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ANTI BACTERIAL ACTIVITY OF 1,2-DIHYDROPYRIDINONE DERIVATIVES

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Abstract: In this paper we describe the anti bacterial activity of newly synthesized derivatives of 1,2-dihydropyridinones 1-20 evaluated for their In vitro screening antibacterial activities of in dimethylsulfoxide (DMSO) were performed by the broth dilution method using nutrient agar against Gram-negative bacteria Pseudomonas aeruginosa, Klebsiella aerogenes, Chromobacterium violaceum, and Gram-positive bacteria Bacillus subtilis, Bacillus sphaericus and Staphylococcus aureus at 100µg/ml concentration. The minimum inhibitory concentration (MIC) was done by the broth dilution method. The presence of substituents especially methyl, chloro, fluoro and dimethoxy groups when attached to phenyl ring increases the activity notably. Among the compounds 1,3,5,6,16 and 18 displayed potent activity towards both gram positive and gram negative bacteria.

Keywords-triazolo[1,8]naphthyridines, anti bacterial activity.

I. INTRODUCTION

Among various heterocyclic molecules, nitrogen heterocyclic molecules have proven as potential compounds[1] in crop protection chemicals, functional materials and medicinal chemistry.[2] Different methods were developed for synthesis of nitrogen heterocyclic molecules[3] *via* metal catalysed[4] and organocatalysed reactions.[5]

Nitrogen heterocyclic molecules, in particular synthesis[6] of 2-pyridinones[7] have received much attention because of their potential applications in various fields (Figure 1).[8] For example amrinone and milrinone were used as cardiotonics.[9] Perampanel is identified as an important molecule for the treatment of Parkinson's disease.[10] 2-Pyridinone derivatives were showing properties like antihypertensive,[11] antitumor,[12] antibiotic,[13] antiviral,[14] antibacterial,[15] thrombin inhibition,[16] tissue factor VIIa inhibition,[17] human chymase inhibition[18] and human leukocyte elastase inhibition.[19] Some of the 2-pyridinone derivatives have been used as dyes.[20] Significant number of natural products are having 2-pyridinone core unit in their chemical structure.[21] Most of these molecules are exhibiting interesting biological and pharmacological properties.[22] Substituted enaminones have been useful for the synthesis of several nitrogen-containing heterocycles.[23]

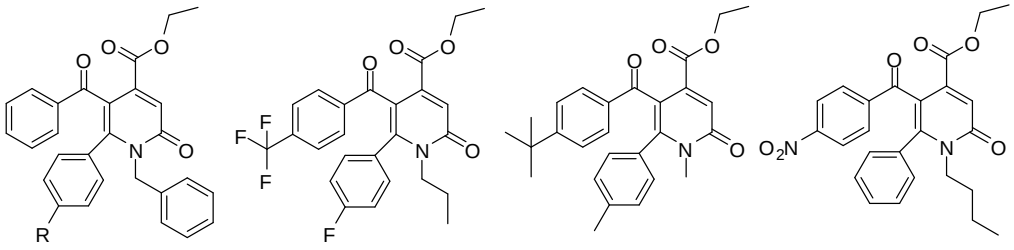


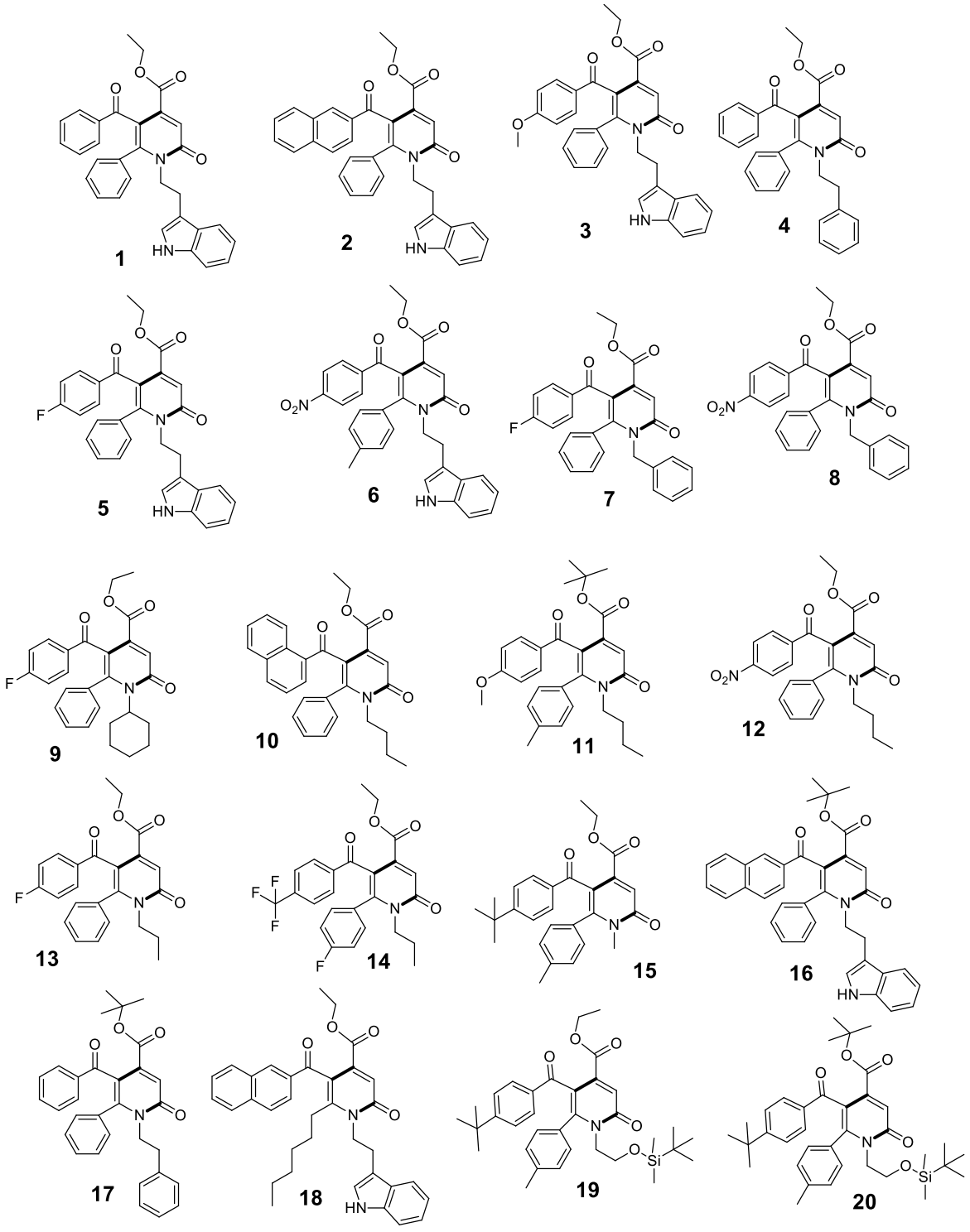
Figure 1

II. Experimental Section

Antibacterial activity

In vitro screening antibacterial activities of **1-20 (Scheme I)** in dimethylsulfoxide (DMSO) were performed by the broth dilution method using nutrient agar against Gram-negative bacteria *Pseudomonas aeruginosa*, *Klebsiella aerogenes*, *Chromobacterium violaceum*, and Gram-positive bacteria *Bacillus subtilis*, *Bacillus sphaericus* and *Staphylococcus aureus* at 100µg/ml concentration. The minimum inhibitory concentration (MIC) was done by the broth dilution method[21]. The ready-made nutrient broth medium (HiMedia, 25g) was suspended distilled water (100ml) and heated until it dissolved completely. The medium and test tubes were autoclaved at a pressure of 15lb/inc^2 for 25 min. A set of

sterilized test tubes with nutrient broth medium was capped with cotton plugs. The test compound is dissolved in dimethylsulfoxide(DMSO) at a concentration of 100µg/ml and added to the first test tube, which is serially diluted. A fixed 0.5ml volume of overnight culture is added to all the test tubes and then incubated at 35˚C for 24h. After 24h, these tubes were measured for turbidity. Ciprofloxacin and Trimethoprim were used as standards for comparison. Results are given in **Table 1**.



Scheme I

III. Results and discussions

The results of antibacterial screening reveal that compounds **1-20** displayed good activity. The compounds **1,3,5,6,16** and **18** exhibited significant activity. However, the degree of inhibition varied both with test compound as well as with the bacteria used in the present investigation. In conclusion, almost all the series of compounds **1-20** showed good activity by inhibiting growth of all the bacteria to a greater extent. These remarkable results may be due to the presence of the indole ring linked to substituted pyridine. Some of the compounds may be used as bacteriocides after a detailed study.

Table1. Antibacterial activity data of compounds **1-20**

	MIC[a,b]					
	Gram-positive			Gram-negative		
Compound	*B.substilis*	*B.sphaerius*	*S.aureus*	*P.aeruginosa*	*K.aerogenes*	*C.violaceum*
1	17	20	19	27	24	23
2	20	26	22	31	27	25
3	24	20	21	24	28	27
4	19	21	18	31	24	24
5	21	24	22	25	27	27
6	18	20	20	24	25	22
7	23	27	20	37	29	26
8	22	26	27	33	27	27
9	25	28	27	37	29	31
10	21	26	24	30	27	25
11	22	25	30	35	26	27
12	19	21	19	31	22	24
13	20	26	27	33	27	27
14	21	26	24	30	27	25
15	23	27	20	37	24	26
16	18	22	20	22	23	20
17	25	28	27	37	27	30
18	16	21	21	22	21	22
19	24	25	29	32	24	27
20	25	27	19	31	22	28
Ciproflaxacin	**20**	**25**	**20**	**30**	**25**	**25**
Trimethoprim	**21**	**23**	**21**	**28**	**22**	**25**

Notes: [a]Negative control(DMSO)-no activity
[b]Concentration 100µg/ml.

IV. CONCLUSION

Among the compounds **1,3,5,6,16** and **18** displayed potent activity towards both gram positive and gram negative bacteria. Rest of the compounds exhibited moderate to good activity against both the bacteria. These remarkable results may be due to the presence of the indole ring linked to substituted pyridine.

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