

Synthesis and Antimicrobia Activity of New Thiiazolidine-4-One Derivatives



Pharma

KEYWORDS : Thiiazolidine-4-one, thioglycolic acid, antimicrobial

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ABSTRACT

Present article is sincere attempt to synthesis series of 3-(2-aminophenyl)-2-(4-hydroxyphenyl)-1,3-thiazolidin-4-one derivatives were synthesized from 4-[(E)-[(2-aminophenyl) imino] methyl] phenol, Schiff base by condensation reaction. 4-[(E)-[(2-aminophenyl) imino] methyl] phenol synthesized by using aldehydes and o-phenylenediamine and cyclization of the compound were done by thioglycolic acid. The compounds obtained were purified by column chromatography using silica gel. The chemical structures of the compounds were confirmed using IR, ¹H-NMR and mass spectroscopy. All the synthesized compounds were screened for their preliminary antimicrobial properties. Some of the compounds exhibited promising antimicrobial activities.

INTRODUCTION:

Heterocyclic compounds occupy a central position among those molecules that makes life possible. The chemistry of heterocyclic compounds has been an interesting field of study for a long time. Thiiazolidine-4-ones containing thiazole moiety. It had been synthesized by 6-aminocoumarin, isatin, primary amines, and aromatic aldehydes¹. Present Thiiazolidinones are the derivatives of thiiazolidine which belong to an important group of heterocyclic compounds containing sulfur and nitrogen in a five member ring. The nucleus is also known as wonder nucleus because it gives out different derivatives with all different types of biological activities. The 4-thiazolidinone ring system is a core structure in various synthetic pharmaceutical agents, displaying a broad spectrum of biological activities such as, anthelmintic², anti-cancer³, anti-tumor⁴, Antiproliferative⁵, antitubercular⁶, antidiabetic⁷, anti-inflammatory, analgesic⁸, anti-convulsant⁹, antimicrobial and antioxidant¹⁰.

MATERIAL AND METHOD:

All the solvents and chemicals were obtained from S. D. Fine-Chem Ltd Mumbai and were purified by standard procedures. Melting points were determined in open capillary and were uncorrected. IR spectra in KBr disc were recorded on Perkin-Elmer-Spectrum-one FT-IR spectrophotometer. ¹H NMR spectra were recorded in DMSO-d₆ with a BRUKER NMR 500 MHz spectrophotometer. Mass spectra were recorded on LCMS 2010A, SHIMADZU mass spectrophotometer. Purity of the compounds was checked by TLC using silica gel 'G' plates. Synthesis of 3-(2-aminophenyl)-2-(3-nitrophenyl)-1,3-thiazolidine-4-one derivatives synthesized by using two steps.

Synthesis of N-(3-nitrobenzylidene)benzene-1,2-diamine:

Compound N-(3-nitrobenzylidene)benzene-1,1-diamine was synthesized by using a mixture of o-nitrobenzaldehyde (1 mol) and o-phenylenediamine (1 mol) were taken in a round bottom flask. Then 100 ml of dry methanol was added into the mixture. This mixture was refluxed for 7 hrs. Then the progress of the reaction was monitored by TLC. After completion of reaction product was poured into crushed ice and filtered.

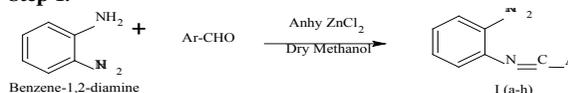
Synthesis of 3-(2-aminophenyl)-2-(3-nitrophenyl)-1,3-thiazolidin-4-one:

Compound-I (1 mol) was taken into round bottom flask and 30 ml of DMF solution added into it. Then (1 mol) of thioglycolic acid was added into the solution. And 0.3 gm of anhydrous zinc chloride was added into the reaction mixture. The reaction mixture was refluxed for 20-22 hrs. The progress of the reaction was monitored by TLC. After completion of the reaction precipitate was added into the crushed ice and washed with cold water. Obtained solid material was filtered and scratched to obtain solid product dried in desiccators. Solid material was confirmed by melting point and purified by column chromatography technique by using different solvents¹¹.

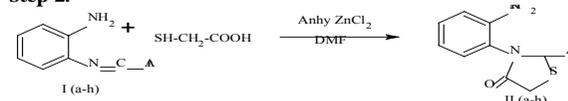
matography technique by using different solvents¹¹.

Scheme:

Step-1:



Step-2:



Physical and spectral data:

Compound II-a: Composition; C (62.92%) H (4.93%) N (9.78%) O (11.17%) S (11.20%); IR (KBr) cm⁻¹; 3174.30 (C=N str), 1602.91(C=O str), 1356.98(C=S str), ¹H NMR (DMSO) δ ppm ; -NH₂ = δ6.134 (s), Ar C-H = δ7.484-δ 8.722 (m), -CH₂ = δ4.213 (s); MASS LCMS DMSO; 316.2 (M⁺).

Compound II-b: Composition; C (63.46%) H (4.99%) Cl (11.71%) N (9.25%) S (10.59%); ¹H NMR (DMSO) δ ppm ; -NH₂ = δ5.615 (s), Ar C-H = δ7.283-δ 8.860 (m), -CH₂ = δ4.243 (s), MASS LCMS DMSO; 304.1 (M⁺).

Compound II-f: Composition; C (59.98%) H (4.65%) O (12.29%) N (10.76%) S (12.32%); IR (KBr) cm⁻¹; 3367.62(N-H str), 1346.48(C-S str), 817.24(C-H str), 1153.47(C-O-C str); ¹H NMR (DMSO) δ ppm ; -NH₂ = δ6.272 (s), Ar C-H = δ7.245-δ7.816 (m), -CH₂ = δ4.353 (s); MASS LCMS DMSO; 260.3 (M⁺).

4.3. Table No- 1: DIFFERENT SUBSTITUTIONS:

COMPOUNDS	Ar	Molecular formula	Molecular weight	Melting point
II-a		C ₁₃ H ₁₀ N ₂ O ₃ S	315.34 gm	221°C
II-b		C ₁₂ H ₉ N ₂ O ₂ S	260.31 gm	219°C
II-c		C ₁₂ H ₁₀ N ₂ O ₃ S	324.60 gm	265°C
II-d		C ₁₃ H ₁₁ ClN ₂ O ₃ S	364.79 gm	209°C
II-e		C ₁₄ H ₁₂ N ₂ O ₂ S	300.37 gm	219°C
II-f		C ₁₇ H ₁₄ N ₂ O ₂ S	286.31 gm	212°C
II-g		C ₁₇ H ₁₅ N ₂ O ₃ S	315.34 gm	224°C

Antimicrobial activity:

The sterilized (autoclaved at 120 °C for 30 min) nutrient agar medium (40-50 °C) was inoculated with the suspension of microorganisms and mixture was transferred to sterile petri dishes and allowed to solidify. In each plate cups of 6 mm diameter bores were made at equal distances using sterile steel borer. Ofloxacin and Amikacin standard drugs were inserted with 0.1 ml of DMSO; other was filled with 0.1 ml of synthesized compounds solution in sterile DMSO. Then plates were kept in refrigerator for 30 min to allow the diffusion of sample to the surrounding agar medium. The plates were incubated at 37±2 °C for 24 hrs and observed for antimicrobial activity. The zone of inhibition diameter were measured and compared with that of standard, the values are tabulated¹².

Table no.2 : Antimicrobial activity of synthesized compounds:-

COM-POUNDS	Conc. in µg/ml	Zone of inhibition in mm		
		E.coli	Klebsilla pneumoniae	Staphylococcus aureus
II-a	50	14	7	8
	100	15	8	9
	150	16	10	10
	200	15	13	11
II-b	50	16	9	9
	100	18	10	10
	150	21	11	12
	200	22	13	15
II-c	50	14	7	8
	100	15	8	9
	150	17	10	10
	200	21	13	10
II-d	50	16	10	8
	100	15	11	10
	150	17	11	12
	200	18	13	14
II-e	50	10	8	7
	100	12	10	8
	150	16	12	10
	200	20	15	11
II-f	50	10	5	6
	100	11	7	8
	150	15	9	10
	200	16	10	11
II-g	50	16	9	7
	100	17	10	9
	150	21	10	10
	200	22	11	11
II-h	50	12	10	8
	100	14	11	10
	150	15	13	12
	200	17	14	14
AMIKACIN	100	34	31	32
OFLOXACIN	100	32	32	33

RESULT AND DISCUSSION:

Obtained substituted thiazolidine-4-ones are purified by making use of column chromatography technique, with the help of different solvent system. Melting points of the synthesized compounds is determined in melting point apparatus and are uncorrected. Analytical and spectral data (IR, ¹H-NMR, MASS spectra) of all synthesized compounds were in full agreement with proposed structure. All the synthesized compounds were tested for their antibacterial activity using Amikacin and Ofloxacin as standards. The data of table-2 indicate that among all the compounds, compounds II-a, II-b, II-c, II-d, II-e, II-f, II-g and II-h were found to highly active against gram negative bacteria *E.coli*. All Compounds showed minimum activity against gram positive bacteria *Staphylococcus aureus*. Compounds II-a, II-b, II-c, II-d, II-e, II-f, II-g and II-h were showed moderate activity against *Klebsilla pneumoniae*.

CONCLUSION

In conclusion, we have synthesized 3-(2-aminophenyl)-2-(3-nitrophenyl)-1,3-thiazolidin-4-one analogues (II-a-h) and evaluated them for *in vitro* studies for antimicrobial activity at various concentrations checked against *E.coli*, *Staphylococcus aureus* and *Klebsilla pneumoniae* bacteria. The investigation of antimicrobial screening of the synthesized compounds reveals that almost all the synthesized compounds showed good activity against all bacterial strains. So, we concluded that the newly synthesized thiazolidine-4-one derivatives possess synergetic antimicrobial activity. In the case of gram -ve organisms showing good activity due to the presence of highly electro negative group substitution which already has antimicrobial activity which will increase the activity with thiazolidine-4-one. Therefore the newly synthesized thiazolidine-4-ones derivatives may serves as a lead molecule for further modification to obtain clinically useful novel entities in the new millennium.

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