110

SYNTHESIS AND SPECTRAL STUDY OF SUBSTITUTED-[1, 2, 4]–DITHIAZOLIDINES [HYDROCHLORIDE]

Kavita. M.Heda
Department of Chemistry,
Shri R. L. T. College of Science,Akola (M.S.)
India

****

Abstract: Newly synthesized 3-thio-4-aryl-5-tolyl-[1, 2, 4]-dithiazolidine [hydrochloride] have been prepared by the interaction of several Ammonium aryl dithiocarbamate with N-p-tolyl-S-chloro isothiocarbamoyl chloride in refluxing chloroform medium. The newly synthesized compounds have been characterized by analytical and IR, ^{1}H NMR and Mass spectral studies.

Keywords: Ammonium aryl dithiocarbamate, N-p-tolyl-S-chloro isothiocarbamoyl chloride, -[1, 2, 4]-dithiazolidine

Introduction: Dithiazolidine constitutes a major role in the synthesis of various heterocyclic moieties. They act as active precursors in synthetic heterocyclic chemistry. Synthesis of a series of novel five member ring containing nitrogen and sulphur are well known[1]. A small heterocyclic ring containing nitrogen and sulphur have been under investigation for a long time because of their important properties. Synthesis, structural properties and antimicrobial activities of various [1, 2, 4]-dithiazolidine have been reported earlier[2]. The literature survey revealed that the [1,2,4]- dithiazolidine have been found to possess potent anti-tumors, anti-tuberculosis[3,4], anti-diabetic and anti-cancer[5] and anti inflammatory[6] properties.

Thiocarbamides and their heterocyclic derivatives have gained recently much interest as inhibitors of Human Immunodeficiency Virus (HIV)[7] and Therapeutic agents[8]. Some of the heterocyclic derivatives of thiocarbamides are found to possess diverse pharmacological activities like antifungal and anti-tubercular agents. In view of utility of thiocarbamides, N-aryl-S-chloro isothiocarbamoyl chloride have been used in synthesis of substituted [1, 2, 4] dithiazolidine by interacting with Ammonium aryl dithiocabamates. The drug containing 1, 2, 4-dithiazolidines show a diverse range of physiological activities, antimicrobial[9-10], anti-inflammatory[11-13], anti-ulcer[14-15], and anti-cancer[16]. Here is reported the synthesis of several 3-thio-4-aryl-5-tolyl-[1, 2, 4]-dithiazolidine [hydrochloride] (3a-d) have been synthesized by the interaction of several Ammonium aryl dithiocarbamate (1a-d) with N-p-tolyl-S-chloro isothiocarbamoyl chloride (2). The required Ammonium aryl dithiocarbamate (1a-d) were obtained by the interaction of interaction of different amines with carbon disulphide and Ammonia.

Results and discussion

Several 3-thio-4-aryl-5-tolyl-[1, 2, 4]-dithiazolidine [hydrochloride] (3a-d) have been synthesized by the interaction of several Ammonium aryl dithiocarbamate (1a-d) with N-p-tolyl-S-chloro isothiocarbamoyl chloride (2). in $CHCl_3$. After condensation, the solvent was distilled off to obtain a sticky residue. This residue was triturated several times with petroleum ether (60-80^{0}C) to afford a pale yellow solid (3a-d). The product was found to be non-desulphurrizable when boiled with alkaline lead acetate solution. The IR spectra of products shows bands due to Ar-H, C-H, C=N, C-C, C-N, C=S, C-S, S-S stretching and ^{1}HNMR spectra of products distinctly displayed signals due to aromatic protons and Acetyl protons. The Mass spectrum of product was also observed. The identities of these new 3-thio-4-aryl-5-tolyl-[1, 2, 4]-dithiazolidine [hydrochloride]have been

established on the basis of usual chemical transformations and also IR, ^{1}HNMR and Mass spectral studies[17-19].

Experimental

General 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. 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.

Synthesis of Ammonium aryl dithiocarbamate[20] (1a-d)

The compound Ammonium aryl dithiocarbamate was prepared by drop wise addition of Amine [9ml] in ice cold mixture of ammonium [15ml, density 0.88] and carbon disulphide [7.5ml] followed by the vigorous shaking. The reaction mixture was allowed to stand for 30min heavy precipitate of Ammonium aryl dithiocarbamate separates out. Filter it and dry it.

Synthesis of N-p-tolyl-S-chloro isothiocarbamoyl chloride (2)

N-p-tolyl-S-chloro-isothiocarbamoyl chloride (**2**) was prepared by passing a calculated amount of chlorine from p-tolyl isothiocyanate.

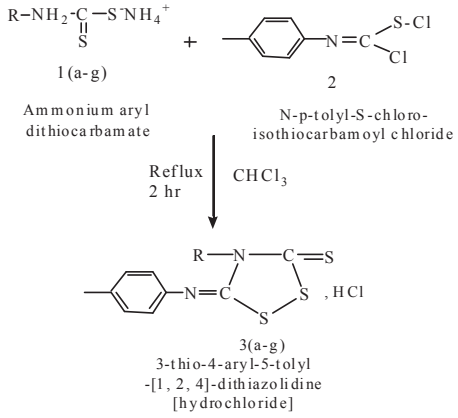
3a:-**Synthesis of 3-thio-4-aryl-5-tolyl-[1, 2, 4]-dithiazolidine [hydrochloride]**

A mixture of Ammonium phenyl dithiocarbamate (1a-d) and N-tolyl-S-chloro isothiocyanocarbamoyl chloride was gently refluxed for 2 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 **(3a)**.

3a: IR (KBr) :u 3155.5 (Ar-H), 2951.0 (C-H aliphatic), 1593.2 (C=N), 1508.3 (C-C), 1131.0 (C-N), 1143.7 (C=S), 752.2 (C-S), 503.4 (S-S), cm^{-1};^{1}H NMR (ä in ppm, $CDCl_3$): ä 7.94-7.22 (9H, m),;ä 2.358-2.353 (3H, s, CH_3) Mass (m/z): 316 (M^+), 300, 225, 211 , Anal. Calcd for $C_{15}H_{12}N_2S_3$, HCl: C, 56.96; H, 3.79; N, 8.86; S, 30.37; Found: C, 56.92; H, 3.75; N, 8.90; S, 30.35.

On the basis of all above facts the product with m. p. 122°C was assigned the structure 3-thio-4-phenyl-5-tolyl-[1, 2, 4]-dithiazolidine [hydrochloride]

When the reaction of N-p-tolyl-S-chloro-isothiocarbamoyl chloride was extended to several other Ammonium phenyl dithiocarbamate corresponding 3-thio-4-aryl-5-tolyl-[1, 2, 4]-dithiazolidine [hydrochloride] (3b-d**)**have been isolated.



Where, R= (a) Phenyl, (b) o-nitro-phenyl, (c) m-nitro-phenyl, (d) p-nitrol-phenyl,

3b:IR (KBr) :u3040.1 (Ar-H), 2780.7 (C-H aliphatic), 1580.0 (C=N), 1541.1 (C-C), 1100.4 (C-N), 1207.4 (C=S), 715.5 (C-S), 535.7 (S-S), cm^{-1};^{1}H NMR (ä in ppm, $CDCl_3$): ä 7.94-7.22 (8H, m),;ä 2.358-2.353 (3H, s, CH_3) Mass (m/z): 361(M^+), 335, 315, 259, Anal. Calcd for $C_{15}H_{12}N_3O_2S_3$, HCl: C, 49.86; H, 3.32; N, 11.63; S, 26.59; Found: C, 49.90-; H, 3.38; N, 11.70; S,

26.62.

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

Compd	Yield %	R_f	M.P. °C	Analysis (%): Found (calcd)	
				N	S
3a	80.00	0.67	122	8.90(8.86)	30.35(30.37)
3b	75.00	0.70	128	11.70(11.63)	26.62(26.59)
3c	66.38	0.50	134	11.60(11.63)	26.60(26.59)
3d	50.34	0.48	130	11.72(11.63)	26.68(26.59)

C and H analysis was found satisfactory in all cases.

Conclusion:

In this research work, the characterizations of newly synthesized products were established on the basis of IR, ^{1}H NMR, & Mass spectral studies. Various 3-thio-4-aryl-5-tolyl-[1, 2, 4]-dithiazolidine [hydrochloride] were synthesized and yield of product ranged from 50-80%.

Acknowledgement

Authors are thankful to SAIF, CDRI, Chandigarh for providing the spectral data and also Dr. V. D. Nanoty for encouragement and necessary facilities.

References:

1. A. Dandia, R. Singh, S. Khaturia, C. Merienne, G. Morgant, and Loupy A, Bioorg Med Chem., 1; **14(7)**, (2006), 2409-17.

2. P. R. Kawle. P. Deohate, and B. N. Berad, Int. J. of Chem. Sci., **10**(2012),895-900.

3. K. M. Heda, S. P. Deshmukh, International Journal of Heterocyclic Chemistry, Vol.25 (2015), 141-142

4. R.M. Kharate, P.P. Deohate, and B.N. Berad, Int. J. Chem. Sci., 7(4), (2009), 2843.

5. P. T. Agrawal, S. P. Deshmukh, J. Indian Chem. Soc., **86**, (2009), 645-648.

6. P. Manna, R. Singh, K.K. Narang, and S.K. Manna, Indian J. Chem.,**44B**, (2005)1880.

7. Wilkerson W. W., Dax S.,Cheatham W. W.; J. Med. Chem.; **40**, (1997), 4079-4088.

8. Nefzi A., Ostresh J. M.,Houghten R. A.;Chem. Rev.; **97**,(1997), 449-472.

9. Z. A. Kaplancikli, G. Turan-Zitouni, A. Ozdemir, G. Revial, Eur. J. Med. Chem., **43,** (2008), 155-159.

10. N. A. Al-Masoudi, Y. A. Al-Soud, M. Irene. Lagoja, Carbohy. Res., **318**, (1999), 67-74.

11. A. M. Abdel-Megeed, H. M. Abdel-Rahman, Gamal-Eldien S.,Eur. J. Med. Chem**.,44**, (2009**)**, 117-123.

12. P. X. Franklin, A. D. Pillia, P. D. Rathod, S. Yerande, M. Nivsarkar, H. Padh, K. K. Vasu, V. Sudarsanam, Eur. J. Med. Chem., **43**, (2008), 129-134.

13. V. B. Jadhav, M. V. Kulkarni, V. P. Rasal, S. S. Biradar, M. D. Vinay, Eur. J. Med. Chem., **43**, (2008), 1721-1729.

14. R. K. Rawal, R. Tripathi, S. B. Katti, C. Pannecouque, Erik De Clercq, Eur. J. Med. Chem., **43, (**2008), 2800-2806.

15. K Ishihara, T Ichikawa, Y Komuro, S Ohara and K Hotta, Arzneim Forsch, Drug Res, **44 (**1994**)**, 827.

16. D. Havrytyuk, L. Mosula, B. Zimenkovsky, O. Vasylenko, A Gzella and R. Lesyk, Eup. J. Med. Chem., **45(11)** (2010), 5012.

17. 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).

18. N.B. Colthup, L.H. Daly and S.E. Wibereley, Introduction to Infrared and Raman spectroscopy "Academic Press, New York, (1964).

19. D.H.Williams and L.Fleming, Spectroscopic Meyhods in Organic Chemistry", 4th ed., Tata-McGraw- Hill, (1988).

20. B.S. Furniss, A.J. Hannaford, W.G. Smith, A.R. Tatchell, "Vogel text book of practical organic, chemistry", FLBS,4th ed.; p (a) 456 (b), 649 (1980).

❑❑❑