Silica Sulfuric Acid (SSA): An Efficient and Heterogeneous Catalyst for Organic Transformations

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Abstract: Silica sulfuric acid (SSA) has been used as an efficient solid acidic catalyst for many organic reactions. In this review, we wish to report some applications of this catalyst in organic synthesis.

Keywords: Silica sulfuric acid (SSA), heterogeneous catalyst, organic reactions.

1. INTRODUCTION

In recent years, heterogeneous catalysts have gained more importance due to environeconomic factors. They have successfully been utilized in several organic transformations to minimize undesirable waste causing environmental pollution. The concept of utilization of catalysts and reagents adsorbed on insoluble inorganic supports is increasingly popular. Reactions with such catalysts and reagents often have the advantages of ease of setup and work-up, mild reaction conditions, increased yield and greater selectivity. Silica supported catalysts and reagents are gaining considerable attention because of higher activity of the catalyst due to the larger surface area and better selectivity. In addition, they have high mechanical and thermal stability, easiness in handling, low toxicity, non-corrosive nature, particularly low price, air tolerance, simplicity in separation of the catalyst after completion of the reaction and reusability of the catalyst, which make it promising for both academic and industrial applications.

Silica sulfuric acid has received considerable attention as an efficient, inexpensive, eco-friendly, highly reactive, available, non-toxic and recyclable catalyst for various organic transformations, affording the corresponding products in excellent yields with high selectivity. Some applications of SSA have been reviewed by Salehi *et al.* in 2006 [1]. In the following sections, we wish to update some recent advances in applications of SSA in organic synthesis.

1.1. Preparation of Silica Sulfuric Acid

A 500 mL suction flask was equipped with a constant pressure dropping funnel containing chlorosulfonic acid (23.3 g, 0.2 mol) and a gas inlet tube for conducting HCl gas over an adsorbing solution i.e. H_2O. Then 60.0 g of silica gel was charged in to the flask. Chlorosulfonic acid was added drop wise over a period of 30 min at room temperature. HCl gas evolved from the reaction vessel immediately. After the addition was complete, the mixture was shaken for 30 min. SSA was obtained (76 g) as a white solid [2].

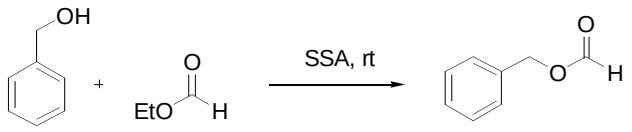
2. APPLICATIONS OF SSA IN FUNCTIONAL GROUP TRANSFORMATIONS

2.1. Protection of Functional Groups

2.1.1. Protection of Hydroxyl Groups

2.1.1.1. Formylation of Alcohols

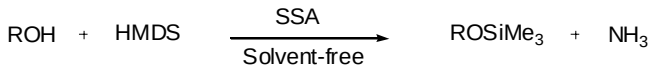
O-Formylation could be the method of choice for protecting an alcoholic group in a complex synthetic sequence because deformylation can be selectively effected in the presence of acetate or other ester protecting groups. Further, if the alcoholic group is planned to be oxidized later in the synthetic scheme, there is no need to deprotect the formylated alcoholic group, and direct oxidation under Oppenauer conditions can be realized [3]. A mixture of ethyl formate and a catalytic amount of silica sulfuric acid as suitable formylating systems can formylate various alcohols to their corresponding formate ester derivatives under mild, nearly neutral and heterogeneous conditions at room temperature with good to excellent yields (Scheme **1**). Chemoselectivity, the cheapness and availability of the reagents, nearly neutral and heterogeneous conditions, easy and clean work-up and high yields are some advantages of this protocol [4].



Scheme 1.

2.1.1.2. Silylation of Hydroxyl Groups

Protection of the hydroxyl functional group is an important process in multi-step synthesis. At room temperature, alcohols and phenols can be efficiently protected with hexamethyldisilazane (HMDS) in the presence of silica sulfuric acid in good to excellent yields (Scheme **2**). The catalyst can be recycled for subsequent reactions without any appreciable loss of efficiency. In this method, SSA was found to be an efficient and simple catalyst for the silylation of various hydroxyl substrates with HMDS under very mild conditions in high yields. In addition, SSA is cheap, stable, easy to handle, nontoxic and separated by filtration [5].



Scheme 2.

2.1.1.3. Fischer Type Glycosylation

Fischer glycosylation, a widely used technique for the preparation of simple alkyl or aryl glycosides, has a few drawbacks including the use of strong mineral acids, excess alcohols, high temperature and long reaction times. The following protocol highlights a modification using sulfuric acid immobilized on silica as catalyst for the preparation of glycosides from free sugars such as D-glucose, D-galactose, D-mannose, L-rhamnose, L-fucose, N-acetyl-D-glucosamine and D-maltose with a diverse range of alcohols to afford a series of useful sugar derivatives in good to excellent yields (Scheme **3**). This strategy is equally applicable for large-scale preparations [6].

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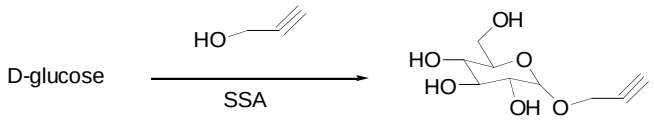
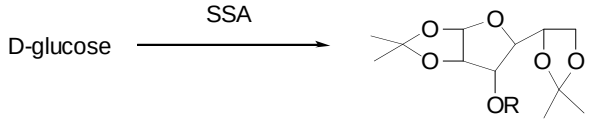


Scheme 3.

2.1.1.4. Synthesis of O-isopropylidene Sugar Derivatives

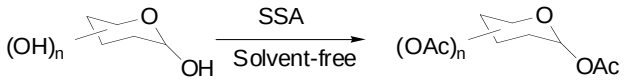
Sulfuric acid immobilized on silica proved to be an efficient catalyst for the synthesis of O-isopropylidene sugar derivatives from reducing sugars. The method is very simple and economic for large-scale synthesis in which the catalyst is recovered and reused several times (Scheme **4**). Reactions with D-glucose, D-galactose, D-mannose, L-rhamnose, L-arabinose, D-xylose and L-sorbose led to the formation of the corresponding thermodynamically stable di-O- and/or mono-O-isopropylidene derivatives in good to excellent yields [7].



Scheme 4.

2.1.1.5. Acetylation of Sugars

Acetylation of sugars catalyzed by silica sulfuric acid has been reported (Scheme **5**). In this reaction, SSA shows a highly catalytic nature, easy to handle procedure, short reaction time, recycle exploitation, insensitivity to air and moisture, and excellent isolated yields. The catalyst could be recycled at least five times [8].



Scheme 5.

In another work, SSA has been used as an efficient and safe alternative promoter for acetalation and subsequent acetylation of sugar glycosides using stoichiometric reagents without work-up. The synthesis of different types of per-O-acetylated acetals/ketals has been achieved from various types of O- and S-glycosides in excellent yields (Scheme **6**). This strategy is compatible with various glycosides, including acid labile p-methoxyphenyl glycosides, and is equally applicable to large-scale synthesis [9].

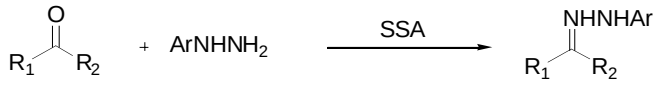
2.1.2. Protection of Amines

2.1.2.1. Synthesis of N-acylsulfonamides

N-Acylsulfonamides have received considerable attention due to their diverse biological activities as precursors of therapeutic agents for Alzheimer's disease [10], antibacterial inhibitors of tRNA synthetases [11], antagonists for Angiotensin II [12], and Leukotriene D4-receptors [13]. Silica sulfuric acid catalyzes efficiently the reaction of sulfonamides with both carboxylic acid anhydrides and chlorides under solvent-free and heterogeneous conditions (Scheme **7**). All the reactions have been done at room temperature and the N-acylsulfonamides have been obtained with high yields and purity via an easy work-up procedure [14].

2.1.2.2. Preparation of Phenylhydrazones and 2,4-dinitro Phenylhydrazones

SSA is an effective catalyst for the conversion of carbonyl compounds to their corresponding phenylhydrazones and 2,4-dintrophenylhydrazones under solvent-free conditions (Scheme **8**). This procedure provides an easy, mild, efficient, versatile, and general methodology for the protection of different classes of carbonyl compounds, and we feel that it may be a suitable addition to methodologies already present in the literature [15].

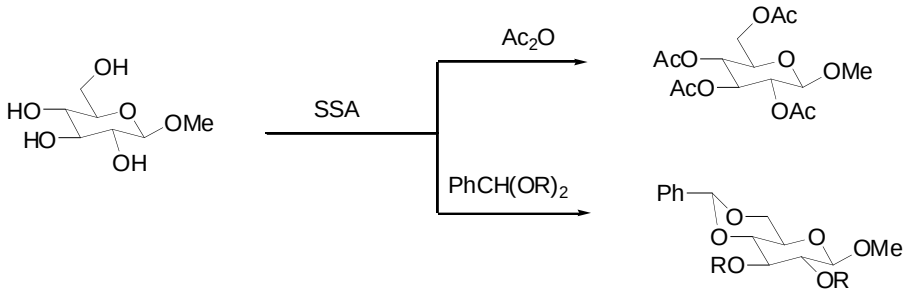


Scheme 8.

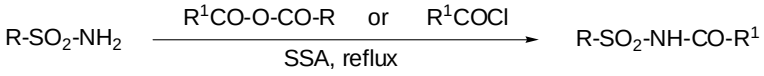
2.1.2.3. Synthesis of N-sulfonylimines

Recently, the synthesis and application of N-sulfonylimines from aldehydes and sulfonamides has been found to be very useful in organic chemistry. N-sulfonylimines are powerful synthetic intermediates in organic synthesis [16,17]. N-sulfonylimines have been successfully synthesized by the reaction of aldehydes with sulfonamides in the presence of SSA (Scheme **9**). In this method, SSA as a solid acid catalyst can offer definite advantages over traditional catalysts in terms of operational simplicity, short reaction time, non-polluting conditions and high yields for the synthesis of N-sulfonylimines [18].

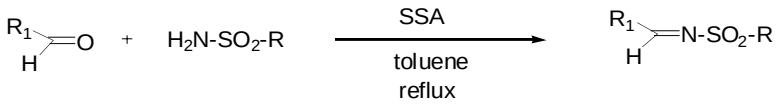
In another work, SSA has been used for the synthesis of N-sulfonylimines via the condensation of sulfonamides with isatin as well as aldehydes under solvent-free conditions (Scheme **10**) [19].



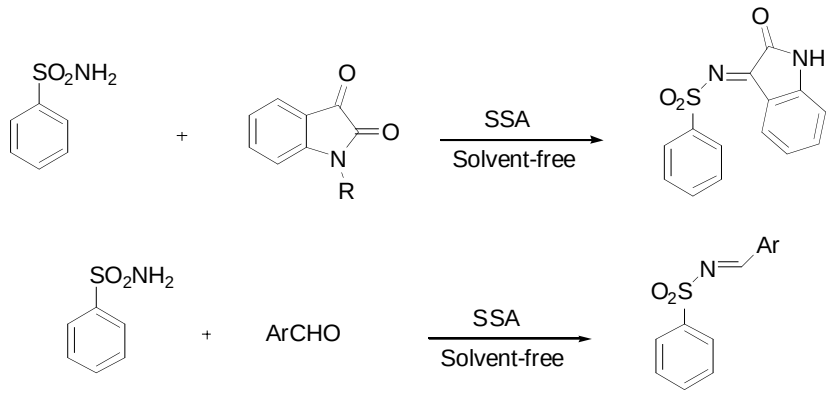
Scheme 6.



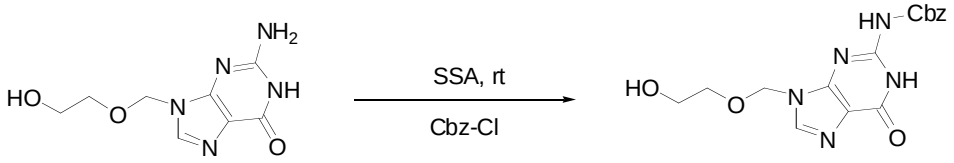
Scheme 7.



Scheme 9.



Scheme 10.



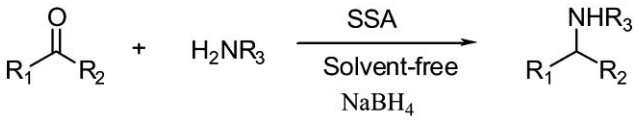
Scheme 11.

2.1.2.4. Cbz-protection of Amines

The benzyloxycarbonyl (Cbz) protected the amido are useful synthetic precursors for various pharmaceuticals and natural products [20,21]. The Cbz group is a very important functionality for the protection of amines and amine derivatives, since it can be easily removed by catalytic hydrogenation without any side reactions, and is stable to basic and most aqueous acidic conditions [22]. A simple, facile, and chemoselective N-benzyloxycarbonylation of amines using silica sulfuric acid that proceeds under solvent-free conditions at room temperature has been achieved (Scheme **11**). These reactions are applicable to a wide variety of primary (aliphatic and cyclic), secondary amines, amino alcohols, and heterocyclic amines [23].

2.1.2.5. Reductive Amination of Aldehydes and Ketones

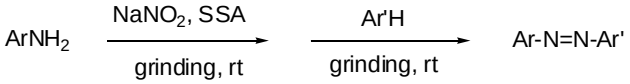
The reductive amination reaction remains one of the most powerful and widely utilized transformations available to practitioners of chemical synthesis in the modern era [24]. A regioselective and convenient procedure for preparation of amines by reductive amination of aldehydes and ketones using sodium borohydride in the presence of sulfuric acid supported on silica gel as an active, inexpensive, and recoverable catalyst under heterogeneous and solvent-free conditions at room temperature has been described (Scheme **12**). The advantages of this system, such as simple workup procedure, regioselective and rapid reduction, excellent yields, energy savings, avoidance of solvent waste dangers and toxicity, neutral reaction conditions, and use of safe and inexpensive reagents with no special handling techniques (which is important from an environmental point of view) make this method a good alternative to the existing methods [25].



Scheme 12.

2.1.2.6. Diazotization and Diazo Coupling Reactions

Diazonium salts are useful synthetic building blocks in organic synthesis. A convenient, rapid, one-pot method for the synthesis of azo dyes has been developed by the sequential diazotization–diazo coupling of aromatic amines with $NaNO_2$, silica sulfuric acid and coupling agents under solvent-free conditions at room temperature. Using this method, several types of aromatic amine, containing electron-withdrawing groups as well as electron-donating groups, were rapidly converted to the corresponding azo dyes in good yield (Scheme **13**). This method has some advantages over traditional methods which include mild reaction conditions at room temperature, short reaction time and easy experimental work-up procedure [26].



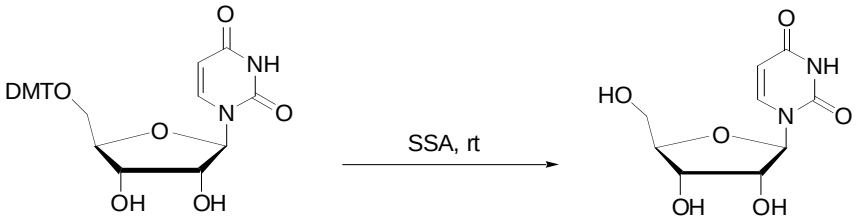
Scheme 13.

2.2. Deprotection Reactions

2.2.1. Hydrolysis of the Terminal O-isopropylidene Group of Sugar Derivatives

Sulfuric acid immobilized on silica proved to be an efficient catalyst for selective hydrolysis of the terminal O-isopropylidene

Scheme 14.



Scheme 15.

group of sugar derivatives. Reactions with di-O-isopropylidene derivatives of D-glucose, D-mannose, D-fructose and L-sorbose led to the formation of the corresponding mono-O-isopropylidene derivatives in good to excellent yields (Scheme **14**). The method is very simple and economic for large-scale synthesis in which the catalyst is recovered and reused for several runs [27].

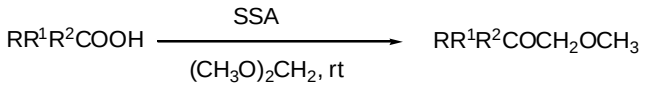
2.2.2. Detritylation of 5'-tritylated Nucleosides

A rapid, mild and highly efficient procedure for the chemoselective deprotection of triphenylmethyl (trityl, Tr), p-anisyldiphenylmethyl (monomethoxytrityl, MMT) and di-(p-anisyl)phenylmethyl (dimethoxytrityl, DMT) groups from nucleoside tritylethers has been established. The deprotection has been achieved at room temperature, using a catalytic amount of silica sulfuric acid in acetonitrile. The trityl nucleosides have been deprotected in 2-17 min without any depurination (Scheme **15**). This method offers several advantages including: (i) The acid sensitive glycosidic bond in nucleosides is not cleaved by SSA, (ii) Chemoselective removal of the trityl moiety from nucleoside trityl ethers in the presence of other acid sensitive hydroxyl protecting groups was possible using a catalytic amount of SSA, and (iii) SSA is an inexpensive and non toxic catalyst, which can be easily prepared, recycled and reused [28].

2.3. Esterification Reactions

2.3.1. Methoxymethylation of Alcohols

Methoxymethylation of a variety of alcohols has been performed using formaldehyde dimethoxy acetal in the presence of SSA at room temperature under solvent-free conditions (Scheme **16**). The methoxymethyl ethers (MOM-ethers) have been obtained in high yields and purity. This procedure has demonstrated that silica sulfuric acid could be used for the methoxymethylation of primary, secondary, and tertiary alcohols by formaldehyde dimethoxy acetal. The notable advantages of this method are mild reaction conditions, high yields, cheapness, safety, eco-friendliness, and recyclability of the catalyst [29].

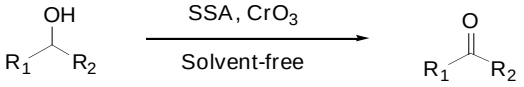


Scheme 16.

3. OXIDATION REACTION

3.1. Oxidation of Alcohols

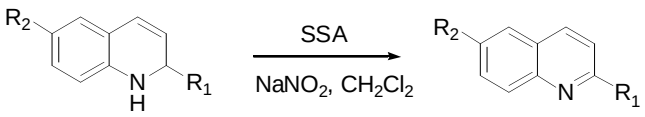
Oxidation of alcohols to carbonyl compounds constitutes one of the fundamental transformations in organic synthesis. A rapid method for the selective oxidation of primary and secondary alcohols to the corresponding carbonyl compounds using CrO_3/silica sulfuric acid has been developed (Scheme **17**) [30].



Scheme 17.

3.2. Aromatization of 1,2-dihydroquinolines

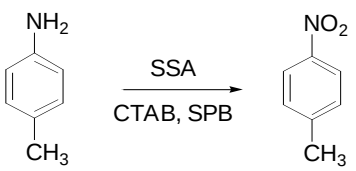
A combination of SSA and $NaNO_2$ in the presence of wet-SiO_2 has been used as an effective oxidizing agent for the oxidation of 1,2-dihydroquinolines to their corresponding quinoline derivatives in dichloromethane at room temperature with excellent yields (Scheme **18**). The notable advantages of this method are mild reaction conditions, high yield, cheapness, safety, eco-friendliness, and recyclability of the silica sulfuric acid [31].



Scheme 18.

3.3. Oxidation of Aromatic Amines to their Corresponding Nitro Compounds

Electron-donating substituted anilines have been converted to their corresponding nitro compounds with sodium perborate in the presence of a catalytic amount of silica sulfuric acid under micellar media in moderate to good yields (Scheme **19**). Some advantages of the proposed system are oxidation of different anilines to the desired nitro compounds without observing any side products, direct conversion of the amino group to the related nitro functional group, so that the nitro group will be created in the exact position and the problem of regioselectivity will be solved, and application of a catalytic amount of silica sulfuric acid as a low cost solid acid [32].

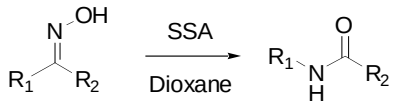


Scheme 19.

4. SYNTHESIS OF AMIDE DERIVATIVES

4.1. Beckmann Rearrangement of Oximes

The conversion of ketoxime into corresponding amide, known as Beckmann rearrangement, is a common method used in organic chemistry and is also a topic of current interest. Silica sulfuric acid has been proved to be a good catalyst for liquid-phase Beckmann rearrangement of oximes in dried dioxane at room temperature (Scheme **20**). Excellent conversion and selectivity were acquired in the Beckmann rearrangement of cyclohexanone oxime. The catalyst system was recycled and reused. This Beckmann rearrangement of ketoximes can be conducted with silica sulfuric acid as catalyst under mild condition, excellent conversion and selectivity were obtained [33].



Scheme 20.

5. THE USE OF SSA IN CARBON-CARBON COUPLING REACTIONS

5.1. Synthesis of β-amino Ketones

Mannich reactions are among the most important carbon-carbon bond forming reactions in organic synthesis [34]. They provide β-amino carbonyl compounds, which are important synthetic intermediates for various pharmaceuticals and natural products [35]. At room temperature, the direct Mannich-type reaction of a variety of in situ generated aldimines using aldehydes and anilines with ketones in a three-component reaction has been efficiently catalyzed by SSA in EtOH. This rapid reaction afforded the corresponding β-amino ketones in good yields with excellent stereoselectivities and catalyst was recyclable (Scheme **21**). The significant features of this procedure include: (i) high yields, (ii) good stereoselectivities, (iii) facile operations, (iv) recyclable catalysts, and (v) non-toxic solvents [36].

5.2. Synthesis of bis(indolyl)alkanes

Bis(indolyl)methanes are known to promote estrogen metabolism in both women and men, and are expected to have an application in the prevention of breast cancer [37]. Silica sulfuric acid has been found to be a mild, efficient and reusable solid acid catalyst in electrophilic substitution reaction of indoles with carbonyl compounds to afford the corresponding bis(indolyl)alkanes in excellent yields under solvent-free conditions (Scheme **22**) [38].

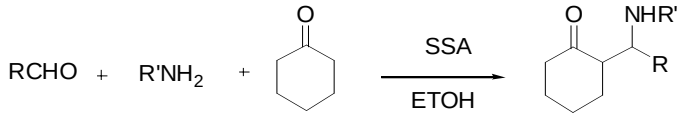
5.3. Friedel-Crafts Alkylation of Indoles

Indoles and their derivatives occur in nature and have a variety of biological activities [39]. The 1,4-conjugate addition of indoles to nitro olefins has been efficiently carried out using an environmentally benign catalyst, silica sulfuric acid, at ambient temperature (Scheme **23**). This reaction has been demonstrated that silica sulfuric acid is a superior acid catalyst for the alkylation of indoles with nitro olefins. This procedure has the advantages of mild reaction conditions, high yields of products, short reaction times, and simple experimental/product-isolation techniques, which make it a useful and attractive process for the synthesis of alkylated indole derivatives [40].

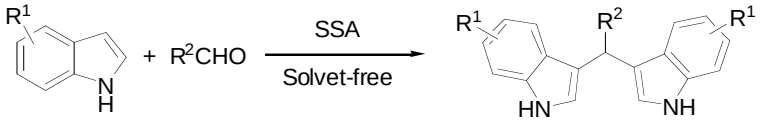
6. SSA-CATALYZED HETEROCYCLIC COMPOUNDS SYNTHESIS

6.1. Synthesis of 3-aminoimidazo[1,2-a]pyridines and Pyrazines

The imidazo[1,2-a]pyridine and imidazo[1,2-a]pyrazine moieties constitute a class of biologically active compounds that are potentially anti-inflammatory [41], antibacterial agents [42], inhibitors of gastric acids secretion [43], calcium channel blockers [44], and sedative-hypnotic drugs, such as Zolpidem and Alpidem [45]. The synthesis of 3-aminoimidazo[1,2-a]pyridines and 3-aminoimidazo[1,2-a]pyrazines through a condensation reaction of 2-aminopyridine or 2-aminopyrazine, aldehyde, and alkyl or aryl isocyanide in high yields at room temperature in the presence of silica sulfuric acid was accomplished (Scheme **24**) [46].

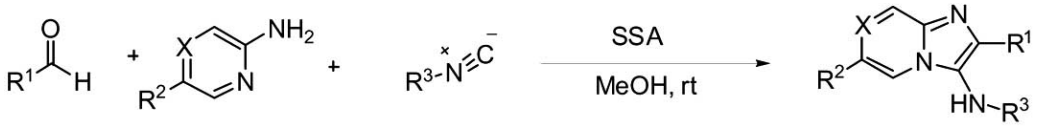


Scheme 21.



Scheme 22.

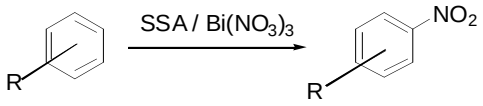
Scheme 23.



Scheme 24.

6.2. Nitration of Aromatic Compounds

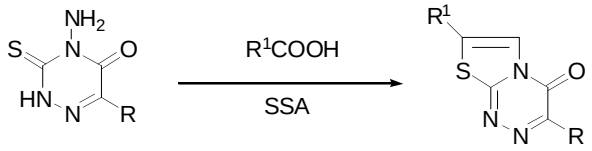
Aromatic nitro compounds are important starting materials for the manufacture of various industrial products such as pharmaceuticals, dyes and plastics. A number of aromatic compounds have been nitrated to the corresponding nitroaromatic derivatives with the use of supported bismuth (III) nitrate on silica sulfuric acid under solvent-free conditions (Scheme **25**). This procedure for the nitration of aromatic compounds with supported bismuth (III) nitrate on SSA under solvent-free conditions is effective for both activated and deactivated substrates [47].



Scheme 25.

6.3. Synthesis of [1,3,4] thiadiazolo [2,3-*c*][1,2,4] triazin-4-ones

[1,3,4]Thiadiazolo[2,3-c][1,2,4]triazin-4-ones have been prepared by one pot condensation and cyclization of 4-amino-[1,2,4]triazine-3-thione-5-ones with various aromatic carboxylic acids in the presence of silica gel sulfuric acid in solventless condition (Scheme **26**). In comparison with the presently available synthetic method for the synthesis of [1,3,4]thiadiazolo[2,3-c][1,2,4]triazin-4-ones, which uses neat sulfuric acid [48b] and phosphorus oxychloride [48a,c], and shows drawback from the standpoint of yield, price, and its hazardous nature, the efficiency of the present work is apparent from the availability of inexpensive sulfuric acid and high yields. Also, due to the lack of solvent, the workup procedure is easy [49].



Scheme 26.

6.4. Synthesis of thiazolo[3,2-*b*]1,2,4-triazoles

3-Mercapto-1,2,4-triazoles have been condensed with allyl bromide, and regioselectively cyclized to give 2,3-dihydro-3-methylthiazolo[3,2-b]1,2,4-triazoles (Scheme **27**). This protocol has developed a facile and eco-friendly method for the synthesis of thiazolo[3,2-*b*]1,2,4-triazoles using SSA as an efficient catalyst [50].

6.5. Synthesis of aryl-14H-dibenzo-[*a,j*]xanthens

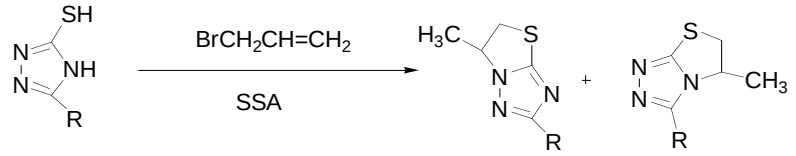
Considerable interest has been focused on the synthesis of xanthenes; in particular, benzoxanthenes have attracted much attention in recent years because of their wide range of biological and pharmacological applications [51]. The one-pot synthesis of aryl-14H-dibenzo[a,j]xanthenes has been described from a known reaction between substituted aldehydes and β-naphthol in the presence of heterogeneous catalyst, silica sulfuric acid, under conventional heating as well as solvent-free conditions to afford good to excellent yields (Scheme **28**). This methodology addresses the current drive toward green chemistry due to the cheapness and easy availability of the substrate, simple workup, high yield, easy handling, non-toxicity of the catalyst, and reusability of the catalyst [52].

6.6. Synthesis of Trisubstituted Imidazoles

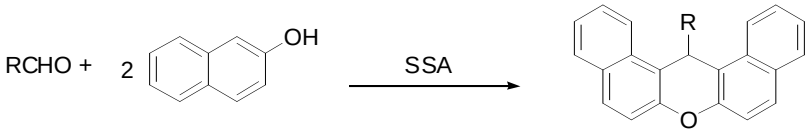
Multi-substituted imidazoles are an important class of compounds in the field of pharmaceuticals and exhibit a wide spectrum of biological activities [53]. Trisubstituted imidazoles have been synthesized in high yields in the presence of silica sulfuric acid as an inexpensive solid acid catalyst under solvent-free classical heating conditions as well as using microwave irradiation (Scheme **29**). The silica sulfuric acid can be recovered for the subsequent reactions and reused without any appreciable loss of efficiency. Low corrosiveness, safety, less waste, ease of separation and recovery are advantages of this method [54].

6.7. Conjugate Addition of thiols to α,β-unsaturated Ketones

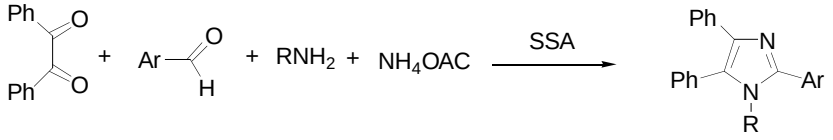
Conjugate addition of thiols to α,β-unsaturated ketones to form a carbon-sulfur bond constitutes a key reaction in biosynthetic processes as well as in organic synthesis. Silica sulfuric acid has been found to be useful and highly efficient catalyst for conjugate addition of thiols to α,β-unsaturated ketones under solvent-free



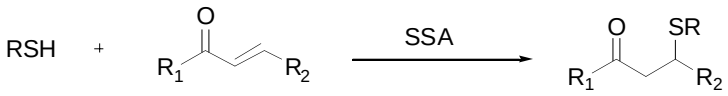
Scheme 27.



Scheme 28.



Scheme 29.

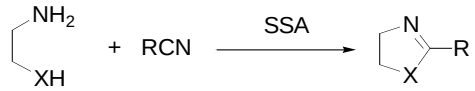


Scheme 30.

conditions at room temperature (Scheme **30**). Short reaction time, high yields, and avoidance of anhydrous conditions should make this protocol a useful alternative to existing methods [55].

6.8. Synthesis of Oxazolines and Imidazolines

A practical, efficient and inexpensive method for the synthesis of 2-oxazolines and 2-imidazoline from the reaction of nitriles with β-aminoalcohols and ethylenediamine (EDA), respectively, using silica sulfuric acid as a heterogeneous catalyst under reflux conditions has been reported (Scheme **31**). This catalyst has been successfully applied for the chemoselective conversion of dicyanobenzenes to their corresponding mono and bis-oxazolines. The application of ultrasonic irradiation has improved the yields and reduced the reaction time. The use of silica sulfuric acid is feasible because of its easy preparation, easy handling, stability, easy recovery, reusability, good activity and eco-friendliness. The method offers several noteworthy advantages including good yields of products and easy work-up. On the other hand, ultrasonic irradiation has increased the catalytic activity and higher product yields have been obtained [56].



Scheme 31.

6.9. Preparation of 2H-indazol[2,1-b]phthalazine-triones

Phthalazine derivatives have some biological activities such as anticonvulsant [57], cardiotonic [58], and vasorelaxant [59] properties. Silica sulfuric acid has been used as an efficient and reusable heterogeneous catalyst for the preparation of 2H-indazol[2,1-b]phthalazine-1,6,11(13H)-trione derivatives from the three-component condensation reaction of phthalhydrazide, dimedone, and aromatic aldehydes under solvent-free conditions in good to excellent yields and short reaction time (Scheme **32**). The methodology is safer than those using conventional catalysts like H_2SO_4 and H_3PO_4 with respect to the amount, hazard and reaction conditions. In addition, the catalyst could be successfully recovered and recycled at least for five runs without significant loss in activity [60].

6.10. Synthesis of Oxindole Derivatives

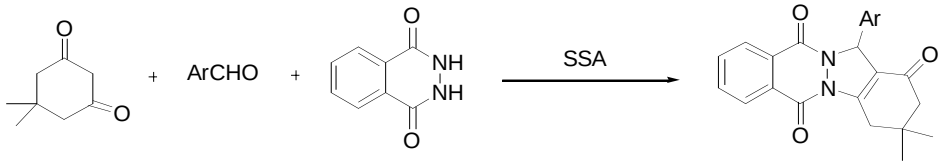
Isatins are familiar for their manifold biological activity. Some derivatives of isatin are key intermediates in the synthesis of natural products [61]. Silica sulfuric acid has catalyzed efficiently the electrophilic substitution reaction of an indoles with various isatins in dichloromethane to afford the corresponding oxindoles derivatives in high yields at room temperature (Scheme **33**). The catalyst exhibited remarkable reusable activity. This method offers several advantages including high yield of products, short reaction time, recyclability of the catalyst and easy experimental workup procedure [62].

6.11. Synthesis of Pyrazoles, Diazepines, β-enaminones

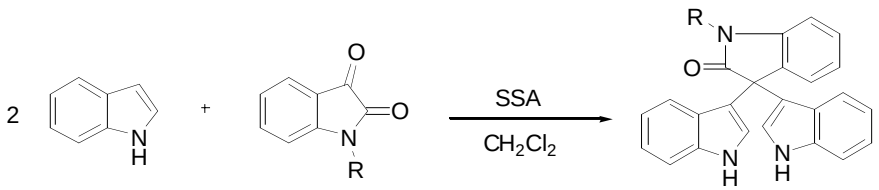
Pyrazoles and diazepines are valuable bioactive heterocycles, which are shown to possess important biological and pharmaceutical activities such as antimicrobial, antiviral, antitumor, anti-inflammatory, antifungal, antidepressant, and anticonvulsant activities [63]. Silica-supported sulfuric acid has been utilized as a heterogeneous recyclable catalyst for highly efficient regio- and chemoselective condensation of hydrazines, diamines, and primary amines with various β-dicarbonyl compounds at room temperature to afford pyrazoles, diazepines, and β-enaminones under solvent-free conditions within 5-15 min (Scheme **34**). The solvent-free conditions, simple experimental procedure, mildness of the conversion, clear reaction profiles, high yields and chemo- and regioselectivities, short reaction time, and low cost, stability, and reusability of the catalyst are the noteworthy advantages of the protocol [64].

6.12. Chemoselective-nitrosation of β-diketones

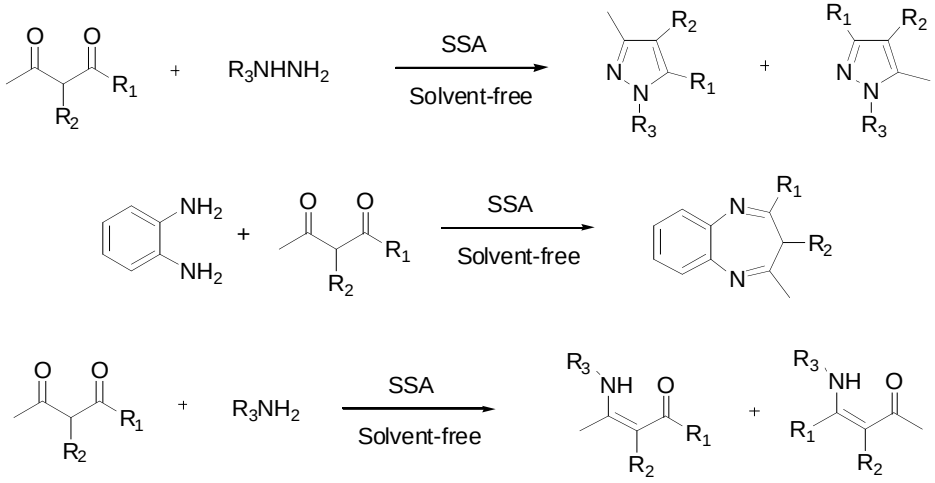
A combination of silica sulfuric acid and sodium nitrite in the presence of wet SiO_2 has been used as an effective nitrosating agent for the nitrosation of β-diketones to their corresponding α-nitroso or α-oximinoketones under mild and heterogeneous conditions in



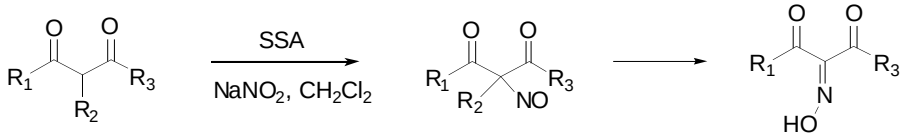
Scheme 32.



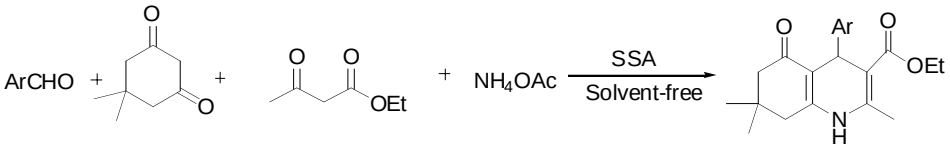
Scheme 33.



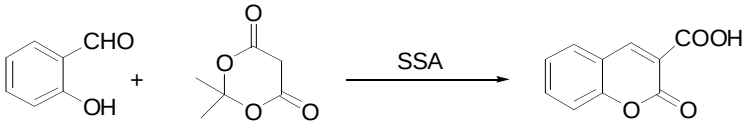
Scheme 34.



Scheme 35.



Scheme 36.



Scheme 37.

moderate to excellent yields (Scheme **35**). The low cost and the availability of the reagents, easy and clean work-up, and high yields make this an attractive method for organic synthesis [65].

6.13. Synthesis of Polyhydroquinoline Derivatives

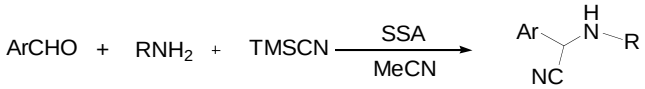
In recent years, much attention has been focused on the synthesis of 1,4-dihydropyridyl compounds because of their significant biological activities [66]. An efficient Hantzsch four-component condensation reaction for the synthesis of polyhydroquinoline derivatives has been reported under two conditions: solvent-free conventional heating and energy-saving microwave irradiation (Scheme **36**). The process is simple and environmentally benign, and the use of a heterogeneous and reusable catalyst, high yields, and short reaction time are the key features of this protocol [67].

6.14. Synthesis of Coumarin-3-carboxylic Acids

Coumarin-3-carboxylic acid (2-oxo-2H-chromene-3-carboxylic acid) subunit appears in a vast range of natural products and, due to the high levels of biological activity exhibited by many such compounds [68], has been duplicated in numerous synthetic compounds exhibiting pharmaceutical activity [69]. Synthesis of substituted coumarin-3-carboxylic acid via Knoevenagel condensation of meldrum's acid with ortho-hydroxyaryl aldehydes in solventless system has been described (Scheme **37**). This method has the additional advantages of mild conditions, easiness of set up and of work up, inexpensive and reusable catalyst [70].

6.15. Synthesis of α-aminonitriles

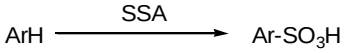
α-Amino nitriles are versatile precursors for the synthesis of α-amino acids [71], various nitrogen and sulfur containing heterocycles such as imidazoles, thiadiazoles [72] and pharmaceuticals [73]. A simple, convenient, and practical method for the synthesis of α-amino nitriles via one-pot three component condensation of aldehydes, amines and trimethyl silyl cyanide in the presence of a catalytic amount of SSA in good yields has been achieved (Scheme **38**). The low cost and low toxicity of the catalyst, fast reaction time, simple experimental procedure, recyclability of the catalyst, selectivity and high yields of the desired nitrile are the advantages of this method [74].



Scheme 38.

6.16. Sulfonation of Aromatic Rings

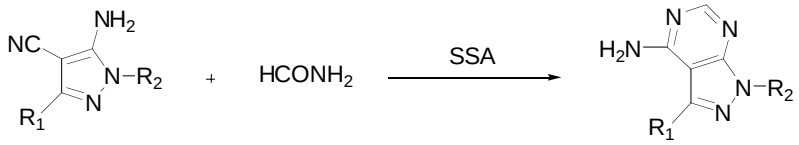
The sulfonation of aromatic compounds is very important, and many aromatic hydrocarbons have been sulfonated [75]. Direct and chemoselective sulfonation of aromatic compounds with silica sulfuric acid in 1,2-dichloroethane or under solvent-free conditions has been developed (Scheme **39**). The advantage of this methodology is the availability of the starting materials, simplicity of sulfonation procedure under heterogeneous system, clean and straightforward work-up, short reaction time, high yields without formation of sulfones as by-products [76].



Scheme 39.

6.17. Synthesis of 4-amino-pyrazol[3,4-d]pyrimidine Derivatives

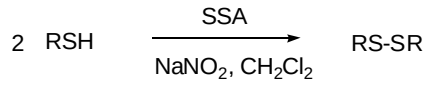
Silica-supported sulfuric acid has been used for the synthesis of 4-amino-pyrazol[3,4-d]pyrimidine derivatives from the reaction of 1-substituted-5-amino-4-cyano-pyrazoles and formamide under classical heating and microwave irradiation (Scheme **40**). The microwave-solid acid combination, leads to a nice and convenient catalytic synthesis of 4-amino-pyrazol[3,4-d]pyrimidines with much reduced reaction time compared to traditional conditions [77].



Scheme 40.

6.18. Production of Thionitrites and Disulfides

Thiols have been readily converted to their corresponding thionitrites with a combination of silica sulfuric acid, wet SiO_2 and sodium nitrite in dichloromethane at room temperature (Scheme **41**). Silica sulfuric acid is a good proton source in terms of convenience, cheapness, easy production, insolubility to all organic solvents. Practical and efficient nitrosation-oxidation of thiols has been achieved by the present methodology. The cheapness and availability of the reagents, easy procedure and work-up make this method attractive for the large-scale operations [2].



Scheme 41.

6.19. Synthesis of 1,5-benzodiazepines

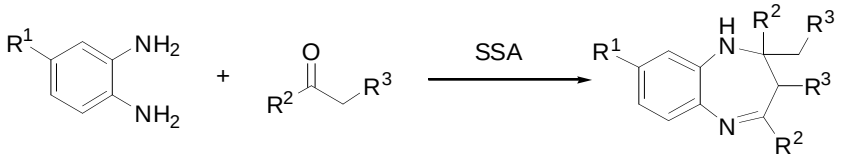
Benzodiazepines and their derivatives are very important compounds for their pharmacological properties [78]. SSA was found to be an efficient catalyst for the synthesis of biological significant, 1,5-benzodiazepines in good yields under solvent-free condition (Scheme **42**). The used method had several advantages including mild conditions, good yields, use of inexpensive, recyclable and reusable catalyst, mild reaction conditions, simple operation and work-up [79].

6.20. Synthesis of Quinoxalines

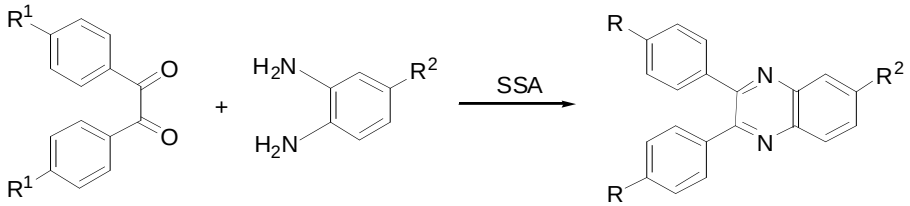
Quinoxalines are important heterocycles in medicinal chemistry [80]. A variety of quinoxalines were synthesized in good yields in the presence of SSA as a catalyst at room temperature (Scheme **43**). It is noteworthy to mention that the catalyst was reusable even after 4 runs in this reaction [81].

6.21. Pechmann Reaction

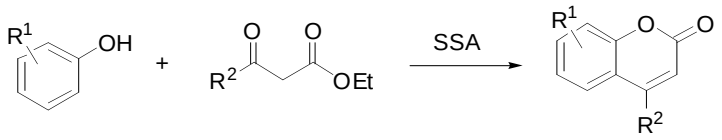
Coumarins and their derivatives form an elite class of compounds, occupying an important place in the realm of natural products and synthetic organic chemistry [82]. SSA can be used as an alternative to conventional acid catalysts in the Pechmann condensation of phenols with β-ketoester, leading to the formation of substituted coumarins (Scheme **44**). The method is simple, cost-effective, solvent-free and gives good yields in a short reaction time [83].



Scheme 42.



Scheme 43.



Scheme 44.

CONCLUSION

In this review, some applications of silica sulfuric acid as a reusable, green, inexpensive, convenient, easy to handle, non-toxic, available and efficient catalyst for various organic transformations have been discussed. We believe that a great number of acid catalyzed organic reactions could be performed using this catalyst, and its use has been growing rapidly.

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REFERENCES

[1] Salehi, P.; Zolfigol, M.A.; Shirini, F.; Baghbanzadeh, M. Silica sulfuric acid and silica chloride as efficient reagents for organic reactions. *Curr. Org. Chem.*, **2006**, *10*, 2171-2189.

[2] Zolfigol, M.A. Silica sulfuric acid/$NaNO_2$ as a novel heterogeneous system for production of thionitrites and disulfides under mild conditions. *Tetrahedron*, **2001**, *57*, 9509-9511.

[3] Ram, R.-N.; Meher, N.-K. Selective formylation of alcohols in the presence of phenols with chloral. *Tetrahedron*, **2002**, *58*, 2997-3001.

[4] Zolfigol, M.A.; Chehardoli, G.; Dehghanian, M.; Niknam, K.; Shirinid, F.; Khoramabadi-Zad, A. Silica sulfuric ccid and $Al(HSO_4)_3$: As efficient catalysts for the formylation of alcohols by using ethyl formate under heterogeneous conditions. *J. Chin. Chem. Soc.*, **2008**, *55*, 885-889.

[5] Ghafuri, H.; Eftekhari-Sis, B.; Hashemi, M.M. Silica sulfuric acid as a reusable catalyst for efficient and simple silylation of hydroxyl groups using Hexamethyldisilazane (HMDS). *Phosphorus. Sulfur. Silicon. Relat. Elem.*, **2007**, *182*, 1645-1651.

[6] Roy, B.; Mukhopadhyay, B. Sulfuric acid immobilized on silica: an excellent catalyst for Fischer type glycosylation. *Tetrahedron Lett.*, **2007**, *48*, 3783-3787.

[7] Rajput, V.K.; Mukhopadhyay, B. Sulfuric acid immobilized on silica: an efficient reusable catalyst for the synthesis of O-isopropylidene sugar derivatives. *Tetrahedron Lett.*, **2006**, *47*, 5939-5941.

[8] Wu, H.; Shen, Y.; Fan, L.Y.; Wana, Y.; Sh, D.Q. Solid silica sulfuric acid (SSA) as a novel and efficient catalyst for acetylation of aldehydes and sugars. *Tetrahedron*, **2006**, *62*, 7995-7998.

[9] Mukhopadhyay, B. Sulfuric acid immobilized on silica: an efficient promoter for one-pot acetalation-acetylation of sugar derivatives. *Tetrahedron Lett.*, **2006**, *47*, 4337-4341.

[10] Hasegawa, T.; Yamamoto, H.A. Practical synthesis of optically active (*R*)-2-propyloctanoic acid: therapeutic agent for alzheimer's disease. *Bull. Chem. Soc. Jpn.*, **2000**, *73*, 423-428.

[11] Banwell, M.G.; Crasto, C.F.; Easton, C.J.; Forrest, A.K.; Karoli, T.; March, D.R.; Mensah, L.; Nairn, M.R.; O'Hanlon, P.J.; Oldham, M.D.; Yue, W. Analogues of SB-203207 as inhibitors of tRNA synthetases. *Bioorg. Med. Chem. Lett.*, **2000**, *10*, 2263-2266.

[12] Chang, L.L.; Ashton, W.T.; Flanagan, K.L.; Chen, T.B.; O'Malley, S.S.; Zingaro, G.J.; Siegl, P.K.S.; Kivlighn, S.D.; Lotti, V.J.; Chang, R.S.L.; Greenless, W.J. Triazolinone biphenylsulfonamides as angiotensin II receptor antagonists with high affinity for both the AT1 and AT2 subtypes. *J. Med. Chem.*, **1994**, *37*, 4464-4478.

[13] Musser, J. H.; Kreft, A.F.; Bender, R.H.W.; Kubrak, D.M.; Grimes, D.; Carlson, R.P.; Hand, J.M.; Chang, J. N-[(Arylmethoxy)phenyl] carboxylic acids, hydroxamic acids, tetrazoles, and sulfonyl carboxamides. Potent orally active leukotriene D4 antagonists of novel structure. *J. Med. Chem.*, **1990**, *33*, 240-245.

[14] Massah, A.R.; Adibi, H.; Khodarahmi, R.; Abiri, R. Majnooni, M.B.; Shahidi, Sh.; Asadi, B.; Mehrabib, M.; Zolfigol, M.A. Synthesis, *in vitro* antibacterial and carbonic anhydrase II inhibitory activities of N-acylsulfonamides using silica sulfuric acid as an efficient catalyst under both solvent-free and heterogeneous conditions. *Bioorg. Med. Chem.*, **2008**, *16*, 5465-5472.

[15] Kiasat, A.R.; Kazemi, F.; Nourbakhsh, K. $H_2SO_4O_2$ as an efficient catalyst for the preparation of phenylhydrazones and 2,4-dinitrophenylhydrazones under solvent-free conditions. *Phosphorus Sulfur Silicon Relat. Elem.*, **2004**, *179*, 569-573.

[16] Prakash, G.K.S.; Mandal, M.; Olah, G.A. Nucleophilic trifluoromethylation of *N*-tosyl aldimines. *Synlett*, **2001**, 77-78.

[17] Davis, F.A.; Reddy, R.T.; Weismiller, M.C. (-)-alpha, alpha.-Dichlorocamphorsulfonyloxaziridine: a superior reagent for the asymmetric oxidation of sulfides to sulfoxides. *J. Am. Chem. Soc.*, **1989**, *111*, 5964-5965.

[18] Lijun, G.; Li, Y. A facile procedure for synthesis of N-sulfonylimines catalyzed by silica sulfate solid acid. *Chem. J. Int.*, **2005**, *7*, 077049ne.

[19] Zare, A.; Hasaninejad, A.; Shekouhy, M.; Moosavi Zare, A.R.A. Green solventless protocol for the synthesis of N-sulfonylimines in the presence of silica sulfuric acid as an efficient, heterogeneous and reusable catalyst. *Org. Prep. Proced. Int.*, **2008**, *40*, 457-463.

[20] Kim, T.H.; Chun, J.C. N-Benzyloxycarbonyl-2-methylaminothiazoline as a selective benzyloxycarbonylating reagent of amines. *Bull. Korean. Chem. Soc.*, **2003**, *24*, 157-158.

[21] Papageorgiou, E.A.; Gaunt, M.J.; Yu, J.-Q.; Spencer, J.B. Selective hydrogenolysis of novel benzyl carbamate protecting groups. *Org. Lett.*, **2000**, *2*, 1049-1051.

[22] Fieser, L.F. In *Reagents for organic synthesis*; John Wiley and Sons: New York, **1967**; Vol. *1*, p. 109.

[23] Gawande, M.B.; Polshettiwar, V.; Varmab, R.S.; Jayarama, R.V. An efficient and chemoselective Cbz-protection of amines using silica-sulfuric acid at room temperature. *Tetrahedron Lett.*, **2007**, *48*, 8170-8173.

[24] Storer, I.R.; Carrera, D.E.; Ni, Y.; MacMillan, D.W.C. Enantioselective organocatalytic reductive amination. *J. Am. Chem. Soc.*, **2006**, *128*, 84-86.

[25] Alinezhad, H.; Tajbakhsh. M.; Zare, M. Reductive amination of aldehydes and ketones under heterogeneous and solvent-Free conditions using Sodium-Borohydride and Silica-Gel-supported sulfuric acid. *Synth. Commun.*, **2009**, *39*, 2907-2916.

[26] Zarei, A.; Hajipour, A.R.; Khazdooz, L.; Mirjalili, B.F.; Najafi, A. Chermahini rapid and efficient diazotization and diazo coupling reactions on silica sulfuric acid under solvent-free conditions. *Dye Pigm.*, **2009**, *81*, 240-244.

[27] Rajput, V.K.; Roy, B.; Mukhopadhyay, B. Sulfuric acid immobilized on silica: an efficient reusable catalyst for selective hydrolysis of the terminal O-isopropylidene group of sugar derivatives. *Tetrahedron Lett.*, **2006**, *47*, 6987-6991.

[28] Khalafi-Nezhad, A.; Parhami, A.; Soltani Rad, M.N.; Zolfigol, M.A.; Zare, A. A catalytic method for chemoselective detritylation of 5'-tritylated nucleosides under mild and heterogeneous conditions using silica sulfuric acid as a recyclable catalyst. *Tetrahedron Lett.*, **2007**, *48*, 5219-5222.

[29] Niknam, Kh.; Zolfigol, M.A.; Khorramabadi-Zad, A.; Zare, R.; Shayegh, M. Silica sulfuric acid as an efficient and recyclable catalyst for the methoxymethylation of alcohols under solvent-free conditions. *Catal. Commun.*, **2006**, *7*, 494-498.

[30] Heravi, M.M.; Farhangi, N.; Beheshtiha, Y.Sh. Ghassemzadeh, M. Tabar-Hydar, K. Sulfuric acid adsorbed on silica gel and chromium(VI) oxide: rapid and selective oxidation of alcohol in solvent-free condition. *Ind. J. Chem. Sect. B: Org. Chem.*, **2004**, *43*, 430-431.

[31] Niknam, K.; Karami, B.; Zolfigol, M.A. Silica sulfuric acid promoted aromatization of 1,2-dihydroquinolines by using $NaNO_2$ as oxidizing agent under mild and heterogeneous conditions. *Catal. Commun.*, **2007**, *8*, 1427-1430.

[32] Habibi, D.; Zolfigol, M.A.; Safaiee, M. Silica sulphuric acid as an efficient catalyst for the catalytic and metal-free Oxidation of aromatic amines to their corresponding nitro compounds with Sodium Perborate under micellar Media. *South. Afr. J. Chem.*, **2008**, *61*, 93-96.

[33] Xiao, L.F.; Peng, J.J.; Xia, C.G. A novel method for beckmann rearrangement of oximes with silica sulfuric acid under mild condition. *Chin. Chem. Lett.*, **2006**, *17*, 617-620.

[34] Arend, M.; Westermann, B.; Risch, N. Modern variants of the Mannich

Reaction. *Angew. Chem., Int. Ed*., **1998**, *37*, 1044-1070.

[35] Muller, R.; Goesmann, H.; Waldmann, H. *N,N*-Phthaloylamino acids as chiral auxiliaries in asymmetric Mannich-Type reactions. *Angew. Chem.,Int. Ed*., **1999**, *38*, 184-187.

[36] Wu, H.; Shen, Y.; Fan, L.Y.; Wan, Y.; Zhang, P.; Chen, C.F.; Wang. Stereoselective synthesis of β-amino ketones via direct Mannich-type reaction catalyzed with silica sulfuric acid. *Tetrahedron*, **2007**, *63*, 2404-2408.

[37] Karthik, M.; Tripathi, A.K.; Gupta, N.M.; Palanichamy, M.; Murugeson, V. Zeolite catalyzed electrophilic substitution reaction of indoles with aldehydes: synthesis of bis(indolyl)methanes. *Catal. Commun*., **2004**, *5*, 371-375.

[38] Pore, D.M.; Desai, U.V.; Thopate, T.S.; Wadgaonkar, P.P. A mild, expedient, solventless synthesis of bis(indolyl)alkanes using silica sulfuric acid as a reusable catalyst. *Arkivoc*, **2006**, *12*, 75-80.

[39] Sundberg, R.J. *The chemistry of Indoles*. Academic Press: New York, **1996**, 113.

[40] Hari, G.S.; Nagaraju, M.; Murthy, M.M. Silica sulfuric acid-catalyzed Friedel-Crafts alkylation of Indoles with nitro olefins. *Synth. Commun*., **2008**, *38*, 100-105.

[41] Maruyama, Y.; Anami, K.; Terasawa, M.; Goto, K.; Imayoshi, T.; Kadobe, Y.; Mizushima, Y. Anti-inflammatory activity of an imidazopyridine derivative. *Arzneim. Forsch*, **1981**, *31*, 1111-1118.

[42] Rival, Y.; Grassy, G.; Michel, G. Synthesis and antibacterial activity of some Imidazo [1,2-α]pyrimidine derivatives. *Chem. Pharm. Bull*., **1992**, *40*, 1170-1176.

[43] Kaminski, J.J.; Wallmark, B.; Briving, C.; Andersson, B.M. Antiulcer agents. 5. Inhibition of gastric H^+/K^+-ATPase by substituted imidazo[1,2-a]pyridines and related analogs and its implication in modeling the high affinity potassium ion binding site of the gastric proton pump enzyme. *J. Med. Chem*., **1991**, *34*, 533-541.

[44] Sanfilippo, P.J.; Urbanski, M.; Press. J.B.; Dubinsky, B.; Moore, J.B. Synthesis of (aryloxy)alkylamines. Novel imidazo-fused heterocycles with calcium channel blocking and local anesthetic activity. *J. Med. Chem*., **1988**, *31*, 2221-2227.

[45] Trapani, G.; Franco, M.; Ricciardi, L.; Latrofa, A.; Genchi, G.; Sanna, E.; Tuveri, F.;Cagetti, E.; Biggio, G.; Liso, G. Synthesis and binding affinity of 2-Phenylimidazo[1,2-*a*]pyridine derivatives for both central and peripheral benzodiazepine receptors. A new series of high-qffinity and selective ligands for the peripheral type. *J. Med. Chem*., **1997**, *40*, 3109-3118.

[46] Shaabani, A.; Soleimani, E.; Maleki, A. One-pot three-component synthesis of 3-aminoimidazo[1,2-*a*]pyridines and -pyrazines in the presence of silica sulfuric acid. *Monatsh. Chem*., **2007**, *138*, 73-76.

[47] Hajipour, A.R.; Zarei, A.; Ruoho, A. E. Supported Bismuth(III) Nitrate on silica sulfuric acid as useful reagent for nitration of aromatic compounds under solvent-free conditions. *Russ. J. Org. Chem.*, **2005**, *41*, 1493-1495.

[48] a) Golgolab, H.; Lalezari, F.; Hosseini-Gohari, L. 1,3,4-Thiadiazolo[2,3-*c*]-*as*-triazines and *s*-triazolo [3,4-6]-1,3,4-thiadiazoles. *J. Heterocycl. Chem.*, **1973**, 387-390; b) Mizutani, M.; Sanemitsu, Y. 1,2,4-triazines. III. A convenient and general synthesis of 4*H*-[1,3,4]thiadiazolo[2,3-*c*][1,2,4]triazin-4-ones. *J. Heterocycl. Chem.*, **1982**, 1577-1578; c) Shivarama Holla, B.; Gonsalues, R.; Sooryana rajana, B.; Shenoy, Sh.; Gopalakrishna, H.N. Synthesis of some new biologically active bis-(thiadiazolotriazines) and bis-(thiadiazolotriazinyl) alkanes. *Farmaco*, **2001**, *56*, 899-903.

[49] Heravi, M.M.; Ramezanian, N.; Sadeghi, M.M.; Ghassemzadeh, M. Synthesis of [1,3,4]thiadiazolo[2,3-C][1,2,4]triazin-4-ones using sulfuric acid supported onto silica gel in solventless system. *Phosphorus Sulfur Silicon Relat. Elem*., **2004**, *179*, 1469-1472.

[50] Heravi, M.M.; Khademalfoghara, H.R.; Sadeghi, M.M.; Khaleghi, Sh.; Ghassemzadeh, M. Solvent free regioselective cyclization of 3-allylmercapto-1,2,4-triazoles to thiazolo[3,2-b]1,2,4-triazoles over sulfuric acid adsorbed on silica gel. *Phosphorus Sulfur Silicon Relat. Elem*., **2006**, *181*, 377-380.

[51] Poupelin, J.P.; Saint-Ruf, G.; Foussard-Blanpin, O.; Marcisse, G.; Uchida-Ernouf, G.; Lacroix, R. Develop an alternate route for the synthesis of xanthenes. *Eur. J. Med. Chem*., **1978**, *13*, 67-71.

[52] Hunnur, R.K.; Sunilkumar, B.; Kumar, P.S.; Srinivasulu, N.; Udupi, R.H.; Hima bindu, V. Silica sulfuric acid: a simple, efficient, and reusable heterogeneous catalyst for the one-pot synthesis of aryl-14H-dibenzo-[a_j]xanthenes under conventional heating and solvent-free conditions. *Chem. Heterocycl. Compd*., **2008**, 44,

[53] Lombardino, J.G.; Wiseman, E.H. Preparation and antiinflammatory activity of some nonacidic trisubstituted imidazoles. *J. Med. Chem*., **1974**, *17*, 1182-1188.

[54] Shaabani, A.; Rahmati, A.; Farhangi, E.; Badri, Z. Silica sulfuric acid promoted the one-pot synthesis of trisubstituted imidazoles under conventional heating conditions or using microwave irradiation. *Catal. Commun*., **2007**, *8*, 1149-1152.

[55] Pore, D.M.; Soudagar, M.S.; Desai,a, U.V.; Thopatea, T.S.; Wadagaonkar, P.P. Potassium phosphate or silica sulfuric acid catalyzed conjugate addition of thiols to α,β-unsaturated ketones at room temperature under solvent-free conditions. *Tetrahedron Lett*., **2006**, *47*, 9325-9328.

[56] Mohammadpoor-Baltork, I.; Mirkhani, V.; Moghadam, M.; Tangestaninejad, Sh.; Zolfigol, M.A.; Abdollahi-Alibeik, M.; Khosropour, A.R.; Kargar, H.; Hojati, S.F. Silica sulfuric acid: A versatile and reusable heterogeneous catalyst for the synthesis of oxazolines and imidazolines under various reaction conditions. *Catal. Commun*., **2008**, *9*, 894-901.

[57] Grasso, S.; DeSarro, G.; Micale, N.; Zappala, M.; Puia, G.; Baraldi, M.; Demicheli, C. Synthesis and anticonvulsant activity of novel and potent 6,7-Methylenedioxyphthalazin-1(2*H*)-ones. *J. Med. Chem*., **2000**, *43*, 2851-2859.

[58] Nomoto, Y.; Obase, H.; Takai, H.; Teranishi, M.; Nakamura, J.; Kubo, K. Studies on Cardiotonic Agents. II. : Synthesis of novel phthalazine and 1,2,3-Benzotriazine derivatives. *Chem. Pharm. Bull*., (Tokyo) **1990**, *38*, 2179-2183.

[59] Watanabe, N.; Kabasawa, Y.; Takase, Y.; Matsukura, M.; Miyazaki, K.; Ishihara, H.; Adachi, K.H. 4-Benzylamino-1-chloro-6-substituted phthalazines: Synthesis and inhibitory activity toward phosphodiesterase 5. *J. Med. Chem*., **1998**, *41*, 3367-3372.

[60] Shaterian, H.R.; Ghashang, M.; Feyzi, M. Silica sulfuric acid as an efficient catalyst for the preparation of 2H-indazolo[2,1-b]phthalazine-triones. *Appl. Catal*., **2008**, *345*, 128-133.

[61] Garden, S.J.; Torres, J.C.; Ferreira, A.A.; Silva, R.B.; Pinto, A.C. A modified sandmeyer methodology and the synthesis of (±)-convolutamydine A. *Tetrahedron Lett*., **1997**, *38*, 1501-1504.

[62] Azizian, J.; Mohammadi, A.A.; Karimi, N.; Mohammadizadeh, M.R.; Karimi, A.R. Silica sulfuric acid a novel and heterogeneous catalyst for the synthesis of some new oxindole derivatives. *Catal. Commun*., **2006**, *7*, 752-755.

[63] Hatheway, G.J.; Hansch, C.; Kim, K.H.; Milstein, S.R.; Schimidt, C.L.; Smith, R.N.; Quin, F.R. Antitumor 1-(X-aryl)-3,3-dialkyltriazenes, 1: Quantitative structure-activity relationships vs L1210 leukemia in mice. *J. Med. Chem*., **1978**, *21*, 563-574.

[64] Chen, X.; She, J.; Shang, Z.C.; Wu, J.; Zhang, P. Room-temperature synthesis of pyrazoles, diazepines, -enaminones, and -enamino esters using silica-supported sulfuric acid as a reusable catalyst under solvent-free conditions. *Synth. Commun*., **2009**, *39*, 947-957.

[65] Zolfigol, M.A.; Choghamarani, A.G. Silica sulfuric acid/$NaNO_2$ as a novel heterogeneous system for the chemoselective nitrosation of diketones under mild conditions. *Phosphorus Sulfur Silicon Relat. Elem*., **2003**, *178*, 1623-1629.

[66] Shan, R.; Velazquez, C.; Knaus, E.E. Syntheses, calcium channel agonist-antagonist modulation activities, and nitric oxide release studies of nitrooxyal-
kyl-1,4-dihydro-2,6-dimethyl-3-nitro-4-(2,1,3-benzoxadiazol-4-yl)pyridine
-5-carboxylate racemates, enantiomers, and diastereomers. *J. Med. Chem*., **2004**, *47*, 254-261.

[67] Mobinikhaledi, A.; Foroughifar, N.; Bodaghi Fard, M.A.; Moghanian, H.; Ebrahimi, S.; Kalhor. M. Efficient one-pot synthesis of polyhydroquinoline derivatives using silica sulfuric acid as a heterogeneous and reusable catalyst under conventional heating and energy-saving microwave irradiation. *Synth. Commun*., **2009**, *39*, 1166-1174.

[68] Murray, R.D.H.; Mendez, J.; Brown, S.A. The *natural coumarins: occurrence, chemistry and biochemistry*. John Wiley & Sons, New York, **1982**.

[69] Meuly, W.C. *Kirk-Othmer encyclopedia of chemical technology*, 3rd ed. JohnWiley& Sons, New York, **1979**, *196*, p. 7.

[70] Hekmatshoar, R.; Rezaei, A.; Beheshtiha, Y.Sh. Silica sulfuric acid: A versatile and reusable catalyst for synthesis of coumarin-3-carboxylic acids in a solventless system. *Phosphorus Sulfur Silicon Relat. Elem*., **2009**, *184*, 2491-2496.

[71] Shafran, Y.M.; Bakulev, V.A.; Mokrushin, V.S. Synthesis and properties of α-aminonitriles. *Russ. Chem. Rev*. **1989**, *58*, 148-162.

[72] Weinstock, L.M.; Davis, P.; Handelsman, B.; Tull, R. General synthetic system for 1,2,5-thiadiazoles. *J. Org. Chem*., **1967**, *32*, 2823-2829.

[73] Barrett, G.C. *Chemistry and biochemistry of the amino acids*; Ed.; Chapman and Hall: London, **1985**.

[74] Oskooie, H.A.; Heravi, M.M.; Sadnia, A.; Jannati, F.; Behbahani, F.K. H_2SO_4/Silicagel: Highly efficient catalyst for the synthesis of α-aminonitriles using trimethysilyl cyanide. *Monatsh. Chem*., **2008**, *139*, 27-29.

[75] Khelevin, R.N. Sulfonation and related reactions. *J. Org. Chem*., USSR **1987**, *23*, 1709-1721.

[76] Hajipour, A.R.; Mirjalili, B.B.F.; Zarei, A.; Khazdoozc, L.; Ruoho, A. E. A novel method for sulfonation of aromatic rings with silica sulfuric acid. *Tetrahedron Lett*., **2004**, *45*, 6607-6609.

[77] Heravi, M.M.; Rajabzadeh, G.; Bamoharram, F.F.; Seifi, N. An eco-friendly catalytic route for synthesis of 4-amino-pyrazolo[3,4-d]pyrimidine derivatives by Keggin heteropolyacids under classical heating and microwave irradiation. *J. Mol. Catal. A Chem*., **2006**, *256*, 238-241.

[78] (a) Schultz, H. *Benzodiazepines*; Springer: Heidelberg, **1982**; (b) Landquist, J.K. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A.R., Rees, C. W. (Eds.); Pergamon: Oxford **1984**; Vol. 1, p. 166.

[79] Shobha, D.; Adharvana Ch.M.; Mukkanti, K.; Ahn, K.H. Silica gel-supported sulfuric acid catalyzed synthesis of 1,5-benzodiazepine derivatives. *J. Heterocycl. Chem.*, **2009**, *46*, 1021-1033.

[80] (a) Jaso, A.; Zarranz, B.; Aldana, I.; Monge, A. Synthesis of new quinoxaline-2-carboxylate 1,4-dioxide derivatives as anti-mycobacterium tuberculosis agents. *J. Med. Chem*., **2005**, *48*, 2019-2025; (b) Carta, A.; Paglietti, G.; Nikookar, M.E.R.; Sanna, P.; Sechi, L.; Zanetti, S. Novel substituted quinoxaline 1,4-dioxides with *in vitro* antimycobacterial and anticandida activity. *Eur. J. Med. Chem.*, **2002**, *37*, 355-366.

[81] Shaabani, A.; Maleki, A. An efficient solid acid promoted synthesis of quinoxaline derivatives at room temperature. *Chin. J. Chem*., **2007**, *25*, 818-821.

[82] Kennedy, R.O.; Zhorenes, R.D. Coumarins: Biology, applications and mode of action, John Wiley and Sons: Chichester, **1997**.

[83] Rad-Moghadam, K.; Montazeri, N. Coumarin synthesis via pechmann condensation on silica-supported. Sulfuric acid under microwave irradiation. *Asian. J. Chem*., **2009**, *21*, 499-503.

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