Original Research Paper

Volume-9 | Issue-7 | July - 2019 | PRINT ISSN No. 2249 - 555X

Pharmacy

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF SUBSTITUTED THIAZOLIDINONE DERIVATIVES AS ANTIMICROBIAL AGENTS

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ABSTRACT A series of compounds were synthesized from 2-imino-5-phenyl-1, 3-thiazolidin-4-one which was prepared from a one-pot three component condensation reaction of benzaldehyde, thio urea and chloroform in the presence of potassium hydroxide under Reeve's condition. All the newly synthesized compounds 3(a-e) were characterized by IR, 1HNMR, 13C NMR spectral data. All the compounds were screened for their anti bacterial and antifungal activities.

KEYWORDS : Anisaldehyde, Benzaldehyde, Salicyladehyde, P-chlorobenzaldehyde, 4 -dimethyl amino Benzaldehyde.

INTRODUCTION

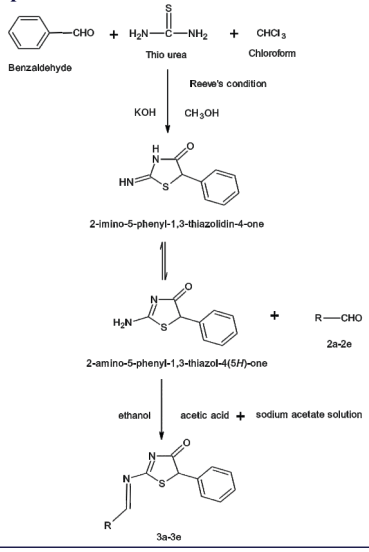
In the recent past, there has been a considerable interest and enthusiasm in developing novel small heterocyclic moieties possessing significant biological activities. The presence of thiazole moiety in the structure of several naturally occurring molecules with important antibiotic, immunosuppressive and antitumor activities has been well known for long. Small ring heterocycles containing nitrogen, sulfur and oxygen have been under investigation for a long time because of their important medicinal properties [1].

MATERIALS AND METHODS:

Materials

Thio urea, benzaldehyde, chloroform, methanol, potassium hydroxide, absolute ethanol, anisaldehyde, Salicyladehyde, P-chlorobenzaldehyde, Sodium acetate, Glacial acetic acid, 4 -dimethyl amino Benzaldehyde. All reagents and solvent were of analytical grade and were used as received without further treatment.

Scheme of the present work



General Procedure For The Synthesis Of 2-imino-5-phenyl-4-thiazolidinone

Thio urea (0.1mole) was dissolved in 25ml of methanol and fused with bezaldehyde (0.1mole) and chloroform (0.1mole) in presence of 4 ml of potassium hydroxide solution and refluxed for 4 hours at 50◦c in Reeve's condition. The reaction mixture was transferred into a beaker and cooled in an ice bath. The product was recrystallized using methanol and washed with cold methanol. Yield=92.2%. [2]

Synthesis Of 2-imino-5-phenyl-4-thiazolidinone Derivatives

2-amino 5-phenyl- 4-thiazolidinone (0.01 mole) taken in a 100ml round bottom flask and 20 ml of ethanol was poured into it. To that 2 to 4 drops of sodium acetate solution and 1 ml of Glacial acetic acid were added. After that different substituted aromatic aldehydes (0.01 mole) were added to the reaction mixture and then refluxed for 9 hours at 50◦c. the Then the reaction mixture was transferred into the beaker and cooled in a ice bath. It was filtered, dried and purified by recrstallization using enthanol. Yield=92.2%.

SCHEME DETAILS

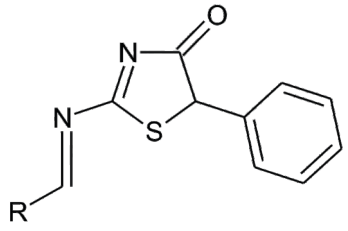
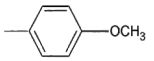
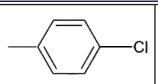
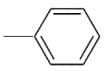
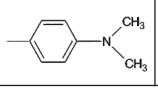


Table: 1: List of title compounds

S. No	Compound Code	R	IUPAC name
1	3a		2-{[(1*E*)-(4-methoxyphenyl) methylene] amino}-5-phenyl-1,3-thiazol-4(5*H*)-one
2	3b		2-{[(1*E*)-(2-hydroxyphenyl) methylene] amino}-5-phenyl-1,3-thiazol-4(5*H*)-one

3	3c		2-{[(1*E*)-(4-chlorophenyl) methylene]amino}-5-phenyl-1,3-thiazol-4(5*H*)-one
4	3d		5-phenyl-2-{[(1*E*)-phenylmethylene] amino}-1,3-thiazol-4(5*H*)-one
5	3e		2-({(1*E*)-[4-(dimethylamino) phenyl]methylene}amino)-5-phenyl-1,3-thiazol-4(5*H*)-one

Preliminary QSAR studies:

Table 2: Physico-chemical parameters of the synthesized compounds

Compound Code	Molecular formula	Molecular weight	% yield	Melting point	Rf value	Log p
3a	$C_{17}H_{14}N_2O_2S$	310.3702	88	156-158	0.82	3.03
3b	$C_{16}H_{12}N_2O_2S$	296.3436	90	153-154	0.78	2.91
3c	$C_{16}H_{11}C_lN_2OS$	314.7893	85	140-141	0.72	3.65
3d	$C_{16}H_{12}N_2OS$	280.3442	72	149-140	0.88	2.97
3e	$C_{18}H_{17}N_3OS$	323.42	95	166-168	0.84	3.08

Table 3: Molecular Property

Compound code	Log p	Polar surface area	No of atoms	No of H-bond acceptors	No of H-bond donors	No of rule of 5 violations	No of rotatable bonds	volume
3a	3.03	51.03	22	4	0	0	4	270.62
3b	2.91	62.03	21	4	1	0	3	253.09
3c	3.65	41.80	21	3	0	0	3	258.61
3d	2.97	41.80	20	3	0	0	3	245.07
3e	3.08	45.04	23	4	0	0	4	290.98

Table 4: Bioactivity score of compounds

Compound code	GPCR Ligand	Ion channel Modulator	Kinase inhibitor	Nuclear receptor ligand	Protease Inhibitor	Enzyme inhibitor
3a	-0.60	-0.60	-0.58	-0.66	-0.71	-0.34
3b	-0.57	-0.61	-0.57	-0.59	-0.66	-0.26
3c	-0.60	-0.54	-0.61	-0.73	-0.76	-0.34
3d	-0.66	-0.56	-0.65	-0.78	-0.79	-0.31
3e	-0.51	-0.52	-0.46	-0.48	-0.63	-0.29

Spectral Characterization of Synthesized Compounds

Compound 3a

IR Spectral Data: C=N (oxime) – 1678.0, C=N str (ring) – 1512.2, C=O – 1756.1, C-H (aromatic stretch) - 3166.7, C=C (aromatic) – 1595.3, C-O – 1261.0

^{1}H-NMR Spectrum of Compound 3a: 7.84- 7.98(4H, m) (Ar-H), 8.43-8.8(1H, s) (-N=CH), 3.9 (3H, s) (-OCH_3)

Compound 3b

IR Spectral Data: C=N (oxime) – 1614.5, C=N str (ring) – 1590.8, C=O – 1760.1, C-H (aromatic stretch) - 3173.7, C=C (aromatic) – 1475.0, OH (phenolic) – 3380.7

Compound 3c

IR Spectral Data: C=N (oxime) – 1690.1, C=N str (ring) – 1431.8, C=O – 1753.6, C-H (aromatic stretch) - 3168.2, C=C (aromatic) – 1478.4, Cl (stretch) – 729.0

Compound 3d

IR Spectral Data: C=N (oxime) – 1691.5, C=N str (ring) – 1432.2, C=O – 1756.6, C-H (aromatic stretch) - 3171.6, C=C (aromatic) – 1568.9.

1713.048, C-H (aromatic stretch) - 3165.582, C=C (aromatic) – 1593.375, C=C (str

Compound 3e

IR Spectral Data:C=N (imine) – 1648.219, C=N str (ring) – 1465.168, C=O – 1710.33, C-H (aromatic stretch) - 3173.637, C=C(aromatic) – 1547.830,C-N (alkyl) – 1163.370, C-N (aryl) – 1311.96

^{1}H-NMR Spectrum of Compound 3e: 7-26- 7.73(m, 9H, Ar-H), 6.67-6.69(6H, CH=C), 3.068 (s, H, N=CH)

Table 5: Invitro Antibacterial activity of the synthesized compounds

Sl. no	Compound code	Name of the organisms	Zone of inhibition in mm			
				Concentration(µg/ml)		
			Std 1mg/ml	1000µg	750µg	500µg
1	3a	*Bacillus subtilis*	40	30	23	22
		Staphylococcus aureus	43	22	10	8
		Escherichia coli	22	22	13	10
		Salmonella typhi	30	14	11	9
2	3b	*Bacillus subtilis*	40	30	22	22
		Staphylococcus aureus	43	27	13	10
		Escherichia coli	22	11	10	10
		Salmonella typhi	30	15	11	9
3	3c	*Bacillus subtilis*	40	22	21	19
		Staphylococcus aureus	43	23	9	8
		Escherichia coli	22	11	10	9
		Salmonella typhi	30	13	9	8
4	3d	*Bacillus subtilis*	40	22	21	21
		Staphylococcus aureus	43	22	8	8
		Escherichia coli	22	13	12	10
		Salmonella typhi	30	11	10	10
5	3e	*Bacillus subtilis*	40	27	20	19
		Staphylococcus aureus	43	22	10	10
		Escherichia coli	22	11	11	10
		Salmonella typhi	30	13	9	9

RESULT AND DISCUSSION

Chemistry and synthesis:

- 2-imino-5-phenyl-4-thiazolidinone condensed with substituted aromatic aldehydes (anisaldehyde, salicyaldehyde, para-chloro benzaldehyde, benzaldehyde and 4-dimethylaminobenzaldehyde) in presence of ethanol, Glacial acetic acid and sodium and acetate to form corresponding substituted 2-imino-5-phenyl-4-thiazolidinone derivatives.
- FT-IR and ^{1}H-NMR, ^{13}C-NMR spectral data of the titled compounds were in correlation with the expected structure.

PHARMACOLOGICAL EVALUATIONS:

Invitro antibacterial and antifungal activities:

- All synthesized novel substituted thiazolidinone compounds were tested against Gram positive organism such as *Bacillus subtilis* and Gram negative organisms such as *Escherichia coli* and *Salmonella typhi* and fungus *Candida albicans* at a concentration of 1000, 750, 500, µg/ml by disc diffusion method.
- All the compounds showed moderate to potent antibacterial and antifungal activities when compared with ***Ampicillin*** concentration of 1mg/ml (20 µl) and ***Amphotericin-B*** concentration of 1mg/ml (20 µl) respectively as standard.
- All the compounds 3a, 3b, 3c, 3d exhibited significant antibacterial activity against *Bacillus subtilis* and moderate effect to the *Staphylococcus aureus*. Less effective against *Salmonella typhi and Escherichia coli* when compared with standard.
- All the compounds 3a, 3b, 3c, 3d, 3e exhibited significant antifungal activity when compared with standard.

REFERENCES

1. Ashraf Mashrai, Ayaz Mahmood Dar, Shafia Mir and Shamsuzzaman. Strategies for the Synthesis of Thiazolidinone Heterocycles, Journal of Medicinal Chemistry, (Los Angeles) 6:280-291. doi:10.4172/2161-0444.1000358, apirl 30, 2016.
2. N.Sunitha, R.Gopi Krishna, R.Lalitha and V.Rajkumar. Synthesis and biological evaluation of new thiazolidinone derivatives. International Journal ofMedicinal Chemistry & Analysis, Vol 6 (1); 2016: P. 19-26.