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NOTE

Synthesis, Characterization and Antibacterial Activity of 2-[(Substituted phenyl)]-3-[(2-methyl-4-thiazolyl)acetamido]-Thiazolidin-4-Ones

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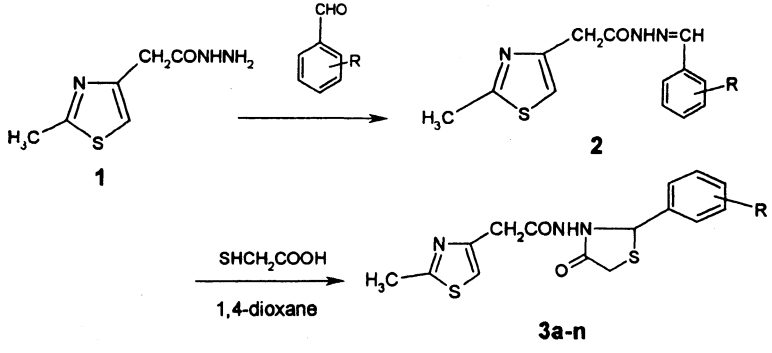
2-[(Substituted phenyl)]-3-[(2-methyl-4-thiazolyl)acetamido]thiazolidin-4-ones were synthesized by reacting the Schiff's bases of 2-methylthiazole-4-acetic acid hydrazide with thioglycolic acid. The title compounds were characterized by spectral data and were screened for antibacterial activity. Some of these thiazolidinones show promising activity.

Key Words: Synthesis, Antibacterial activity, 2[(Substituted phenyl)]-3-[(2-methyl-4-thiazolyl)acetamido]thiazolidin-4-ones.

Thiazoles are shown to possess array of biological activities, antiinflammatory[1, 2], antitubercular[3] and antimicrobial[4]. Thiazolidinones also exhibit a variety of biological activities such as antitubercular[5], anticonvulsant[6], antifungal[7], antibacterial[8] and antitumour[9]. These observations prompted us to combine the two moieties with the hope of producing new compounds with augmentation in antibacterial activity.



Scheme

IR (KBr) spectra were recorded on Shimadzu FTIR 8700. ^{1}H NMR spectra were recorded on EM 390 CW-NMR 90 MHz using TMS as internal standard. Mass spectra were recorded on a Finigan Mat 8230 MS-GC.

Synthesis of 2-[(2-chlorophenyl)]-3-[(2-methyl-4-thiazolyl)acetamido]-thiazolidin-4-one (3a): 2-Methylthiazole-4-acetic acid hydrazide is synthesized by reported method[10]. The hydrazide obtained was refluxed with salicylaldehyde for 2 h to get the Schiff's base (4N′-(2-hydroxyphenylidene hydrazido)-2-methyl thiazole-4-yl-acetamide). The Schiff's base was refluxed with thioglycolic acid in 1,4-dioxane with a pinch of fused zinc chloride[11] for 12 h. The reaction mixture was concentrated, cooled to room temperature and poured into cold water. The separated solid was washed with cold water, dried and recrystallized from ethyl alcohol; yield 93%. Similarly, the other thiazolidinone derivatives were synthesized (**3b–n**) and their physical data along with antibacterial activities are reported in Table-1.

Characterization of 2-[(4-chlorophenyl)]-3-[(2-methyl-4-thiazolyl)]-acetamido]thiazolidin-4-one (3j): IR (KBr, cm^{-1}), 3153 ν(N—H); 2922 ν(C—H); 1687 ν(C=O of carboxamide); 856 ν(C=O of Tz); 759 ν(C—Cl); 723 ν(C—S—C). PMR spectrum ($CDCl_3$) δ : 8.6, 1H (s, NH); 7.8–7.2 6H {m, Ar—H (5) + thiazole (1H)}; 1.6–1.4 5H {CH_3(3H) + CH_2C=O (2H)-merged}; 1.3–1.2, 2H (s, CH_2-thiazole). Mass spectrum 367 (M^{+1}); 40 (100%); other peaks are at 332, 222, 165, 139, 111, 75, 63 and 40.

Antibacterial activity: The final compounds were screened for antibacterial activity by agar diffusion method[12] at a concentration of 100 μg/0.1 mL using two Gram +ve and two Gram –ve organisms. The activity was compared with amoxicillin (conc. 100 μg/0.1 mL) as standard. Results are recorded in Table-1.

TABLE-1
PHYSICAL DATA AND ANTIBACTERIAL ACTIVITY OF 2-[(SUBSTITUTED PHENYL)]-3-[(2-METHYL-4-THIAZOLYL)ACETAMIDO]THIAZOLIDIN-4-ONES

Compd.	R	m.f. (m.w.)	m.p. (°C)	Zone of inhibition in mM			
				E.c	*P.a*	*B.s*	*S.a*
3a	2-OH	$C_{15}H_{15}N_3O_3S_2$ (249)	170	12	13	15	14
3b	2-Cl	$C_{13}H_{12}N_3OSCl$ (367.5)	104	—	9	8	8
3c	4-N(Me)$_2$	$C_{17}H_{20}N_4O_2S_2$ (376)	180	9	10	11	12
3d	2-NO_2	$C_{14}H_{14}N_4O_4S_4$ (378)	124	9	10	11	12
3e	5-Cl-2-OH	$C_{15}H_{14}N_3O_3S_2Cl$ (343.5)	130	15	14	20	18
3f	2-Furfuryl	$C_{13}H_{13}N_3O_3S_2$ (323)	136	10	11	10	11
3g	4-OH-3-OMe	$C_{16}H_{17}N_3O_4S$ (379)	138	14	20	18	20
3h	4-OMe	$C_{16}H_{17}N_3O_3S_2$ (363)	154	17	15	19	17
3i	H	$C_5H_{15}N_3O_2S_2$ (333)	150	16	14	18	16
3j	4-Cl	$C_{15}H_{14}N_3O_2S_2Cl$ (367.5)	120	8	12	9	11
3k	4-OH	$C_{15}H_{15}N_3O_3S_2$ (349)	210	9	11	10	10
3l	5-Br-2-OH	$C_{15}H_{14}N_3O_3S_2Br$ (427.9)	140	8	12	21	19
3m	4NO_2	$C_{14}H_{14}N_4O_4S_2$ (378)	118	10	9	9	11
3n	4-OCH$_2$COOH-3-OMe	$C_{17}H_{19}N_3O_9S_2$ (425)	150	10	10	20	19
Standard	Amoxicillin			20	20	25	22

Compound **3g** showed very good activity against all the organisms except *Escherichia coli* whereas compounds **3e** and **3l** showed good activity against *Bacillus subtilis* and *Staphylococcus aureus* while other compounds have moderate or negligible activity compared to that of the standard.

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