Indian J.Sci.Res. 13 (1): 126-130, 2017 ISSN: 0976-2876 (Print)
ISSN: 2250-0138 (Online)

SYNTHESIS AND BIOLOGICAL ACTIVITY OF HETEROCYCLIC AZLACTONE AND IMIDAZOLINE DERIVATIVES

RUBY AHMED[1]

Department of Chemistry, Shibli National P.G. College, Azamgarh, Uttar Pradesh, India

ABSTRACT

A series of oxazol-5(4H)-ones were prepared by cyclization , condensation of O-Hydroxy Hippuric acid with various aromatic aldehydes in presence of acetic anhydride and sodium acetate in catalytic amounts. Synthesised compounds were confirmed and characterized by various spectral techniques like IR, HNMR, Mass Spectroscopy and Carbon, Hydrogen and Nitrogen analysis.

KEYWORDS: Hippuric acid, IR, HNMR, AZLACTONE.

The study incorporates the topic AZLACTONE, because it provides a basic skeleton structure and which is also a part of great importance for its drug characteristics. The basic nucleus imidazole, emerges from the drug intermediate azlactone. The azlactone possess oxazolone moiety. Azlactones are known to exhibit antifungal, antibacterial and anti-inflammatory activities. They are also of great importance to produce penicillin type of drug intermediates, and they are also useful to produce synthetic hormonal compounds (Abdallah et.al., 1985 & 1981).

Imidazole is a planar five membered hetrocyclic ring system with three carbon and two nitrogen atoms in 1 and 3 positions. Imidazolones are keto dihydro imidazoles. Imidazolone that is known as oxyimidazoline is a five membered heterocyclic ring system having nitrogen atom in 1 and 3 positions and carbonyl group in 5 position. Oxoimidazoline, which is also known as imidazolinone is reported to exhibit a wide variety of therapeutic activities , such as sedative, hypnotic, central nervous system depressant etc. imidazolinone derivatives have alse been reported to possess antihistaminic, antihypertensive, and antiparkinsonian activities (Ahmed and Mokhtar 1985 & Borrellet.al., 2004).

The 4-arylidene-2-phenyl oxazol-5(4H)-ones thus prepared are converted into new imidazolinone derivatives by reaction with aryl amines. All the past observation and essential role of heterocyclic azlactone derivatives and imidazolinone derivatives, in certain biological reactions encouraged, to explore various derivatives of this heterocyclic compound (Cornforth et.al., 1949 & EL-Nawawy and EL-Kheshin 1960).

The search for a new chemical structure as a biocide ,is to decrease or prevent the environmental pollution. To raise the success rate of the search, more and more design and optimization procedure such as – structure activity relationship are adopted (Evans, 1965 & Finny, 1971).

The imidazolinone herbicides were discovered in 1970's by scientists at American Cyanide Company. The discovery of imidazolinone herbicide has led to the development of various class of herbicides. Because of their versatility, low toxicity and environmental safety, these herbicides are used in many different crops and play a vital role in production of food and fibre throughout the world. The imidazolinone represent one of the new class of herbicides that will lead ahead. Due to the importance of imidazolinone in weed control in agriculture , a great deal of research has been conducted on the efficacy and potential use of these compounds to weed control (Ian and Alan, 2014 & Kadous et.al., 1979).

The derivatives of imidazolinone sulfonamide general structure has attracted the attention of many scientists to find out biologically and significantly active derivatives. Different biological effects of these compounds were studied as herbicides during 1980s. four new herbicidal alasses emerged that were potent, selective, broad-spectrum inhibitors of plant growth . The herbicide groups are sulphonyl ureas, imidazolinones, triazolopyrimidine, and pyrimidinyl thio benzoate, yet all share the same site of action- namely acetoacetate synthase (ALS), a key enzyme in biosynthesis of branched chain amino acids, leucine, isoleucine and valine. They are able to control a very wide spectrum of troublesome annual grass and broad leaf weeds with very low dose (Koscelny et.al. & Kumar et.al., 1996).

Furthermore, formulations have proved to be both foliar and soil active, with very low toxicity to

[1]Corresponding author

mammals. Chlorsulfuran, tribenuron-methyl and imazamethabenzen give selective weed control in crops. sulfonamide is an active herbicidal group against grassy broad leaf weeds in low dose. Synthesis of new imidazolinone sulfonamide derivatives may give herbicidal activity against grassy and broad leaf weeds in different field crops (Mayo and Rochester, 2015 & Morsy et.al., 1981).

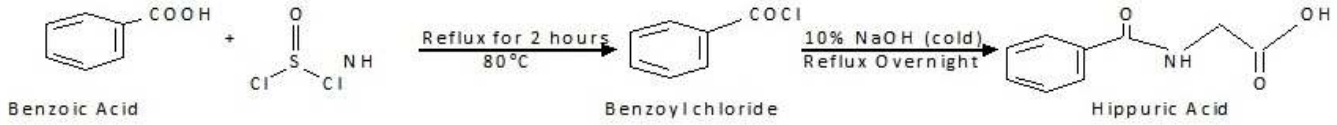
All the past observations and essential role of heterocyclic azlactone derivatives and imidazolinone derivatives ,in certain biological reactions , prompt us to synthesise various heterocyclic derivatives (Montazeri, 1995 & Pawan et.al., 2012).

MATERIALS AND METHODS

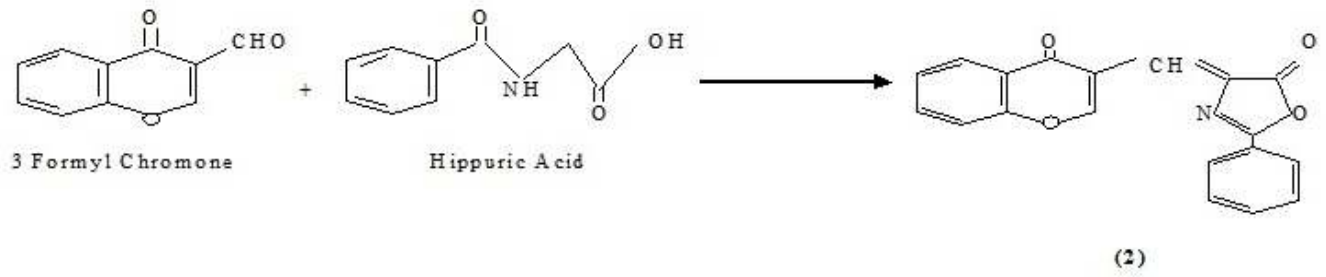
General Method for the Synthesis of Compound 2

A mixture of N-benzylglycine (Hippuric acid) (0.01 ml) and 3-formylchrome (compound 1) (0.01ml) in acetic anhydride (15ml) and in presence of freshly fused sodium acetate (0.5gm) were heated and refluxed on water bath for 1 hour. After cooling, the resulting oxazolone was washed , first with 50%aqueous alcohol then with ether and recrystallized from alcohol-acetone.

The synthesised compound will be analysed by IR spectra, HNMR spectroscopy and mass spectrometry. Elemental analysis too was carried out to get the percentage composition of carbon, hydrogen, nitrogen and oxygen.



Synthesis of Hippuric Acid



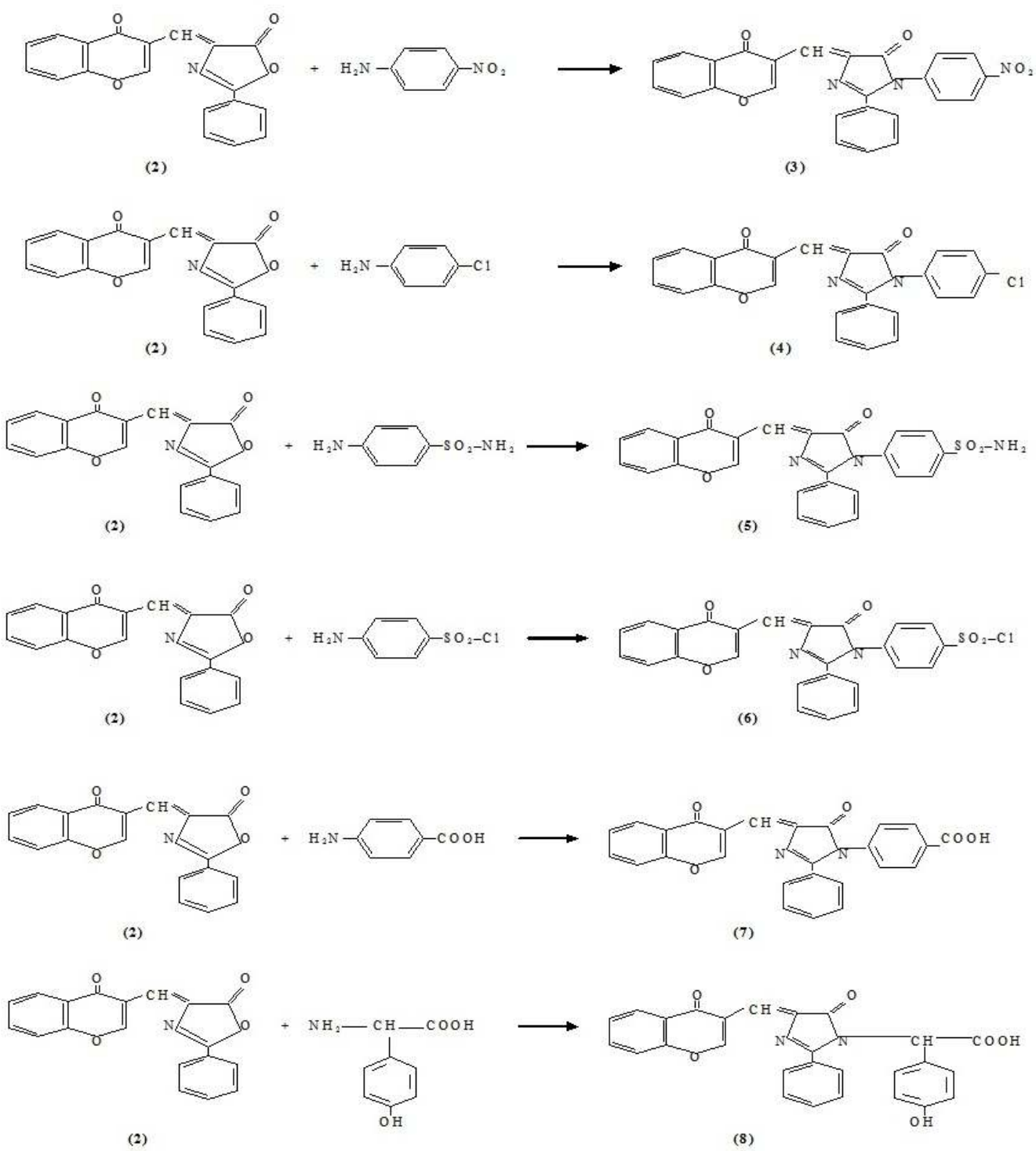
Synthesis of Compound (2)

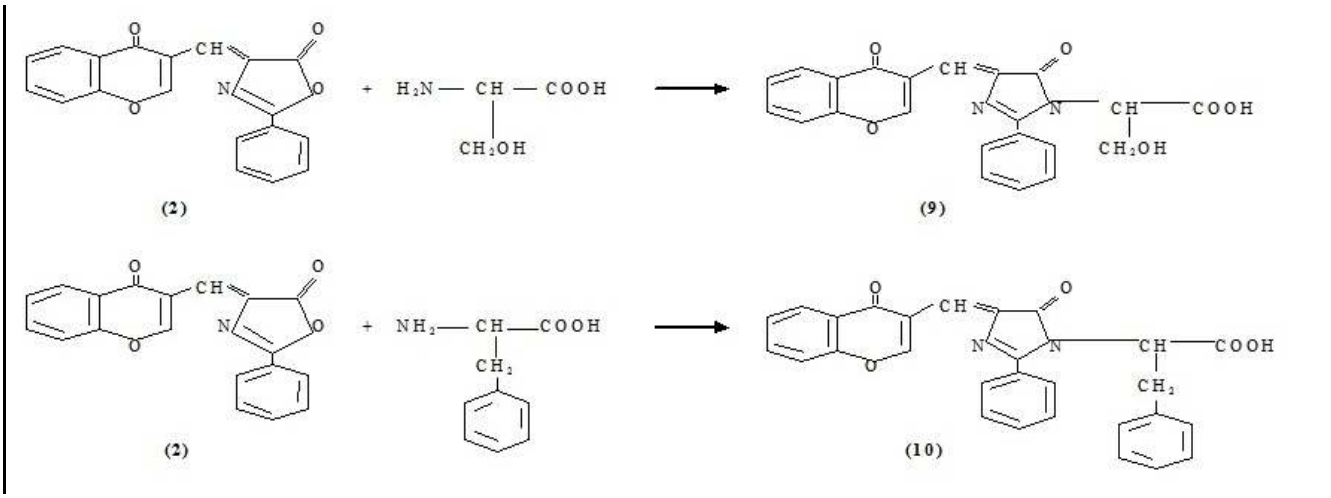
General Method for the Synthesis of Compounds (3-16)

Amixture of compound 2 (0.01ml) and feshly prepared sodium acetate (0.8 gm) and aryl amine of amino acid esters and substituted hydrazine (0.01 ml) in glacial acetic acid (10 ml) were refluxed for 2 hours. After cooling , the mixture, its yield was calculated. The compound was analysed for its chemical nature , structure and elemental constituents.

Likewise , the whole series of compounds (3 – 16) were synthesised, and analysed.

Once the derivatives (compounds 3 -16) are prepared, they underwent biological screening. Their biological activity as a herbicide, fungicide or bactericide was tested on various strains of micro organism.


(2)
(3)
(4)
(5)
(6)
(7)
(8)



Synthesis of Various Derivatives of Compound (2)

BIOLOGICAL ACTIVITY

The antimicrobial activity of the newly synthesised compounds was compared with known antibiotics like Ampicillin, Penicilline and Tetracycline. Antimicrobial activity was studied against gram positive bacteria (Staphylococcus aureus) and gram negative bacteria (Escherichia coli). Antimicrobial screening was carried out by cup-plate method at a concentration of 50µgm/ml in solvent DMF. Zone of inhibition was measured in mm. Antimicrobial activity of the synthesised compounds was compared with standard drugs Ampicillin, Penniciline and Tetracycline at the same concentration.

CONCLUSION

Reaction of 3 formylchromone with hippuric acid to form compound 2, namely 1, 3-oxazol-5(4H)-one ring as starting material for synthesis of compounds 3-10.

This is aimed to incorporate their heterocyclic biologically active moieties into new heterocyclic systems. This research work was in continuation to previous work, where chromone and its derivatives were synthesised and their structure analysed by infra red spectroscopy, NMR spectroscopy, mass spectroscopy, and elemental analysis. In this work new five membered nitrogen heterocyclic derivatives of chromone were synthesised. The carbonyl group of chromone is reactive and has considerable significance in biological activity too. It is reactive towards nucleophiles and thus enables the synthesis of a wide variety of heterocyclic compounds.

These affect a wide variety of enzymatic reactions. Commonly occuring reactions include oxidative, reductive, hydrolytic and conjugative alteration of the target molecule.

Once synthesised , these compounds proved as effective antimicrobial agents.

REFERENCES

Abdallah E.A.M, Morsy F.A., Saleh M.S. and Kadous E. A., 1985. Relation between chemical chemical structure andInsecticidal activity. Part VI. Effect of phenylarsonic and their N-oryl-thiomronium salts against mosquite Larvae.6th Arab Pesticide Conf. Tanta Univ.

Abdallah E.A.M, Mokhtar H.M. and Mosry F. A., 1981. Relation between chemical structure and insecticidalactivity part V. Biological activity of 2-methyl-6-styrylpyridiue dicarboxylic acid and its derivatives. Prec.4th Arab pesticide Conf. Tanta Univ. III A: 215-245

Ahmed A.H. and Mokhtar H., 1985. Structure activity relationships “Fungitoxicity and phytotoxicity of 3-athoxy carbonyl-5-stytyl pyrazole derivatives. Alex. J. Agric. Res., **30**(3):1583-1592.

Borrell J. I., Schuler E., Teixidó J. and Michelotti E. L., 2004. Design and synthesis of two pyrazole libraries based on o-hydroxyacetophenones. Mol Divers., **8**(2):147-57.

Cornforth J. W., Clarke H. T., Johnson J. R., and Robinson R., 1949. Chemistry of Penicillin.

PrincetonUniversity Press, Princeton, New Jercey. 778.

EL-Nawawy A. S. and EL-Kheshin S. A., 1960. The relationbetween chemical structure and biological activity. Part1.The Principle of covalent electrovalent organic molecule. Alex. J. Agric. Research, **891**: 277.

Evans V. R. M., 1965. The Chemistry of the Antibiotics used in Medicine. Angewandte Chemie., **78**(14):724.

Finny D.J., 1971. Probit Analysis, third ed. Cambridge University Press, London. 318P.Gulidov, A. M. and E.D. Narezhnaga. 1994. Herbicidesin winter wheat. Zashchita Rastennii (Moskva), **8**:18.

Ian C. and Alan M. J., 2014. Diversity-OrientedSynthetic Strategies Applied to Cancer Chemical Biologyand Drug Discovery, Molecules, **19**(11):17221-17255.

Kadous E. A., EL-Shazly A.M. and EL-Din A.T., 1979.Structure Fungicidal activity relationship of someorgano-arsonates. Proc. 3rd Arab Pesticides Conf. Tanta Univ., **2**:640-654.

Koscelny I.A. and Peeper T.F., 1996. Herbicides impregnatedinto granular Fertilizer carriers for broadleaf weed scontrol in winter wheat-Weed Technology, **10**: 531-534.

Koscelny I.A., Peeper T.F. and Krenzar E.G., 1996. Sulfonylurea herbicides affect hard red wheat forage and grainyield. Weed Technology, **10**: 531-534.

Kumar L., Singh D. and Pahuja S.S., 1996. Evaluation of triben uron for control broad leaf weeds in wheat.Haryana Agric. Univ. J. of Res., **26**(3): 199-201.

Mayo C. and Rochester M.N., 2015. Howard Walter Florey-Production of Penicillin Mayo Clin Proc., **90**(6):63-64.

Morsy F. A., Soliman S. M. S. and EL-Abdallah A. M., 1981. Relation between chemical structure andinsecticidal activity Part I. Insecticidal properties of Naryl thiouronium salts of o-tolylarsonate. Proc. 4th Arab pesticide Conf. Tanta Univ., **3**(1): 197-205.

Montazeri M., 1995. Interaction of tribenuron and graminicides in wheat. Procudings of an International British crop protection conference, Brighton, **2**:753-756.

Pawan K, Sureash K., Rana S.S. and Navell C., 2012. Combination of Pinoxadin with other herbicides againstComplex weed flora in wheat. Hndian J. of Weed Science, **44**(4): 225.

Punia S.S., Yadav D., Yadav A., Malik R.S. and PolMaler Y., 2008. Bioeffecacy and phytotoxicity of herbicidesMPH-206 for Control of Complex weed flora in wheat. Indian J. of weed Science, **40**(3-4): 176-179.

Rakesh N. M. and Desai K. R., 2005. Studies on Synthesis of Some Novel Heterocyclic Azlactone Derivatives and Imidazolinone Derivatives and theirantimicrobial activity. E-Journal of Chemistry, **2**(1):4-51.

Sabra F.S., Kassem F.A. and Khalifa M., 1999. Effectiveness of herbicidal treatments against weeds in wheat and their action on yield and yield components. J. pest. Control and Environ. Sci., **7**(3): 103 - 121.

Savjani J. K. and Gajjar A.K., 2011. Pharmaceutical importance and synthetic strategies for imidazolidine-2-thione and imidazole-2-thione derivatives. Pak J Biol Sci., **14**(24):1076-1089.

Thomas J. M. and Cline J. F., 1985. Modification of the neubauer technique to assess toxicity of hazardous chemicals in soils. Environmental Toxicology and Chemistry, **4**(2): 201–207.

Yutilov Y.M, 2005. Imidazopyridines: 1- and 3-Deazapurines. Advances in Heterocyclic Chemistry **89**:159-270.