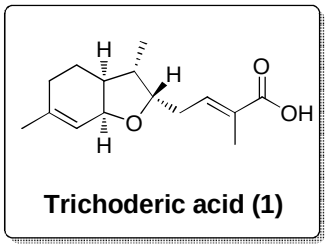
The thesis entitled "***Stereoselective Total Synthesis of Trichoderic acid and Development of Catalyst-free Green Methodologies on or in Aqueous Medium***" has been divided into three chapters.

Statement of Problem

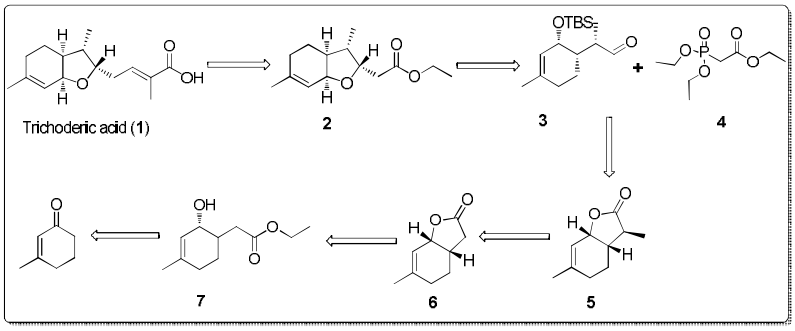
CHAPTER I: Stereoselective first total synthesis of Trichoderic acid

Introduction : The isolation of a bisabolane-type sesquiterpene, trichoderic acid (1) reported by Wu et al in 2011, from the culture broth of Trichoderma sp. PR-35, an endophytic fungus isolated from Paeonia delavayi. It has been evaluated for its antibacterial and antifungal activities in addition to this the extract also shown biological properties such as: sedative, analgesic, and anti-inflammatory agent, and also a remedy for cardiovascular.



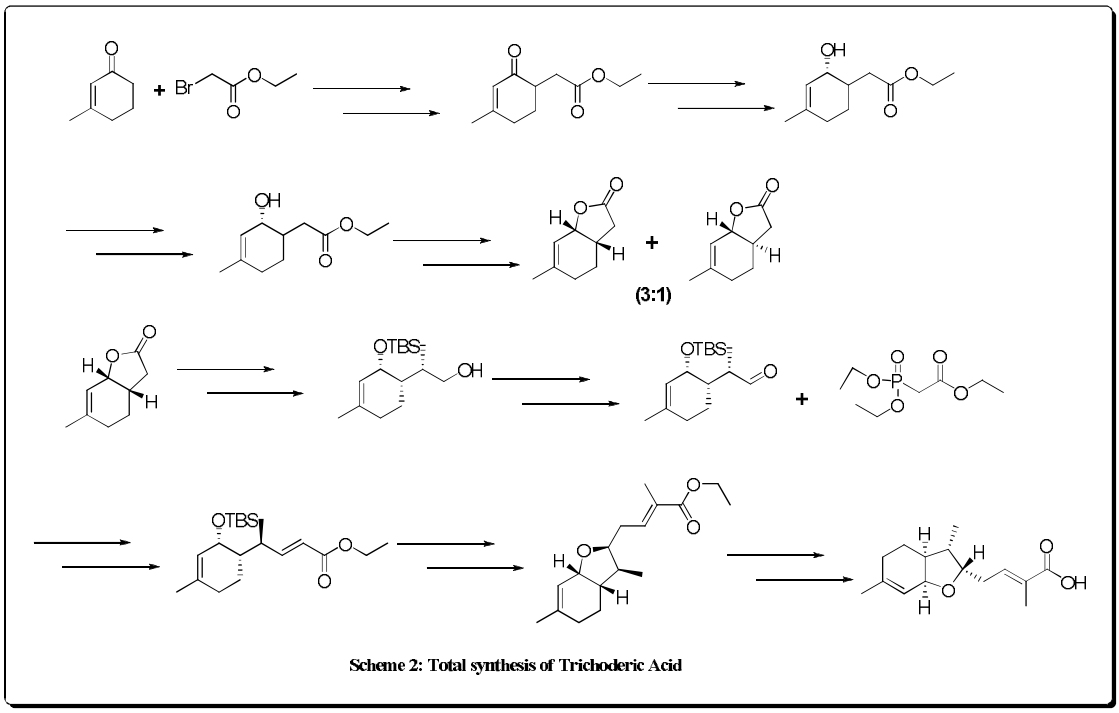
Trichoderic acid (1)

Methodology (Retrosynthetic analysis): The stereoselective total synthesis of Trichoderic acid (**1**) starts from commercially available 3-methylcyclohex-2-enone. The key steps involved in this synthesis were stereoselective reduction, alfa-methylation of lactone and *trans*-witting coupling by Horner-Emmons Reagent obtain Trichoderic ester.



Scheme 1. Retrosynthetic analysis of Trichodericacid

Results and discussion:



Scheme 2: Total synthesis of Trichoderic Acid

Conclusion: In conclusion, successful synthesis of trichoderic acid (**1**) was accomplished from 3-methyl cyclohexenone by stereoselective reduction, Horner-Emmons Reagent and intramolecular oxa-Michael reactions as key steps.

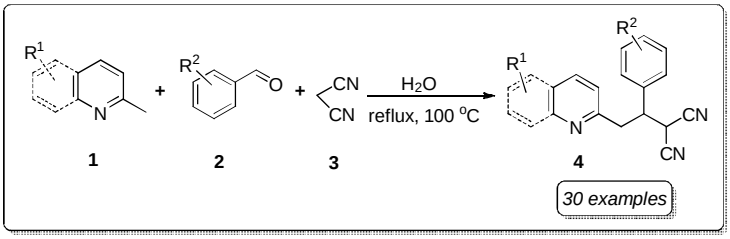
<u>CHAPTER II</u>: This chapter describes the development of new synthetic methodologies on azaarenes under catalyst-free conditions on water. These azaarene derivatives were evaluated for biological properties as well as photophysical properties.

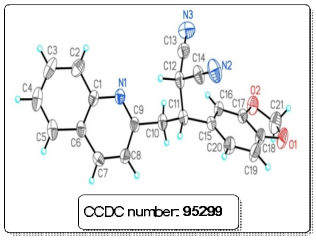
<u>Section A</u>:

A catalyst-free one-pot three-component approach for the synthesis of 2-(1-aryl-2-(azaaryl)ethyl)malononitriles via sp^3 C-H activation of 2-methyl azaarenes.

Combinatorial libraries of 2-(1-aryl-2-(azaaryl)ethyl)malononitriles derivatives have been synthesized by catalyst-free one-pot three-component protocol and employing water as a solvent. Simple reaction, open air reaction and easy isolation are added advantages of this

method. The method is applicable for aryl as well as heteroaryl system and provides a convenient access for the synthesis of novel quinoline derivatives. All the 2-(1-aryl-2-(azaaryl)ethyl)malononitrile derivatives were evaluated for their antimicrobial activity against Gram-positive bacteria (*Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Bacillus cereus*) and Gram-negative bacteria (*Pseudomonas aeruginosa*). Some of the compounds exhibited good antibacterial activity against both Gram-positive pathogens and Gram negative species.

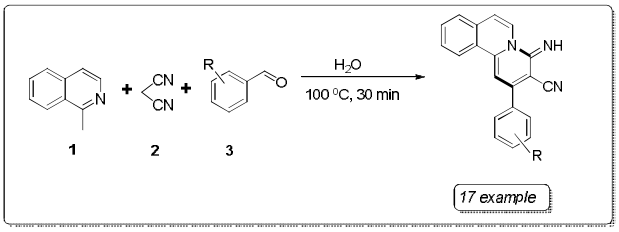


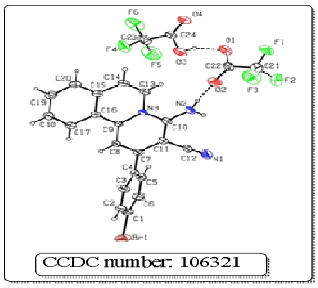


Scheme 2. Catalyst-free one-pot three-component synthesis of 2-(1-aryl-2-(azaaryl)ethyl)malononitriles

<u>Section B</u>: A domino green method for the rapid synthesis of novel fused isoquinoline derivatives via Knoevenagel/Michael/cyclisation reactions on aqueous media and their photophysical properties

An expedient, eco-friendly and green-protocol have been developed for the synthesis of novel 4-imino-2-aryl-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile derivatives via Knoevenagel/Michael/cyclisation reactions in one-pot under catalyst-free condition on aqueous medium. These products exhibited UV-Vis absorption and photoluminescence properties. Structure of the product was confirmed by single x-ray crystallography.





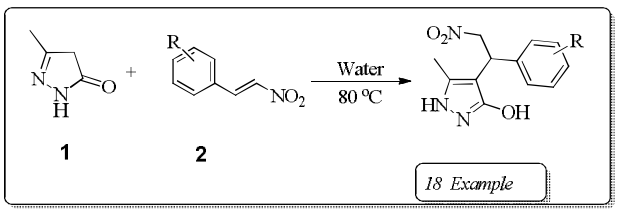
Scheme 3. Catalyst-free one-pot three-component synthesis of 4-imino-2-aryl-4H-pyrido[2,1-a]isoquinoline-3-carbonitrile derivatives

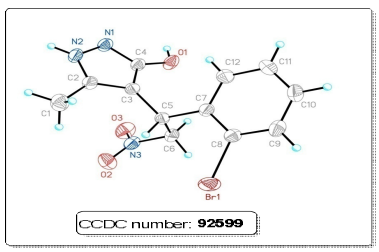
<u>CHAPTER-III</u>: This chapter describes the development of new synthetic methodologies for catalyst-free Michael addition/Friedel-Crafts alkylation of pyrazolone and tetrahydroisoquinoline with β-nitrostyrenes. These protocols are eco-efficient and eco-friendly using water as a reaction meadium, this chapter is further divided into two sections.

<u>Section A</u>:

A Catalyst Free Michael Addition of 3-Methyl-2-Pyrazolin-5-one to β-nitrostyrenes "On Water": A Green protocol for facile synthesis of 4-(1-aryl-2-nitroethyl)-3-methyl-1H-pyrazol-5-ol

A highly efficient and green protocol has been developed for the synthesis of 4-(1-aryl-2-nitroethyl)-3-methyl-1H-pyrazol-5-ol via Michael addition of 3-Methyl-2-Pyrazolin-5-one with β-nitrostyrenes under catalyst-free conditions on aqueous medium. A series of 4-(1-aryl-2-nitroethyl)-3-methyl-1H-pyrazol-5-ols have been synthesized in good to excellent yield. C-alkylated product was observed exclusively with 3-Methyl-2-Pyrazolin-5-one without formation of N-alkylated product.



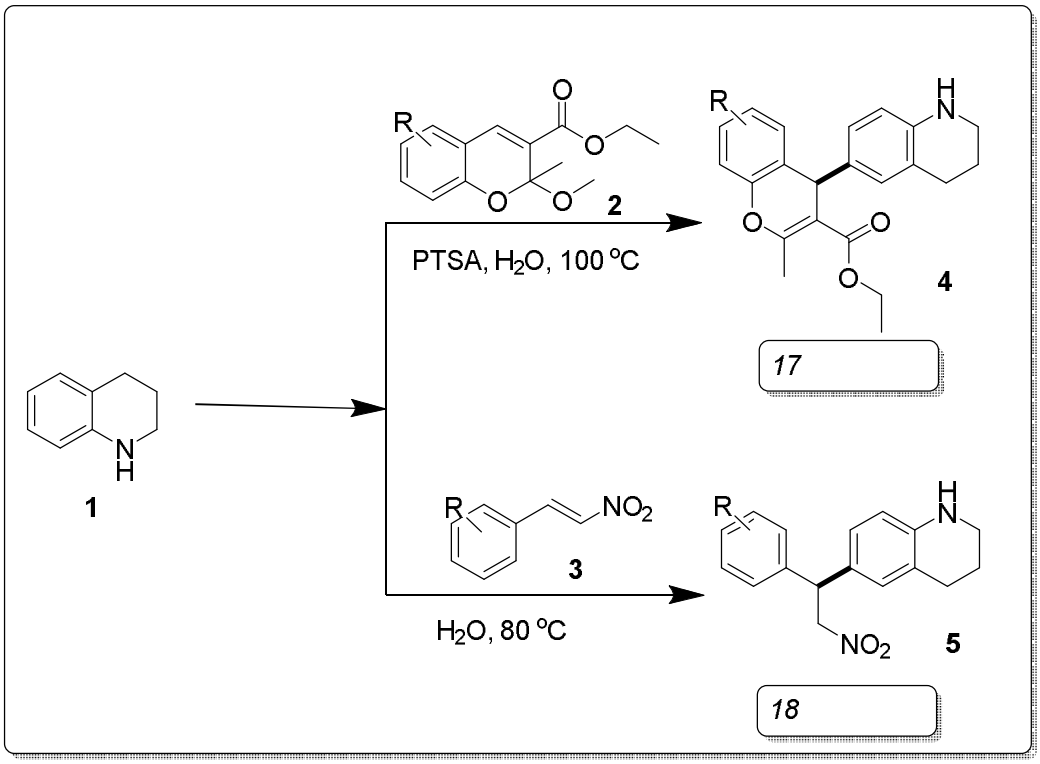


Scheme 4. Michael addition of 3-methyl-2-pyrazolin-5-one to the β-nitrostyrenes.

<u>Section B</u>:

Efficient and eco-friendly protocol for the synthesis of novel 6-substituted Tetrahydroquinolines via C6-functionalisation of Tetrahydroquinolines with chromene acetals and β-nitrostyrenes in aqueous meadium

A facile, novel and eco-efficient method has been developed for the C6-functionalisation of unprotected tetrahydroquinoline (THQ) with chromenes and β-nitrostyrenes to afford novel 6-substituted tetrahydroquinolines in aqueous medium.



Scheme 4. Synthesis of C6-functionalized THQ derivatives.