Asian Journal of Chemistry Vol. 20, No. 6 (2008), 4335-4338

Synthesis and Antibacterial Activity of Aminobenzylated Mannich Bases of Amides

K.C. CHALUVARAJU* and K. ISHWARBHAT†
Department of Pharmaceutical Chemistry, Bharathi College of Pharmacy
Bharathi Nagara, Mandya-571 422, India
E-mail: chaluvarajukc@gmail.com

In the present study some aminobenzylated mannich bases are reported and were obtained by reacting morpholine, benzaldehyde with various amides under mannich condition. The compounds were characterized and screeened for antibacterial activity.

Key Words: Synthesis, Antibacterial activity, Mannich bases.

INTRODUCTION

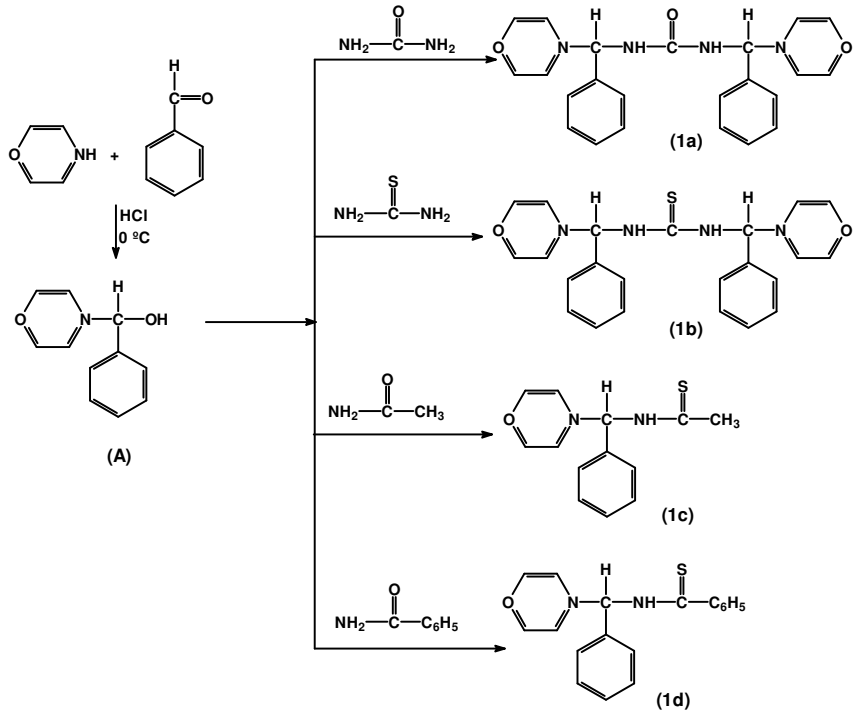
Mannich bases are important compounds owing to their wide range of biological and industrial applications. They have been found to possess pharmacological activities such as local anaesthetic[1], antibacterial[2], antifungal[3], antitubercular[4], analgesic and antiinflammatory[5], diuretic[6], *etc*. In view of the above biological importance of the mannich bases, we report here the synthesis of some aminobenzylated mannich bases of amides.

Benzaldehyde reacts with cyclic secondary amine like morpholine to form an intermediate N-cyclic phenylcarbinol [A], which when condensed with an amide containing an active hydrogen such as urea, thiourea, acetamide and benzamide gives aminobenzylated mannich bases **1a** to **1d** (**Scheme-I**). The spectral data obtained for compounds **1a** to **1d** were in good agreement with assigned structure of the synthesized aminobenzylated mannich bases.

EXPERIMENTAL

Melting points of the synthesized compounds were determined in open capillary tubes and are uncorrected. IR spectra were recorded (KBr) on Jasco FTIR-4100 spectrometer. ^{1}H NMR spectra was recorded on AMX-400 NMR spectrometer using TMS as internal standard. The purity of the compounds were checked using TLC on coated silica gel plates by single spots where the mobile phase was chloroform:methanol mixture (70:30), iodine as visualizing agent.

†Department of Pharmaceutical Chemistry, NGSM Institute of Pharmaceutical Sciences, Nanthoor, Mangalore-575 005, India.



Scheme-I: Synthesis of aminobenzylated mannich bases

1,3-*bis*-N-(Morpholinobenzyl)urea (1a): To an aqueous solution of urea (3.0 g, 0.05 mol), ice cold morpholine (9.0 mL, 0.1 mol) was added dropwise and stirred to get a clear solution. A drop of HCl was added and the reaction mixture was then cooled and ice cold ethanolic benzaldehyde (9.0 mL, 0.1 mol) was added dropwise and stirred for about 24 h in an ice bath. The resulting mixture was allowed to stand at room temperature with occasional shaking for about 3 weeks. The crystalline solid obtained was washed with sufficient water and then recrystallized from chloroform. Yield 63.20 %, m.p. 166-170 ºC. IR (KBr, ν_{max}, cm^{-1}): 3332 (NH), 1634 (C=O) and 1117 (C-N-C of morpholine). ^{1}H NMR: 10.1-10.0 (s, 2H of NH), 7.7-7.0 (m, 10H of Ar-H), 5.7-5.3 (s, 2H of methyline), 3.8-3.5 (t, 8H, -OCH_2 of morpholine), 3.1-2.8 (t, 8H, -NCH_2 of morpholine).

1,3-*bis*-N-(Morpholinobenzyl)thiourea (1b): The compound **1b** was prepared according to the procedure above **1a** using thiourea (1.5 g, 0.025 mol), morpholine (4.5 mL, 0.05 mol) and benzaldehyde (4.5 mL, 0.05 mol) and recrystallized from methanol. Yield 74.66 %, m.p. 118-129 ºC. IR (KBr,

ν_{max}, cm^{-1}): 3290 (NH), 1295 (C=S) and 1115 (C-N-C of morpholine). ^{1}H NMR: 7.7-7.0 (m, 10H of Ar-H), 6.0 (s, 2H of NH), 5.0-4.8 (s, 2H of methyline), 3.9-3.6 (t, 8H, -OCH_2 of morpholine), 3.5-3.4 (t, 8H, -NCH_2 of morpholine).

N-(Morpholinobenzyl)acetamide (1c): The compound **1c** was prepared according to the procedure above **1a** using acetamide (0.59 g, 0.01 mol), morpholine (0.9 mL, 0.01 mol) and benzaldehyde (0.9 mL, 0.01 mol) and recrystallized from chloroform. Yield 88.62 %, m.p. 86-94 ºC. IR (KBr, ν_{max}, cm^{-1}): 3402 (NH), 1661 (C=O) and 1130 (C-N-C of morpholine). ^{1}H NMR: 7.7-7.0 (m, 5H of Ar-H), 6.3-6.1 (s, 1H of NH), 5.7-5.4 (s, 1H of methyline), 3.8-3.6 (s, 3H, -$COCH_3$) 3.0 (t, 4H, -OCH_2 of morpholine), 2.7-2.4 (t, 4H, -NCH_2 of morpholine).

N-(Morpholinobenzyl)benzamide (1d): The compound **1d** was prepared according to the procedure above **1a** using benzamide (1.21 g, 0.01 mol), morpholine (0.9 mL, 0.01 mol) and benzaldehyde (0.9 mL, 0.01 mol) and recrystallized from ethanol. Yield 93.12 %, m.p. 82-86 ºC. IR (KBr, ν_{max}, cm^{-1}): 3291 (NH), 1636 (C=O) and 1111 (C-N-C of morpholine). ^{1}H NMR: 8.0-7.2 (m, 10H of Ar-H), 6.2-6.0 (s, 1H of NH), 5.0-5.2 (s, 1H of methyline), 3.8-3.6 (t, 4H, -OCH_2 of morpholine), 2.7-2.5 (t, 4H, -NCH_2 of morpholine).

Antibacterial activity: All the newly synthesized aminobenzylated mannich bases (**1a** to **1d**) were screened for their antibacterial activity against *E. coli, B. subtilis* and *S. aureus* using cup-plate agar diffusion method[7]. The compounds were tested at concentration of 20, 30 and 40 µg/mL. Ciprofloxacin was used as a standard drug. The antimicrobial activity was determined[8] using the following relationship and results are tabulated in Table-1.

$$\%\text{Activity} = \frac{Y - 0.6}{X - 0.6} \times 100$$

where, X = the diameter in mm of the inhibition zone of ciprofloxacin, Y = the diameter in mm of the inhibition zone by compounds.

TABLE-1
ANTIMICROIAL ACTIVITY (%) OF COMPOUNDS (**1a-d**)
AT 20 30 AND 40 µg/mL

Compound	*E. coli*	*S. aureus*	*B. subtilis*
1a	53	47	59
1b	56	51	58
1c	62	50	60
1d	59	54	61
Ciprofloxacin	100	100	100

RESULTS AND DISCUSSION

The newly synthesized aminobenzylated mannich bases of amides are found comparatively potent antibacterial agent to ciprofloxacin. They can prove to be drugs having minimum side effects and also having comparatively low cost.

ACKNOWLEDGEMENTS

The authors wish to thank the Principal Bharathi College of Pharmacy, Bharathi Nagara, Director, Principal NGSM Institute of Pharmaceutical Sciences, Mangalore for providing the facilities. The authors are thankful to the director IISc, Bangalore for the spectral data.

REFERENCES

1. S.C. Chaturvedi, G.K. Patnaik, B.N. Dhawan and V.K. Dixit, *Indian J. Pharm.*, **17**, 155 (1985).
2. B.S. Holla and M.K. Shivananda, *Indian J. Heterocycl. Chem.*, **13**, 85 (2003).
3. S.N. Pandeya, P. Yogeeshwari, D. Sriram and G. Nath, *Indian J. Pharm. Sci.*, **64**, 209 (2002).
4. S. Joshi, N. Khosla, D. Khare and R. Sharda, *Bioorg. Med. Chem. Lett.*, **15**, 221 (2005).
5. D.K. Nair, A. Mishra and M.S. Vijay Kanth, *Asian J. Chem.*, **17**, 943 (2005).
6. D.A. Koechel and G.O. Rankin, *J. Med. Chem.*, **21**, 764 (1978).
7. A.L. Barry, The Antimicrobial Susceptibility Test: Principle and Practices, IlluSlea and Febiger, Philadelphia (1997).
8. M.F. Sydney and J.M. Wiliam, Diagnostic Microbiology, C.V. Mosby Company, London (1982).

(*Received*: 23 April 2007; *Accepted*: 1 March 2008) AJC-6389