IJARSCT

International Journal of Advanced Research in Science, Communication and Technology

International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal

ISSN: 2581-9429

Volume 6, Issue 8, April 2026

Impact Factor: 8.2

Synthesis of Tetrahydro[b]pyran Derivatives Catalyzed by Zn Doped Cobalt Tartrate

Mahesh Walle
Sundarrao More Arts, Commerce and Science College Poladpur-Raigad
mahesh.walle@gmail.com

Abstract: *The synthesis of tetrahydro[b]pyran derivatives represents a significant advancement in heterocyclic chemistry, particularly through the application of Zn-doped cobalt tartrate as a novel, efficient catalyst. Tetrahydro[b]pyran scaffolds are essential structural motifs in natural products, pharmaceuticals, and bioactive molecules, exhibiting diverse biological activities such as antimicrobial, anticancer, and anti-inflammatory properties. The optimized protocol involves the condensation of aromatic aldehydes, active methylene compounds (e.g., malononitrile), and cyclic 1,3-diketones (e.g., dimedone or 1,3-cyclohexanedione) in aqueous ethanol under mild reflux conditions (75–80°C). The Zn doping enhances the Lewis acidity of the cobalt tartrate framework, facilitating dual activation of electrophiles and nucleophiles via coordinated hydrogen bonding and metal coordination, thus promoting rapid cyclization with excellent regioselectivity. A model reaction with 4-chlorobenzaldehyde, malononitrile, and dimedone afforded the corresponding 2-amino-tetrahydrobenzo[b]pyran in 94% isolated yield within 1 hour using 10 mol% catalyst. Catalyst characterization via FT-IR, XRD, SEM-EDX, and TGA confirmed the successful incorporation of Zn into the cobalt tartrate matrix, revealing high surface area and thermal stability.*

Keywords: tetrahydro[b]pyran

1. Introduction

The tetrahydro[b]pyran derivatives attracted researcher widely as they have various pharmacological properties like diuretics, anticancer, spasmolytic, anti-anaphylactin agent and cognitive enhancer for the treatment of neurodegenerative disease such as alzheimer, amyoprophic lateral sclerosis, Parkinson's disease, Huntington's disease, Down's syndrome and Schizophernia and myoclonus[1].

The copper doped tartarates has been grown in silica gel and many of tartarate compound found application in medical, pharmaceutical and industrial fields due to their special properties, for example injection of Na-Cr tartarate increases the susceptibility to the transplanted sarcoma to the effect of X-rays, calciphylatic responses of various ferrous tartarate compounds prevents anemia of champagene, ferrous tartarate is used to tan skin and manganese tartarate crystals are used as chemical temperature indicator[2].

The synthesis of heterocyclic compound containing oxygen atom like 3,3-arylidene bis(4-hydroxycoumarin) has been reported recently by using ferrite as catalyst[3], where as some compounds containing nitrogen atom was synthesized like quinoline and dihydropyramidines by using tartarate as catalyst[4].

Synthesis of tetrahydrobenzo[b]pyran was traditionally promoted by strong bases, ligands, strong acids or high temperature in the presence of volatile organic compounds like ammonium chloride[5], fructose[6], hexadecyl-dimethylbenzyl ammonium bromide[7], pthalimide-N-Oxyl[8], tetramethyl ammonium hydroxide[9], palladium nanoparticals[10], (S)-Proline[11], diammonium hydrogen phosphate[12], hexadecyltrimethyl ammonium bromide[13], molecular iodine[14], LiBr[15], MgO[16], ionic liquids[17], perfluorooctonoate[18] and potassium phosphate[19]. Some of the 2-amino-tetrahydrobenzo[b]pyrans can be used as photoactive materials[20]. All of these methods have cons and pros but now a day's researcher would like to go for more eco-friendly method which can minimize the hazardous byproducts.

DOI: 10.48175/IJARSCT-33164

In present work we reported an efficient, environment benign and economic green synthesis of tetrahydrobenzo[b]pyran using various aromatic aldehydes, malononitrile and dimedone in presence of $ZnCo_2(C_4H_4O_6)_3.6H_2O$ as catalyst in aqueous media at reflux condition. The catalyst has potential of water solubility and can be recoverable which can be efficiently used for 2-3 cycles.

Experimental

The melting points were determined on an electrothermal apparatus and the temperature was not calibrated. IR spectra were recorded as thin films on KBr using Spectrum 400 spectrophotometer. The ^{13}CNMR spectra were recorded on a Bruker AVANCE NEO 500 MHz NMR spectrometer. Sample solution was prepared in DMSO containing tetramethyl silane (TMS) as an internal reference. Mass spectra were recorded on a Water S, Q-TOF MICROMASS (ESI-MS) at 70 eV.

All chemical reagents were commercially available and purified with standard methods before use. Solvents were dried in routine ways and redistilled.

General procedure for preparation of catalyst $ZnCo_2(C_4H_4O_6)_3.6H_2O$

The Zn-doped cobalt tartrate complex was synthesized by mixing cobalt(II) chloride and zinc(II) sulfate in stoichiometric ratios, followed by the addition of tartaric acid as a ligand under controlled conditions. An appropriate amount of cobalt(II) chloride hexahydrate ($CoCl_2·6H_2O$) was dissolved in distilled water. Similarly, zinc (II) sulfate heptahydrate ($ZnSO_4·7H_2O$) was dissolved in distilled water. The prepared $CoCl_2$ and $ZnSO_4$ solutions were mixed in a 2:1 molar ratio (i.e., 2 moles of Co^{2+} for every 1 mole of Zn^{2+}) in a reaction vessel. The molar ratio of cobalt to zinc was critical for achieving the desired Zn-doped cobalt tartrate complex. 10 % aqueous Tartaric acid ($C_4H_6O_6$) was then added slowly to the mixture of metal solutions till complete precipitation. Tartaric acid acted as a ligand, coordinating with both cobalt and zinc ions to form the Zn-doped cobalt tartrate complex.

General procedure for the synthesis of tetrahydrobenzo[b]pyran

The mixture of aromatic aldehyde (1mmol), malononitrile (1mmol), dimedone (1mmol), water (10 ml) and $CuFe_2(C_4H_4O_6).6H_2O$ (10 mol%) was prepared properly by using glass rod and refluxed, the progress of the reaction was monitored by TLC by using ethyl acetate and n-hexane (20:80) as solvent system. After completion of reaction the mixture was cooled and poured on 20 ml crushed ice. The solid product was filtered, washed with water, dried and recrystallized by using ethanol to get corresponding tetrahydro[b]pyran. The products were confirmed by melting point, IR and ^{1}HNMR spectrum.

Result and Discussion

Initially, the catalyst was prepared and reported elemental analysis was compared with observed data of weight % of Zn-Co tartrate complex which was quite similar. The synthesized metal complexes are powdered solid, colored and stable towards air and moisture at room temperature as shown in table 1. XRD and TEM data of tartrate complex were compared with standard data and found to be very similar to reported data which confirmed the formation of complex.

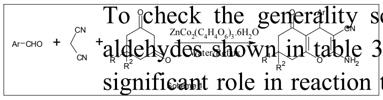
Element	Wt%	Atomic %
O	49.45	76.75
Co	24.72	10.42
Zn	17.33	6.58

Table 1 Observed weight % of Zn-Co tartrate complex

The synthesis of tetrahydrobenzo[b]pyran was carried out by using 4-nitro benzaldehyde as model reaction in different conditions like temperature, reaction time, solvent selection etc. as shown in table 2. When reaction carried out in catalyst free condition by only stirring at room temperature no product was formed till 45 minutes, whereas by reflux at 60°C in ethanol the product formed after 2.5 hours and eventually in presence of $ZnCo_2(C_4H_4O_6)_3.6H_2O$ commendable product was formed within 30 minutes. It was observed 10 mol % of the catalyst was sufficient to promote the reaction without losing its activity and could be reuse for frequent cycles. The catalyst demonstrates remarkable recyclability (up to 8 cycles with <5% leaching) and broad substrate scope, accommodating electron-rich and electron-deficient aldehydes with yields ranging from 90–95%.

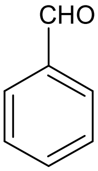
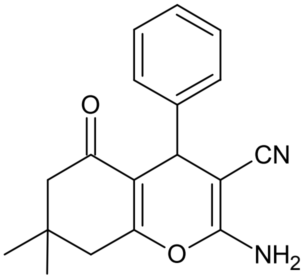
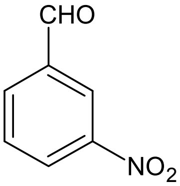
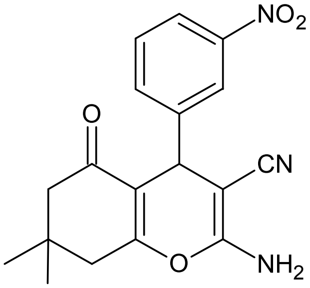
Entry	Catalyst	Reaction Condition	Time (Min.)	Yield %
1	Without Catalyst	EtOH/Stirring/RT	60	No product
2	Without catalyst	EtOH/60°C	120	70
3	$ZnCo_2(C_4H_4O_6)_3.6H_2O$	$EtOH:H_2O$/60°C	60	78
4	$ZnCo_2(C_4H_4O_6)_3.6H_2O$	H_2O/60°C	30	90

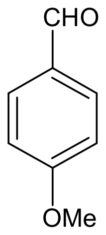
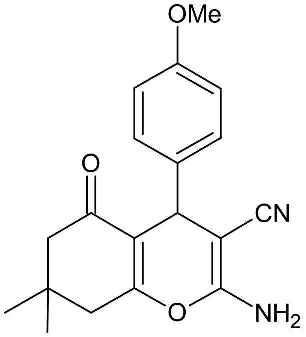
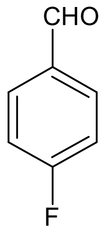
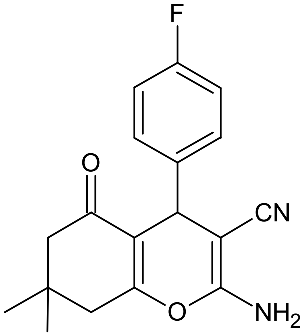
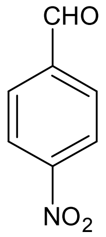
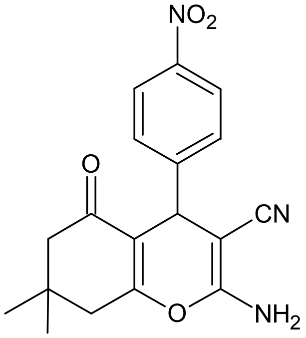
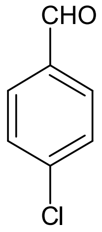
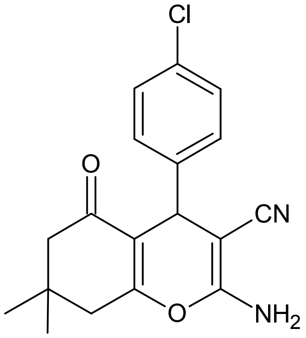
Table 2 optimization of reaction condition



Scheme 1

To check the generality scope of this new methodology, we performed reaction of various substituted aromatic aldehydes shown in table 3. The nature of substituent like electron donating and electron withdrawing has played no significant role in reaction time and yield of corresponding products. The reaction was carried out in water hence has attractive feature as carried out neatly and solvent free. This would provide us very easy work up and no complicated isolation method was required. The metal tartrate acts similar to Lewis acid which can provide possible conditions.

Sr.No.	Aldehyde	Product	Time (Min.)	Yield (%)	M.P.	
					Obtained	Reported
1			30	90	232-234	234-235
2			30	92	210-212	214-216

3			30	90	202-204	201-202
4			30	90	222-224	220-221
5			30	95	178-180	179-180
6			30	95	212-214	215-217

DOI: 10.48175/IJARSCT-33164

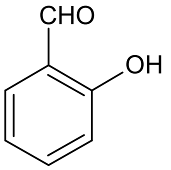
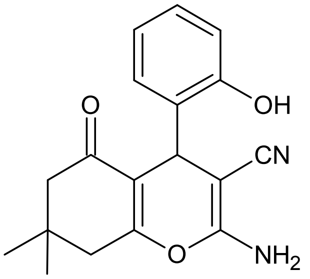
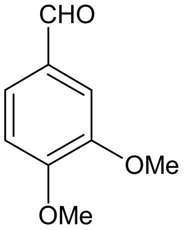
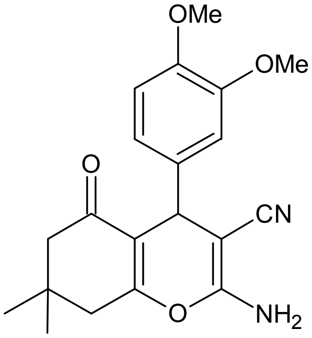
7			30	92	226-228	224-226
8			30	90	210-212	215-217

Table 3. Reactions of various substituted aromatic aldehydes with good yield

2. Conclusion

In conclusion we have developed mild, efficient, environment benign method for the synthesis of series of biological active Tetrahydrobenzo[b]pyran derivatives by using water soluble and reusable catalyst $ZnCo_2(C_4H_4O_6)_3.6H_2O$. The present method has simple procedure, easy work-up, lesser time, solvent free condition and high yield compared to many reported methods. The given method is green and need not any hazardous solvent.

REFERENCES

1. Sheikhhosseini, E., Ghazanfari, D. & Nezamabadi, V. A new method for synthesis of tetrahydrobenzo [b] pyrans and dihydropyrano [c] chromenes using p-dodecylbenzenesulfonic acid as catalyst in water. (2013).

2. Mathivanan, V. & Haris, M. Characterization of pure and copper-doped iron tartrate crystals grown in silica gel. *Pramana* **81**, 177–187 (2013).

3. Walle, M. R., Pansare, D. N., Kamble, S. S., Pawar, R. P. & Ingale, R. D. SYNTHESIS OF 1, 8-DIOXOOCTAHYDROXANTHENE AND 3, 3-ARYLIDENE BIS (4-HYDROXYCOUMARIN) DERIVATIVES. *EUROPEAN CHEMICAL BULLETIN* **8**, 101–104 (2019).

4. Pawar, S. S., Patil, C. S., Tadke, V. B., Dhanmane, S. V. S. & Pawar, R. P. COPPER-NICKEL TARTARATES COMPOSITES: A REUSABLE AND GREEN CATALYSTS FOR THE SYNTHESIS OF QUINOLINES AND DIHYDROPYRIMIDINES DERIVATIVES. *EUROPEAN CHEMICAL BULLETIN* **5**, 221–224 (2016).

5. Pagore, V., Tekale, S. U., Jadhav, V. B. & Pawar, R. P. Ammonium chloride catalyzed microwave-assisted synthesis of tetrahydrobenzo [b] pyrans. *Iranian Journal of Catalysis* **6**, 189–192 (2016).

6. Pourpanah, S. S., Habibi-Khorassani, S. M. & Shahraki, M. Fructose-catalyzed synthesis of tetrahydrobenzo [b] pyran derivatives: Investigation of kinetics and mechanism. *Chinese Journal of Catalysis* **36**, 757–763 (2015).

7. Jin, T.-S. *et al.* Hexadecyldimethyl benzyl ammonium bromide: an efficient catalystfor a clean one-pot synthesis of tetrahydrobenzopyran derivatives in water. *Arkivoc* **14**, 78–86 (2006).

8. Dekamin, M. G., Eslami, M. & Maleki, A. Potassium phthalimide-N-oxyl: a novel, efficient, and simple organocatalyst for the one-pot three-component synthesis of various 2-amino-4H-chromene derivatives in water. *Tetrahedron* **69**, 1074–1085 (2013).

9. Balalaie, S., Sheikh-Ahmadi, M. & Bararjanian, M. Tetra-methyl ammonium hydroxide: An efficient and versatile catalyst for the one-pot synthesis of tetrahydrobenzo [b] pyran derivatives in aqueous media. *Catalysis Communications* **8**, 1724–1728 (2007).

10.Saha, M. & Pal, A. K. Palladium (0) nanoparticles: a novel and reusable catalyst for the synthesis of various pyran derivatives. (2012).

11.Balalaie, S., Bararjanian, M., Amani, A. M. & Movassagh, B. (S)-Proline as a neutral and efficient catalyst for the one-pot synthesis of tetrahydrobenzo [b] pyran derivatives in aqueous media. *Synlett* **2006**, 263–266 (2006).

12.Balalaie, S., Bararjanian, M., Sheikh-Ahmadi, M., Hekmat, S. & Salehi, P. Diammonium hydrogen phosphate: An efficient and versatile catalyst for the one-pot synthesis of tetrahydrobenzo [b] pyran derivatives in aqueous media. *Synthetic Communications* **37**, 1097–1108 (2007).

13.Jin, T.-S., Wang, A.-Q., Wang, X., Zhang, J.-S. & Li, T.-S. A clean one-pot synthesis of tetrahydrobenzo [b] pyran derivatives catalyzed by hexadecyltrimethyl ammonium bromide in aqueous media. *Synlett* **2004**, 0871–0873 (2004).

14.Bhosale, R. S. *et al.* Molecular iodine: An efficient catalyst for the synthesis of tetrahydrobenzo [b] pyrans. *Synthetic Communications* **37**, 4353–4357 (2007).

15.Saini, A., Kumar, S. & Sandhu, J. S. A new LiBr-catalyzed, facile and efficient method for the synthesis of 14-alkyl or aryl-14H-dibenzo [a, j] xanthenes and tetrahydrobenzo [b] pyrans under solvent-free conventional and microwave heating. *Synlett* **2006**, 1928–1932 (2006).

16.Seifi, M. & Sheibani, H. High surface area MgO as a highly effective heterogeneous base catalyst for three-component synthesis of tetrahydrobenzopyran and 3, 4-dihydropyrano [c] chromene derivatives in aqueous media. *Catalysis letters* **126**, 275–279 (2008).

17.Godse, V. W. *et al.* L-Pyrrolidine-2-Carboxylic Acid Sulfate: A New Ionic Liquid for the Synthesis of Bioactive Tetrahydrobenzo [b] pyrans. *Organic Preparations and Procedures International* **49**, 363–369 (2017).

18.Wang, L.-M., Shao, J.-H., Tian, H., Wang, Y.-H. & Liu, B. Rare earth perfluorooctanoate [RE (PFO) 3] catalyzed one-pot synthesis of benzopyran derivatives. *Journal of fluorine chemistry* **127**, 97–100 (2006).

19.Pore, D. M., Undale, K. A., Dongare, B. B. & Desai, U. V. Potassium phosphate catalyzed a rapid three-component synthesis of tetrahydrobenzo [b] pyran at ambient temperature. *Catalysis letters* **132**, 104–108 (2009).

20.Armesto, D., Horspool, W. M., Martin, N., Ramos, A. & Seoane, C. Synthesis of cyclobutenes by the novel photochemical ring contraction of 4-substituted 2-amino-3, 5-dicyano-6-phenyl-4H-pyrans. *The Journal of Organic Chemistry* **54**, 3069–3072 (1989).

21.Salvi, P. P. *et al.* Brønsted acidic ionic liquids promoted cyclocondensation reaction: Synthesis of 1, 8-dioxo-octahydroxanthene. *Comptes Rendus Chimie* **14**, 883–886 (2011).

22.Muthu, T., Anand, K., Sureshkumar, M. & Gengan, R. M. Eco-friendly approach: Graphene like boron nitride modified calcium material for the synthesis of 2-amino-4H-pyran-3-carbonitrile derivatives. *Adv. Mater. Lett* **7**, 790–794 (2016).

23.Mousavi, M. R., Maghsoodlou, M. T., Noori, F. & Hazeri, N. A Facile and Efficient Synthesis of Tetrahydrobenzo [b] pyrans Using Sucrose as Green, Inexpensive, Natural and Biodegradable Catalyst. *Organic Chemistry Research* **1**, 66–71 (2015).

24.Rupnar, B. D., Pagore, V. P., Tekale, S. U., Shisodia, S. U. & Pawar, R. P. L-Tyrosine catalysed mild and efficient synthesis of dihydropyrano [2, 3c] pyrazole under microwave irradiation. *Der Chemica Sinica* **8**, 229–234 (2017).

25.Bhagat, D. S. *et al.* SYNTHESIS OF TETRAHYDROBENZO [b] PYRAN DERIVATIVES USING THIAMINE HYDROCHLORIDE (VB1) AS A GREEN CATALYST. *EUROPEAN CHEMICAL BULLETIN* **6**, 211–214 (2017).

26.Boumoud, B., Debbache, A., Boumoud, T., Boulcina, R. & Debache, A. Aqua Mediated One-Pot Synthesis of 2-Amino-tetrahydrobenzo[b]pyran Derivatives Catalyzed by Mg(NO3)2•6H2O. *Letters in Organic Chemistry* **11**, 475–479 (2014).

27.Efficient One-Pot Synthesis of Bis(4-hydroxycoumarin)methanes in the Presence of Sulfonic Acid Functionalized Nanoporous Silica (SBA-Pr-SO3H) - Ziarani - 2013 - Journal of the Chinese Chemical Society - Wiley Online Library. https://onlinelibrary.wiley.com/doi/abs/10.1002/jccs.201200530