Synthesis and characterization of some novel benzothiazole derivatives.

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Abstract- A series of some novel benzothiazole derivatives were synthesized from the 2-(4-aminophenyl) benzothiazol-5-ol, which was synthesized by the Jacobson method using Lawesson's reagent. Acyl and amide derivative were synthesized by catalyzed condensation method, named as 2- chloro-N-(4-(4-(5-hydroxybenzothiazole-2yl)phenyl)acetamide (P101), N-(4-(5- hydroxy benzothiazole-2-yl)phenyl)-4-methyl benzamide (P102), N-(4-(5-hydroxy benzothiazole-2-yl)phenyl) benzamide (P103), 4-((4-(5-hydroxybenzothiazol-2-yl)phenyl)amino)-4-oxobut-2 enoicacid (P104), 1-(4-(5-hydroxybenzo thiazole -2-yl)phenyl)-1N-Pyrrole-2,5-dione(P105), 2-(diphenyl amino)-N-(4-(5-hydroxy benzothiazol-2yl) phenyl) acetamide(P106), 3-(4-(5-hydroxy benzothiazol-2-yl)phenyl)-2-iminothiazolidin-4-one (P107),5-benzylidene-3-(4-(5-hydroxybenzothiazol-2-yl) phenyl)-2-imino thiazolidin-4-one (P108), 4-((4-(5-hydroxy benzothiazol-2-yl)phenyl)diazenyl) phenyl4methoxybenzoate (P109).The structures of the compounds were confirmed by NMR and IR spectral data.

Key words-Benzothiazole, synthesized, Lawesson's reagent.

1.Introduction-The best of biologically active agrochemicals and pharmaceuticals used in industrial application extending from cosmectics, data storage, reprography and plastics are heterocyclic in nature. Heterocycles make an enormously significant class of compounds. In the study of organic chemistry heterocycles have occupied a major and magnificent research area.[1-3]

Heterocycles are also useful compounds for their synthetic value as synthetic intermediate, protecting group, chiral auxillaries,organic reagents in organic synthesis.[4-6] Therfore, new methods developed to synthesized heterocycles have been paid too much attention.The alkaloids have a main cluster of naturally occurring heterocyclic compounds. Alkaloids such as Ergotamine: indole based and Cinchonine : quinolone based exhibited antimigraine and antimalarial activities respectively, they contain basic N-atoms. A triazole based alkaloid: Posaconazole has also been used as antifungal drug.[7-10]

Heterocyclic compounds can be segregated into heteroaromatic and hetero alicyclic types. In general, the chemistry of hetero alicyclic compounds is identical to that of their aliphatic parallel such as ether, amide, amines, thioether etc. Their properties are especially impacted by the occurrence of ring strain.[11-13]

The compounds enclosing benzothiazole fraction are of excessive attention and have been broadly used in pharmaceutical chemistry and agricultural division. In calculation, benzothiazole forms an imperative pharmacophore in herbicidal, fungicidal and insecticidal agents.[14,15]

The Aim of the present study is to synthesize some benzothiazole derivatives from 2-(4-aminophenyl)benzothiazol-5-ol as starting compound in which NH2 and endocylic N functions are suitably situated to enable reaction with common electrophillic agents to form a variety of fused heterocyclic derivatives.

2. EXPERIMENTAL

2.1 Synthesis of 2-(4-aminophenyl)benzothiazol-5-ol (1) [16]

It was synthesized in four steps as follows:

Step I: Preparation of [(4-hydroxyphenyl)-4-azaneyl) (4-nitrophen)] methanone (a)

To a solution of p-amino phenol and p- nitrobenzoylchloride,pyridine (40 ml) was added followed by the addition of toluene (30 ml) and the mixture was refluxed for 5hrsThe product obtained was recrystallized from alcohol. Yield: 60%, m.p- 150^{0}C

Step II: Preparation of N-(4-hydroxyphenyl)-4nitrobenzo thioamide (b)

To an ethanolic solution of compound a, Lawesson's reagent [2,4-Bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide] (0.6 molar eq) was added. The mixture was heated for 2hrs after which it was dried and recrystallised from alcohol.

Yield: 65%, m.p :160^{0}C

Step III: Preparation of 2-(4-nitrophenyl)benzothiazol-6-ol (c)

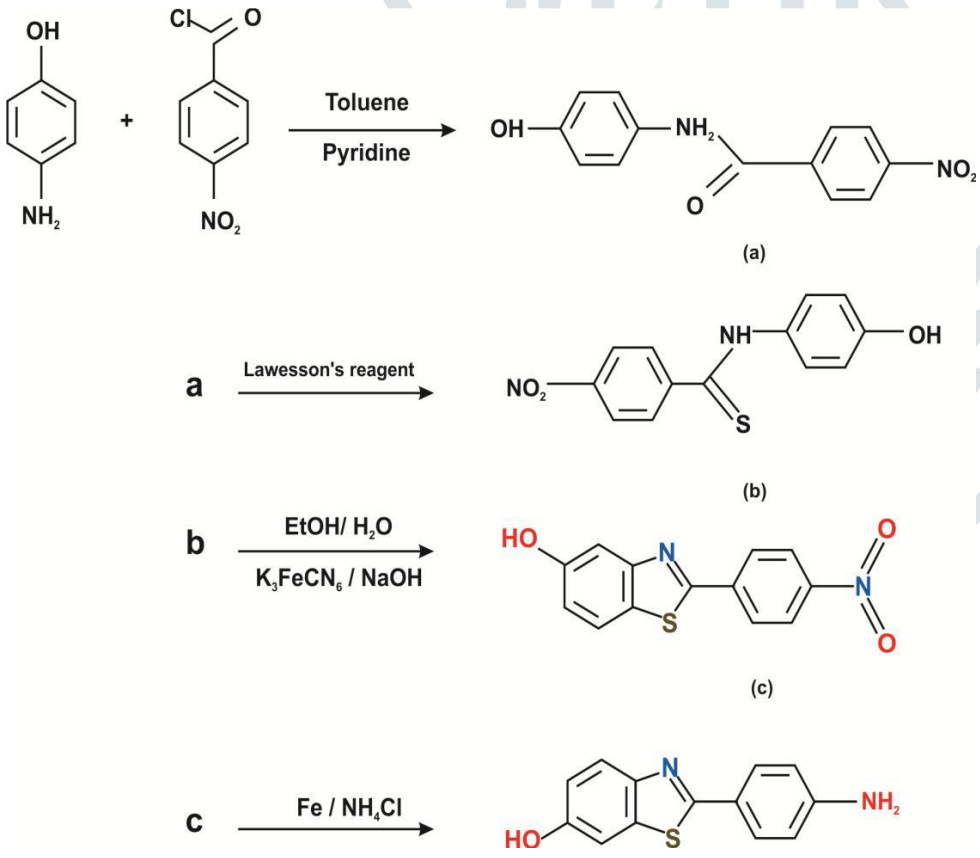
To a benzene solution of compound b,0.5 ml ethanol and 1ml NaOH was added. The freshly prepared aqueous potassium ferricynide(2-3 molar equivalent) was added to a cooled solution in an ice bath and stirred at room temperature. Then the mixture was neutralized with 1M HCl. The organic layer was removed and residue was washed with water and recrystallised from alcohol.

Yield: 50 % ,m.p-120^{0}C

Step IV: Preparation of 2-(4-aminophenyl)benzothiazol-5-ol (1)

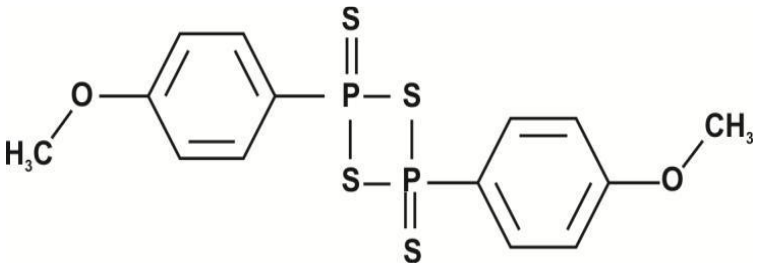
To an ethanolic solution of compound c, 10 ml water,4 g iron powder and 7g ammonium chloride was added. The mixture was stirred at 850C for one hr. cooled at room temp. then filtered and washed with water and recrystallised from alcohol.

Yield: 65%,m.p-148^{0}C.



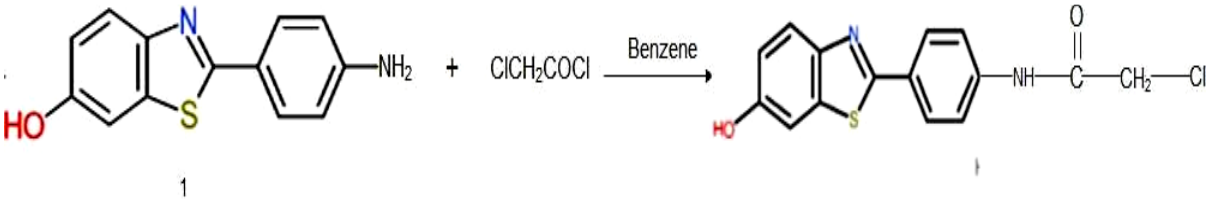
Synthesis of 2-(4-aminophenyl)benzothiazol-5-ol (1)

Lawesson's Reagent



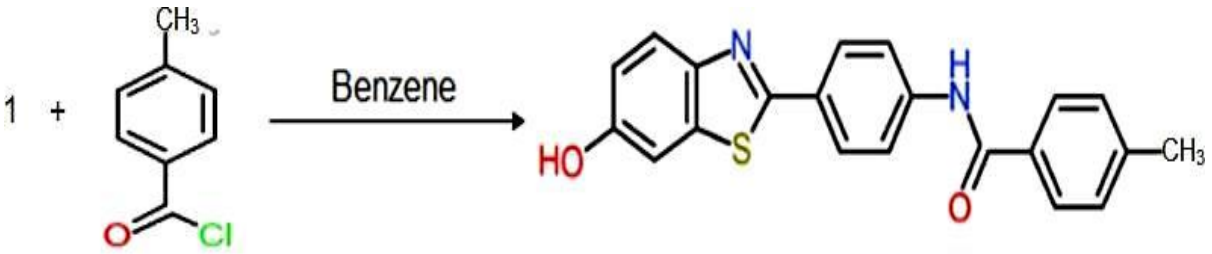
2.2 Synthesis of Acyl derivatives of Benzothiazole (P101-P103) [17]

A solution of the reactant (chloroacetyl chloride/4-methyl benzoyl chloride/benzoyl chloride) in benzene(100ml) was gradually added to solution of 1, the starting compound (0.0055mole) in dry benzene(100ml).The reaction mixture was refluxed on a water bath for 2hrs.The product obtained was washed with 5% sodium bicarbonate solution.Finally again washed with water,dried and recrystallized from alcohol.



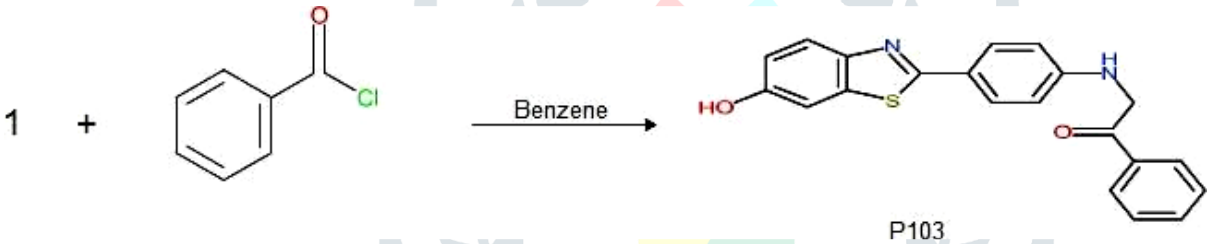
1 P101

2-chloro-N-[4-(4-(5-hydroxybenzothiazole -2yl)phenyl]acetamide(P101)



P102

N-[4-(5-hydroxy benzothiazole-2-yl)phenyl]-4-methyl benzamide(P102)

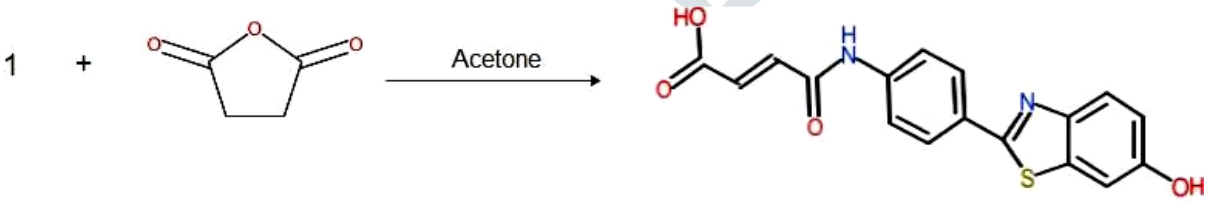


P103

N-[4-(5-hydroxy benzothiazole-2-yl)phenyl] benzamide(P103)

2.3 Synthesis of 4- [(4-(5-hydroxybenzothiazol-2-yl)phenyl)amino]-4 oxobut-2-enoicacid(P104) [18]

The solution of maleic anhydride (0.01mol) in dry acetone (80ml) was prepared and added to a solution of 1 in dry acetone (30ml) The mixture was cooled in ice and was stirred for 1 hr. The product (P104) obtained was filtered,washed,dried and recrystallised from alcohol.

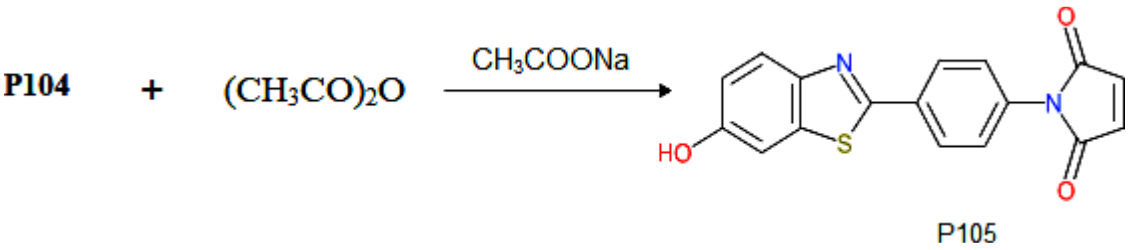


P104

4-((4-(5-hydroxybenzothiazol-2-yl)phenyl)amino)-4-oxobut-2-enoicacid(P104)

2.4 Synthesis of 1-[4-(5-hydroxybenzothiazole-2-yl)phenyl]-1N pyrrole- 2, 5- dione(P105) [19]

A mixture of P104 and acetic anhydride (20ml) was added to sodium acetate solution and refluxed for 2hrs. The homogeneous solution was cooled to room temperature, then poured into excess cold water with vigorous stirring. The product (P105) obtained was filtered, washed with water, dried and finally recrystallised from alcohol.

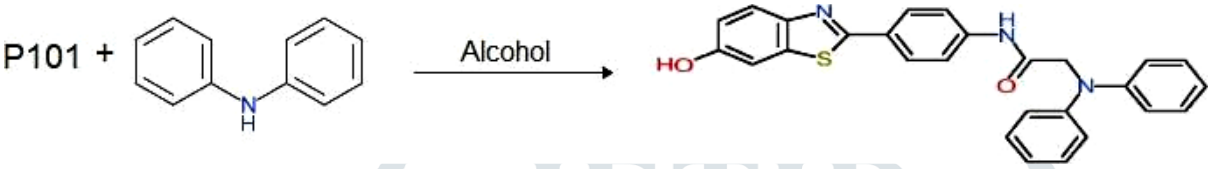


P105

1-(4-(5-hydroxy benzothiazole-2-yl)phenyl)-1N-Pyrrole-2,5-dione(P105)

2.5 Synthesis of 2-(diphenylamino)-N-[4-(5-hydroxy benzo thiazol-2-yl) phenyl]acetamide(P106) [20]

The solution of P101(0.01 mol)) was prepared in absolute alcohol (25ml) into which diphenyl amine(0.01 mol) was added. The mixture was refluxed on water bath for 4 hrs. The product(P106) obtained was filtered, dried and recrystallized from alcohol.



P106

2-(diphenyl amino)-N-(4-(5-hydroxy benzo thiazol 2yl)phenyl)acetamide (P106)

3. RESULTS AND DISCUSSIONS

3.1Proposed mechanism for the synthesis of P101- P103

The acylation of benzothiazole involves the condensation of 1 with acyl chlorides giving P101-P103.

3.2Proposed mechanism for the synthesis of P104

This reaction involves the addition of amino group of 1 to carbonyl group of maleic anhydride resulting in latter's ring opening and giving 4 (4-(5-hydroxybenzothiazol-2-yl)phenyl)amino)-4-oxobut-2-enoicacid(P104).

3.3 Proposed mechanism for the synthesis of P105

The conversion of P104 to P105 was achieved by acetylating P104 with sodium acetate and acetic anhydride which(acetyl drivatives) then undergoes cyclization to give 1-(4-(5-hydroxy benzothiazole-2-yl)phenyl)-1N-Pyrrole-2,5-dione(P105)

3.4 Proposed mechanism for the synthesis of P106

This is a simple condensation between P101 and diphenylamine involving nucleophilic attack by secondary amine on the electrophilic carbon of P101 to give 2-(diphenylamino)-N-(4-(5-hydroxybenzothiazol-2-yl)phenyl)acetamide (P106)

3.5 The Spectral data of the synthesized compounds are as followes-

Spectral data of 2-chloro-N-[4-(4-(5-hydroxybenzothiazole- 2yl)phenyl]acetamide (P101)

IR (KBr) Cm^{-1}	3479 (O–H), 3387 (N–H), 1659 (C=O) etc.
^{1}HNMR (400MHzDMSO) ppm	8.32 (O–H),8.16N–H), 6.6–7.7 (Ar–H),2.53 (CH_2)
^{13}CNMR (400MHzDMSO) ppm	162.92,154.05,148.78,140.63,130.02,128.97114.85,79.12,78.47,40.11,39.70,39.07,38.86

Spectral data of N-[4-(5-hydroxy benzothiazole-2-yl)phenyl]-4-methyl benzamide (P102)

IR (KBr) Cm^{-1}	3487 (N–H) ,3155 (C–H) etc.
^{1}HNMR (400MHzDMSO) ppm	9.30 (O–H) 6.7734,–8.3264 (Ar–H) , 5.2 (N–H) 3.48 (CH_3)
^{13}CNMR (400MHzDMSO) ppm	155.44,134.61,129.07,127.65 ,125.91,122.41,118.66,108.65,79.25,78.60,40.11,39.90,39.27,39.06,38.85

Spectral data of N-[4-(5-hydroxy benzothiazole-2-yl)phenyl] benzamide (P103)

IR (KBr) Cm^{-1}	3500 (O–H) ,3377 (N–H) etc.
^{1}HNMR (400MHzDMSO) ppm	9.57 (O–H) , 6.8–7.83 (Ar–H) , 5.9 (N–H)
^{13}CNMR (400MHzDMSO) ppm	163.01,154.08,148.87,140.77,130.49,128.87,123.30,122.30,115.51,114.93

Specral data of 4-[(4-(5-hydroxy benzothiazole-2-yl)phenyl)amino]-4- oxobut-2-enoic acid (P104)

IR (KBr) Cm^{-1}	3409 (O–H phenol) , 3069 (N–H) , 1732 (C=Oacid) ,1703 (C=O amide)
^{1}HNMR (400MHzDMSO) ppm	10.43 (COOH) ,9.57 (Ph–OH) , 6.08–8.32 (Ar– H) 5.3235 (N–H) 4.83 (CH=CH)
^{13}CNMR (400MHzDMSO) ppm	163.01,154.08,148.87,140.77,130.49,130.08,128.87,123.30,123.15,115.51,114.93,79.03,78.70,78.37,40.17,39.96, 39.13,38.92

Spectral data of 1-[4-(5-hydroxy benzothiazole-2-yl)phenyl]-1N- Pyrrole-2,5-dione (P105)

IR (KBr) Cm^{-1}	3726.81 (O–H) , 1739.06 (C=O) etc.
^{1}HNMR (400MHz DMSO) ppm	8.21 (O–H) ,7.0–7.2 (Ar–H) ,6.8 (CH=CH)
^{13}CNMR (400MHz DMSO) ppm	155.44,134.61,129.07,127.43,125.91,122.41,118.66,108.65,79.25,79.13,78.60,40.11, 39.69,39.27,39.06,38.85

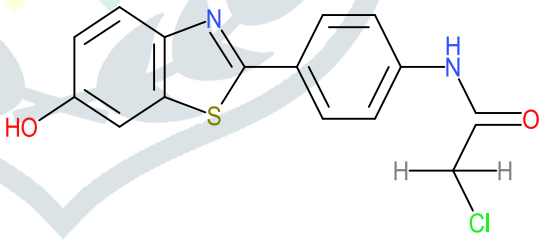
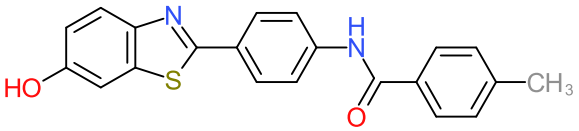
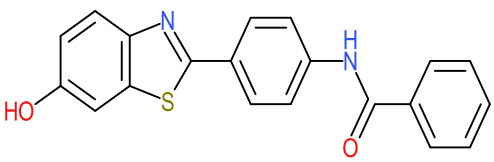
Spectral data of 2-(diphenyl amino)-N-(4-(5-hydroxy benzo thiazol-2- yl)phenyl)acetamide (P106)

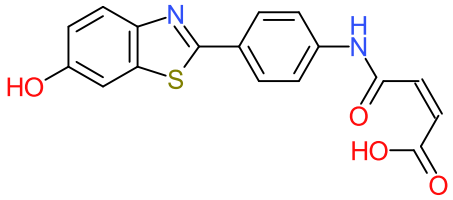
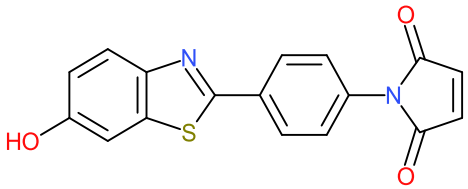
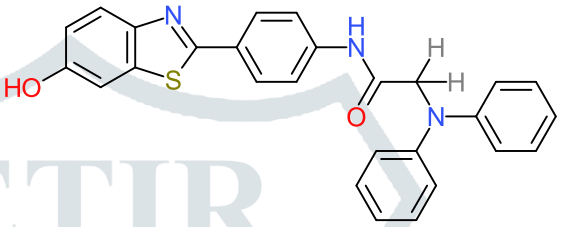
IR (KBr) Cm^{-1}	3239 (OH/NH), 3030 (Ar–CH), 1740 (C=O) etc.
^{1}HNMR (400MHzDMSO) Ppm	8.27 (Ph–OH),6.55–7.72 (Ar –H),2.5066 (CH2)
^{13}CNMR (400MHzDMSO) ppm	167.57,165.91,163.02,160.76,159.76,154.12,152.87,151.56,148.87,140.78,136.90,128,10,123,16,119.43,115.67,113.14,112.59,112.54

4. CONCLUSSION

The present work describes convenient methods for the synthesis of Benzothiazole derivatives. Benzothiazole derivatives were synthesized from the 2-(4-aminophenyl) benzothiazol-5-ol, which was synthesized by the Jacobson method using Lawesson's reagent. six compounds (P101-P106) of acyl and amide derivative were synthesized by catalyzed condensation method, named as 2- chloro-N-(4-(4-(5-hydroxybenzothiazole-2yl)phenyl)acetamide (P101), N-(4-(5- hydroxy benzothiazole-2-yl)phenyl)-4-methyl benzamide (P102), N-(4-(5-hydroxy benzothiazole-2-yl)phenyl) benzamide (P103), 4-((4-(5-hydroxybenzothiazol-2-yl)phenyl)amino)-4-oxobut-2 enoicacid (P104), 1-(4-(5-hydroxybenzo thiazole -2-yl)phenyl)-1N-Pyrrole-2,5-dione(P105), 2-(diphenyl amino)-N-(4-(5-hydroxy benzothiazol-2yl) phenyl) acetamide(P106).

Table : Summary of the synthesized compounds.

Product code	Structure
P101	
P102	
P103	

Product code	Structure
P104	
P105	
P106	

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