Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Molecular Catalysis A: Chemical 237 (2005) 93–100
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
www.elsevier.com/locate/molcata

Sulfated zirconia as an efficient catalyst for organic synthesis and transformation reactions

Benjaram M. Reddy *, Pavani M. Sreekanth, Pandian Lakshmanan

Inorganic and Physical Chemistry Division, Indian Institute of Chemical Technology, Hyderabad 500007, India

Received 21 February 2005; received in revised form 20 April 2005; accepted 20 April 2005
Available online 4 June 2005

Abstract

The efficacy of sulfated zirconia catalyst was investigated towards various acid-catalyzed organic syntheses and transformation reactions in the liquid phase. The SO_4^{2-}/ZrO_2 efficiently catalyzes synthesis of 1,5-benzodiazepine derivatives, electrophilic substitution of indoles with aldehydes to afford the corresponding bis(indolyl)methanes, synthesis of 3,4-dihydropyrimidinones, synthesis of diaryl sulfoxides, and tetrahydropyranylation of alcohols and phenols. Various advantages associated with these protocols include, simple work-up procedure, solvent-free conditions, short reaction times, high product yields and easy recovery and reusability of the catalyst. The SO_4^{2-}/ZrO_2 catalyst was obtained by immersing a finely powdered hydrous $Zr(OH)_4$ into 1 M H_2SO_4 solution and subsequent drying and calcination at 923 K. The $Zr(OH)_4$ was prepared from aqueous $ZrOCl_2{\cdot}8H_2O$ solution by hydrolysis with dilute ammonium hydroxide. The bulk and surface properties of the prepared catalysts were examined by X-ray powder diffraction, BET surface area, ammonia-TPD and Raman spectroscopy techniques. All characterization results revealed that the incorporated sulfate ions show a significant influence on the surface and bulk properties of the ZrO_2. In particular, XRD and Raman results suggest that impregnated sulfate ions stabilize the metastable tetragonal phase of ZrO_2 at ambient conditions. Ammonia-TPD and BET surface area results indicate that sulfated catalyst exhibits enhanced acid strength and specific surface area than that of unprompted ZrO_2.

Keywords: Solid superacid; Sulfated zirconia; Benzodiazepines; Bis(indolyl)methanes; 3,4-Dihydropyrimidinones; Diaryl sulfoxides; Tetrahydropyranylation

1. Introduction

Acid-catalyzed organic reactions are numerous and the usage of solid acid catalysts is very rampant in several industrial and environmental processes [1]. It can be said that solid acids are the most important heterogeneous catalysts used today, considering in terms of both the total amounts used and the final economical impact. According to a recent review of industrial acid–base catalysis, of the 127 processes identified, over 115 are solid acid-catalyzed [2]. It clearly indicates the significance of these materials and the scope of their commercial exploitation. The use of conventional liquid acids and Lewis acids such as, H_2SO_4, HCl, HF, $AlCl_3$, BF_3, $ZnCl_2$ and SbF_5 pose significant risks in handling, containment, disposal and regeneration due to their toxic and corrosive nature. There is an exigent need to eliminate the aggressive and ecologically harmful mineral acids to carry out a large number of acid-catalyzed industrial processes. This can be achieved by the development of strong solid acid catalysts that are stable, regenerable and active at moderate temperatures.

Over the past few years, the preparation and characterization of zirconia based solid acids has been receiving much attention, among other solid acids such as clays, zeolites, heteropolyacids and ion exchange resins, due to their superior catalytic activity for hydrocarbon conversions [3,4]. These catalysts are finding numerous applications in oil refinery and petrochemical industries. Among the promoted ZrO_2 solid acid catalysts, the SO_4^{2-}/ZrO_2 become more popular due to its high activity for light alkane isomerizations even at low

* Corresponding author. Tel.: +91 40 2716 0123; fax: +91 40 2716 0921.
E-mail addresses: mreddyb@yahoo.com, bmreddy@iict.res.in (B.M. Reddy).

1381-1169/$ – see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.molcata.2005.04.039

temperatures. Many large volume applications based on sulfated zirconia are reported in the literature, especially in the petroleum industry for alkylation, isomerization and cracking reactions [5–8].

In recent times, inorganic solid acid-catalyzed organic transformations are gaining much attention due to the proven advantage of heterogeneous catalysts, like simplified product isolation, mild reaction conditions, high selectivities, ease in recovery and reuse of the catalysts and reduction in the generation of wasteful byproducts [9–11]. In that connection we were interested in investigating various industrially important organic reactions aimed at replacing toxic and corrosive reagents, noxious or expensive solvents and multistep process, with single step solvent-free ones by using environmentally benign solid acid catalysts. Interestingly, sulfated zirconia exhibits excellent activity for a wide range of organic synthesis and transformation reactions. In this paper we report the SO_4^{2-}/ZrO_2 catalyzed various organic synthesis and transformation reactions and the advantages associated with these catalyst systems.

2. Experimental

2.1. Catalyst preparation

About 25 g of $ZrOCl_2{\cdot}8H_2O$ (Fluka, GR grade) was dissolved in doubly distilled water. To this clear solution, dilute aqueous ammonia was added drop-wise from a burette with vigorous stirring until the pH of the solution reached 8. The obtained precipitate was washed with distilled water until free from chloride ions and dried at 393 K for 24 h. To prepare sulfated ZrO_2 catalyst, a portion of the obtained hydrous zirconia sample was ground to fine powder and immersed in 1 M H_2SO_4 solution (30 ml) for 30 min. Excess water was evaporated on a water-bath and the resulting sample was oven-dried at 393 K for 12 h and calcined at 923 K for 4 h in air atmosphere and stored in vacuum desiccator. For the purpose of comparison an unpromoted ZrO_2 was also prepared by calcining the hydrous zirconia at 923 K for 4 h in air atmosphere.

2.2. Catalyst characterization

The powder X-ray diffraction patterns of the prepared samples have been recorded on a Siemens D-5000 diffractometer by using Cu Kα radiation source and a scintillation counter detector. The XRD phases present in the samples were identified by using JCPDS data files. The BET surface area of the sample was determined by nitrogen physisorption at liquid nitrogen temperature on a Micromeritics Gemini 2360 instrument by taking 0.162 nm^2 as the area of cross-section for N_2 molecule. Prior to analysis, the samples were oven-dried at 393 K for 10 h and flushed with argon gas for 1 h. Raman spectra were obtained on a DILOR XY spectrometer equipped with a CCD detector. The spectra were recorded in the range of 100–4000 cm^{-1} and a spectral resolution of 2 cm^{-1} using the 514.5 nm exciting line from an argon ion laser (Spectra Physics, USA). The temperature programmed desorption (TPD) measurements using ammonia probe molecule were carried out on an AutoChem 2910 instrument (Micromeritics, USA). A thermal conductivity detector was used for continuous monitoring of the desorbed ammonia and the areas under the peaks were integrated using GRAMS/32 software. Prior to TPD studies, samples were pre-treated at 473 K for 1 h in a flow of ultra pure helium gas (40 ml min^{-1}). After the pre-treatment, the sample was saturated with 10% ultra pure anhydrous ammonia gas (balance He, 60 ml min^{-1}) at 373 K for 2 h and subsequently flushed with He (60 ml min^{-1}) at 373 K for 2 h to remove the physisorbed ammonia. The heating rate for the TPD measurements, from ambient to 1073 K, was 10 K min^{-1}. All flow rates mentioned are at normal temperature and pressure (NTP).

2.3. Activity studies

All chemicals used in this study were commercially available and used without further purification. All the reactions were carried out in the liquid phase batch mode by taking a mixture of reactants and catalyst in a round bottom flask and stirred/refluxed for appropriate times. Completion of the reaction was monitored by TLC. After completion of the reaction, catalyst was recovered by simple filtration and reused. The products were recovered from the filtrate, concentrated on a rotatory evaporator and chromatographed on a silica gel column to afford pure products (isolated yields). NMR and mass spectroscopy techniques were used to analyze the products and compared with the authentic samples.

3. Results and discussion

The surface and bulk properties of ZrO_2 and SO_4^{2-}/ZrO_2 catalysts were examined by various spectroscopic and non-spectroscopic techniques namely, X-ray powder diffraction, BET surface area, ammonia-TPD and Raman spectroscopy. The XRD patterns of ZrO_2 and SO_4^{2-}/ZrO_2 samples calcined at 923 K are shown in Fig. 1. The corresponding phase composition, crystallite size and BET surface area results are presented in Table 1. As can be seen from Fig. 1, the hydrous zirconia sample calcined at 923 K is in poorly crystalline form with a mixture of monoclinic and tetragonal phases. On the other hand, the sulfated sample exhibits prominent lines due to tetragonal phase indicating that the impregnated sulfate ions show a strong influence on the phase modification of zirconia from thermodynamically more stable monoclinic to the metastable tetragonal phase. It can be observed from Table 1 that the sulfated zirconia shows smaller crystallite size and more tetragonal phase when compared to unpromoted ZrO_2. It appears from XRD results (Fig. 1 and Table 1) that the incorporated sulfate ions retard the forma-

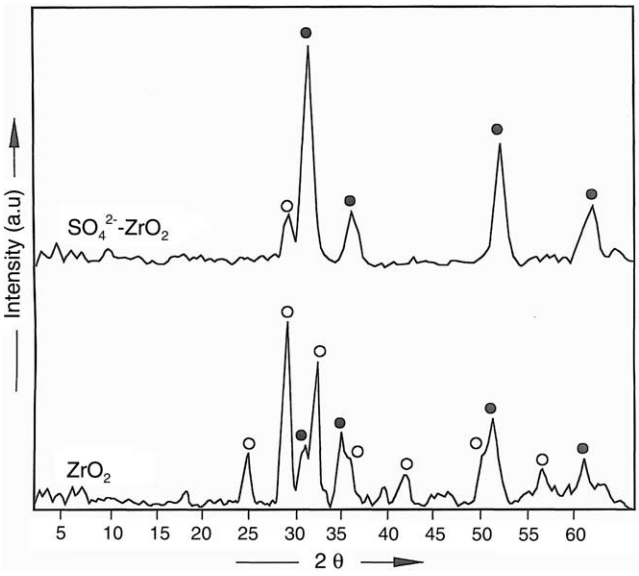


Fig. 1. X-ray powder diffraction patterns of pure and sulfate promoted zirconia samples calcined at 923 K. (●) Characteristic lines due to tetragonal zirconia; (○) characteristic lines due to monoclinic zirconia.

tion of larger crystallites of zirconia and stabilize them in the metastable tetragonal phase [12]. In the absence of promoters, calcination of hydrous zirconia normally leads to the formation of thermodynamically more stable monoclinic form with large crystallite sizes [13]. The specific surface area of SO_4^{2-}/ZrO_2 sample is also higher than that of ZrO_2 (Table 1). Ammonia-TPD results revealed two temperature maximums on both the samples indicating the presence of two different types of acids sites with different acid strength distribution. The total amount of ammonia desorbed in the case of sulfated sample is much higher than that of pure ZrO_2. It clearly indicates that impregnated sulfate ions show a strong influence on the acidic properties of the zirconia. The Raman spectrum of unprompted ZrO_2 exhibited prominent bands due to a mixture of monoclinic (180, 188, 221, 331, 380, 476 and 637 cm^{-1}) and tetragonal (148, 290, 311, 454 and 647 cm^{-1}) phases and the bands due to tetragonal phase were less intense than the peaks due to monoclinic phase [14,15]. Whereas in the spectrum of sulfated zirconia catalyst bands representing the tetragonal phase were more intense. A strong band at 1032 cm^{-1} with a shoulder was also observed in the spectrum of SO_4^{2-}/ZrO_2 sample. This is due to hydrated sulfate groups attached to the zirconia support [16]. Raman results supported the observations made from XRD studies, wherein sulfation increased the proportion of tetragonal phase [17]. The charaterization results are in agreement with the earlier published papers wherein sulfation inhibited the crystal growth and increased the specific surface area and stabilized the tetragonal phase of zirconia [3,4,7].

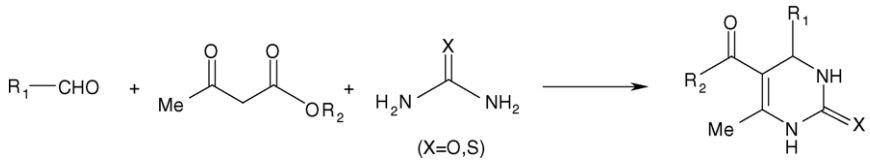
3.1. Synthesis of 3,4-dihydropyrimidin-2(1H)ones

Dihydropyrimidinones (DHPMs) are important class of compounds due to their diverse therapeutic and pharmacological applications. Many functionalized derivatives of DHPMs are known to act as anti-hypertensive agents, alpha-la-antagonists, nueropeptide Y (NPY) antagonists and also serve as integral backbones of several calcium channel blockers [18,19]. Several marine alkaloids containing the dihydropyrimidinone units are found to exhibit diverse biological activities as anti-viral, anti-bacterial, anti-tumor and anti-inflammatory agents [20,21]. Among those, batzelladine alkaloids have been found to be potential HIV gp-120-CD4 inhibitors [22]. In view of these reasons, this family of compounds received a great deal of attention towards their synthesis. The general method for the synthesis of DHPMs involves three-component condensation reaction between aldehyde, β-keto ester and urea under strong acidic conditions. This reaction was first reported by Biginelli in 1893, but suffers from low product yields especially with substituted aromatic aldehydes [23]. Subsequently several modifications were reported for the Biginelli condensation reaction to improve the yields. Apart from this classical one-pot Biginelli reaction many multistep protocols were also reported for the synthesis of DHPMs [24]. The Biginelli reaction was carried out employing many reagents such as lanthanum chloride, manganese acetate, montmorillonite KSF, silica-supported sulfuric acid and metal triflates [25–27]. Most of these reported catalysts suffer from various drawbacks such as stringent reaction conditions, tedious work-up procedures, long reaction times, use of stoichiometric amounts of catalysts and some of the catalysts employed are expensive. In view of these reasons, still many efforts are going on to develop greener, faster and high yield protocols for this reaction. Herein, we report a facile method for the synthesis of 3,4-dihydropyrimidone-2(1*H*)–ones by a one-pot condensation reaction between an aldehyde, β-keto ester and urea or thiourea under solvent-free conditions catalyzed by sulfated zirconia (Scheme 1).

The reaction was performed by taking a mixture of stoichiometric amounts of an aldehyde, β-keto ester and urea/thiourea along with a catalytic amount of sulfated zirconia in a round bottom flask and heated at 373 K for an appropriate time. The reaction proceeds efficiently under these conditions and the dihydropyrimidinones are produced

Table 1
BET surface area, amount of monoclinic and tetragonal phases of ZrO_2 and their crystallite size, and total acidity

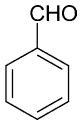
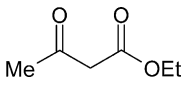
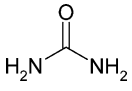
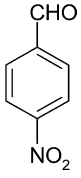
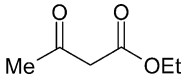
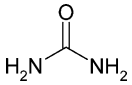
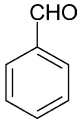
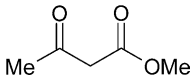
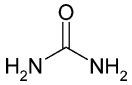
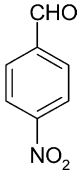
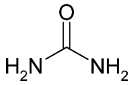
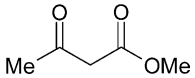
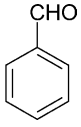
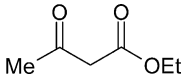
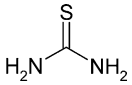
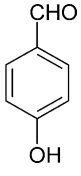
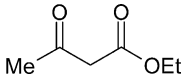
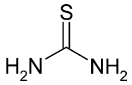
Catalyst	BET SA	Monoclinic		Tetragonal		NH_3 desorbed
	($m^2\ g^{-1}$)	Amount (%)	Size (nm)	Amount (%)	Size (nm)	($ml\ g^{-1}$)
ZrO_2	42	76	11.2	24	13.0	5
SO_4^{2-}/ZrO_2	100	20	07.3	80	12.3	16



Scheme 1.

in excellent yields in short reaction times (40–60 min). Aromatic aldehyde bearing either electron withdrawing or electron donating groups reacted smoothly and produced the corresponding dihydropyrimidinones in high yields and high purity. These results are compiled in Table 2. This procedure offers several advantages including mild reaction conditions, greater selectivity, high product yields as well as simple experimental and isolation procedure, which makes it useful and attractive process for large scale synthesis of these compounds.

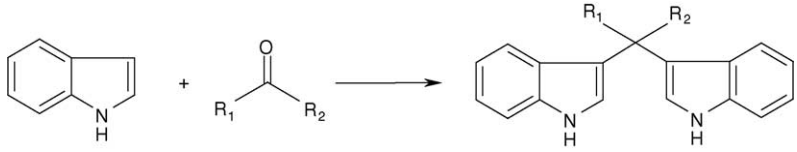
Table 2
Sulfated zirconia catalyzed synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones

Entry	Aldehyde	Beta-keto ester	Urea/thiourea	Yield
1				90
2				88
3				92
4				90
5				80
6				82

3.2. Synthesis of bis(indolyl)methane derivatives

Indoles and their derivatives are important intermediates in organic synthesis and widely featured in variety of pharmacologically active compounds [28]. During the past few years a large number of natural products containing bis(indolyl)methanes and bis(indolyl)ethanes have been isolated from both marine and terrestrial sources and some of them were found to exhibit interesting biological activity [29]. Therefore, there is a great deal of interest in the synthesis of this class of compounds. The acid-catalyzed reaction of electron rich heterocyclic compounds like indoles and pyrroles with *p*-dimethylaminobenzaldehyde is known as Ehrlich test [30]. Generally, bis(indolyl)methanes are synthesized by the analogous reactions of Ehrlich test, where indoles react with aliphatic or aromatic aldehydes/ketones in the presence of an acid catalyst to produce azafulvenium salts. These azafulvenium salts can undergo further addition with a second indole molecule to produce bis(indolyl)methanes [31]. Protic-acids as well as Lewis acids are known to promote these reactions [32,33]. The use of various other reagents such as lanthanide triflates, clays, ion exchange resins and zeolites have also been studied for this reaction [34–36]. However, a major problem associated with the conventional Lewis acid catalysts is that they deactivate or some times even decompose due to the nitrogen containing reactants. Moreover, many of these Lewis acid reagents are required in stoichiometric amounts.

In this study, we successfully synthesized bis(indolyl) methanes by electrophilic substitution reaction of indole with various aldehydes in the presence of sulfated zirconia catalyst (Scheme 2). This reaction was carried out by taking a mixture of aldehyde and indole (1:2.5 mole ratio) in a round bottomed flask and stirred for an appropriate time at room temperature along with the catalytic amount of sulfated zir-



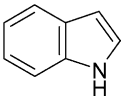
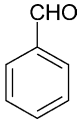
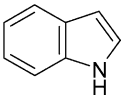
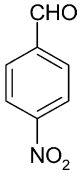
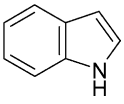
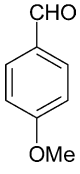
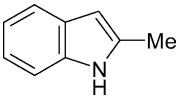
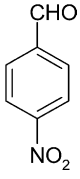
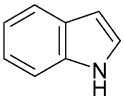
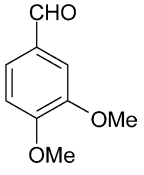
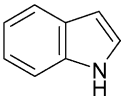
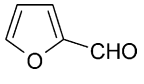
Scheme 2.

conia. Under these optimized conditions various aldehydes smoothly reacted with indole and furnished corresponding bis(indolyl)methanes in excellent yields in short reaction times. These results are summarized in Table 3. Under similar conditions the unpromoted ZrO_2 failed to produce the desired products in good yields. It can be noted from Table 3 that sulfated zirconia is an efficient catalyst for the synthesis of bis(indolyl)methanes in terms of product yields, reaction temperature and reaction times.

3.3. Synthesis of 2,3-dihydro-1H-1,5-benzodiazepines

Benzodiazepines and their polycyclic derivatives are an important class of bioactive compounds. Many functionalized benzodiazepines are widely used as anti-convulsant, anti-anxiety, analgesic, sedative, anti-depressive and hypnotic agents [37]. These compound also finding applications as dyes for acrylic fibers and anti-inflammatory agents [38]. 1,5-Benzodiazepines are key intermediates for the synthesis of various fused ring compounds such as triazolo-, oxadiazolo- and oxizino-diazepines [39]. Due to their broad spectrum of biological activity, these compounds received a lot of attention towards their synthesis. The general method for the synthesis of 1,5-benzodiazepines involves an acid-catalyzed condensation of *o*-phenylenediamines with α,β-unsaturated carbonyl compounds or β-halo ketones or ketones. Many reagents have been utilized for this reaction including polyphosphoric acid-SiO_2, $BF_3{\cdot}OEt_2$, $NaBH_4$, $Yb(OTf)_3$, MgO-$POCl_3$, and more recently acetic acid under microwave conditions [40–42]. In this study various 1,5-benzodiazepine derivatives were synthesized by the condensation reaction of *o*-phenylenediamine with various ketones using the sulfated zirconia catalyst under solvent-free conditions (Scheme 3).

Table 3
Sulfated zirconia catalyzed synthesis of bis(indolyl)methanes

Entry	Indole	Aldehyde	Yield
1			85
2			84
3			78
4			82
5			73
6			78

Scheme 3. The condensation reaction (Scheme 3) was carried out by taking a mixture of *o*-phenylenediamine and ketone in a 1:2.5 mole ratio into a round bottom flask along with the catalytic amount of sulfated zirconia and the reaction mixture was stirred at ambient conditions for an appropriate time. In the presence of sulfated zirconia catalyst various ketones were found to react efficiently with substituted *o*-phenylenediamines giving high yields of 1,5-benzodiazepines. Cyclic ketones like cyclohexanone also reacted smoothly to produce the corresponding fused ring benzodiazepines. The results of this reaction are summarized in the Table 4. Under identical conditions unpromoted ZrO_2 was found to exhibit very negligible activity. Therefore, the observed high yields can be attributed to the superacidity of the sulfated zirconia catalyst.

3.4. Synthesis of diaryl sulfoxides

Sulfoxides and sulfones are important intermediates for the synthesis of large variety of organic sulfur compounds in the field of drugs and pharmaceuticals [43,44]. Recently, sulfoxides have received much attention as important chiral auxiliaries in asymmetric synthesis and in carbon–carbon bond forming reactions [45]. Usually, sulfoxides are prepared by indirect methods, which involve reduction of sulfones [46], oxidation of sulfides [47], and the reaction of organometallic reagents with sulfinic acid esters, mixed anhydrides or sulfines [48]. In addition to these indirect processes, diaryl sulfoxides can also be synthesized by the Friedel–Crafts sulfinylation of arenes using Lewis as well as Brönsted acids [49,50]. Some other methods like, addition of aryl Grignard reagents to thionyl chloride and reaction of SO_2 with arenes in the presence of magic acid also produce diaryl sulfoxides [51]. Very recently, this transformation has been reported with

Table 4
Sulfated zirconia catalyzed synthesis of 1,5-benzodiazepine derivatives

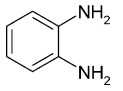
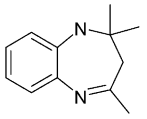
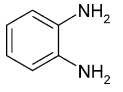
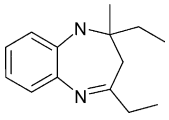
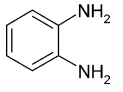
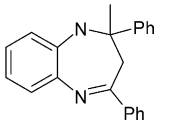
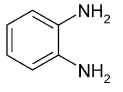
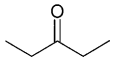
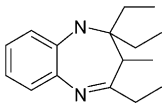
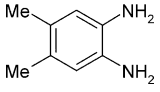
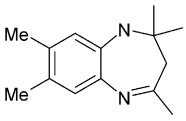
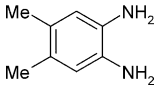
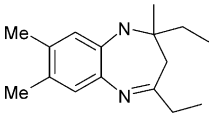
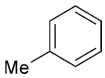
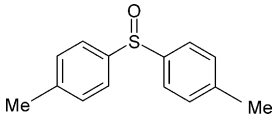
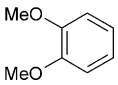
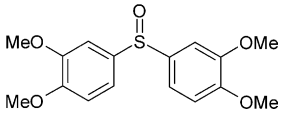
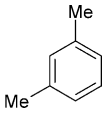
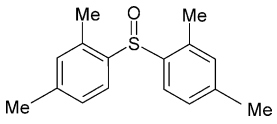
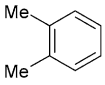
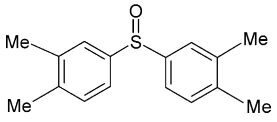
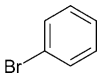
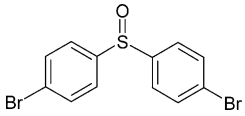
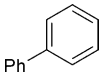
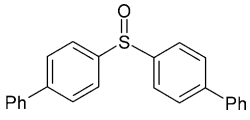
Entry	Diamine	Ketone	Product	Yield
1				94
2				91
3				96
4				84
5				94
6				91

Table 5
Sulfated zirconia catalyzed synthesis of diaryl sulfoxides

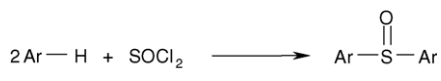
Entry	Arene	Product	Yield
1			90
2			92
3			85
4			83
5			88
6			80

metal triflates and in the presence of ionic liquids [52]. However, many of these methods have limitations that include, use of hazardous, corrosive and expensive reagents, formation of a mixture of products containing sulfonium salts and chlorinated byproducts along with the desired sulfoxides. Accordingly, a simple and high yielding one-pot approach for the synthesis of diaryl sulfoxides under mild reaction conditions is highly desirable. Our systematic investigations on this reaction revealed that sulfated zirconia efficiently catalyzes this reaction (Scheme 4).

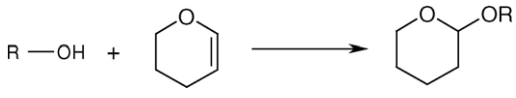
This reaction (Scheme 4) was carried out by taking arene and thionyl chloride (2:1 mole ratio) with catalytic amount of sulfated zirconia in a round bottom flask and stirred for an appropriate time under solvent-free conditions. Under these reaction conditions several substituted arenes reacted smoothly with thionyl chloride leading to the formation of corresponding diaryl sulfoxides in good to excellent yields. The efficiency of sulfated zirconia catalyst for the synthesis of diaryl sulfoxides with various activated and non-activated arenes is presented in Table 5. Major advantages associated with this procedure are cleaner reaction profiles, mild reaction conditions, shorter reaction times and operational simplicity.

3.5. Tetrahydropyranylation of alcohols and phenols

Tetrahydropyranylation is one of the most frequently used processes in organic synthesis for the protection of hydroxyl groups [53]. This is mainly due to high stability of resulting THP ethers in variety of reaction conditions, such as reduction, oxidation, strongly acidic and basic media, as well as ease in the deprotection of formed THP ethers [54]. Under acidic conditions alcohols and phenols react with 3,4-dihydropyran (DHP) to give tetrahydropyranyl ethers. Varieties of reagents have been reported for this reaction including protic-acids, Lewis acids, ion exchange resins, clays and expensive metal triflates [55–57]. Many of these methods are associated with several drawbacks such as long reaction times, severe refluxing conditions and some of the reagents employed are expensive.

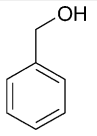
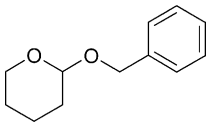
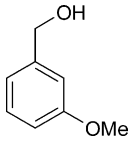
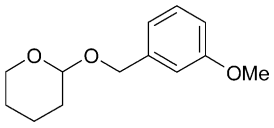
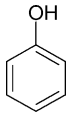
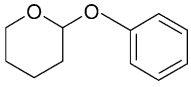
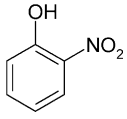
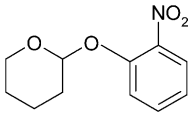
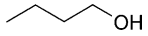
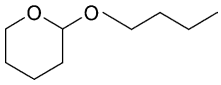
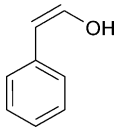
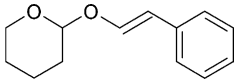


Scheme 4.



Scheme 5.

Table 6
Sulfated zirconia catalyzed tetrahydropyranylation of alcohols and phenols

Entry	Alcohol	Product	Yield
1			94
2			96
3			84
4			90
5			94
6			92

In this study a variety of alcohols and phenols were treated with 3,4-dihydro-2-*H*-pyran in the presence of catalytic amount of sulfated zirconia under solvent-free conditions at room temperature (Scheme 5). Tetrahydropyranyl ethers were produced in excellent yields at less reaction time [58]. The catalytic results obtained with sulfated zirconia are summarized in Table 6. The present procedure for tetrahydropyranylation is quite simple and can be employed for a wide range of hydroxy compounds.

4. Conclusions

The solid acid catalyst sulfated zirconia was found to catalyze efficiently a variety of organic synthesis and transformation reactions leading to the formation of various pharmacologically/biologically important molecules such as 1,5-benzodiazepines, bis(indolyl)methane derivatives and dihydropyrimidinones. Simple work up procedure, milder reaction conditions and shorter reaction times are some of the advantages associated with the sulfated zirconia catalyzed processes. More importantly this catalyst is able to facilitate an increasing number of solvent-free conversions. This opens up a broad field of possible applications for ZrO_2-based catalysts in organic synthesis and transformation reactions.

Acknowledgement

P.M.S and P.L. thank Council of Scientific and Industrial Research (CSIR), New Delhi for the award of senior research fellowships.

References

[1] A. Corma, H. Garcia, Chem. Rev. 103 (2003) 4307.
[2] K. Tanabe, W.F. Hölderich, Appl. Catal. A: Gen. 181 (1999) 399.
[3] K. Arata, Adv. Catal. 37 (1990) 165.
[4] K. Arata, Appl. Catal. A: Gen. 146 (1996) 3.
[5] X. Li, K. Nagaoka, L.J. Simon, J.A. Lercher, J. Catal. 230 (2005) 229.
[6] B.H. Davis, R.A. Keogh, R. Srinivasan, Catal. Today 20 (1994) 219.
[7] G.D. Yadav, J.J. Nair, Microporous Mesoporous Mater. 33 (1999) 1.
[8] X. Song, A. Sayari, Catal. Rev. Sci. Eng. 38 (1996) 329.
[9] J.H. Clark, Acc. Chem. Res. 35 (2002) 791.
[10] A. Corma, Chem. Rev. 95 (1995) 599.
[11] T. Okuhara, Chem. Rev. 102 (2002) 3641.
[12] A. Khodakov, J. Yang, S. Su, E. Iglesia, A.T. Bell, J. Catal. 177 (1998) 343.
[13] D.J. Zalewski, S. Alerasool, P.K. Doolin, Catal. Today 53 (1999) 419.
[14] M. Scheithauer, R.E. Jentoft, B.C. Gates, H. Knözinger, J. Catal. 191 (2000) 271.
[15] M. Scheithauer, R.K. Grasselli, H. Knözinger, Langmuir 14 (1998) 3019.
[16] C. Morterra, G. Cerrato, S. Ardizzone, C.L. Bianchi, M. Signoretto, F. Pinna, Phys. Chem. Chem. Phys. 4 (2002) 3136.
[17] B.M. Reddy, P.M. Sreekanth, V.R. Reddy, J. Mol. Catal. A: Chem. 225 (2005) 71.
[18] C.O. Kappe, Eur. J. Med. Chem. 35 (2000) 1043.
[19] C.O. Kappe, Tetrahedron 49 (1993) 6937.
[20] B.B. Snider, Z. Shi, J. Org. Chem. 58 (1993) 3828.
[21] L.E. Overman, M.H. Rabiniwitz, P.A. Renhowe, J. Am. Chem. Soc. 117 (1995) 2657.
[22] A.D. Patil, N.V. Kumar, W.C. Kokke, M.F. Bean, A.J. Freyer, C. Debrosse, S. Mai, A. Trunch, D.J. Faulkner, B. Carte, A.L. Breen, R.P. Hertzberg, R.K. Johnson, J.W. Westley, B.C.M. Ports, J. Org. Chem. 60 (1995) 1182.
[23] P. Biginelli, Gazz. Chim. Ital. 23 (1893) 360.
[24] C.O. Kappe, D. Kumar, R.S. Varma, Synthesis (1999) 1799.
[25] G. Sabita, G.S.K.K. Reddy, K.B. Reddy, J.S. Yadav, Tetrahedron Lett. 44 (2003) 6497.
[26] R. Varala, M.M. Alam, S.R. Adapa, Synlett (2003) 67.
[27] A.S. Paraskar, G.K. Dewkar, A. Sudalai, Tetrahedron Lett. 44 (2003) 3305.
[28] R.J. Sundberg, The Chemistry of Indoles, Academic Press, New York, 1970.
[29] T.R. Garbe, M. Kobayashi, N. Shimizu, N. Takesue, M. Ozawa, H. Yukawa, J. Nat. Prod. 63 (2000) 596.
[30] P. Ehrlich, Medicin Woche (1901) 151.
[31] W. Remers, Chem. Heterocycl. Compd. 25 (1972) 1.
[32] M. Roomi, S. Mac Donald, Can. J. Chem. 48 (1970) 139.
[33] J. Banarji, A. Chatterjee, S. Manna, C. Pascard, T. Parange, J. Shoolery, Heterocycles 15 (1981) 325.
[34] J.S. Yadav, B.V.S. Reddy, C.V.S.R. Murthy, G.M. Kumar, Ch. Madan, Synthesis (2001) 783.
[35] C.J. Magesh, R. Nagarajan, M. Karthik, P.T. Perumal, Appl. Catal. A: Gen. 266 (2004) 1.
[36] X. Mi, S. Luo, J. He, J.P. Cheng, Tetrahedron Lett. 45 (2004) 4567.
[37] H. Schutz, Benzodiazepines, Springer, Heidelberg, 1982.
[38] R.C. Haris, J.M. Straley, US Patent 1,537,757 (1968).

[39] K.V.V. Reddy, P.S. Rao, D. Ashok, Synth. Commun. 30 (2000) 1825.
[40] M. Balakrishna, B. Kaboudin, Tetrahedron Lett. 42 (2001) 1127.
[41] M. Pozarentzi, J.S. Stephanatou, C.A. Tsoleridis, Tetrahedron Lett. 43 (2002) 1755.
[42] B.M. Reddy, P.M. Sreekanth, Tetrahedron Lett. 44 (2003) 4447.
[43] H.L. Holland, Chem. Rev. 88 (1988) 473.
[44] E. Block, Angew. Chem. Int. Ed. Engl. 31 (1992) 1135.
[45] M.C. Carreno, Chem. Rev. 95 (1995) 1717.
[46] I.W.J. Still, F.J. Ablenas, J. Org. Chem. 48 (1983) 1617.
[47] Y.J. Chen, Y.U. Huang, Tetrahedron Lett. 41 (2000) 5233.
[48] J. Drabowicz, P. Kielbasinski, M. Mikolajczyk, in: S. Patai, Z. Rappoport, C.J.M. Stirling (Eds.), The Chemitry of Sulfones and Sulfoxides, Wiley, New York, 1988 (Chapter 8).
[49] G.A. Olah, J. Nishimura, J. Org. Chem. 39 (1974) 1203.
[50] G.A. Olah, E.R. Marinez, G.K.S. Prakash, Synlett (1999) 1397.
[51] K.K. lalli, D.S. Nagvekar, J. Org. Chem. 56 (1991) 1867.
[52] J.S. Yadav, B.V.S. Reddy, R.S. Rao, S.P. Kumar, K. Nagaiah, Synlett (2002) 784.
[53] T.W. Greene, P.G.M. Wuts, Protective Groups in Organic Synthesis, second ed., J. Wiley, New York, 1991.
[54] S. Hoyer, P. Laszlo, Synthesis (1986) 655.
[55] Y.G. Wang, X.X. Wu, Z.Y. Jiang, Tetrahedron Lett. 45 (2004) 2973.
[56] B. Tamami, K.P. Borujeny, Tetrahedron Lett. 45 (2004) 715.
[57] T. Mineno, Tetrahedron Lett. 43 (2002) 7975.
[58] B.M. Reddy, P.M. Sreekanth, Synth. Commun. 32 (2002) 3561.