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Studies on 4-Thiazolidinones: Part-1: Preparation and Antimicrobial Activity of 2-Aryl-3-(p- cumenyl)-5-H/methyl-4-thiazolidinones.

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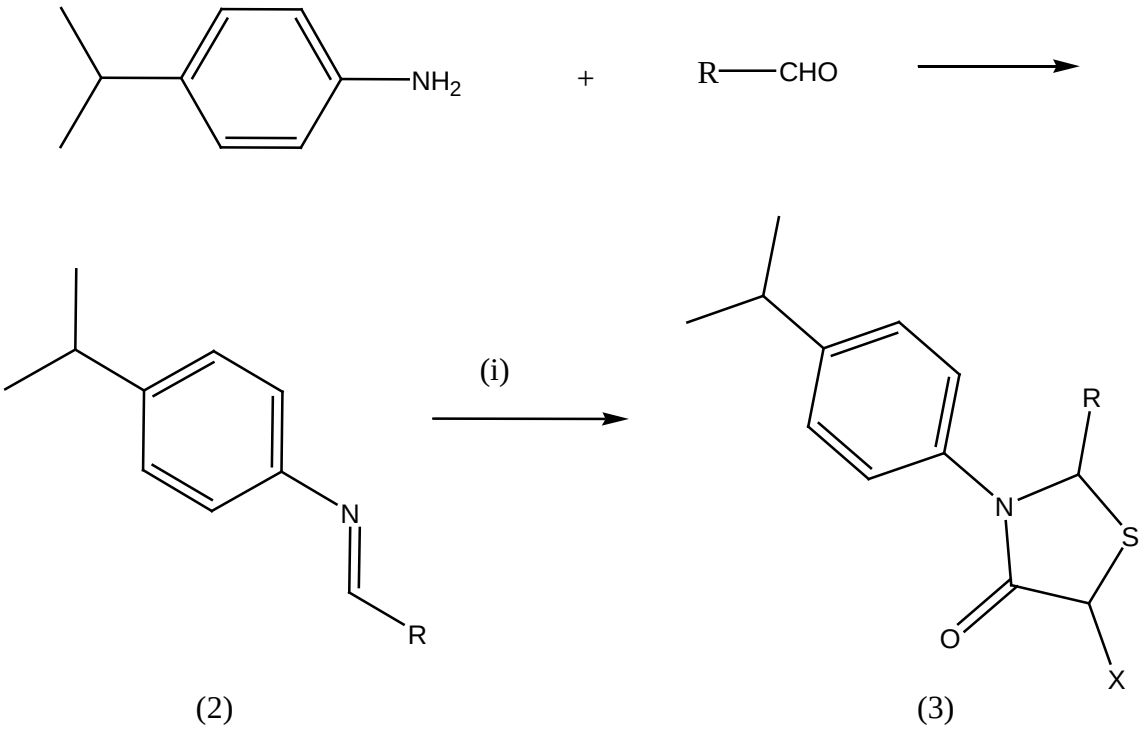
Abstract: Some new 4-thiazolidinones have been prepared by the condensation of Schiff's bases from p- cumidine with thioglycolic and thiolactic acids. The structures of the compounds have been delineated by IR, NMR and MASS spectral study. The products have been screened for antimicrobial activity; most of the compounds proved active.

Key words: p- Cumidine, thioglycolic acid, thiolactic acid, Schiff's bases, 4-thiazolidinones, antimicrobial activity.

INTRODUCTION

Several substituted 4-thiazolinones have been found to have many physiological activities[1-10]. In continuation of our work to incorporate theses molecules into the p-cumidine moiety to explore the unknown pharmacological, herbicidal and insecticidal activity of p-cumidinederivatives,the synthesis of 4-thiazolidinones of type (3) has been schematised in 2 steps by the condensation of Schiff's bases (2) from p-cumidine and aryl aldehydes with thioglycolic and thiolactic acid. The structures of the products have been characterised by IR, NMR, and MASS spectral study. The products have been screened for antimicrobial activity. Most of the compounds exhibited more activity than the reference antibiotic drugs.

Reaction Scheme:



(2) (3)

(i) SH-CHX-COOH, $ZnCl_2$Anhy, 120'C
R = Aryl
X = H/CH_3

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Experimental :

All the melting points were determined in open capillaries and are uncorrected. The IR spectra (KBr) were recorded on a Shimadzu DR-1-435 spectrophotometer, the ^{1}H NMR spectra on Hitachi R-1200 (60 MHz) spectrometer and mass spectra on Jeol D-300 mass spectrometer.

4- Nitrobenzalamino–p-cumene (2):

4- Nitrobenzaldehyde (0.01 M) and p-cumidine (0.01M) were refluxed in ethanol for 9-10 hrs. The contents were poured into ice containing acid and filtered. The product was treated with ether and crystallised from ethanol. Yield 76%, m.p. 86^{o}c.

2-(4'-Nitrophenyl)-3-N-(p-cumenyl)-5-H-4-thiazolidinone (3):

A mixture of 4- Nitrobenzalamino–p-cumene (0.0025 M, 0.67 gm.) and mercapto acetic acid (0.0025 M, 0.182 ml.) was fused at 120^{o}c for 10-12 hours. The reaction mixture was cooled and treated with 10% $NaHCO_3$solution. The product was isolated and recrystallised from ethanol. Yield 59%, m.p. 130^{o}c.

IR (KBr) : 3080 (C-H str. asym.), 1690 (C=O str.), 1360 (N=O str.), 1216 (C-N vib.), 718 (C-S-C Str.) cm^{-1}.

PMR (TFA) : 7.09-8.20 (m, 8H, Ar-H), 6.14(s, 1H, -CH),3.86(s, 2H, -CH_2),2.60-3.18(h, 1H, -CH$(CH_3)_2$), 1.2-1.23 (d, 6H , -CH$(CH_3)_2$ δ ppm.

MS : m/z : 209 (base peak), 176,162,146,135,120,91,77,65,51,42.

2-(4'-Nitrophenyl)-3N-(p-cumenyl)-5-methyal-4-thiazolidinone (3):

A mixture of 4-Nitrobenzalamino–p-cumene (0.002 M, 0.54 g.) and thiolactic acid (0.0025 M, 0.22 ml) was heated in oil bath at 115-120^{o}c for 12 hrs. The resulting mixture was treated with 10% $NaHCO_3$ solution. The product was isolated and recrystallised from ethanol. Yield 68%, m.p. 126^{o}c.

IR (KBr) : 3085 (Ar C-H str.), 1695 (C=O str.), 1375 (N=O str.), 1220 (C-N vib.), 690 (C-S-C Str.) cm^{-1} .

PMR (TFA): 7.0-8.3 (m, 8H, Ar-H), 6.30 (s, 1H, -CH), 4.39-4.7 (q, 1H,-CH –CH_3), 2.61-3.20 (h, 1H, -CH $(CH_3)_2$), 1.77-1.93 (d, 3H , -CH(CH_3),1.14-1.25 (d, 6H –CH-$(CH_3)_2$) δ ppm.

MS : m/z : 356 , 341 , 253 , 206 , 179(base peak), 135 ,105 ,91,77, 65.

Similarly, other 4- thiazolidinones were prepared (Table-1).

RESULTS AND DISCUSSION

4-Thiazolidinones showed characteristic C=O str. absorption around 1690, C-N vib. at 1215,C-S-C str. at 718, C-H bending at 1340 and asym.C-H str. of CH_3 at 2945 cm^{-1}. In NMR spectral study –CH$(CH_3)_2$ proton showed doublet at 1.12-1.23; -CH$(CH_3)_2$, heptet at 2.50-3.18; -CH_2(thiazolidinone moiety), singlet at 3.86; -CH (thiazolidinone moiety) singlet at 6.14 and Ar-Hmultiplet at 7.09-8.20 δ ppm.

From the antimicrobial activity data most of the compounds proved more or equally active at a concentration of 50µg in comparison to reference drugs like Ampicillin (12-25mm), Chloramphenicol(13-23mm), Norfloxacin(23-25mm) and Griseofulvin(25mm) against microbes like Bacillus megaterium(B.m.), Staphylococcus citrus(S.c.), Escherichia coli(E.c.), Salmonella typhosa(S.t.) and fungi Aspergillusniger(A.n.).4-Hydroxy-3-methoxyphenyl derivative(11) remarkably proved active against Staphylococcus citrus (26 mm) and Aspergillusniger (21mm).Styryl(5)and 2-Hydroxyphenyl derivative(8) exhibited good activity againstSalmonella typhosa (22mm).3-Nitrophenyl derivative (14) showed maximum activity against Salmonella typhosa (20mm) and Aspergillusniger (20mm).

Table 1: Physical and Analytical Data

No.	R	Physical & Analytical Data X = H M.P. °C	Yield %	N % found(Calcd.)	Physical & Analytical Data X = CH_3 M.P. °C	Yield %	N % found(Calcd.)
1.	Phenyl	140	40	4.62 (4.71)	127	55	4.40 (4.50)
2.	3-Aminophenyl	105	75	8.88 (8.97)	110	61	8.49 (8.49)
3.	4-Aminophenyl	110	55	8.91 (8.97)	116	69	8.51 (8.59)
4.	4-chlorophenyl	125	65	4.15 (4.22)	131	51	3.97 (4.05)
5.	Styryl	98	51	4.27 (4.33)	69	52	4.08 (4.15)
6.	3,4-Dimethoxyphenyl	140	43	3.80 (3.92)	120	50	3.69 (3.77)
7.	2'-Furyl	243	62	4.79 (4.88)	210	72	4.58 (4.65)
8.	2-Hydroxyphenyl	110	67	4.39 (4.47)	61	67	4.18 (4.28)
9.	3-Hydroxyphenyl	98	52	4.37 (4.47)	95	52	4.20 (4.28)
10.	4-Hydroxyphenyl	105	59	4.41 (4.47)	90	61	4.16 (4.28)
11.	4-Hydroxy -3-methoxyphenyl	100	44	4.01 (4.08)	95	53	3.81 (3.92)
12.	2- methoxyphenyl	133	62	4.20 (4.28)	126	50	4.01 (4.10)
13.	2-Nitrophenyl	72	41	8.09 (8.19)	107	55	7.28 (7.86)
14.	3-Nitrophenyl	95	39	8.11 (8.19)	115	52	7.76 (7.86)
15.	4-Nitrophenyl	125-130	59	8.17 (8.19)	126	67	7.78 (7.86)
16.	4- methoxyphenyl	105	60	4.19 (4.28)	-	-	-

Table 2: Antimicrobial Activity Data

No.	R	Antimicrobial Activity Data (Zones of inhibition in mm) X = H B.m.	S.c.E.c.	S.t.A.n.			Antimicrobial Activity Data (Zones of inhibition in mm) X = CH_3 B.m.	S.c.E.c.	S.t.A.n.		
1.	Phenyl	16	11	18	18	17	14	14	17	17	18
2.	3-Aminophenyl	15	17	17	16	14	14	14	15	18	17
3.	4-Aminophenyl	13	13	17	17	16	13	11	18	19	15
4.	4-chlorophenyl	14	11	17	16	18	15	11	17	16	16
5.	Styryl	12	14	21	22	19	16	17	20	17	17
6.	3,4-Dimethoxyphenyl	12	24	19	16	20	13	13	14	17	14
7.	2'-Furyl	11	12	18	17	13	13	16	18	18	17
8.	2-Hydroxyphenyl	15	18	18	22	12	13	15	16	21	15
9.	3-Hydroxyphenyl	12	12	17	19	12	18	15	15	18	14
10.	4-Hydroxyphenyl	12	12	17	20	12	18	15	15	18	14
11.	4-Hydroxy -3-methoxyphenyl	17	26	17	19	21	14	16	14	19	18
12.	2- methoxyphenyl	12	11	17	18	13	14	11	12	16	16
13.	2-Nitrophenyl	12	14	19	17	14	15	15	15	20	17
14.	3-Nitrophenyl	13	15	17	15	15	15	19	16	20	20
15.	4-Nitrophenyl	12	15	19	19	18	16	11	17	20	15
16.	4- methoxyphenyl	13	13	17	19	14	-	-	-	-	-

Table 3: Antimicrobial Activity Data of Standard Antibiotics :

Sr. No.	Microbes	Standard antibiotics (zone of inhibition)
1.	B.megaterium	Ampicillin (16mm)
2.	S.citrus	Chloramphenicol (17mm)
3.	E.coli	Norfloxacin (24mm)
4.	S.typhosa	Chloramphenicol (13mm)
5.	A.niger	Griseofulvin (25mm)

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Graphical Abstract

(1) The title of the paper :

STUDIES ON 4-THIAZOLIDINONES : PART-1 : PREPARATION AND ANTIMICROBIAL ACTIVITY OF 2-ARYL-3-(P-CUMENYL)-5-H / METHYL-4-THIAZOLIDINONES.

(2) The family names of the authors preceded by the initials of the given names:

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(4) A summary :

Some new 4-thiazolidinones have been prepared by the condensation of Schiff's bases from p- cumidine with thioglycolic and thiolactic acids. The structures of the compounds have been delineated by IR, NMR and MASS spectral study. The products have been screened for antimicrobial activity. Most of the compounds exhibited more activity than the reference antibiotic drugs.

(5) A small diagram or other informative illustration that shows the most striking feature of the paper in pictorial form

R = Aryl
X = H / CH_3