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Synthesis and biological evolution of 3-aryl-2-(2-chloro-6-iodoquinonlin-3'yl)-4-thiazolidinones

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ABSTRACT

Thiazolidin-4-ones **(3a-g)** have been synthesized by the cyclocondesation at thioglycalic acid with N-aryl-2-chloro-6-iodo quinonin-3-yl azomethine **(2a-g)** which in turn have prepared by the action of amines on 2-chloro-6-iodo-quinoline-3-charboxaldihyde1. The structure of the compound **(2)** and **(3)** have been confirmed from elemental analysis, further supported by IR, ^{1}H NMR and Mass Spectral data. All the products have been screened form their antimicrobial activity against several microbe.

INTRODUCTION

In the course of work on new pharmacologically active thiazonidiniones, extensive efforts have been made to find more potential agents. Thiazolidinones[1-6] are endowed with variety of pharmacological activities such as analgesic, anticonvulsant, antifungal, anesthetics, antibacterial and industrially important as stabilizer. The key intermediate 2-Chloro-6-iodoquinole-3-carboxaldehyde also possesses pharmacological activity[7]. This observation led us to synthesis some new thiazolidanone derivatives bearing 2-chloro-6-iodo quinoline nucleus.

The starting compounds 2-chloro-6-iodo-quinolin-3-carbaldehyde **(1)** on treatment with different aromatic amine in ethanol afforded corresponding N-Aryl-2-chloro-6-iodoquinolin-3-yl azomethines **(2a-g)**.

The compounds **(2a-g)** on cyclization with mercaptoacetic acid furnished compounds **(3a-g)**. The constitution of all the products have been characterized using elemental analyses, IR, 1H NMR and mass spectral studies. All the compounds were screened for their antimicrobial activity against different strains of bacteria and fungi.

EXPERIMENTAL

All the melting points were determined in an open capillary tube and are uncorrected. Thin layer chromatography was used for monitoring the reaction and to check purity. IR spectra (KBr disc) were recorded on Shimadzu-8400 spectrophotometer and ^{1}H NMR spectra were recorded on 300 MHz spectrophotometer using TMS as internal standard. Mass spectra were recorded on 300 MHz spectrophotometer using TMS as an internal standard. Mass spectra were recorded on JEOL SX 102/DA 6000 spectrophotometer. All the compounds gave satisfactory elemental analysis.

Preparation of 2-chloro-6-iodo-quinoline-3-carbolldehyde (1)

Dimethyl formamide (0.125 mole, 9.13 gm) was cooled to 0^0C in flask equipped with drying tube and phosphorous oxychloride (0.35 mole, 53.7gm) was added dropwise with stirring to this solution, 4-iodo acetanilide (0.05 mol, 7.45 gm) was added and the content were heated under refluxe for 12 hours on a water bath. The product was isolated and crystallized from ethyl acetates yield 50% ,mp 206'C, found C, 37.80; H,1.4; N,4,40%, C10H5ClNOI, requires

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TABLE 1: Physical data of compound (2a-g) and (3a-g)

Sr.no.	R	Yield %	M.P ^{0}C	Mol. formula	Elemental analysis (Found) calcd.(%)		
					C	H	N
(2a)	-C_6H_5	65	158	$C_{16}H_{11}N_2ICl$	(48.91)48.95	(2.53)2.57	(7.10)7.13
(2b)	-4-IC_6H_4	78	140	$C_{16}H_9N_2I_2Cl$	(37.02)37.06	(1.71 1.75	(5.36)5.40
(2c)	-4-NO_2-C_6H_4	70	190	$C_{16}H_9N_3O_2ICl$	(43.89)43.94	(2.02)2.07	(9.55)9.60
(2d)	4-OH-C_6H_4	60	170	$C_{16}H_9N_3IO_2Cl$	(47.01)47.03	(2.43)2.47	(6.81)6.86
(2e)	4-F-C_6H_6	75	180	$C_{16}H_{11}N_2IClF$	(46.74)46.80	(2.19)2.21	(6.77)6.82
(2f)	2-CH_3,4-CL,C_6H_3	60	150	$C_{17}H_{11}N_2Cl_2I$	(46.25)46.29	(2.47)2.51	(6.33)6.35
(2g)	2,4$(CL)_2$-C_6H_3	65	190	$C_{16}H_8N_2Cl_3I$	(41.60)41.64	(1.71)1.75	(6.02) 6.07
(3a)	-C_6H_5	65	200	$C_{18}H_{12}ClIN_2OS$	(46.28)46.32	(2.54)2.59	(5.95) 6.00
(3b)	-4-IC_6H_4	70	140	$C_{18}H_{11}ClI_2N_2OS$	(36.44)36.48	(1.83)1.87	(4.67)4.73
(3c)	4-NO_2-C_6H_4	66	>200	$C_{18}H_{11}ClIN_3O_3S$	(42.21)42.25	(2.12)2.17	(8.17)8.21
(3d)	4-OH C_6H_4	75	250	$C_{18}H_{12}ClIN_2O_2S$	(44.74)44.79	(2.52)2.51	(5.76)5.80
(3e)	4-FC_6H_4	60	198	$C_{18}H_{11}ClFIN_2OS$	(44.55)44.60	(2.22)2.29	(5.72)5.78
(3f)	2-CH_3 ,4-Cl-C_6H_4	72	190	$C_{19}H_{13}Cl_2IN_2OS$	(44.25)44.29	(2.50)2.54	(5.40) 5.44
(3g)	3,4 $(Cl)_2$ –CH_3	55	180	$C_{18}H_{10}Cl_3IN_2OS$	(40.32)40.36	(1.82)1.88	(5.16)5.23

TABLE 2 : Antibacterial and antifungal activity data of compound (2a-g) and (3a-g)

Sr. no.	Antibacterial Zone of inhibition in mm				Antifungal zone of inhibition in mm
	P.Valgius	*S.Aureous*	*B.Mega*	*E.coli*	*A.niner*
(2a)	15	12	12	13	11
(2b)	10	17	17	17	24
(2c)	24	15	15	24	15
(2d)	27	16	16	14	18
(2e)	27	14	14	8	12
(2f)	14	18	18	18	13
(2g)	20	17	17	15	17
(3a)	14	12	12	13	20
(3b)	13	15	15	24	22
(3c)	12	17	18	17	18
(3d)	14	16	12	14	12
(3e)	20	13	14	16	13
(3f)	24	12	17	25	18
(3g)	22	22	13	18	17
Ofloxacin	32	27	24	22	0
Ciprofloxacin	12	34	26	22	0
Griseofulvin	0	0	0	0	26

C,37.97; H,1.58; N,4.43%.

Preparation of aryl-2-chloro-6-iodo quinoline 3-yl azomethine (2f)

A mixture of 2-Chloro-6-iodoquinolin-3-carbaldehyde (0.01 mole) and 2-Methyl, 4-chloro aniline (0.01 mole, 1.42gm) was refluxed in DMF on oil bath for 6 hours in presence of con. H_2SO_4. The contents were cooled and product isolated was crystallized from DMF. Yield 60%, m.p. 150^{0}C. (Found: C, 46.25; H, 2.47; N,.6.33%, Calcd. from $C_{16}H_{10}N_2Cl$;C, 46.29; H, 2.51; N,6.35%). IR(KBr) cm^{-1}: 2921, 2842(C-H Alkane), 3020 (-CH Aromatic), 1577(C=C),1609 (C=N quinolone), 735 (C-Cl), ^{1}H NMR (δ ppm): 7.19-8.55 (m, 9H, Ar-H), 8.84 (s, 1H, -CH=N). Similarly other derivatives of **(2a-g)** are prepared by the condensation of **(1)** with different aryl amines and their physical data are recorded in (TABLE 1).

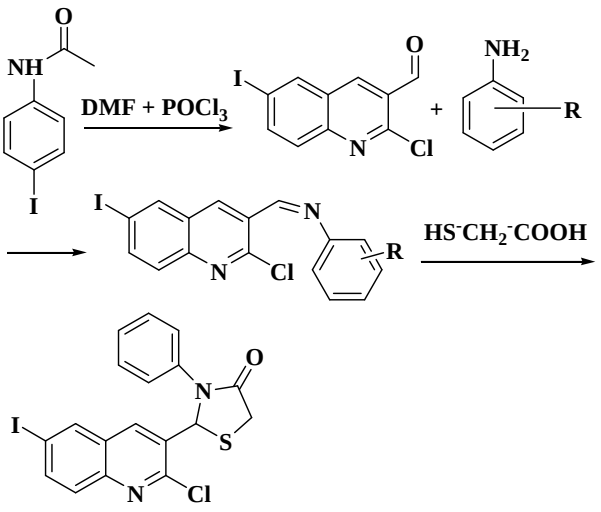
Preparation of 3-Aryl-2- (2-chloro-6-iodoquinoline-3;-yl)thiazolidinones (3f)

A mixture of N-(2-Methyl, 4-chloro-phenyl)-2-chloro-6-iodo quinolin-3-yl azomethine **(2f)** and thiogycolic acid (0.01 mole, 1ml) was heated on an oil bath for 24 hours, cooled and treated with 10% sodium carbonate solution. The resulting mass was crystallized from DMF. Yield 72%, m.p. 190^{0}C. (Found: C, 44.25; H, 2.50; N 5.40%, Calcd. from $C_{19}H_{11}ClN_2ISO$; C, 44.29; H, 2.54; N, 5.44%). IR (KBr) cm-^{1}: 2920, 2858 (C-H Alkane), 3020 (C-H Aromatic), 1639 (C=N Imine), 1654(-C =O Thiazolidinone), 699 (C-S-C), ^{1}H NMR (δ ppm): 2.17 (s, 3H,- CH_3), 3.66 (s,2H, -CH_2 Thiazolidinone), 7.05, 8.02(m,8H,Ar-H +Thia. H)

Like wise other compounds from **(3a-g)** in similar way from **(2a-g)** were synthesized and their physical data are presented in (TABLE 1).

Biological activity

The antimicrobial activity was assayed using cup-plate diffusion method[8] by measuring the zones of inhibition in mm. All the compounds were screened *in vitro* for their antimicrobial activity against bacterial strains like *Bacillus megaterium, Staphylococcus aureus, Escherichia coli, Proteus vulgaris* and fungi,



SCHEME

Aspergillus niger at a concentration 40μg. Known antibiotics like Ofloxacin (22-32mm), Ciprofloxacin (21-32mm), and Greseofulvin (26mm) were used for comparison purpose. The data are recorded in (TABLE 2).

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