

## Synthesis and Antimicrobial Activity of New 3-Amino sulphonyl[3'-chloro-4'-(substituted phenyl)-2'-oxo azetidine]indole

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A series of new 3-amino sulphonyl[3'-chloro-4'-(substituted phenyl)-2'-oxo azetidine]indole derivatives (**5a-j**) have been prepared from the respective 3-(substituted benzylidene hydrazine) sulphonyl indoles (**4a-j**) by treating with chloroacetyl chloride in presence of ethanol. The required substituted benzylidene hydrazino sulphonyl indoles (**4a-j**) were obtained from hydrazino sulphonyl indole (**3**) by condensing with appropriate aromatic aldehydes. Chloro-sulphonyl indole (**2**) when treated with hydrazine yielded the respective hydrazides. 3-Aminosulphonyl [3'-chloro-4'-(4-nitro phenyl)-2'-oxo azetidine]indole showed moderate to good antimicrobial activity.

**Key Words:** Indole derivatives, Azetidine, Antimicrobial activity.

### INTRODUCTION

Substituted indoles are associated with psychotropic<sup>1</sup>, antiinflammatory<sup>2-5</sup>, CNS depressant, anticonvulsant and antimicrobial activities. The azetidinone moiety is known to potentiate the biological activity<sup>6-8</sup>. Azetidinone containing fused indole moieties are likely to be shown enhanced biological activities.

### EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. IR spectra were recorded on Shimadzu FTIR-3000 instrument, <sup>1</sup>H NMR spectra were recorded on Bruker 300 MHz spectrophotometer using TMS as an internal standard. The purity of synthesized compounds was routinely checked by TLC.

#### Synthesis of 3-chloro sulphonyl indole (**2**)

Equimolar proportions of indole (0.01 mol) and chlorosulphonic acid was added drop by drop and it was shaken from time to time to ensure thorough

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mixing. The reaction mixture was kept on boiling water bath for another 30 min in order to complete the reaction. The mixture was then added slowly to crushed ice. The product was rinsed with a little ice water. The resultant product was filtered and washed with a little cold water and recrystallized from ethanol. The purity was established by single spot on TLC plates. The solvent used was chloroform : methanol (95 : 5). m.p. 67°C, yield 68%.

### Synthesis of 3-hydrazino sulphonyl indole (3)

To a boiling solution of compound **2** (0.01 mol) in absolute ethanol (50 mL) hydrazine hydrate (99%, 0.01 mol) was added and the resulting solution was refluxed for 4 h. Excess of solvent was distilled off and the solid thus obtained, filtered, washed with water and recrystallized from ethanol. The purity was established by single spot on TLC plates. The solvent used was chloroform : methanol (95 : 5). m.p. 73°C, yield 73%.

### Synthesis of 3-(substituted benzylidene hydrazino)sulphonyl indole, 4 (a–j)

Compound **3** (0.01 mol) and equimolar proportion of different aldehydes and anhydrous sodium acetate (0.82 g) was added to 75 mL of glacial acetic acid in round-bottomed flask. It was refluxed for 4 h using double surface condenser with a calcium chloride guard tube. The reaction mixture was kept to overnight. The mixture was added to water, the solid thus obtained filtered and recrystallized from ethanol.

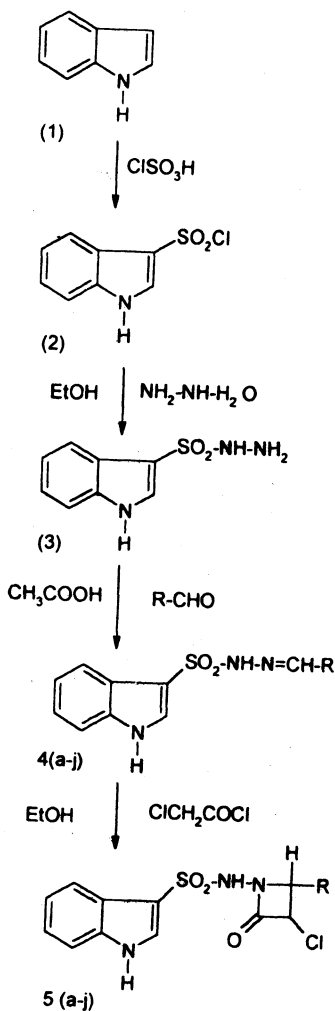
### Synthesis of certain 3-amino sulphonyl[3'-chloro-4'-(substituted phenyl)-2'-oxo azetidine]indole, 5 (a–j)

A mixture of compound **4** (0.01 mL) in ethanol (100 mL) and chloroacetyl chloride (0.01 mol) was heated under reflux for 2 h, cooled and treated with aqueous sodium hydroxide. The solid thus obtained was filtered and recrystallized from ethanol to give the final compound (**Scheme-1**).

The IR spectra of **5b** (KBr,  $\text{cm}^{-1}$ ) 1630 ( $\beta$ -lactam ring (C=O)), 3100 (CH, stretching, Ar), 1366 ((SO<sub>2</sub>—NH), 1108 (chlorobenzene), 1512 (C=C, stretching, Ar), <sup>1</sup>H NMR (CDCl<sub>3</sub>), 4.55–4.61 (d, 1H, C<sub>4</sub>H<sub>1</sub> azetidinone), 6.2–6.3 (m, 4H, Ar—H), 7.56–7.66 (s, 1H, SO<sub>2</sub>NH), 9.24–9.32 (s, 1H, NH of indole exchangeable with

D<sub>2</sub>O). Similarly, other members of **5** (a–j) were prepared and their physical and analytical data are presented in Table-1.

All the compounds were screened *in vitro* for their antimicrobial activity against bacteria *Staphylococcus aureus*, *Escherichia coli* and fungi *Candida albicans* using DMF as solvent by agar-cup plate method<sup>9</sup> at 100  $\mu\text{g/mL}$  concentration. After 24 h of incubation at 37°C, the zones of inhibition were measured in mm. The activity was compared with known antibiotics like Amoxicillin and Griseofulvin.



Scheme-1

## RESULTS AND DISCUSSION

Synthesized compounds have been screened from their antimicrobial activities against the strains of *S. aureus*, *E. coli* and *C. albicans* at a concentration of 100  $\mu\text{g/mL}$ . The maximum activity was found in **5a**, **5b**, **5d** and **5e** for *S. aureus*, **5e**, **5f**, **5h**, **5i** and **5j** were active against *E. coli*. Most of the compounds were found moderately active against *C. albicans*. Antimicrobial data are listed in Table-2.

TABLE-1  
PHYSICAL AND ANALYTICAL DATA OF COMPOUNDS 5(a-j)

Comp. No.	R	m.f.	m.w.	m.p. (°C)	Yield (%)	% Found (calcd.)		
						C	H	N
5a	2-chlorophenyl	C <sub>15</sub> H <sub>12</sub> O <sub>2</sub> SN <sub>3</sub> Cl	409	78	60	49.65 (49.87)	3.02 (3.17)	10.44 (10.20)
5b	4-chlorophenyl	C <sub>15</sub> H <sub>12</sub> O <sub>2</sub> SN <sub>3</sub> Cl	409	74	64	49.74 (49.87)	3.12 (3.17)	10.06 (10.20)
5c	2-nitrophenyl	C <sub>15</sub> H <sub>12</sub> O <sub>4</sub> SN <sub>4</sub>	385	73	66	52.68 (52.90)	3.06 (3.37)	14.28 (14.54)
5d	3-nitrophenyl	C <sub>15</sub> H <sub>12</sub> O <sub>4</sub> SN <sub>4</sub>	385	77	68	52.82 (52.90)	3.18 (3.37)	14.32 (14.54)
5e	4-nitrophenyl	C <sub>15</sub> H <sub>12</sub> O <sub>4</sub> SN <sub>4</sub>	385	75	68	52.74 (52.90)	3.48 (3.37)	14.64 (14.54)
5f	4-methylphenyl	C <sub>18</sub> H <sub>16</sub> O <sub>3</sub> SN <sub>3</sub>	354	70	60	60.76 (61.01)	4.36 (4.51)	11.74 (11.86)
5g	2-methoxyphenyl	C <sub>18</sub> H <sub>16</sub> O <sub>4</sub> SN <sub>3</sub>	370	68	62	58.28 (58.37)	4.46 (4.32)	11.18 (11.35)
5h	4-methoxyphenyl	C <sub>18</sub> H <sub>16</sub> O <sub>4</sub> SN <sub>3</sub>	370	66	63	58.08 (58.37)	4.16 (4.32)	11.38 (11.35)
5i	2,4-dichlorophenyl	C <sub>17</sub> H <sub>12</sub> O <sub>3</sub> SN <sub>3</sub> Cl <sub>2</sub>	443	76	65	45.86 (46.04)	2.36 (2.48)	9.28 (9.48)
5j	4,6-dichlorophenyl	C <sub>17</sub> H <sub>12</sub> O <sub>3</sub> SN <sub>3</sub> Cl <sub>2</sub>	443	78	69	45.92 (46.04)	2.38 (2.48)	9.30 (9.48)

TABLE-2  
ANTIMICROBIAL ACTIVITY DATA OF COMPOUNDS (5a-j)

Compound No.	R	Zone of Inhibition (mm)		
		<i>S. aureus</i>	<i>E. coli</i>	<i>C. albicans</i>
5a	2-chlorophenyl	24	20	18
5b	4-chlorophenyl	26	19	20
5c	2-nitrophenyl	20	17	16
5d	3-nitrophenyl	24	18	17
5e	4-nitrophenyl	22	26	19
5f	4-methylphenyl	20	26	21
5g	2-methoxyphenyl	18	16	20
5h	4-methoxyphenyl	21	24	18
5i	2, 4-dichlorophenyl	16	22	16
5j	2, 6-dichlorophenyl	18	24	17

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