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NOTE

Effect of Substituents on N-(1-Piperidinobenzyl)acetamide and N-(1-Morpholinobenzyl)acetamide and Their Antimicrobial Activity

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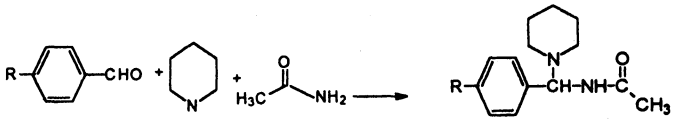
Substituted N-(1-piperidinobenzyl)acetamide (PBA) and N-(1-morpholinobenzyl)acetamide (MBA) compounds have been synthesized and characterized by IR, UV and ^{1}H-NMR spectral analysis. The antimicrobial activity of the compounds has been studied in detail.

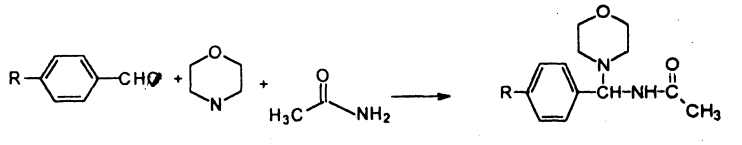
Key Words: N-(1-Piperidinobenzyl)acetamide; N-(1-Morpholinobenzyl)acetamide, Antimicrobial activity.

It is well known from the literature that compounds containing amide moiety as a functional group have been found to possess donor properties and biological activities[1-5]. In continuation of our interest in the antimicrobial study[6, 7], we have synthesized some substituted N-(1-piperidinobenzyl) acetamide (PBA) and N-(1-morpholinobenzyl) acetamide (MBA) compounds and studied the antimicrobial activity to find out the substituent effect on PBA and MBA.

SCHEME



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



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

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. ^{1}H-NMR spectra ($CDCl_3$) were recorded on a JEOL FX-90X instrument. Muller-Hinton agar was used for testing the susceptibility of microorganisms to antibacterial agents using the well-diffusion technique.

General procedure for preparation of PBA and MBA

The PBA and MBA compounds have been prepared[8, 9] by the reaction of appropriate benzaldehyde with the mixture of acetamide and piperidine or morpholine in 1 : 1 : 1 mole ratio.

All the compounds are stable at room temperature and show UV absorption around 270–290 nm. The IR and ^{1}H-NMR spectral features are as follows:

Infrared bands of PBA observed at 3340, 1642 and 1100 cm^{-1} have been assigned to ν(NH), amide ν(C=O) and ν(C—N—C) of piperidine group respectively. Similarly, the infrared bands of MBA observed at 3285, 1626 and 1120 cm^{-1} have been assigned to ν(NH), amide ν(C=O) and ν(C—N—C) of morpholine group respectively. These spectral assignments are consistent with the literature reports[8, 9].

The ^{1}H-NMR spectra of PBA/MBA displayed the expected signals. PBA exhibits a multiplet signal at 7.3–7.5 δ (Ar—H), 6.8 δ (d, 1H, CH), 5.6–5.8 δ (1H, NH), 2.4–2.7 δ (piperidine N-CH_2), 2.2 δ (s, CH_3) and 1.2–1.5 δ (piperidine CH_2). Similarly, MBA shows a multiplet signal at 7.2–7.5 δ (Ar—H), 6.6 δ (d, 1H, CH). 5.7–5.8 δ (1H, NH), 3.5–3.7 δ (morpholine OCH_2), 2.4–2.6 δ (morpholine N-CH_2) and 2.3 δ (s, CH_3).

The PBA and MBA compounds were tested for antimicrobial activity against *S. aureus, B. subtilis* (Gram positive) and *E. coli, P. auroginosa* (Gram negative) bacteria by well diffusion method[10]. The results are presented in Table-1. The

TABLE-1
ANTIBACTERIAL ACTIVITY OF N-(1-PIPERIDINOBENZYL)ACETAMIDE (PBA) AND N-(1-MORPHOLINOBENZYL)ACETAMIDE (MBA)

No.	Compound	Inhibition zone (mm) at concentration (100 μg/10 μL)			
		S. aureus	*E. coli*	*B. subtilis*	*P. auroginosa*
1.	H-PBA	10	11	11	13
2.	4-CH_3-PBA	8	9	9	12
3.	4-OCH_3-PBA	6	8	8	10
4.	4-Cl-PBA	12	14	13	16
5.	4-CN-PBA	16	17	15	18
6.	H-MBA	11	12	10	14
7.	4-CH_3-MBA	9	10	8	12
8.	4-OCH_3-MBA	7	8	7	9
9.	4-Cl-MBA	13	13	13	15
10.	4-CN-MBA	16	16	16	17

order of activity of PBA and MBA compounds towards *S. aureus, E. coli, B. subtilis* and *P. auroginosa* is: $CN > Cl > H > CH_3 > OCH_3$. It is found that the inhibitory action gets enhanced with the introduction of electron-withdrawing cyano and chlo[illegible]roups in the phenyl ring. The compounds, however, with electron-releasing [illegible]hyl and methoxy groups are lesser active compared to unsubstituted phenyl [illegible]. It appears that there is a linear relationship between logarithm of zone of inhibition and Hammet substituent constant. The substituent constant (σ) for H, CH_3, OCH_3, Cl and CN is 0, –0.17, –0.27, 0.23 and 0.66. According to Hammet, substituents that enhance activity relative to unsubstituted benzene ring will have positive σ values ($\sigma > 0$).

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