Summary of the Project

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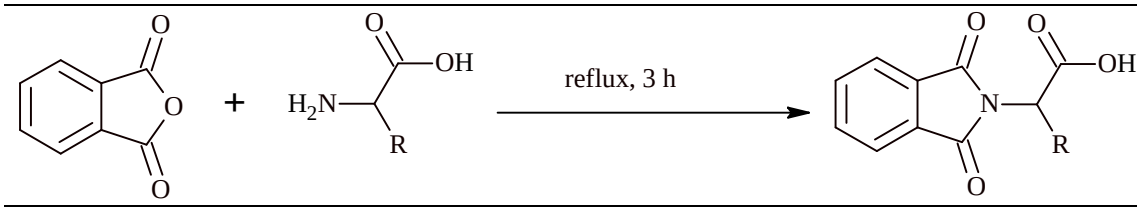
- **Department** : Chemistry
- **Name of College**: Jankidevi Bajaj college of Science, Wardha (M.S.)
- **UGC approval Letter No. and Date**: 47-629/13 (WRO) dated 20th May 2014
- **Title of the Research Project**: Synthesis and biocidal activity of benzene-1,2-dicarboxamide of amino acids
- **Date of starting the project**:20th May 2014 ,
  Date of completion of project: 19th May 2016

Summary

1. Synthesis of Venlafaxine Derivative of Amino Acid–Carboxamide & Antibacterial and Molecular Modeling Study:

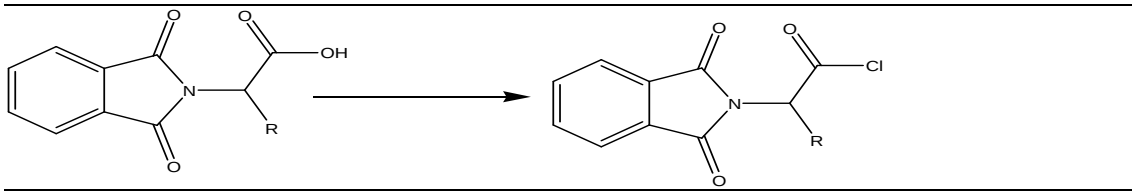
In the present work , we have reported the synthesis of Carboxamide derivatives of the amino acid (4d-4g) which shows potent biocidal activity. Since, Venlafaxine is an antidepressant drug, we have synthesized the derivative of venlafaxine having free NH2 group to enhance its reactivity during synthesis of its carboxamide derivatives. Free amino analogue of venlafaxine (3b) also shows potential activity against some bacteria/ fungi. The synthesis of 3b has been carried out by the novel method using a unique combination of NaBH4 /CoCl2 as a reducing agent for reduction of nitrile group. Synthesis of the venlafaxine derivative of the amino acid–carboxamide has been carried out via Coupling of N-phthaloyl derivatives of amino acid and their chlorinated products (1a-1g/2a-2g). Venlafaxine derivative of amino acid–carboxamide (-CONH) (4a-4g) screened for their antibacterial activity against certain bacterial strains viz. Escherichia Coli (MTCC-390), Enterococcus feacalis (MTCC-2729) ,Klebsialla pneumoniae (MTCC-3384) and Staphylococcus aureus (MTCC- 96) and they shows potent antibacterial activity against these bacteria. Moreover, molecular docking study of carboxamide derivatives (4a-4g) carried out to explore their binding affinity with protein Bovine Serum Albumin (BSA) using computer aided drug discovery /docking software HEX 8.0.0. All the compounds possess excellent binding affinity with BSA. This Protein-Ligand interaction plays a significant role in structural based drug designing.

Scheme 1.1 : Synthesis of N-phthaloyl amino acids (1a-1g)

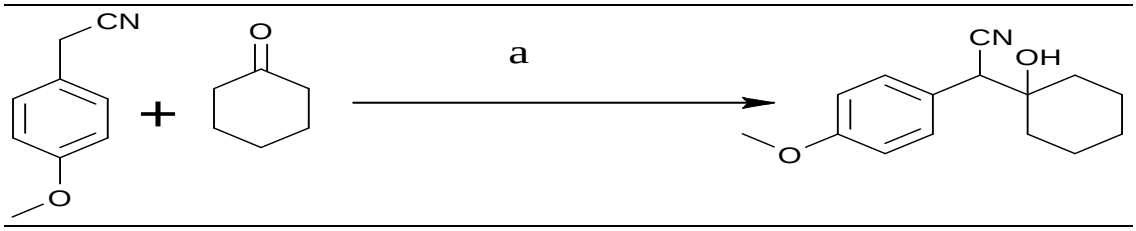


R = -H, -CH_3 , -CH (CH_3)$_2$, -CH_2CH (CH_3)$_2$, -$CH_2CH_2SCH_3$, -CH_2Ph, -CH_2Ph (pOBn).

Scheme 1.2 : Synthesis of N,N-phthaloyl amino acid chlorides (2a-2g)

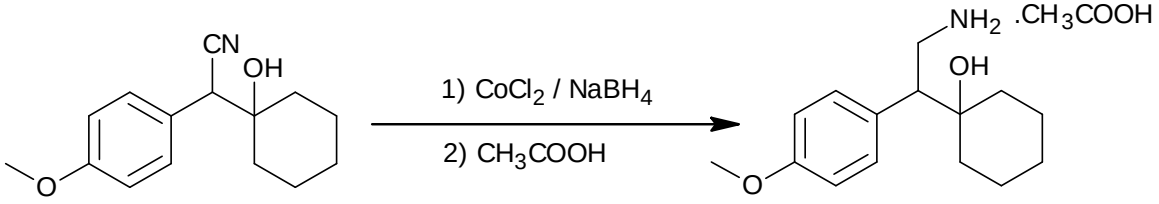


Scheme 1.3 : Synthesis of1-[Cyano(4 methoxyphenyl)methyl]cycloalkanol (3a)



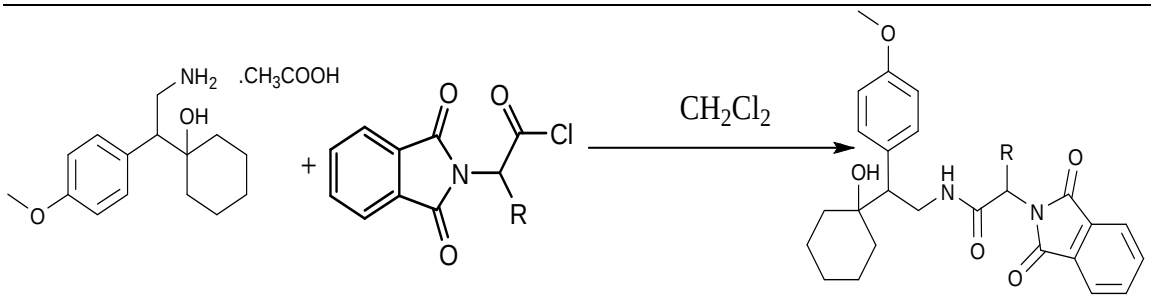
(a= TBAHS/NaOH)

Scheme 1.4: Synthesis of acetate salt of 1-(2-amino-1-(4-methoxyphenyl)ethyl) cyclohexanol(3b)



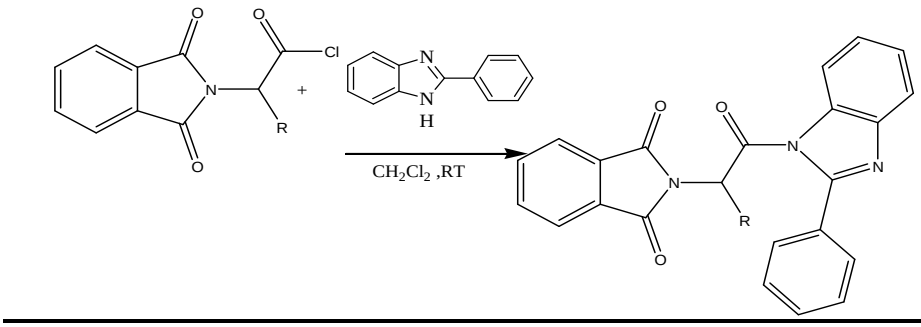
(b= $NaBH_4$ and $CoCl_2$ in 2:1 THF: H_2O)

Scheme 1.5 : Synthesis of venlaflaxine derivatives of amino acids-carboxamide (**4a-4g)**



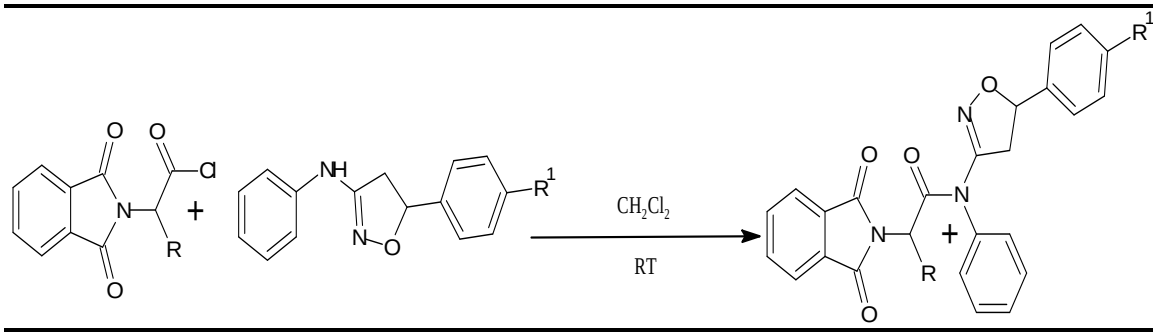
Although our proposed objectives for the projects are achieved as described above, additionally we also synthesized carboxamides (-CONH) derivatives of N-heterocycles viz. Benzimidazole, Isoxazoline , Quinazoline and Dihydropyridine. These carboxamide derivatives of various N-heterocycles also found to show good antibacterial activity against some bacteria and excellent binding affinity with BSA protein. As the final conclusion, we believed that the protocol developed by us will discover new horizons of series of potent bioactive drugs which are useful for the future endeavors. Our aim to develop a green, environmentally benign and recyclable technologies are fulfilled which is clearly implicated by the methodologies. The catalysts / solvents / reaction conditions used for the synthesis of a aforesaid heterocyclic nucleus containing carboxamide derivatives of amino acids are prototypical examples of green synthesis systems. Since they are non-toxic / less toxic, recyclable, affords excellent atom economy, shorter reaction time and simple work-up procedure and gives appreciable yields under the conditions which we have developed. These green methodologies support the invention of more environmentally friendly chemical processes which reduce or eliminate the generation of hazardous substances. Schemes are given below.

2. Microwave assisted coupling of substituted benzimidazole with N-pthaloyl amino acids and their antimicrobial study/ docking screening

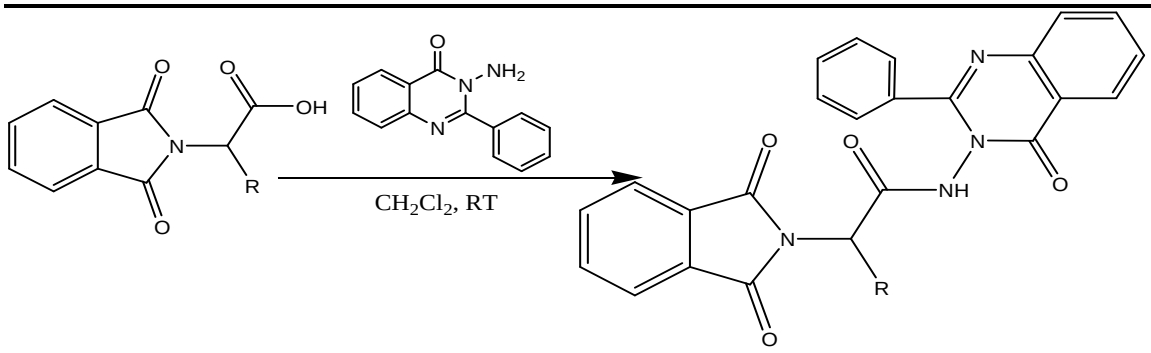


R^1 = p-Cl , p-NO_2

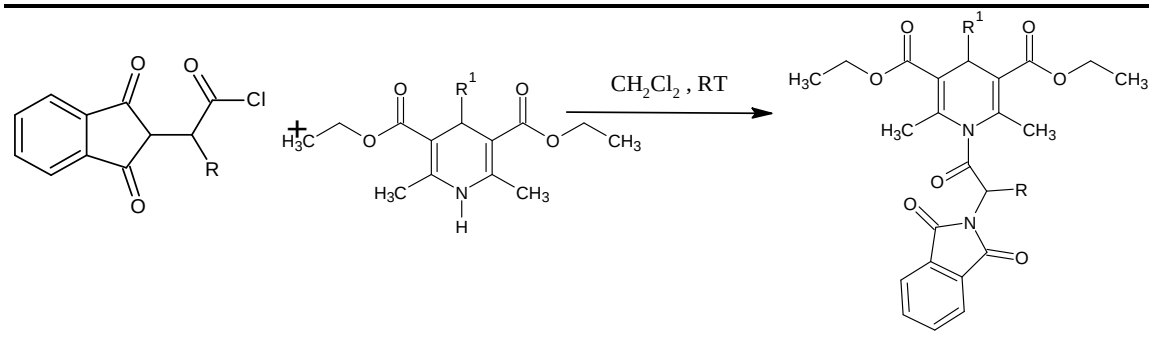
3. Coupling reactions of N-pthaloyl amino acids with substituted 3-phenylamino-5-(substituted phenyl) isoxazolines



4. Carboxamide synthesis via coupling of N-pthaloyl amino acids with amino substituted quinazoline



5. Synthesis of Carboxamide of N-pthaloyl amino acids with substituted 1.4-dihydropyridine-3,5-dicarboxylate and their docking / antimicrobial evaluation



R^1 = 4-$C_6H_5NO_2$, Sparfloxacin

Ecofriendly microwave assisted synthesis, atom economy, green catalysis are some of the green aspects of these schemes.