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"DESIGN AND SYNTHESIS OF NEW SERIES OF 5-[3-(SUBSTITUTEDPHENYL)-1-{4-[2-(4-CHLOROPHENYL)-4-OXO-1,3-THIAZOLIDIN-3-YL]PHENYL]PROP-2-EN-1-YL}PYRIMIDINE-2,4,6-TRIONE DERIVATIVES"

Nital N. Patel[1] and Pankaj S. Patel*[2]

[1]Department of Chemistry, Sheth LH Science College, Mansa Research Scholar of Gujarat University, Ahmedabad.
[2]Head, Chemistry Department, Sheth L. H. Science College, Mansa

***Corresponding Author: Dr. Pankaj S. Patel**

Head, Chemistry Department, Sheth L. H. Science College, Mansa.

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ABSTRACT

Heterocyclic Compounds have so far been synthesized mainly due to the wide range of biological activities. Thiazolidinone plays an important role in biological field. From these reviews we synthesized a new series of 5-[3-(substitutedphenyl)-1-{4-[2-(4-chlorophenyl)-4-oxo-1,3-thiazolidin-3-yl]phenyl]prop-2-en-1-yl}pyrimidine-2,4,6-trione derived from 3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-2-(4-chlorophenyl)-1,3-thiazolidin-4-one and barbituric acid in CH_3COOH. The title compounds were characterized by element analysis, IR, NMR and spectral data. All the compounds were tested for their antibacterial and antifungal activities by Cup Borer method.

KEY WORDS: Thiazolidinone, Trion, IR, NMR, Cup Borer method.

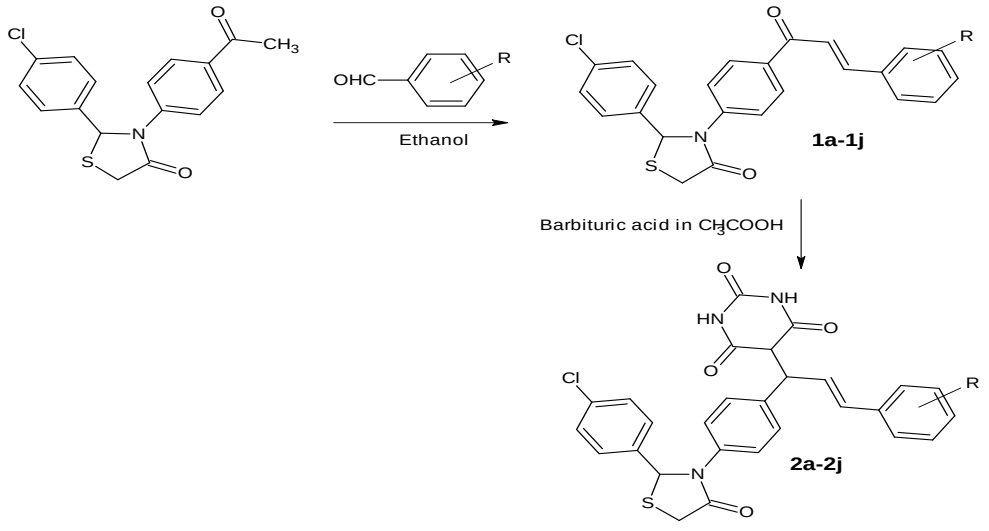
INTRODUCTION

One of the most fruitful paradigms for discovery of new bioactive chemical entities is starting with established structural cores, known to be part of other bioactive molecules.[1] Barbiturates exhibit a broad range of biological activities, including sedative[2], anticancer[3], antibacterial[4], antioxidant[5], hypnotic[6], anti-convulsant[7], immuno-modulating[8], radio-sensitizing[9], and gelatinase inhibiting.[10]

EXPERIMENTAL

All reagents were of analytical reagent grade and were used without further purification, All the product were synthesized and characterized by their spectral analysis. Melting points were taken in open capillary tube. The IR spectra were recorded on Bruker Model; Alpha, Laser Class1, made in Germany and Brooker instrument used for NMR Spectroscopy was 500 MHz and tetramethyl silane used as internal standard. Solvent used were DMSO. Purity of the compounds was checked by TLC on silica-G plates. Anti-microbial activities were tested by Cup-Borer method.

Reaction Scheme



Preparation of 3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-2-(4-chlorophenyl)-1,3-thiazolidin-4-one.(1a-1j) To the solution of 3-(4-acetylphenyl)-2-(4-chlorophenyl)-1,3-thiazolidin-4-one (0.01M) in absolute ethanol (50 ml), substituted aldehyde (0.01M) and 2% NaOH (10 ml) were added and refluxed for 10 hours. After refluxing the reaction mixture was concentrated, cooled, filtered and neutralized with dil. HCl. The solid residue thus obtained was crystallized by absolute ethanol. **IR(1g), cm^{-1}**: 3288 (-OH), 3045 (=CH), 2948(-CH stretching), 1739 (>C=O stretching), 1521 (>C=C< Aromatic), 1438 (-CH_3- bend), 1347 (C-N), 822(C-Cl), 651 (C-S-C). **^{1}H-NMR (1d-DMSO, δ ppm):** 3.339 (2H, s, -CH_2-), 5.810 (1H, s, >CH-), 6.15-7.923(13H, m, Ar-H), 7.945 (2H, d, -CH=CH-).

Preparation of 5-[3-(substitutedphenyl)-1-{4-[2-(4-chlorophenyl)-4-oxo-1,3-thiazolidin-3-yl]phenyl]prop-2-en-1-yl}pyrimidine-2,4,6-trione (2a-2j)

A mixture of Preparation of 3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-2-(4-chlorophenyl)-1,3-thiazolidin-4-one (0.01M) in 15ml ethanol, barbituric acid (0.01M) and gl. acetic acid (15ml) was refluxed for 8 hrs. in oil bath. The contents were poured into ice and the product was isolated and crystallized from ethanol. **IR (2i), cm^{-1}**: 3312 (>NH-), 3085 (=CH), 2980 (-CH stretching), 1725 (>C=O stretching), 1512 (>C=C< Aromatic), 1456 (-CH_2- bend), 1410 (-CH_3), 1290 (C-N), 1252 (C-O-C), 812 (C-Cl), 687 (C-S-C).**^{1}H-NMR (2e-DMSO, δ ppm)**: 3.311(2H, s, -CH_2-), 3.913(2H,d,-CH<), 5.935(1H, s, >CH-),6.987 (1H, s, -CH=CH-), 9.017 (1H, s, -OH), 10.076(2H, s, -NH-), 6.550-7.720 (12H, m, Ar-H)

Table 1: ***Physical constant of 2a-2j.***

Comp'd	R	M.F.	Yield %	M.P. °C	Elemental Analysis		
					% C Found (Calcd)	% N Found (Calcd)	% H Found (Calcd)
2a	-2-Cl	$C_{28}H_{21}Cl_2N_3O_4S$	85	191	59.34 (59.37)	7.39 (7.42)	3.71 (3.74)
2b	-4-Cl	$C_{28}H_{21}Cl_2N_3O_4S$	81	185	59.35 (59.37)	7.38 (7.42)	3.72 (3.74)
2c	-3,4- $(OCH_3)_2$	$C_{30}H_{26}ClN_3O_6S$	87	196	60.85 (60.86)	7.08 (7.10)	4.41 (4.43)
2d	-H	$C_{28}H_{22}ClN_3O_4S$	67	184	63.18 (63.21)	7.87 (7.90)	4.15 (4.17)
2e	-2-OH	$C_{28}H_{22}ClN_3O_5S$	73	179	61.35 (61.37)	7.66 (7.67)	4.04 (4.05)
2f	-4-OH- 3-OCH_3	$C_{29}H_{24}ClN_3O_6S$	70	205	60.23 (60.26)	7.24 (7.27)	4.15 (4.18)
2g	-4-OH	$C_{28}H_{22}ClN_3O_5S$	75	195	61.34 (61.37)	7.64 (7.67)	4.04 (4.05)
2h	-4-$N(CH_3)_2$	$C_{30}H_{27}ClN_4O_4S$	83	186	62.65 (62.65)	9.69 (9.74)	4.71 (4.73)
2i	-4-OCH_3	$C_{29}H_{24}ClN_3O_5S$	85	182	61.94 (61.97)	7.45 (7.48)	4.28 (4.30)
2j	-3-NO_2	$C_{28}H_{21}ClN_4O_6S$	73	190	58.25 (58.28)	9.68 (9.71)	3.64 (3.67)

Table 2: ***Antimicrobial activities of 2a-2j.***

Sr. No.	Comp. No.	R	Zone of Inhibitions in mm		
			Antibacterial activity		Antifungal activity
			E. coli	S. aureus	C. albicans
1	2a	-2-Cl	18	19	14
2	2b	-4-Cl	16	15	NA
3	2c	-3,4- $(OCH_3)_2$	NA	18	15
4	2d	-H	14	16	18
5	2e	-2-OH	15	14	17
6	2f	-4-OH- 3-OCH_3	12	15	14
7	2g	-4-OH	14	17	15
8	2h	-4-$N(CH_3)_2$	17	13	16
9	2i	-4-OCH_3	16	18	14
10	2j	-3-NO_2	14	16	13
11	SD - 1	Penicillin	15	17	-

12	SD - 2	Kanamycin	17	19	-
13	SD - 3	Baycor 25 w.p.	-	-	18
14	SD - 4	Amphotericin	-	-	20
15	Solvent	DMF	11	12	12

RESULTS AND DISCUSSION

Antibacterial activity

Against Escherichia Coli

From screening results, substituted derivatives 2a and 2h possesses very good activity against Penicillin and Kanamycin. The compounds 2d and 2j was shown minimum antibacterial activity. 2c was found to be inactive against Escherichia Coli. Rest of all compounds were found to show good to moderate activity against Saccharomyces as compared to the standard drug Kanamycin.

Against Staphylococcus aureus

Biological evaluation of present investigation revealed the maximum antibacterial activity was shown by the compound 2a and 2c. The minimum antibacterial activity was shown by the compound 2e and 2h. The remaining compounds were found to show good to moderate activity against Staphylococcus aureus as compared to the standard drug Kanamycin.

Antifungal activity

Against Candida albicans

Biological evaluation of present investigation revealed the maximum antifungal activity was shown by the compound 2d and 2e. The minimum antifungal activity was shown by the compound 2a, 2f and 2i. 2b was found to be inactive against Escherichia Coli. Rest of all compounds were found to show good to moderate activity against Saccharomyces as compared to the standard drug Amphotericin.

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