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NOTE

Synthesis and antimicrobial activity of 2-aryl-3-[3′-(2″,4″,6″-trichlorophenoxymethyl)-5′-mercapto-1′,2′,4′-triazol-4′-yl]-5-substituted-4-thiazolidinones

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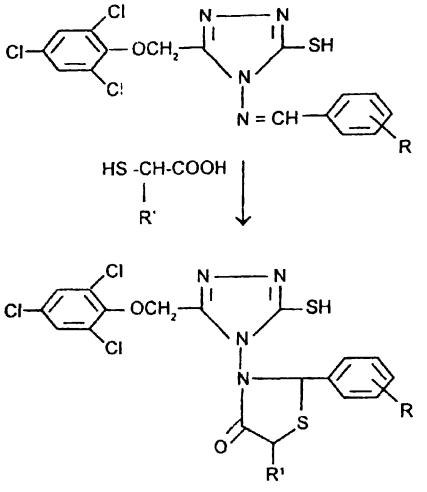
Abstract : Some new 4-thiazolidinones derivatives have been prepared and evaluated for antibacterial activity. Characterization was made with elemental analysis, IR, NMR and mass spectral studies.

Keywords : Thiazolidinones, synthesis.

Compounds having 4-thiazolidinone nucleus possess various therapeutic and biological activities[1]. We have synthesised thiazolidinones and their derivatives with both aromatic and heterocyclic substituents in the position 2 and 3 respectively.

The cycloaddition of thioglycolic acid, thiolactic acid and thiomalic acid to 3-(2′,4′,6′-trichlorophenoxymethyl)-4-(*N*-benzylidinylamino)-5-mercapto-1,2,4-triazole[2] yielded the corresponding 4-thiazolidinone derivatives according to the Scheme 1 given below.



where, R^1
1a-j = H
2a-j = $-CH_3$
3a-j = $-CH_2COOH$

R = **a**, H; **b**, 2-OH; **c**, 2-Cl; **d**, 2-NO_2; **e**, 3-NO_2; **f**, 4-NO_2; **g**, 2-OCH_3; **h**, 4-OCH_3; **i**, 3-OCH_3, 4-OH; **j**, 4-$N(CH_3)_2$

Scheme 1

Results and discussion

Antimicrobial activity :

The compounds were screened for antibacterial activity against *E. coli*, *S. aureus*, *S. typhi* and *B. subtilus* at two test concentration in dimethyl sulphoxide by cup-plate method[3]. All the observations are given in Table 1.

Experimental

All m.ps. were taken in open capillaries using Toshniwal apparatus and are uncorrected. IR spectra (KBr) were recorded on Shimadzu IR 460 spectrophotometer. ^1H NMR spectra on Perkin-Elmer R-32 spectrometer and mass spectra on a Jeol D-300 instrument.

2-Phenyl-3-[3′-(2″,4″,6″-trichlorophenoxymethyl)-5′-mercapto-1′,2′,4′-triazol-4′-yl]-5(H)-4-thiazolidinones (**1a**) : A mixture of 3-(2′,4′,6′-trichlorophenoxymethyl)-4-(*N*-benzylidinylamino)-5-mercapto-1,2,4-triazole (0.01 mol) and thioglycolic acid (0.012 mol) was heated in oil bath at 115–120° for 12–15 h.The resulting product was isolated using sodium bicarbonate and crystallized from DMF,(60%),m.p.115°; ν_{max} 2963–2966 ($-CH_2$-str.),1682(C=O str., thiazolidinone),1303–1319 (-C=N-str.),1030–1049 and 1250–1265 (-C-O-C str.),813–833 (1 : 4 sub), 671–679 cm^{-1} (C–Cl); δ (DMSO) 2.507 (1H, s, Ar-SH), 3.334 (2H, s, Ar-O-CH_2-Ar), 8.079 (1H, s, -N-CH), 7.557 (1H, s, $-CH_2$-), 8.519 (2H, s, Ar-H), 7.201–8.436 (4H, m, Ar-H); *m/z*; **1e** 530, 243, 275, 184, 175, 135, 92, 77, 65, 64. All other compounds (**1b-j**) were prepared by similar procedure (yields 60–75%) : **1b**, m.p.190°; **c**, 148°; **d**, 140°; **e**, 125°; **f**, 205°; **g**, 128°; **h**, 120°; **i**, 170°; **j**, 165°.

Table 1. Physical data and antimicrobial activity of compounds **1a-j**, **2a-j** and **3a-j**

Compd.	R	M.p. (°C)	Yield (%)	Antibacterial activity								Anti T.B activity
				E. coli		*S. aureus*		*S. typhi*		*B. subtilus*		Minimum inhibitory
				200 (mcg/ml)	2000 (mcg/ml)	200 (mcg/ml)	2000 (mcg/ml)	200 (mcg/ml)	2000 (mcg/ml)	200 (mcg/ml)	2000 (mcg/ml)	concentration against $H_{37}Rv$
1a	H	115	60	–	–	++	++	–	–	–	–	
1b	2-OH	190	68	–	+	–	+	–	–	++	++	Not active
1c	2-Cl	148	62	–	–	+	++	+	+	–	+	Not active
1d	2-NO_2	140	68	–	–	++	++	–	–	–	–	
1e	3-NO_2	125	60	++	++	++	++	–	–	–	–	
1f	4-NO_2	205	62	–	–	++	++	–	–	–	–	200 mcg/ml
1g	2-OCH_3	128	65	++	++	++	++	–	–	–	–	
1h	4-OCH_3	120	70	+	+	+	+	+	+	+	+	200 mcg/ml
1i	3-OCH_3, 4-OH	170	59	+	+	+	+	+	+	++	++	
1j	4-$N(CH_3)_2$	165	75	+	+	–	–	+	+	+	+	200 mcg/ml
2a	H	119	55	+	+	+	+	+	+	+	+	
2b	2-OH	168	65	+	+	+	+	+	+	+	+	
2c	2-Cl	155	58	+	+	+	+	+	+	+	+	Not active
2d	2-NO_2	135	62	+	+	+ +	++	+	+	+	+	Not active
2e	3-NO_2	109	60	+	+	+	+	+	+	+	+	
2f	4-NO_2	115	65	+	+	+	+	+	+	–	+	Not active
2g	2-OCH_3	130	62	–	+	–	+	–	–	+	+	
2h	4-OCH_3	137	68	+	+	–	+	–	+	+	+	Not active
2i	3-OCH_3, 4-OH	160	55	–	+	–	+	–	+	+	+	
2j	4-$N(CH_3)_2$	153	70	–	+	–	+	–	+	–	+	Not active
3a	H	100	62	+	+	–	+	+	+	+	+	
3b	2-OH	120	65	+	+	–	+	–	+	+	+	Not active
3c	2-Cl	150	56	+	+	+	+	+	+	+	+	
3d	2-NO_2	146	69	+	+	–	+	+	+	–	+	
3e	3-NO_2	165	68	+	+	–	+	+	+	+	+	
3f	4-NO_2	175	72	+	+	+	+	+	+	+	+	200 mcg/ml
3g	2-OCH_3	125	65	+	+	+	+	+	+	+	+	
3h	4-OCH_3	155	68	+	+	+	+	+	+	+	+	200 mcg/ml
3i	3-OCH_3, 4-OH	185	60	+	+	+	+	+	+	+	+	200 mcg/ml
3i	4-$N(CH_3)_2$	170	62	+	+	+	+	–	+	–	+	

All compounds gave satisfactory C, H and N analysis.

– Not active, (0–10 mm) = + mildly active, (10–18 mm) = ++ moderately active (19 mm, up) = +++ highly active.

2-Phenyl-3-[3′-(2″,4″,6″-trichlorophenoxymethyl)-5′-mercapto-1′,2′,4′-triazol-4′-yl]-5-methyl-4-thiazolidinones (**2a**) : A mixture of 3-(2′,4′,6′-trichlorophenoxymethyl)-4-(*N*-benzylidinylamino)-5-mercapto-1,2,4-triazol (0.01 mol) and thiolactic acid (0.01 mol) was heated at 120–125° for 12 h. The reaction mixture was cooled and treated with 10% sodium bicarbonate solution.The product was isolated and crystallised from ethanol, (55%), m.p.119°; ν_{max} 2912–2970 (-CH_2- str.), 1682–1686 (C=O str., thiazolidinone), 1303–1362 (-C=N- str.), 1038–1049 and 1246–1265 (-C-O-C str.), 814–833 (1 : 4 sub.), 671–687 cm^{-1} (C–Cl); δ (DMSO) 2.500 (1H, s, Ar-SH). 3.518 (2H, s, Ar-O-CH_2-Ar), 7.877 (1H, s, -N-CH). 7.453 (1H, q, -*C*H-CH_3,). 1.534 (3H, d, *J* 6.6 Hz. -CH-*C*H_3). 8.487 (2H, s, Ar-H), 7.188–8.261 (4H, m, Ar-H); *m/z*; **2e** 457, 459, 238, 239, 240, 184, 186, 175, 176, 177, 135, 92,

77, 65. All other compounds (**2b-j**) were prepared by similar procedure; (yields 55–70%); **2b**, m.p.168°; **c**, 155°; **d**, 135°; **e**, 109°; **f**, 115°; **g**, 130°; **h**, 137°; **i**, 160°; **j**, 153°.

2-Phenyl-3-[3′-(2″,4″,6″-trichlorophenoxymethyl)-5′-mercapto-1′,2′,4′-triazol-4′-yl]-5-carboxymethyl-4-thiazolidinones (**3a**) : A mixture of 3-(2′,4′,6′-trichlorophenoxymethyl)-4-(*N*-benzylidinylamino)-5-mercapto-1,2,4-triazol (0.01 mol) and thiomalic acid (0.01 mol) was heated at 160° for 2–4 h.The temperature was then raised to 180° for 30 min. The product was dissolved in sodium bicarbonate solution and reprecipitated by 10% hydrochloric acid and crystallized from ethanol, (62%), m.p. 100°; ν_{max} 3668 (-OH str.), 2912–2970 (-CH_2- str.), 1686–1693 (C=O str., thiazolidinone),1315–1342 (-C=N- str.), 1038–1049 and 1246–1265 (-C-O-C str.), 814–833 (1 : 4 sub.), 671–698 cm^{-1} (C-Cl); δ (DMSO) 2.500 (1H, s, Ar-SH), 3.336 (2H, s, Ar-O-CH_2-Ar), 7.915 (1H, s, -N-CH), 7.520 (1H, t, -*C*H-CH_2COOH), 3.825 (2H, aryl acid, d, *J* 11 Hz, CH-*C*H_2COOH), 8.584 (2H, s, Ar-H), 7.008–7.633 (4H, m, Ar-H),11.477 (1H, acid, s, -COOH); *m/z*; **3e** 499, 481, 314, 315, 284, 285, 256, 135, 92, 77, 65. All other compounds (**3b-j**) were prepared by similar procedure (yields 56–72%); **3b**, m.p.120°; **c**, 150°; **d**, 146°; **e**, 165°; **f**, 175°; **g**, 125°; **h**, 155°; **i**, 185°; **j**, 170°.

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