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NOTE

Synthesis and Antibacterial Activity of N′-(Substituted Phenylidene Hydrazido)-2-Methylthiazole-4-yl Acetamides

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Arylidene derivatives of ethyl-2-methylthiazole-4-acetic acid were synthesized by condensing ethyl ester of 2-methyl thiazole-4-acetic acid and hydrazine hydrate followed by the reaction with respective aldehydes. These are characterized on the basis IR, NMR and mass spectral data. The synthesized compounds were evaluated for antibacterial activity against organisms *Pseudomonas aeruginosa, Bacillus subtilis, Escherichia coli and Staphylococcus aureus.*

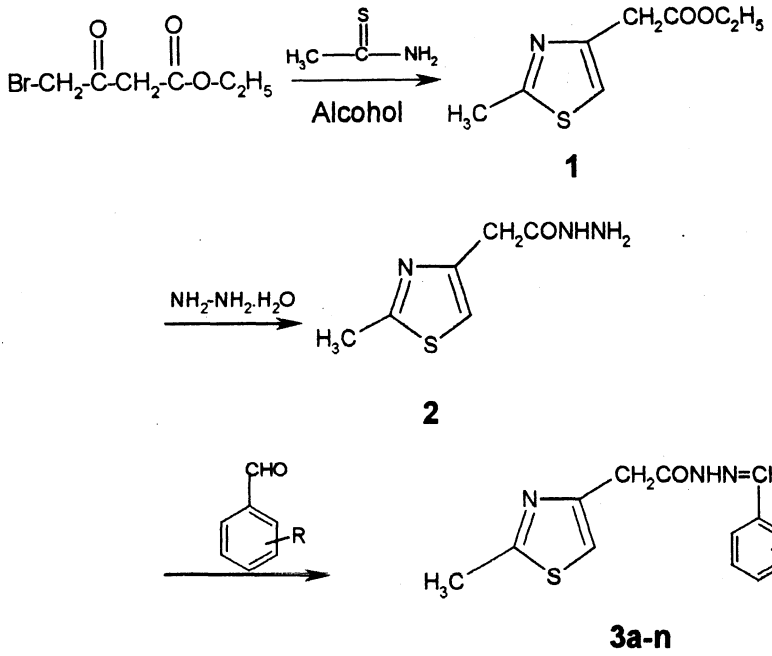
Key Words: Ethyl-2-methyl thiazole-4-acetate, Arylidene derivatives, Antibacterial activity.

Thiazoles and their substituted ring systems have been shown to possess good antimicrobial, analgesic and antiinflammatory activities[1–3]. Arylidene derivatives show an array of biological activities such as antimicrobial, antiinflammatory and antitubercular activities[4–6]. In continuation with our previous work on arylidene derivatives of 1,2,4-trizoles and thiazoles, more compounds of similar nature have been synthesized and evaluated for antibacterial activity.

Synthesis of ethyl-2-methylthiazole-4-acetate (1): Ethyl bromo aceto- acetate, prepared by treating ethyl acetoacetate and bromine, was reacted with thioacetamide in ethyl alcohol. This was allowed to stand for 16 h. 2 N HCl was added and the mixture was washed with ether. The aqueous portion was mixed with excess of solid sodium bicarbonate. The oily, immiscible thiazole acetic acid ester formed was isolated by extraction with ether, yield 82%.

Synthesis of 2-methylthiazole-4-acetic acid hydrazide (2): Compound **1** and hydrazine hydrate were mixed in ethyl alcohol and refluxed for 3 h. The

alcohol was distilled off[7] to get the hydrazide which was recrystallized from benzene and ethyl acetate, yield 84%.



Scheme-1

Synthesis of N′ (substituted phenylidene hydrazido)-2-methylthiazole-4-yl acetamide (3a–n): Compound **2** and respective aldehydes were taken in ethyl alcohol and refluxed for 2 h. The 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[8], yield 80–90%.

Characterization of N′ (4-methoxy phenylidene hydrazido)-2-methyl thiazole-4-yl acetamide (3h): IR (KBr, cm^{-1}): 3242 ν(N—H); 1668 ν(C=O, str.); 1552 ν(NH bending); 1249 ν(C=N); 1178 ν(C—S). PMR spectrum ($CDCl_3$) δ: 10.1, 1H (s, N=CH); 0.2, 1H (s, NH); 8.1–6.8 5H {m ArH(4) + thiazole (1H)}; 4.3, 2H (s, CH_2CO); 3.8, 3H (t, OCH_3); 2.8–2.6, 3H (d, CH_3). Mass: 289(M+), 177, 150, 134, 113 (100%), 91, 71, 63, 40.

Antibacterial activity: Title compounds are evaluated for antibacterial activity by agar diffusion method[9] at a concentration of against the test organisms. The zones of inhibition were compared with std. amoxicillin (concentration 100 μg/0.1 mL). Results obtained are recorded in Table-1.

Compounds **3e** and **3l** showed good activity against all the organisms. All other compounds had moderate or negligible activity compared to that of the standard.

TABLE-1
ANTIBACTERIAL ACTIVITY OF N′ (SUBSTITUTED PHENYLIDENE HYDRAZIDO)-2-METHYLTHIAZOLE-4-yl ACETAMIDES

Compound	m.f.	m.p.	m.w.	R	Zone of inhibition in mM			
					E.c	*P.a*	*B.s*	*S.a*
3a	$C_{15}H_{15}N_3O_3S_2$	186	349.0	2-OH	12	13	15	14
3b	$C_{13}H_{12}N_3OSCl$	110	367.5	2-Cl	—	9	8	8
3c	$C_{17}H_{20}N_4O_2S_2$	210	376.0	4-N(Me)$_2$	9	10	11	12
3d	$C_{14}H_{14}N_4O_4S_2$	136	378.0	2-NO_2	9	10	11	12
3e	$C_{15}H_{14}N_3O_3S_2Cl$	165	343.5	5-Cl-2-OH	15	14	20	18
3f	$C_{13}H_{13}N_3O_3S_2$	142	323.0	2-Furfuryl	10	11	10	11
3g	$C_{16}H_{17}N_3O_4S_2$	140	379.0	4-OH-3-OMe	14	20	18	20
3h	$C_{16}H_{17}N_3O_3S_2$	175	363.0	4-OMe	17	15	19	17
3i	$C_5H_{15}N_3O_3S_2$	162	333.0	H	16	14	18	16
3j	$C_{15}H_{14}N_3O_2S_2Cl$	190	367.5	4-Cl	8	12	9	11
3k	$C_{15}H_{15}N_3O_3S_2$	220	349.0	4-OH	9	11	10	10
3l	$C_{15}H_{14}N_3O_3S_2Br$	154	427.9	5-Br-2-OH	8	12	21	19
3m	$C_{14}H_{14}N_4O_4S_2$	124	378.0	4NO_2	10	9	9	11
3n	$C_{17}H_{19}N_3O_9S_2$	184	425.0	4-OCH_2COOH-3-OMe	10	10	20	19
Std.	Amoxicillin				20	20	25	22

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