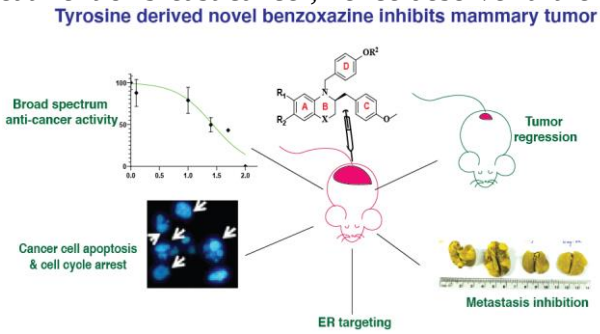
List of 10 best papers of the applicant highlighting the important contributions in them briefly

1. **Tyrosine-Derived Novel Benzoxazine Active in Rat Syngenic Mammary Tumor Model of Breast Cancer**

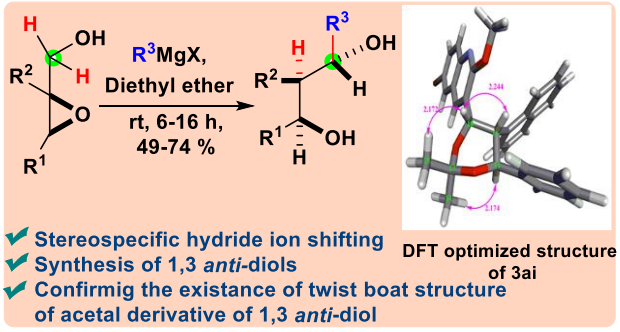
Amit Kumar Jana, Jyotsana Singh, Asha Ganesher, Amit Kumar, Arpita Banerjee, Deepak Kumar, Sarvesh Kumar Verma, Ashok Kumar Sharma, Rabi Sankar Bhatta, Rituraj Konwar, Gautam Panda J. Med. Chem. 2021, 64, 16293−16316

In continuing efforts of improving benzoxazepine derivatives as anti-breast cancer agent, a new chemical entity, benzoxazine was designed from scaffold morphing. Structure activity relationship studies revealed that H, -OMe, $-CF_3$ and -F were well tolerated on R_1 and R_2 position of ring **A** and R^2 as $-CH_2CH_2N(CH_2)_4$ (N-ethyl pyrrolidine) and $-CH_2CH_2N(CH_2)_5$ (N-ethyl piperidine) chain on ring D increased activities (**Series B, Figure 3**). **13d** selected as lead compound (IC_{50} : 0.20 to 0.65 µM), induces apoptosis, cell cycle arrest, loss of mitochondrial membrane potential in breast cancer cells. Compound **13d** was formulated into **13d-f** using cyclodextrin to improve its solubility for pharmacokinetic, *in vivo* efficacy study. Both **13d** and **13d-f** regressed tumor growth at concentration of 5 mg/Kg and 20 mg/Kg better than tamoxifen without any mortality in rat syngenic mammary tumor model. Collectively, our data suggest that tyrosine-derived novel benzoxazine **13d** could be a potential lead for the treatment of breast cancer, hence deserve further in-depth studies



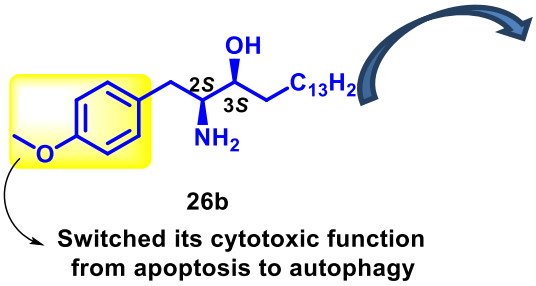
2. **A Tandem Semipinacol Rearrangement/aldehyde Arylation or Alkylation of Trisubstituted 2,3-Epoxy Alcohols with Grignard reagents for Functionalized 1,3-diols**; Amit Kumar, Gaurav Sharma, Sanjeev K Shukla, Gautam Panda, Journal of Organic Chemistry 2022, 87, 12, 7696-7711

A tandem semipinacol rearrangement/aldehyde arylation or alkylation reaction leading to formation of functionalized 1,3-diols bearing three consecutive tertiary stereocenters is identified from the reaction of various new trisubstituted 2,3-epoxy alcohols with numerous Grignard reagents. The observed 1,3-diols exist in anti-configuration which is confirmed by the 2D-NOESY, crystal structure of acetonide of one of the 1,3-diol analogues **3ai** and further DFT studies.

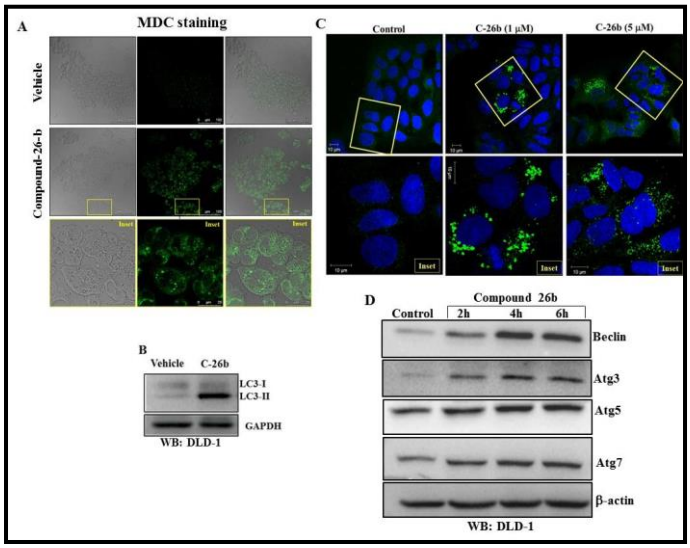


3. **New Spisulosine Derivative Promotes Robust Autophagic Response to Cancer Cells**; Asha Ganesher, Priyank Chaturvedi, Sanjeev Meena, Dipak Datta, Gautam Panda, European Journal of Medicinal Chemistry, 2020, 188, 112011

Therapy resistance by evasion of apoptosis could be one of the hallmarks of human cancer. Therefore, restoration of cell death by non-apoptotic mechanisms is critical to successfully overcome therapy resistance in cancer. By rational drug design approach, here we try to provide evidence that subtle changes in the chemical structure of spisulosine completely switched its cytotoxic function from apoptosis to autophagy. Our most potent molecule (**26b**) in a series of 16 synthesized derivatives of Spisulosine showed robust autophagic cell death in diverse cancer cells sparing normal counterpart. Compound **26b** mediated lethal autophagy induction was confirmed by formation of characteristic autophagic vacuoles, LC3 puncta formation, upregulation of signature autophagy markers like Beclin and ATG family proteins. Altogether, we have detected novel autophagy inducer small molecule which can be tested further for drug discovery research.

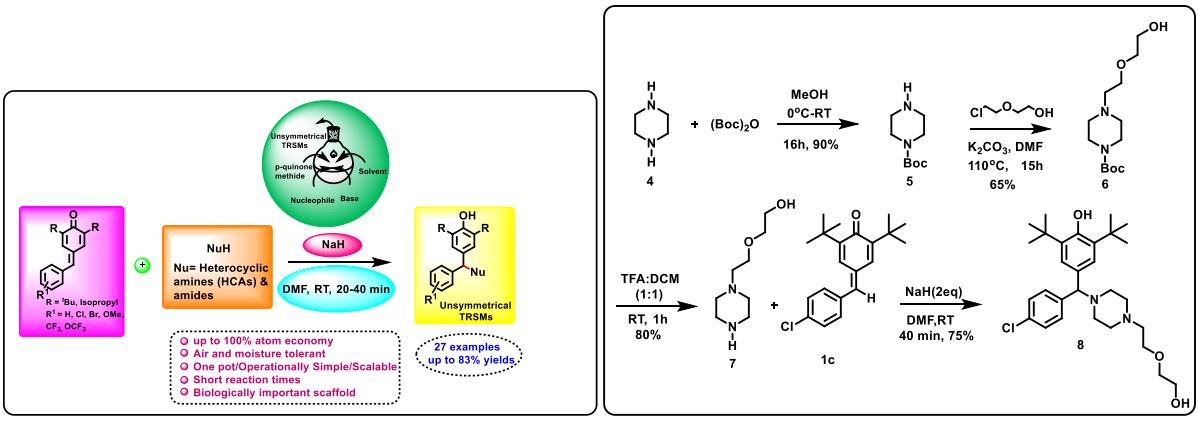


Compound 26b promotes Autophagic cell death



4. **Base mediated 1,6- Aza-Michael addition of heterocyclic amines and amides to p-QMs leading to Meclizine, Hydroxyzine and Cetirizine like architectures**, Deblina Roy, Gautam Panda, Synthesis 2019, 51, 4434-4442 (10.1055/s-0039-1690677)

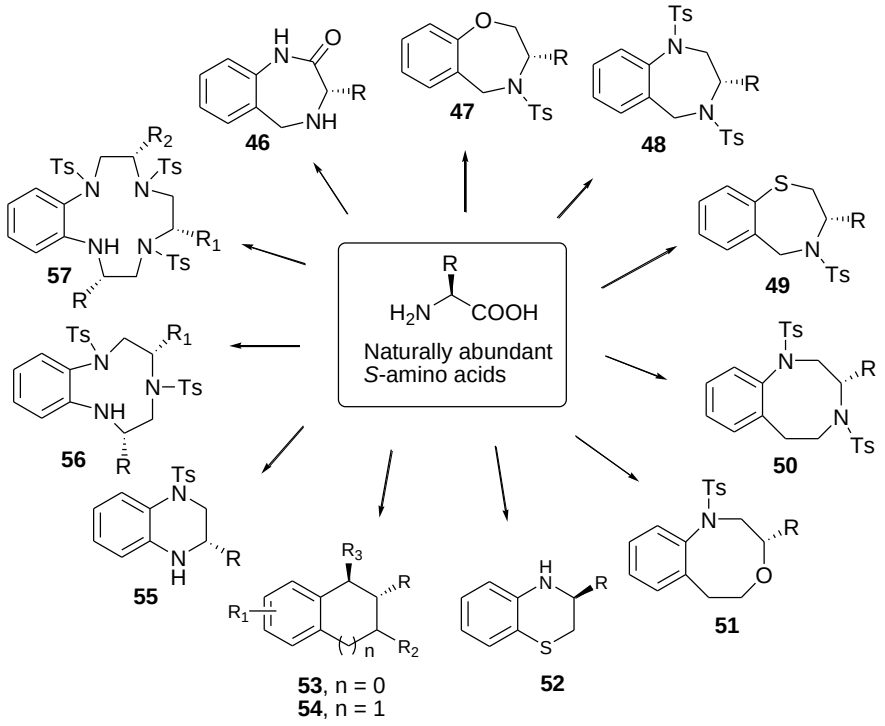
Reported herein is an expeditious, cost-effective synthetic methodology for a wide range of nitrogen containing unsymmetrical trisubstitutedmethanes (TRSMs). The synthesis involves base mediated 1,6- conjugate addition of heterocyclic amines and amides to substituted p-QMs giving the unsymmetrical TRSMs in moderate to very good yields (up to 83%) in one pot. The low-cost, mild temperature, high atom economy and yields, easy scale up, broad substrate scope are some of the salient features of this protocol. The methodology could further be extended for the synthesis of biologically important first generation antihistamines Meclizine, Hydroxyzine and Cetirizine like molecules highlighting the utility of the work. Importantly, the presence of halo substituent in most of the molecules allows for further late stage functionalization which paves way for generation of chemical library in drug discovery.



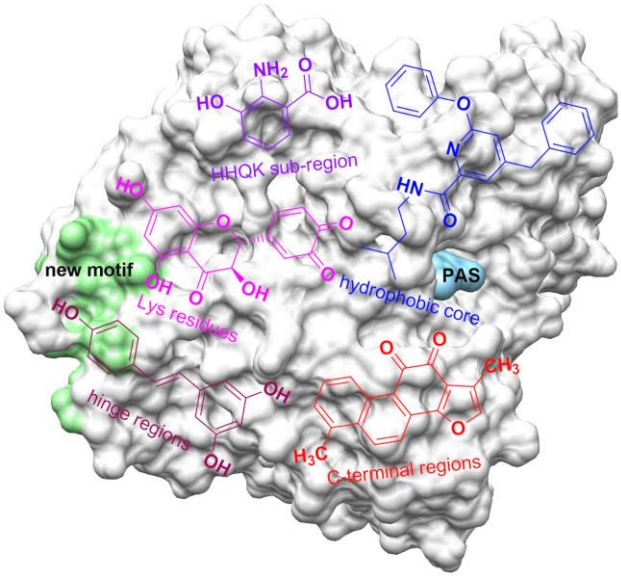
Synthesis of Hydroxyzine and Cetirizine like molecules

5. **QUEST FOR STEROIDOMIMETICS: AMINO ACIDS DERIVED STEROIDAL AND NONSTEROIDAL ARCHITECTURES,** Shagufta, Irshad, Ahmad and Gautam Panda, European Journal of Medicinal Chemistry 133 (2017) 139-151

The chiral pool amino acids have been utilized for the construction of steroidal and non-steroidal architectures in quest for steroidomimetics. Chirality derived from amino acids based architectures provide new and easy to incorporate chiral chemical space which otherwise very difficult to introduce and comprising of several synthetic steps for asymmetric steroids. The different and exciting ligand-receptor interactions may arise from the use of each enantiomer of amino acids that have been introduced in chiral steroidal backbone. The ring A and D of steroidal architectures can be mimicked through phenyl group of amino acid tyrosine. Mitsunobu reaction, nucleophilic substitution and elimination etc. were utilized for constructing diverse tri and tetracyclic steroidal skeleton as well as benzofused seco-steroids from amino acids. Promising biological activities related to hormonal disorders were observed from these benzofused amino acids derived steroidal and nonsteroidal molecules



6. **Perspectives on Inhibiting beta-Amyloid Aggregation through Structure-Based Drug Design.**
Pankaj Mishra, Senthil Raja Ayyannan, Gautam Panda *ChemMedChem 2015, 10, 1467-1474*



Targeting amyloid beta (Aβ) remained the most desired strategy in Alzheimer's disease (AD) drug discovery research. Many peptides specifically targeting the Aβ aggregates are known encompassing efforts from the industrial and academic research point of view. However, in clinical term, not much success has been gained with peptide research and in turn, small drug-like chemicals hold promising avenue and are already globally recognised. Also Aβ-aggregation inhibitions constitute the most important part in the multifunctional drug design regimen for AD. Unfortunately, rational drug design approaches with small molecules are still in the beginning stages. In this work our endeavours are to highlight, update and elaborate the structural anatomy of Aβ and known inhibitors for their best possible utilization in structure-based drug design approach to gain specific inhibitors. Further, we are also presenting the first review report of targeting a previously unknown region of the enzyme acetylcholinesterase, the N-terminus (7-20 sub-region) which was experimentally elucidated to participate in Aβ-aggregation and deposition.

7. **Thiophene containing Trisubstituted Methanes [TRSMs] as identified lead against Mycobacterium Tuberculosis; *European Journal of Medicinal Chemistry*, Volume 95, 5 May 2015, Pages 357-368**
Priyanka Singh, Sudipta Kumar Manna, Amit Kumar Jana, Tiash Saha, Pankaj Mishra, Saurav Bera, Maloy Kumar Parai, Srinivas Lavanya Kumar M., Sankalan Mondal, Priyanka Trivedi, Vinita Chaturvedi, Shyam Singh, Sudhir Sinha and **Gautam Panda**;
Triarylmethanes (TRAMs) and thiophene containing trisubstituedmethanes (TRSMs) have been reported by us, having potential against Mycobacterium tuberculosis and Mycobacterium fortuitum strains, respectively. Further, extension through synthesis and biological evaluation of novel TRSMs resulted into an identified lead 36 (S006-830) [(diisopropyl-(2-{4-[(4-methoxy-phenyl)- thiophen-2-yl-methyl]-phenoxy}-ethyl)-amine)

with MIC; 1.33 mg/L, non-toxic against Vero C-1008 cell line with selectivity index >10, ex-vivo efficacy equivalent to first line TB drugs-isoniazid (INH), rifampicin and pyrazinamide in the mouse and human bone marrow derived macrophages tuberculosis model, respectively and CFU count of 2.2 x 107 (approximately 15 fold lesser than untreated mice (31 x 107) with comparable efficacies to ethambutol (EMB) (1.27 x 107) and PZA (1.9 x 107). Further, S006-830 also showed potent bactericidal activity against multi-drug resistant and single-drug resistant clinical isolates of M. tuberculosis.

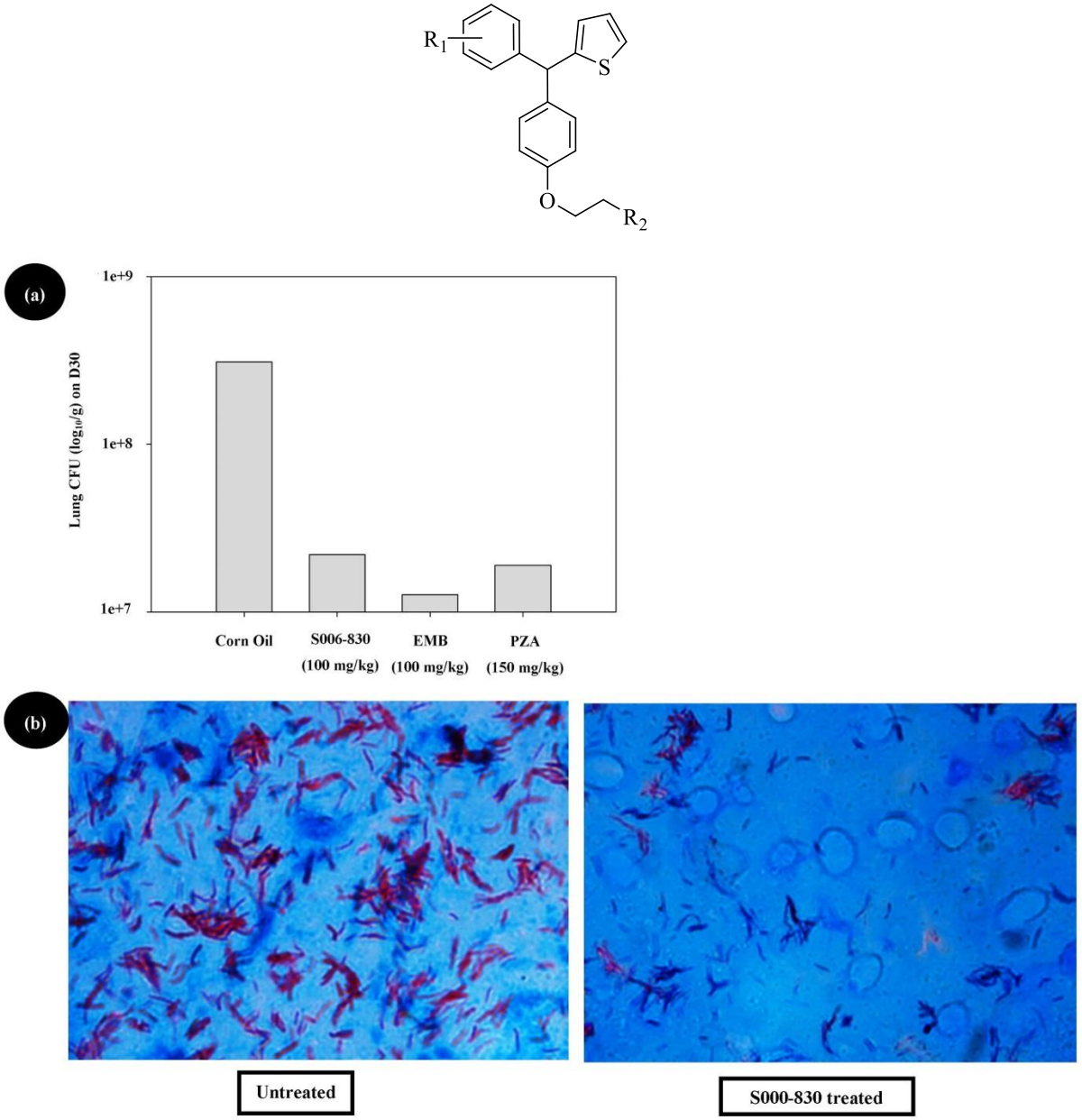


Figure. Results of *in vivo* protection experiments in mice infected (i.v.) with *M. tuberculosis* $H37R_v$.

A) **S006-830** treated mice (100 mg/kg body wt, by oral gavage, 6 d/w, x 4w) showed appx.15 fold reduction in CFU in lungs, which was equivalent to in vivo efficacy of standard drugs ethambutol (EMB) and pyrazinamide (PZA) B) represents the Z-N staining of lung homogenate untreated and treated with **S006-830**

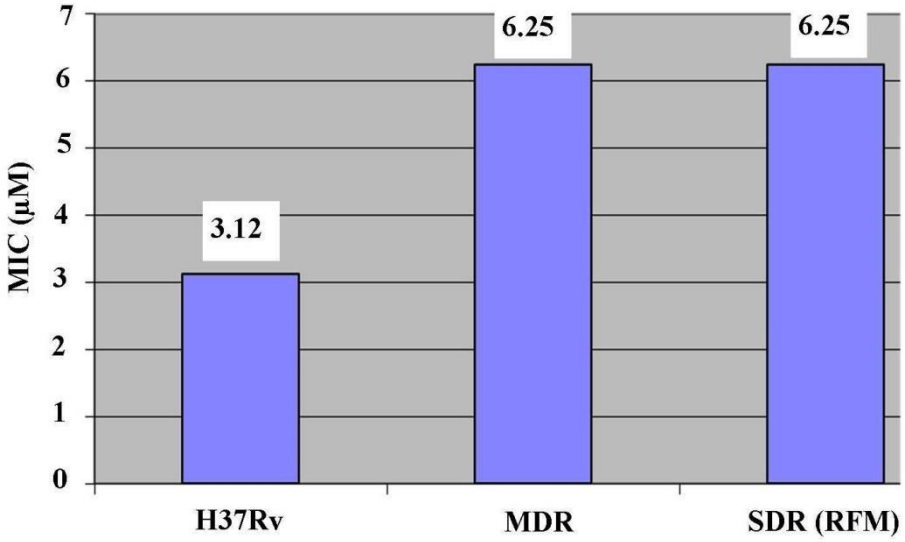
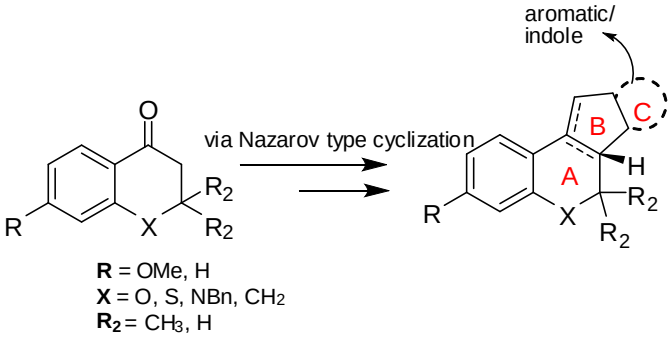


Figure. Activity of **36 (S006-830)** against sensitive (H37Rv), single- and multi- drug resistant *M. tuberculosis*

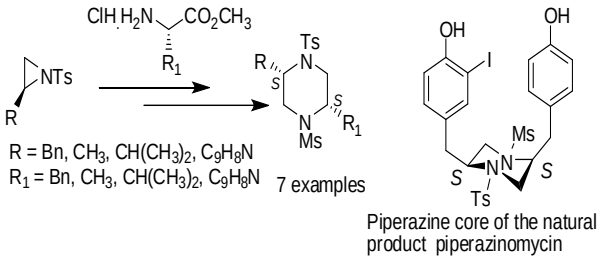
8. **Application of Nazarov type electrocyclization to access [6-5-6] and [6-5-5] core embedded new Polycycles: an easy entry to tetrahydrofluorene scaffolds related to Taiwaniaquinoids and C-*nor*-D *homo*steroids** Singh, R.; and **Panda, G**.:, *Org. Biomol. Chem.*, **2011**, *9*, 4782-4790 (**selected as cover page article)**.

We have reported an easy, general and expedient route to access variety of uncommon hetero [6-5-6]ABC tetrahydrofluorene cores resembling all carbotricyclic [6-5-6] tetrahydrofluorene cores present in Taiwaniaquinoids as well as in C-nor-D-homo steroids. Efforts have also been made to synthesize several hetero [6-5-5] tricyclic systems via Nazarov type cyclization. This is first such heteroaromatic Nazarov system which showed excellent regioselectivity under very mild reaction conditions using just 2 mol% $Sc(OTf)_3$, providing high yielding functionalized scaffolds that could serve as valuable building blocks towards Diversity Oriented Synthesis



9. **Regioselective Ring-Opening of Amino Acid-Derived Chiral Aziridines: an Easy Access to cis-2, 5-Disubstituted Chiral Piperazines** Samanta, K.; and **Panda, G.**:; *Chemistry an Asian Journal*, **2011,** *6*, 189-197.

Four-step efficient synthetic strategy for cis-2,5-disubstituted chiral piperazines derived from amino acids based aziridines are described. First report of BF3.OEt2 mediated highly regioselective ring opening of less reactive N-Ts chiral aziridines by α-amino acids methyl ester hydrochloride followed by Mitsunobu cyclization are the key reaction steps. This protocol was used in an attempt to construct the piperazine core framework of natural product (+)- piperazinomycin.



10. **Total Synthesis of (-)-Balanol, its all Stereoisomers, their N-tosyl analogues and fully protected Ophiocordin: An easy access to hexahydroazepine cores from Garner aldehydes** Srivastava, A. K., and **Panda, G**.:. *Chemistry A European Journal*, **2008,** *14*, 4675-4688.

Total synthesis of Protein Kinase C (PKC) inhibitor (-)-Balanol and its all stereoisomers are described starting from easily available Garner aldehydes. Diastereoselective Grignard reaction on Garner aldehydes and ring closing metathesis are the key steps for the construction of hexahydroazepine subunits. The benzophenone subunits were constructed through coupling of properly functionalized aromatic aldehyde and bromo components. The synthetic route constitutes a convenient and scalable reaction sequence to generate all the stereoisomers of balanol. The methodology is further explored for the synthesis of N-tosyl-analogues of balanol and fully protected antifungal antibiotic ophiocordin.