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SYNTHESIS AND BIOLOGICAL EVALUATION OF NOVEL SCHIFF BASE DERIVATIVES

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ABSTRACT

A series of novel Schiff base derivatives N-[[2-Chloro-7-(trifluromethyl)quinoline-3-yl}methylene]aryl amine were synthesized and evaluated for their antibacterial and antifungal activity. The structures of the synthesized compounds were determined by IR, NMR, Mass Spectroscopy and elemental analysis.

Key Words: Schiff base, Quinoline, Antifungal. Antibacterial.

INTRODUCTION

Azomethines are generally known as Schiff bases to honour a great chemist Schiff, who synthesized such compounds[1]. These are the compounds containing characteristic –C=N- group. They are well known intermediate for the preparation of azetidinones, thiazolidinones, aryl acetamides and many other derivatives. The reaction between amine and formaldehyde followed by further reaction with compounds having active hydrogen gives manich bases.

Azomethines can be formed by the reaction of a primary amine with various aldehydes (other then HCHO) with the simultaneous removal of water. The loss of water, give an imine, corresponds to the "Crotonaldehyde stage" of the aldol condensation. Several methods have been reported for the preparation of azomethines. Sampat and Mehta gave the detail study report on heterocyclic Schiff bases legends derived from pyrazole 2-caboxy aldehyde and pyridine-2-carboxy aldehyde with o-toludine, p-toludine and aniline. Chang and Pan reported some Schiff bases derived from amino phenols and aromatic aldehydes[2]. More et al.[3] have marked the

biological activity of Schiff bases synthesized from aminothiazoles. Selvam et al. have prepared sulfonamide and its derivatives as anti-HIV agents[4].

The azomethine derivatives of 1,2,4-triazole have been found to be potent drug pharmaceutical industries and possess a wide spectrum of biological activity[5-8]. Wei et al.[9] have synthesized new type of Schiff bases containing triazole ring which are observed to be potential fungicides. Yadawe and Patil have reported some azomethines which were screened for their antibacterial and antifungal. Holla et al. have documented azomethine bearing triazole moiety. which possess good antibacterial activity[11].

Owing to their characteristic properties like, manifestations of novel structures, thermal stabilities, abnormal magnetic properties, relevant biological properties, high synthesis flexibility, different coordinating ability and medicinal utility, a wide range of these compounds have been synthesized and studied extensively[13-30].

MATERIALS AND METHODS

All the chemicals used were of pure grade (Finar and Sigma Aldrich). The melting points of all compounds were determined by open capillary method and were uncorrected.

Synthesis of 2-Chloro 7-trifluoromethyl 3- Carbaldehyde (Compound-2)

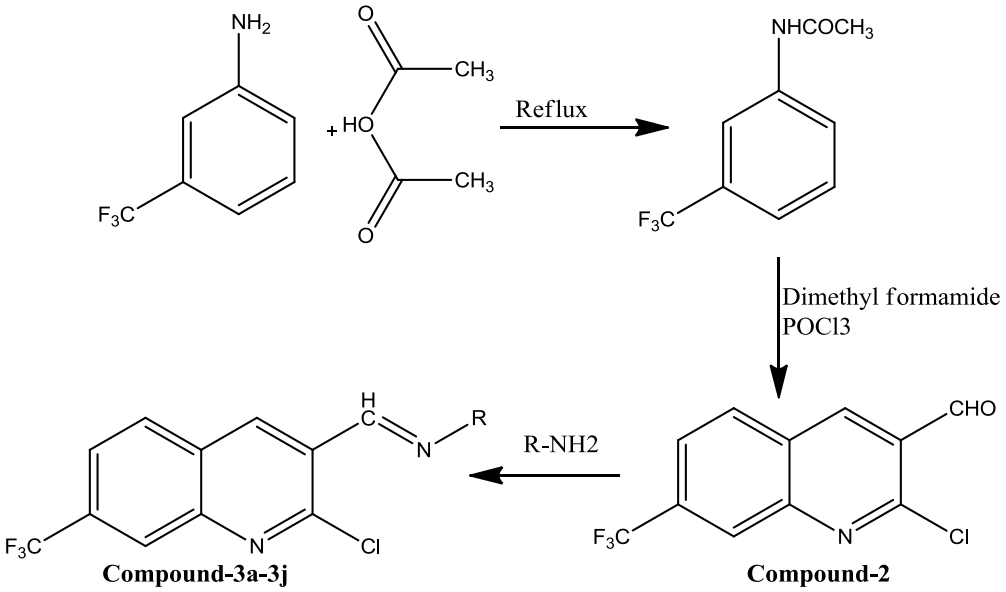
To an ice-cooled solution of N,N-dimethylformamide (10.95g, 0.15 mol) and Phosphoryl chloride (53.7 g, 0.35 mol) was added drop wise under cooling,stirring for 1/2 hr add m-tri Fluoro Acetinilide (10.15g, 0.05 mole) and CTBAB (cetyl tetrabutylammonium bromide) Start heating slowly to 75°c for 20 hrs. A mixture of poured in ice and temp maintain 0 to 10° for 1hr. Product was isolated and filter and wash by water. Crystallized from ethyl acetate. Yield (9.77g, 68%) m.p. 170-175^{O}C

Synthesis of N-[{2-chloro-7-(trifluoromethyl) quinoline-3-yl} methylene] benzenamine, (3a-3j)

A mixture of 2-Chloro 7-trifluoromethyl 3- Carbaldehyde (0.01M, 2.22gm) and different aromatic aldehydes was taken in ethanol and 2-3 drops of gl. acetic acid was added and the

reaction mixture was refluxed for 10 hours. The product was isolated and crystallized by absolute alcohol.

Scheme



Compound-3a-3j **Compound-2**

RESULTS AND DISCUSSION

All the synthesized final compounds were first purified by successive recrystallization using appropriate solvents. The purity of the synthesized compounds was checked by performing thin layer chromatography and determining melting points. Then the synthesized compounds were subjected to spectral analysis such as IR and NMR to confirm the structures. All the analytical details show satisfactory results. Our titled compounds are known to possess antimicrobial activity; the compounds were screened for their antibacterial and antifungal activity by cup-plate method. Two gram positive bacteria such as B.mega, and S.aureus two gram negative bacteria such as E.coli and P.valgaris and a fungal species such as A.Niger is tested for the activities. The concentration of 40 μg/ml of our titled compounds has been used. Ampicillin, Amoxicilline, Norfloxacin and Penicilline have been used as standards for anti-bacterial activity and greseofulvin have been used as standards for anti-fungal activity. All the compounds have shown mild to moderate activities.

Table:I-Characterization of N-[{2-Chloro-7-(trifluoromethyl)quinoline-3-yl}methylene] benzenamine

Sr No 1	Molecular Formula 2	R 3	M.P °C 5	Yield % 6	% of Nitrogen	
					Calcd	Found
1a	$C_{17}H_{10}ClF_3N_2$	C_6H_5-	130	70	8.37	8.35
1b	$C_{17}H_{10}ClF_3N_2O$	4-OH-C_6H_4-	133	72	7.99	8.05
1c	$C_{18}H_{12}ClF_3N_2O$	4-OCH_3- C_6H_4-	128	75	7.68	7.70
1d	$C_{17}H_9ClF_4N_2$	4-F- C_6H_4-	144	74	7.94	8.00
1e	$C_{17}H_9Cl_2F_3N_2$	4-Cl- C_6H_4-	152	69	7.59	7.95
1f	$C_{19}H_{15}ClF_3N_3$	4(N,NdiCH_3)- C_6H_4-	110	61	11.12	11.15
1g	$C_{17}H_9ClF_3N_3O$	3-NO_2- C_6H_4-	160	78	11.07	11.11
1h	$C_{17}H_9Cl_2F_3N_2$	2-Cl-C_6H_4-	155	70	7.59	8.06
1i	$C_{17}H_9BrCl_2F_3N_2$	2-Br-C_6H_4-	159	73	6.77	6.83
1j	$C_{18}H_{12}ClF_3N_2$	4-CH_3- C_6H_4-	135	70	8.03	8.10

Table:II-Biological Activity

Compounds	*B.mega*	*S.aureus*	*E.coli*	*P.valgaris*	*A.niger*
1a	20	18	18	14	19
1b	16	14	19	16	16
1c	13	10	13	10	21
1d	11	20	12	12	22
1e	21	19	17	15	20
1f	13	14	11	19	12
1g	15	12	15	10	10
1h	09	17	11	11	13
1i	10	13	14	17	14
1j	14	14	20	14	11

Ampicillin	23	22	21	25	-
Amoxicillin	22	23	21	24	-
Norfloxacin	24	17	23	19	-
Penicillin	25	24	19	20	-
Greseofulvin	-	-	-	-	25

CONCLUSATION

The work has approached towards the synthetic and biological approach of these wonder molecules. Anti-bacterial property of the synthesized compounds has exhibited very good inhibition; all compounds have exhibited mild activity towards gram positive becteria B. mega, S. aureous, when all compound shows mild activity against gram negative becteria E. coli and P.aeruginosa as compare to four standard. But the systematic substitution at various position and other derived compounds have shown remarkable antifungal properties. The compounds 2d and 2c have exhibited outstanding activity towards A.niger. The remaining compounds have shown poor antifungal activity indicating less biological importance for a synthetic chemist.

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