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Synthesis, Characterization and Antibacterial Activity of Some Schiff Bases of 2-Amino-3-(N-Tolyl Carboxamido)-4,5,6,7-Tetrahydro Benzo (b) Thiophenes

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2-Amino-3-(N-tolyl carboxamido)-4,5,6,7-tetrahydro benzo (b) thiophenes (**I–III**) were synthesized by Gewald reaction. Later, the compounds **I–III** were treated with ten different substituted arylaldehydes to yield thirty new Schiff bases (**I a–j to III a–j**). The compounds were characterized by spectral data and were screened for antibacterial activity. Some of these Schiff bases exhibited promising activity.

Key Words: Synthesis, Thiophenes, Schiff bases, Antibacterial activity.

INTRODUCTION

A number of thiophenes[1–4] and Schiff bases[5–8] were reported to possess different biological activities like antitubercular, bacteriostatic and antifungal activities. These observations stimulated us with a presumption that Schiff bases of thiophenes (**I–III**) would produce new compounds of better antibacterial activity. Hence an attempt was made by us to synthesize thirty new thiophene Schiff bases for antibacterial studies.

EXPERIMENTAL

The UV spectra were recorded on Shimadzu 1601 spectrometer. IR (KBr) were recorded on FT-IR 8201. H^1 NMR spectra were recorded on Brucker DPX 200. The chemical shift values are in δ ppm.

General Method for the Synthesis of the New Schiff Bases

Synthesis of Schiff Base of 2-Amino-3-(N-*o*-Tolyl Carboxamido)-4,5,6,7,-Tetrahydro Benzo (b) Thiophene (Ia): The starting compound 2-amino-3-(N-tolyl carboxamido)-4,5,6,7-tetrahydro benzo (b) thiophenes (**I-III**) were synthesised by already reported procedure[9]. Later to the compound 2-amino-3-(N-*o*-tolyl carboxamido)-4,5,6,7-tetrahydro benzo (b) thiophene (**I**) (2.86 g, 0.01 M) in ethanol (40 mL) was added salicylaldehyde (1.22 g, 0.01 M) and catalytic amount of glacial acetic acid (1 mL). The product separated out on warming and then cooled, filtered, washed with ethanol, dried and recrystallized from DMF : Water

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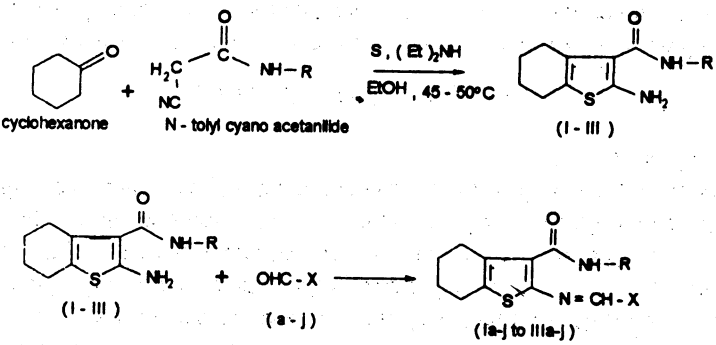
mixture (5 : 1) to yield bright yellow coloured crystalline compound. Yield 90%, m.p. 208°C. The other compounds reported in Table-1 were prepared in the same manner.

All the synthesised compounds **(Ia–j–III a–j)** were screened for their antibacte-



SCHEME-1

rial activity by cup diffusion method[10] at a concentration of 50 μg/mL using 02 gram +ve and 02 gram –ve bacteria. The zone of inhibition was measured in mm and reported in Table-1. The activity was compared with ampicillin (50 μg/mL) as standard.

RESULTS AND DISCUSSION

All the synthesized compounds are bright coloured solids. Melting points are uncorrected. Elemental analyses were within ±0.4% of their calculated values.

The formation of the starting compounds 2-amino-3-(N-tolyl carboxamido)-4,5,6,7-tetrahydro benzo (b) thiophenes **(I-III)** were confirmed by the presence of specific IR peaks at 750 cm^{-1} due to *o*-tolyl group, 780 cm^{-1} due to *m*-tolyl group, 830 cm^{-1} due to *p*-tolyl group, 1618 cm^{-1} (—CONH—), 2858–2731 cm^{-1} (—S—CH—), 3282 cm^{-1} (—NH—), 3458 cm^{-1} ($—NH_2$).

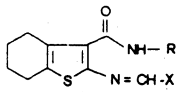
The formation and the purity of the new Schiff bases **(I a–j to III a–j)** were confirmed by the difference in m.p. R_f values and specific IR peaks between 609 cm^{-1} (C—Cl aromatic), 750–740 cm^{-1} (*o*-tolyl $—CH_3$ group), 830–810 cm^{-1} (*p*-methyl aromatic), 1307 cm^{-1} (—OH aromatic), 1370–1330 cm^{-1} (—C—aromatic), 1660–1640 cm^{-1} (—CH=N— of Schiff's bases), 2860–2840 cm^{-1} ($—OCH_3$) and ^1H NMR spectra as follows.

Ib = 8.5 (s, 1H, —CH=), 8.0 (d, 1H, —NH—), 7.0–7.75 (m, 8H, Arom), 4.0 (s, 3H, $—OCH_3$ Arom), 2.5 (s, 1H, $—CH_3$ Arom), 2.0 and 3.0 (m, 8H, tetramethelenic protons).

Ic = 8.5 (s, 1H, —CH=), 8.0 (d, 1H, —NH—), 7.0–7.75 (m, 7H, Arom), 4.0 (s, 6H, $—OCH_3$ Arom), 2.5 (s, 3H, $—CH_3$ Arom), 2.0 & 3.0 (m, 8H, tetramethelenic protons).

IIa = 8.5 (s, 1H, —CH=), 7.75–8.0 (d, 2H, —NH and —OH protons), 6.75–7.25 (m, 8H, Arom), 2.25 (s, 3H, $—CH_3$ Arom), 1.8 and 2.75 (m, 8H, tetramethelenic protons).

TABLE-1
PHYSICAL AND ANTIBACTERIAL DATA OF COMPOUNDS I a-j TO III a-j



(Ia-j - III a-j)

Comp. No.	R	X	(m.p.) °C	Recrystallization solvent	Zone of inhibition in mm			
					S.a.	*S.e.*	E.c.	S.t.
Ia	*o*-Tolyl	2-hydroxy phenyl	208	DMF:WATER	18	21	NA	NA
Ib	*o*-Tolyl	4-methoxy phenyl	178	DMF:WATER	NA	NA	NA	NA
Ic	*o*-Tolyl	3,4-trimethoxy phenyl	138	DMF:WATER	NA	NA	NA	NA
Id	*o*-Tolyl	3,4,5-trimethoxy phenyl	122	ETHANOL	14	16	NA	NA
Ie	*o*-Tolyl	2-nitro phenyl	216	DMF:WATER	16	14	NA	NA
If	*o*-Tolyl	3-nitro phenyl	176	DMF:WATER	19	15	NA	NA
Ig	*o*-Tolyl	4-methyl phenyl	154	DMF:WATER	NA	NA	NA	NA
Ih	*o*-Tolyl	4-dimethyl amino phenyl	164	DMF:WATER	NA	NA	NA	NA
Ii	*o*-Tolyl	3-methoxy-4 hydroxy phenyl	216	DMF:WATER	18	16	NA	NA
Ij	*o*-Tolyl	4-chloro phenyl	178	DMF:WATER	22	19	16	NA
IIa	*m*-Tolyl	2-hydroxy phenyl	212	DMF:WATER	20	24	NA	NA
IIb	*m*-Tolyl	4-methoxy phenyl	182	DMF:WATER	NA	NA	NA	NA
IIc	*m*-Tolyl	3,4-dimethoxy phenyl	144	DMF:WATER	NA	NA	NA	NA
IId	*m*-Tolyl	3,4,5-trimethoxy phenyl	152	ETHANOL	16	15	NA	NA
IIe	*m*-Tolyl	2-nitro phenyl	218	DMF:WATER	18	15	NA	NA
IIf	*m*-Tolyl	3-nitro phenyl	180	DMF:WATER	17	16	NA	NA
IIg	*m*-Tolyl	4-methyl phenyl	146	DMF:WATER	NA	NA	NA	NA
IIh	*m*-Tolyl	4-dimethyl amino phenyl	172	DMF:WATER	NA	NA	NA	NA
IIi	*m*-Tolyl	3-methoxy-4 hydroxy phenyl	208	DMF:WATER	17	17	NA	NA
IIj	*m*-Tolyl	4-chloro phenyl	186	DMF:WATER	24	21	18	NA
IIIa	*p*-Tolyl	2-hydroxy phenyl	202	DMF:WATER	22	24	NA	NA
IIIb	*p*-Tolyl	4-methoxy phenyl	186	DMF:WATER	NA	NA	NA	NA
IIIc	*p*-Tolyl	3,4-dimethoxy phenyl	176	DMF:WATER	NA	NA	NA	NA
IIId	*p*-Tolyl	3,4,5-trimethoxy phenyl	154	ETHANOL	16	18	NA	NA
IIIe	*p*-Tolyl	2-nitro phenyl	204	DMF:WATER	18	17	NA	NA
IIIf	*p*-Tolyl	3-nitro phenyl	178	DMF:WATER	20	15	NA	NA
IIIg	*p*-Tolyl	4-methyl phenyl	158	DMF:WATER	NA	NA	NA	NA
IIIh	*p*-Tolyl	4-dimethyl amino phenyl	210	DMF:WATER	NA	NA	NA	NA
IIIi	*p*-Tolyl	3-methoxy-4 hydroxy phenyl	206	DMF:WATER	20	18	NA	NA
IIIj	*p*-Tolyl	4-chloro phenyl	206	DMF:WATER	26	24	21	NA
Ampicillin					40	32	28	26

S.a. = S. aureus, S.e. = S. epidermis, E.c. = E. coli, S.t. = S. typhi.

IIh = 8.5 (s, 1H, —CH=), 7.5 (d, 1H, —NH—), 6.75–7.75 (m, 8H, Arom), 3.0–3.25 (d, 9H, —CH_3 Arom and —$N(CH_3)_2$), 1.75–2.5 (m, 8H, tetramethelenic protons).

IIIi = 8.5 (s, 1H, —CH=), 7.25–7.6 (m, 9H, —NH, —OH and Ar—H), 4.0 (s, 3H, —OCH_3 Arom), 2.5 (s, 3H, —CH_3 Arom), 1.9 and 3.2 (m, 8H, tetramethelenic protons).

IIIe = 8.5 (s, 1H, —CH=), 7.25–7.6 (m, 9H, —NH and Ar—H), 2.5 (s, 3H, —CH_3 Arom), 1.9 and 3.2 (m, 8H, tetramethelenic protons).

A comparative study of MIC values (Table-1) of these compounds reveals that 18 compounds were exhibiting interesting antibacterial activities, however not on par with that of standard employed.

The compounds having 2-hydroxy phenyl substituent, 3,4,5-trimethoxy phenyl substituent, 2-nitro or 3-nitro phenyl substituent, 3-methoxy, 4-hydroxy phenyl substituent at X were exhibiting antibacterial activity against gram positive organisms only, and no activity against gram negative organisms. Whereas the compounds **Ij, IIj, IIIj** with 4-chloro phenyl substituent at X were active against both gram positive bacteria and *E.coli* only.

It is also interesting to note that the compounds **IIIa, IIId, IIIe, IIIf, IIIi** and **IIIj** containing *p*-tolyl substituent at R of thiophene showed a better antibacterial activity than the active compounds of series **I** and **II.**

Finally out of the 30 compounds screened for antibacterial activity, 12 compounds were possessing least antibacterial activity and 18 compounds were found to possess moderate antibacterial activity when compared to the standard.

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