalhydrazide, benzaldehyde and malononitrile. Initially, a comparison of the catalytic activity of C@TiO_2-SO_3H-ILs was done for the model reaction and it was found that both C@TiO_2-SO_3H-IL1 and C@TiO_2-SO_3H-IL2 gave the desired product in almost same reaction time (**Table 2**). However, C@TiO_2-SO_3H-IL1 gave higher product yield in comparison to C@TiO_2-SO_3H-IL2, thereby exhibiting enhanced catalytic activity for the synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones. The catalytic activity of C@TiO_2-SO_3H-IL1 was also compared to its precursors, nano-titania, amorphous carbon, non-sulfonated carbon@titania, sulfonated carbon, [dmim][Cl] and C@TiO_2-SO_3H under the optimized reaction conditions. The results presented in **Table 5** clearly showed the superiority of C@TiO_2-SO_3H-IL1 over its precursors and also depicted its role as efficient solid acid catalyst for the present protocol. Thereafter, other reaction parameters such as amount of catalyst and temperature were screened to test the efficiency of the C@TiO_2-SO_3H-IL1 and the results are summarized in **Table 3** and **Table 4**. Since we wished to study the catalytic activity of C@TiO_2-SO_3H-IL1 in aqueous media, therefore all reaction parameters were optimised using water as solvent. To study the effect of catalyst amount, the model reaction was carried out in the presence of various amounts of catalyst. As can be seen

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from the results shown in **Table 3**, the optimum catalyst amount was again found to be 0.1 g (2.7 mol% SO_3H) to obtain best results. Further, the effect of temperature on the model reaction was studied by carrying out the reaction at room temperature, 60, 80, 100 and 110 °C in aqueous media. It was observed that reaction temperature had a significant influence both on the reaction time and product yield. At room temperature, no product formation was observed, whereas, an increase in the reaction temperature from 60 to 100 °C lead to a significant increase in yield from 56 to 95% (**entries 6-8, Table 4**). The optimum reaction temperature for the desired organic transformation was thus selected to be 100 °C. To establish the scope of the present catalytic system, we examined a wide variety of aldehydes containing either electron-withdrawing or electron-donating groups and found that aldehydes with electron-withdrawing groups furnished excellent yield of the corresponding products in shorter reaction times in comparison to aldehydes with electron-donating groups. The developed protocol was also applied to heteroaromatic and aliphatic aldehydes, and good results were obtained (**entries 10-12, Table 7**).

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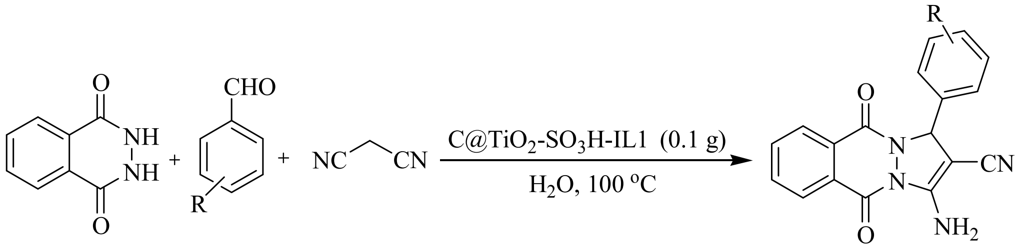
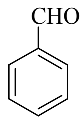
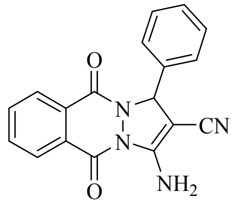
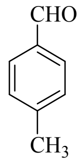
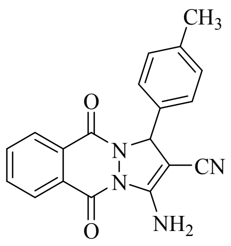
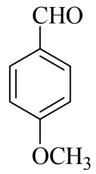
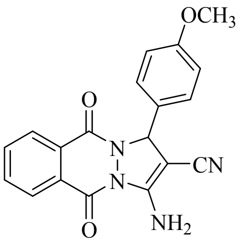
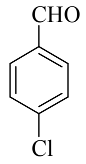
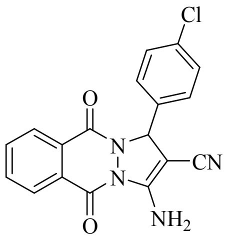
Table 7. C@TiO_2-SO_3H-IL1 catalyzed one-pot synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones[a]



Entry	Aldehyde	Product	Time (h)	Yield[b] (%)	m.p./lit. m.p.(°C)
1			20	95	277-278/276-278[31]
2			25	92	235-236/236-238[31]
3			25	91	239-240/240-242[31]
4			15	92	270-271/273-276[31]

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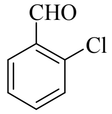
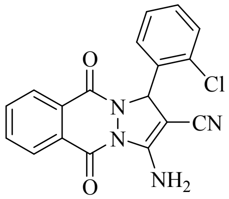
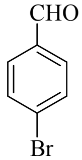
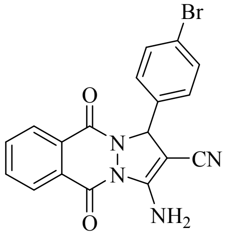
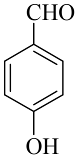
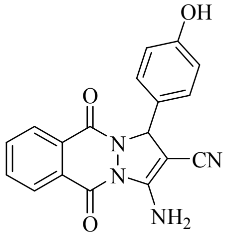
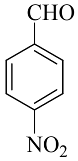
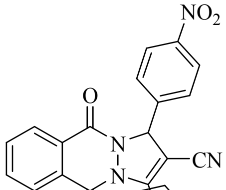
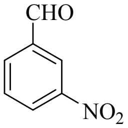
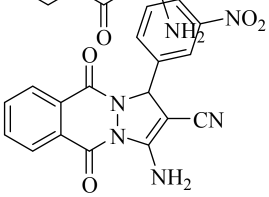
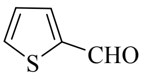
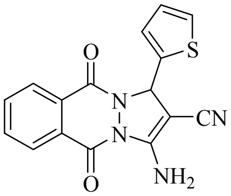
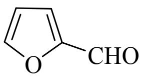
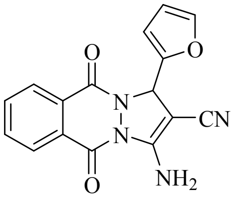
5			20	94	258-259/257-259^{31}
6			15	92	264-265/263-265^{32}
7			15	94	270-271/270-272^{33}
8			15	96	226-227/227-229^{34}
9			15	95	271-272/269-271^{31}
10			15	90	245-246/244-246^{31}
11			15	90	288-289/290-292^{31}

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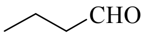
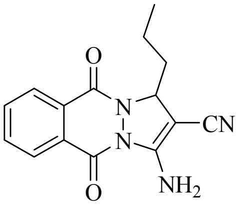
12			30	80	221-223/220-222[22]

[a]Reaction conditions: phthalhydrazide (1 mmol), aldehyde (1 mmol), malononitrile (1 mmol) and C@TiO_2-SO_3H-IL1 (0.1 g, 2.7 mol% SO_3H) at 100 °C in water (5 mL). [b]Isolated yield.

The plausible mechanism for C@TiO_2-SO_3H-IL1 catalyzed one-pot synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones is represented in **Scheme 3**. Initially, the carbonyl carbon of aldehyde (activated by C@TiO_2-SO_3H-IL1) undergoes Knoevenagel condensation with malononitrile to form intermediate **1**. The intermediate **1** then undergoes Michael type addition with phthalhydrazide, followed by intramolecular concerted cyclization assisted by C@TiO_2-SO_3H-IL1 to afford 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives.

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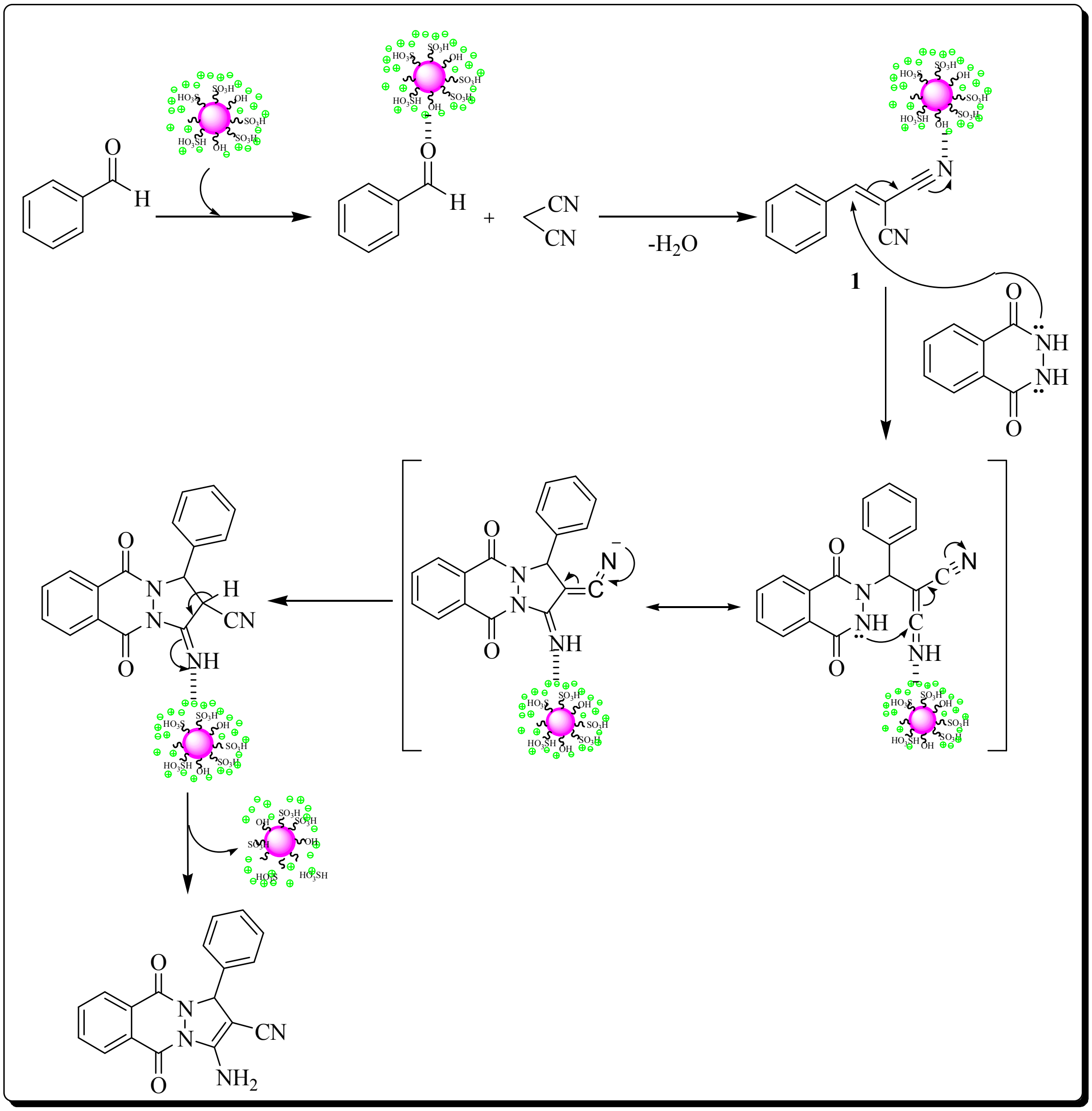

Scheme 3. Proposed mechanism for C@TiO$_2$-SO$_3$H-IL1 catalyzed one-pot synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones.

3. Recyclability

To examine the reusability and stability of SO$_3$H groups in C@TiO$_2$-SO$_3$H-IL1, multiple recycling experiments were performed for the one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones (**entry 1, Table 6; entry 1, Table 7**). At the end of reaction, the catalyst was recovered by simple filtration and reused for the subsequent reactions. For every new reaction cycle, the amount of reactants was taken in

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accordance with the amount of catalyst recovered in the previous reaction run. The reusability of the recovered catalyst was tested for five consecutive runs and it was observed that the conversion and yield of products were comparable to the fresh catalyst, indicating that the synthesized catalyst is highly stable and can be used for several runs (**Fig. 5**). Moreover, the sulfur content of the recovered catalyst obtained after five runs was found to be almost the same as fresh catalyst. These results suggest the higher stability of sulfonic groups in C@TiO_2-SO_3H-IL1 and confirmed that the developed catalyst is truly heterogeneous in nature.

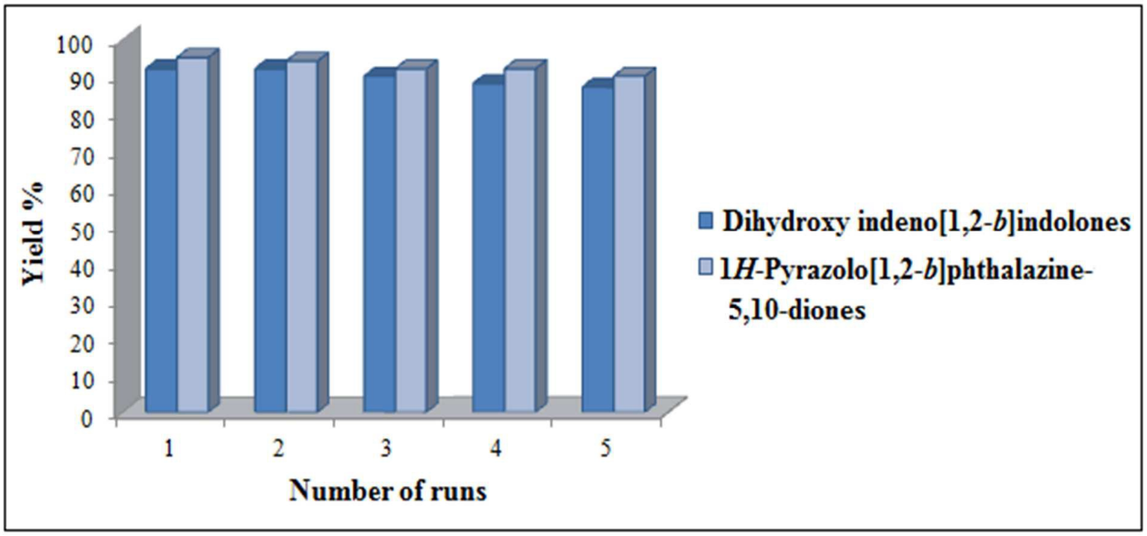

Fig. 5 Recyclability of C@TiO_2-SO_3H-IL (**entry 1, Table 6; entry 1, Table 7**).

4. Conclusion

To summarise, we have developed a novel catalytic system that showed remarkable activity and stability in water for the one-pot multicomponent synthesis of various substituted indeno[1,2-*b*]indole-9,10-dione derivatives and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones. In addition, the reported methodology involves the use of environmentally friendly and mild conditions. The developed catalytic system has ample scope to be utilized further towards the development of green methodologies.

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5. Experimental

5.1 Reagents and instrumentation

All reagents and starting materials were obtained commercially from Sigma-Aldrich and Merck, and were used as received without any further purification unless otherwise noted. The ^{1}H and ^{13}C NMR data were recorded using DMSO-d_6 or $CDCl_3$+DMSO-d_6 or CD_3COCD_3 on Bruker Avance III (400 MHz) spectrometer. The FTIR spectra were conducted using Thermo Nicolet, Avatar 370 spectrophotometer. XRD was recorded using Bruker AXS D8 Advance in 2θ the range of 10-80° and mass spectral data was recorded on Bruker Esquires 3000 (ESI). CHNS analysis was carried out on ThermoFinnigan FLASH EA 1112 series. Scanning electron microscopy studies were conducted on JEOL Model JSM-6390LV Scanning Electron Microscope, High Resolution Transmission Electron Microscopy studies (HRTEM) were performed using FEI, Tecnai G2, F30 Transmission electron microscope. EDX analysis was carried out using JEOL Model JED-2300 and TGA was recorded on Perkin Elmer, Diamond TG/DTA.

5.2 General procedure for the synthesis of ionic liquid coated sulfonated carbon@titania composites (C@TiO_2-SO_3H-ILs)

In the first step, sulfonated carbon@titania composites (C@TiO_2-SO_3H) were prepared according to the method already reported in our previous publication[35]. In the second step, coating of ionic liquid, [dmim][Cl] or [dmim][BF_4] on C@TiO_2-SO_3H was done to obtain C@TiO_2-SO_3H-IL1 and C@TiO_2-SO_3H-IL2 respectively. In a typical procedure, to the solution of appropriate ionic liquid ([dmim][Cl] or [dmim][BF_4], 0.2 g) in acetonitrile (30 mL) taken in a round bottom flask (50 mL), C@TiO_2-SO_3H (1 g) was added and the resulting solution was stirred at room temperature for 30 minutes. Thereafter, acetonitrile was removed using a rotary evaporator to get a black solid, which was finally dried under vacuum for 1 h to obtain C@TiO_2-SO_3H-ILs.

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5.3 General procedure for the C@TiO$_2$-SO$_3$H-IL1 catalyzed one-pot multicomponent synthesis of indeno[1,2-b]indole-9,10-diones

A mixture of amine (1 mmol), dimedone (1 mmol), C@TiO$_2$-SO$_3$H-IL1 (0.1 g, 2.7 mol% SO$_3$H) and water (5 mL) was taken in a round bottom flask (25 mL) and stirred at 60 °C for 30 min (**Table 6**). Afterwards, ninhydrin (1 mmol) was added and the reaction mixture was again stirred for the appropriate time. After completion of the reaction (as monitored by TLC), ethyl acetate (30 mL) was added and the catalyst was filtered. The organic layer was washed with water (100 mL) and dried over anhyd. Na$_2$SO$_4$. The combined organic extracts were concentrated in vacuum to get the crude product, which was further purified by re-crystallization from ethanol.

5.4 General procedure for the one-pot synthesis of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones

To a mixture of phthalhydrazide (1 mmol), aldehyde (1 mmol), malononitrile (1 mmol) and C@TiO$_2$-SO$_3$H-IL1 (0.1 g, 2.7 mol% SO$_3$H) in a round bottom flask (25 mL), water (5 mL) was added and the reaction mixture was stirred at 100 °C for the appropriate time. The progress of the reaction was monitored by TLC (**Table 7**). After completion of the reaction, the reaction mixture was diluted with hot ethyl acetate (5×10 mL) and filtered. The organic layer was washed with water (100 mL) and dried over anhyd. Na$_2$SO$_4$. Finally, the product was obtained after removal of the solvent under reduced pressure followed by crystallization from methanol.

The structures of the products were confirmed by FTIR, ^{1}H NMR, ^{13}C NMR, mass spectral data and comparison with authentic samples obtained commercially or prepared according to the literature methods.

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Graphical abstract

Ionic liquid coated sulfonated carbon@titania composites for the one-pot synthesis of indeno[1,2-*b*]indole-9,10-diones and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones in aqueous media

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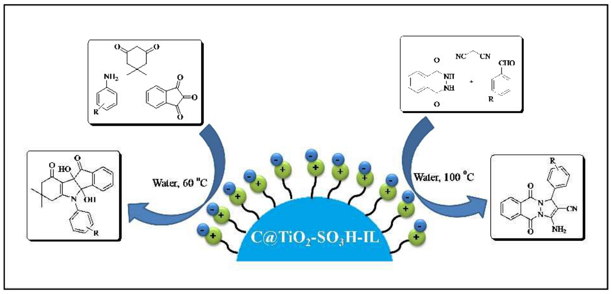
A novel and efficient ionic liquid based solid Bronsted acid catalyst has been designed and explored as a recyclable catalytic system for multicomponent synthesis in an aqueous reaction media.



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Crystal structure of ethyl 4-(2-chlorophenyl)-2-methyl-4*H*-pyrimido[2,1-*b*][1,3]benzothiazole-3-carboxylate

Balbir Kumar, Manmeet Kour, Satya Paul, Rajni Kant and Vivek K. Gupta

Acta Cryst. (2015). E**71**, o669

Acta Cryst. (2015). E**71**, o669 Kumar *et al.* · $C_{20}H_{17}ClN_2O_2S$

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Crystal structure of ethyl 4-(2-chlorophenyl)-2-methyl-4*H*-pyrimido[2,1-*b*][1,3]benzothiazole-3-carboxylate

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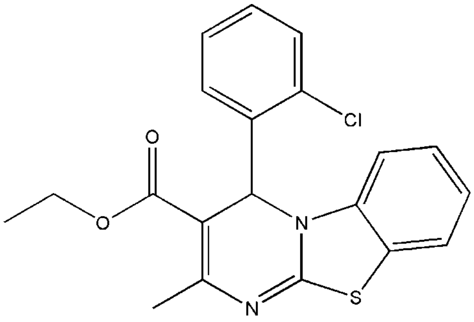
In the title compound, $C_{20}H_{17}ClN_2O_2S$, the dihedral angle between the planes of the benzothiazole fused ring system (r.m.s. deviation = 0.024 Å) and the chlorobenzene ring is 89.62 (12)°. The ester C—O—C—C side chain has an *anti* orientation [torsion angle = −155.2 (3)°]. In the crystal, weak aromatic π–π stacking interactions are observed between the phenyl and pyrimidine rings [centroid–centroid seperation = 3.666 (2) Å].

Keywords: crystal structure; pyrimido[2,1-*b*][1,3]benzothiazole; ester; biological activity.

CCDC reference: 1406433

1. Related literature

For biological activities of benzothiazoles, see: Landreau *et al.* (2002); Russo *et al.* (1985). For a related structure, see: Sankar *et al.* (2015).



2. Experimental

2.1. Crystal data

$C_{20}H_{17}ClN_2O_2S$
$M_r = 384.87$
Triclinic, $P\bar{1}$
$a = 8.9049\ (8)$ Å
$b = 8.9275\ (10)$ Å
$c = 12.3564\ (11)$ Å
$\alpha = 88.434\ (8)^\circ$
$\beta = 83.536\ (7)^\circ$
$\gamma = 66.201\ (10)^\circ$
$V = 892.90\ (15)$ Å^3
$Z = 2$
Mo $K\alpha$ radiation
$\mu = 0.35$ mm^{-1}
$T = 293$ K
0.30 × 0.20 × 0.20 mm

2.2. Data collection

Oxford Diffraction Xcalibur Sapphire3 diffractometer
Absorption correction: multi-scan (*CrysAlis PRO*; Oxford Diffraction, 2010)
$T_{\min} = 0.880$, $T_{\max} = 1.000$
6440 measured reflections
3477 independent reflections
2275 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.033$

2.3. Refinement

$R[F^2 > 2\sigma(F^2)] = 0.053$
$wR(F^2) = 0.142$
$S = 1.03$
3477 reflections
237 parameters
H-atom parameters constrained
$\Delta\rho_{\max} = 0.64$ e Å^{-3}
$\Delta\rho_{\min} = -0.35$ e Å^{-3}

Data collection: *CrysAlis PRO* (Oxford Diffraction, 2010); cell refinement: *CrysAlis PRO*; data reduction: *CrysAlis PRO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012); software used to prepare material for publication: *PLATON* (Spek, 2009).

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Supporting information for this paper is available from the IUCr electronic archives (Reference: HB7475).

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supporting information

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Crystal structure of ethyl 4-(2-chlorophenyl)-2-methyl-4*H*-pyrimido[2,1-*b*][1,3]benzothiazole-3-carboxylate

Balbir Kumar, Manmeet Kour, Satya Paul, Rajni Kant and Vivek K. Gupta

S1. Experimental

To a mixture of ethylacetoacetate (1.0 mmol, 0.13 g), 2-chlorobenzadehyde (1.0 mmol, 0.14 g) and 2-aminobenzothiazole (1.0 mmol, 0.152 g) in a round bottom flask (25 ml), C/TiO_2·SO_3·$SbCl_2$ (0.1 g) was added and the reaction mixture was heated at 363 K under solvent-free conditions for 1 h. Hot ethanol (2 × 5 ml) was added to the reaction mixture and the catalyst was separated by simple filteration. Removal of the solvent under reduced pressure afforded the product, which was further crystallized from ethanol as yellow crystals (Yield: 88%).

S2. Refinement

All the H atoms were geometrically fixed and allowed to ride on their parent C atoms, with C—H distances of 0.93–0.96 Å; and with U_{iso}(H) = 1.2U_{eq}(C), except for the methyl group where U_{iso}(H) = 1.5U_{eq}(C).

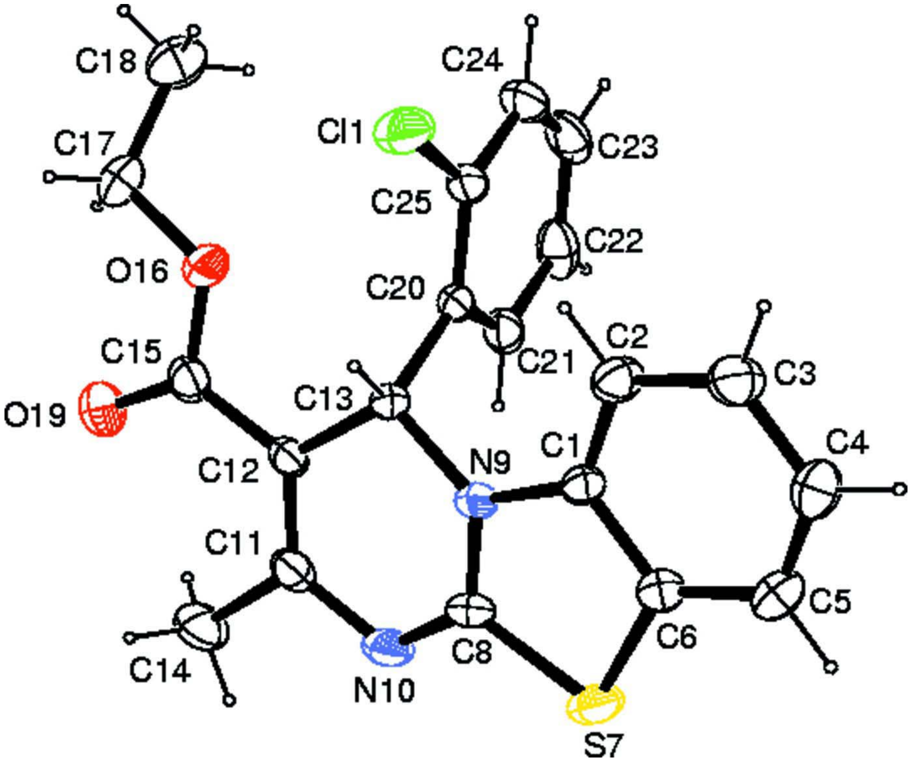

Figure 1

ORTEP view of the molecule with displacement ellipsoids drawn at the 40% probability level.

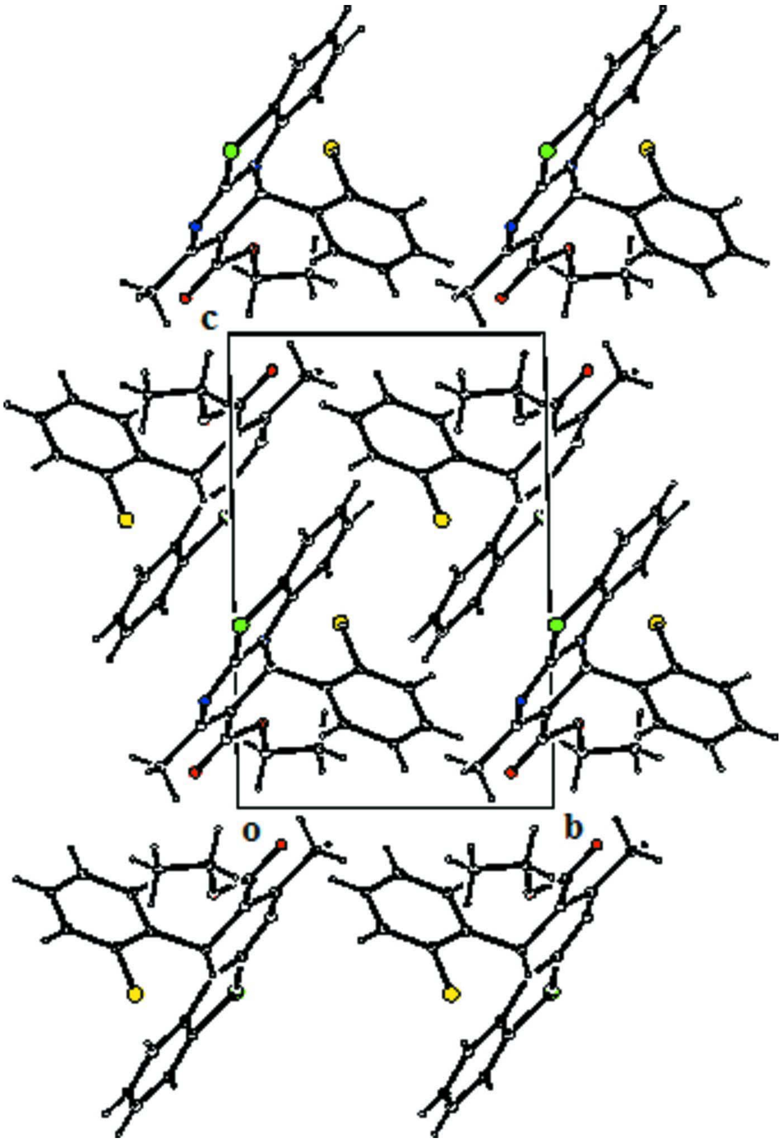

Figure 2

The packing arrangement of molecules viewed down the *a* axis.

Ethyl 4-(2-chlorophenyl)-2-methyl-4*H*-pyrimido[2,1-*b*][1,3]benzothiazole- 3-carboxylate

Crystal data

$C_{20}H_{17}ClN_2O_2S$
$M_r = 384.87$
Triclinic, $P\overline{1}$
Hall symbol: -P 1
$a = 8.9049$ (8) Å
$b = 8.9275$ (10) Å
$c = 12.3564$ (11) Å
$\alpha = 88.434$ (8)°
$\beta = 83.536$ (7)°
$\gamma = 66.201$ (10)°
$V = 892.90$ (15) Å^3

$Z = 2$
$F(000) = 400$
$D_x = 1.431$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 1737 reflections
$\theta = 4.1–27.4°$
$\mu = 0.35$ mm^{-1}
$T = 293$ K
Block, colourless
0.30 × 0.20 × 0.20 mm

Data collection

Oxford Diffraction Xcalibur Sapphire3 diffractometer	6440 measured reflections
Radiation source: fine-focus sealed tube	3477 independent reflections
Graphite monochromator	2275 reflections with $I > 2\sigma(I)$
Detector resolution: 16.1049 pixels mm^{-1}	$R_{\text{int}} = 0.033$
ω scans	$\theta_{\text{max}} = 26.0°$, $\theta_{\text{min}} = 3.9°$
Absorption correction: multi-scan (*CrysAlis PRO*; Oxford Diffraction, 2010)	$h = -10\rightarrow10$
$T_{\text{min}} = 0.880$, $T_{\text{max}} = 1.000$	$k = -10\rightarrow10$
	$l = -9\rightarrow15$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.053$	H-atom parameters constrained
$wR(F^2) = 0.142$	$w = 1/[\sigma^2(F_o^2) + (0.0556P)^2 + 0.235P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.03$	$(\Delta/\sigma)_{\text{max}} < 0.001$
3477 reflections	$\Delta\rho_{\text{max}} = 0.64$ e Å^{-3}
237 parameters	$\Delta\rho_{\text{min}} = -0.35$ e Å^{-3}
0 restraints	
Primary atom site location: structure-invariant direct methods	

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	y	z	U_{iso}*/U_{eq}
S7	0.83804 (10)	0.01946 (11)	0.38623 (8)	0.0592 (3)
Cl1	0.02890 (10)	0.33670 (11)	0.39074 (8)	0.0648 (3)
N9	0.5363 (3)	0.0924 (2)	0.35456 (18)	0.0370 (6)
C25	0.1519 (4)	0.3941 (3)	0.2942 (2)	0.0431 (7)
C12	0.4497 (3)	−0.0172 (3)	0.2052 (2)	0.0368 (7)
O16	0.1721 (3)	0.0825 (2)	0.17927 (17)	0.0531 (6)
N10	0.7388 (3)	−0.0979 (3)	0.2270 (2)	0.0503 (7)
C21	0.4011 (4)	0.3408 (3)	0.1786 (2)	0.0445 (7)
H21	0.5087	0.2715	0.1531	0.053*
C8	0.6924 (3)	−0.0008 (3)	0.3117 (2)	0.0427 (7)
C20	0.3121 (3)	0.2857 (3)	0.2573 (2)	0.0345 (6)
C15	0.3219 (4)	−0.0328 (3)	0.1475 (2)	0.0446 (7)
O19	0.3434 (3)	−0.1335 (3)	0.0766 (2)	0.0719 (7)
C13	0.3919 (3)	0.1118 (3)	0.2977 (2)	0.0341 (6)
H13	0.3110	0.0911	0.3495	0.041*
C1	0.5264 (3)	0.1829 (3)	0.4491 (2)	0.0370 (7)

C11	0.6124 (4)	−0.1115 (3)	0.1764 (2)	0.0443 (7)
C3	0.4058 (4)	0.3661 (4)	0.6003 (3)	0.0553 (9)
H3	0.3125	0.4372	0.6429	0.066*
C24	0.0834 (4)	0.5496 (4)	0.2540 (3)	0.0612 (10)
H24	−0.0238	0.6201	0.2795	0.073*
C2	0.3873 (4)	0.2860 (4)	0.5114 (2)	0.0473 (8)
H2	0.2829	0.3019	0.4944	0.057*
C17	0.0396 (4)	0.0912 (4)	0.1179 (3)	0.0608 (9)
H17A	−0.0047	0.0128	0.1455	0.073*
H17B	0.0815	0.0642	0.0419	0.073*
C6	0.6823 (4)	0.1580 (3)	0.4765 (2)	0.0439 (7)
C14	0.6786 (4)	−0.2416 (4)	0.0879 (3)	0.0640 (10)
H14A	0.6468	−0.3300	0.1087	0.096*
H14B	0.7969	−0.2819	0.0772	0.096*
H14C	0.6343	−0.1959	0.0214	0.096*
C5	0.6991 (4)	0.2383 (4)	0.5662 (3)	0.0561 (9)
H5	0.8031	0.2214	0.5845	0.067*
C4	0.5604 (4)	0.3422 (4)	0.6264 (3)	0.0601 (9)
H4	0.5697	0.3978	0.6861	0.072*
C23	0.1744 (5)	0.5998 (4)	0.1761 (3)	0.0675 (11)
H23	0.1283	0.7051	0.1491	0.081*
C18	−0.0923 (5)	0.2586 (5)	0.1279 (4)	0.0812 (12)
H18A	−0.1419	0.2802	0.2021	0.122*
H18B	−0.1747	0.2677	0.0813	0.122*
H18C	−0.0457	0.3365	0.1069	0.122*
C22	0.3327 (5)	0.4969 (4)	0.1373 (3)	0.0594 (10)
H22	0.3932	0.5316	0.0839	0.071*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S7	0.0328 (4)	0.0641 (5)	0.0699 (6)	−0.0056 (4)	−0.0153 (4)	−0.0055 (5)
Cl1	0.0374 (5)	0.0726 (6)	0.0751 (6)	−0.0129 (4)	−0.0018 (4)	−0.0116 (5)
N9	0.0318 (13)	0.0316 (11)	0.0424 (14)	−0.0058 (10)	−0.0106 (11)	0.0003 (10)
C25	0.0382 (16)	0.0343 (14)	0.0534 (19)	−0.0077 (13)	−0.0169 (15)	−0.0053 (13)
C12	0.0402 (16)	0.0244 (12)	0.0425 (16)	−0.0089 (12)	−0.0075 (14)	−0.0002 (12)
O16	0.0401 (12)	0.0549 (12)	0.0632 (14)	−0.0144 (10)	−0.0165 (11)	−0.0126 (11)
N10	0.0361 (14)	0.0421 (13)	0.0579 (17)	−0.0002 (11)	−0.0040 (13)	−0.0080 (13)
C21	0.0514 (19)	0.0383 (15)	0.0456 (18)	−0.0177 (14)	−0.0141 (16)	−0.0004 (13)
C8	0.0324 (16)	0.0349 (14)	0.0517 (18)	−0.0028 (12)	−0.0107 (14)	0.0046 (14)
C20	0.0341 (15)	0.0295 (13)	0.0395 (16)	−0.0100 (12)	−0.0131 (13)	−0.0019 (12)
C15	0.0512 (19)	0.0349 (15)	0.0499 (18)	−0.0189 (14)	−0.0085 (16)	0.0017 (14)
O19	0.0711 (17)	0.0584 (14)	0.0851 (18)	−0.0210 (13)	−0.0161 (15)	−0.0285 (13)
C13	0.0299 (14)	0.0297 (13)	0.0421 (16)	−0.0097 (11)	−0.0104 (13)	0.0026 (12)
C1	0.0351 (16)	0.0344 (14)	0.0413 (16)	−0.0112 (12)	−0.0152 (13)	0.0058 (13)
C11	0.0492 (18)	0.0291 (14)	0.0487 (18)	−0.0092 (13)	−0.0068 (15)	−0.0011 (13)
C3	0.050 (2)	0.0590 (19)	0.0467 (19)	−0.0105 (16)	−0.0080 (16)	−0.0088 (16)
C24	0.053 (2)	0.0373 (17)	0.081 (3)	0.0000 (16)	−0.028 (2)	−0.0075 (17)

C2	0.0403 (17)	0.0554 (18)	0.0430 (17)	−0.0143 (15)	−0.0111 (15)	−0.0004 (15)
C17	0.052 (2)	0.068 (2)	0.074 (2)	−0.0304 (18)	−0.0224 (19)	−0.0030 (18)
C6	0.0400 (17)	0.0410 (15)	0.0484 (18)	−0.0121 (13)	−0.0129 (15)	0.0037 (14)
C14	0.058 (2)	0.0497 (18)	0.068 (2)	−0.0050 (17)	−0.0011 (19)	−0.0180 (18)
C5	0.048 (2)	0.064 (2)	0.060 (2)	−0.0208 (17)	−0.0246 (18)	0.0024 (18)
C4	0.065 (2)	0.066 (2)	0.053 (2)	−0.0261 (19)	−0.0207 (19)	−0.0087 (18)
C23	0.087 (3)	0.0312 (16)	0.079 (3)	−0.0107 (19)	−0.042 (2)	0.0046 (18)
C18	0.064 (3)	0.082 (3)	0.098 (3)	−0.022 (2)	−0.043 (2)	0.008 (2)
C22	0.092 (3)	0.0491 (19)	0.051 (2)	−0.039 (2)	−0.021 (2)	0.0095 (16)

Geometric parameters (Å, º)

S7—C8	1.741 (3)	C11—C14	1.505 (4)
S7—C6	1.744 (3)	C3—C4	1.379 (4)
Cl1—C25	1.735 (3)	C3—C2	1.388 (4)
N9—C8	1.353 (3)	C3—H3	0.9300
N9—C1	1.413 (3)	C24—C23	1.370 (5)
N9—C13	1.481 (3)	C24—H24	0.9300
C25—C24	1.376 (4)	C2—H2	0.9300
C25—C20	1.394 (4)	C17—C18	1.479 (5)
C12—C11	1.360 (4)	C17—H17A	0.9700
C12—C15	1.462 (4)	C17—H17B	0.9700
C12—C13	1.536 (3)	C6—C5	1.390 (4)
O16—C15	1.338 (3)	C14—H14A	0.9600
O16—C17	1.448 (3)	C14—H14B	0.9600
N10—C8	1.296 (4)	C14—H14C	0.9600
N10—C11	1.394 (4)	C5—C4	1.359 (4)
C21—C22	1.385 (4)	C5—H5	0.9300
C21—C20	1.389 (4)	C4—H4	0.9300
C21—H21	0.9300	C23—C22	1.374 (5)
C20—C13	1.521 (3)	C23—H23	0.9300
C15—O19	1.216 (3)	C18—H18A	0.9600
C13—H13	0.9800	C18—H18B	0.9600
C1—C2	1.370 (4)	C18—H18C	0.9600
C1—C6	1.394 (4)	C22—H22	0.9300

C8—S7—C6	91.01 (14)	C23—C24—C25	119.5 (3)
C8—N9—C1	114.1 (2)	C23—C24—H24	120.2
C8—N9—C13	121.6 (2)	C25—C24—H24	120.2
C1—N9—C13	123.8 (2)	C1—C2—C3	118.5 (3)
C24—C25—C20	121.5 (3)	C1—C2—H2	120.7
C24—C25—Cl1	117.2 (3)	C3—C2—H2	120.7
C20—C25—Cl1	121.3 (2)	O16—C17—C18	109.4 (3)
C11—C12—C15	121.0 (2)	O16—C17—H17A	109.8
C11—C12—C13	121.9 (2)	C18—C17—H17A	109.8
C15—C12—C13	117.1 (2)	O16—C17—H17B	109.8
C15—O16—C17	116.6 (2)	C18—C17—H17B	109.8
C8—N10—C11	115.9 (2)	H17A—C17—H17B	108.2

C22—C21—C20	121.3 (3)	C5—C6—C1	120.7 (3)
C22—C21—H21	119.3	C5—C6—S7	128.0 (2)
C20—C21—H21	119.3	C1—C6—S7	111.2 (2)
N10—C8—N9	127.7 (3)	C11—C14—H14A	109.5
N10—C8—S7	120.5 (2)	C11—C14—H14B	109.5
N9—C8—S7	111.8 (2)	H14A—C14—H14B	109.5
C21—C20—C25	117.5 (3)	C11—C14—H14C	109.5
C21—C20—C13	119.1 (2)	H14A—C14—H14C	109.5
C25—C20—C13	123.4 (3)	H14B—C14—H14C	109.5
O19—C15—O16	121.7 (3)	C4—C5—C6	118.6 (3)
O19—C15—C12	126.3 (3)	C4—C5—H5	120.7
O16—C15—C12	112.0 (2)	C6—C5—H5	120.7
N9—C13—C20	110.1 (2)	C5—C4—C3	120.9 (3)
N9—C13—C12	108.4 (2)	C5—C4—H4	119.6
C20—C13—C12	112.7 (2)	C3—C4—H4	119.6
N9—C13—H13	108.5	C24—C23—C22	120.9 (3)
C20—C13—H13	108.5	C24—C23—H23	119.5
C12—C13—H13	108.5	C22—C23—H23	119.5
C2—C1—C6	120.2 (2)	C17—C18—H18A	109.5
C2—C1—N9	128.0 (2)	C17—C18—H18B	109.5
C6—C1—N9	111.9 (2)	H18A—C18—H18B	109.5
C12—C11—N10	123.1 (2)	C17—C18—H18C	109.5
C12—C11—C14	125.1 (3)	H18A—C18—H18C	109.5
N10—C11—C14	111.8 (3)	H18B—C18—H18C	109.5
C4—C3—C2	121.1 (3)	C23—C22—C21	119.2 (4)
C4—C3—H3	119.5	C23—C22—H22	120.4
C2—C3—H3	119.5	C21—C22—H22	120.4

C11—N10—C8—N9	−2.2 (5)	C15—C12—C13—C20	−65.5 (3)
C11—N10—C8—S7	176.9 (2)	C8—N9—C1—C2	−179.2 (3)
C1—N9—C8—N10	178.7 (3)	C13—N9—C1—C2	8.4 (4)
C13—N9—C8—N10	−8.7 (5)	C8—N9—C1—C6	1.1 (3)
C1—N9—C8—S7	−0.4 (3)	C13—N9—C1—C6	−171.3 (2)
C13—N9—C8—S7	172.18 (18)	C15—C12—C11—N10	178.2 (3)
C6—S7—C8—N10	−179.5 (3)	C13—C12—C11—N10	−0.7 (4)
C6—S7—C8—N9	−0.3 (2)	C15—C12—C11—C14	−2.0 (5)
C22—C21—C20—C25	−0.7 (4)	C13—C12—C11—C14	179.1 (3)
C22—C21—C20—C13	178.5 (2)	C8—N10—C11—C12	6.8 (4)
C24—C25—C20—C21	0.4 (4)	C8—N10—C11—C14	−173.1 (3)
Cl1—C25—C20—C21	178.98 (19)	C20—C25—C24—C23	−0.2 (4)
C24—C25—C20—C13	−178.9 (2)	Cl1—C25—C24—C23	−178.8 (2)
Cl1—C25—C20—C13	−0.3 (4)	C6—C1—C2—C3	1.1 (4)
C17—O16—C15—O19	−5.8 (4)	N9—C1—C2—C3	−178.6 (3)
C17—O16—C15—C12	172.5 (2)	C4—C3—C2—C1	−0.5 (5)
C11—C12—C15—O19	5.4 (5)	C15—O16—C17—C18	−155.2 (3)
C13—C12—C15—O19	−175.7 (3)	C2—C1—C6—C5	−0.8 (4)
C11—C12—C15—O16	−172.8 (3)	N9—C1—C6—C5	179.0 (3)
C13—C12—C15—O16	6.1 (4)	C2—C1—C6—S7	179.0 (2)

C8—N9—C13—C20	−110.7 (3)	N9—C1—C6—S7	−1.3 (3)
C1—N9—C13—C20	61.2 (3)	C8—S7—C6—C5	−179.4 (3)
C8—N9—C13—C12	12.9 (3)	C8—S7—C6—C1	0.9 (2)
C1—N9—C13—C12	−175.2 (2)	C1—C6—C5—C4	−0.2 (5)
C21—C20—C13—N9	64.4 (3)	S7—C6—C5—C4	−179.9 (3)
C25—C20—C13—N9	−116.4 (3)	C6—C5—C4—C3	0.8 (5)
C21—C20—C13—C12	−56.7 (3)	C2—C3—C4—C5	−0.5 (5)
C25—C20—C13—C12	122.5 (3)	C25—C24—C23—C22	0.3 (5)
C11—C12—C13—N9	−8.7 (4)	C24—C23—C22—C21	−0.6 (5)
C15—C12—C13—N9	172.4 (2)	C20—C21—C22—C23	0.9 (4)
C11—C12—C13—C20	113.4 (3)		