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NOTE

Synthesis and Antimicrobial Activity of Substituted N-(1-piperidinobenzyl)nicotinamide: A Structure-Reactivity Study

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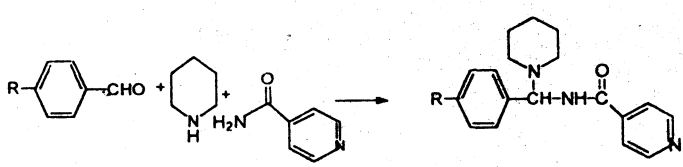
Substituted N-(1-piperidinobenzyl)nicotinamide compounds have been prepared and characterized by IR, UV and ^{1}H-NMR spectral analysis.The antimicrobial activities of the comipounds have been studied.

Key Words: Synthesis, Antimicrobial, Substituted N-(1-piperidinobenzyl)nicotinamide.

Acetamide and its related compounds have been found to possess donor properties and biological activities[1–5]. The literature reveals that there is a little work done on the antimicrobial study of these compounds. As a part of our interest in the antimicrobial study, we have synthesised a new Mannich base, N-(1-piperidinobenzyl)nicotinamide (PBN) (**Scheme**) and its complexes and studied the antimicrobial activity to find out the substituent effect on PBN.



R= H, CH_3, OCH_3, Cl, CN **PBN**

Scheme

All the compounds are stable at room temperature. The spectral studies and characterization of PBN compounds are as follows:

The IR bands of the PBN observed at 3300, 1640 and 1100 cm^{-1} have been assigned to ν(NH), amide ν(C=O) and ν(C—N—C) of piperidine group respectively. In the IR spectra of all the complexes, the ν(NH) band remained at the same position as in the free ligand, indicating that the secondary nitrogen is not coordinated.

The ^{1}H NMR spectra of PBN displayed the expected signals. PBN exhibits a multiplet signal at 6.5–7.5 δ(m, Ar-H and pyridine–H), 8.0–8.1 δ(d, CH), 8.2–8.6

δ(pyridine–H), 5.8-5.9 δ(d, sec. amide NH), 2.5–2.6 δ (piperidine N—CH_2), 2.4 δ (s, CH_3) and 1.5 δ(piperidine CH_2).

Antimicrobial Study: The PBN compounds were tested for antimicrobial activity. Mueller-Hinton agar was used for testing the susceptibility of micro organisms to antibacterial agents by well diffusion method[6], using DMF as solvent, at a concentration of 100 μg/10 μL against gram positive *(Staphylococcus aureus)* and gram negative *(Escherichia coli)* bacteria. The minimum inhibitory concentration **(MIC)** values were determined at the end of an incubation period of 24 h at 37°C .

The results are presented in Table–1 for PBN. The results show that all the compounds are antimicrobially active. The order of activity of PBN compounds for both *Staphylococcus aureus* and *Escherichia coli* is ·

$$CN > Cl > H > CH_3 > OCH_3$$

TABLE-1
ANTIBACTERIAL ACTIVITY OF N-(1-PIPERIDINOBENZYL)NICOTINAMIDE (PBN)

No.	Compound	Inhibition zone (mm) at concentration (100 μg/10 μL)	
		S. aureus	*E. coli*
1.	H—PBN	12	14
2.	4-CH_3—PBN	11	11
3.	4-OCH_3—PBN	9	10
4.	4-Cl—PBN	15	17
5.	4-CN—PBN	18	19

It is obvious that the inhibitory action gets enhanced with the introduction of electron-withdrawing cyano and chloro groups in the phenyl ring. The compounds, however, with electron-releasing substituents such as methyl and methoxy groups are lesser active compared to unsubstituted phenyl ring. Among the compounds 4-CN PBN was found to be most active for both *S. aureus* and *E. coli.* It appears that there is linear relationship between logarithm of zone of inhibition and Hammet substituent constant. The substituent constants (σ) for —H, —CH_3, —OCH_3, —Cl and —CN are 0, –0.17, –0.27, 0.23 and 0.66 respectively. According to Hammet, substituents that enhance activity relative to unsubstituted benzene ring will have positive values (σ > 0). The structural characterization of the PBN complexes is now in progress and will be reported soon. The present study proves that the title compounds may find application for therapeutic purposes in human diseases provided they are nontoxic to human body.

All the chemicals were of AR grade. IR spectra were recorded on a Perkin-Elmer 783 spectrophotometer. KBr disc method was used for recording the IR spectra. UV spectra were recorded on Shimadzu 160 UV-visible spectrophotometer. Muller-Hinton agar was used for testing the susceptibility of microorganisms to antibacterial agents using the well-diffusion technique.

General procedure for preparation of PBN

The PBN compounds have been prepared by the reaction of appropriate

aldehyde with the mixture of nicotinamide and piperidine in 1 : 1 : 1 mole ratio **(Scheme)**.

Synthesis of metal complexes using PBN

Ni(II), Cu(II), Co(II) and Zn(II) complexes have been synthesized using PBN as ligand. PBN was dissolved in chloroform and mixed with an ethanolic solution of the metal salt in 1 : 1 mole ratio.The reaction mixture was gently warmed on a hot water-bath for 1/2 h.

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