



“SODIUM TOLUENE-4-SULFONIC ACID AN EFFICIENT AND GREEN CATALYST FOR THE SYNTHESIS OF TETRAHYDROBENZO [B]PYRAN IN AQUEOUS MEDIUM”

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Abstract:

The synthetic methodology for tetrahydrobenzo[b]pyran by a green approach in aqueous medium catalyzed by Sodium toluene-4-sulfonic acid (STS) represents an environmentally conscious and sustainable method. The utilization of aqueous medium aligns with principles of green chemistry, aiming to minimize environmental impact and promote sustainability in chemical processes. This green synthesis may involve the use of catalysts, such as sodium toluene-4-sulfonic acid known for its water compatibility. The method not only emphasizes the importance of reducing toxic waste and by-products but also contributes to the development of more eco-friendly synthetic routes. This approach showcases the commitment to adopting practices that are both efficient and environmentally responsible in the formation of tetrahydrobenzo[b]pyran.

Key-words: Sodium toluene-4-sulfonic acid (STS), aqueous medium, Green synthesis, Tetrahydrobenzo [b] pyran.

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1.0 Introduction:

Multicomponent reactions play a crucial role in organic synthesis, offering various applications such as high atom economy, simplicity, less reaction times, high yields of products with good purity. They provide an efficient pathway for synthesizing heterocyclic compounds, adding significant value to the design of new compounds. An example of such a compound is 4*H*-benzo(b)pyran, an oxygen-containing heterocyclic compound synthesized from benzaldehyde, active methylene compounds with dimedone using various catalysts in the presence of aqueous medium. This approach represents a green organic transformation [1]. In recent years, the development of sustainable and eco-friendly methodologies for organic synthesis has garnered significant attention in the field of chemical research. The quest for efficient catalytic systems that enable the synthesis of valuable compounds while minimizing environmental impact has been a focal point of investigation. Among these endeavors, the utilization of sodium toluene-4-sulfonic acid as a catalyst has emerged as a promising avenue in organic synthesis, particularly in the formation of tetrahydrobenzo [b] pyran. The tetrahydrobenzo [b]pyran scaffold represents a structurally diverse and pharmacologically significant motif found in various biologically active compounds, including pharmaceuticals, agrochemicals, and natural products. Consequently, the development of sustainable methodologies for the synthesis of tetrahydrobenzo[b]pyran has attracted considerable interest from both academic and industrial perspectives. The use of water as a reaction medium holds immense appeal in organic synthesis due to its abundance, non-toxic nature,

and environmental compatibility. Aqueous environments offer an advantageous platform for green chemistry practices, facilitating the design of processes that minimize the use of organic solvents and reduce waste generation. In this context, the catalytic prowess of sodium toluene-4-sulfonic acid in aqueous media presents an intriguing prospect for the synthesis of tetrahydrobenzo[b]pyran. Its efficacy as a catalyst, coupled with its benign environmental footprint, underscores its potential as an efficient and environmentally benign alternative in the pursuit of sustainable synthetic methodologies. This present work explores the recent advancements and applications of sodium toluene-4-sulfonic acid as a catalyst in the synthesis of tetrahydrobenzo[b]pyran in aqueous media. Through a critical analysis of existing literature and experimental findings, this work intends to elucidate the mechanistic insights, reaction pathways, and catalytic performance of sodium toluene-4-sulfonic acid, thereby contributing to the burgeoning field of green chemistry and sustainable synthesis strategies. Recently 4*H*-benzo[b]pyran and its analog have garnered attention because of their potential biological and medicinal characteristic properties. These compounds show important applications in the treatment of diseases such as Alzheimer's, AIDS, Huntington's, Parkinson's, and Down syndrome. Additionally, 4*H*-benzopyran finds use in cosmetics, food additives, agrochemicals, and photoactive materials. Researchers have focused on synthesizing anticancer, antianaphylactic, and antibacterial agents [2]. Moreover, these compounds have shown promise in clinical way in disease of schizophrenia and myoclonus [3-4].

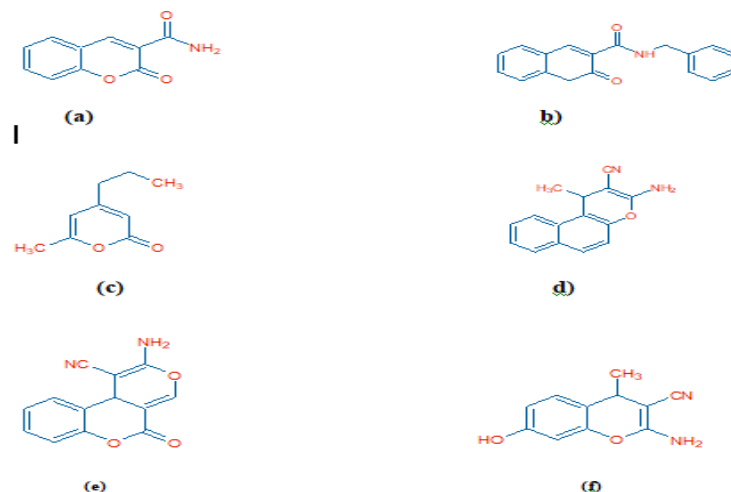


Fig.3.1: Biological Active tetrahydrobenzo[b]pyran Molecules

The tetrahydrobenzo[b]pyran is a heterocyclic compound. It was synthesized by three components such as aldehyde, malononitrile and dimedone. It is synthesized by using various catalyst and solvents.

2.0 Result and Discussion:

The synthesis of tetrahydrobenzo[b]pyran utilizing STS as a catalyst in an aqueous medium exhibited notable efficiency. The STS-catalyzed reaction proceeded smoothly and resulted in the formation of tetrahydrobenzo[b]pyran in high yields. STS demonstrated significant promise as a green catalyst due to its advantageous characteristics. Its water solubility facilitated the use of an aqueous medium, reducing the requirement for hazardous organic solvents. This environmentally benign feature aligns well with the principles of green

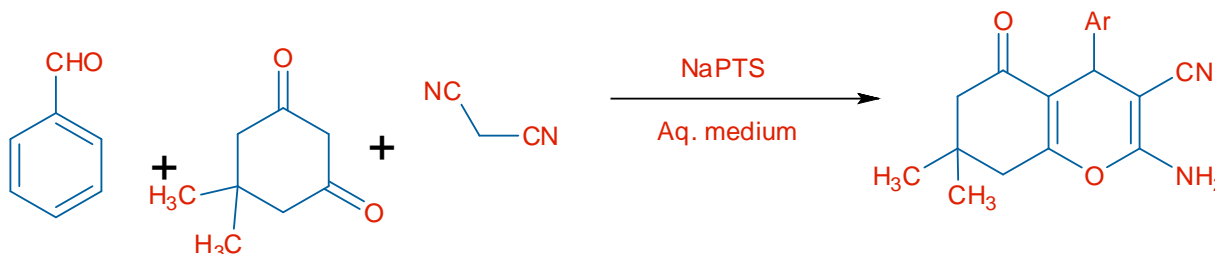
chemistry. The reaction yield achieved using STS as a catalyst was substantial, surpassing previously reported methods. High yields of tetrahydrobenzo[b]pyran were obtained, highlighting the efficacy of STS in promoting this reaction. The selectivity of the reaction catalyzed by STS was noteworthy. The formation of tetrahydrobenzo[b]pyran occurred predominantly with minimal side products or undesired by-products, indicating the high selectivity of STS as a catalyst in this transformation. While the exact mechanism of the STS-catalyzed synthesis of tetrahydrobenzo[b]pyran in aqueous media requires further elucidation, preliminary insights suggest potential pathways involving protonation of the carbonyl group and subsequent cyclization.

Table-2.1: Screening of conditions for synthesis of 5-amino-pyrazole-4-carbonitrile:

Entry	Solvent/ Catalyst	Time	Yield
1	Water	60 hrs	trace
2	Ethanol	40 hrs	trace
3	Water + Ethanol(1:1)	30 hrs	40%
4	Water + 40% NaPTS	40 min	92%

Mainly we focus on the selection of more sustainable and green synthetic process for present scheme. For the synthesis of tetrahydrobenzo[b]pyran we screening various solvents like water, ethanol, mixture of water and ethanol (1:1) and found that for this organic transformation require longer reaction time and poor yield of the product. Then we select the STS in aqueous medium for this organic synthesis and found that the high yield of the product within short reaction time (Table 2.1). This is due to

STS acts as surface active agent and it increase the solubility of reactant molecules in may fold access. We screen the reaction condition by using reactant as aldehyde (1mmol), malononitrile (1mmol), and dimedone (1mmol) (Scheme 2.1) and got the maximum yield in 5ml STS in aqueous medium at room temperature. Then use different derivatives of benzaldehyde with electron donating and withdrawing group getting good to excellent yields of corresponding tetrahydrobenzo[b]pyran (Table 2.2).



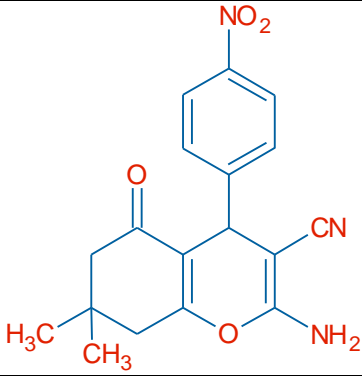
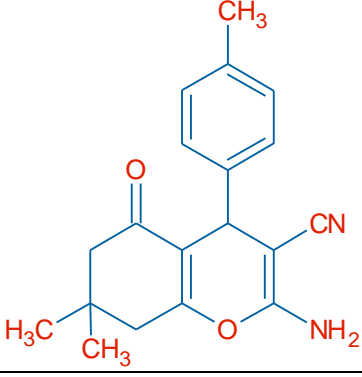
Scheme-2.1: Synthesis of Tetrahydrobenzo[b]Pyran catalyzed by sodium toluene-4- Sulfonic acid in aqueous medium

Another advantageous aspect of STS was its potential for reusability. After the reaction, the catalyst could be easily separated from the reaction mixture, and its effectiveness remained relatively consistent upon successive runs, contributing to its economic viability. While the exact mechanism of

the STS-catalyzed synthesis of tetrahydrobenzo[b]pyran in aqueous media requires further elucidation, preliminary insights suggest potential pathways involving protonation of the carbonyl group and subsequent cyclization.

Table No.2.2: The synthesis of Tetrahydrobenzo[b]Pyran

Sr. No.	Tetrahydrobenzo[b]Pyran	Time min	Yield %	Melting Point °C
1		40	92	227-240
2		40	93	204-208
3		45	86	200-202
4		40	85	174-175
5		50	85	210-212

6		80	80	232-234
7		90	84	214-216

This method exhibits a noteworthy capability to tolerate the presence of functional groups such as -NO₂, -OH, and -OCH₃ under the reaction conditions. Moreover, the catalyst, Sodium toluene-4-sulfonic acid, showcases reusability up to four times without a noticeable decrease in its catalytic activity. While prior reports have often focused on synthesizing 4H-benzopyran under basic conditions, our success lies in demonstrating the recyclability of Sodium toluene-4-sulfonic acid as a Lewis acid catalyst for the promotion of tetrahydrobenzo[b]pyran synthesis. In-depth analysis using various spectroscopic techniques, including IR, ¹H and ¹³C NMR, as well as mass spectral data, provides valuable insights into the formation of the desired product. This comprehensive characterization enhances our understanding of the reaction mechanism and the structural attributes of the synthesized tetrahydrobenzo[b]pyran.

3.0 Experimental Section:

General:

Chemicals from Loba and Sigma-Aldrich chemical companies, without further purification, were utilized. Reactions underwent monitoring via thin-layer chromatography (TLC) on silica gel plates using UV light. Melting points, determined using the EQ 730A-EQUIPTRONICS electrical melting point apparatus, are reported as uncorrected values for the products. Infrared spectra were obtained with a Perkin-Elmer FTIR spectrometer, examining samples as KBr discs at 5% w/w. Gas

Chromatography used to determine the mass of molecule. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker Ascend 400 MHz spectrometer, utilizing DMSO as a solvent and TMS as an internal reference.

General Procedure

The mixture of dimedone, aldehyde, and malononitrile 1 mmol each in 5mL aqueous solution of sodium toluene-4-sulfonic acid and stirred leading to final product, 4H-benzo[b]pyran, obtained and re-crystallized in ethanol.

Spectroscopic Data

2-amino-3-cyano-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro 4H-benzopyran:

¹H NMR: 1.06 (3H,s), 1.15 (3H, s), 2.29 (2H, d, J = 14.0 Hz), 2.51 (2H, s), 4.54 (1H, s), 4.67 (2H, s, 4), 7.44 (2H, d, J = 11.6 Hz), 8.21 (2H, d, J = 11.6 Hz). The ¹³C NMR: δ 27.29, 28.75, 32.25, 35.54, 46.99, 50.37, 58.20, 112.75, 120.01, 128.74, 129.56, 131.55, 144.19, 158.93, 163.09, and 196.17. MS resonate at m/z 329 (M+), 312, 302, 266, 245, 216, 161, and 133.

2-Amino-3-carbonitrile-4-(4-chlorophenyl)-5-oxo-5,6,7,8-tetrahydro-4H-pyran IR: 3373, 3311, 2827, 2192, 1648 cm⁻¹, ¹H NMR spectrum (300 MHz), δ 0.928 (3H,s) δ 1.016 (3H,s), δ 2.108 (2H,d,J=15.9 Hz), 2.262(2H,d J=15.9 Hz), δ 2.48(2H,s) 4.174(1H,s), 7.074(2H,d) 7.165 & 7.348 (2H,dJ=8.4 Hz).

4.0 Conclusion

The utilization of Sodium toluene-4-sulfonic acid as a catalyst for the synthesis of tetrahydrobenzo[b]pyran in an aqueous ethanol solvent has proven to be a pivotal advancement in the realm of sustainable catalysis. This study demonstrated the efficacy of Sodium toluene-4-sulfonic acid in promoting the formation of tetrahydrobenzo[b]pyran, offering a greener and more efficient synthetic route compared to conventional methods. The successful synthesis of tetrahydrobenzo[b]pyran underscored the catalytic prowess of Sodium toluene-4-sulfonic acid, facilitating the formation of the desired product under mild reaction conditions. The use of aqueous ethanol as a solvent further exemplified the environmentally benign nature of this catalytic system, aligning with the principles of green chemistry by minimizing the use of hazardous or non-renewable solvents. The insights gained from this study not only highlight the efficiency and selectivity of Sodium toluene-4-sulfonic acid as a catalyst but also emphasize the potential for developing sustainable synthetic methodologies in organic chemistry. The use of Sodium toluene-4-sulfonic acid in aqueous ethanol offers a promising avenue for further exploration in the synthesis of diverse bioactive compounds and pharmaceutical intermediates, contributing to the ongoing efforts in environmentally conscious synthesis strategies. The application of Sodium toluene-4-sulfonic acid as a catalyst for tetrahydrobenzo[b]pyran synthesis in an aqueous ethanol medium represents a significant stride towards sustainable and eco-friendly synthetic routes, fostering the development of greener chemical processes with wide-ranging implications in pharmaceutical and material science applications.

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6.0 Disclosure statement

The authors declare no potential conflict of interest.

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