

Indian Science Technology and Engineering facilities Map (I-STEM)

Invites application for

1. Partial financial support for using R&D facilities in other institutions through the I-STEM web portal to Users from Academic Institutions and Start-ups (Format-1)

Format for requesting support for accessing and using facilities through the I-STEM web portal.

(i) Details of the Personal Information

- a. **Name of the Researcher:** ANSHRA NOUSHEEN
- b. **Name of the Institution:** PALAMURU UNIVERSITY
- c. **Name of the Department:** Department of CHEMISTRY
- d. **Degree registered for:** Ph.D
- e. **Mob. No.:** +916305806586
- f. **Email ID:** anshranousheen27@gmail.com

(ii) Project/Research topic Details:

Project Title/Research Title: Electrochemical synthesis of 2,3-dihydrobenzofuran derivatives by cyclic voltammetry and their DNA cleavage and antioxidant activity.

- a. **Sub area:** Heterocyclic chemistry and biological activities
- b. **Area Description:** Organic chemistry and medicinal chemistry
- c. **Aims & Objective (in Bullets):**
 - To design a set of new Diastereoselective Heterocyclic compounds by using Electrochemical organic synthesis.
 - Characterization of all the designed molecules using spectroscopic techniques such as NMR, HRMS and Single crystal XRD for at least one compound among the series of analogs.
 - To synthesize compounds for the development of SAR studies and evaluation of their DNA cleavage and antioxidant activity by DPPH assay.
 - To screen various reaction conditions (solvent conditions, various types of catalyst if necessary, green protocol, E-factor) to achieve efficiency in the reaction.

d. **Duration (MM/YYYY):** 07/2023 (6 months)

e. Project Summary (1000 words):

Oxygen containing heterocyclic substructure possess potent immune suppressive activities [1], among which 2,3-dihydrobenzofuran structures corresponds to one of the most important biomaterial [2] found as a key structural element in the neo-lignans [3-5], which are a disparate family of biologically active plant enzymes. These compounds possess a wide range of biological activities comprising antitumor and immunosuppressive activities. Attributed to their significant biological and neuroprotective potential of 2,3-dihydrofuran biomaterials has become an important willing in the synthetic community.

Electrochemical synthesis is recognized as one of the most powerful and sustainable methods in organic chemistry [6-7]. Electrochemical methods are more and more widely used for the study of electroactive compounds in pharmaceutical forms and

physiological fluids due to their simple, rapid, and economical properties [8]. The field of electrochemical synthesis has developed rapidly over the last decade and provided alternative synthetic methods without using stoichiometric amounts of chemical oxidants or reductants. The importance of sustainable and green synthetic protocols for the synthesis of fine chemicals has rapidly increased during the last decades in an effort to reduce the use of fossil fuels and other finite resources. The replacement of common reagents by electricity provides a cost- and atom-efficient, environmentally friendly, and inherently safe access to novel synthetic routes [9].

In the present protocol we report a superficial and Eco-friendly synthesis of dihydrobenzofuran derivatives has been performed at platinum electrode by electrochemical oxidation of aromatic alcohol in the presence of active methylene groups. Electrochemical organic synthesis has to be done in an undivided cell at environmental conditions.

f. Technical Details

a. **TRL:**

The proposed project will be executed within six months. The component-wise work plan has been given below.

1st month: Required chemicals will be procured and initiate the synthesis of the intermediates.

2nd & 3rd month: Optimizing the reaction conditions for the formation of the target compounds. Synthesis and their characterization using spectroscopic techniques.

4th month: Preparation of the library of target compounds and structural elucidation using spectral studies.

5th month: Evaluation of biological activity including DNA cleavage and antioxidant activity by DPPH assay

6th month: Submission of the project report to I-STEM. Submission of the manuscript and filing a patent.

b. **Design & development:**

The synthesis of 2,3-dihydrofuran moiety has become an important aspiration in the synthetic section. As a consequence, synthetic Organic chemists also took a fascinate considerable recognition for the development of methods to synthesize fused 2,3-dihydrobenzofuran component (Fig1).

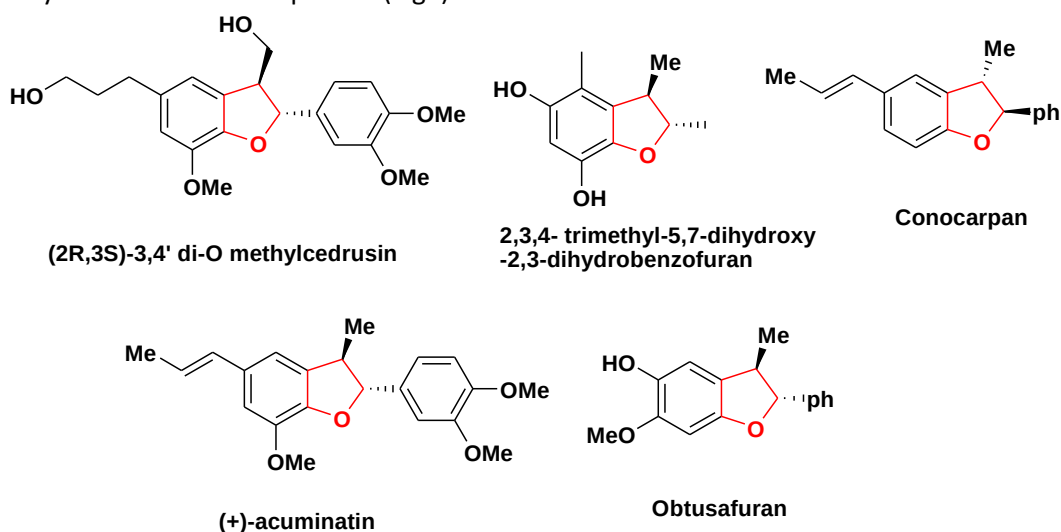
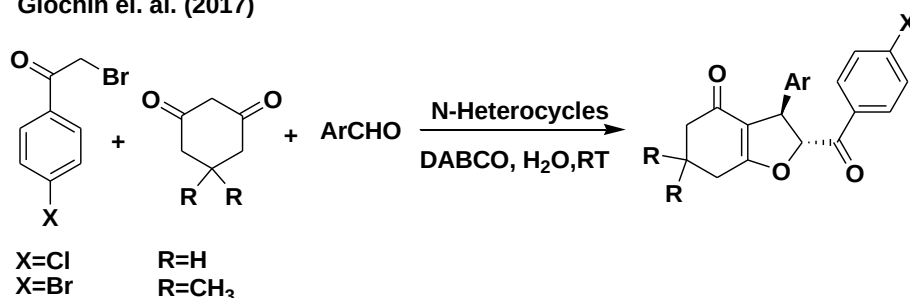


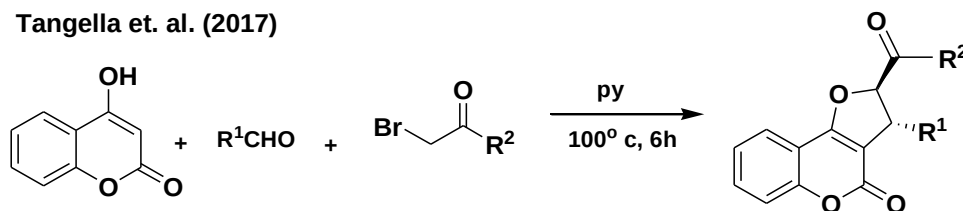
Fig1: Chemical structures of biologically active 2,3-dihydrobenzofuran derivatives

In spite of that, many synthetic procedures have been reported for the preparation of 2,3-dihydrobenzofurans. Osyanin et. al developed a simple, general route for the preparation of 1,2-dihydronaphtho[2,1-b] furans and 2,3- dihydrobenzofurans, starting from phenolic Mannich bases and pyridinium ylides has been developed with excellent diastereoselectivity [10] Golchin et. al. 2017 [11] Tangella et. al. 2017 [12], Havasian et. al. 2018 [13], anshra et. al. 2022[14], independently reported simple, general route for the preparation of 2,3-dihydrobenzofuran via a succession one-pot, two-step tandem reaction started with pyridinium ylide, aromatic aldehyde, dimedone, or 4-hydroxycoumarin with different bases which leads to the development of 2,3-dihydro furans by domino Michael addition-proton exchange-annulation through intramolecular cyclisation arrangement (scheme1).

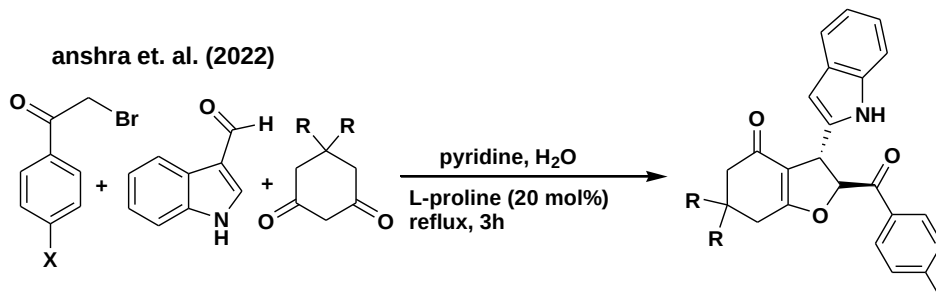
Glochin et. al. (2017)



Tangella et. al. (2017)



anshra et. al. (2022)



Scheme1:Previously reported synthetic methods for the preparation of 2,3-dihydrobenzofurans

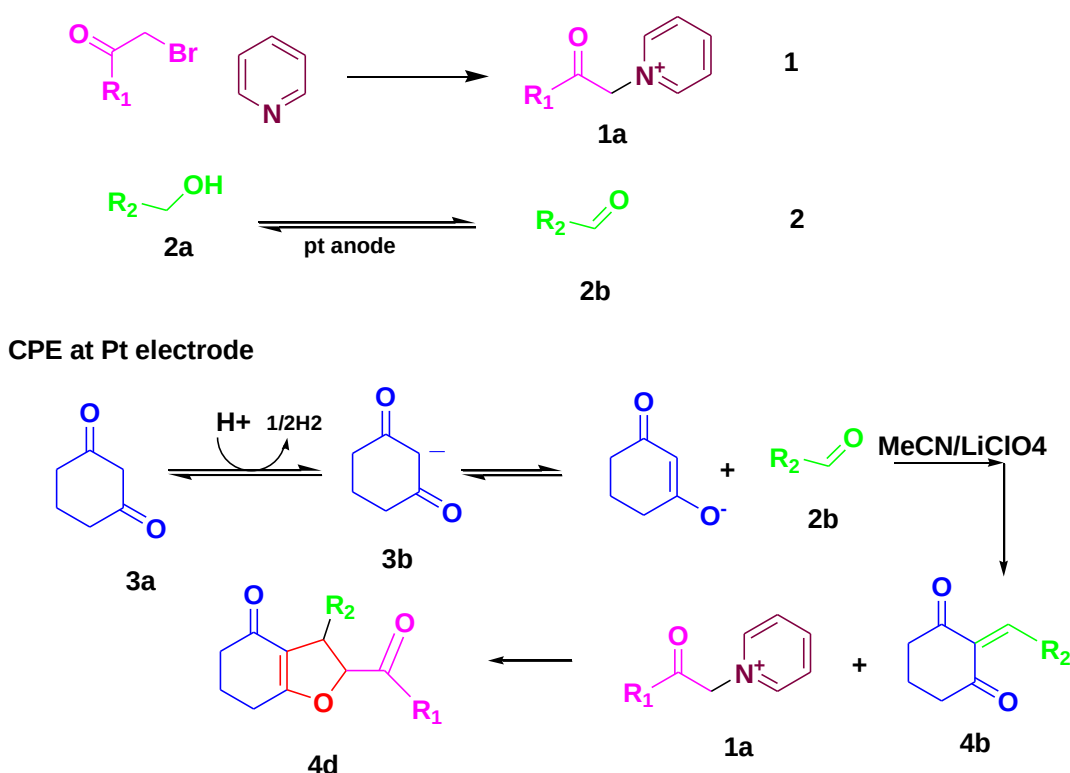
However, there are few disadvantages observed in previous reports such as harsh reaction conditions, expensive transition metal reagents or catalysts, longer reaction times and less substrate scope.

c. Methodology:

Considering these preliminary observation, a library of 2,3-dihydrobenzofuran derivatives were designed. These products were easily obtainable in high yields from the corresponding aromatic alcohol with active methylene groups by the following literature procedures [15]. Dihydrofurans synthesis presumably occurs via a pyridinium ylide, aromatic alcohol, dimedone, or 4-hydroxycoumarin with different bases through electrochemical method by using cyclic voltammetry which leading to

the formation of 2,3-dihydro furans through domino Michael addition-proton exchange-annulation via intramolecular cyclization sequence.

Cyclic voltammetry of 1 mM solution of aromatic alcohol can be recorded in acetonitrile solution containing LiClO₄ as supporting electrolyte at an ambient temperature. The experiment has to be carried out using a three electrode compartment cell both working and counter electrodes were platinum plates. The potential of the working electrode was measured vs saturated calomel electrode(SCE) as reference electrode at scan rate of 0.01 V s⁻¹. The results of the voltammetric experiments shows two anodic peaks which correlate to conversion of aromatic alcohol to aromatic aldehyde by one electron process and reveals no reduction peak potential. The result indicates that the electro oxidation contains a conversion within a one electron oxidation process. the anodic oxidation of aromatic alcohol 2a in the presence of different active methylene groups. The anodic oxidation of aromatic alcohol leads to the tranformation of the corresponding aromatic aldehyde 2b by removal of electrons. Electrochemically generated aromatic aldehyde 2b is highly reactive intermediate which undergo knoevenagel condensation with base of active methylene compounds 3a and further undergoes Michael type of conjugated addition with pyridinium base ylide 1a. The intermediate formed undergoes intramolecular cyclization and aromatization to give the desired product 4d [16-17] as shown in below scheme2.



Scheme2: Plausible mechanism for the formation of trans 2,3-dihydrofuran derivatives

Reference:

1. M. Antoszczak, D. Otto-Slusarczyk, M. Kordylas, M. Struga, A. Huczynski, Synthesis of lasalocid-based bioconjugates and evaluation of their anticancer activity, ACS Omega 7 (2022) 1943.

2. F. Bertolini, M. Pineschi, Recent progress in the synthesis of 2,3-dihydrobenzofurans, *Org. Prep. Proced. Int.* **41** (2009) 385–418.
3. X. Ma, J. Yang, C.L. Brown, C. Wang, S. Deng, R. Ke, S. Xu, M. Huang, X. Yang, Y. Feng, Cytotoxic neolignans from the traditional Chinese medicine *Daphniphyllum macropodum* miq, *RSC Adv.* **7** (2017) 52970–52976.
4. R. Guo, P. Zhao, X. Yu, G. Yao, B. Lin, X. Huang, S. Song, (±)-Pinnatifidones A-D, four pairs of highly modified neolignan enantiomers with a rare spirocyclohexanone skeleton from *Crataegus pinnatifida*, *Org. Chem. Front.* **8** (2021) 953–960.
5. K. Dong, C.Y. Zhao, X.J. Wang, L.Z. Wu, Q. Liu, Bioinspired selective synthesis of hetero dimer 8-5' or 8-O-4' Neolignan analogs, *Org. Lett.* **23** (2021) 2816–2821.
6. Kosuke Yamamoto, Masami Kuriyama, and Osamu Onomura, Anodic Oxidation for the Stereoselective Synthesis of Heterocycles, *Acc. Chem. Res.* (2019) DOI: 10.1021/acs.accounts.9b00513.
7. Xihao Chang, Qinglin Zhang and Chang Guo, Asymmetric Electrochemical Transformation, *Angew. Chem.* DOI: <http://dx.doi.org/10.1002/anie.202000016>.
8. Ke-Jin Jiao, Yi-Kang Xing, Qi-Liang Yang, Hui Qiu and Tian-Sheng Mei, Site-Selective C–H Functionalization via Synergistic Use of Electrochemistry and Transition Metal Catalysis, *Acc. Chem. Res.* (2020) DOI: <https://dx.doi.org/10.1021/acs.accounts.9b00603>.
9. Masanori Morimoto, Masamitsu Urakawa and Koichiro Koma, Electrochemical Synthesis of Dihydrobenzofurans and Evaluation of Their Insect Antifeedant Activities (2017) DOI: 10.5650/jos.ess17022.
10. A. Vitaly Osyanin, V. Dmitry Osipov and N. Yuri Klimochkin, Reactions of o-Quinone Methide with pyridinium Methylides: a diastereoselective synthesis of 1,2-Dihydronaphtho [2,1-b] furans and 2,3-dihydrobenzofurans, *J. Org. Chem.*, (2013) **78**, 5505.
11. Sajedeh Golchin, Mohammad Hossein Mosslemin, Afshin Yazdani-Elah-Abadi and Nasim Shams, DABCO- catalysed multi-component domino reactions for the synthesis of diverse and densely functionalized benzofurans in water, *Res Chem Intermed.*, (2017) **43**, 1735.
12. Yellaiah Tangella, Kesari Lakshmi Manasa, V. Laxma Nayak, Manda Sathish, B. Sridhar, Abdullah Alarifi, Narayana Nagesh and Ahmed Kamal, An efficient one-pot approach for the regio- and diastereoselective synthesis of trans-dihydrofuran derivatives: cytotoxicity and DNA-binding studies, *Org. Biomol. Chem.*, (2017) **15**, 6837.
13. Azadeh Havasian, Elham Heydaripour, Mohammad Reza Nateghi, Mohammad Hossein Mosslemin and Forough Kalantari Fotouh, synthesis, characterization and application of monodisperse poly l-dopa microspheres, *Turk J Chem.*, (2018) **42**, 1370.
14. Anshra Nousheen, Munugala Chandrakant, Banoth Karuna Sagar and Vijaya Laxmi Somarapu, Novel diastereoselective trans 2, 3-dihydrobenzofuran derivatives: Tandem synthesis, crystal structure, antioxidant and anticancer activity, *Journal of Molecular Structure* **1261** (2022) 132899.
15. Alireza Asghari, Anahita Gholami, Mohammad Bakherad and Mohsen Ameri, A green, simple, catalystfree, and efficient method for electroorganic synthesis of new benzofuran derivative, *J IRAN CHEM SOC* (2017) DOI 10.1007/s13738-017-1149-2.
16. Mohammad Mazloun-Ardakani, Alireza Khoshroo, Davood Nematollahi and Bibi-Fatemeh Mirjalili, Electrochemical Study of Catechol Derivatives in the Presence of β -diketones: Synthesis of Benzofuran derivative, *J. Electrochem. Soc.* (2012) DOI:

10.1149/2.029212jes.

17. Jyoti Malviya, R. K. P. Singh, Shashi Kala, and L. K. Sharma, Anodic Synthesis of New Benzofuran Derivatives Using Active Methylene Group at Platinum Electrode, Russ. J. Electrochem. (2018) DOI: 10.1134/S1023193518030096.

d. Facilities and Instrumentation required:

- Nuclear Magnetic Resonance (NMR) spectrometer for structural elucidation of all the synthesized compounds.
- Single crystal XRD for the structural elucidation of the compounds.

e. Consumables (Scientific materials):

S.no	Biological Activities	Institute with the facility	Charge per sample analysis(Rs.)	No. of samples	Total amount(Rs.)
1	DNA Cleavage	Averin biotech laboratories	4,000/-	15	60,000/-
2	Antioxidant	Averin biotech laboratories	2,000/-	15	30,000/-
				Total	90,000/-

S.no	Characterization	Institute with the facility	Charge per sample analysis(Rs.)	No. of samples	Total amount(Rs.)
1	¹ H NMR	Spark analyticals	300/-	15	4,500/-
2	¹³ C NMR	Spark analyticals	1,000/-	15	15,000/-
3	Mass spectra	Spark analyticals	250/-	15	3,750/-
4	Single crystal XRD	IICT Hyderabad	5,000/-	1	5,000/-
				Total	28,250/-
	Consumables			Total	1,50,00/-
				Grand Total(excluding travel)	2,68,250/-

g. Expected output and outcome

h. Industry/Institute Collaboration: yes

(i) **Name of the Collaborating Industry/Institute:** Koneru Lakshmaiah Education Foundation

(ii) Collaboration Details:

For cyclic voltammetry (electrochemical synthesis)

Dr. Pradeep Kumar Brahman
Associate Professor
Department of Chemistry
Koneru Lakshmaiah Education Foundation
Guntur, Andhra Pradesh, 522502.

(iii) **Additional Details if any**

i. **Funding required from I-STEM (with justification):**

Details of Requirements & Mode of the Engagement: (Attach the quotation for the consumables)

- (i) Short term Engagement:
 - a. Usage of testing/characterization facilities across the country (Characterization Mode)
 - i. **Testing Charges:** 1,18,250/-
 - ii. **Consumable charges:** 1,50,000/-
 - iii. **Travel Cost (Boarding and Lodging, if any):** 10,000/-
 - b. Usage of fabrication and testing facilities across the country (Fabrication Mode)
 - i. Fabrication and testing Charges
 - ii. Consumable charges (if any)
 - iii. Travel Cost (Boarding and Lodging, if any)
- (ii) Medium term Engagement:
 - a. Execution of project in any one of the Host Institution (Project Mode)
 - a. Fabrication and or testing Charges
 - b. Consumable charges (if any)
 - c. Travel Cost (Boarding and Lodging, if any)
 - b. Execution of project in Multi Host Institutions (Project Mode)
 - a. Fabrication and or testing Charges
 - b. Consumable charges (if any)
 - c. Travel Cost (Boarding and Lodging, if any)

(Round-trip to the Host Institution by 2nd class (Non-AC) railway via the nearest route)

Details of User's Bank Account:

(Please send a copy of the cancelled cheque/copy of the passbook carrying all the information needed)

Beneficiary Name (User's name): ANSHRA NOUSHEEN

PAN: BUBPN9706L

Bank Account No.: 62247904425

Name of the Branch: SBI Main Branch, MBNR

IFSC Code: SBIN0020184

Note: Proposed proposal must be executed within stipulated duration (max. 6 month) to avoid fund availability issues. Travel form will be provided by the I-STEM office. The users will submit the technical report, original invoice (duly signed by the Head of the Institution) raised by the Host Institution through I-STEM portal only along with a copy of the travel forms and original tickets through post to the Nodal Officer, I-STEM, Indian Institute of Science, Bangalore. A scan copy of all the documents may be sent in advance.

Generally used abbreviations

a/c	= Account	dep	= Deposit	Pr	= Principal
Adj	= Adjustment	Dft		Proc	= Processing Charge
Amt	= Amount	Dish		rd	= Recurring Deposit
Ar	= Arrear	DR		Ret/Rtn	= Return
bal	= Balance	DoB		Rnd	= Round of
Capn	= Capitalization	eft		ansfer	SB
chg/ch	= Charge	Inop		SC	= Short Credit
Chq	= Cheque	Ins		SI/So/SORD	= Standing Instruction
Clos	= Closure	int/in		S/D/W/H/o	= Son/Daughter/Wife/Husband of
Coll	= Collection	lon/li		tr/rtr/xfer	= Transfer
Comm	= Commission	min		TT	= Telegraphic Transfer
CDR/CORR	= Correction	os	= Outstanding	txn	= Transaction
CR	= Credit	P & T	= Postage & Telegram	Wdi	= Withdrawal
cash	= Cash	Pos	= Point of Sale	+MOD Bal	= total balance (SB+linked MOD a/c)



स्टेट बैंक ऑफ़ हैदराबाद

032YYNNN1203201111Y20101B05C03N04904P02

CIF NO : 72114609361
Account No : 62247904425
Customer Name: Miss. ANSHRA NOUSHEEN

S/D/W/H/o: M D ZAHEER UDDIN
Address: H-NO-3-2-182 VEERANNAPET

STATE BANK OF INDIA
Clock Tower Br.-20184
Mahabubnagar-509 001.
IFSC Code: SBIN0020184

In MAHABUBNAGAR
Phone:
Email (Provision for Future use)
D.O.B. (If Minor): 27/08/1998

H.O. 2039

State Bank of Hyderabad

MAHABUBNAGAR MAIN BR.
NEAR CLOCK TOWER

Phone: 242351

Email: mbn_sbmbrn@sbhi.co.in

Branch Code: 20184
Date of Issue: 24/09/2012
24/09/2012 401815 20184
IFSC: SBIN0020184

शाखा प्रबंधक
Branch Manager



Ansha
Signature of the applicant

Dr S. Vijiya Laxmi
Signature of the Guide

Dr S. Vijiya Laxmi
Assistant Professor
Department of Chemistry
Palamuru University
Mahabubnagar-509001, T.S.