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APPLICATIONS OF SULFATED TIN OXIDE (STO) IN ORGANIC SYNTHESIS - FROM 2016 TO 2021

Narsimhaswamy Dubasi[a] and Ravi Varala[b]*

[a]Saimerak Pharma, Dallas, Texas-75220, USA
[b]Scrips Pharma, Mallapur-500076, Hyderabad, Telangana, India
✉Corresponding Author: ravivarala@gmail.com; Ph: +91-9618286529

Abstract – In this mini-review, authors have briefed about the applications of sulfated tin oxide (STO) as bifunctional catalyst in various C-C, C-hetero bond formations. Synthesis of biologically relevant pyranoquinolines, benzimidazoles, benzodiazepines, fully substituted pyridines, dihydropyridines and isoxazoles were performed by heterogeneous recyclable and reusable solid acid catalyst, STO. In addition, methodologies such as *N*-Boc protection of amines, production of renewable less viscous, high-density fuel molecules from α-pinene, selective production of MeCl from CH_4, esterification, *tert*-butylation and conversion of glucose into value added 5-hydroxymethylfurfural, were established by using STO as catalyst.

CONTENTS

1. INTRODUCTION

Sulfated tin oxide (hereafter referred to as STO) has tremendous attention during past few years in the fields of catalysis and organic synthesis, owing to its low cost, greater stability, non-corrosive, reuse and recyclability, high efficiency and large surface area.[1]

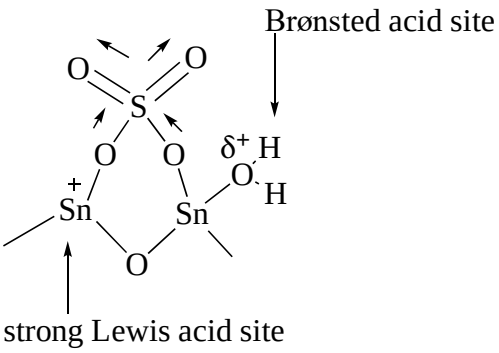


Figure 1. STO as bi-functional catalyst

STO possesses both Brønsted acid sites derived from sulfates on the surface of metal oxides, Lewis acid sites derived from metal oxides. Due to which they have been extensively exploited as a solid acid heterogeneous catalyst in a variety of synthetic organic methodologies (Figure 1). Thus, STO is acting as a bi-functional catalyst.[2,3]

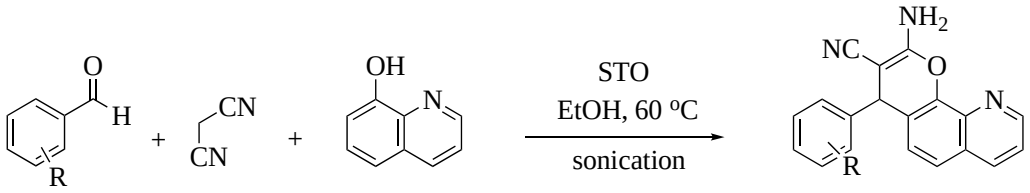
Preparation of STO was done by treating of $SnCl_2$ with NH_4OH to form stannous hydroxide, which was then equilibrated with H_2SO_4, followed by calcination at 500 °C.[4] Varala et al. published a related review covering until 2015.[1] The present update is an extension of the research work carried out during 2016-2021, across the world.

2. RECENT APPLICATIONS OF STO (DURING 2016-2021)

2-1. Synthesis of Heterocycles

2-1-1. Synthesis of 2-amino-4*H*-pyranoquinolines

The quinoline derivatives play a vital role in several pharmacologically relevant natural products.[5] Varala et al. have recently developed ultrasound irradiated synthesis of 2-amino-4*H*-pyranoquinolines in excellent yields using heterogeneous reusable STO as catalyst in ethanol at 60 °C, from different aldehydes, malononitrile and 8-hydroxyquinoline (Scheme 1).[6] Thus, an operationally simple one-step C-C and C-O bond construction reaction was developed.



Isolated yields: 91-96%; Time: 1-3 h; 6 examples (R=H/4-OMe/4-Br/4-OH/2-Cl/2-Br)

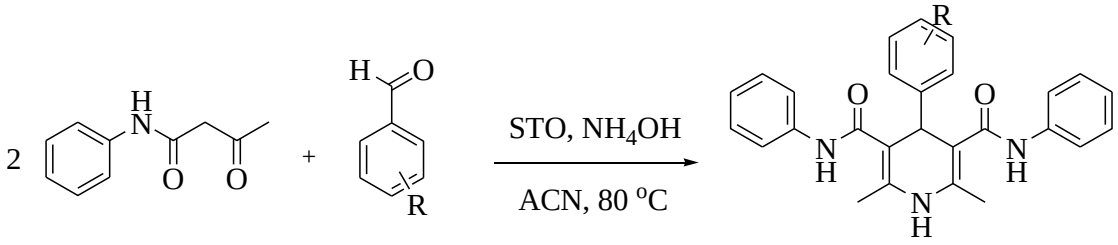
Scheme 1. STO-catalyzed synthesis of 2-amino-4*H*-pyranoquinolines

The strategy followed in this method gives an additional feature like, easy setup, less reaction time, effortless decantation, good yields and consequently create an utmost contribution to green chemistry. The Lewis and Brønsted acidic nature of STO triggers the resultant condensed product to bond with 8-hydroxyquinoline and forms the intermediate compound, which further cyclizes to yield the corresponding product.

2-1-2. Synthesis of 1,4-dihydropyridine derivatives

2-1-2-1. Varala and co-workers

1,4-Dihydropyridines are a group of pyridine-based molecules possessing a magnificent set of biological and therapeutic potentials. Dihydropyridines show diverse range of biological activities.[7,8] They exploited STO as an excellent heterogeneous catalyst for the one-pot synthesis of dihydropyridine derivatives *via* Hantzsch reaction using substituted aldehydes, NH_4OH and acetoacetanilide in acetonitrile at 80 °C (Scheme 2).[9] No significant loss of the efficiency of the catalyst was observed even after five cycles.



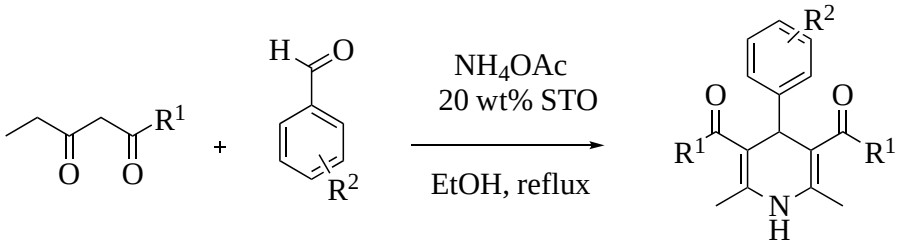
Isolated yields: 86-94%; Time: 2.5-3.5 h; 6 examples (R=H/4-$N(Me)_2$/4-Br/2- NO_2/4-OH/4-OMe)

Scheme 2. STO-catalyzed synthesis of dihydropyridine derivatives

The mechanism of this reaction proceeds STO as Brønsted acid catalyst, initially through a Michael addition, followed by an intramolecular tandem sequence, that may take place in the formation of the final product.

2-1-2-2. Munde and co-workers

The authors have synthesized biologically relevant 1,4-dihydropyridine derivatives *via* one-pot condensation of aromatic aldehydes, β-keto esters, and ammonium acetate by using STO as solid super acid heterogenous catalyst in ethanol at reflux condition (Scheme 3).[10] The yields of all synthesized compounds were in the range of 82-92%. No significant loss in the yield and selectivity of product was observed over five cycles. However, the authors did not discuss about reaction mechanism.



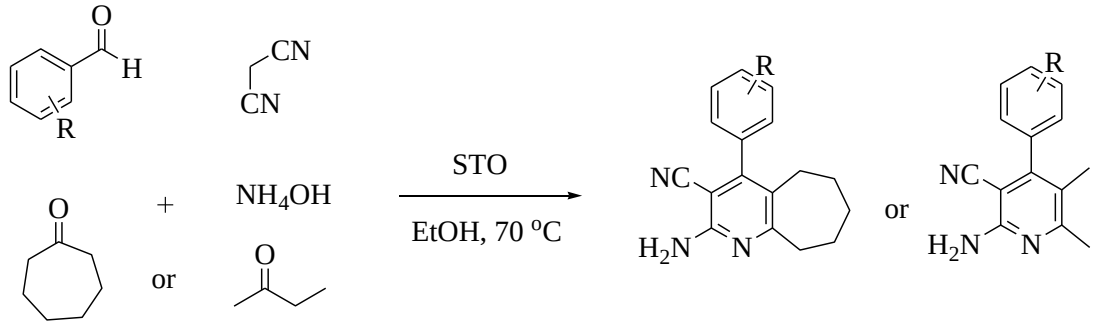
R^1=OEt or OMe

Isolated yields: 82-92%; Time: 1-5 h; 12 examples

Scheme 3. STO-catalyzed synthesis of 1,4-DHPs

2-1-3. Synthesis of fully functionalized pyridines

In view of exhibiting wide range of metabolic activities, pyridine ring occupies prominent position in several biologically relevant compounds.[11] Varala and co-workers published STO-catalyzed cyclocondensation of the synthesis of fully functionalized pyridines from substituted aldehydes, malononitrile, aliphatic ketone and ammonium hydroxide in ethanol at 70 °C (Scheme 4).[12] Due to cooperating contribution of its Lewis and Brønsted acidic sites, as shown in Figure 1, efficacy of the catalyst is enhanced.



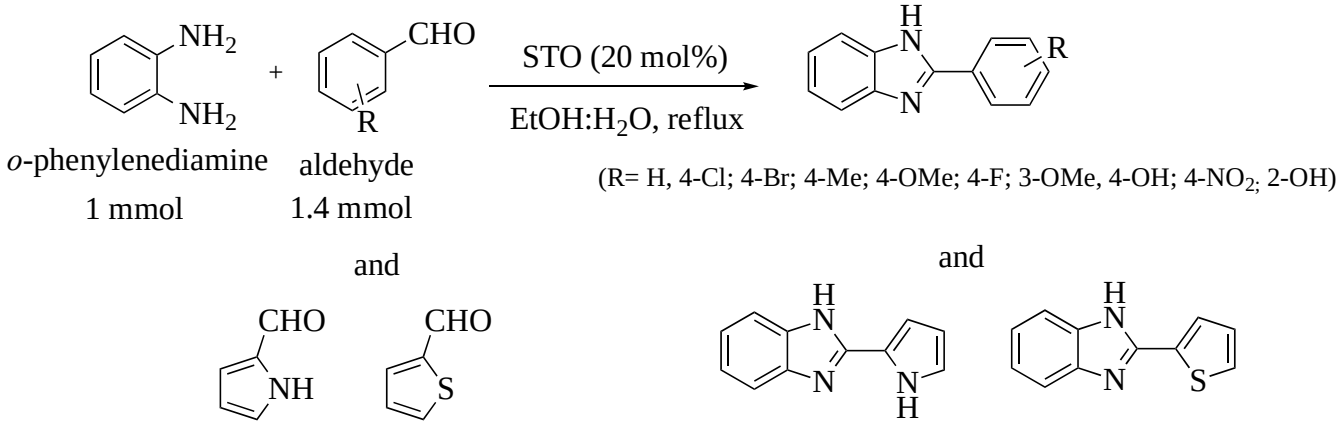
Isolated yields: 82-95%; Time: 1.5-3.5 h; 14 examples (R=H/4-$N(Me)_2$/4-Br/4-OMe/2-Cl/2-OMe)

Scheme 4. STO-catalyzed synthesis of fully functionalized pyridines

Nano sized STO catalyst is compatible with several substrates and reusable. No significant loss of the efficiency of the catalyst was observed up to five cycles. However, the authors did not discuss about reaction mechanism.

2-1-4. Synthesis of benzimidazoles

Benzimidazoles have practical applications in medicinal chemistry ascribed to its diverse biological functions.[13] Munde et al. developed a novel methodology for the synthesis of benzimidazoles using STO as a catalyst by utilizing aromatic aldehydes and *o*-phenylenediamine in the solvent system H_2O:EtOH (1:1 v/v) under reflux (Scheme 5).[14] Reusability and wide substrate scope are key outcomes of the work.



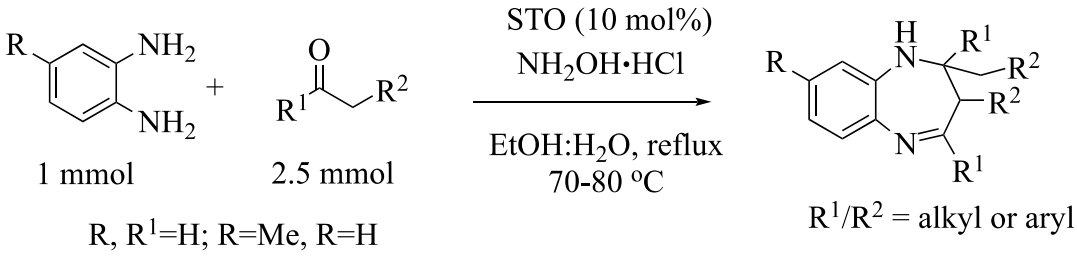
Isolated yields: 84-94%; Time: 1.1-2.6 h; 11 examples

Scheme 5. STO-catalyzed synthesis of benzimidazoles

However, the authors did not discuss about reaction mechanism.

2-1-5. Synthesis of 1,5-benzodiazepine derivatives

Benzodiazepines are crucial nitrogen containing heterocyclic compounds that own a varied array of pharmacological and therapeutic properties.[15] In addition, Munde and co-workers reported STO-catalyzed synthesis of 1,5-benzodiazepine derivatives using the same optimized reaction parameters (Scheme 6).[16] No significant loss of the efficiency of the catalyst was observed up to five cycles. The protocol developed was mild, clean, high yielding and environmentally benign. However, the authors did not discuss about reaction mechanism.

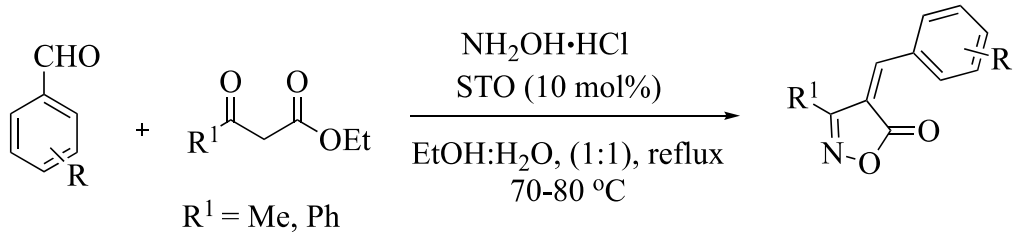


Isolated yields: 80-90%; Time:2-2.6 h; 10 examples

Scheme 6. STO-catalyzed synthesis of benzodiazepine derivatives

2-1-6. Synthesis of 4-arylmethylidene-3-substituted-isoxazol-5(4*H*)-ones

Isoxazoles are one of the prominent pharmaceutically relevant heterocycles, which attracted synthetic and medicinal chemists to explore.[17] In this study, Pawar et al. reported a STO-catalyzed green methodology by adopting one-pot multi-component synthesis of 4-arylmethylidene-3-substituted-isoxazol-5(4*H*)-ones from β-keto ester, aldehydes and hydroxylamine hydrochloride (Scheme 7).[18]



Isolated yields: 82-91%; Time: 6-25 min; 13 examples

Scheme 7. STO-catalyzed synthesis of 4-arylmethylidene-3-substituted-isoxazol-5(4*H*)-ones

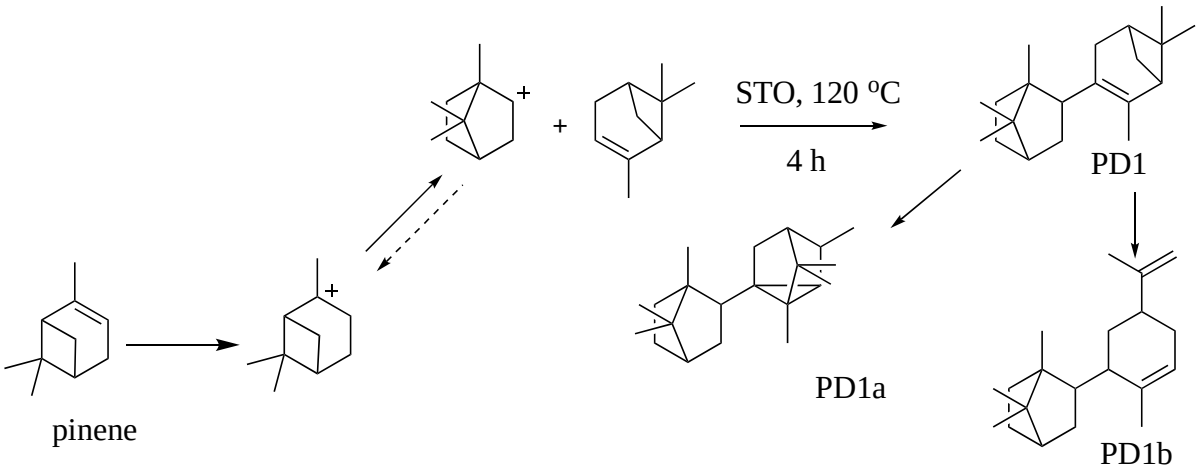
The method includes several advantages such as the use of STO as a heterogeneous catalyst, short reaction time, affording high yields of the corresponding products. The method is operationally simple, environmentally benign, and a time-saving protocol; hence it is superior and constitutes a valuable addition to the existing methods for the preparation of target compounds by one-pot multi-component approach. The plausible mechanism for the STO catalyzed synthesis of 4-arylmethylidene-3-substituted-isoxazol-5(4*H*)-ones, involves the formation of an oxime intermediate followed by a cyclic intermediate during the reaction *via* strong Lewis acidic sites at Sn.

2-2. Miscellaneous reactions

2-2-1. Coupling reactions of α-pinene to produce dimeric hydrocarbon products (fuels)

It is well known that coupling reactions of α-pinene to produce dimeric hydrocarbon products that act as renewable less viscous, high-density fuel molecules. Choi et al.[19] presented the role of STO (calcined at

550 °C) as Brønsted acid site for the partial coupling reaction of α-pinene from turpentine to give excellent possible yield of dimeric products (near about 50%) in solvent-free conditions (Scheme 8).



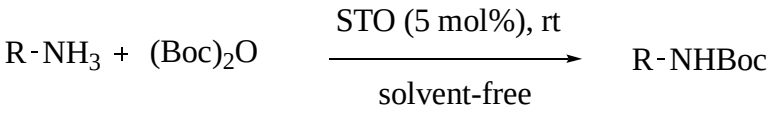
[PD: Possible dimeric structures]

Scheme 8. STO-catalyzed synthesis of high-density fuel molecules

By applying a suite of physicochemical characterizations, it is shown that the strong Lewis acid sites on STO generated by the interaction of Sn and surface sulfate groups are mainly responsible for the highly selective CH_4 conversion.

2-2-2. *N*-Boc (N-*tert*-butoxycarbonyl) protection of aliphatic, aromatic and cyclic amines

Reddy and co-workers published solvent-free productive protocol for the *N*-Boc (N-*tert*-butoxycarbonyl) protection of aliphatic, aromatic and cyclic amines using 5 mol% STO at ambient temperature (Scheme 9).[20] Faster reaction times, reusability, excellent yields and neat conditions are the salient features of this work. However, the authors did not discuss about reaction mechanism.

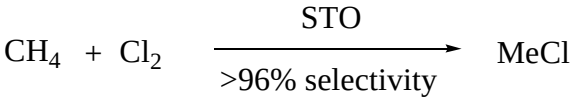


Isolated yields: 93-99%; Time: 1-6 min; 12 examples (R=aromatic, aliphatic and cyclic)

Scheme 9. STO-catalyzed synthesis of *N*-Boc amines

2-2-3. Gas phase catalytic chlorination of CH_4

Selective production of MeCl from CH_4 is a great challenge because of the involvement of radical process. Kim and others,[21] developed an efficient STO catalyzed gas phase catalytic chlorination of CH_4 (Scheme 10). Strong Lewis acidic sites are found to be responsible for this selectivity by cleaving Cl_2 molecules in heterolytic approach as confirmed from DFT calculations.

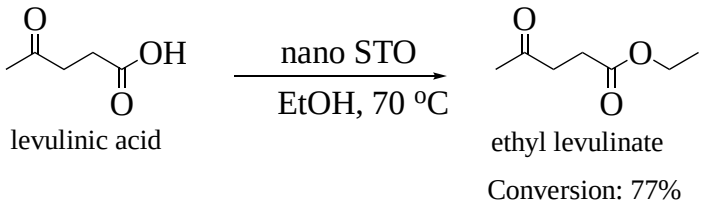


Gas-phase catalytic chlorination of CH_4, T= 350 °C

Scheme 10. STO-catalyzed synthesis of selective production of MeCl from CH_4

2-2-4. Esterification of levulinic acid

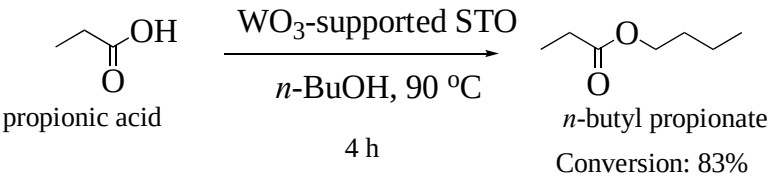
Levulinate esters are valuable compounds, which can be used as fuel additives, solvents and plasticizers. In particular, ethyl levulinate, which is directly, used as a diesel-miscible biofuel in regular diesel engines. Popova et al.[22] reported the acid mediated esterification of levulinic acid in the presence of nano STO (Scheme 11). Catalyst is very stable and they did not observe any leaching after 3 cycles, which was demonstrated by XRD and TG data of the spent catalyst. The authors proposed reaction mechanism involving participation of both Brønsted and Lewis acid sites for catalytic esterification of levulinic acid with ethanol.



Scheme 11. STO-catalyzed esterification of levulinic acid

2-2-5. Esterification of propionic acid

Alaya et al.[23] reported the preparation, characterization and catalytic activity of WO_3 supported sulfated tin oxide nano-crystalline catalyst (Scheme 12). They exploited the catalyst to optimize a model catalytic system for the esterification of propionic acid with *n*-butanol. Lewis acid sites were found to be more effective on catalyzing the esterification reaction.

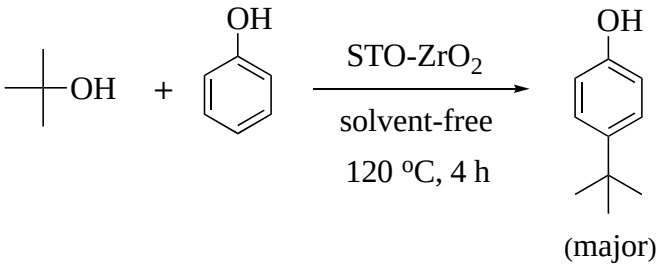


Scheme 12. WO_3 supported STO-catalyzed esterification of propionic acid

2-2-6. *tert*-Butylation of phenol

Tsilomelekis and co-workers[24] reported the characterization of STO-ZrO_2 catalyst and their catalytic performance on the *tert*-butylation of phenol (Scheme 13). Comparison of the catalytic performance of all

sulfate oxides in the *tert*-butylation of phenol, it was found that SnO_2 -rich samples show high *tert*-butyl alcohol (TBA) conversion, with monoalkylated phenols (TBP) as the primary product under solvent-free conditions. Lewis acid sites were found to be more effective on catalyzing the butylation reaction.



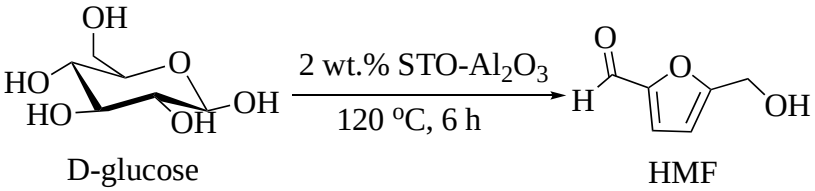
Scheme 13. STO-ZrO_2-catalyzed *tert*-butylation of phenol

2-2-7. Esterification of free fatty acids (FFA)

Nuithitikul and co-workers[25] compared catalytic activities of sulfated cobalt-tin and sulfated aluminium-tin mixed oxides for esterification of free fatty acids in crude palm oil to produce corresponding methyl esters. They found that SO_4^{2-}/Al_2O_3-SnO_2 had higher catalytic activity than SO_4^{2-}/Co_2O_3-SnO_2. The presence of Lewis and Brønsted acid sites in its structure catalyzed esterification reaction.

2-2-8. Conversion of D-glucose to 5-hydroxymethylfurfural (HMF)

Innovative catalysts to convert biomass carbohydrates in high value products are of an immense interest for the chemical industry and biorefineries. Lopes et al.[26] exploited Al_2O_3-promoted sulfated tin oxide for effective chemo-selective conversion of glucose to 5-hydroxymethylfurfural (Scheme 14). Brønsted acid sites had a vital role in promoting glucose and fructose dehydration to HMF.



D-glucose HMF

Maximum yield =19%

Scheme 14. Al_2O_3 promoted STO-catalyzed chemo-selective conversion of glucose to 5-hydroxymethylfurfural

3. CONCLUSION

The authors have presented the very recent applications of sulfated tin oxide (STO) both in catalysis as well as in organic synthesis. Lewis acid and Brønsted acidic sites make STO to act as bifunctional catalyst and has enormous scope for upcoming researchers to exploit the catalyst by fine-tuning into nanomaterials and there by applying in catalysis. We do hope that the update covering from 2016 to 2021

would attract researchers exploiting nano and heterogeneous reusable STO catalyst in several organic transformations leading to produce diverge range of biologically relevant heterocyclic compounds.

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Narsimhaswamy Dubasi completed his Ph. D from Indian Institute of Chemical Technology (CSIR-IICT) Hyderabad, INDIA in Synthetic Organic chemistry (2000-2007). He subsequently conducted his Post-Doctoral Studies in the laboratory of Prof. J. R. Falck, at UT Southwestern Medical Center, Dallas, Texas, USA (2007-2009) in the field of medicinal chemistry and organometallics. After completion of his Post-Doctoral Studies, he moved to India and worked as Associate Principal Scientist at Laxai Avanti Life Sciences. Then he moved to USA, worked in CRO Laboratories, Dallas, Texas and Saimerak Pharma Dallas, Texas, in different areas of chemistry like bioorganic chemistry, process chemistry and medicinal chemistry. Currently, he is working in Belcher Pharmaceuticals, Florida.

Ravi Varala pursued his Ph. D from CSIR-IICT, India during 2000-2006 and went on postdoctoral research in Portugal during 2007-2009. From 2010 to till date, he had gained vast experience in both academic and research fields. During 2015-2016, he was '*Invited Researcher'* (Visiting Scientist) to University of Sao Paulo, Brazil. He has got 90 published research articles of international and national repute. Attended or participated in more than 120 national and international conferences. Has published two books, seven book chapters and eight reviews/perspectives, as on date. Got research collaborations with KSA and Malaysia. Presently, he is working as Scientist in Scrips Pharma, Hyderabad. His fields of research interests are: organic synthesis and catalysis.