Available online at www.pelagiaresearchlibrary.com

Pelagia Research Library

Der Chemica Sinica, 2015, 6(3):59-63

Pelagia Research Library

ISSN: 0976-8505
CODEN (USA) CSHIA5

Synthesis, structural study and biological evaluation of 1,3-thiazine

Reshal Deshmukh

Department of Chemistry, Shivaji Science College, Congress Nagar, Nagpur(MS), India

---

ABSTRACT

The acid base catalysed aldol condensation of 2-hydroxy acetophenone with substituted benzaldehyde and anisaldehyde furnish substituted chalcone which were later treated with diphenyl thiourea and dinitro diphenyl thiourea in ethanol in presence of aqueous potassium hydroxide solution.The reaction mixture was refluxed for 3 hours ,cooled diluted with water and acidified with 1:1 HCl afforded substituted 1,3- Thiazines.

Keywords: Synthesis 1, 3-Thiazine, Condensation, Ring transformation, Antimicrobial, Insecticidal activity.

INTRODUCTION

The multifaceted chemical potential of 1, 3-thiazine- a six membered motif/species containing nitrogen and sulphur in the ring has led to unabated research in their synthetic methodologies. This paper summarizes various methods viz. condensation, cyclo-addition, ring transformations etc. to procure 1,3- thiazines and their derivatives along with biological activities viz. pharmacological and agrochemical etc. Synthetic heterocyclic compounds especially containing heteroatom N, S, O have enormous potential, primarily as agrochemicals, drugs etc. Thiazine a heterocyclic compound having four carbon atoms and one nitrogen and sulphur atom at varied positions in the six membered ring are known to exhibit various kinds of biological activities such as Ca^{2+} antagonist ,blood platelet aggregation inhibitors[**3]** and antipsychotic[**4]** ,antiviral[**5]** , antibacterial[**6]** and antihypertensive agent. In the view of this observation and extension of earlier work, thiazine derivatives have been prepared.

MATERIALS AND METHODS

Section -A

Preparation of Acetophenone:

The 2-Hydroxy-5-chloroacetophenone (IIa) was prepared by Fries migration of p-chlorophenol acetate (Ia) in presence of $AlCl_3$, mp. 55^oC

Preparation of 2-Hydroxy- 3-bromo-5-chloroacetophenone (IIb):

The 2-Hydroxy- 3-bromo-5-chloroacetophenone (IIb) was prepared by the bromination of acetophenone (IIa) with bromine in acetic acid mp. 90^0C.

Section -B

Preparation of Chalcones:

Acetophenone (IIa-d) on condensation with aldehydes gave corresponding chalcones. The following chalcones were prepared.

Condensation with Anisaldehyde:

2-Hydroxy- 3-bromo-5-chloro-4-methoxychalcone (IIIa) mp. 172^{0}C

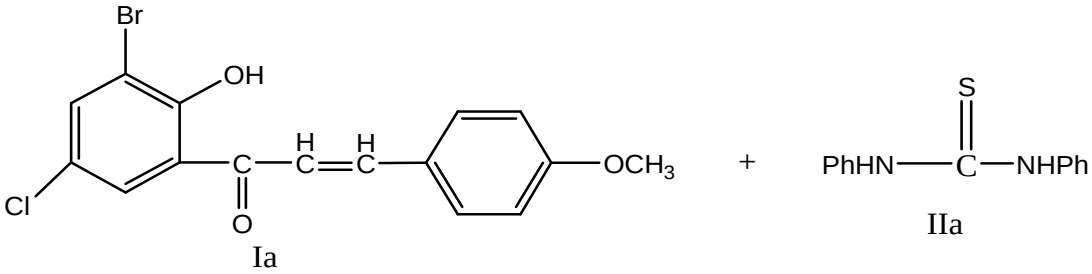
Condensation with Benzaldehyde:

2-Hydroxy- 3-bromo-5-chloro chalcone (IIIb). mp 124^{0}C

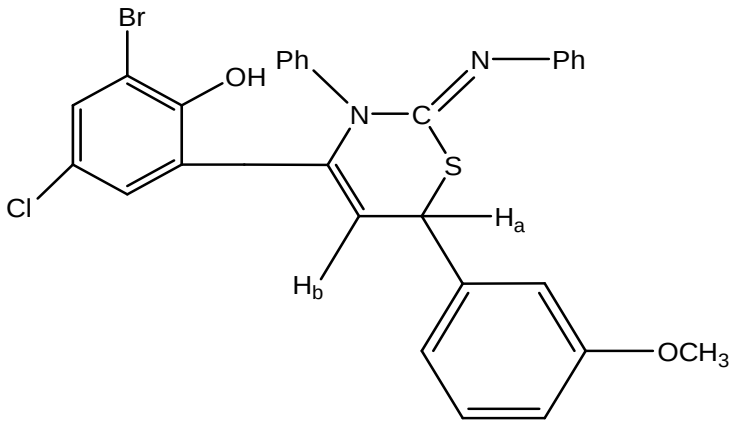
Section C

1.Preparation of 4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-(4-anisylphenyl)-2-imino-6-H-2,3-diphenyl-1,3-thiazine.(IIIa)

A mixture of 2-Hydroxy- 3-bromo-5-chloro-chalcone (IIIa) (0.01mole) , diphenyl thiourea (IIa)(0.02mole) and aqueous potassium hydroxide (0,02mole) in ethanol (30ml) was rerluxed for about three hours. It was then diluted with water and acidified by 1:1 dil HCl. A solid obtained was crystallized from ethanol to get the product 4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-(4-anisylphenyl)-2-imino-6-H-2,3-diphenyl-1,3-thiazine.(IIIa) mp. 158^{0}C, yield 68%



Ia IIa



IIIa

The following 1,3-Thiazines were prepared by extending the above method as listed in Table-1

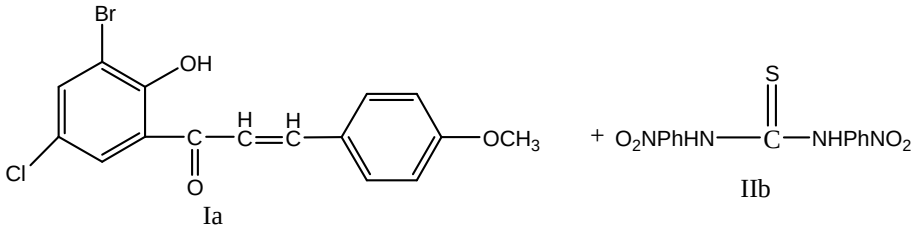
1. 4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-(4-anisylphenyl)-2-imino-6-H- 2,3- diphenyl-1,3-thiazine**.(IIIa)**
2. 4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-phenyl-2-imino-6-H-2,3- diphenyl- 1,3- thiazine**.(IIIb)**
3. 4-(2-hydroxy-5-chlorophenyl)-6- (4-anisylphenyl)-2-imino-6-H-2,3- . diphenyl- 1,3-thiazine**.(IIIc)**
4. 4-(2-hydroxy-5-chlorophenyl)-6- phenyl-2-imino-6-H-2,3-diphenyl-1,3- thiazine**.(IIId)**

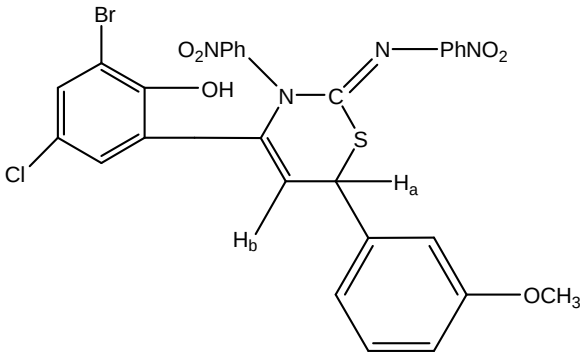
Table-1

Sr.no	Chalcone	Thiourea	1,3-Thiazine	Mp^{0}C
1.	2-Hydroxy-3-bromo- 5-chloro-4-anisylchalcone (Ib)	Diphenyl thiourea(IIa)	4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-(4-anisylphenyl)-2-imino-6-H-2,3-diphenyl-1,3-thiazine.**(IIIa)**	158
2.	2-Hydroxy-3-bromo-5-chlorochalcone**(Ib)**	*Diphenyl* thiourea(IIa)	4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-phenyl-2-imino-6-H-2,3-diphenyl-1,3-thiazine.**(IIIb)**	179
3.	2-Hydroxy- 5-chloro-4-anisylchalcone **(Ic)**	Diphenyl thiourea(IIa)	4-(2-hydroxy-5-chlorophenyl)-6- (4-anisylphenyl)-2-imino-6-H-2,3-diphenyl-1,3- thiazine.**(IIIc)**	196
4.	2-Hydroxy- 5-chlorochalcone **(Id)**	Diphenyl thiourea(IIa)	4-(2-hydroxy-5-chlorophenyl)-6- phenyl-2-imino-6-H-2,3-diphenyl-1,3-thiazine.**(IIId)**	228

2 .Preparation of 4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-(4-anisylphenyl)-2-imino-6-H-2,3-dinitro-phenyl-1,3-thiazine.(IIIe)

A mixture of 2-Hydroxy- 3-bromo-5-chloro-chalcone (III) (0.01mole) , dinitro diphenyl thiourea (0.02mole) and aqueous potassium hydroxide (0,02mole) in ethanol (30ml) was rerluxed for about three hours. It was then diluted with water and acidified by 1:1 dil HCl. Asolid obtained was crystallized from ethanol to get the product 4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-2-imino-6-H-2,3-dinitrodiphenyl-1,3-thiazine.(IIIe) mp. 157^{0}C, yield 68%





IIIe

The following 1,3-Thiazines were prepared by extending the above method as listed in Table-II

1. 4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-(4-anisylphenyl)-2-imino-6-H-2,3-dinitro-phenyl-1,3- thiazine.(IIIe)
2 4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-phenyl-2-imino-6-H-2,3-dinitro-phenyl-1,3-thiazine.(IIIf)
3. 4-(2-hydroxy-5-chlorophenyl)-6-(4-anisylphenyl) -2-imino-6-H-2,3-.dinitrophenyl-1,3-thiazine.(IIIg)
4. 4-(2-hydroxy-5-chlorophenyl)-6- phenyl-2-imino-6-H-2,3-dinitrophenyl-1,3-. thiazine.(IIIh)

Table-II

Sr.no	Chalcone	Thiourea	1,3-Thiazine	Mp^{0}C
1	2-Hydroxy-3-bromo- 5-chloro-4-anisylchalcone (Ia)	Dinitrophenyl thiourea(IIb)	4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-(4-anisylphenyl)-2-imino-6-H-2,3-dinitro-phenyl-1,3-thiazine**.(IIIe)**	157
2	2-Hydroxy-3-bromo-5-chlorochalcone(Ib)	Dinitrophenyl thiourea(IIb)	4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-phenyl-2-imino-6-H-2,3-dinitro-phenyl-1,3-thiazine**.(IIIf)**	131
3	2-Hydroxy- 5-chloro-4-anisylchalcone **(Ic)**	Dinitrophenyl thiourea(IIb)	4-(2-hydroxy-5-chlorophenyl)-6-(4-anisylphenyl)- 2-imino-6-H-2,3-dinitrophenyl-1,3-thiazine**.(IIIg)**	99
	2-Hydroxy- 5-chlorochalcone (Id	Dinitrophenyl thiourea(IIb)	4-(2-hydroxy-5-chlorophenyl)-6- phenyl-2-imino-6-H-2,3-dinitrophenyl-1,3-thiazine**.(IIIh)**	149

RESULTS AND DISCUSSION

I) ***Synthesis of 4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-(4-anisylphenyl)-2-imino-6-H-2,3-diphenyl-1,3-thiazine.(IIIa)***

1,3- Thiazines were synthesized by dissolving substituted chalcone (Ia) (chloro,bromo, nitro) in diphenyl thiourea (IIa) in presence of aqueous potassium hydroxide in 30ml ethanol .The reaction mixture was refluxed for about 3hours .It was then diluted with water and acidified by 1:1dilute HCl.Asolid obtained was crystallized from ethanol to get the product 4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-(4-anisylphenyl)-2-imino-6-H-2,3-diphenyl-1,3-thiazine.(IIIa)

1.The compound (IIIa) is reddish yellow coloured crystalline solid mp179^0
2.It gives violet colouration with neutral $FeCl_3$ solution.
3.It gives deep blue colouration with concH_2SO_4 solution showing the absence of
4.Purity of the compound was tested by TLC
- C –CH = CH- linkage.
5 The I.R and NMR spectra of the compound (IIIa)

Literature value cm-1	Observsd value	Assignment
3600-3000	3400-3200	-NH stretching
1700-1580	1620	-OH stretching
1620-1550	1585	>C=N stretching
1300-900	1268	-C-H stretching
780-650	720	C-Cl stretching
750-550	650	C-Br stretching

6. The PMR spectrum of the compound (IIIa) was recorded as:

Peak observed	Multiplicity	Assignment
3.88	S	3H,-OCH_3
6.96	S	1H,-C-CH-S-
6.99	S	1H,-C=CH
7.4-8.0	M	6H,Ar-H and 2H, -NH
13.69	S	1H,Ar-OH

All these observation confirms the structure of compound(IIIa)

II) ***Synthesis of 4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-(4-anisylphenyl)-2-imino-6-H-2,3-dinitro-phenyl-1,3-thiazine.(IIIe)***

1,3- Thiazines were synthesized by dissolving substituted chalcone (Ia) (chloro,bromo, nitro) in dinitro diphenyl thiourea (IIb) in presence of aqueous potassium hydroxide in 30ml ethanol .The reaction mixture was refluxed for about 3hours .It was then diluted with water and acidified by 1:1dilute HCl. A solid obtained was crystallized from ethanol to get the product 4-(2-hydroxy-3-bromo-5-chlorophenyl)-6-(4-anisylphenyl)-2-imino-6-H-2,3-dinitrophenyl-1,3-thiazine.(IIIe)

1.The compound (IIIa) is yellow coloured crystalline solid mp131^0
2.It gives violet colouration with neutral $FeCl_3$ solution.
3.It gives deep blue colouration with concH_2SO_4 solution showing the absence of
- C –CH = CH- linkage.

4.Purity of the compound was tested by TLC.
5 The I.R and NMR spectra of the compound(IIIe)

Literature value cm-1	Observsd value	Assignment
3600-3000	3400-3200	-NH stretching
1700-1580	1620	-OH stretching
1620-1550	1585	>C=N stretching
1300-900	1268	-C-H stretching
780-650	720	C-Cl stretching
750-550	650	C-Br stretching
1500-1300	1350	C-NO_2 stretching

6. The PMR spectrum of the compound (IIIe) was recorded as:

Peak observed	Multiplicity	Assignment
3.88	S	3H,-OCH_3
6.96	S	1H,-C-CH-S-
6.99	S	1H,-C=CH
7.4-8.0	M	6H,Ar-H and 2H, -NH
13.69	S	1H,Ar-OH

All these observation confirms the structure of compound(IIIe)

III.*) Antimicrobial Activity of Synthesised Compounds*

The 1,3-thiazines when screened in vitro against some common bacteria viz. E. coli,S. aureaus, B. subtilis, P. argenosa it was noticed that most of all these compounds have shown remarkable inhibitory activity.

An assay of newly synthesized 1,3-thiazines revels that, almost all the compounds were strongly active against all the test pathogens B. subtilis, P. argenosa. Their inhibitory impact on the bacterial growth is remarkable.

Table-1: Antibacterial activities of test compounds

S. No.	Test Compounds	Zone of inhibition (mm)			
		. E. coli	*,S. aureaus*	*. B.subtilis*	*P. argenosa*
1	IIIa	26	22	24	27
2	IIIb	16	18	20	22
3	IIIc	21	23	24	20
4	IIId	18	18	20	21

Table-2: Antibacterial activities of test compounds

S. No.	Test Compounds	Zone of inhibition (mm)			
		. E. coli	*,S. aureaus*	*. B.subtilis*	*P. argenosa*
1	IIIe	20	23	30	25
2	IIIf	18	20	19	18
3	IIIg	22	25	20	22
4	IIIh	14	12	16	24

REFERENCES

[1]Fadda A.A, Khalil AM&EL-Habbal MM,*J Indian Chem Soc*,68 **1991**,393
[2]PandeyVK,Saxena S.K&Bajpai,*IndianJournalChemistry*,43B,**2004**,1015
[3]Bhatt AK, Karadia HG & Shah PR, *Indian Journal of Heterocyclic Chemistry*,13,**2004**,281
[4]F.H.Z.Haider ,*J. Pharma . Res*.,4(4) , 2263 92012)
[5] SK Doifode; MP Wadekar; S Rewatkar. *Orient. J. Chem.*, **2011,** 27(3), 1265-1267.
[6]F. H. Z. Haider, J. *Pharm. Res.*, 4(4),2263**2012**
[7]Farooque Haider Zulfequar Haider *Journal of chemical and Pharmaceutical Research*,**2010**,4(4):2263-2267.
[8]Keerthi kumar.B et al. *Journal of Pharmacy Research*. 4(1); **2011** 274-275.