15. 1, 3, 5 Thiadiazines: Synthesis, Characterization and Biological Studies of Newly Synthesized Compounds [Hydrochloride]

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Abstract

A new series of 3-Aryl((-Cl- aniline)-4-S-benzyl-6-p-tolylimino-2-phenylimino-2,3-dihydro-[1,3,5] thiadiazine [Hydrochloride] were synthesized by the interaction of 1-Aryl(-Cl-aniline)-5-p-tolyl-2-S-benzyl-2,4- isodithiobiuretes with phenyl isocyanodichloride. The identities of these newly synthesized compounds have been established on the basis of usual chemical transformations and IR, ^{1}H NMR and Mass spectral analysis. The polarimetric study of all compounds was carried out.

The progress achieved in the synthesis of heterocyclic compounds with biological potential is due to improvement of the methodological study of tested substance. Several five and six member aromatic systems having these compounds were screened for their antibacterial and antifungal activities against–Escherichia coli, Staphylococcus aureus. These compounds show appreciable activity towards these microorganisms.

Keywords:- 2,4- isodithiobiuretes, phenyl isocyanodichlorides, -1, 3, 5-thiadiazines, Antimicrobial Activity etc.

Introduction

1, 3, 5-thiadiazines and their rearranged product 1, 3, 5-triazines have been shown to possess brightening and fiber finishing properties in textile industry[1,2], symmetric triazines have also been used as chain lengthing agents in polyurethane, polymerization[3],azodye, paints, plastic and rubber[4]. They are also used as fungicidal[5], insecticidal[6], and as medicinal compounds. The literature survey reveals that the heterocyclic compounds having 1, 3, 5-thiadiazines nucleus enhanced pharmaceutical, medicinal, agricultural and industrial values.

The chemistry of heterocyclic compounds continues to explore the field of carbohydrate chemistry. Literature survey also revealed that the heterocyclic derivatives of sugar possess

antimicrobial[7-9], and antitumor activity[10-12]. Thiadiazines and their derivativs acts as antifibrinolytic [13], cardiotonic[14], anesthetic, cardiovascular and hypometabolic agents[15].

Materials and Methods

All chemicals were research grade. Melting points determined are uncorrected. IR spectra were recorded in KBr on a FT-IR Perkin-Elmer RXI (4000-450cm^{-1}) spectrophotometer. ^{1}H NMR measurements were performed on a Bruker DRX-300 (300 MHz FT NMR) NMR spectrometer in $CDCl_3$ solution with TMS as internal reference. The Mass spectra were recorded on a THERMO Finnigan LCQ Advantage max ion trap Mass spectrometer. Optical rotation $[\alpha]_D^{31}$ measured on a Equip-Tronics Digital Polarimeter EQ-800 at 31^{0}C in $CHCl_3$. Thin layer chromatography (TLC) was performed on silica Gel G and spots were visualized by iodine vapour. The compounds describe in this paper were first time synthesized by the multistep reaction protocol

Results and discussion

Several 3-Aryl ((-Cl- aniline)-4-S-benzyl-6-p-tolylimino-2-phenylimino-2,3-dihydro-[1,3,5] thiadiazine [Hydrochloride] (3a-d) have been synthesized by the interaction of 1-Aryl(-Cl- aniline)-5-p-tolyl-2-S-benzyl-2,4-isodithiobiurets (2a-d) and phenyl isocyanodichloride (1). To the chloroform suspension of Phenyl isothiocyanate chlorinated on chlorination assembly .This chlorinated solution was added to 1-Aryl (-Cl- aniline)-5-p-tolyl-2-S-benzyl-2,4-isodithiobiuret in chloroform medium . Then the reaction mixture was reflux for 3 hrs. And a sticky mass obtained as a residue was triturated several times with petroleum ether (60-80^{o}C).. A product will separate out.

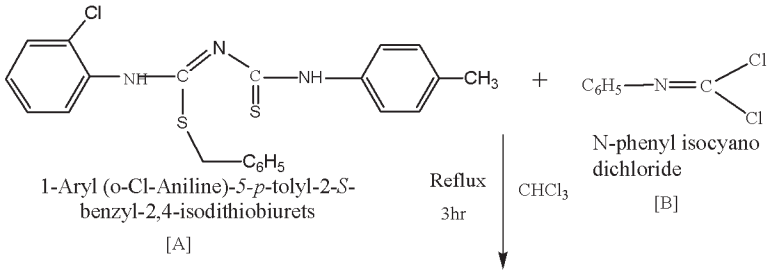
The IR spectra of products shows bands due to Ar-H, N-H, C=N, C-N, C-S stretching and ^{1}HNMR spectra of products distinctly displayed signals due to aromatic protons and aliphatic Protons. The Mass spectrum of product was also observed. The identities of these newly synthesized compounds have been established on the basis of usual chemical transformations and also IR, ^{1}H NMR and Mass spectral studies[16-18].

Experimental

Synthesis of 3-Aryl (o-Cl- aniline)-4-S-benzyl-6-p-tolylimino-2-phenylimino-2,3-dihydro-[1,3,5] thiadiazine[Hydrochloride]

3-Aryl (o-Cl- aniline)-4-S-benzyl-6-p-tolylimino-2-phenylimino-2,3-dihydro-[1,3,5] thiadiazine[Hydrochloride] was prepared by the interaction of 1-Aryl (o-Cl- aniline)-5-p-tolyl-2-

S-benzyl-2,4-isodithiobiurets and phenyl isocyanodichloride in chloroform medium. A chloroform solution of Phenyl isocyanodichloride was mixed with the chloroform solution of 1-Aryl (o-Cl- aniline)-5-p-tolyl-2-S-benzyl-2,4-isodithiobiuret. Then the reaction mixture was reflux on boiling water bath for 3 hr during which evolution of HCl was noticed. The progress of reaction was monitored by TLC. After completion of the reaction, the reaction mixture was brought to room temperature and the solvent removed under reduced pressure to obtain residue. This residue was triturated several times with petroleum ether (60-80°C) to afford a pale yellow solid.

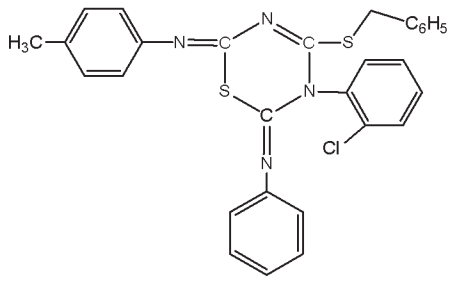


1-Aryl (o-Cl-Aniline)-5-*p*-tolyl-2-*S*-benzyl-2,4-isodithiobiurets
[A]

Reflux
3hr

$CHCl_3$

N-phenyl isocyano dichloride
[B]



3-Aryl
(o-Cl-aniline)-4-*S*-benzyl-6-*p*-tolylimino-2-phenylimino-2,3-dihydro-1,3,5-thiadiazine
Hydrochloride

Where, R= (a) Phenyl, (b) o-Cl- aniline, (c) m- Cl- aniline , (d) p-Cl- aniline,

3a: IR (KBr):υ 3201 (Ar-H), 2877 (Ali-H), 1523 (C=N), 1450 (C-C), 1323 (C-N), 694 (C-S). H NMR (δ in ppm, $CDCl_3$): δ 7.63 -6.91 (19H, m, Ar. H), δ 4.27- 2.26 (5H, m, Ali. H) Mass (m/z): 490 (M^+), 477, 387, 300, 91; Anal. Calcd for $C_{29}H_{24}N_4S_2$. C, 70.73; H, 4.87; N, 11.38; S, 13.00; Found: C, 70.70; H, 4.85; N, 11.40; S, 13.04.

On the basis of all above facts the product with m. p. 98°C was assigned the structure 3-Aryl(Phenyl)-4-S-benzyl-6-p-tolylimino-2-phenylimino 2,3-dihydro- [1,3,5] thiadiazine [Hydrochloride]

When the reaction of phenyl isocyanodichloride was extended to several other 1-Aryl (-Cl- aniline)-5-p-tolyl-2-S-benzyl-2,4-isodithiobiurets corresponding 3-Aryl (-Cl-aniline)-4-S-

benzyl-6-p-tolylimino-2-phenylimino 2,3-dihydro- [1,3,5] thiadiazine [Hydrochloride] has been synthesized.

3b: IR (KBr):υ 3030 (Ar-H), 2872 (Ali-H), 1566 (C=N), 1475 (C-C), 1267 (C-N), 792 (C-S). H NMR (δ in ppm, $CDCl_3$): δ 8.08 -6.56 (18H, m, Ar. H), δ 4.42- 1.59 (5H, m, Ali. H) Mass (m/z): 526 (M^+), 425, 403, 91; Anal. Calcd for $C_{29}H_{23}N_4S_2Cl.HCl.$,: C, 66.15; H, 4.37; N, 10.64; S, 12.16; Found: C, 66.20; H, 4.40; N, 10.70; S, 12.20.

Table -1: Physical data for characterization of 3-Aryl (-Cl-aniline)-4-S-benzyl-6-p-tolylimino-2-phenylimino 2,3-dihydro- [1,3,5] thiadiazine [Hydrochloride] (3a-d)

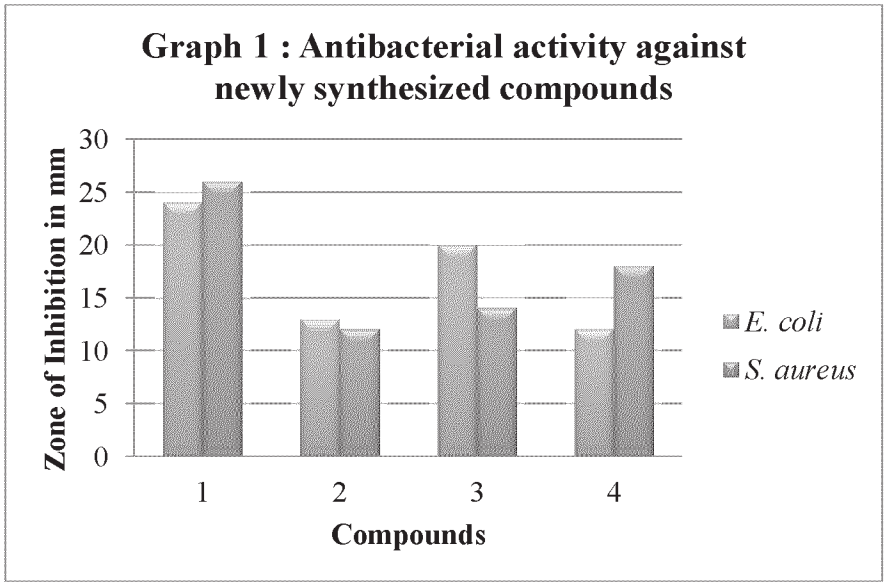
Compd	Yield %	R_f	M.P. ^0C	Analysis (%): Found (calcd)	
				N	S
3a(Aniline)	75.00	0.55	98	11.40(11.38)	13.04(13.00)
3b(o-Cl- aniline)	55.00	0.40	125	10.70 (10.64)	12.20 (12.16)
3c(m-Cl- aniline)	68.00	0.45	143	10.60 (10.64)	12.21(12.16)
3d(p-Cl- aniline)	79.00	0.52	102	10.68 (10.64)	12.00 (12.16)

C and H analysis was found satisfactory in all cases.

Antimicrobial activity[19]

All the compounds have been screened for both; antimicrobial and antifungal activity by using disc diffusion assay. For this, sterial filter paper disc (6 mm) impregnated with fixed doses of compounds was placed on pre-innoculated surface. The disc bearing plates were incubated at 37ºC for 24 h. After incubation, zone diameters were measured. The compounds were taken at a concentration or 1 mg/mL using dimethyl sulphoxide as a solvent. Amikacin (100 µg/mL) was used as standard for antibacterial. The compound was screened for antibacterial activity against Eschrichia coli, Staphylococcus aureus, in nutrient agar medium. It has been observed that all the compounds showed good activity against both; bacteria.

Compound	**Escherichia coli**	**Staphylococcus aureus**
1) Aniline	24mm	26mm
2) o-chloro	13mm	12mm
3) p-chloro	20mm	14mm
4) m-chloro	12mm	18mm
Amikacin	28mm	26mm



Zone of inhibition in mm. (15 or less) resistance, (16-20 mm) moderate and more than

Conclusion

In this research work, the characterizations of newly synthesized products were established on the basis of UV, IR, ^{1}H NMR, & Mass spectral studies. Various 3-Aryl (-Cl-aniline)-4-S-benzyl-6-p-tolylimino-2-phenylimino 2,3-dihydro- [1,3,5] thiadiazine [Hydrochloride] were synthesized and yield of product ranged from 68-82%.

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