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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL STUDIES OF NEWLY SYNTHESIZED -1, 3, 5-THIADIAZINES

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Abstract: *Serial of 3-Aryl-4-S-benzyl-6-p-tolylimino-2-phenylimino-2,3-dihydro-[1,3,5] thiadiazine[Hydrochloride] has been synthesized by the interaction of 1-Aryl-5-p-tolyl-2-S-benzyl-2,4- isodithiobiuretes with phenyl isocyano dichloride in refluxing chloroform medium. Initially evolution of hydrochloric gas to obtain 3-aryl-4-S-benzyl-6-p-tolylimino-2-phenylimino-2,3-dihydro-1,3,5thiadiazines [hydrochloride]. Constitutions of synthesized compound have been delineated on the basis of chemical transformation, elemental determination, and IR, NMR and Mass spectral studies. These compounds were screened for their antibacterial and antifungal activities against–Escherichia coli, Proteus vulgaris, Staphylococcus aureus, Salmonella typhimurium, Klebsiella pneumonie, Psudomonas aeruginosa, Aspergillus Niger and Candida albicance. These compounds show appreciable activity towards these microorganisms.*

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INTRODUCTION

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. Thin layer chromatography (TLC) was performed on silica Gel G and spots were visualized by iodine vapour. The compounds were screened for their antibacterial and antifungal activities by the disc diffusion assay method[21]. The compounds describe in this paper were first time synthesized by the multistep reaction protocol.

1] Preparation of phenyl isocyanodichloride

a] Preparation of phenyl isothiocyanate: [22]

Place a 500ml conical flask in freezing mixture of ice and salt. Add to it 30 ml of conc. Ammonia solution and 15ml of pure carbon disulphide. Stir the mixture and run in 19 ml of aniline about 15 min. Stir for a further 30min and allow standing for another 30min. A heavy ppt of Ammonium phenyl dithiocarbamate separates. Filter it and dry it.

Transfer the salt to a 2lit R.B. flask. By 2-3 extractions with 100ml portion of distilled water. To this solution of 50gm of lead nitrate in distilled water with constant stirring. Lead sulphide ppt is observed. Steams distill the mixture into a receiver containing 10ml of 0.5ml H_2SO_4 as long as organic material passes over. Separate the oil; dry it over anhydrous Calcium Chloride or Magnesium Sulphate.

b] Preparation of phenyl isocyanodichloride

Through the chloroformic solution of phenyl isothiocyanate, chlorine gas was bubbled maintaining the temperature of the system below 10^{o}C. After the addition of chlorine was completed, the yellow reaction mixture was diluted with 40-50ml petroleum ether (60-80^{o}C). The solvent was then removed by distillation under vacuume. The whole operation was repeated several times with petroleum ether then phenyl isocyanodichloride was obtained as pale yellow oil.

2] Synthesis of 1-Aryl-5-*p*-tolyl-2-*S*-benzyl-2,4-isodithiobiurets (2a-j)

a) Preparation of 1-Aryl-*S*-benzyl isothiocarbamide

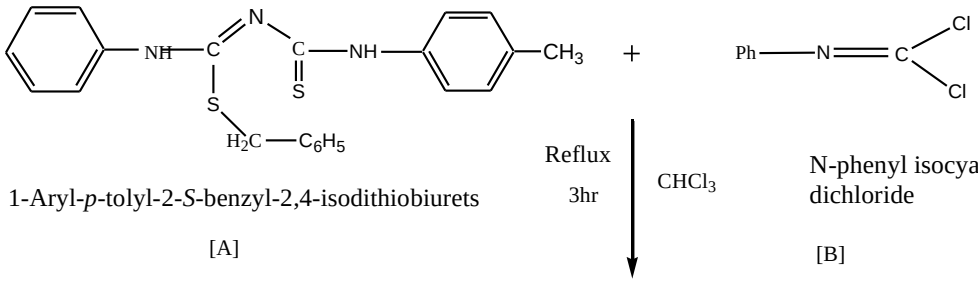
To the ethanolic suspension of phenyl thiocarbamide was added benzyl chloride and the reaction mixture was reflux for 90 min . Afterward the reaction mixture was cooled and rendered basic with dil. ice cold NH_4OH and a sticky residue was obtained which on standing for 1 to 2 hrs. solidifies. It was filtered and wash with petroleum ether**.**

b) Preparation of 1-Aryl-5-*p*-tolyl-2-*S*-benzyl-2,4-isodithiobiurets

Several 1-Aryl-5-*p*-tolyl-2-*S*-benzyl-2,4-isodithiobiurets have been prepared by the interaction of 1-Aryl-*S*-benzyl isothiocarbamide and *p*-tolyl isothiocyanate in benzene medium . To the benzene solution of 1-Aryl-*S*-benzyl isothiocarbamide , *p*-tolyl isothiocyanate was added .This reaction mixture was then reflux over a boiling water bath for 3 hrs. after completion of the reaction, solvent benzene was distilled off and the sticky mass obtained as residue was triturated several times with petroleum ether . A white product separated out crystallised from ethanol.

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

3-Aryl-4-*S*-benzyl-6-*p*-tolylimino-2-phenylimino-2,3-dihydro-[1,3,5] thiadiazine[Hydrochloride] was prepared by the interaction of 1-Aryl-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-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^{o}C) to afford a pale yellow solid.

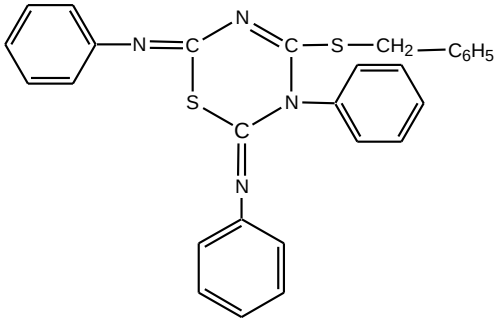


1-Aryl-*p*-tolyl-2-*S*-benzyl-2,4-isodithiobiurets

[A]

N-phenyl isocyano dichloride

[B]



3-Aryl-4-*S*-benzyl-6-*p*-tolylimino-2-phenylimino-2,3-dihydro-1,3,5-thiadiazine [hydrochloride]

Where, R= (a) Phenyl, (b) *o*-tolyl, (c) *m*-tolyl , (d) *p*-tolyl,

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-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-5-*p*-tolyl-2-*S*-benzyl-2,4-isodithiobiurets corresponding 3-Aryl-4-*S*-benzyl-6-*p*-tolylimino-2-phenylimino 2,3-dihydro- [1,3,5] thiadiazine [Hydrochloride] has been synthesized.

3b: IR (KBr):υ 3028 (Ar-H), 2866 (Ali-H), 1566 (C=N), 1494 (C-C), 1315(C-N), 702 (C-S). H NMR (δ in ppm, $CDCl_3$): δ 7.66 -7.21 (18H, m, Ar. H), δ 4.56- 1.42 (8H, m, Ali. H) Mass (m/z): 505 (M^+), 405; Anal. Calcd for $C_{28}H_{22}N_4S_2$,: C, 70.44; H, 4.61; N, 11.74; S, 13.41; Found: C, 70.69; H, 4.65; N, 11.70; S, 13.45.

Table -1: Physical data for characterization of compounds (3a-d)

Compd	Yield %	R_f	M.P. ^{0}C	Analysis (%): Found (calcd)	
				N	S
3a	80.00	0.67	98	11.40(11.38)	13.04(13.00)
3b	79.00	0.72	92	11.70(11.74)	13.45(13.41)
3c	82.00	0.48	102	11.68(11.74)	13.40(13.41)
3d	81.00	0.51	108	11.72(11.74)	13.35(13.41)

C and H analysis was found satisfactory in all cases.

Antimicrobial activity:

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 37°C for 24 h. After incubation, zone diameter 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 and fluconazole (100µg/mL) as a standard for antifungal activity. The compound were screened for antibacterial activity against *Eschrichia coli, Proteus vulgaris, Staphylococcus aureus, Salmonella typhi, Klebsiella pneumonie* and *Psudomonas aeruginosa* in nutrient agar medium and for, antifungal activity against *Aspergillus niger* and *Candida albicance* in potato dextrose agar medium. It has been observed that all the compounds showed good activity against both; bacteria and fungi.

Compound	*E. coli*	*S. aureus*	*P. vulgaris*	*P. aeruginosa*	*S. typhi*	*K. pneumonie*	*A. niger*	*C. albicance*
1(3a)	17	16	20	19	18	21	19	20
2(3b)	10	15	15	12	20	19	20	21
3(3c)	18	14	19	17	15	18	17	19
4(3d)	14	19	18	18	19	20	20	19
Amikacin	18	21	23	19	20	21		
Fluconazole							24	24

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

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REFERENCES:

1. K. Tsujihara, M. Ozeki, T. Morikawa, M. Kawamori, Y. Akaike and Y. Arai, *J. Med. Chem*., **25**, 441 (1982).
2. T. K. Lindhorst and C. Kieburg, *Synthesis*, **10**, 1228 (1995).
3. C. Ortizmellet, J. Balanco , L. Jose, G. Fernandez and M. Jose, Fuentes, *J. Carbohydr. Chem*., **12**, 487 **(**1993).
4. R. D. Ghuge and S. P. Deshmukh, *Int. J. Chem. Sci.,* **9(3) ,** 1391 (2011).
5. P. R. Mahalle, G.V. Korpe and S. P. Deshmukh , *Ind.J.Heterocyclic Chem*., **18**, 161 (2008).
6. M. T. Sangole and S. P. Deshmukh , *J. Ind. Chem. Soc*., **88**, 739 (2011).
7. Tayade D.T., Ph.D. Thesis, Amravati Univ, 1996.
8. Paranjape M. G., *J. Indian Chem. Soc.*, 1966, 42- 45.
9. Shelke M. E. and Tayade D.T., *AJC*, 2006; **18**(3): **18**(4): 3137-3138.
10. Shelke M. E., *JPAM*, 2007; 1(1): 123-125.
11. Shelke M. E., Ph.D. Thesis, Amravati Univ., 2005.
12. Richard S, Robi S. and Jackson P., *J. Am. Chem. Soc.*, 1951; **84**: 589.
13. Jackson P., Joseph A. and Podell T., *J. Am. Chem. Soc.*, 1961; 123: 169.
14. Elvino Fako, Shirley D. and George Hitching, *J. Am. Chem. Soc.*, 1951; **73**: 3760.
15. Birtwell S., Curd F. H. S., Hendry J. A. and Rose F. L., *J. Chem. Soc.*, 1948; **16** : 53.
16. Bamberger E., *Ber Dtsch. Chem, Ges*,, 1883; **16**: 1460.

17. Rathke B., *Ber. Dtsch. Chem. Ges.*, 1878; **11**: 963.
18. R. M. Silverstein, G. C. Bassler and T. C. Morrill, *Spectrometric Identification of Organic Compounds*", 5th ed., John Wiley and Sons, Inc, New York, (1991).
19. N.B. Colthup, L.H. Daly and S.E. Wibereley, *Introduction to Infrared and Raman spectroscopy* "Academic Press, New York, (1964).
20. D.H.Williams and L.Fleming*, Spectroscopic Meyhods in Organic Chemistry*", 4th ed., Tata-McGraw- Hill, (1988).
21. Collee JG and Marr W Laboratory control of anti-microbial therapy. In: college JG, Duguid JP, Fraser AG, Marmion BP (eds) Mackie and Mc Cartney *Practical Medical Microbiology*. 14th edition. Edinburgh Churchill Livingeston, (1996), 114-115.
22. Furniss, A.J. Hannaford, W.G. Smith, A.R. Tatchell , "Vogel text book of practical organic chemistry", FLBS, 4th ed.; p (a) 456 (b)