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A New Route Synthesis and Characterization of Novel Spiro-Heterocyclic Compounds From Semicarbazones

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Abstract

Now a day's synthesis of heterocyclic compounds is the major research in field of organic and medicinal chemistry is due to the extensive pharmacological activities of these compounds, synthesis of these type of pharmacological active heterocyclic compounds are achieved by varying substituent. The main object of this type of synthesis is to study the activity related aspects of pharmacophore group of the heterocyclic compounds and to enhance the yield if compound is biologically active.Since spiroheterocyclic compounds also pharmacologically active compounds, spiropyrrolidines are synthesized by the reaction of Isatin and L-proline with semicarbazone by 1,3 dipolar cycloaddition reaction. The formation of spiroheterocyclic compound is confirmed by the ^{1}H NMR and ^{13}C NMR.

Keywords: spiropyrrolidines, Pharmacophore group, pharmacological active, semicarbazone, 1,3 dipolar cycloaddition reaction.

1. Introduction

Many Heterocyclic compounds found wide application in the medicinal chemistry due to their pharmacological and biological activities such as analgesic agent, tranquilizers and neurons transmitters, Amoxycillin is an antibiotic and rantidine as an gastro resistant drug etc. contains a heterocyclic ring as a part of their structure. Heterocycles are synthesized with a focus on studying the physiological effects that these compounds can trigger and the synthetic routes that can providewith greater supply of these compounds than that nature can produce.

There are so many heterocyclic compounds like thiadiazoles, oxadiazoles and triazoles which found to be an adverse biological and pharmacological properties such as antimicrobial, antiviral and insecticidal activities.

The present approach is concerned with the synthesis, characterization of small molecules of medicinal interest due to versatility Spiro - heterocyclic compounds. The reaction of isatin and L-proline with semicarbazone gave the corresponding spiropyrrolidines. Intermolecular 1,3-dipolarcycloaddion reaction of azomethine ylides, generated through decarboxylation route, with various semicarbazone as dipolarophiles has been investigated. A new class of functionalized spiroheterocycles with pyrrolidine moiety has been synthesized. Characterization of the product is carried out by means of various spectral methods.

Isatin and its derivatives have extensively used as an key intermediates in organic synthesis due to their excellent biological and pharmacological activities.

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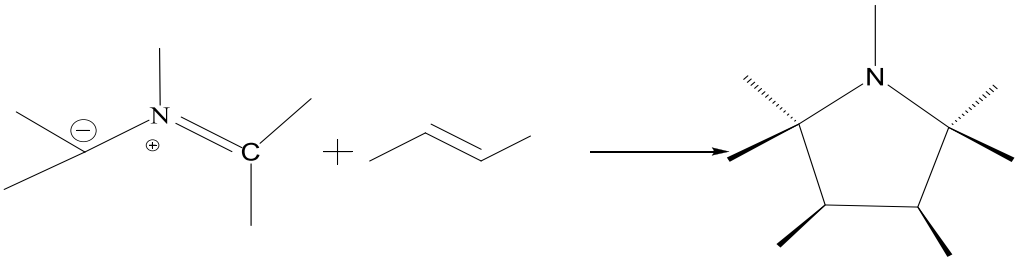
Isatin is also a core constituent of many alkaloids and drug as well as dyes. Isatin is also core constituent of the pesticides. Literature survey reveals that various derivatives of isatin possess diverse activities such as antibacterial, antifungal, antiviral, anti HIV, antimicobacterial,, anticancer, anti-inflammatory and anticonvulsant activity.

Isatin offers an unprecedented opportunity to a chemist to the synthesis of a wide variety of heterocyclic compounds. This is because isatin exists completely in the dicarbonyl form with its 3-carbonyl group being more reactive, than 2-carbonyl group towards nucleophilic reagents. This variation in the reactivity of its two carbonyl groups coupled with the observed, facile opening the ring under the influence of hydroxylic nucleophilic reagents provides additional advantages towards accomplishing the desired synthetic goals using isatins. Besides its versatility in synthesis, the ubiquity of this nucleus in chemical literature is undoubtedly a consequence of the multifarious biological response which its derivatives elicit in combating a variety of body ailments.

The 1,3-Dipolar cycloaddition, also known as Huisgen cycloaddition or Huisgen reaction. This reaction belonging to concerted pericyclic cycloadditions. Rolf Hhuisgen first saw the prospects of varying the 1,3-dipole and its value for synthesis of 5-membered is classic reaction in organic chemistry. The history of 1,3-dipoles goes back to Curtius, who in 1883 discovered diazoacetic ester.

The 1,3-dipolar cycloaddition reaction of azomethine ylides with alkenes leads to the formation of the pyrrolidines. 1,3-dipolar cycloaddition reaction of azomethine ylides from highly substituted heterocyclic compounds.



1 2 Scheme I 3

Azomethine ylides are unstable species which have to be prepared in situ. A number of methods have been developed for the generation of azomethine ylides, such as proton abstraction from imine derivatives of R-amino acids, thermolysis or photolysis of aziridines, and dehydrohalogenation of imonium salts. The reaction of azomethine ylides with alkenes has been investigated from a theoretical point of view inorder to understand the reaction course, selectivity, and influence of Lewis acids on the reaction. The product can be used as new catalyst or serve as important biologically active molecules.

Spiro-cyclic compounds have attracted the attention of organic chemists due to their biologically interesting spiroisocazoline derivatives. Manikandan and his coworkers done their work in the construction of novel unique structural and reactivity pattern. 1, 3-dipolar cycloaddtion offers a convenient route for the construction of five membered heterocyclic compounds. The 1, 3-dipolar cycloaddition reaction has been applied to the synthesis of natural products such as sugar derivatives, β-lactams, aminoacids and alkaloids. Isooxazoline derivatives have been extended to many natural product synthesis and also proved to be an efficient precursor for many synthetic intermediates including γ-amino alcohols, β-hydroxy ketones etc. The high synthetic versatility and the pharmacological importance have prompted to synthesize some spiroheterocyclic derivatives, and also to study their biological applications, the reactions of the versatile 1, 3-dipole nitrile oxide with 9-

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arylidene anthrone have been studied.

S.Kathiravan and his coworkers reported (E)5H-2-(arylidine)-5-phenyl-6,7-di-hydrothiazolo[2,3-b]benzo[h]quinazolines through are giosel-ective 1,3-dipolar cycloaddition reaction with azomethine ylide derived from ninhydrin and sarcosine to give a new class of complex dispiropyrrolidines in good yield. The structures of the synthesized cycloadducts have been elucidated by spectral methods

.T. Augustine and his coworkers reported the cycloaddition reaction of azomethine ylides, generated through decarboxylation, with (E)-3-arylidene-4-chromanones and Chalcones as dipolarophiles. A high degree of regioselectivity has been observed in the synthesis of a new class of functionalized dispiroheterocyclic compounds bearing chromanone, chalcones and acenaphthenequinone framework[18,19]. Spiro-oxindole ring system represents an important class of naturally occurring substances characterised by highly pronounced biological properties. Oxindole derivatives are found to be potent aldose reductase inhibitors(ARI) , which help to treat and prevent diabetic complications arising from elevated levels of sorbitol.

Spiro-cyclic compounds have attracted the attention of organic chemists due to their unique structural and reactivity pattern. 1, 3-dipolar cycloaddtion offers a convenient route for the construction of five membered heterocyclic compounds. The 1, 3-dipolar cycloaddition reaction has been applied to the synthesis of natural products such as sugar derivatives, β-lactams, aminoacids and alkaloids. Isooxazoline derivatives have been extended to many natural product synthesis and also proved to be an efficient precursor for spiropyrrolidines and their application in different field. As a part of our ongoing research program in the area of cycloaddition reaction of azomethine ylides with semicarbazones, we herein report the highly regioselective synthesis of spiro pyrrolidines through 1,3–dipolar cycloaddition methodology. The prepared compounds were many synthetic intermediates including γ-amino alcohols, β-hydroxy ketones etc. The high synthetic versatility and the pharmacological importance have prompted to synthesize some biologically interesting spiroisocazoline derivatives. Manikandan and his coworkers done their work in the construction of novel spiroheterocyclic derivatives, and also to study their biological applications, the reactions of the versatile 1, 3-dipole nitrile oxide with 9-arylidene anthrone have been studied.

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The literature survey shows that some work has been carried out in characterized by spectroscopic techniques and its biological applications like antibacterial studies were carried out.

2. Experimental Section

All chemicals used were of analytical grade, supplied from Sigma-Aldrich and used as received. The first step in this synthesis

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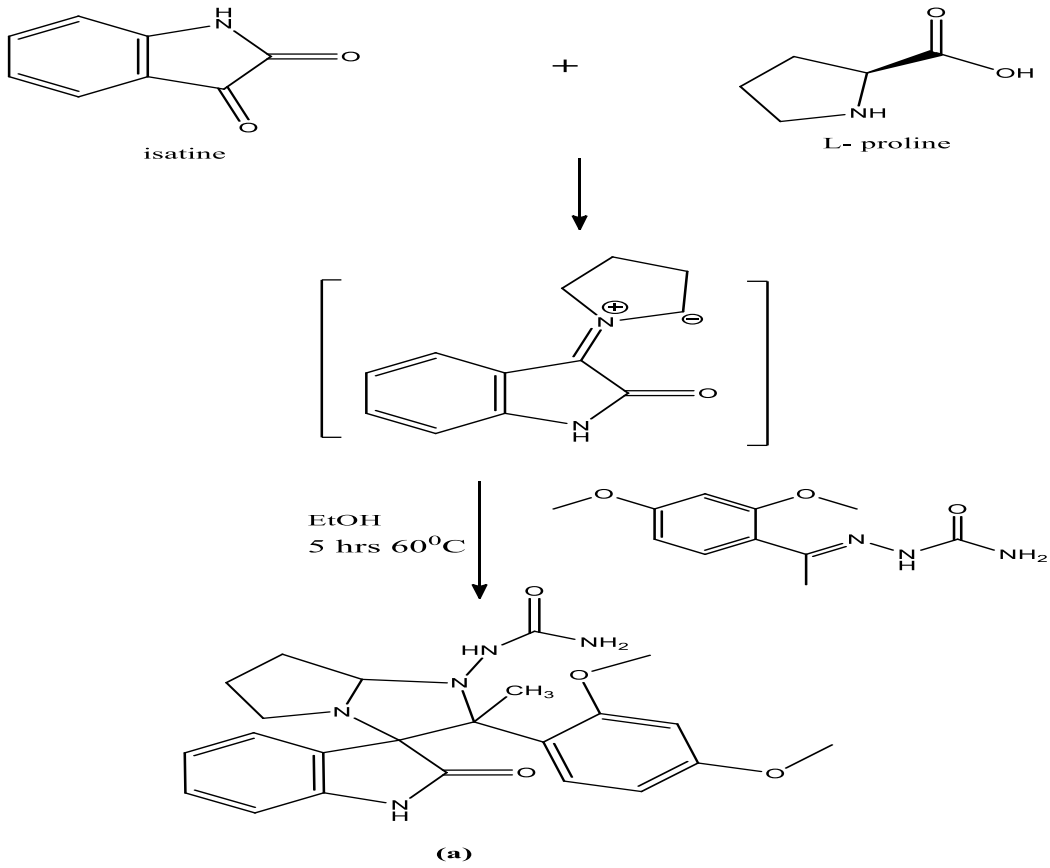
involves nucleophilic addition reaction between acetophenone and semicarbazide hydrochloride using the literature procedure. The second step involves 1,3-Dipolar cycloaddition reaction between formed semicarbazoneand dipolarphiles. The structures of these products were established by physical and spectral methods.

Synthesis of Spiro[5.3']oxidolino(4-methyl(2,4dimethoxyphenyl)hexahydro[pyrrolo[2,3]imidazole]-2-yl]diamide:-

A mixture of isatin(0.147g, 1 mmole), L-proline(0.115g. mmole) and 2-(1-(2,4-dimethoxyphenyl)ethylidene)hydrazinecarboxamide(0.237g,1mmole) in ethanol(40 ml) was refluxed for 5 hours at a temperature of 60°C. After the reaction was over, the reaction mixture was extracted with ethanol and dried; then it was recrystallized using acetone. The melting point and chemical yield are 185°C - 189°C and 80.7% **(a)**.

Scheme II



Scheme 1

Synthesis of spiro[5.3']oxidolino(4-methyl-(2-methoxynaphthalen 1yl)hexahydro [pyrrolo[2,3] imidazole]-2-yl]diamide:

A mixture of isatin (0.147 g, 1 mmole), L-proline (0.115 g. 1 mmole) and 2-(1-(2-methoxynapthalen-1yl)ethylidene)hydrazinecarboxamide (0.257 g, 1 mmole) in ethanol(40 ml) was refluxed for 5 hours at a temperature of 60°C. After the reaction was over, the reaction mixture was extracted with ethanol and dried; then it was recrystallised with acetone. The melting point and chemical yield are 130°C -135°C and 78.%

(b)Synthesis of spiro[5.3']oxidolino(4-methyl-(1-methoxynaphthalen-2-yl)hexa-hydro[pyrrolo[2,3]imidazole]-2-yl]diamide:

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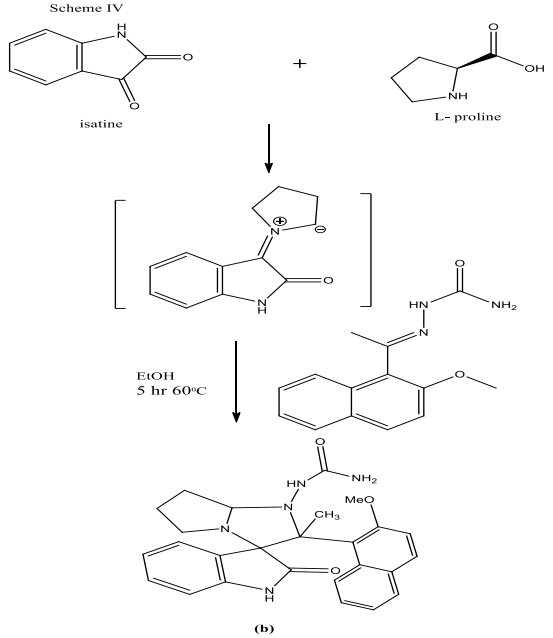
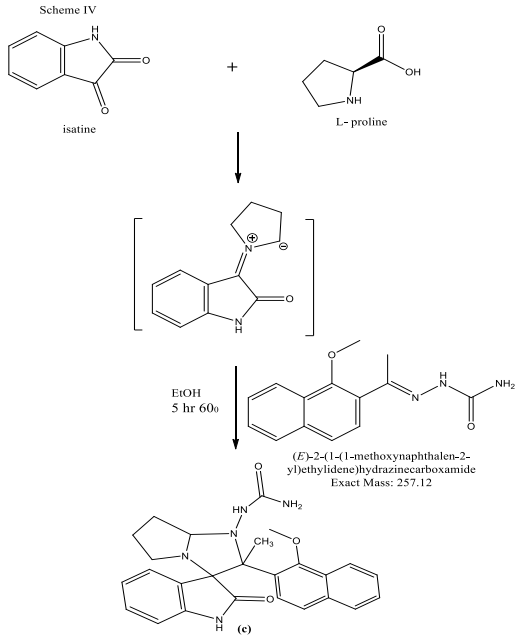
A mixture of isatin (0.147 g, 1 mmole), L-proline (0.115 g. 1 mmole) and 2-(1-(1-methoxynapthalen-2-yl)ethylidene)hydrazinecarboxamide (0.257 g, 1 mmole) in ethanol(40 ml) was refluxed for 5 hours at atemperature of 60°C. After the reaction was over, the reaction mixture was extracted with ethanol and dried; then it was recrystallised with acetone. The melting point and chemical yield are 105°C -111°C and 42%.



Scheme 2



Scheme 3

3. Results and discussion

***Spiro compound (a)*:** IR (KBr): 1609, 1711 cm-1, 1230cm^{-1}1035cm^{-1}; ^{1}H NMR (DMSO/400 MHz): δ 2.16(s,3H), 3.72(s,6H OCH_3)1.25-1.59 (m, 2H), 2.59 (t, -NCH), 6.3-7.5 (m,aromatic), 6.3-9.5 (-NH,-NH2 protons); ^{13}C-NMR (DMSO/400 MHz): δ77.81,151,191,162,14.4, 83

Spiro compound 11: IR (KBr): 1605, 1721 cm-^{1}1230cm^{-1}1035cm^{-1}; 1H NMR (DMSO/400 MHz): δ 2.36 (s,3H), 3.72(s,3H OCH_3) 7.63 (S, -CONH), 3.1(t, -NCH), 6.9-7.58(m,aromatic),6.3-9.5 (-NH,-NH2 protons); 13C-NMR (DMSO/400 MHz): δ 77.81, 155, 195, 165, 13.14,83.

Spiro compound 15: IR (KBr): 1620, 1718 cm^{-1}1230cm^{-1}1035cm^{-1}, 1H- NMR (DMSO/400 MHz): δ 2.56 (s,3H), 7.41 (S, -CONH), 3.72(s,3H OCH_3), 2.56 (t, -NCH), 6.74-7.63 (m,aromatic), 6.9-9.08 (-NH,-NH2 protons); 13C-NMR (DMSO/400 MHz): δ 77.95,152.46, 186, 186, 161, 18.25, 83,

4. Conclusion

From the above synthesized compound, compound (a) get in higher yield than other two compounds. From the literature study it is clear that compounds like (a) shows higher biological and pharmacological activity than compound (b) and (c).

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5. References

1. RamuP.a, Augustine Arul Prasad T.*b, Scholastica Mary Vithiyac and S. Arul Antonyd, Scholar research library(2014, 6(4):30-36)
2. MEENAKSHI SHARMA1*,VATSALASONI1, VANDANA SINGH1 ,IJCPS Vol. 3, No. 5, Sep-Oct 2014(ISSN:2319-6602)
3. Koch, M. A.; Schuffenhauer, A.; Scheck, M.; Wetzel, S.; Casaulta, M.; Odermatt, A.; Ertl, P.; and Waldmann,.H. Proc. Natl. Acad. Sci. U.S.A. 102, 17272-77, (2005)
4. Agarwal A., Sharma M., Agrawal M., and Kishore D., E-Journal of Chemistry, 9(3), 1305-1312, (2012).
5. Manju P., Neeraj K. S., and Priyanka K. K.J., J.Adv.Sci.Res, 2(2), 35-44 (2011).