



## Synthesis, spectral studies and antibacterial screening of some novel derivatives of 2-Pyrrolidinones based on Schiff base

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### ABSTRACT

2-Pyrrolidinones are one of the heterocyclic compounds with very important biological activities. In this view, it was proposed to synthesize some novel 2-Pyrrolidinones from Schiff bases. Here the synthesis of 2-Pyrrolidinones using 1-N-phenyl-3-phenyl-4-formyl pyrazole (PFP), Schiff bases and succinic anhydride under basic condition in presence of ethanol. The structures of synthesized were assigned on the basis of elemental analysis, IR and <sup>1</sup>H NMR spectroscopy data. These compounds were screened for their anti-bacterial activity.

**Keywords:** 2-Pyrrolidinones, Antibacterial activity, Schiff bases, PFP.

### INTRODUCTION

Heterocyclic compounds are the well known class of compounds for its biological applications out of which 2-pyrrolidinone occupy unique position due to dominate applications [1-5]. 2-pyrrolidinone are heterocyclic compounds which possess wide range of biological activities such as anti bacterial and anti fungal [6-7]. Various 2-pyrrolidinone derivatives were prepared by condensation of Schiff base of PFP and succinic anhydride. Also further some of benzimidazole derivatives were synthesized by condensation of some of 2-pyrrolidinone derivatives with o-phenylene diamine [8-12]. It is an industrial solvent for polymers, chlordane, DDT, sorbitol, glycerol, iodine, sugars. It is used in speciality printers ink. It is used as plasticizer and coalescing agent for acrylicstyrene emulsion type floor polishes. It is prepared from glutamic acid [13-15]. Adam, Waldemar and Zhang, Aimin studied the high  $\beta$ -facial selectivity through chelation of magnesium ions in the DMD epoxidation of  $\beta$ -unsaturated imides with chiral pyrrolidinone auxiliaries. Estimation of the lipophilicity of antiarrhythmic and antihypertensive active-1-substituted pyrrolidin-2-one and Pyrrolidine derivatives was carried out by Kulig, Katarzyna and Malawska, Barbara. In the present communication, we report the reaction of different Schiff base derivatives with succinic anhydride to form pyrrolidinone. The structures of various synthesized compounds were assigned on the basis of elemental analysis, IR and <sup>1</sup>H NMR spectral data. These compounds were also screened for anti bacterial activities.

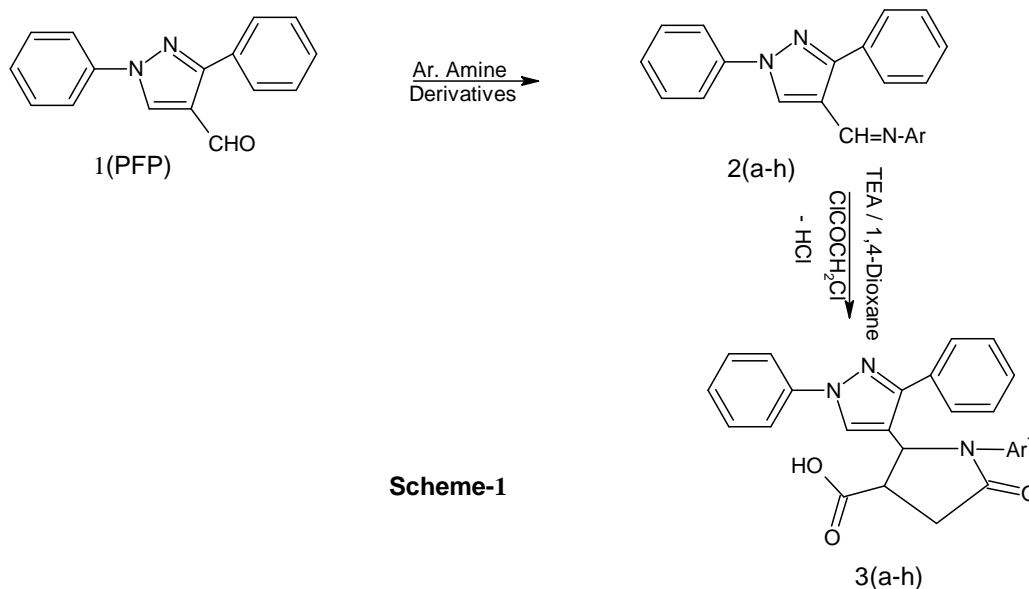
### MATERIALS AND METHODS

Various Schiff bases of pyrazole and sulphonamide (2a-h) on heterocyclization reactions with Succinic anhydride gave the desired products 2-pyrrolidinones (3a-h). Their structures have been characterized on the basis of their analytical and spectral data. The research work is scanned in Scheme-1 and the experimental procedures for the synthesis of the series of compounds have been adopted according to the reported method [17].

#### Synthesis of sulfonamide derivatives of Arylidine-[1-N-phenyl-3-phenyl- pyrazole] (2a-h)

The various Schiff bases (2a-h) of 1-N-phenyl-3-phenyl-4-formyl pyrazole (PFP) (**1**) have been prepared in the similar manner. The procedure is as follow:

A mixture of equimolar amount of 1-N-phenyl-3-phenyl-4-formyl pyrazole (PFP) (0.01 mole) (1) and various aromatic amino sulfonamides (0.01 mole) in 50 ml acetic acid was refluxed for about 10-12 hrs. on oil bath with TLC monitoring. The reaction mixture was cooled and it was poured into ice water and extracted with ethyl acetate and water and finally dried over anhydrous sodium sulfate. The solvent was evaporated to give the solid product. It was crystallized from ethyl acetate-hexane using decolorizing charcoal to give various anils (i.e. Schiff bases) (2a-h).



No.	sulfonamide derivative	Structure
2a	4-amino-N-phenylbenzene-sulfonamide	
2b	4-amino-N-4'-chloro phenylbenzene-sulfonamide	
2c	4-amino-N-4'-bromo phenylbenzene-sulfonamide	
2d	4-amino-N-4'-nitro phenylbenzene-sulfonamide	
2e	4-amino-N-4'-methyl phenylbenzene-sulfonamide	
2f	4-amino-N-2',6'-dichloro-4'-nitro phenylbenzene Sulfonamide	
2g	N-[(4-aminophenyl)-sulfonyl]acetamide	
2h	4-amino-N-2-pyrimidinylbenzenesulfonamide	

The analytical and spectral data of the Schiff bases of 1-N-phenyl-3-phenyl-4-formyl pyrazole (PFP) (1) are described as follows:

**Synthesis of 5-[1-N-phenyl sulphonamide-3-phenyl-pyrazole]-2-oxo-1-N-aryl-1H-pyrrolidinone-4-carboxylic acid (3a-h)**

Succinic anhydride (0.1mole) and an imine (2a-h) (0.1mole) were heated at reflux in chloroform (30ml) for about 5 hours with TLC monitoring. After the mixture was allowed to stand for 2 days, the solid was filtered. The product thus formed was recrystallized from ethanol to give pure in good Synthesis of 5-[1-N-phenyl sulphonamide-3-phenyl-pyrazole -2-oxo-1-N-aryl-1H-pyrrolidinone-4-carboxylic acid (3a-h) yield.

**Table -1. Physical Constant of 2-pyrrolidinones derivatives (3a-h)**

Compd.	R	Mol. Formula (Mol. Wt)	m.p. (°C)	Yield %	% of C,H,N Calcd. / Found			
					C	H	N	S
<b>3a</b>	C <sub>12</sub> H <sub>12</sub> N <sub>2</sub> O <sub>2</sub> S-	C <sub>32</sub> H <sub>26</sub> N <sub>4</sub> O <sub>5</sub> S 578	173-174 °C	67%	66.4	4.5	9.7	5.5
					66.3	4.4	9.7	5.4
<b>3b</b>	C <sub>12</sub> H <sub>11</sub> N <sub>2</sub> O <sub>2</sub> SCl-	C <sub>32</sub> H <sub>25</sub> N <sub>4</sub> O <sub>5</sub> SCl 612.5	157-158 °C	66%	62.7	4.1	9.1	5.2
					62.5	4.0	9.0	5.1
<b>3c</b>	C <sub>12</sub> H <sub>11</sub> N <sub>2</sub> O <sub>2</sub> SBr-	C <sub>32</sub> H <sub>25</sub> N <sub>4</sub> O <sub>5</sub> SBr 657	170-172 °C	64%	58.4	3.8	8.5	4.8
					58.2	3.7	8.4	4.7
<b>3d</b>	C <sub>12</sub> H <sub>11</sub> N <sub>3</sub> O <sub>4</sub> S-	C <sub>32</sub> H <sub>25</sub> N <sub>5</sub> O <sub>7</sub> S 623	173-174 °C	65%	61.6	4.0	11.2	5.1
					61.5	3.5	11.0	5.0
<b>3e</b>	C <sub>13</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub> S-	C <sub>33</sub> H <sub>28</sub> N <sub>4</sub> O <sub>5</sub> S 592	157-158 °C	68%	66.9	4.7	9.4	5.4
					66.8	4.5	9.4	5.3
<b>3f</b>	C <sub>12</sub> H <sub>9</sub> N <sub>3</sub> O <sub>4</sub> SCl <sub>2</sub> -	C <sub>32</sub> H <sub>23</sub> N <sub>5</sub> O <sub>7</sub> SCl <sub>2</sub> 692	167-168 °C	67%	55.5	3.3	10.1	4.6
					55.4	3.2	10.0	4.6
<b>3g</b>	C <sub>8</sub> H <sub>10</sub> N <sub>2</sub> O <sub>3</sub> S-	C <sub>28</sub> H <sub>24</sub> N <sub>4</sub> O <sub>6</sub> S 543	180-182 °C	68%	61.9	4.4	10.3	5.9
					61.8	4.3	10.3	5.8
<b>3h</b>	C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> S-	C <sub>30</sub> H <sub>24</sub> N <sub>6</sub> O <sub>5</sub> S 580	184-185 °C	63%	62.0	4.1	14.5	5.5
					62.0	4.0	14.3	5.5

**Compound-3a**

Infrared Spectral Features cm<sup>-1</sup>: 3054,1600,1532-Aromatic C-H, 1667-C=O of COOH, 1717-C=O of pyrrolidinone. PMR spectral Features (δ,ppm) : 6.3-8.1 (multiplet aromatic + H of pyrazole + H of SO<sub>2</sub>NH), 5.15 (H, S, C<sub>5</sub>), 4.7 (H, S, C<sub>4</sub>), 2.5 - 2.7 (H, d, C<sub>2</sub>), 3.4 - 3.8 (2H, t, C<sub>3</sub>), 12.9 (H, s, COOH)

**Compound-3b**

Infrared Spectral Features cm<sup>-1</sup>: 3030, 1600,150-Aromatic C-H, 1670 C=O of COOH, 1717- C=O of pyrrolidinone. PMR spectral Features (δ,Ppm): 6.3-8.1(multiplet aromatic H of pyrazole + H of SO<sub>2</sub>NH), 12.9 (H, S, COOH), 5.15 (H, S, C<sub>5</sub>), 4.7 (H, S, C<sub>4</sub>), 2.5 - 2.7 (H, d, C<sub>2</sub>), 3.4 - 3.8 (2H, t, C<sub>3</sub>).

**Compound-3c**

Infrared Spectral Features cm<sup>-1</sup>:3030, 1600,1500-Aromatic C-H, 1670-C=O of COOH, 1717-C=O of pyrrolidinones. PMR spectral Features (δ,ppm):6.1-8.1(multiplet aromatic H of pyrazole + H of SO<sub>2</sub>NH),12.92 (H, s, COOH), 5.15 (H, S, C<sub>5</sub>), 4.7 (H, S, C<sub>4</sub>), 2.5 - 2.7 (H, d, C<sub>2</sub>), 3.4 - 3.8 (2H, t, C<sub>3</sub>).

**Compound-3d**

Infrared Spectral Features cm<sup>-1</sup>: 3030, 1600, 1500-Aromatic C-H, 1690-C=O of COOH, 1717-C=O of pyrrolidinones. PMR spectral Features (δ,ppm): 6.3-8.1(multiplet aromatic H of pyrazole + H of SO<sub>2</sub>NH), 12.92 (H, s, COOH), 5.15 (H, s, C<sub>5</sub>), 4.7 (H, s, C<sub>4</sub>), 2.5 - 2.7 (H, d, C<sub>2</sub>), 3.4 - 3.8 (2H, t, C<sub>3</sub>).

**Compound-3e**

Infrared Spectral Features cm<sup>-1</sup>: 3030, 1600, 1500-Aromatic C-H, 1670-C=O of COOH, 1717-C=O of pyrrolidinones. PMR spectral Features (δ,ppm): 6.1-8.1(multiplet aromatic H of pyrazole + H of SO<sub>2</sub>NH), 1.16 (3H, s, CH<sub>3</sub>), 12.92 (H, s, COOH), 5.15 (H, s, C<sub>5</sub>), 4.7(H, s, C<sub>4</sub>), 2.5 - 2.7 (H, d, C<sub>2</sub>), 3.4 - 3.8 (2H, t, C<sub>3</sub>).

**Compound-3f**

Infrared Spectral Features cm<sup>-1</sup>: 3030, 1600, 1500-Aromatic C-H, 1670-C=O of COOH, 1717-C=O of pyrrolidinones. PMR spectral Features (δ,ppm): 6.3-7.9(multiplet aromatic H of pyrazole + H of SO<sub>2</sub>NH), 12.92 (H, s, COOH), 5.15 (H, s, C<sub>5</sub>), 4.7 (H of C<sub>4</sub>), 2.5 - 2.7(H, d, C<sub>2</sub>), 3.4 - 3.8 (2H, t, C<sub>3</sub>).

**Compound-3g**

Infrared Spectral Features  $\text{cm}^{-1}$ : 3030, 1600, 1500-Aromatic C-H, 1670-C=O of COOH, 1717-C=O of pyrrolidinones. PMR spectral Features ( $\delta$ ,ppm): 6.3-7.9-(multiplet aromatic H of pyrazole + H of  $\text{SO}_2\text{NH}$ ), 2.0 (3H, s,  $\text{COCH}_3$ ), 12.92 (H, s, COOH), 5.15 (H, s,  $\text{C}_5$ ), 4.7(H, s,  $\text{C}_4$ ), 2.5 - 2.7 (H, d,  $\text{C}_2$ ), 3.4 - 3.8 (2H, t,  $\text{C}_3$ ).

**Compound-3h**

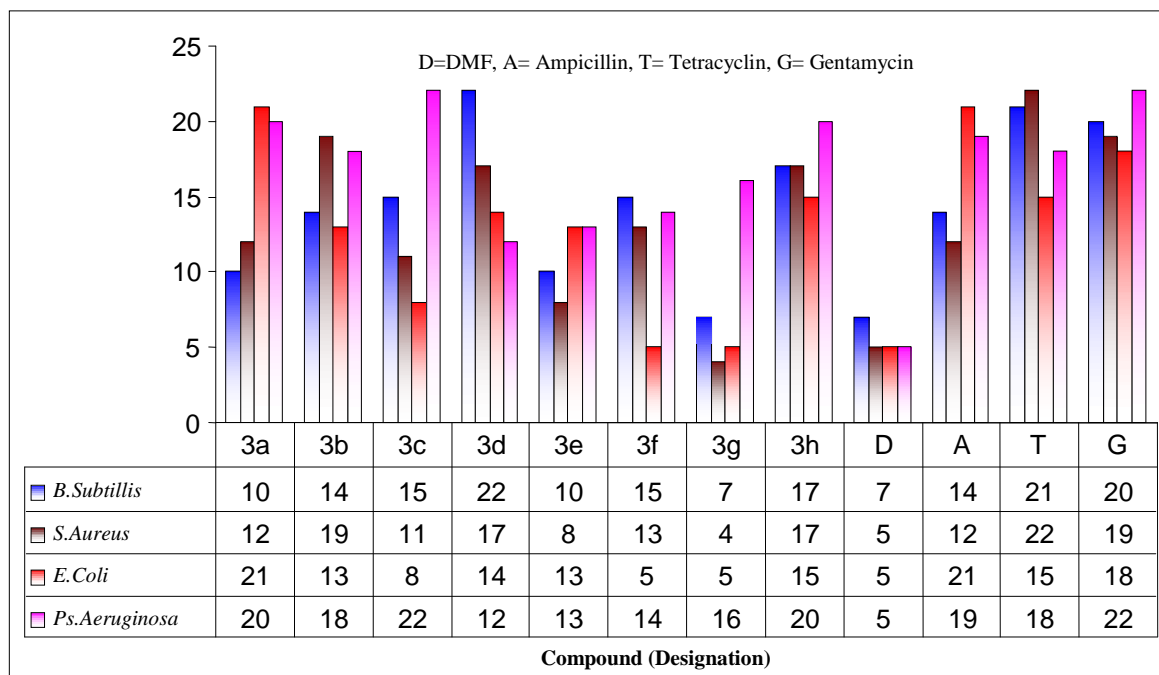
Infrared Spectral Features  $\text{cm}^{-1}$ : 3030, 1600, 1500-Aromatic C-H, 1670-C=O of COOH, 1717-C=O of pyrrolidinones. PMR spectral Features ( $\delta$ ,ppm): 5.9-7.9-(multiplet aromatic H of pyrazole + H of  $\text{SO}_2\text{NH}$ ), 12.92 (H, s, COOH), 4.7-5.15 (H, d,  $\text{C}_5\text{H}$ ).

**Table-2. Antimicrobial activity of Standards and Solvent (DMF)**

No.	Name of compound	Zone of inhibition (in mm)			
		Gram positive		Gram negative	
		<i>B.Subtillis</i>	<i>S.Aureus</i>	<i>E.Coli</i>	<i>Ps.Aeruginosa</i>
1	DMF	7	5	5	5
2	Ampicillin	14	12	21	19
3	Tetracyclin	21	22	15	18
4	Gentamycin	20	19	18	22
5	Chloramphenicol	21	23	17	24

**Table: 4 Antimicrobial activity 5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-phenyl sulphonamide-pyrrolidinone-4-carboxylic acid (3a-h)**

Compound (designation)	Zone of Inhibition (in mm)			
	Gram positive		Gram negative	
	<i>B.Subtillis</i>	<i>S.Aureus</i>	<i>E.Coli</i>	<i>Ps.Aeruginosa</i>
3a (1)	10	12	21	20
3b (2)	14	19	13	18
3c (3)	15	11	08	22
3d (4)	22	17	14	12
3e (5)	10	08	13	13
3f (6)	15	13	05	14
3g (7)	07	04	05	16
3h (8)	17	17	15	20

**Fig 1. Zone of Inhibition → Compounds (3a-3h)**

## RESULTS AND DISCUSSION

Structures of azomethines, arylidene-[1-N-phenyl-sulfonamide-3-phenyl-pyrazole] (2a-h). As we know that the azomethines are the crucial material for the preparation of heterocyclic compounds like 2H-pyrrole-2-ones, 2-pyrrolidinones, etc. These azomethines (2a-h) on cyclocondensation reaction with succinic anhydride affords the biologically active 2-pyrrolidinones derivatives (3a-h). (Table 2-3)

Their structures were confirmed by analytical and spectral data. The C, H, N and S contents of the prepared compounds were consistent with their predicted structures as shown in Scheme-1. The infrared spectra show the band in the region  $1680-1700\text{cm}^{-1}$  for carbonyl group of 2-pyrrolidinone ring.

The NMR spectra show a singlet at  $5.1\delta$  for CH proton at position-5 in the 2-pyrrolidinone ring and a triplet at  $6.2-7.1\delta$  for CH protons at position-4 of the 2-pyrrolidinone ring. All other signals are at their respective positions for the respective protons in the NMR spectra.

The acid group of 2-pyrrolidinone derivatives was reacted easily with o-phenylene diamine to give corresponding 2-benzimidazole derivatives of 2-pyrrolidinone. Here in this chapter we are trying this reaction for compounds 3a, 3b, 3c and 3d and 2-benzimidazole derivatives. The reaction scheme was shown in scheme-1.

The analytical and spectral data of the compounds are shown Table-1 for the 3(a-h) compounds.

## CONCLUSION

In conclusion, a set of Arylidene [1-N-phenyl-3-phenyl-pyrazole] (2a-h) and 5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-phenyl sulphonamide-pyrrolidinone-4-carboxylic acid (3a-h) was prepared in 2-Pyrrolidinones based on Schiff base derivatives. Compound (2a-h) and (3a-h) with the potencies similar to or better than those of ampicillin, tetracycline, gentamycin and chloramphenicol against *B.Subtillis*, *S.Aureus*, *E.Coli* and *Ps.Aeruginosa*, worth further investigation. (Fig. 1)

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