CURRICULUM VITAE

Dr. MUKTHAPURAM PRATHAP REDDY
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Objective:

Motivated and enthusiastic synthetic chemist, looking for the right position in the field of Medicinal chemistry and Synthetic chemistry, where I can perform my research on effectiveness, efficiency, integrity, and diligence.

Research experiance:

Research Associate: (March 2022 to present) Supervisor: Dr. Amarnath Natarajan, University of Nebraska Medical Center, Omaha, Nebraska, USA.

- Practical and efficient gram-scale synthesis of BTE-EN1: A heterobifunctional anticancer agent.
- Isatin -derived spirocyclic α-methylene-γ-butyrolactams as NFκB pathway inhibitors

Senior scientist II: (January 2019 to November 2021) STA Pharmaceutical Co., Ltd. a WuXi AppTec company**,** Shanghai, China.

- Involved in the Process development for the late-phase API molecules.

Postdoctoral scholar: (September 2016-December 2018) Supervisor: Dr. Ding Ke, Jinan University, Guangzhou, China.

- Design and Synthesis of New Selective Fibroblast Growth Factor Receptor 4 (FGFR4) Inhibitors and FGFR4 degraders.

Doctoral Research Fellow: (April 2010-Feb 2016) Supervisor: Dr. B. Surendar Reddy, CSIR-Central Drug Research Institute, Lucknow, India.

- Involved in the development of new methodologies for organic synthesis.
  - New synthetic strategies to heterocycles such as Oxazoles (using N-Bromo succinimide) pyrazines and quinoxalines (using Molecular Iodine) and Aromatic Carboxylic Acids, Cinnamic acid derivatives (using Aryl/vinyl Ketones via C-C bond cleavage).
- Involved in the development of bioactive cationic excipients.
  - Cationic lipo-benzamides

- Cationic lipid-oxazole Hybrids
- Cationic lipid derivatives of natural product Cordiarimide-A

Highlights:

- ✓ Designing and executing the multi-step synthesis of bioactive molecules and development of new methodologies for organic synthesis
- ✓ Capable of doing both collaborative and independent projects
- ✓ Experienced in milligram to kilogram scale reactions.
- ✓ Acquired with purification techniques such as Flash Chromatography, Column Chromatography, Preparative and thin layer chromatography.
- ✓ Apart from bench work, I am actively involved in literature search and manuscript preparation
- ✓ Well versed with the data interpretation.

Academic credentials:

Postdoctoral scholar (Medicinal Chemistry)

Supervisor: Dr. Ding Ke, Prof. of medicinal chemistry, Dean, School of Pharmacy, Jinan University, Guangzhou, China. (September 2016- December 2018)

Ph.D. (Medicinal & Synthetic Chemistry)

Research Supervisor: Dr. B. Surendar Reddy, Scientist, CSIR-Central Drug Research Institute, Lucknow, India. (April 2010-Februry 2016)

Master of Science (Organic Chemistry)

Sri Krishnadevaraya University, Anantapur, India. (July 2007-March 2009)

Bachelor of Science (Maths, Physics, Chemistry)

Sri Krishnadevaraya University, Anantapur, India. (April 2003- May 2006)

Accomplishments:

2012	Senior Research Fellowship, Council of Scientific and Industrial Research (CSIR), India
2010	Junior Research Fellowship, Council of Scientific and Industrial Research (CSIR), India

Publications & Patents

1	Surendar Reddy Bathula,* **Prathap Reddy M**‡, Deependra K S‡, Komal S‡, Pushpa S, Amit D, Banerjee ‡ Contributed equally.	siRNA delivery using a cationic-lipid-based highly selective human DNA ligase I inhibitor	***ACS Appl. Mater. Interfaces.*, 2018**, *10* (2), 1616–1622
2	Tushar J, **Prathap reddy M**, Komal S, Ravi O, Garima P, Kalyan M, Surendar Reddy B*, Banerjee D*.	Biofilm inhibition and anti-Candida activity of a cationic lipo-benzamide molecule with twin-nonyl chain	***Bioorg. Med. Chem. Lett.*, 2018,** *28* (10), 1776-1780
3	Surendra Reddy Bathula*, Durga Rao K, Komal S, **Prathap Reddy M**, D. Banerjee, D. K. Singh	Cationic lipid derivatives of cordiarimide: A useful as anti cancer agents by targeting Human DNA ligase-I	***US Patent Application* 20170137462**
4	Tushar J, **Prathap reddy M**, Satya P, Komal S, Garima P, Kalyan M, Surendar Reddy B*, Banerjee D*.	Chain-length-specific anti-Candida activity of cationic lipo-oxazoles: a new class of quaternary ammonium compounds.	***J. Med. Microbiol.*, 2017**, *66* (12), 1706-1714
5	Sathyanarayana P, Atul U, Ravi O, **Prathap Reddy M**, Surendar Reddy B*	Iodine-catalyzed oxidative C–C bond cleavage for benzoic acids and benzamides from alkyl aryl ketones	***RSC Adv.*, 2016**, *6*, 22749-22753
6	Sathyanarayana P, Ravi O, **Prathap Reddy M**, Surendar Reddy B*	Copper catalyzed oxygen assisted C-(CNOH)-C (alkyl) bond cleavage: A facile conversion of aryl/vinyl ketones to aromatic acids	***Org. Bio. Mol. Chem.*, 2015** *13* (37), 9681-9685
7	**Prathap Reddy M**,‡ Durga Rao K,‡ Sathyanarayana P, Ravi P, Ruchir Kant, Surendar Reddy B* ‡ contributed equally.	Iodine-mediated oxidative annulation for one-pot synthesis of pyrazines and quinoxalines using a multipathway coupled domino strategy	***Chem. Commun.*, 2014**, *50*, 13517–13520
8	Surendar Reddy B,* **Prathap Reddy M**, Durga Rao K, Sathyanarayana P, Sridhar Reddy M.	Access to Di- and Tri substituted Oxazoles by NBS-Mediated Oxidative Cyclisation of N-Acyl Amino Acid Derivatives	***Eur. J. Org. Chem.*, 2013**, 4552-4557
9	**Prathap Reddy M**, Rishi. K. G, Komal S, Rohit. C, Srinivas. K, Mishra. D. P, Surendar Reddy B*	Anticancer siRNA delivery by new anticancer molecule: A novel combination strategy for cancer cell killing	***Eur. J. Med. Chem.*, 2012**, *56*, 400–408

Conferences and Symposia Participated:

- ✓ Participation and Poster presentation in "**2023 College of Pharmacy Research Day**" held at University of Nebraska Medical Center, Omaha, NE, USA. (May 23rd, 2023).
- ✓ Participation and Poster presentation in "**Cancer Prevention and Control Symposium (CPCS-2023)**" held at University of Nebraska Medical Center, Omaha, NE, USA. (February 17th, 2023).
- ✓ Participated in "**11th International Symposium for Chinese Medicinal Chemists (ISCMC 2018)**" held at Zhengzhou University, Zhenezhou, China. (August 24-26, 2018).
- ✓ Participation and Poster presentation in "**21st ISCB International Conference on Current Trends in Drug Discovery and Developments" (ISCBC-2015)** CSIR-Central Drug Research institute (CSIR-CDRI), Lucknow, India (February 24-28, 2015).
- ✓ Participation and Poster presentation in "**International Conference on Chemical Biology Disease Mechanisms and Therapeutics (ICCB-2014)**" held at CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad, India (February 6-8, 2014).
- ✓ Participated in "**National Seminar on Modern Trends in Analytical Methods of Analysis**" held at Sri Krishnadevaraya University, Anantapur, Andhra Pradesh, India. (December 25-27, 2008).

Service to the Scientific Community:

- ✓ Reviewer for *RSC Advances*, *Bioorg. Med. Chem.*, *Heterocyclic Communications*, *J. Braz. Chem. Soc.*, *SynOpen*, *J. Chem.*

Personal data:

Date of Birth : 05th February, 1985
Nationality/Sex/Marital status: Indian/Male/Married

References:

1. Dr. Amar Natarajan, PhD
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2. 1. Dr. Manish Kumar Chourasia
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3. **Dr. Ke Ding**
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Declaration:

I hereby declare that the information given above is true and I hold the responsibility of its aunthentically.

Place: Banglore, India (MUKTHAPURAM PRATHAPREDDY)

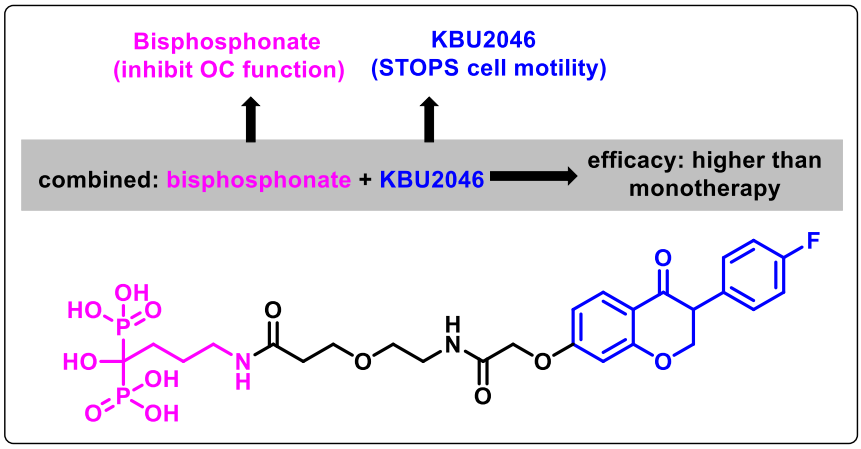
Research Summary:

Currently, I am working as a Postdoctoral research associate under Prof. Amarnath Natarajan, University of Nebraska Medical Center, Omaha, NE, USA where I am responsible for the small molecule inhibitors and scale up of BTE-EN1 for pre-clinical development. Details are given below.

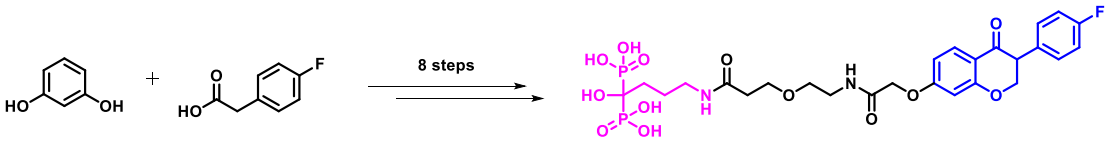
Ia) Practical and efficient gram-scale synthesis of BTE-EN1: A heterobifunctional anticancer agent

3(4-fluorophenyl)chroman-4-one (KBU2046) binds to the interface of HSP90b/CDC37 interface and inhibits osteoclast (OC) mediated bone destruction. Bisphosphonates are the most widely prescribed and used medications for the treatment of osteoporosis. Three oral bisphosphonates (alendronate, risedronate, and ibandronate) are approved by the U.S. Food and Drug Administration (FDA). A heterobifunctional compound generated by conjugating

alendronate (bis) and KBU2046 through a linker yields, Dual-Acting Bone-Defender (DABD) which was more effective than KBU2046 + bis or the individual components. The reported synthesis of a DABD BTE-EN1 required 11 steps and had an overall yield of 0.7%.

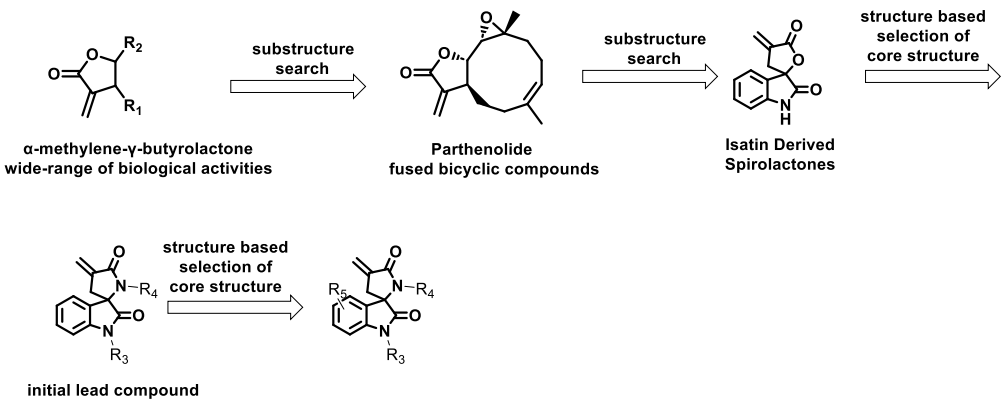


To enable scale up of BTE-EN1 for pre-clinical development, here we optimized the route and the process that resulted in reducing the number of synthetic steps from 11 to 8 and increased the overall yield from 0.7% to 11% (~16-fold increase).



- Reducing synthetic steps from 11 to 8
- Increased the overall yield from 0.7% to 11%

Ib) Isatin -derived spirocyclic α-methylene-γ-butyrolactams as NFκB pathway inhibitors:



Structure-based strategy to design a new class of NF-κB inhibitors.

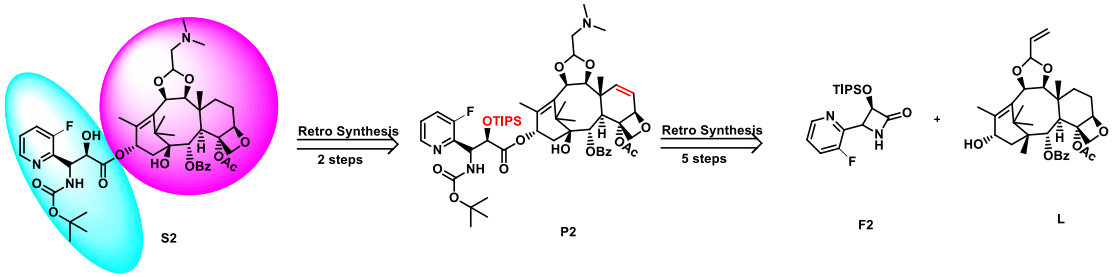
Inhibitor **κ**-B kinase β (IKKβ) is a key enzyme in the canonical NF**κ**B pathway. Constitutive activation (ca) of IKK□ has been observed in various tumors and tissue specific expression of

ca-IKK□ in the presence of oncogenic insults results in aggressive disease. The majority of IKKβ inhibitors reported are ATP competitive inhibitors that reversibly bind IKKβ, with four ATP competitive IKK□ inhibitors entered clinical trials, and none were approved by the FDA. Development of covalent IKKβ inhibitors is an alternate strategy to target IKK□ and the NF□B pathway. We reported an analog with an isatin-derived spirocyclic α-methylene-γ-butyrolactone core which covalently engaged IKKβ. However, the stability of the γ-butyrolactone in the biological matrix was a concern. To address this here we report the synthesis of an isatin-derived spirocyclic α-methylene-γ-butyrolactam library. The library was generated using an aza-Wittig reaction followed by a zinc catalyzed aza-Barbier reaction. The library was then screened for the inhibition of TNF-□ induced IKKβ mediated NF**κ**B activity in a cell-luciferase reporter assay. The hits were counter-screened in cell-based luciferase reporter assays that specifically reported transcriptional activity associated with p53 or AP1. The relevant chemistry, biology and the associated structure activity relationship is reported.

II). Process development in late-phase manufacturing process of the drug candidate.

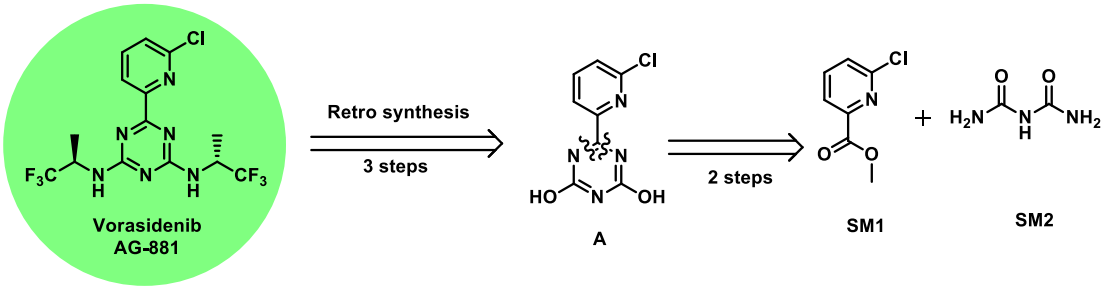
Tesetaxel, an investigational, orally administered chemotherapy agent that belongs to a class of drugs known as taxanes, which are widely used in the treatment of cancer.

I am primarily involved in the process development of last seven (7) steps of this molecule. The structure of Tasetaxel and retro synthesis is shown in the figure below.



Vorasidenib is a promising brain-penetrant dual mIDH1/2 inhibitor under late-stage development for the treatment of low-grade mIDH glioma, and it has shown promising clinical activity in early clinical trials.

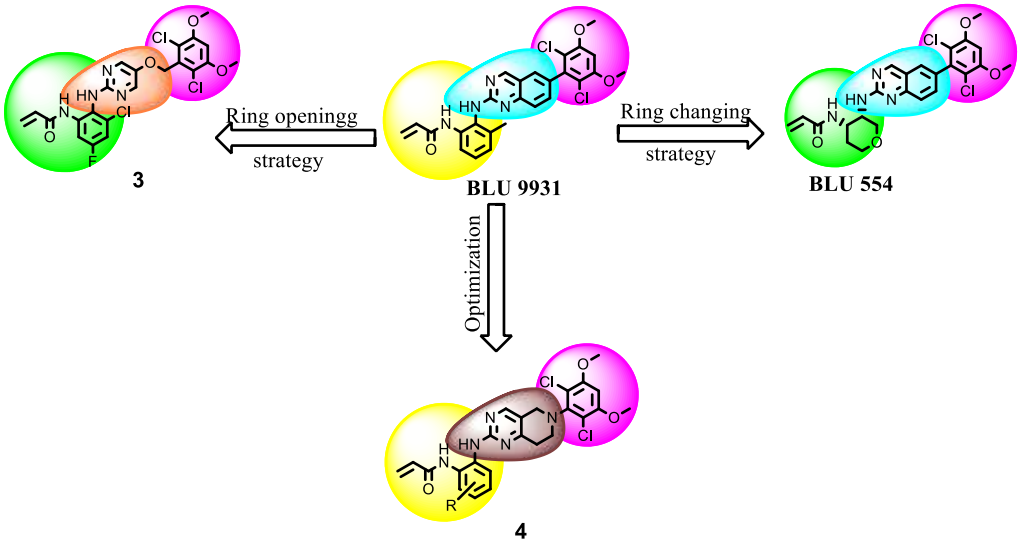
I am primarily involved in the process development of this molecule's 5-step process. The general structure and retro synthesis of this molecule is shown in the figure below.



III). Design and Synthesis of Tetrahydropyrido-pyrimidin-2-amine Derivatives as New Selective Fibroblast Growth Factor Receptor 4 (FGFR4) Inhibitors

A number of small molecule FGFR inhibitors with different selectivity profiles have been developed into clinical investigation for the management of FGFR-driven human cancers. Given the fact that the FGFR family share significant sequence homology in their kinase domains, it is a considerable challenge to develop selective FGFR4 inhibitors over the other family members. Most recently, BLU9931 was discovered as the first selective FGFR4 inhibitor. Most recently, BLU554, a structurally related derivative of inhibitor BLU9931, was advanced into early-stage clinical investigation (clinical trial ID NCT02508467).

Our group also, a series of 2-aminopyrimidine derivatives were designed and synthesized as highly selective FGFR4 inhibitors **3** by using ring opening strategy. The clinical report of the compound is eagerly awaited. Nevertheless, it is still highly valuable to identify new selective FGFR4 inhibitors for anticancer drug discovery. Herein, we describe the design, synthesis and biological evaluation of a series of 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-2-aminederivatives as new selective FGFR4 inhibitors (**4**).

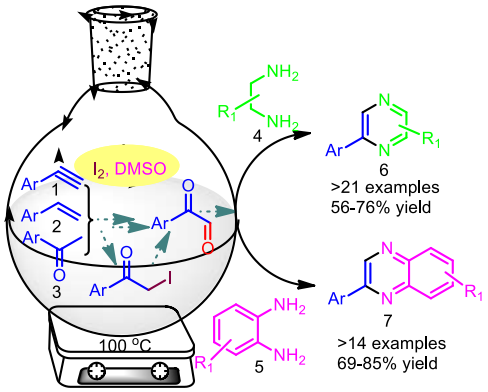


IV). Development of new methodologies and its application towards synthesis of biologically important hybrid molecules

I have played a major role in the development of efficient synthetic approaches for the construction of various biologically significant heterocycles such as oxazoles, pyrazines, quinoxalines and carbocycles like Aromatic Carboxylic Acids, Cinnamic acid derivatives by utilizing commercially available precursors. Through these methodologies, we created numerous diversely functionalized small molecules and few bioactive hybrid molecules, which were screened against various disease areas.

IVa). Iodine-mediated oxidative annulation for one-pot synthesis of pyrazines and quinoxalines using a multipathway coupled domino strategy.

Chem. Commun. 2014, 50, 13517–13520

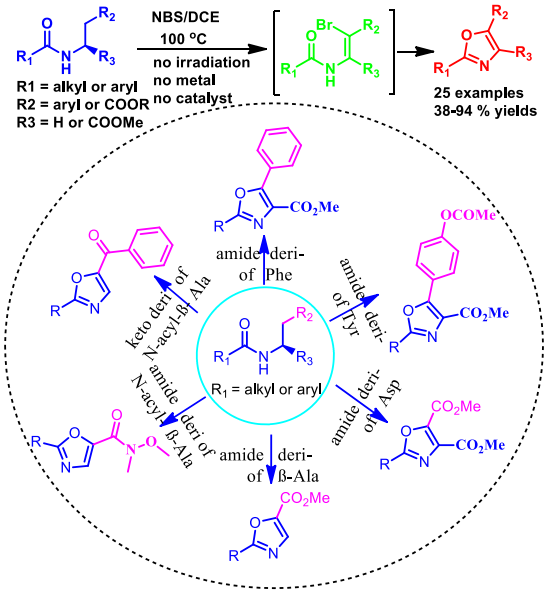


An efficient iodine-mediated oxidative annulation of aryl acetylenes–arylethenes–aromatic ketones with 1,2-diamines for the synthesis of pyrazines and regioselective synthesis of quinoxalines by using multipathway coupled domino.

IVb). Access to Di- and Tri substituted Oxazoles by NBS-Mediated Oxidative Cyclisation of N-Acyl Amino Acid Derivatives.

Eur. J. Org. Chem. 2013, *4552–4557*

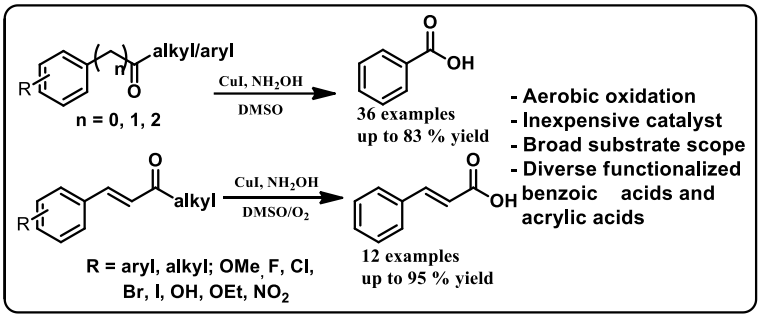
A remarkably simple method for the synthesis of di- and tri-substituted functionalized oxazoles under metal- and catalyst-free conditions is described. An iterative bromination and debromination of N-acylated amino acid derivatives with NBS as the sole reagent cleanly led to various substituted oxazoles.



IVc). Copper Catalyzed Oxygen Assisted C-(CNOH)-C (alkyl) Bond Cleavage: A Facile Conversion of Aryl/vinyl Ketones to Aromatic Acids

***Org. Bio. Mol. Chem.*, 2015*13* (37), 9681-9685**

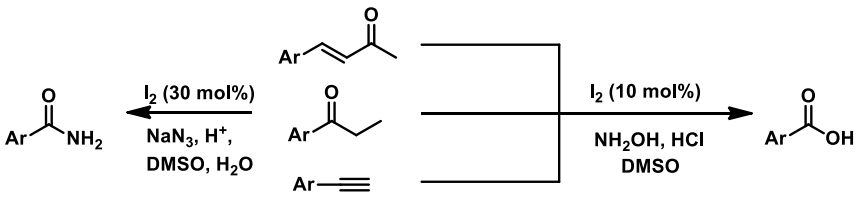
Herein, we reported a simple, eco friendly oxidant; inexpensive catalyst and multipath way method to convert aryl/vinyl alkyl ketones to corresponding acids via unprecedented cleavage of alkyl groups adjacent to keto group is reported.



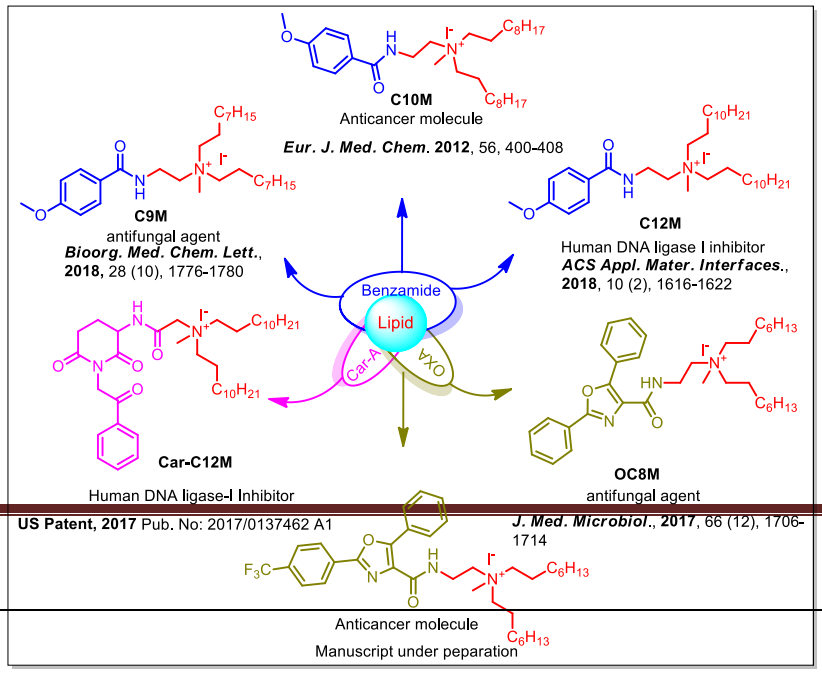
IVd). Iodine-catalyzed oxidative C–C bond cleavage for benzoic acids and benzamides from alkyl aryl ketones

***RSC Adv.*, 2016**, *6*, 22749-22753

Iodine-catalyzed oxidative C–C bond cleavage has been performed for the facile synthesis of both benzoic acids and benzamides from readily available alkyl aryl ketones. Additionally, benzylidene acetones and phenylacetylenes were also converted to the corresponding aromatic acids under the same conditions.



V). Development of bioactive cationic excipients



I have played a major role in the development of bioactive cationic excipients. Based on the initial results, our lab received a grant from EMPOWER project, New Delhi. Under this project with the help of other students in our laboratory, I have actively involved in the synthesis of various bioactive cationic excipients. A representative figure is shown in the figure above.

Va). The molecule with a ten-carbon chain-length (**C10M**) significantly inhibited proliferation of cancer cells via arresting the cell cycle predominantly in the G1 phase. C10M effectively mediated siRNA delivery in vitro. The combined anticancer effect of the delivery of C10M together with its survivin-targeting siRNA cargo was significantly superior to that of agent alone. (***Eur. J. Med. Chem.* 2012,** *56, 400–408)*

Vb). The molecule with a twelve-carbon chain-length (**C12M**) selectively and efficiently inhibited the enzyme activity of hLigI, compared to other human ligases (hLigIII β and hLigIV/XRCC4) and bacterial T4 DNA ligase. Furthermore, upon hydration with equimolar cholesterol, C12M produced antiligase cationic liposomes, which transfected survivin siRNA and showed significant inhibition of tumor growth. ***(ACS Appl. Mater. Interfaces.*, 2018**, *10* (2), 1616–1622)

Vc). The molecule with a nine-carbon chain-length (**C9M**) inhibited growth of both Candida albicans and non-albicans strains and is equally active against pairs of azole sensitive and resistant clinical isolates of C. albicans. Compound C9M also inhibited different stages of Candida biofilms. (***Bioorg. Med. Chem. Lett.*, 2018,** *28* (10), 1776-1780)

Vd). Octyl chain analogue of oxazole showed promising anti-fungal activity. Compound **OC8M** was active against both fluconazole-sensitive and resistant clinical isolates of Candida albicans as well as non-albicans Candida strains. It also inhibited the adhesion of C. albicans cells to a polystyrene surface and restricted biofilm formation. (***J. Med. Microbiol.*, 2017**, *66* (12), 1706-1714)

Ve). The molecule with a twelve-carbon chain-length (**Car-C12M**) significantly inhibited proliferation of PC-3 (prostate cancer), HepG2 (liver cancer), MCF-7 (breast cancer) and

NIH/3T3 (non cancer) cells. Furthermore, the derivative exhibited DNA ligase I inhibition. (***US*** **Patent Application 20170137462)**