Bhaskar Reddy Manda, PhD

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RESEARCH HIGHLIGHTS

- Regio selective synthesis of unusual Tröger's base analogues under Vilsmeier–Haack conditions. Further cytotoxic evaluation of these molecules led to identification of seven compounds possess cytotoxicity against human breast cancer cell line (MDAMB-231).
- Synthesis of two flexible Tröger's base ditopic molecular receptors C4TB and C5TB incorporating monoaza crown ether for bisammonium ion complexation.
- Developed CuI-catalyzed amination method for the synthesis of symmetrical & unsymmetrical Tröger's base derivatives.
- Synthesis of new α-amino phosphonate Tröger's base derivatives.
- Synthesis and Antitubercular evaluation of Cardanol and Glycerol-based lipophilic β-amino alcohol derivatives.
- Synthesized of potential fluorescent biodiesel markers based on cardanol and glycerol.

PROFESSIONAL SYNOPSIS

- A well experienced professional with 12+ years of experience in research & development (Industrial 5.5 years and academics 6.9 years).
- Planning and execution of chemistry activities on daily and weekly basis.
- Expertise in handling of databases like Sci-finder/Reaxys for literature searches.
- Expertise in chemistry related software's like Chem Draw/Chem Office, ISIS Draw, Windows, Microsoft office etc.
- Characterization and spectral analysis of complex organic compounds using 1D (^{1}H, ^{13}C, DEPT) and 2D NMR (HMBC, HMQC, COSY, NOESY), FTIR and MASS spectra.

ACADEMICS

Post-Doctoral fellowship in Organic chemistry from Federal University of Mato Grosso do Sul, Campo Grande, Brazil-Apr 2015 to Mar 2016 (**Supervisor**: Prof. Adilson Beatriz; **Research Topic**: Design, synthesis and biological evaluation of Cardanol derivatives.

Post-Doctoral fellowship in Organic chemistry from University of Sao Paulo, Sao Paulo, Brazil-Apr 2016 to Dec 2016 (**Supervisor**: Prof. Iolanda Cuccovia) **Research Topic**: Micellar effects of *N,N,N*-trimethyl-*N*-hexadecylammonium chloride on aromatic nucleophilic substitution by Cysteine derivatives.

Ph.D. in Synthetic Organic Chemistry from CSIR-Indian Institute of Chemical Technology, Hyderabad, India -Jul 2009 to Jun 2014 (**Supervisor**: Dr. Alla Manjula; **Research Topic**: Tröger's base as a versatile synthon: Design, synthesis of novel Tröger's base analogues and their applications in medicinal and supramolecular chemistry).

Masters of Science (Organic Chemistry); 2006-2008; from Kakatiya University, Warangal, Telangana; Secured 71%: 1st class.

Bachelor of Science (Chemistry); 2003-2006, from Osmania University, Hyderabad, Telangana; Secured 87%: 1st class.

CORE COMPETENCIES

- Effectively managing FTE projects for timely delivery while handling a multi-level team of chemistry professionals
- Guide the chemist on the bench in solving various synthesis bottlenecks to complete the work plan on promised timelines
- In case of repeated failures or complex chemistry personally undertake and demonstrate
- Identifying, collecting, processing, analysing and cataloguing data, according to the established protocol, procedures & standards, as appropriate to specific objectives of the research study
- Implement GLPs, laboratory notebook writing & documentation as per SOP and safety compliance
- Mentoring and motivating the team for efficient productivity
- Ensure timely submission of weekly reports, active participation in the teleconferences with client
- Vast experience in synthesis, isolation & purification of organic compounds by a wide range of modern synthetic organic chemistry methods and their characterization using spectroscopic techniques [FT-IR, NMR, LC-MS, and HPLC]
- Handling multi step organic synthesis in pharmaceutical company (Scale-up from 0.05g to 500g) and separation of organic compounds by chromatographic methods
- Entering data into appropriate database, performing routine basic manipulation, analysis & interpretation of data
- Planning and organising day-to-day on-site research activities and resolving procedural and logistical problems as appropriate to the timely completion of research objectives
- Setting up, calibrating, operating and maintaining a variety of laboratory research equipment as specified by the requirements of the research study

- Conducting literature survey to understand & execute synthesis of organic compounds; contributing to the publication and/or presentation of results. Taking initiative to drive quality within the organization to achieve the global standards

PROFESSIONAL EXPERIENCE

June' 21-till date **Research Scientist with Sai Life Sciences Ltd., Hyderabad**

- To handle 6-8 FTE (20 FTE program) and actively involved in the schematic representation of target compounds (Expected delivery: ~15 mg)
- Preparation of quotations and proposals. Actively involved in purchase & sourcing decisions pertaining to project raw materials
- Project execution support, as required. Scale-up the reactions, suitable reagents, wok up conditions, analysis of the results, logical and quick solutions as part of trouble shooting and co-ordination with CFTs like stores, engineering & SCM etc.
- Laboratory Maintenance: Assigning responsibilities to chemists for good maintenance of chemist cabin (no structures outside, LNBs are properly arranged etc.,) glassware breakage record and monthly review and chemical inventory file and quarterly review.
- Responsible for timely communication towards project progress with clients in form of weekly TC on current chemistry

Oct' 18-May'21 **Associate Scientist with GVK Bio Sciences Ltd., Hyderabad**

- Manage 3-4 chemists.
- Preparation of quotations and proposals. Actively involved in purchase & sourcing decisions pertaining to project raw materials
- Responsible for carrying out literature search using various scientific data bases such as Sci-Finder and Reaxys, and design synthetic schemes to prepare target molecules. Identify customer requirements from the inquiries shared.
- Worked on the bench while coordinating with team members in the lab.
- Synthesis, purification, and identification of chemical intermediates and target compounds on milligram-to-gram scale.
- Working independently on research projects as assigned, in addition to implement independent thinking and judgment in the absence of established protocols and procedures.
- Maintain lab records and also knowledge sharing, training to trainees.
- Generated weekly reports and data cards as per the client requirements.
- To ensure the quality standards of samples before shipping them to the clients.
- Contributed for overall success of the project by performing all other duties as assigned.
- Keeping up to date with relevant scientific and technical developments.

Jan' 17-Sep'18 **Co-Founder & Managing Director with Manda Laboratories, Hyderabad**

- Maintain all the company protocols and had interaction with various departments to get permission for company.
- Established Start-up Company and active participation in company related documentation.
- Day-to-day meetings with clients to get projects on PO basis. Communication: Weekly updates at TCs, email, responses within 24 h, discuss synthetic challenges, plans for targets, bi-products observed.
- Worked for few China and Canada clients on PO projects.
- To handle 4 chemists and 1 PhD chemist.
- Preparation of quotations and proposals. Responsible for carrying out literature search using various scientific data bases such as Sci-Finder and Reaxys, and design synthetic schemes to prepare target molecules. Identify customer requirements from the inquiries shared.
- Actively involved in purchase & sourcing decisions pertaining to project raw materials
- Handled various PO projects from 5mg to 25kg scale. Experience in handling reactions at pilot scale level and handled 100L to 500L reactors.
- Worked on the bench while coordinating with team members in the lab. Synthesis, purification, and identification of chemical intermediates and target compounds on milligram-to-gram scale. Expertise in reaction optimization, Process R&D and technology transfer of various projects.
- Maintain the quality and timelines for product delivery.

Sep' 14-Mar'15 **Senior Research Associate with GVK Biosciences, Hyderabad**

- Synthesis, purification, and identification of chemical intermediates and target compounds on milligram-to-gram scale.
- Working independently on research projects as assigned, in addition to implement independent thinking and judgment in the absence of established protocols and procedures.
- Maintain lab records and also knowledge sharing, training to trainees.
- Generated weekly reports and data cards as per the client requirements.
- To ensure the quality standards of samples before shipping them to the clients.
- Contributed for overall success of the project by performing all other duties as assigned.
- Keeping up to date with relevant scientific and technical developments.

HONORS & AWARDS

- Qualified all India GATE-2009 with 97.8 percentile (All India 129th Rank) – **2008**.
- Qualified Joint CSIR and UGC-NET conducted by C S I R (Govt. of India) – **2007 & 2008**.
- Qualified BARC qualification exam for Technical Assistant post – **2008.**
- Junior Research Fellowship Awarded by Council of Scientific and Industrial Research (CSIR), India, **2009-2011.**
- Senior Research Fellowship Awarded by Council of Scientific and Industrial Research (CSIR), India, **2011-2014.**
- PNPD-CAPES postdoctoral fellowship from CNPQ, Govt. of Brazil – **2015**.
- FAPESP postdoctoral fellowship from FAPESP, Govt. of Brazil – **2016**.

PUBLICATIONS

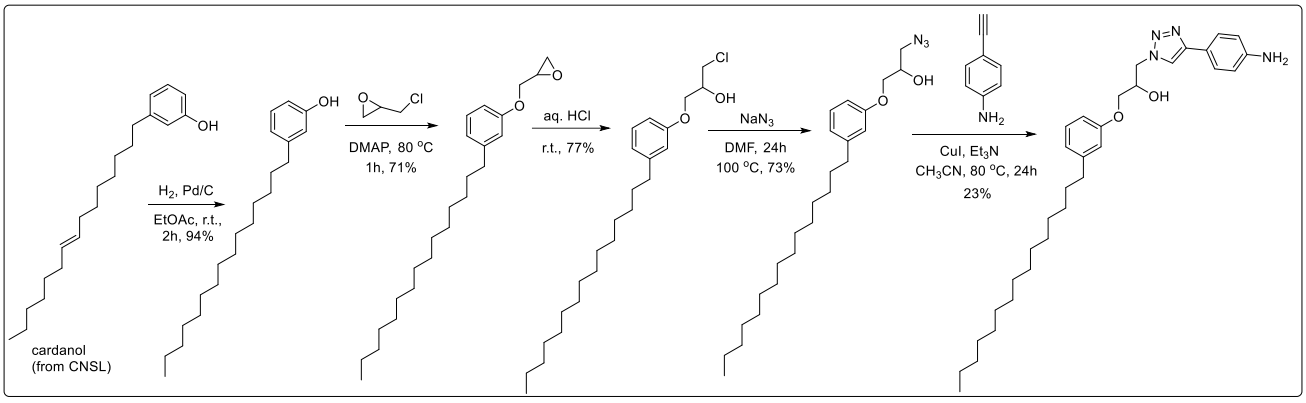
- Regioselective Synthesis of Dimethylamino- or Arylalkylamino- Crowned Troger's Base Analogues under Vilsmeier-Haack Conditions. **M. Bhaskar Reddy**, A. Manjula, B. Vittal Rao, B. Sridhar. Eur. J. Org. Chem. **2012**, 312-319.
- Discovery of Troger's Base Analogues as Selective Inhibitors against Human Breast Cancer Cell Line: Design, Synthesis and Cytotoxic Evaluation. **M. Bhaskar Reddy**, A. Manjula, G. Roopa Jones, A. Anthony. Eur. J. Med. Chem. **2014,** 39-47.
- Design and Synthesis of Troger's Base Ditopic Receptors: Host-Guest Interactions, a Combined Theoretical and Experimental Study. **M. Bhaskar Reddy**, M. Shailaja, A. Manjula, G. Narahari Sastry, K. Sirisha, and A. V. S. Sharma. Org. Biomol. Chem. **2015**, 13, 1141.
- CuI-catalyzed amination of Troger's base halides: a convenient method for synthesis of unsymmetrical Troger's bases. **M. Bhaskar Reddy**, P. Gal Reddy, A. Manjula. RSC Advances **2016**, 6, 98297.
- Synthesis of Troger's base bis(α-Aminophosphonates). **M. Bhaskar Reddy**, P. Gal Reddy, A. Manjula. Arkivoc **2016** (iv), 246-260.
- Insights for Diastereoselective Synthesis of Cyclic α-Sulfinyl and Sulfanyl Oximes. **M. Bhaskar Reddy**, Roberto Gomes, D. R. Paiva, Adilson Beatriz. Tetrahedron Letters, 58, ***2017***, 2240-2243.
- Synthesis, Antibacterial and Antitubercular Evaluation of Cardanol and Glycerol-Based Lipophilic β-Amino Alcohol Derivatives. **M. Bhaskar Reddy**, Prasad A N, Narendar R T, Lacerda Jr V, Barbosa L R, Santos H, Romao W, Pavan F R, Ribeiro C M, dos Santos E A, Marques M R, de Lima D P, Micheletti A C, Beatriz A. J. Braz. Chem. Soc, **2017**, 29, 639-648.

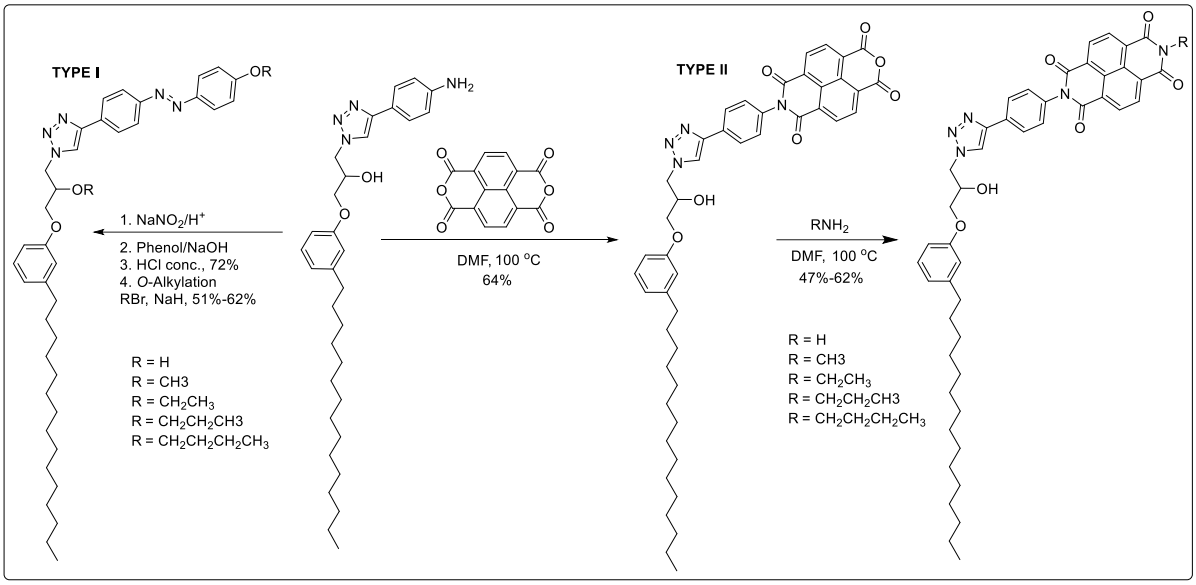
Research Summary

Postdoctoral Work:

Scheme 1:

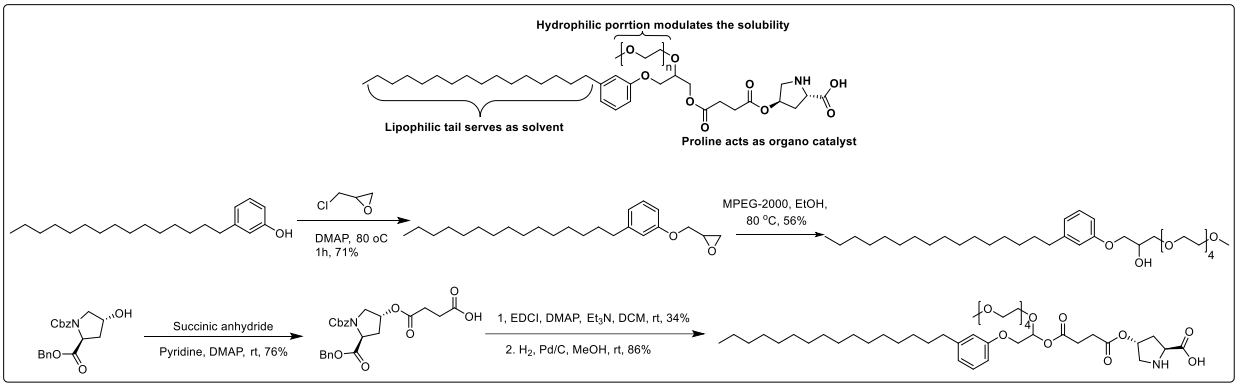
The cashew plant is the source of a wide variety of bioactive compounds consisting of phenolic lipids, mainly present in the spongy shells of cashew nuts. The liquid in the cashew nut shell generated after nut roasting in the food industry, which is usually treated as waste. However, it contains high amount of cardanol that could be used as a building block and are of innumerable applications. We provide an alternative to use cardanol and glycerol as building blocks to produce amphiphilic molecules. The meta-triazolaniline presented a high fluorescent signal at low concentration (4 ppm), revealing to be the best candidate for a fuel marker. The amphyphylic triazoanilines synthesized from cardanol and glycerol, have photo-physical properties which allow their use in the development of fluorescent biomarkers with applicability in the biodiesel quality control.





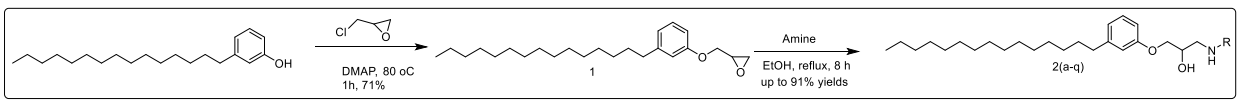
Scheme 2:

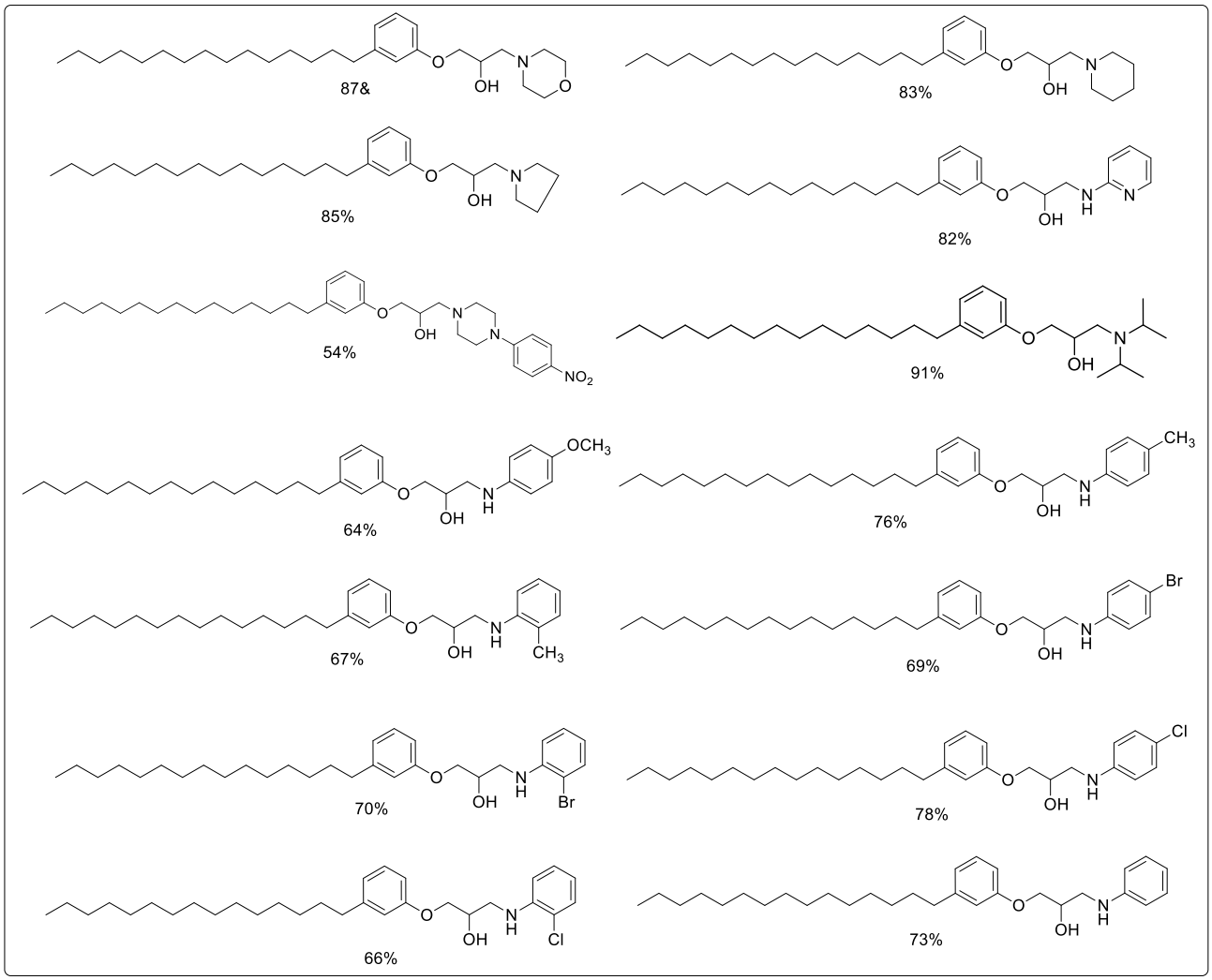
Micellar catalysis provides a means for synthesizing novel and conventional materials in aqueous media, resulting in improved reaction rates and eliminating the need for organic solvents. Here, we attempted the synthesis of a catalyst derived from Cardanol and glycerol which is having a lipophilic tail serves as solvent for organic substrates; hydrophilic part modulates the solubility in aqueous medium, and proline unit introduced as well for organo catalysis. The target molecule synthesis achieved successfully in good yield over 5 steps. However, further use of the obtained molecule was not pursued.



Scheme 3:

Herein, we report the synthesis of novel amino alcohol derivatives based on cardanol and glycerol were achieved in good yields. In addition, we evaluated the in vitro antimicrobial activity against Gram-positive (Staphylococcus aureus, standard and clinical strains), Gram-negative (Escherichia coli) and M. tuberculosis bacterial strains. The bioassay results indicated that four compounds showed activity against S. aureus, including the clinical resistant strain, with MIC (minimum inhibitory concentration) ranging from 3.90 to 15.60 µg mL-1 and M. tuberculosis, with MIC90 (minimum inhibitory concentration required to inhibit the growth of 90% of organisms) ranging from 3.18 to 7.36 µg mL-1.

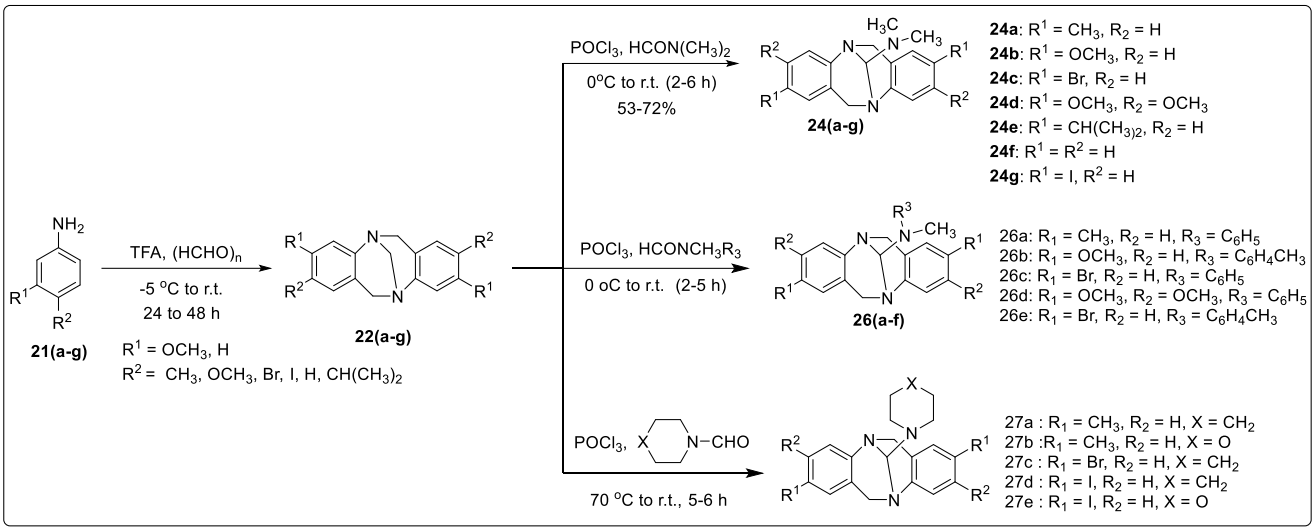




Doctoral Work:

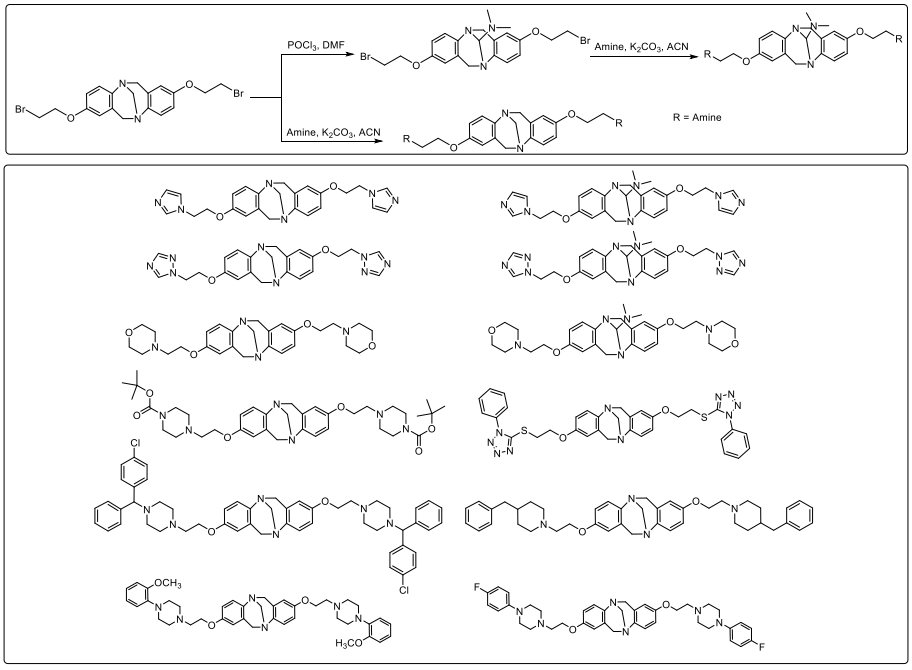
Scheme I:

A library of structurally diverse Tröger's base analogues has been constructed via unusual amination of methylene bridge employing Vilsmeier-Haack conditions as well as by the incorporation of five and six membered heterocycles on the aromatic core of Tröger's base framework. The constructed structurally diverse frameworks were evaluated for their cytotoxic activities against a panel of three human cancer lines A549 (lung adenocarcinoma), MDAMB-231 (breast) and SK-N-SH (neuroblastoma). From the activity profile obtained, a redesign of Tröger's base analogues led to the construction of more potent molecular entities. The study led to development of a series of compounds with MDAMB-231 cell line specific cytotoxicity. Of the 30 compounds synthesized and evaluated, 7 compounds were found to possess cytotoxicity that is equivalent or better than standard drug doxorubicin against MDAMB-231 cell line while only one compound was found to be active against SK-N-SH cell line. Improved and promising anticancer activity of the synthesized Tröger's base compounds provides the basis for further exploration of these molecules as therapeutics, specifically against breast cancer.



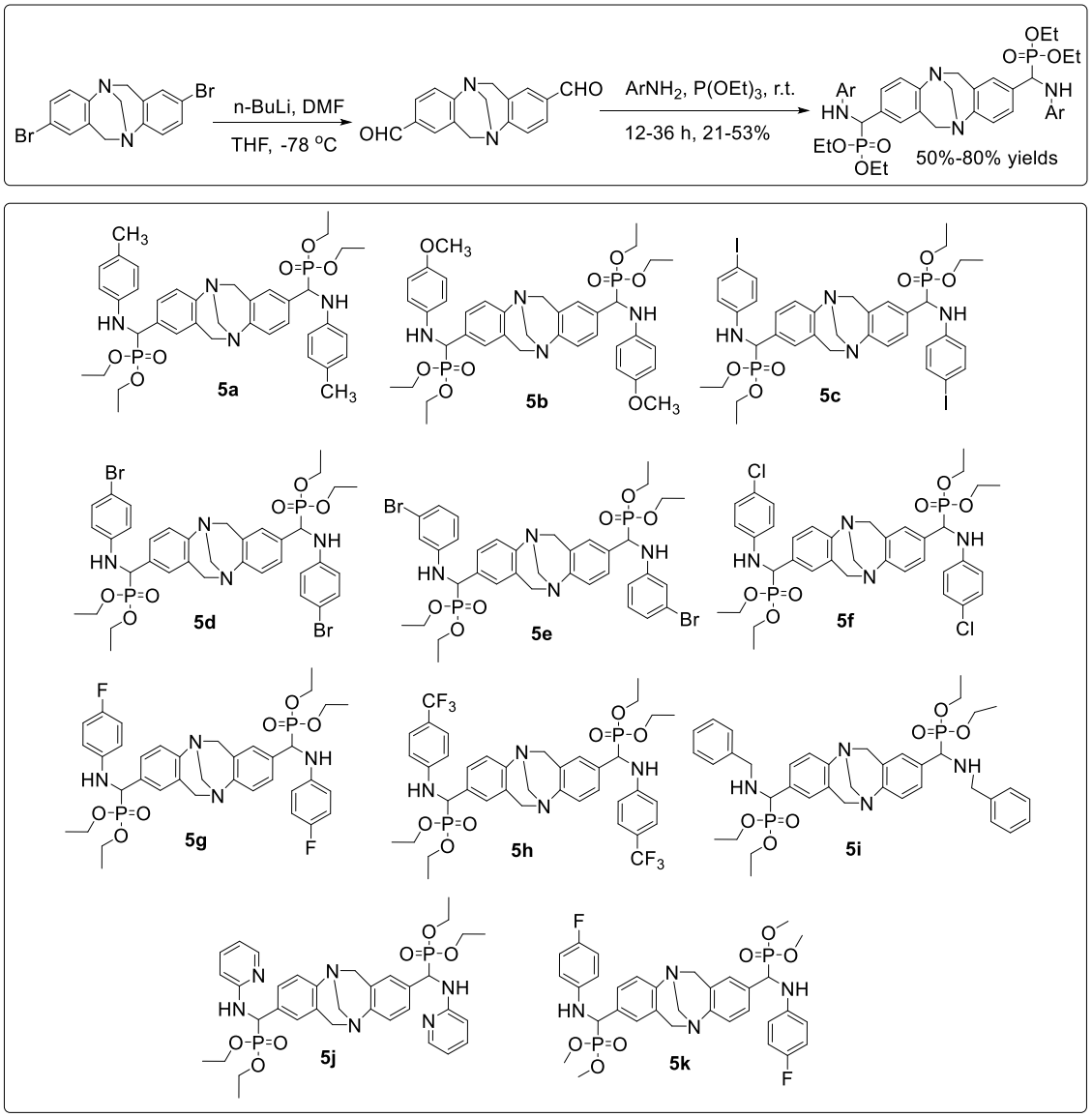
Scheme II:

Several redesigned compounds synthesized in the second phase (shown in below scheme) were effective inhibitors against MDAMB-231 cell line and better than doxorubicin. Improved and promising anticancer activity of the synthesized Tröger's base compounds provides the basis for further exploration of these molecules as therapeutics, specifically against breast cancer.



Scheme III:

A straightforward and efficient introduction of α-aminophosphonate moiety on Tröger's base is described for the first time. A series of novel Tröger's base bis(α-aminophosphonates) were synthesized by using Tröger's base dialdehyde as a versatile synthon. In a multicomponent one pot Kabachnik-Fields protocol, Tröger's base dialdehyde, substituted anilines and triethyl phosphite were reacted under solvent and catalyst free conditions. However, this method has limitations such as longer reaction times and low yields. Employing Pudovik method, phosphonates were synthesized in high yields and shorter reaction times from corresponding imines in the presence of TMSCl. The Pudovik approach provides a convenient method for the synthesis of Tröger's base bis(α-aminophosphonates) when compared to Kabachnik-Fields protocol.

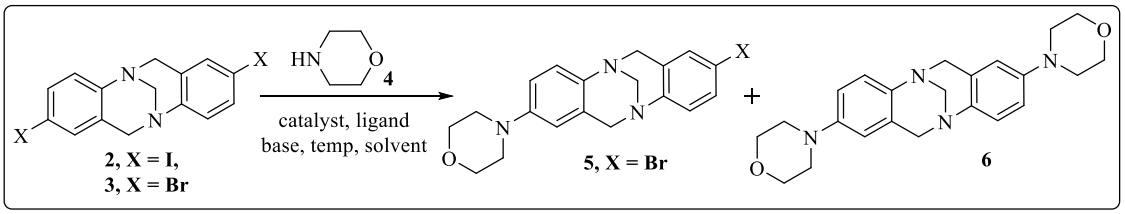


Scheme IV:

A convenient method for the amination of Troger's base halides has been developed via copper catalysed coupling reactions. This reaction proceeds in moderate to good yields. The protocol has been utilized to produce two different classes of Troger's base derivatives, one bearing identical substituents on both the aryl rings and the other featuring two different substituents on the aryl rings.

Tröger's base dihalides (bromo/iodo) were prepared by the condensation of corresponding anilines with paraformaldehyde in presence of TFA. At the outset, the amination of 2,8-dibromo-6,12-dihydro-5,11-methanodibenzo[b,f][1,5]diazocine with morpholine was chosen as a model reaction to screen the various reaction parameters. The screening has been performed in the presence of CuI (20 mol%), proline (40 mol%) and K_2CO_3 (3 eq) in DMSO at 90 °C under nitrogen atmosphere. As anticipated, unsymmetrical and symmetrical trogers base compounds were isolated and identified by 1HNMR and LCMS. Using this protocol, several symmetrical and unsymmetrical trogers base analogues were synthesised. This method could be useful for further diversification of Tröger's base dihalide employing various amine derivatives. Total 12 analogues synthesised.

Table 1: Optimization reaction conditions for the amination of Tröger's base dihalide with morpholine.

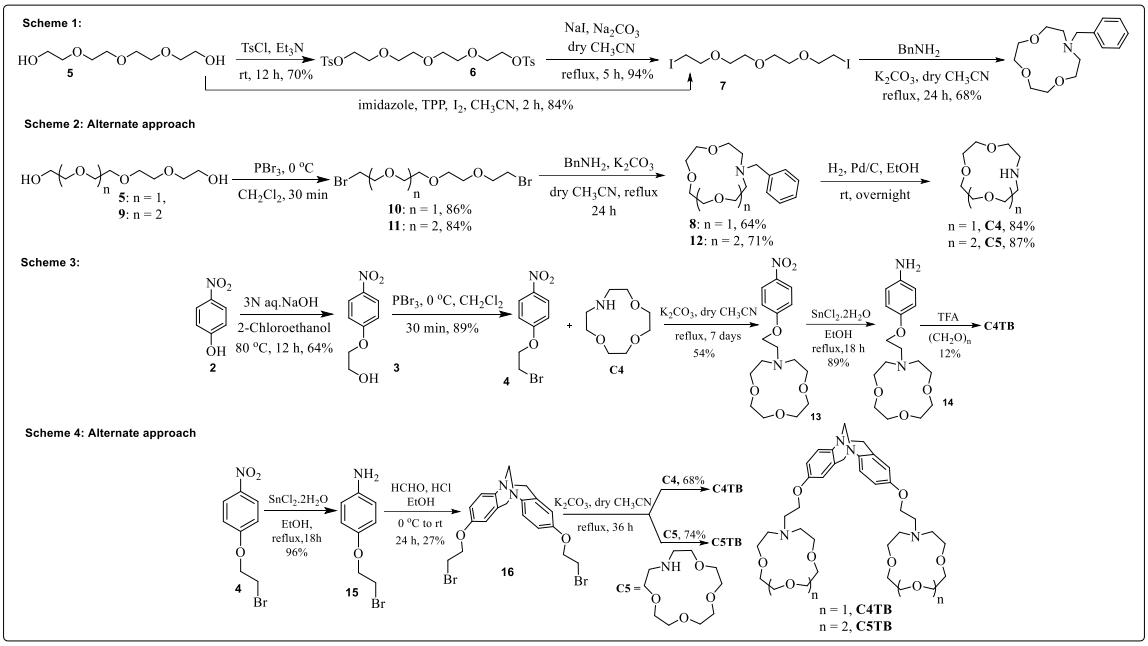


Entry	X	Catalyst	Ligand	Base	Temp (°C)	Solvent	Time (h)	Yield % (**5/6**)[a]
1	Br	CuI	Proline	K_2CO_3	90	DMSO	24	18/34[b]
2	Br	CuI	Proline	K_2CO_3	90	DMSO	40	13/35[b]
3	Br	CuI	Proline	K_2CO_3	120	DMSO	12	trace/68[b]
4	Br	CuI	Proline	K_2CO_3	25	DMSO	24	NR
5	I	CuI	Proline	K_2CO_3	120	DMSO	8	trace/71[b]
6	I	CuI	Proline	K_2CO_3	120	DMF	24	11/-[c]
7	Br	CuI	Proline	K_2CO_3	82	CH_3CN	24	7/-[c]
8	Br	CuI	Proline	K_2CO_3	120	Toluene	24	NR
9	Br	CuI	Proline	K_2CO_3	120	HMPA	36	NR
10	Br	CuBr	Proline	K_2CO_3	120	DMSO	24	12/14[d]
11	Br	CuCl	Proline	K_2CO_3	120	DMSO	48	13/trace[e]
12	Br	CuOAc	Proline	K_2CO_3	120	DMSO	24	NR
13	Br	-	Proline	K_2CO_3	120	DMSO	24	NR
14	Br	CuI (10%)	Proline	K_2CO_3	90	DMSO	24	13/trace[g]
15	Br	CuI (10%)	Proline	K_2CO_3	120	DMSO	24	9/24[g]
16	Br	CuI (10%)	Proline (20%)	K_2CO_3	120	DMSO	24	10/13[g]
17	Br	CuI (5%)	Proline (20%)	K_2CO_3	90	DMSO	24	8/-[g]
18	Br	CuI (5%)	Proline (20%)	K_2CO_3	120	DMSO	24	8/-[g]
19	Br	CuI	$NH_2CH_2CH_2OH$	K_2CO_3	90	DMSO	24	9/-[g]
20	Br	CuI	$NH_2CH_2CH_2OH$	K_2CO_3	120	DMSO	24	10/8[g]
21	Br	CuI	$CH_3NHCH_2CH_2NHCH_3$	K_2CO_3	90	DMSO	24	14/8[g]
22	Br	CuI	$CH_3NHCH_2CH_2NHCH_3$	K_2CO_3	120	DMSO	24	trace/48[g]
23	Br	CuI	Proline	Cs_2CO_3	90	DMSO	24	17/38[f]

Reaction conditions: Tröger's base (TB) (1 mmol), amine (5 mmol), CuI (0.2 mmol, 20 mol%), L-Proline (0.4 mmol, 40 mol%), and base (3 mmol) in DMSO under nitrogen except otherwise mentioned. [a]Isolated yields. [b]5-15% of TB was recovered. [c]up to 60% of TB was recovered. [d]28% of TB was recovered. [e]45% of TB was recovered. [f]14% of TB was recovered. [g]26-63% of TB was recovered. NR: no reaction.

Scheme V:

Two flexible Tröger's base ditopic receptors C4TB and C5TB incorporating monoaza crown ether were designed and synthesized for bisammonium ion complexation. A comprehensive study of host–guest interactions was established by ^{1}H NMR spectroscopy and DFT calculations. Bisammonium chloride with a shorter alkyl chain spacer showed the highest affinity for the receptors.



Conclusion:

- Worked for different synthetic projects and performed various reactions for C-C, C-O, C-N bond formation ranging from 1mg (Catalyst/ligand Kit-Screening for C-C, C-N, C-O bond formation) to 25kg (PO based).
- I am familiar with handling of various oxidising and reducing reagents (on large scale), photochemical reactions etc.
- Toxic (like KCN, NaCN etc), pyrophoric (BuLi, DIBAL-H, LDA, LAH etc.) reagents have been used on large scale following proper safety protocols.