Oriental Journal of Chemistry Vol. **26**(1), 243-246 (2010)

Synthesis and biological studies of some novel formazans

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(Received: August 03, 2009; Accepted: September 18, 2009)

ABSTRACT

A new series of formazans (3a-3l) were synthesized containing the INH moiety, INH upon reaction with substituted aromatic aldehydes yields the Schiff bases (2a-2c). Schiff bases on condensation with different diazonium salts will give formazans. The structure of the final newly compounds were assigned on the basis of IR, ^{1}H NMR and MASS spectral data. All the compounds of this series were evaluated for their *In-vitro* antibacterial and antifungal activity. Some of the compounds showed promising biological activity.

Key words: Formazans, azo compounds, Schiff bases, anti bacterial and anti fungal activity.

INTRODUCTION

Schiff bases exhibit good antibacterial activity and pharmacological activity. These agents are one of the important synthons for the synthesis of a variety of heterocyclic compounds. Further more, formazans nucleus is known to be pharmacophoric in nature. A number of formazans derivatives possess antifertility[1], antiviral[1], anti-inflammatory[2], antiparkinsonian[3], CNS depressant[4], anticancer, and anti-HIV activities. In the light of the above observations a new series of formazans were synthesized containing the INH moiety.

The title compounds were prepared by the reaction sequence as depicted in Scheme-01. INH upon reaction with substituted aromatic aldehydes in presence of few drops of glacial acetic acid will yields the intermediate schiff bases. Various diazonium salts were prepared by the reaction between amines in glacial acetic acid and HCl was diazotized in the cold condition with sodium nitrite. The prepared diazonium salts were condensed with INH moiety in a mixture of DMF and pyridine to yield the title compounds. The structures of the above compounds were confirmed by IR, ^{1}H NMR and MASS spectral data. The compounds were screened for their in vitro antibacterial and antifungal activity.

EXPERIMENTAL

Thin layer chromatography was used to monitor the reactions and purity of the newly synthesized compounds. The melting points were determined in open capillary tubes are uncorrected. IR spectra were recorded on a Shimadzu Perkin-Elmer 8201 FT-IR spectrophotometer. The ^{1}H NMR spectra were recorded on BRUKER AVANCE II 400 NMR SPECTROMETER in $CDCl_3$ and DMSO-d_6 using TMS as internal reference (chemical shifts in δ ppm). The FAB mass spectra were recorded on

JEOL SX-102/DA-6000 Mass spectrometer operating at 70ev.

Synthesis of Schiff bases

A mixture of hydrazide (0.01 mol) and substituted aromatic aldehydes (0.01 mol) in absolute alcohol (35 ml), in presence of catalytic amount of glacial acetic acid was refluxed for about 6-7 hrs. The reaction mixture was cooled and poured into the crushed ice. The precipitated compound was filtered and washed with water and recrystallised from absolute alcohol. The physical data of schiff bases (2a-2c) is given in Table-01.

2b IR (KBr) (cm^{-1}): 3061 (CH-Ar), 1676 (C=O), 1593 (C=C).

^{1}H-NMR ($CDCl_3$) δ ppm: 3.09 (s,3H, CH_3), 7.14-8.42 (m, 8H, Ar-H, Ar-CH),

11.77 (s, 1H, CONH) MS: m/z: 239[M^+].

2c: IR (KBr) (cm^{-1}): 3037 (CH-Ar), 1664 (C=O), 1544(C=C).

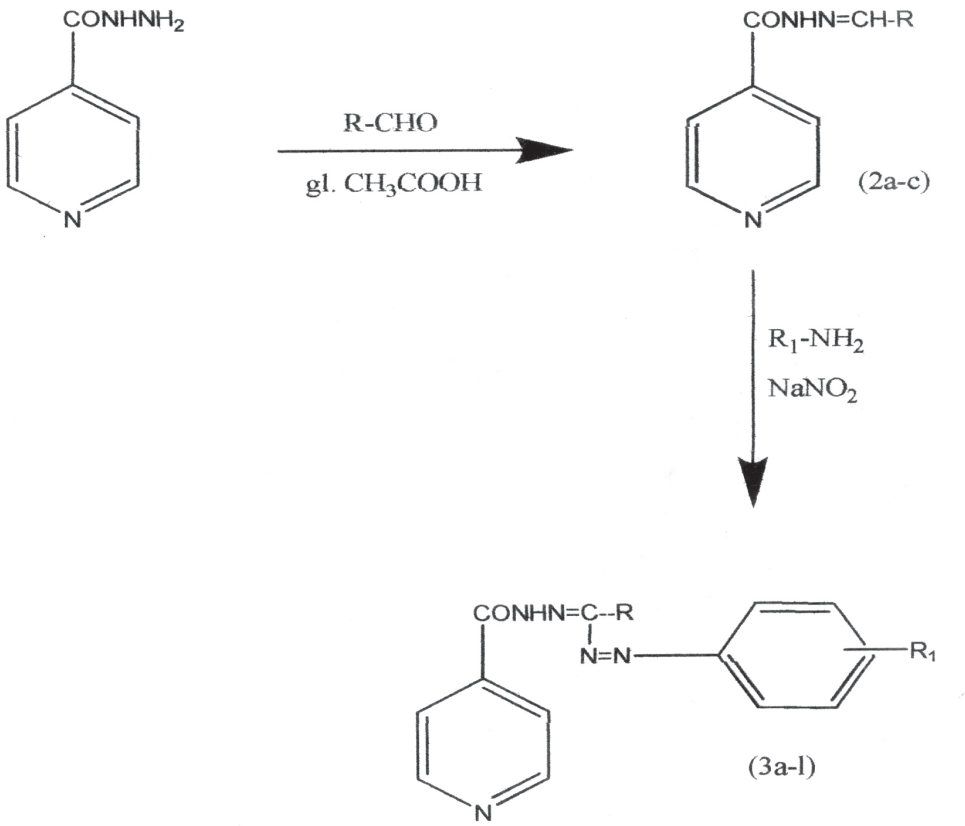
^{1}H-NMR ($CDCl_3$) δppm: 7.32-8.75 (m, 8H, Ar-H, Ar-CH),

11.94(s, 1H, CONH) MS: m/z:259 [M^+].

Synthesis of formazans[7]

The appropriate amine (0.01 mol) in gl.acetic acid (2ml) and HCl (1.5 ml) was diazotized with sodium nitrite (0.2 g in 2ml of water) in the cold (0-5°C) medium. The resultant diazonium chloride solution was added with stirring to the schiff base (0.01 mol in DMF + Pyridine), and the resulting dark coloured solution was left overnight at room temperature and then poured onto crushed ice. The solid thus obtained, was recrystallised from ethanol/ aqueous alcohol.

SCHEME-01



Scheme 1.

3a: IR (KBr) (cm^{-1}) 2915 (CH-Ar), 1656(C=O), 1559(N=N), 1599 (C=C). ^{1}H-NMR ($CDCl_3$) δ ppm: 7.26-8.80 (m, 12H, Ar-H), 10.10(s, 1H, CONH) MS: m/z: 329 [M$^+$].

3g: ^{1}H-NMR ($CDCl_3$) δppm: 2.40 (s,3H, CH_3), 7.20-8.77 (m, 12H, Ar-H), 9.61(s, 1H, CONH).

3h: ^{1}H-NMR ($CDCl_3$) δppm: 2.39 (s,3H, CH_3), 7.34-8.79 (m, 12H, Ar-H),
11.84(s, 1H, CONH). MS: m/z: 422 [M$^+$].

3j: IR (KBr) (cm^{-1}): 1667 (C=O), 1557(N=N), 1595 (C=C). ^{1}H-NMR ($CDCl_3$) δ ppm: 7.30-8.81 (m, 12H, Ar-H), 9.94 (s, 1H, CONH).

3I: IR (KBr) (cm^{-1}): 3110 (CH-Ar), 1680(C=O), 1570(N=N), 1590 (C=C). ^{1}H-NMR ($CDCl_3$) ä ppm:

Table 1: Physical data of Schiff bases (2a-2c)

Comp	R-CHO	m.p. (°C)	% yield
2a	C_6H_5	108	66
2b	4-CH_3	136	68
2c	4-Cl	173	70

Table 2: Physical data of Formazans (3a-3l)

Comp.	R-CHO	R_1-NH_2	MP (°C)	% Yield
3a	C_6H_5	$C_6H_5NH_2$	S	61
3b	C_6H_5	4-CH_3	156	64
3c	C_6H_5	4-Cl	134	66
3d	C_6H_5	Sulphadiazine	176	61
3e	4-CH_3	$C_6H_5NH_2$	144	71
3f	4-CH_3	4-CH_3	116	58
3g	4-CH_3	4-Cl	166	63
3h	4-CH_3	Sulphadiazine	186	69
3i	4-Cl	$C_6H_5NH_2$	154	55
3j	4-Cl	4-CH_3	107	62
3k	4-Cl	4-Cl	192	67
3l	4-Cl	Sulphadiazine	162	63

Table 3: Antimicrobial and antifungal activities of compounds 3a-l

	Diameter of zone of inhibition (mm) at 10µg/ml concentration					
Comp	***S.aureus***	***B.subitilis***	***E.coli***	***P.aeruginosa***	***C.albicans***	***A.niger***
3a	8	11	13	9	10	11
3b	14	13	8	14	11	12
3c	13	9	14	13	8	10
3d	12	11	9	11	11	9
3e	8	12	14	15	12	11
3f	12	12	9	8	13	10
3g	11	10	14	13	12	9
3h	10	10	9	16	10	12
3i	12	8	11	13	13	13
3j	9	11	7	14	12	12
3k	13	11	14	9	11	12
3l	12	11	8	14	10	11
Streptomycin	22	23	24	22	-	-
Griseofulvin	-	-	-	-	23	24
Control (DMF)	-	-	-	-	-	-

7.31-8.76 (m, 12H, Ar-H), 11.78(s, 1H, CONH).
3k: ^{1}H-NMR ($CDCl_3$) ™ppm: 7.34-8.81 (m, 12H, Ar-H), 12.00(s, 1H, CONH).

Similarly other derivatives (3a-3l) were synthesized and their physical data is given in Table-02.

Antibacterial And antifungal activity

The newly synthesized formazans was assayed in vitro for antibacterial activity S.aureus, P.aeruginosa, E.coli and B.subtilis and antifungal activity against C.albicans and A.niger using DMF as solvent at 100 ìg/ml concentration by cup-plate method[8]. After 24 hr of incubation at 37°C, the zones of inhibition were measured in mm. The activity was compared with the known antibiotics viz. Streptomycin and Griseofulvin at the same concentration. The biological data of the compounds (3a-l) is given in table-03.

RESULTS AND DISCUSSION

The antibacterial activity of the newly synthesized compounds in the present investigation was assessed by the cup-plate method. The result of the antibacterial studies are shown in table-3. Among the compounds tested 4b, 4e, 4g, 4i showed good activity against both the gram positive and gram negative pathogenic organisms. The rest of the compounds showed moderate activity against all the four organisms.

In the antifungal activity, the compounds 4b and 4h showed highest activity against both the fungal organisms. The other compounds showed moderate activity.

ACKNOWLEDGEMENTS

The authors are thankful to NITTE Education Trust for providing the necessary facilities. The authors are also grateful to the Directors, RSIC, Chandigarh and CDRI, Lucknow for providing IR, NMR and Mass spectra respectively.

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