DESIGN AND SYNTHESIS OF NOVEL HETEROCYCLIC COMPOUNDS FROM 1,2 & 1,3 - DIKETONE COMPOUNDS AND INVESTIGATES THEIR ANTIMICROBIAL ACTIVITIES

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Abstract
In the present work a some new heterocyclic compound has been prepared by using 1,2 & 1,3-diketones with a amine group present compounds. Since the unsymmetrical 1,2, and 1,3-diketone moiety may have up to three nucleophilic and two electrophilic centers with negligible reactivity differences, selectively performing chemical transformations with substrate at a single centers appears to be very difficult. Because of their closely spaced, highly reactive carbonyl groups, 1,2- diketone and 1,3- diketone molecules have a variety of biological functions.
Keywords: *1, 2 & 1, 3-diketones, 2-Mercaptobenzimidazole,1-Amino-2-naphthol-4-sulfonic acid,2- aminothiophenol, acetamide, ortho phenylenediamine,antimicrobial activity*

Introduction

The important class of compounds known as heterocycles is present in alkaloids, vitamins, hormones, and a variety of natural goods. Furthermore, a wide variety of medications and physiologically active compounds contain them. Most heterocycles are also used in combinatorial, supramolecular, industrial, agricultural, and medical fields. One of the most important intermediates used in synthetic organic synthesis is β-dicarbonyl molecules, whose importance cannot be emphasized.Chemistry throughout this discipline's history. β-dicarbonyl molecule chemistry is strongly related to Michael, Claisen, and Knoevenagel's areas of organic chemistry. In contemporary solid phase chemistry, combinatorial chemistry, pharmaceuticals, and stereo- and enantioselective synthesis, 1,3-dicarbonyl molecules are widely utilized. They are also employed in the C-C formation process.

Nowadays, organic compounds with various heterocyclic ring systems have garnered a lot of interest in chemical and medical research, which may be related to their many therapeutic uses. Benzimidazoles are a class of heterocyclic nitrogen compounds that has both pharmacological and biological properties. Organic chemists have created synthetic heterocycles that are utilized as agrochemicals, dyes, and medications. They are also becoming more and more significant in a variety of other fields, such as adhesives, molecular engineering, and polymers. Because of their diverse variety of biological actions, oxazine derivatives are a significant class of heterocycles that have garnered a lot of synthetic interest. As a heterocyclic, oxazine formally, a chemical can be created by substituting nitrogen and oxygen for carbon (and hydrogen) atoms in benzene and its reduction products. Oxazine derivatives have shown themselves to be useful synthetic intermediaries in recent years. They also exhibit significant biological activity, including sedative, analgesic, antipyretic, and anticonvulsant, antitumor, antimalarial, and antibacterial properties. Drug resistance development is a significant issue nowadays, and creating new classes of chemicals is required to address this issue.

All live cells' metabolism depends on heterocyclic molecules, and the majority of nitrogen-containing fused heterocyclic compounds with five members are physiologically active. Imidazo[2,1-b]thiazoles, imidazo[1,2-c]thiazoles, and their derivatives are among the nitrogen and sulfur-containing heteroaromatic compounds that are known to be physiologically active and have a significant position in medicinal chemistry. These medicinal substances have the potential to effectively treat a wide range of illnesses and Imidazothiazole core structure.

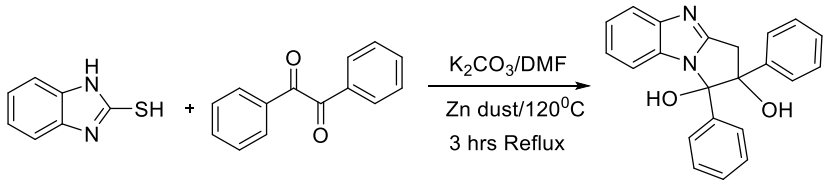
The significance of β-dicarbonyl compounds as one of the most essential intermediates utilised in synthetic organic synthesis cannot be overstated.chemistry throughout the history of this field of study. The fields of organic chemistry that are closely related to the chemistry of β -dicarbonyl molecules include Michael, Claisen, and Knoevenagel. Nowadays, 1,3-dicarbonyl compounds are widely used in modern stereo- and enantioselective synthesis, in medicine, combinatorial chemistry, and solid phase chemistry. They are also utilised in the formation of C-C bonds synthesis and heterocycles, and as flexible intermediates and synthons in multistep and complex organic synthesis.

METHODS OF SYTHESIS OF HETEROCYLIC COMPOUNDS

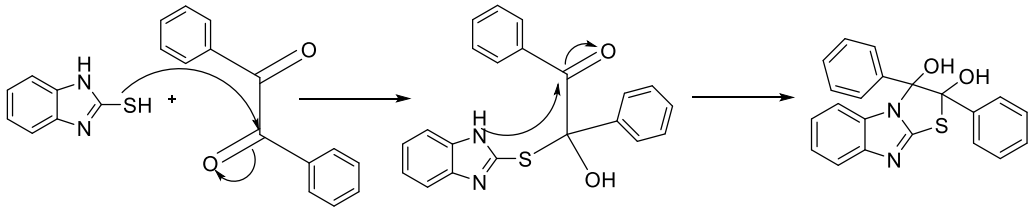
S -1

Synthesis of 2,3-diphenyl-2,3-dihydrobenzo[4,5] imidazo [2,1-b] thiazole- 2,3-diol.

In reaction of 1.05gm of benzil (0.005 mol), 0.75 gm of 2-Mercaptobenzimidazole (0.005 mol), were taken in 100 ml round bottom flask with 15ml DMF in presence K_2CO_3 as a base & Zn dust was added as a catalyst keep on reflux for about 3hr, the reaction mixture poured in crushed ice then solid product is formed ,recrystallization the product by ethyl alcohol and checking a TLC in 5:5 EtOAc /n-hexane.



Mechanism:-



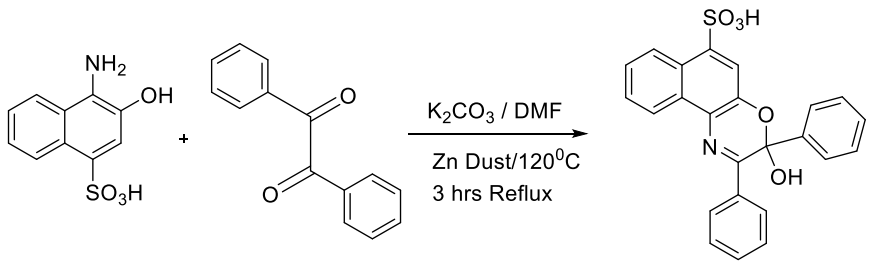
Spectral Analysis:-

Yellowish solid,$C_{21}H_{16}N_2O_2S$ mp- 144-147^{0}C , yield 70%,^{1}H NMR (400 MHz,$CDCl_3$),δ 7.29 – 7.97 (Ar-H), 3.33 (-SCH3), 5.32 (-OH), IR (cm^{-1})- 3726 (-OH) , 3000 (Ar-C=C-H) , 2100 (C=N) 680 (C-S), 1500 (C=C), 1400 (C-C)

S-2

Synthesis of 3-hydroxy-2,3-diphenyl-3H-naptho[2,1-b][1,4]oxazine-6- sulfonic acid.

1.05 gm of benzil (0.005 mol), 1.15 gm of 1-Amino-2-naphthol-4-sulfonic Acid (0.005 mol),were taken in 100 ml RBF with 15 ml DMF in presence K_2CO_3 base & Zn dust was added as a catalyst keep on reflux ,3hr poured the mixture in crushed ice, then acidified with conc.H_2SO_4 , recrystallization , take TLC in 5:5(EtOAc /n-hexane)



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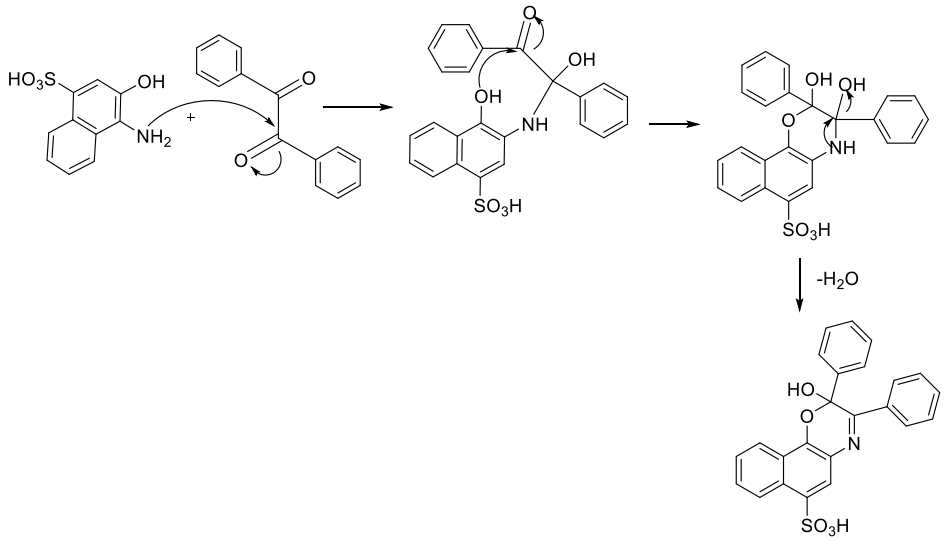


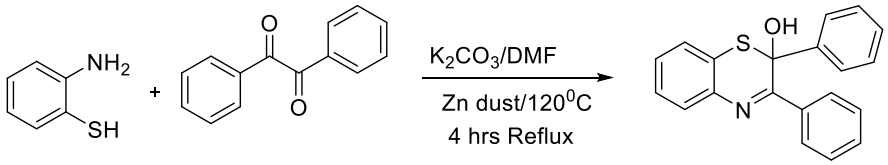
Spectral Analysis:-

black solid, mp- 155-157^{0}C, $C_{24}H_{17}O_5NS$, yield 56%,^{1}H NMR (400 MHz,$CDCl_3$) 7.26 – 7.98 (Ar-H),5.47(-OH),IR(cm^{-1})-3600 (-OH), 3060 (Ar-C=C-H), 1400(-C-C-) 1500(-C=C-),1209(-C-O), 2150(-C=N)

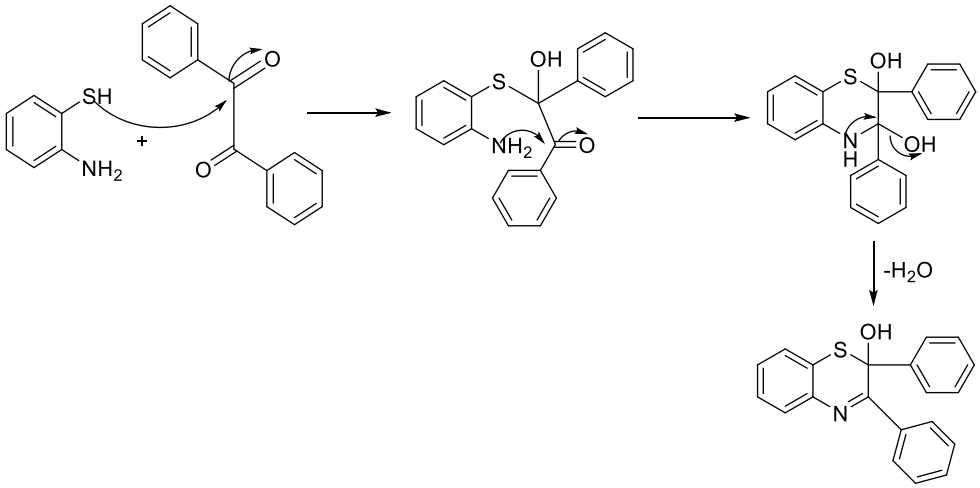
S-3

Synthesis of 2, 3-diphenyl-2H-benzo[b] [1, 4] thiazin-2-ol.

Take 1.05 g of benzil (0.005 mol), 0.6 g of 2-aminothiophenol (0.005 mol), and place them in 100 ml of RBF with 15 ml of DMF in the presence of anhydrous K_2CO_3 as a base. Add Zn dast a catalyst and let the mixture reflux for 4 hours. Pour the mixture into crushed ice, acidify it with diluted HCL, recrystallize it with ethanol, and take TLC in a solvent EtOAc and n-hexane in a ratio 5:5



Mechanism:-



Spectral Analysis:-

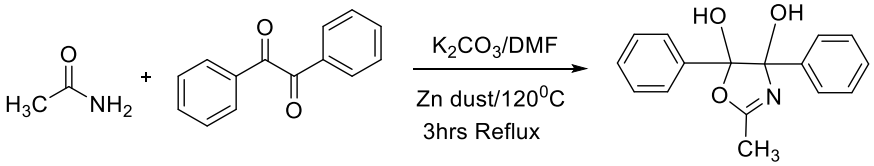
black solid, mp- 98-100^{0}C, $C_{20}H_{15}ONS$, yield 60%,^{1}H NMR (400 MHz,$CDCl_3$) 7.26-7.91 (Ar-H), 5.35(OH),IR(cm^{-1}) 3500(-OH),2200(-C=N),3000(-C=CH-),1577(-C=C-),1448(Ar-C-C),679(-C-S).

S-4

Synthesis of 2-methyl-4, 5-diphenyl-4, 5-dihydrooxazole-4, 5-diol.

Take 1.05 g of benzil (0.005 mol), 0.3 g of acetamide (0.005 mol), and place them in 100 ml of RBF with 15 ml of DMF in the presence of anhydrous K_2CO_3 as a base. Add Zn dust as a catalyst and let the mixture

reflux for 3 hours. Pour the mixture into crushed ice, acidify it with diluted HCL, recrystallize it with ethanol, and take TLC in a solvent EtOAc and n-hexane in a ratio 5:5



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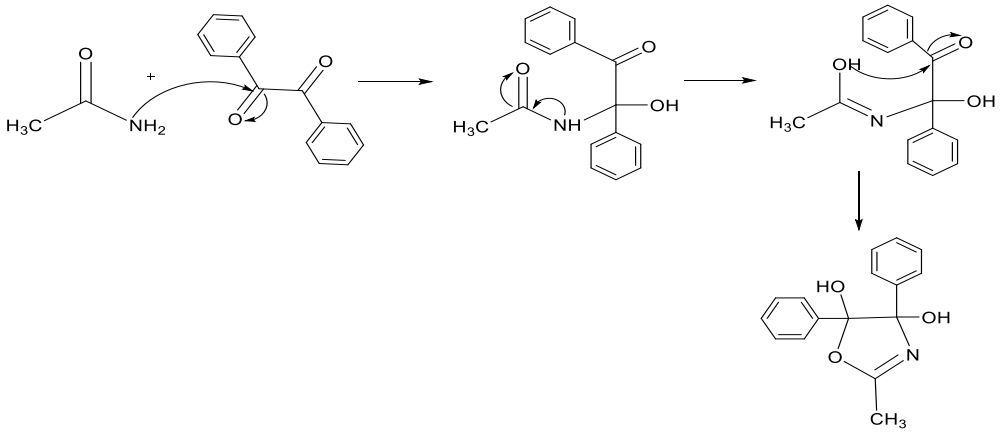


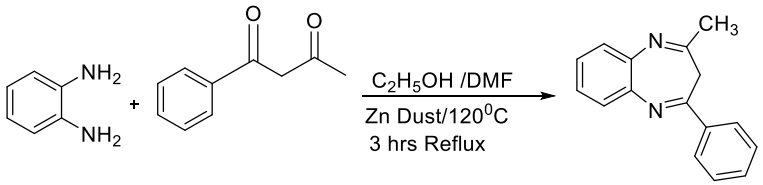
Spectral Analysis:-

Yellow solid, mp- 92-95^{0}C, $C_{16}H_{15}O_3N$, yield 70%, ^{1}H NMR(DMSO d_6 δppm) 7.26 -7.56 (Ar-H) , 1.25 (-CH_3) IR(cm^{-1}) δ 3600(-OH),3036(-C=CH-),2900(-C-CH-), 2200(-C=N),1172(-C-O).

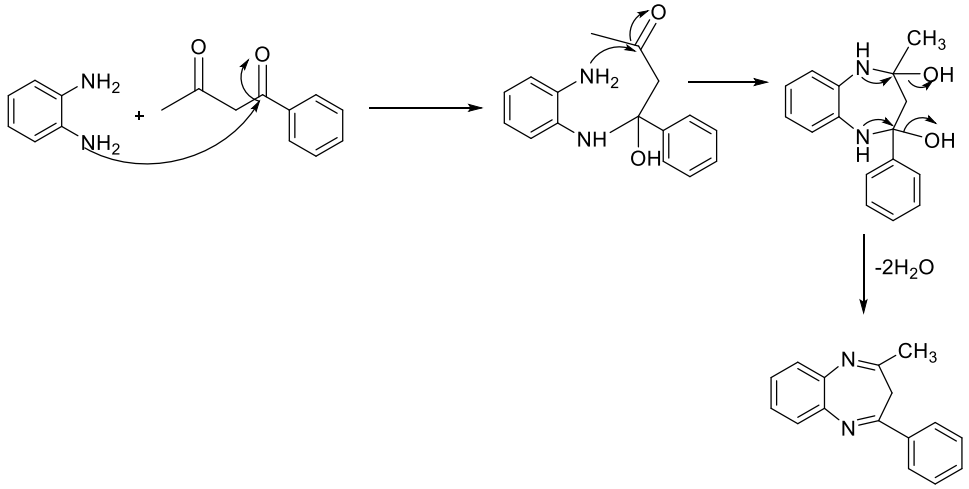
S-5

Synthesis of 2-methyl-4-phenyl-3H-1,5-benzodiazepine.

Take 0.95gm of ortho phenylenediamine (0.005 mol), 0.81 benzoylacetone (0.005 mol) were taken in 100 ml RBF with 15 ml EtOH in presence K_2CO_3 base & Zn dust was added as a catalyst keep on reflux ,3hr poured the mixture in crushed ice, then acidified with conc.H_2SO_4 , recrystallization , take TLC in 5:5(EtOAc /n-hexane)



Mechanism:-



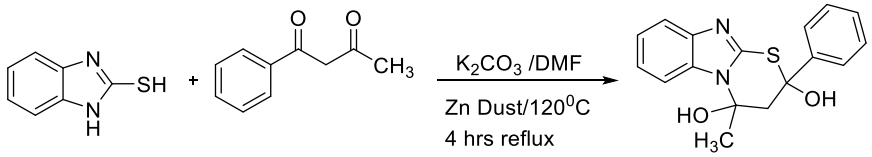
Spectral Analysis:-

Yellow solid, mp- 125-128^{0}C, $C_{15}H_{13}N_2$, yield 65%, IR(cm^{-1}) δ 2929(Ar -C=C-H), 2127(C=N) ,1500(C=C), 3730(-CH_3)

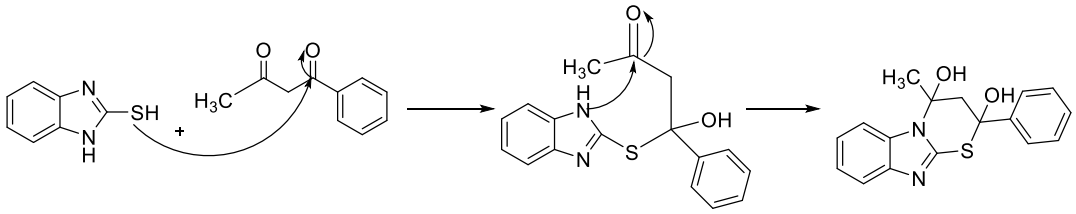
S-6

Synthesis of 4-methyl-2-phenyl-3,4-dihydro-2H-benzo[4,5]imidazo[2,1-b][1,3]thiazine-2,4-diol.

Take 0.8 g of benzoylacetone (0.005mol), 0.7 g of 2- mercaptobenzimidazole (0.005mol), and place them in 100 ml of RBF with 15 ml of DMF in the presence of anhydrous K_2CO_3 as a base. Add Zn dust as a catalyst and let the mixture reflux for 4 hours. Pour the mixture into crushed ice, acidify it with diluted HCL, recrystallize it with ethanol, and take TLC in a solvent EtOAc and n-hexane in a ratio 5:5



Mechanism:-



Spectral Analysis:-

Brown solid, mp- 110-113^{0}C, $C_{17}H_{16}O_2N_2S$, yield 45%, IR(cm^{-1}) δ 3637(OH),3789(CH),3000(C=CH),2358(C=N),1502(C=C),1442(C-C),630(C-S).

Microbial Activity:-

Sr. No.	Compounds	Gram positive Zone of Inhibition in (mm)	Gram negative Zone of Inhibition in (mm)
		S. aureus	***E.Coli***
1	S-1	15	15
2	S-2	NA	NA
3	S-3	15	NA
4	S-4	NA	14
5	S-5	17	NA
6	S-6	NA	NA
7	**Streptomycin**	20	22

- The antimicrobial activity of the synthesized compounds (Scheme-1, Scheme-3, Scheme-4, and Scheme-5) was evaluated by the **agar diffusion method** against Gram-positive *Staphylococcus aureus* and Gram-negative *Escherichia coli*. The antibacterial efficacy was assessed by measuring the **zone of inhibition (mm)** and compared with the standard antibiotic **streptomycin**.
- Scheme-1 exhibited **moderate antibacterial activity** against both *S. aureus* and *E. coli*, showing inhibition zones of 15 mm each, indicating a **broad-spectrum nature** of this compound.
- Scheme-3 showed activity only against *S. aureus* with a zone of inhibition of 15 mm, while no activity was observed against *E. coli*, suggesting **selective Gram-positive antibacterial activity**.
- Scheme-4 demonstrated antibacterial activity exclusively against *E. coli* with a zone of inhibition of 14 mm and showed no effect against *S. aureus*, indicating **selectivity toward Gram-negative bacteria**. Scheme-5 exhibited the **highest activity among the synthesized compounds against** *S. aureus* with a zone of inhibition of 17 mm, but it was inactive against *E. coli*.
- Scheme-2 and Scheme-6 no activity observed against *S.aureus* and *E.coli* .
- The standard drug showed significantly higher zones of inhibition (20 mm against *S. aureus* and 22 mm against *E. coli*), confirming its **superior broad-spectrum antibacterial efficacy**. Although the synthesized compounds displayed lower activity compared to streptomycin, some compounds demonstrated **promising selective antibacterial properties**, which may be further optimized for enhanced antimicrobial potential.

Conclusion

Heterocyclic compounds are essential in drug discovery due to their diverse biological activities. 1,2 or 1,3 diketones are versatile starting materials for the synthesis of various heterocycles. The synthesis of heterocyclic compounds from 1,2 or 1,3 diketones involves multiple steps and transformations. Cyclization reactions of 1,2 & 1,3-diketones with different reagents such as sulfur , nitrogen, or oxygen

nucleophiles result in the generation of heterocyclic scaffolds.Heterocyclic compounds obtained from 1,2 & 1,3-diketones exhibit a wide range of ring sizes and substitution patterns, influencing their physicochemical properties. The synthesis of new heterocyclic compounds from 1,2 & 1,3 diketones is a promising area of research in organic chemistry. By understanding the reaction mechanisms and optimizing synthetic protocols, novel heterocyclic compounds with potential pharmacological activities can be developed. Continued research in this field will contribute to the discovery of new drugs and therapeutic agents.The synthesis of new heterocyclic compounds using based catalysts and 1,2- and 1,3-di ketones is a rapidly evolving field, with a strong focus on the development of green and sustainable methodologies. The use of phase transfer catalysis, supported metal catalysts, and N- Heterocyclic Carbenes (NHC) catalysis, along with the exploration of green and sustainable methods, has been instrumental in the creation of complex heterocyclic structures with high atom utilization and minimal waste. Some synthesized compounds show **moderate to selective antibacterial activity**.**Scheme-1** demonstrates **broad-spectrum potential**.**Scheme-5** is most effective against **Gram-positive bacteria**. Compared to streptomycin, the synthesized compounds exhibit **moderate antibacterial potency**, but certain compounds show promising selective activity and may serve as lead molecules for further optimization.

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