An Green and Efficient Synthesis of Hexahydrospiro[Indoline-3,3′-pyrrolo[1,2-Imidazol] -2-one Derivatives via one-pot Multicomponent Reaction

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Abstract : An efficient and practical protocol to synthesize hexahydrospiro[indoline-3,3'-pyrrolo[1,2-imidazol]-2-one derivatives by one pot multi component reaction of 1,3-dipolar cycloaddition reaction. Based on this methodology, a series of hexahydrospiro[indoline-3,3'-pyrrolo[1,2-imidazol]-2-one were obtained in excellent yields (upto 99%).

Cycloaddition, Derivatives, Multi component reaction, Efficient, Protocol

I. INTRODUCTION

Heterocyclic compounds, or heterocycles, are cyclic compounds in which one or more atoms of the ring are heteroatoms, an atom other than carbon. A variety of atoms, such as N, O, S, Se, P, Si, B, and as can be incorporated into ring structures. The most prevalent heterocyclic compounds are the one that contain the heteroatoms N, O, and S. Heterocycles make an exceedingly important class of compounds and more than half of all known organic compounds are heterocycles. Most of the compounds we know as drugs, vitamins and many other natural products are heterocycles. Alkaloids are natural products containing one or more nitrogen heteroatoms that are found in the leaves, barks, roots, or seeds of plants. Heterocyclic compounds also include many of the biochemical material essential to life. Nucleic acids, the chemical substances that carry the genetic information controlling inheritance, consist of long chains of heterocyclic units held together by other types of materials. There are many naturally occurring pigments, vitamins and antibiotics that are heterocyclic compounds. Modern society is dependent on synthetic heterocycles for use as drugs,[1] pesticides,[2] dyes,[3] and plastics.[4]

Among the approximately 20 million chemical compounds identified by the end of the second millennium, more than two-third of them are fully or partially aromatic and approximately half of them are heterocyclic. The presence of heterocycles in all kinds of organic compounds of inters electronics, biology, optics, pharmacology and material sciences is very well known. Sulfur and nitrogen containing heterocyclic compounds have maintained the interest of synthetic organic chemists over the period.[5] However; heterocycles with other hetero atoms such as oxygen[6] phosphorus[7] and selenium[8] also assume importance. It is pertinent to note that nitrogen heterocycles have been accorded a special place in the view of their diverse and important biological acivities, as illustrated below with a few examples. A variety of benzimidazoles are in use, like thiabendazole and flubendazole (anthelmintic), omeprazole (antiulcerative), astemizole (antihistaminic) and lansoprazole (antihistaminic). The chemistry and pharmacology of benzimidazoles have been of great interest to medicinal chemistry.[9]

Heterocycles are of immense importance biologically and industrially. The majority of pharmaceuticals and biologically active agrochemicals are heterocyclic, while countless additives and modifiers used in industrial applications ranging from cosmetics, reprography, information storage and plastics are heterocyclic in nature.

Many natural and synthetic heterocyclic compounds can and do participate in chemical reactions taking place in the human body. The fundamental manifestations of life the provision of energy, transmission of nerve impulses, metabolism and the transfer of hereditary information are all based on chemical reactions involving the participation of many heterocyclic compounds.

Synthetic heterocycles have widespread therapeutic uses such as antibacterial, antifungal, antimycobacterial, trypanocidal, anti-HIV activity, antileishmanial agents, genotoxic, antitubercular, antimalarial, herbicidal, analgesic, anti-inflammatory, muscle relaxants, anticonvulsant, anticancer, lipid peroxidation inhibitor, hypnotics, antidepressant, antitumoral, anthelmintic and insecticidal agents.[10-16] Large number of synthetic heterocyclic compounds with other important applications such as fungicides, herbicides, anticorrosive agents, photostabilizers, agrochemicals, dyestuff, copolymers, photographic developers, fluorescent whiteners, sensitizers, booster agent, antioxidants in rubber and flavoring agent[17-21] are also known. The essential amino acids proline, histidine and tryptophane,[22] photosynthesizing pigment chlorophyll, the oxygen transporting pigment haemoglobin,[23] the hormones kinetin, heteroauxin and cytokinins[24] are popular heterocyclic compounds.

In view of the above biological importance nitrogen heterocycles in the field of medicine, development of new, efficient and eco-friendly protocols for the construction of heterocycles is accorded great priority. Synthesis *via* one pot multistep transformations, known as tandem, cascade or domino reactions has become important for rapidly accessing complex structures. These transformations minimize enormously the waste generation, labour, time and cost. Hence they are considered to be ecofriendly and green. As the

present investigation has employed one pot multi component reaction for the construction of a series of novel Hexahydrospiro[Indoline-3,3′-pyrrolo[1,2-Imidazol]-2-one Derivatives with good yield.

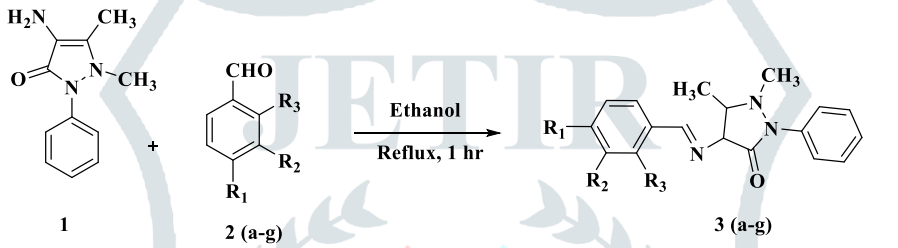
II. EXPERIMENTAL SECTION

2.1 Materials and methods

All the chemicals and reagents were used in this work as analytical grade. *p*-tolualdehyde, 4-methoxybenzaldehyde, 4-nitrobenzaldehyde, 4-bromobenzaldehyde, benzaldehyde, vanilline, *o*-vanilline and 4-aminoantipyrine were purchased from Sigma Aldrich. Isatine and proline were purchased from Alfa Aesar and all the solvents were obtained from laboratory grade. The melting points were measured in open capillary tubes and are uncorrected. The ^{1}H spectra was recorded on a Bruker (Avance) 300 MHz NMR instrument using TMS as an internal standard, $CDCl_3$ and DMSO as a solvent. Standard Bruker software was used throughout. Chemical shifts are given in parts per million (δ-scale) and the coupling constants are given in Hertz. Silica gel-G plates (Merck) were used for TLC analysis with a mixture of pet ether and ethylacetate as an eluent.

2.2. General method for synthesis of 4-aminoantipyrine based chalcones (3a-3g)

4-aminoantipyrine and aromatic aldehydes was dissolved in 10 ml of ethanol, the mixture was refluxed for 1 hr. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and recrystallized with ethanol, to get pure chalcone.



1 + 2 (a-g) → 3 (a-g)

R_1 = CH_3, OCH_3, NO_2, Br, H, OH
R_2 = OCH_3, H
R_3 = OH, H

2.3. Preparation of (*E*)-4-(benzylideneamino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3a)

4-aminoantipyrine **1** (0.5g, 2 mmol) and Benzaldehyde **2a** (0.26g, 2 mmol) was dissolved in 10 ml of ethanol; the mixture was refluxed for 1 hr. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and washed with n-hexane, dried it. Orange solid (98% yield). m.p. 90-92°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.736 (s, 1H), 7.867 (s, 2H), 7.408-7.332 (m, 10H), 3.128 (s, 3H), 2.474 (s, 3H).

2.4. Preparation of (*E*)-1,5-dimethyl-4-((4-methylbenzylidene)amino)-2-phenylpyrazolidin-3-one (3b)

4-aminoantipyrine **1** (1.7g, 8 mmol) and 4-methyl benzaldehyde **2b** (1g, 8 mmol) was dissolved in 10 ml of ethanol; the mixture was refluxed for 1 hr. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and washed with n-hexane, dried it. Orange solid (96% yield). m.p. 103-105°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.733 (s, 1H), 7.764 (d, *J* = 7.7 Hz, 2H), 7.498–7.204 (m, 9H), 3.125 (S, 3H), 2.479 (s, 3H), 2.383 (s, 3H).

2.5. Preparation of (*E*)-1,5-dimethyl-4-((4-methoxybenzylidene)amino)-2-phenylpyrazolidin-3-one (3c)

4-aminoantipyrine **1** (1.5g, 7 mmol) and 4-methoxy benzaldehyde **2c** (1g, 7 mmol) was dissolved in 10 ml of ethanol; the mixture was refluxed for 1 hr. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and washed with n-hexane, dried it. Yellow solid (95% yield). m.p. 80-82°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.703 (s, 1H), 7.812 (d, *J* = 8.04 Hz, 2H), 7.487–7.414 (m, 5H), 7.390–7.272 (m, 2H), 7.003–6.915 (m, 2H), 3.831 (s, 3H), 3.106 (s, 3H), 2.461 (s, 3H).

2.6. Preparation of (*E*)-1,5-dimethyl-4-((4-bromobenzylidene)amino)-2-phenylpyrazolidin-3-one (3d)

4-aminoantipyrine **1** (1.1g, 5 mmol) and 4-bromo benzaldehyde **2d** (1g, 5 mmol) was dissolved in 10 ml of ethanol; the mixture was refluxed for 1 hr. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and washed with n-hexane, dried it. Yellowish Orange solid (98% yield). m.p. 145-147°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.702 (s, 1H), 7.716 (d, *J* = 8.37 Hz, 2H), 7.544–7.261 (m, 8H), 3.163 (s, 3H), 2.481 (s, 3H).

2.7. Preparation of (*E*)-1,5-dimethyl-4-((4-nitrobenzylidene)amino)-2-phenylpyrazolidin-3-one (3e)

4-aminoantipyrine **1** (1.34g, 6 mmol) and 4-nitro benzaldehyde **2e** (1g, 6 mmol) was dissolved in 10 ml of ethanol; the mixture was refluxed for 1 hr. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and washed with n-hexane, dried it. Orange solid (97% yield). m.p. 138-139°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.786 (s, 1H), 8.240 (d, *J* = 8.55 Hz, 2H), 7.967 (d, *J* = 8.58 Hz, 2H), 7.495 (t, *J* = 7.65 Hz, 3H), 7.391–7.261 (m, 4H), 3.224 (s, 3H), 2.514 (s, 3H).

2.8. Preparation of (*E*)-4-((4-hydroxy-3-methoxybenzylidene)amino)-1,5-dimethyl-2-phenylpyrazolidin-3-one (3f)

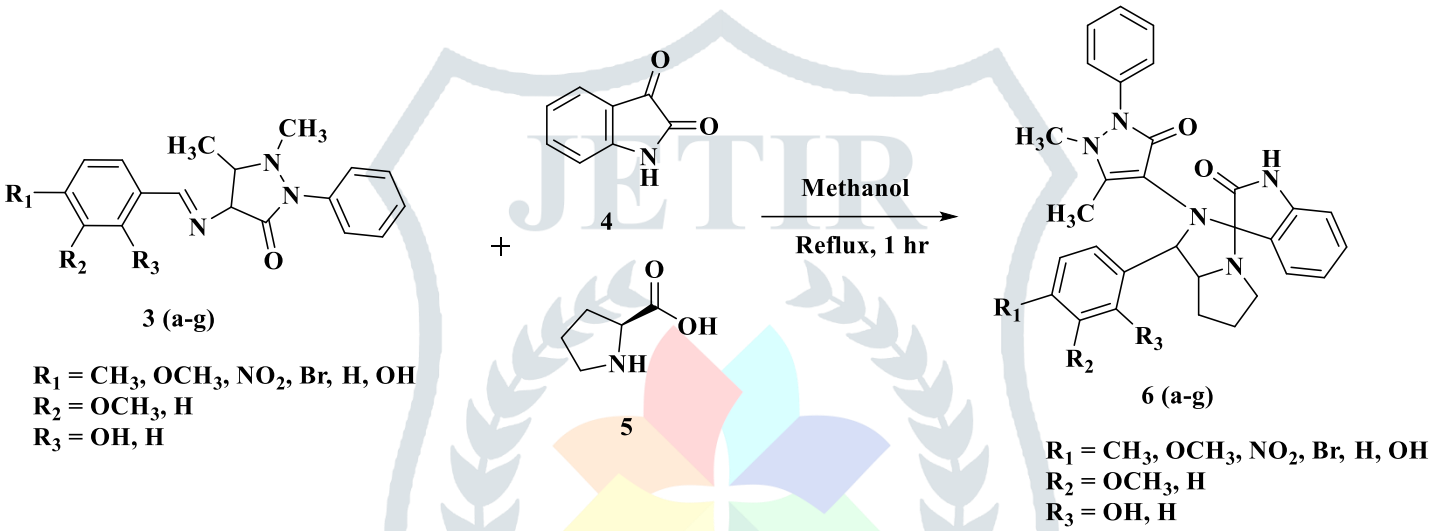
4-aminoantipyrine **1** (0.5g, 2 mmol) and vanillin **2f** (0.37g, 2 mmol) was dissolved in 10 ml of ethanol; the mixture was refluxed for 1 hr. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and washed with n-hexane, dried it. Yellow solid (96% yield). m.p. 123-125°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.649 (s, 1H), 7.466–7.268 (m, 9H), 6.915 (d, *J* = 8.04 Hz, 1H), 6.251 (s, 1H), 3.919 (s, 3H), 3.112 (s, 3H), 2.463 (s, 3H).

2.9. Preparation of (*E*)-4-((2-hydroxy-3-methoxybenzylidene)amino)-1,5-dimethyl-2-phenylpyrazolidin-3-one (3g)

4-aminoantipyrine **1** (0.5g, 2 mmol) and *o*-vanillin **2g** (0.37g, 2 mmol) was dissolved in 10 ml of ethanol; the mixture was refluxed for 1 hr. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and washed with n-hexane, dried it. Yellow solid (95% yield). m.p. 130-132°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 13.897 (s, 1H), 9.800 (s, 1H), 7.505–7.260 (m, 7H), 6.987–6.801 (m, 3H), 3.914 (s, 3H), 3.166 (s, 3H), 2.399 (s, 3H).

2.10. General method for synthesis of hexahydrospiro[indoline-3,3'-pyrrolo[1,2-c]imidazol]-2-one derivatives (6a-6g)

To the mixture of 4-aminoantipyrine based chalcones, isatin and L-proline was dissolved in 5 ml of methanol and refluxed until the completion of reaction as indicated by TLC. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and recrystallized with ethanol, to get pure product without column chromatography.



2.11. Preparation of 2'-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-1'-phenyl-1',2',5',6',7',7a'-hexahydrospiro [indoline-3,3'-pyrrolo[1,2-c]imidazol]-2-one (6a)

To the mixture of (*E*)-4-(benzylideneamino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one **3a** (0.3 mmol), isatin **4** (0.3 mmol) and L-proline **5** (0.5 mmol) was dissolved in 5 ml of methanol and refluxed until the completion of reaction as indicated by TLC. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and recrystallized with ethanol, to get pure product without column chromatography. Greenish yellow solid; (97% yield). m.p. 118–120ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.549 (s, 1H), 8.175-6.697 (m, 14H), 3.121 (s, 3H), 2.416 (s, 3H), 1.768-0.6675 (m, 8H).

2.12. Preparation of 2'-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-1'-(p-tolyl)-1',2',5',6',7',7a'-hexahydrospiro [indoline-3,3'-pyrrolo[1,2-c]imidazol]-2-one (6b)

To the mixture of (*E*)-1,5-dimethyl-4-((4-methylbenzylidene)amino)-2-phenylpyrazolidin-3-one **3b** (0.3 mmol), isatin **4** (0.3 mmol) and L-proline **5** (0.4 mmol) was dissolved in 5 ml of methanol and refluxed until the completion of reaction as indicated by TLC. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and recrystallized with ethanol, to get pure product without column chromatography. Pale green solid; (94% yield). m.p. 110–112ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.509 (s, 1H), 7.893-6.725 (m, 13H), 2.412 (s, 9H), 1.732-0.686 (m, 8H).

2.13. Preparation of 2'-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-1'-(4-methoxyphenyl)-1',2',5',6',7',7a'-hexa hydrospiro[indoline-3,3'-pyrrolo[1,2-c]imidazol]-2-one (6c)

To the mixture of (*E*)-1,5-dimethyl-4-((4-methoxybenzylidene)amino)-2-phenylpyrazolidin-3-one **3c** (0.3 mmol), isatin **4** (0.3 mmol) and L-proline **5** (0.4 mmol) was dissolved in 5 ml of methanol and refluxed until the completion of reaction as indicated by TLC. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and recrystallized with ethanol, to get pure product without column chromatography. Greenish Yellow solid; (98% yield). m.p. 154–156ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.484 (s, 1H), 7.919 (d, *J* = 18.21 Hz, 1H), 7.673 (d, *J* = 8.13 Hz, 3H), 7.435-7.291 (m, 6H), 6.882-6.738 (m, 3H), 3.752 (s, 3H), 3.083 (s, 3H), 2.388 (s, 3H), 2.168-0.724 (m, 8H).

2.14. Preparation of 1'-(4-bromophenyl)-2'-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-1',2',5',6',7',7a'-hexa hydrospiro[indoline-3,3'-pyrrolo[1,2-c]imidazol]-2-one (6d)

To the mixture of (*E*)-1,5-dimethyl-4-((4-bromobenzylidene)amino)-2-phenylpyrazolidin-3-one **3d** (0.2 mmol), isatin **4** (0.2 mmol) and L-proline **5** (0.4 mmol) was dissolved in 5 ml of methanol and refluxed until the completion of reaction as indicated by TLC. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and recrystallized with ethanol, to get pure product without column chromatography. Green solid; (97% yield). m.p. 210–212ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.505 (s, 1H), 7.942 (s, 1H), 7.649 (d, *J* = 6.99 Hz, 1H), 7.498-6.715 (m, 11H), 3.138 (s, 3H), 2.411 (s, 3H), 1.521-0.734 (s, 8H).

2.15. Preparation of 2'-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-1'-(4-nitrophenyl)-1',2',5',6',7',7a'-hexa hydrospiro[indoline-3,3'-pyrrolo[1,2-c]imida zol]-2-one (6e)

To the mixture of (*E*)-1,5-dimethyl-4-((4-nitrobenzylidene)amino)-2-phenylpyrazolidin-3-one **3e** (0.2 mmol), isatin **4** (0.2 mmol) and L-proline **5** (0.4 mmol) was dissolved in 5 ml of methanol and refluxed until the completion of reaction as indicated by TLC. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and recrystallized with ethanol, to get pure product without column chromatography. Brown solid; (95% yield). m.p. 135–137ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.415 (s, 1H), 7.842 (s, 1H), 7.449 (d, *J* = 5.90 Hz, 1H), 7.391-6.624 (m, 11H), 3.027 (s, 3H), 2.341 (s, 3H), 1.430-0.658 (s, 8H).

2.16. Preparation of 2'-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-1'-(4-hydroxy-3-methoxyphenyl)-1',2',5', 6',7',7a'-hexahydrospiro[indoline-3,3'-pyr rolo[1,2-c]imidazol]-2-one (6f)

To the mixture of (*E*)-4-((4-hydroxy-3-methoxybenzylidene)amino)-1,5-dimethyl-2-phenylpyrazolidin-3-one **3f** (0.2 mmol), isatin **4** (0.2 mmol) and L-proline **5** (0.2 mmol) was dissolved in 5 ml of methanol and refluxed until the completion of reaction as indicated by TLC. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and recrystallized with ethanol, to get pure product without column chromatography. Green solid; (97% yield). m.p. 124–126ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 13.384 (s, 1H), 9.424 (s, 1H), 7.444-6.781 (m, 12H), 3.821 (s, 3H), 3.091 (s, 3H), 2.403 (s, 3H), 1.649-0.692 (m, 8H).

2.17. Preparation of 2'-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-1'-(2-hydroxy-3-methoxyphenyl)-1',2',5', 6',7',7a'-hexahydrospiro[indoline-3,3'-pyr rolo[1,2-c]imidazol]-2-one (6g)

To the mixture of (*E*)-4-((2-hydroxy-3-methoxybenzylidene)amino)-1,5-dimethyl-2-phenylpyrazolidin-3-one **3g** (0.4 mmol), isatin **4** (0.4 mmol) and L-proline **5** (0.4 mmol) was dissolved in 5 ml of methanol and refluxed until the completion of reaction as indicated by TLC. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and recrystallized with ethanol, to get pure product without column chromatography. Green solid; (96% yield). m.p. 130–132ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 13.384 (s, 1H), 9.638 (s, 1H), 7.461-6.757 (m, 12H), 3.795 (s, 3H), 3.171 (s, 3H), 2.486 (s, 3H), 1.771-0.713 (m, 8H).

III. RESULTS AND DISCUSSION

Infectious diseases have emerged as a serious cause of morbidity and mortality, with 16.2 percent (equivalent to 57 million) deaths each year worldwide. Hence, WHO has listed such diseases in 2nd place among the lead cause of death. Now, medicinal world has conquered many deadly infectious diseases and immensely brought down the mortality rate to some extent. But still diseases like pneumonia, tuberculosis (TB), typhoid, H1N1, dengue and HIV are matter of big concern at present. Further, emerging antimicrobial resistance has created a major public health dilemma, compounded by a dearth of new antimicrobial options. In addition, the alarming rates of emerging and reemerging microbial threats coupled with increasing antimicrobial resistance, particularly in regard to multi drug resistant Gram-positive bacteria and *Mycobacterium*, are major concerns to the public health as well as scientific communities worldwide.

Antimicrobial drugs have caused a dramatic change not only of the treatment of infectious diseases but of a fate of mankind. Antimicrobial chemotherapy made remarkable advances, resulting in the overly optimistic view that infectious diseases would be conquered in the near future. Antimicrobial resistance is a global public health concern that is impacted by both human and non-human antimicrobial use. The consequences of antimicrobial resistance are particularly important when pathogens are resistant to antimicrobials that are critically important in the treatment of human disease. However, in reality, emerging and re-emerging infectious diseases have left us facing a counter charge from infections. Infections with drug resistant organisms remain an important problem in clinical practice that is difficult to solve.

The greatest impact of the synthesis of heterocyclic chemistry is the development of new pharmaceutically active and efficient compounds. Inventing and developing a new medicine is a long, complex, costly and highly risky process that has few peers in the commercial world. Research and development (R&D) for most of the medicines available today has required 12-24 years for a single new medicine, from starting a project to the launch of a drug product. In addition, many expensive, long term research projects completely fail to produce a marketable medicine. Each step of a synthesis involves a chemical reaction, reagents and conditions need to be designed to give a good yield and pure product. The discovery of new methods and reagents grab the attention of chemists across the world. Optimization is where one or two starting compounds are tested in the reaction under a wide variety of conditions of temperature, solvent, reaction time etc, until the optimum conditions for product, yield and purity are found. Then the researcher tries to extend the method to a broad range of different starting materials to find the scope and limitations.

Heterocyclic compounds by virtue of their specific activity could be employed in the treatment of infectious diseases. Review of literature indicated that nitrogen containing heterocycles find a significant place in the development of pharmacologically important molecules. This gives us an opportunity to explore new molecules. Also the biological activity, stability and toxicity of the

individual mofits are encouraging and well documented. Keeping in view of these observations it was planned to synthesize some nitrogen containing heterocycles especially hexahydrospiro[indoline-3,3'-pyrrolo[1,2-imidazol]-2-one derivatives.

The present research work involves synthesis and characterization of new nitrogen heterocycles carrying interesting pharmacophore like hexahydrospiro[indoline-3,3'-pyrrolo[1,2-imidazol]-2-one derivatives. In the present work first we prepared 1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one derivatives from 4-aminoantipyrine and various aromatic aldehydes. The synthesized products were confirmed by ^{1}H NMR spectroscopy. In NMR spectrum these compounds give signal for NH proton is singlet at 9.733 ppm. The aromatic protons were give signal at aromatic region from 7.778 ppm to 7.204 ppm. The methyl protons were give signal at 2.479 ppm and 2.383 ppm.

Further this synthesized products involved in one pot multicomponent reaction with isatin and L-proline via 1,3-dipolar cycloaddition reaction. The synthesized novel heterocyclic compounds confirmed by ^{1}H NMR spectroscopy. In NMR spectrum these compounds give signal for NH proton is singlet at 9.484 ppm. The aromatic protons were give signal at aromatic region from 7.949 ppm to 6.738 ppm. The methyl protons were give signal at 3.083 and 2.388. The aliphatic protons give signal from 2.168 ppm to 0.724 ppm.

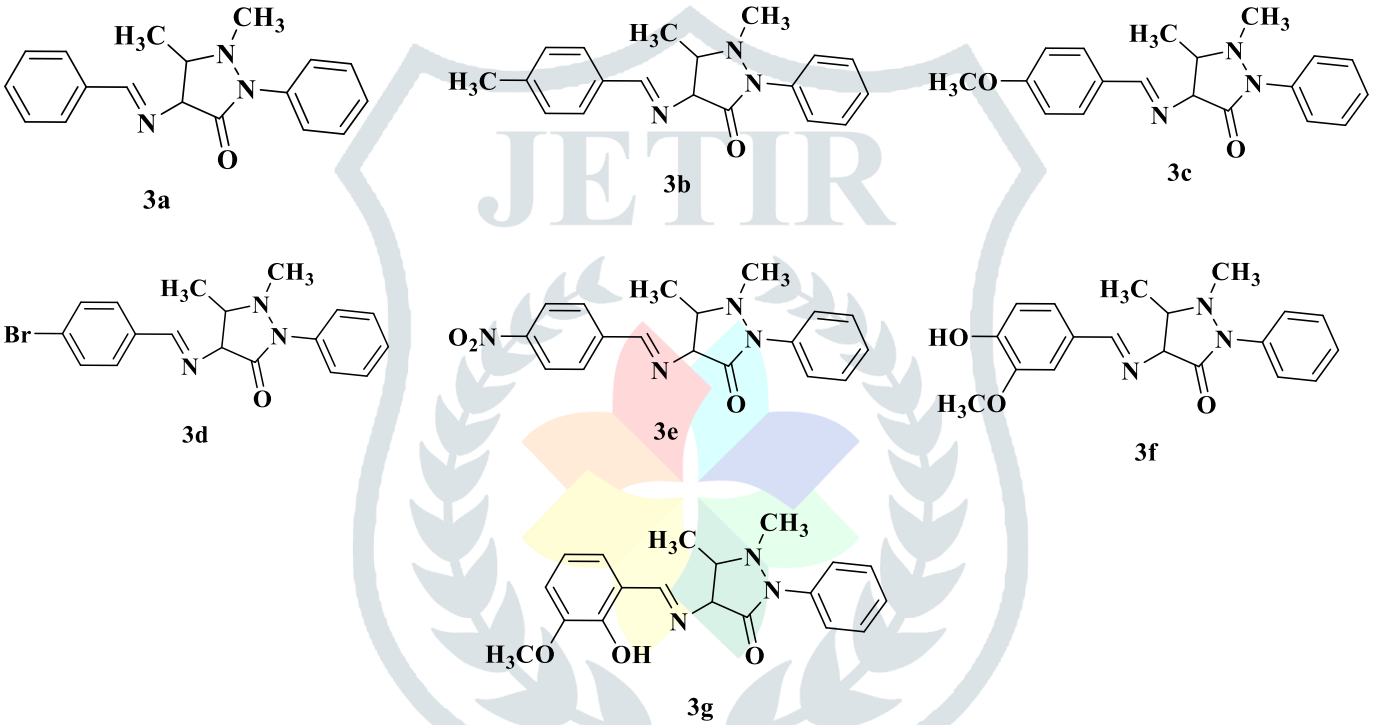
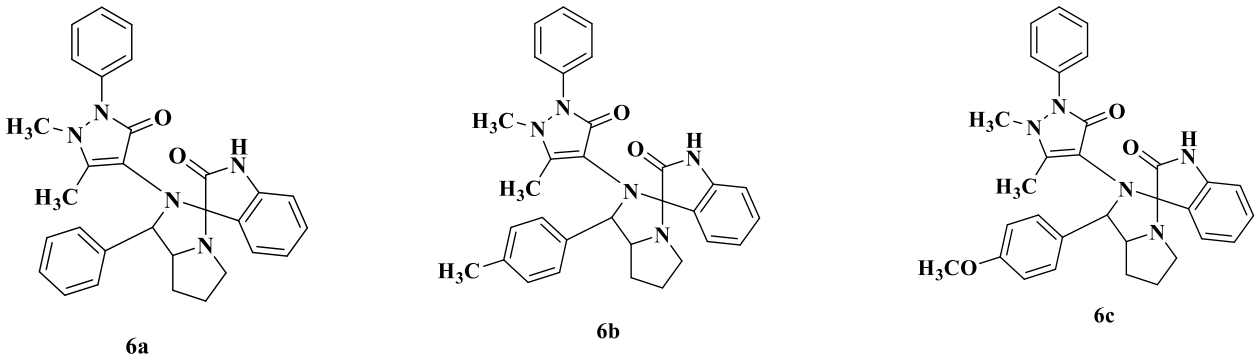


Figure 3.1. Structure of Synthesized 1,5-Dimethyl-2-Phenyl-1,2-Dihydro-3h-Pyrazol-3-One Derivatives



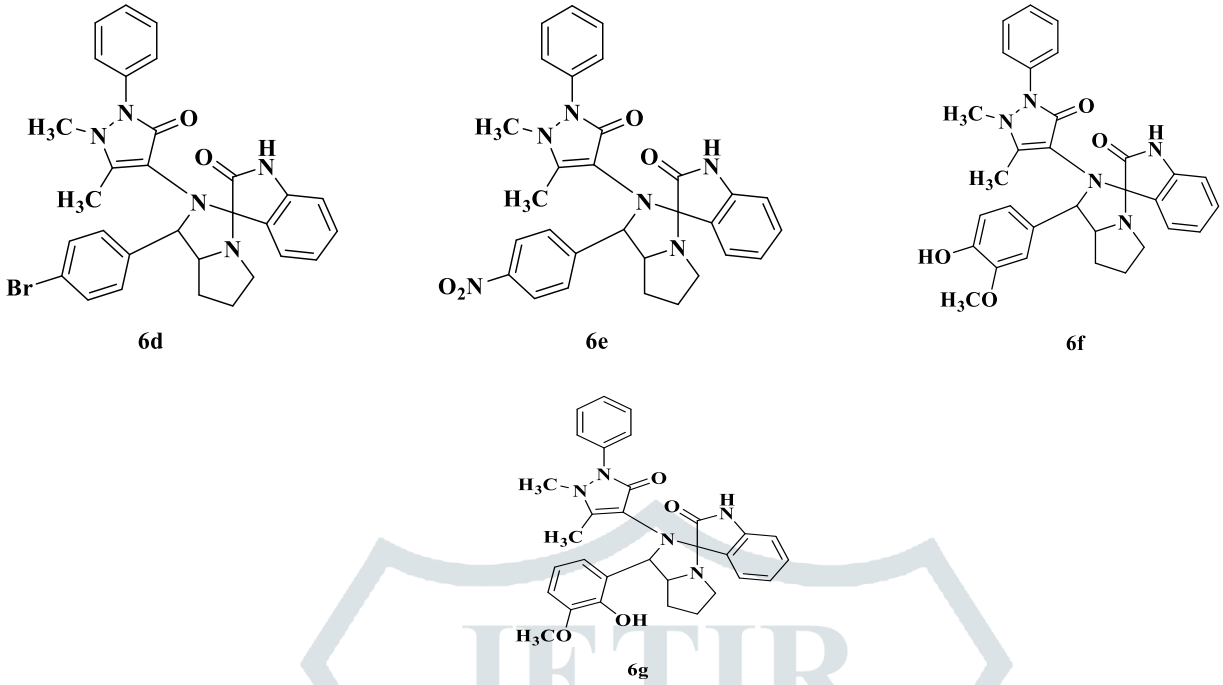


Figure 3.2. Structure of Synthesized Hexahydrospiro[Indoline-3,3'-Pyrrolo[1,2-Imidazol]-2-One Derivatives

IV. CONCLUSIONS

In conclusion, we have developed an efficient and practical protocol to synthesize hexahydrospiro[indoline-3,3'-pyrrolo[1,2-imidazol]-2-one derivatives by one pot multi component reaction of 1,3-dipolar cycloaddition reaction. Based on this methodology, a series of hexahydrospiro[indoline-3,3'-pyrrolo[1,2-imidazol]-2-one were obtained in excellent yields (upto 99%).

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