"SYNTHESIS OF NOVEL SUBSTITUTED AROMATIC COMPOUNDS INVOLVING CYCLO-ADDITION REACTIONS"

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For the SUMMARY of

MAJOR RESEARCH PROJECT REPORT
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IN CHEMISTRY
UNDER FACULTY OF SCIENCE

Submitted by

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A literature survey revealed that these heterocycles possess different types of biological activities like antidibetic, antimicrobial, anthelmintic, anti-inflammatory, analgesic, anticonvulsant, anti-cancer, antidepressant, antibiotic etc. therefore some of them are used as medicaments. Hence more attention is being directed towards the construction of new heterocycles via cycloaddition reaction and the development of efficient synthetic routes for their building. Keeping this objective in view the syntheses of new aromatic compounds were planned with the hope to obtain the molecules with high potency and efficiency. It was also proposed to modify the synthetic routes using moderate, eco-friendly, simple economic and feasible protocols to improve the quality and yields of the products.

The present work was therefore accordingly planned, executed and presented in the form of thesis entitled ***"SYNTHESIS OF NOVEL SUBSTITUTED AROMATIC COMPOUNDS INVOLVING CYCLO-ADDITION REACTIONS".*** The works includes the synthesis of new aromatic compounds and anthracene derivatives via cycloaddition reaction. The details of the synthetic work and characterization and Biological evaluation of novel synthesized molecules and the intermediates have been presented in the thesis in five chapters.

Chapter I: Introduction and literature review:

Gives the general introduction and literature overview of synthetic route for aromatic compounds via cycloaddition reaction mainly Diels-alder reaction. Woodword and Hoffmann introduced the term Pericyclic reaction. Pericyclic reactions are those reactions that occur by a concerted cyclic shift of electrons. These are two key points that characterise a Pericyclic reaction:

a) It is concerted reaction i.e reactant bonds are broken and products are formed with transition state.
b) Pericyclic involves a cyclic shift of electrons

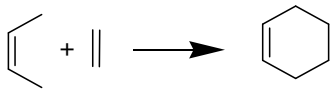
Pericyclic reaction thus highlights cyclic transition state involving π-bonds.

Pericyclic reactions are of four types:

1. Electrocyclic reaction
2. Cycloaddition reaction
3. Sigmatropic rearrangement
4. Group Transfer reaction

From those types, cycloaddition processes have been regarded as the most useful organic chemical reactions. The Diels-alder reaction which is well known[(2)] world famous and is only one example of great class of thermal and photochemical reactions. The facile synthesis of cyclic compounds from acyclic precursors, the high degree of stereoselectivity made numerous near discovseries of (4+2) cycloaddition reaction by several luminaries in the field of organic chemistry during the 20th century.

A cycloaddition reaction is a reaction in which two unsaturated molecules undergo addition reaction to yield a cyclic product. Formation of cyclic product takes place at the expense of one π-bond in each of the reacting partner and gain of two sigma bonds at the end of the both components having π-bonds.

 loss of π-bonds and formation of sigma bonds.

The cycloaddition reaction are classified with respect to three facts of the reaction.

i. The number of electron of each unit participating in cycloaddition.
ii. The nature of orbital changing (π or σ).
iii. The stereochemical mode of cycloaddition.

The [2+2] reaction is that in which the reaction involves two electrons from one reacting component and also two electrons from other component.

Other points discussed in this topic is:

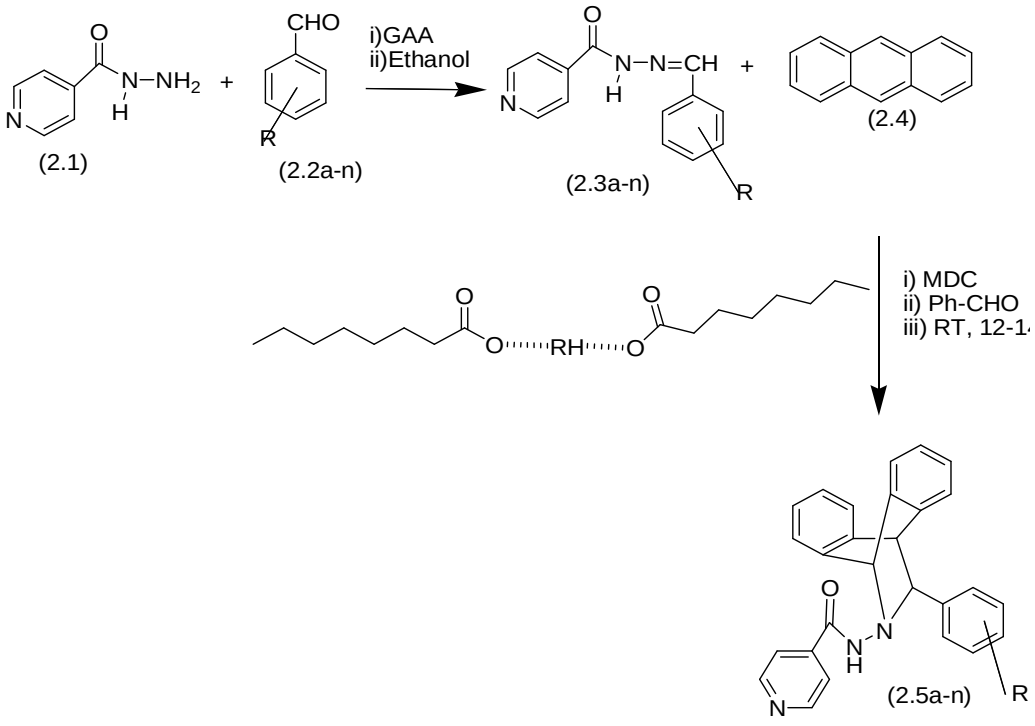
1. Regiocontrol and Beyond: Achieving Stereoselection.
2. Hetero-Diels-Alder Reactions.
3. Diels-Alder Reactions in Disguise: Cloaked Dienes and Dienophiles

4. Daring Applications of the Diels-Alder Reaction in Total synthesis

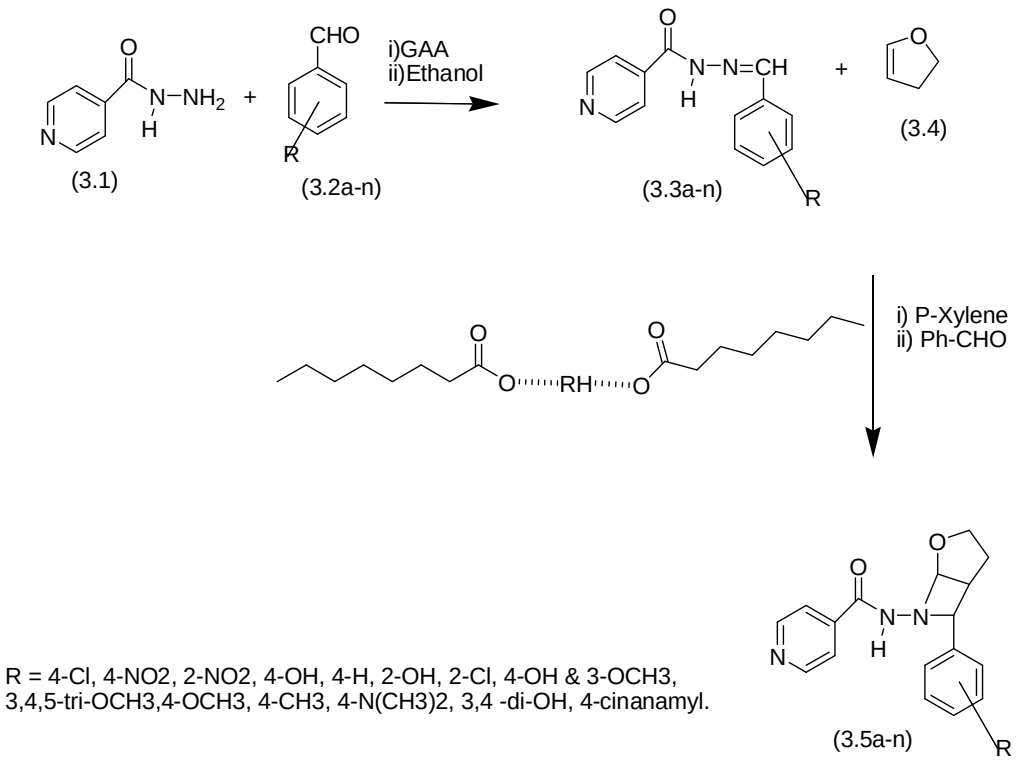
Chapter II: consists Synthesis of N-(2-(substituted phenyl)-2,5-dihydroanthro [7,10b] azet-1(10bH)-yl) isonicotinamide:

Starting with isoniazid different anthracene derivatives were synthesized as per the following scheme and characterized

2.2.2 General Reaction scheme:

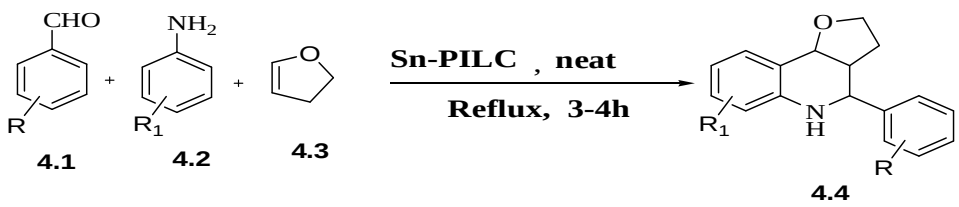


Chapter III: Synthesis of N - (7 - (substituted phenyl) – 4 – oxa – 6 – aza –bicyclo [3.2.0] heptan – 6 - yl) isonicotinamide (3.5a-n): starting with isoniazid different aromatic compounds were prepared via cycloaddition reaction shown in following scheme and characterized.



R = 4-Cl, 4-NO2, 2-NO2, 4-OH, 4-H, 2-OH, 2-Cl, 4-OH & 3-OCH3, 3,4,5-tri-OCH3,4-OCH3, 4-CH3, 4-N(CH3)2, 3,4 -di-OH, 4-cinanamyl.

Chapter IV: Sn-PILC: A novel efficient and recyclable catalyst for one-pot three component Aza-Diels-alder reactions for a facile synthesis of tetrahydropyranoquinoline derivatives under neat conditions. As part of our ongoing research on the chemical synthesis and biological properties of tetrahydroquinoline derivatives, it is proposed to synthesize of tetrahydropyranoquinoline derivatives by using Sn-PILC as catalyst via one-pot three component Aza-Diels-alder reactions under neat conditions which may helpful to society to get pharmacologically more active compounds, reaction scheme shown below. In the present study a novel series of tetrahydroquinoline were synthesized and characterized by means of IR, ^{1}HNMR, ^{13}CNMR, Mass spectral analysis and elemental analysis.



4.1 **4.2** **4.3** **4.4**

Chapter-V: BIOLOGICAL EVALUATION

Provides the screening results for antibacterial activities. Some of synthesized compounds were subjected for pharmacological screening to evaluate antimycobacterial and anticonvulsant screening which shows good results.

Conclusion:

Spectral data of synthesized compounds confirm the formation of novel aromatic compounds involving cycloaddition reaction compounds and Biological evaluation of synthesized compounds shows good activity with respective bacteria.

The work presented in the MRP report as well as Summary significantly contributes to Pericyclic reactions, as first time a considerable number of new sulphur, nitrogen and oxygen heterocyclic analogs have been synthesized by employing convenient / modified synthetic routes. The new molecules synthesized are anthracene derivatives of Isoniazid as main moiety The novel synthesized molecules and intermediates have been obtained in pure forms and are well characterized by using spectral data. Attempts have also been made to provide modified routes so as to enhance rates and yields of the products by using introducing one pot synthetic routes. Carrying reaction neatly, alternative efficient synthetic methods for obtaining reactive intermediates.

Publications:

1. **Megha Rai**, Shivaji Jadhav and Mazahar Farooqui., "A novel, efficient & Cat-RH (II) catalyzed one-pot Aza-dials-alder reaction for facile synthesis of Trihydroquinoline bearing INZ" *J. Med. Chem. & Drug Discovery (*ISSN: 2347-9027)*.,* **2015**,special issue of ACTRA,67-73.

2. **Megha Rai**, Shivaji Jadhav and Mazahar Farooqui., "One pot Aza-Diels-alder reaction for facile synthesis of N-(7-(substituted phenyl)-4-oxa-6-aza-bicyclo [3.2.0] heptan-6-yl) isonicotinamide by using RH (II) catalyst" *Prospectus & Opportunities in Chemical sciences., (978-93-84916-56-5)***2015**,Page.100-102.

3. **Megha Rai,** Shivaji Jadhav and Mazahar Farooqui., "Sn-PILC: A novel efficient and recyclable catalyst for one-pot three component Povarov's inverse-electron-demand hetero Diels-Alder reaction for a facile synthesis of tetrahydropyranoquinoline derivatives under neat conditions" Orbital E-journal of chem. (ISSN 1984-6428), 8(3), 2016. [DOI:http://dx.doi.org/10.17807/orbital.v8i3.801]