CURRICULUM VITAE – RAMESH KARRI

Personal Details

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Academic Chronicle

Aug 2014 to May 2019 : **Ph.D. in Bioinorganic chemistry,**
Shiv Nadar University, India
Title of doctoral dissertation: *Detoxification of Organomercury Compounds: Enzyme Mimetic Studies to Understand the Hg-C Bond Activation by Organomercurial Lyase Enzyme (MerB).*
Name of supervisors: Dr. Gouriprasanna Roy, Associate Professor, IIT-Tirupati, Andhra Pradesh.

Jun 2009 to April 2011 : **Masters of Science (M.Sc.) in Organic Chemistry**
Andhra University, Andhra Pradesh, India
Date awarded: 30th April-**2011**

Aug 2006 to Mar 2009 : **Bachelor of Science (B.Sc.) in Chemistry**
Andhra University, Andhra Pradesh, India
Date awarded: 30th March-**2009**

Professional Experience

Feb 2019 to Dec 2019 : Research Associate, Department of chemistry, Shiv Nadar University (SNU)
Project funded by **CEFIPRA**, **Indo-French** Scientific Collaborative Research Program
Project Title: Metal Chelators derived from imidazole thiones and selones for detoxification
Advisor: Dr. Gouriprasanna Roy (SNU)

Jan 2013 to Aug 2014 : Analyst, Bio-analytical department, **SIPRA LABS. LTD** in Hyderabad, India.
Role: LCMS instrumental analysis of Bio-analytical and food samples.

Awards and Achievements

Jan 2017 : Qualified certificate of **State Level Eligibility Test for Lectureship (SLET-Chemistry)**

Jun 2012 : Qualified certificate of **Graduate Aptitude Test in Engineering (GATE-Chemistry)**

Aug 2014 : Qualified for **PhD Research Fellowship** and **Teaching Assistantship award** from Department of Chemistry, School of Natural Sciences, Shiv Nadar University, India, 2014-2018

Conferences and presentations

Jan 2017 : Invited a poster presentation in 5th International Symposium on "Advanced Biological Inorganic Chemistry (SABIC-2017)", January 7-11, 2017 at Kolkata, organized by the Tata Institute of Fundamental Research (TIFR) and Indian Association for the Cultivation of Science (IACS).

April 2016 : Presented a poster at one day symposium on "Emerging Trends Translational Research in India" 9th April, 2016, Shiv Nadar University, India.

Dec 2015 : Invited a poster presentation in MTIC-XVI Symposium on "Modern Trends in Inorganic Chemistry", Jadavpur University, December 3-5, 2015, West Bengal, India.

Strengths

- Expertise in designing and executing the multi-step synthesis of complex chelating ligands such as **N-heterocyclic carbene (NHC)** based ligands, and also expertise in synthesis of various metal complexes in inert conditions (Shlenkline technique).

- Expertise in performing kinetic studies by spectroscopic techniques (**HPLC, LCMS, NMR, IR and UV**) and skilled in nanomaterial characterization by **TEM, SEM** and **PXRD**. Skilled in crystal growths in various methods and processing as well as structure solution of complex single-crystal X-ray diffraction data having different types of disorder in organic small molecule, organometallic compounds, solvent disorders etc.

- **Computational skills**: Density functional theory (optimization ground state and TS calculations in solution, gas phase, NBO calculations for organometallic reactions).

- Expertise in **cell-culture studies** for metal complexes and ligands (MTT, GSH estimation, antioxidant enzyme activity like GPX, GR and CAT enzyme activity by using micro-plate reader) and Skilled in live-cell imaging studies ROS estimation by fluorescent microscopy.

Research publications

1. Das, R; **Karri, R**.; Chalana, A.; Roy, G.* " Direct Evidence of Neurotoxin Methylmercury Mediated Alkylating DNA Lesions in Living Cells". *Manuscript submitted*.
2. **Karri, R**.; Das, R; Rai. R; Anaswara, G. P.; Roy, G.* " Hg–C Protonolysis by A Functional Model of Bacterial Enzyme Organomercurial Lyase MerB ". *Chem. Comm.*, **2020.** https://doi.org/10.1039/D0CC02232B
3. Chalana, A[#].;**Karri, R**[#].; Roy, G.* "Chemical Degradation of Mercury Alkyls Mediated by Copper Selenide Nanosheets". *Chem. Asian. J.*, **2019**, 14, 4582-4587 (# = equally contributed). https://doi.org/10.1002/asia.201901077
4. **Karri, R**.; Chalana, A.; Binayak. K.; Roy, G.* "Exploiting the κ^2-Fashion Coordination of [Se_2]-donor Ligand L_3Se for Facile Hg–C Bond Cleavage of Mercury Alkyls and Excellent Cytoprotection Against Methylmercury-induced Toxicity". *Chem. Eur. J*., **2019**, 25, 12810-12819 , https://doi.org/10.1002/chem.201902578
5. Rai, R. K.; Chalana, A.; **Karri, R**.; Das, R.; Kumar, B.; Roy, G*. "Role of Hydrogen Bonding by Thiones in Protecting Biomolecules from Copper (I)-Mediated Oxidative Damage". *Inorg. Chem*, **2019**, *58*, 6628–6638.
6. Chalana, A; **Karri, R**.; Das, R.; Kumar, B.; Rai, R, K.; Saxena, H.; Gupta, A.; Banerjee, M.; Jha, K. K.; Roy, G*. "Copper-driven Deselenization: A Strategy for Selective Conversion of Copper Ion to Nanozyme and Its Implication for Copper-related Disorders". *ACS Appl. Mater. Interfaces*, **2019**, *11*, 4766-4776.
7. **Karri, R**.; Chalana, A.; Das, R; Rai,; R. Roy, G.* "Cytoprotective effects of imidazole-based [S_1] and [S_2]-donor ligands against mercury toxicity: a bioinorganic approach". *Metallomics*, **2019**, *11*, 213-225.
8. Mitra, S.; **Karri, R**.; Kumar, P.; Dey, A. B.; Bhattacharya, G.; Roy, G.; Kamil, S. M.; Dhara, S.; Sinha, S. K.; Ghosh, S. K "Re-entrant Direct Hexagonal Phases in a Lyotropic System of Surfactant Induced by an Ionic Liquid ". *Liquid Crystals*, **2019**, *46*, 1327-1339.
9. Das, R.; Banerjee, M.; Rai, R. K.; **Karri, R.**; Roy, G. Metal-free C(sp^2)–H Functionalization of Azoles: K_2CO_3 /I_2 -Mediated Oxidation, Imination, and Amination. *Org. Biomol. Chem*., **2018**, *16*, 4243– 4260.
10. **Karri, R**.; Banerjee, M.; Chalana. A.; Jha, K. K.; Roy, G.* "Activation of the Hg-C Bond of Methylmercury by [S2]-Donor Ligands" *Inorg. Chem*, **2017**, *56*, 12102–12115.
11. Banerjee, M.; **Karri, R**.; Chalana, A; Das, R; Rai, R; Rawat, K.S; Pathak, B; Roy, G.* "Protection of Endogenous Thiols against Methylmercury by Benzimidazole-based Thione via Unusual Ligand Exchange Reactions". *Chem. Eur. J*, **2017**, *23*, 5696-5707. This article is highlighted in "Frontispiece" and selected as "**HOT PAPER**". https://doi.org/10.1002/chem.201605238

12. **Karri, R.**; Banerjee, M.; Rai, R. Roy, G.* "Synthesis and characterization of 1:2 complex of mercury (II) chloride with 1,3-dimethyl-1H-imidazole-2(3H)-thione". *Proc. Natl. Acad. Sci., India, Sect. A Phys. Sci*, **2016,** *86*, 611-617.
13. Banerjee, M.; **Karri, R**.; Rawat, K. S.; Muthuvel, K.; Pathak, B.; Roy, G.* "Chemical Detoxification of Organomercurials". *Angew. Chem. Int. Ed.*, **2015**, *54*, 9323-9327. https://doi.org/10.1002/ange.201504413

Patent

Oct 2017 : Gouriprasanna Roy (Principal Investigator), Mainak Banerjee (Ph.D. Student), **Ramesh Karri** (Ph.D. Student), Ashish Chalana (Ph.D. Student) and Ranajit Das (Ph.D. Student). DERIVATIVES OF IMIDAZOLE AND BENZIMIDAZOLE, METHOD OF PREPARATION AND USE THEREOF.
International Patent Number: WO 2017/168451 A1

May 2020 : Gouriprasanna Roy (Principal Investigator), **Ramesh Karri** (Ph.D. Student), Ranajit Das (Ph.D. Student) and Rakesh Kumar Rai (Ph.D. Student). DERIVATIVES OF IMIDAZOLE AND BENZIMIDAZOLE BASED THIONES AND SELONES AND THE METHOD OF PREPARATION THEREOF.
Patent Filed Number: 202011019228

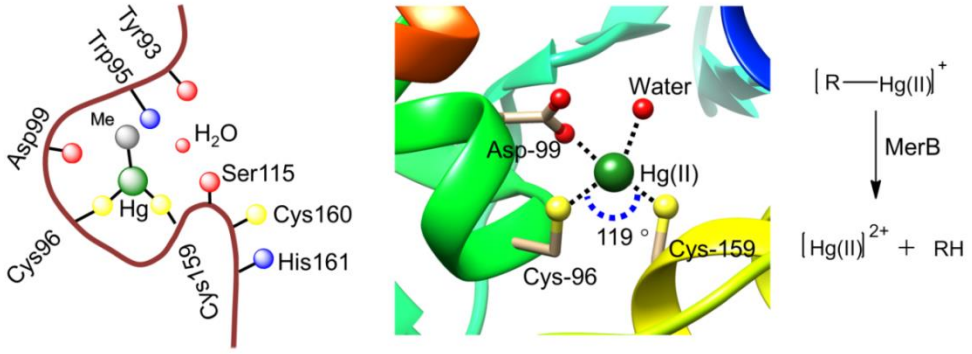
Book Chapter

April 2017: Banerjee, M.; **Karri, R**.; Muthuvel, K, Chalana, A.; Roy, G. "Detoxification of Mercury: Bioremediation to Chemical Degradation, in Handbook of Metal-Microbe Interactions and Bioremediation: Published by Taylor & Francis, Ed: Das, S. and Dash, H. R.; **2017**, 779-792.

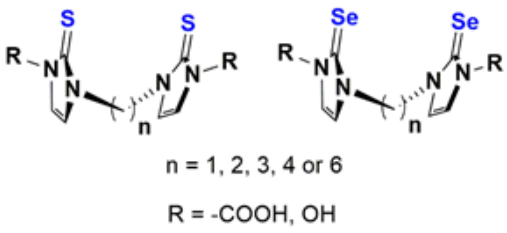
Research summary of doctoral work

My doctoral research work describes the "**Detoxification of Organomercury Compounds: Enzyme Mimetic Studies to Understand the Hg–C Bond Activation by Organomercurial Lyase Enzyme (*MerB*)**". The main objective of this study is to understand the activation of Hg–C bonds by organomercurial lyase enzyme through mimic the active site of an enzyme. Methylmercury ($MeHg^+$) is a ubiquitous environmental pollutant that accumulates at high levels in fish, seafood and rice grains. Thus, the consumption of these contaminated foodstuffs poses a serious health threat to humans and animals. Bacteria are resistant to methylmercury carry *mer* operon that codes for two important Mer enzymes (along with other *Mer* enzymes), namely organomercurial lyase (*MerB*) and mercurial reductase (MerA). The active site of *MerB* consists of a catalytic triad of two cysteines (Cys) residues and one either aspartic acid (Asp) or serine

(Ser) residue. The two Cys residues present at the active site of *MerB* play crucial role in binding the substrate RHg^{+} (R = alkyl, aryl) and facilitates the cleavage of the otherwise inert Hg–C bonds of RHg^{+} to form RH and Hg^{2+} , which is subsequently transferred to another enzyme MerA where it further reduces to volatile Hg^{0}. Whereas the carboxyl group (-COOH) of Asp residue present in the active site of *MerB* donates the proton required for the proteolytic cleavage of R-Hg^{+} bond to form RH.



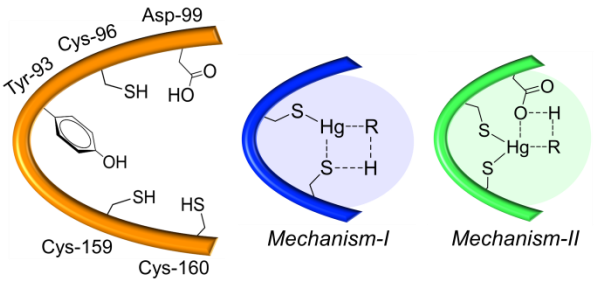
The main goal of my thesis work to develop rich chemistry between organomercurial compounds various [S_2]- or [Se_2]-donor ligands that, somewhat, structurally mimic the active site of organomercurial lyases and cleave the highly inert Hg–C bonds. For this, I have synthesized varieties of imidazole and benzimidazole- based [S_2]- or [Se_2]-donor ligands with various substitution at the nitrogen center of the 5- membered heterocyclic ring and the different spacer length in between the two imidazole or benzimidazole rings and studies their demethylation activity of MeHgX at various reaction conditions. The aim of objective was approached by four parts. Firstly, we understand the coordination behavior of various inorganic mercury salts with imidazole based [S_1]- or [S_2]-donor ligands and their cytotoxicity as well as protective role against $HgCl_2$ induced toxicity in HepG2 cells (***Proc. Natl. Acad. Sci., India, Sect. A Phys. Sci*, 2016,** 86, 611-617 and ***Metallomics*, 2019**,11, 213-225).



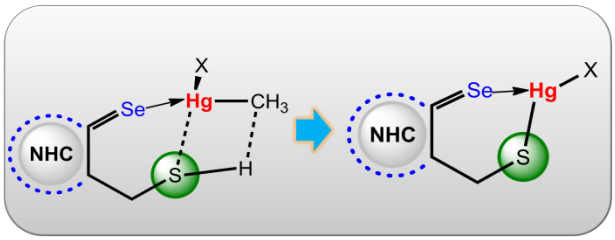
- ***Coordination behavior of [S_1]- or [S_2]-donor ligands***
- ***Activation of Hg-C bonds by [S_2]- or [Se_2]-donor ligands***
- ***Role of spacer length of bis-chalcogenes on Hg-C bond activation and biological significance***
- ***Functional mimic of MerB: Role of substitutional group on cleavage of Hg-C bonds.***

In next step, we studied about the activation of Hg–C bond of various organomercurials by [S_2]-donor ligands and we investigated and identified the novel pathway of dealkylation process by performed extensive kinetic studies by multinuclear NMR (^{1}H, ^{13}C, ^{199}Hg and ^{77}Se) whereas HRMS-QTOF (particularly MS/MS) and SXRD were helpful to identify the intermediates as well as the end products (***Inorg. Chem,* 2017**, 56, 12102–12115, ***Chem. Eur. J,* 2017**, 23, 5696-5707). After conclusion of necessity of two thione based ligands for activation of Hg–C bonds we have checked the demethylation of MeHgCl, the dominant chemical form of $MeHg^{+}$ in marine systems, is extremely slow, even in photochemical process, compared to other $MeHg^{+}$ species that are attached to the strong electron-donating ligands such as I^{-} or GSH. In the third part of my thesis work, we introduced the strong donating ligands such as [Se_2]-donor ligands against MeHgCl and achieved demethylation process almost 35 times faster than the [S_2]-donor ligands. Moreover, the activation of Hg–C bond can depend on mode of coordination such as ***k*^{2}-coordination** as well as softness of ligands which was identified by the tuning the alkyl spacer length between the [S_2]- or [Se_2]-donor ligands. Further, these results were well supported through performed DFT calculation (optimization, NAO analysis) to elucidate the reaction mechanism and to compare reactivity of various ligands **(*Chem. Eur. J,* 2019).**

The last part of my thesis dissertation concluded with three distinct pathway of detoxification process such as chelation, mercury mineralization (***Angew. Chem. Int. Ed.,* 2015**, 54, 9323-9327) and protonation of Hg–C bonds. In this part, the protolytic cleavage was



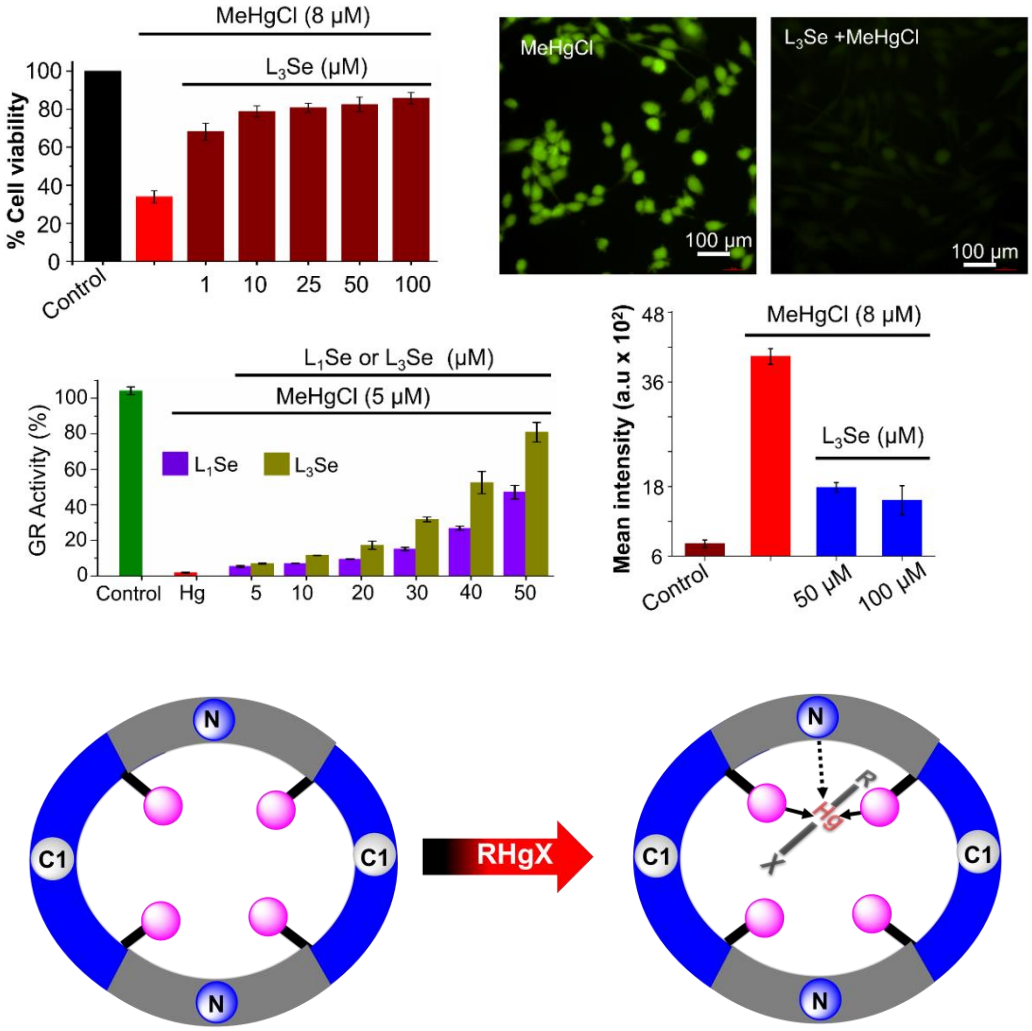
MerB-Active Site and praposed mechanisms

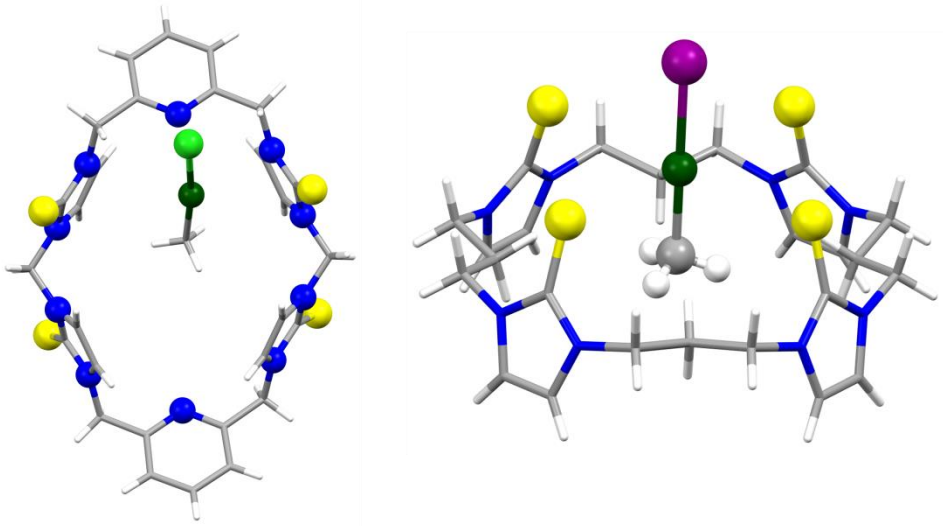


Synthetic functional mimic mechanism

obtained by utilizing various functional group tales as substituents on [S_2]- or [Se_2]-donor ligands. First time a synthetic molecule named as *MerB1*, which showed a unique ability to detoxify a wide variety of organomercurials (RHg^{+}) including $MeHg^{+}$ via Hg–C protonolysis in the absence of any exogenous thiol at room temperature and, thus, acts as a functional model of *MerB*. Negatively charged Se atom of *MerB1* activates the Hg–C bond of RHg^{+} and the –SH group, located close to the RHg^{+} group, simultaneously attack to the Hg center and directly

transfers acidic proton to the activated R group to produce hydrocarbon RH and Hg^{2+} complex (*J. Am. Chem. Soc.* **2019**, *Manuscript under review).* In final part of my thesis, we have shown the *in vitro* studies of the effective compounds to understand the **cytoprotective role** of [S_2]- or [Se_2]-donor ligands against MeHgCl induced toxicity in liver cells by estimating the protective role (*MTT assay*), Inhibition of the ROS production and enhancement of antioxidant enzyme activities.





A part from my thesis work, for the first time, we have developed a imidazole based homoleptic and heteroleptic macrocyclic thiones [S_4] and selones [Se_4] ligands and we exploring the coordination of heavy metals especially organomercurial compounds. In fact, we have succeed to trap the toxic organomercurials by utilizing macrocyclic [S_4] & [Se_4] donor ligands via non-covalent interactions (Unpublished work). However, the synthetic strategy of this study was inspired by couple of research groups (Prof. Paul D. Beer, Prof. Alexander Pothig, Prof. John A. Murphy and Prof. F. Ekkehardt Hahn) specially working on macrocyclic anion receptors as well as metal hosts.