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Synthesis of 2-[substituted phenyl]-3-[(6-methoxy-4-nitro-1,3-benzothiazol-2-yl) amino]-1,3-thiazolidin-4-one

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ABSTRACT

4-thiazolidinone ring is reported to possess significant antitubercular, antibacterial & antifungal activities. 2-nitro-4-methoxy aniline (1), which is derivative of aniline have been found to be biologically interesting compound for many years. From this aniline derivative first we have synthesized 2-amino-4-nitro-6-methoxy benzothiazole (2) which is then treated with hydrazine hydrate to form 2-hydrazino-4-nitro-6-methoxy benzothiazole (3). Compound (3) condensed with 4-dimethylamino benzadehyde, 4-nitro benzaldehyde, 4-chloro benzaldehyde, 4-hydroxy benzaldehyde, 3-hydroxy Benzaldehyde and 2-nitro benzaldehyde to form corresponding hydrazone (4a-4f). These hydrazone heated with mercapto acetic acid by using DMF as solvent and Pinch of anhydrous $ZnCl_2$ for 5-6 hours, to afford 3-[(4-nitro-6-methoxy-1,3-benzothiazol-2-yl)-amino]-2-aryl-1,3-thiazolidin-4-one (5a-5h). These newly synthesized 4-thiazolidinone compounds screened for their antibacterical activity.

Key Words : benzothiazoles, hydrazone, thiazolidizone,

Introduction:

A survey of literature reveals that large work has been carried out on the synthesis of 4-thiazolidinone and known to exhibits various biological activities as antitubercular[1], antiallergic[2]. Schiff-bases give good antibacterial activity and pharmacological application[3]. 4-thiazolidinone ring are reported to possess various biological activities, as antimicrobial, anti-nflammatory, antiviral, antiparasitic and antituberculosis[4-10]. These Schiff-bases can be prepared by the acid catalysed reaction of amine and aldehyde or ketone which shows good fungicidal acivit[11].

4-thiazolidinone give good pharmacological properties[12] are known to exhibits antitubercular[13], antibacterial[14], anticonvulsant[15], antifungal activity[16]. Large work has been carried out on 4-

thiazolidinone but very less information is available about 4-thiazolidinone bearing substituted benzothiazolyl moiety.

The starting compound were prepared by the reaction of 2-nitro-4- aniline and sodium thiocynate to obtained 2-amino-4-nitro-6-methoxy benzothiazole. 2-amino-4-nitro-6-methoxy benzothiazole benzothiazole treated with hydrazine hydrate which then condensed with aldehydes to obtain the hydrazones. Thease hydrazones then treated with thioglycolic acid to obtain the corresponding 4-thiazolidinone.

Experimental

All the melting points were determined in open capillary tube and may be uncorrected. The purity of compound was checked by TLC on silica gel coated glass plate. Infra-red spectra were monitored in KBr palates on Bomen 104 FT infra-red spectrophotometer. H1 NMR spectra were obtained on a Gemani 200 Mz spectrometer with tetra methyl silane as an internal standard.. Elemental analysis was performed on a Heraeus CHN-O rapid analyzer.

Synthesis of 2-amino-4-nitro-6-methoxy benzothiazole

Sodium thiocynate 9.7 gm, (0.1 M) were dissolved in glacial acetic acid (160 ml) and 2-nitro-4-methoxy aniline (16.8 gm, 0.1 M) was added with constant stirring. The mixture of solution was cooled by keeping reaction mixture in ice bath. Bromine (16 gm, 10 ml, 0.1 M) in glacial acetic acid (25 ml) was added with stirring and maintaining temperature below 5°C. The mixture was allowed to stand for one hour at room temp. The resulting hydrobromide was dissolved in hot water and neutralized with 10 % NaOH to obtain base. The amine thus obtained was filtered, washed with water and recrystallized in aq. alcohol to get the product 2-amino-4,6-dichloro benzotiazole.

Yield: 13.5 gm, M.P: 89 °C I.R. (KBr) : 3420 cm^{-1} (Asymmetric stretching of $-NH_2$), 3342 cm^{-1} (N-H Symmetrical stretching of $-NH_2$), 3050 cm^{-1} (Ar-H stretching), 1620 cm^{-1} (-C=N stretching); PMR ($CDCl_3$) δ 3.4 (Singlet, 3H, $-OCH_3$) δ 6.2 (broad, 2H, NH_2), δ 7.0-7.5 (two singlet, 2H, Ar-H)

2-hydrazino-4-nitro-6-methoxy benzothiazole

Hydrazine hydrate (80%, 17 ml) was taken in a flask cooled to 5°C and concentrated HCl (11 ml) was added to it with stirring. The flask was kept at room temp. for few minutes and then

2-amino-4-nitro-6-methoxy benzothiazole (11 gm) was added in portions. Ethylene glycol (44 ml) was added into the flask. The contents of the flask were heated at 150-160°C on an oil bath for three hours. On cooling, the product 2-hydrazino-4-nitro-6-methoxy benzothiazole is obtained. It was filtered at pump, washed with cold water and recrystallized from ethyl alcohol,

Yield: 10.4 gm, M.P: 103 °C I.R. (KBr) : 3455 cm^{-1} (asymmetric N-H stretching in $–NH_2$),3350 cm^{-1} (symmetric N-H stretching in $–NH_2$), 3054 cm^{-1} (Ar-H stretching), 1635 cm^{-1} (-C=N stretching) , 2960 cm^{-1} (C-H stretching in alkane)

General procedure for Synthesis of hydrazone of 2-hydrazino-4-nitro-6-methoxy benzothiazole and substituted aromatic aldehyde (4a-4f)

2-hydrazino-4-nitro-6-methoxy benzothiazole (0.01 M) was added in 50 ml ethanol. In another beaker, aromatic substituted benzaldehyde (0.01 M) and ethanol was mixed well. These two mixture of benzothiazole and aldehyde was refluxed on water bath for three hours in a100 ml round bottom flask, solid separated was allowed to cool. The solid was filtered at pump washed with ethanol and recrystallised from hot benzene.

4a. : Yield: 2.8 gm , M. P. : 142 °C, IR(KBr) : 3040 cm-1 (C-H Stretch in alkane), 3140 (N-H) stretch), 1120 (C= N Stretch), 1280, (C-N Stretch), [Found : C: 62.40 %, H : 54.8 %, N : 17.10 %, O : 4.5 %, S : 9.40 %.], $C_{17}H_{18}N_4OS$ required: C: 62.55 %, H : 56 %, N : 17.16 %, O : 4.9 %, S : 9.82 %.]

General Procedure for synthesis of 3-[(6-methoxy-4-nitro-3-benzothiazol-2-yl)-amino]-2-aryl substituted -1,3-thiazolidin-4-one: (5a- 5f)

The hydrazone (0.0025M) (4a-4f) was refluxed with mercapto acetic acid (0.005M) by using DMF (15 ml) as solvent in 50 ml RBF containing and pinch of anhydrous ZnCl2 for 5-6 hours. The reaction mixture was cooled and pours it on well crushed ice. The solid product obtained was Filtered and washed with cold water. The obtained product was recrystallised from methanol.

Result and Discusion:

The synthesized compounds are characterized by spectroscopic technique. Compound (5a) shows IR absorption at 1740 cm-1 (C=O) stretching and 3163 cm-1 (N-H stretching) while NMR shows 3.8 (s, 3H, O-CH3), 1.8 (s, 6H, CH_3-N-CH_3), compound (5d) shows absorption IR signal at 1734 cm^{-1} (C=O stretching), 3412 cm^{-1} (O-H Stretching) and 3180 cm-1 (N-H stretching). The PMR spectrum of compound (5d) shows signal at 2.3 (s, -CO-CH_2) in

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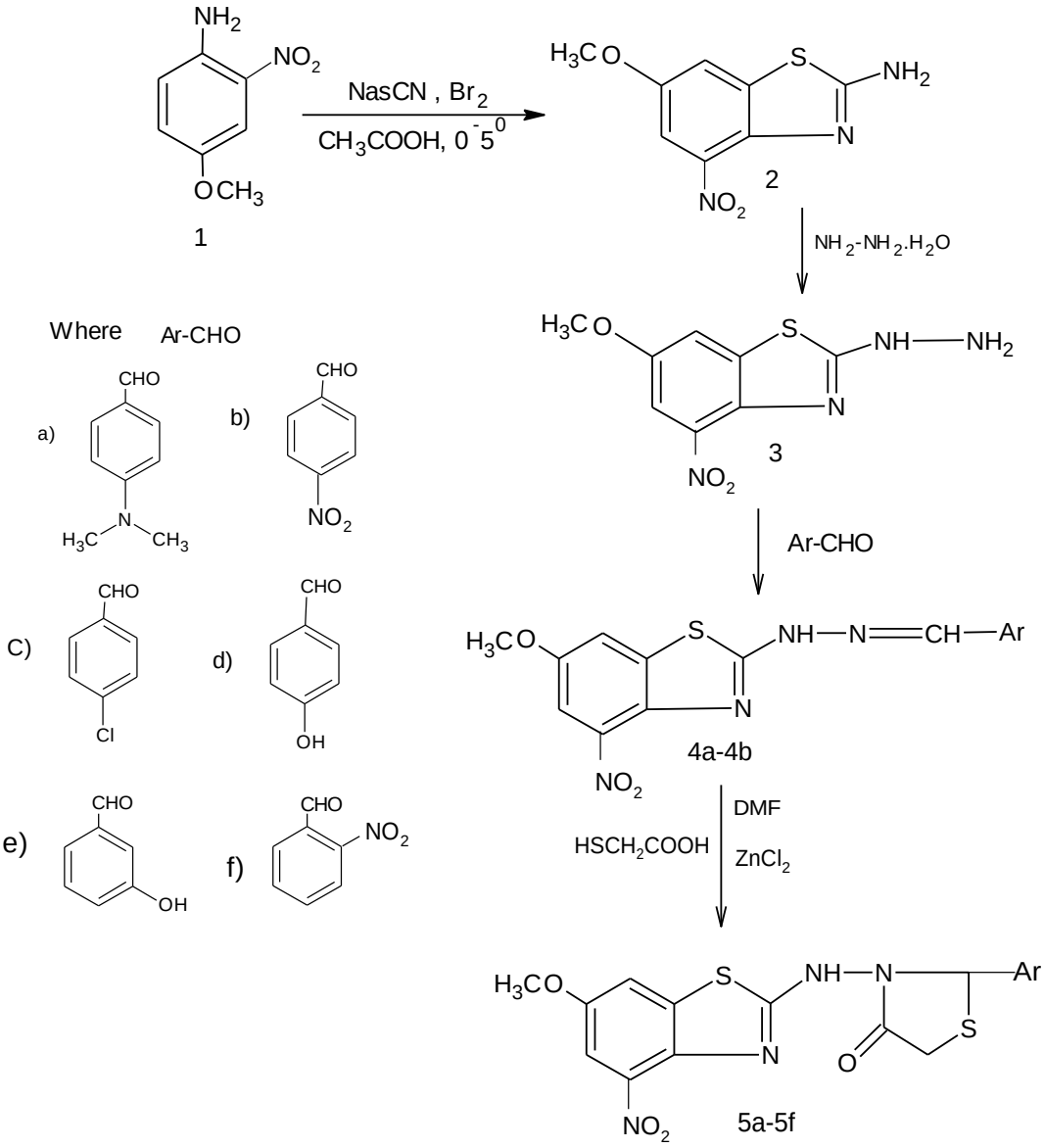
thiazolidinone ring which confirms the formation of the product. Similarly all compounds shows absorption signal 1700-1800 cm^{-1} (C=O stretching), and 3100-3400 cm^{-1} (N-H stretching).

Scheme



Antibacterial Activity

The compound 5a to 5f were tested for their antimicrobial activity by cup plate agar diffusion method against *E.coli* (Gram –ve) *B.subtilis* (Gram +ve), *E. carotovara* and *Xanthomonas citri* using ampicillin, streptomycin. and penicillin as a standard for comparison. The antibacterial screening data of the compounds is presented in table No.1. Dimethyl sulphoxide was used as a control (solvent).

Table : 1

Sr. No.	Comp.	Antimicrobial activity (zone of inhibition in mm)			
		E.coli	*Erwinia*	*Bacillus*	*Xanthom-Onas citri*
1	5a	08	00	04	00
2	5b	06	08	10	08
3	5c	08	04	06	08
4	5d	14	12	13	14
5	5e	12	13	14	12
6	5f	10	10	08	07
Ampicillin		16	18	17	15
Streptomycin		20	18	22	18
Penicillin		15	20	18	17
Control		00	00	00	00

Result and discusion

The compounds 5a to 5f were tested for their antimicrobial activity by the cup plate agar diffusion method against *E. Coli, Erwinla carotovara, Bacillus substilis, and Xanthomonas citri.* The antibacterial screening data of the compound shows compound 5d is more active against *E. Coli, Bacillus and Xanthomonas citri* while compound 5e is more active against *E. Coli, Erwinla carotovara* as compare to other species. The compounds 5d and 5e are more active as compare to other compound. It may be due to presence of –OH group in a substituted thiazolidinone ring.

Referances:

1. Kasel W, Dolezal M, Sidoova E,Odlerova Z and Drasata, *J. Chem. Abstr*., ,**110**,128063e (1989).
2. Ronssel U and Jpn Kokai Tokyo, *Chem. Abstr*, **106**, 156494G, (1987).
3. Warad D.U., Satish C.D., Kulkarni V.H. and bajgur C.S, *Indian J. Chem*, 2000, **39a,** 415. (1987).

4. Capan, G., Ulusoy N., Ergenc N., Kiraz M. *Monatshefte fur Chemie* 1999, 130, 1399, (1987).
5. Vigorita, M. G., Ottana R., Monforte F., Maccari R., Trivato A., Monforte M. T., Zaviano M. F. *Bioorg. Med. Chem. Lett*. 2001, 11, 2791, (1987).
6. Rawal, R. K.; Prabhakar, Y. S.; Katti, S. B.; Clercq, E. *Bioorg. Med. Chem*. 2005, 13, 6771, (1987).
7. Babaoglu, K.; Page, M. A.; Jones, V. C.; McNeil, M. R.; Dong, C.; Naismith, J. H.; Lee, R. E. *Bioorg. Med. Chem. Lett*. 2003, 13, 3227, (1987).
8. Alves, A. J.; Ramos, S. V. V.; Silva, M. J.; Fulcrand, P.; Artis, A. M.; Quero, A. M. *Rev. Farm. Bioquı´m. Univ. Sao Paulo* 34, 77, (1998).
9. Alves, A. J.; Leite, A. C. L.; Santana, D. P.; Beltrao, T. M.; Coelho, *M. R. D. IL Farmaco* 48, 1167, (1993).
10. Bharti, N.; Husain, K.; Garza, M. T. G.; Vega, D. E. C.; Garza, J. C.; Cardenas, B. D. M.; Naqvi, F. *Bioorg. Med. Chem. Lett*. 12, 3475, (2002).
11. Dash B, Mahapatra P.K., Panda D and Patnaik J.M. *Indian Chem. Soc.*, **61**, 1061, (1984).
12. Yadav R, Srivastava S, Srivastava S K. and Srivastava S. D., *Chemistry An Indian Journal*, **1**, 95, (2003).
13. Desai P.S. and Desai K.S., *J. Indian Chem. Soc.* , **71**, 155, (1994).
14. Fadayon M. Kulkarni V.D. and pakdamanA S H, *Asian J. Chem.*, **5** (2), 282, (1993).
15. Srivastava S. K., Srivastava S. and Srivastava S.D., *Indian J. Chem.*, **38B**, 183, (1999).
16. Bhatt J.J., Shah B. R., Trivedi P.B., Undavia N. K. and Desai N.C., *Indian J. Chem.*, **33B**, 189, (1994).