International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.2, No.4, pp 2097-2099, ct-Dec 2010

Synthesis and Spectral Studies of Mannich Bases Derived from 2- Substituted Benzimidazoles

Mohamed G Elerafi , *Mohamed N Ibrahim

Chemistry Department, Faculty of Science, Garyounis University, Benghazi, Libya

Corres.author: mnibrahim46@yahoo.com
melerafi@yahoo.com

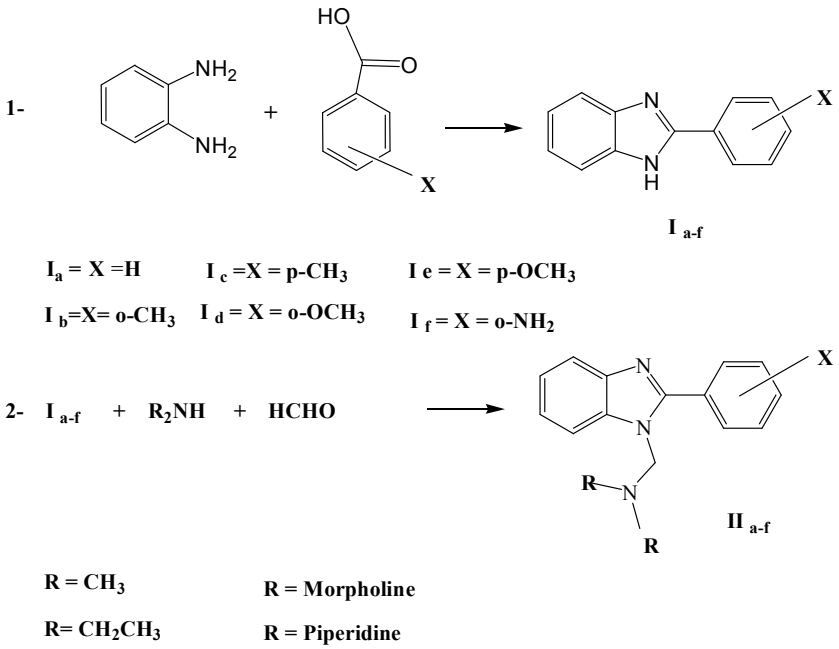
Abstract :
2-substituted benzimidazoles were prepared by reaction of benzoic acid and substituted benzoic acid with o-phenylenediamine, and then treated with secondary amines in the presence of formaldehyde in a Mannich reaction way to give the 1- (substituted methyl)-2- substituted phenyl benzimidazoles. The final products were characterized by physical and spectral analysis.
Key Words: Synthesis, Benzimidazole, Mannich Bases.

Introduction: It is well known that benzimidazole derivatives possess antimicrobial [1, 2], analgesic and anti-inflammatory activities [3, 4], as well as proved to have activities against HIV and cancer [5, 6]. Heterocyclic nucleus and substituted amino group at 1-position of the benzimidazole were reported to be associated with potent anti-inflammatory activity.

Therefore it was thought that preparing Mannich base derivatives from 2-substituted benzimidazoles would probably result in compounds of having high biological activities toward many diseases.

In this study, we continue our work [7] and report the synthesis of a number of Mannich bases derived from substituted benzimidazole, then these compounds were characterized by IR, ^{1}HNMR spectra and elemental analysis.

Experimental : Melting points were determined by Stuart melting point apparatus and are uncorrected. IR spectra were recorded in KBr on Perkin-Elmer 883 spectrometer.^{1}H NMR spectra were recorded by Bruker AC-300 with TMS as an internal standard, the chemical shift are reported as ppm. Elemental analyses were performed by Perkin-Elmer 240.The reaction is carried out according to the reaction scheme outlined below, the first step involve the synthesis of benzimidazole derivatives (I $_{a-f}$), then these compounds were treated with the secondary amines in presence of formaldehyde to obtain the Mannich bases (II $_{a-f}$).



Reaction scheme

General method for synthesis of (2-substituted phenyl) benzimidazole I $_{a-f}$ [8}

A solution of benzoic acid (or substituted benzoic acid) 0.01 mol, and 1, 2-phenylenediamine 0.01 mol, in 20 ml acetic acid was refluxed for 4 hrs, the precipitate obtained after cooling was recrystallized from ethanol. The physical data are given in table 1.

General method for synthesis of Mannich bases of (2-substituted phenyl)- benzimidazole II $_{a-f}$ [8]

N-Mannich bases of 2-substituted phenyl benzimidazole were prepared according to the following procedure. To a solution of 2-substituted phenyl benzimidazoles (0.005 mol) in 10ml ethanol, 0.005 mol of respective secondary amine and 0.005 mol of formaldehyde were added with stirring for 1 hr, then the reaction mixture was refluxed for another hr. On cooling, the product formed was filtered, dried and recrystallized from DMF. Physical data are given in table 1, and the spectral data for these compounds are shown in table 2.

Table 1: Physical data of compounds I $_{a-f}$ and compounds II $_{a-f}$

Compd. No.	Formula	M.P °C	Yield %	Analysis % Calc. (Found) C	H	N
I_a	$C_{13}H_{10}N_2$	291	64	--	--	--
I_b	$C_{14}H_{12}N_2$	233	45	--	--	--
I_c	$C_{14}H_{12}N_2$	201	55	--	--	--
I_d	$C_{14}H_{12}N_2O$	284	36	--	--	--
I_e	$C_{14}H_{12}N_2O$	269	52	--	--	--
I_f	$C_{13}H_{11}N_3$	247	60	--	--	--
II_a	$C_{16}H_{17}N_3$	230	62	76.49(77.01)	6.77(6.43)	16.73(16.34)
II_b	$C_{17}H_{19}N_3$	288	57	76.98(76.45)	7.16(6.89)	15.84(15.28)
II_c	$C_{19}H_{23}N_3$	274	67	77.81(77.37)	7.84(7.51)	14.33(14.82)
II_d	$C_{19}H_{23}N_3O$	296	43	73.78(73.34)	7.44(6.98)	13.59(13.11)
II_e	$C_{19}H_{21}N_3O_2$	283	54	70.58(70.21)	6.50(6.26)	13.00(13.56)
II_f	$C_{19}H_{22}N_4$	276	60	74.50(74.92)	7.18(6.78)	20.91(21.32)

Table 2: Spectral data for compounds II $_{a-f}$

Compds No.	IR , υ cm^{-1}	^{1}H NMR , δ ppm
II $_a$	2998(CH),1625(C=N), 1475 (C-N)	2.276H,s,2CH_3), 4.8(2H,s,CH_2), 7.1-7.7(9H,m, Ar-H)
II $_b$	2986(CH),1630(C=N), 1468(C-N)	2.2(6H,s,2CH_3), 2.3(3H,s,CH_3), 4.6(2H,s,CH_2), 7.2-7.8(8H,m,Ar-H)
II $_c$	3010(CH), 1624(C=N), 1456(C-N)	2.1(6H,s,2CH_3), 2.4(3H,s,CH_3), 4.7(2H,s,CH_2), 7.1-7.8(8H,m,Ar-H)
II $_d$	2987(CH), 1636(C=N), 1448(C-N), 1106(C-O)	1.1-2.4(10H,m,2C_2H_5), 3.7(3H,s,OCH_3), 4.8(2H,s,CH_2), 6.8-7.7(8H,m,Ar-H)
II $_e$	3002(CH),1620(C=N), 1452(C-N), 1180(C-O)	2.3-3.4(8H,m,4CH_2),3.8(3H,s,OCH_3), 4.8(2H,s,CH_2), 6.9-7.8(8H,m,Ar-H)
II $_f$	2969(CH), 1618(C=N), 1432(C-N)	1.0-2.2(10H,m,5CH_2), 4.8(2H,s,CH_2), 6.8-7.8(8H,m,Ar-H)

References

1- Nofal, Z.M., Fahmy, H.H. and Mohamed, H.S., Arch. Pharm. Res., 25, 250(2002)

2- Klimesova, V., Koci, J., Pour, M., Stachel, J., Waisser, K. and Kaustova, J., Eur. J. Med. Chem., 37,409(2002)

3- Sondhi, S.M., Rajvanshi, S., Johar, M. Bharti, N., Azam, A. and Singh, A.K., Eur. J. Med. Chem., 37, 835(2002)

4- Ito, K., Kagaya, H., Fukuda, T., Yoshino, K. and Nose, T., Arzeni-forsch., 32, 499(1982)

5- Rao, A., Carbone, A., Chimirri, A., De Clercq, E., Monforte, A.M., Monforte, P., Pannecouque, C. and Zappala, M., IL. Farmaco, 57, 747(2002)

6- Kumar, D., Jacob, M.R., Reynolds, M.B. and kerwin, S.M., Bioorg. Med. Chem., 10, 3997(2002)

7- Winter, C.A., Risley, E.A. and Nuss, G.W., Proc. Soc. Exp. Biol. Med. Chem., 111, 544(1962); Coburn, R.A., Clark, M.T., Evans, R.T. and Genus, R.J., J. Med. Chem., 30(1), 205(1987); Isasi, S.B., etal, Bioorg. Med. Chem., 16(16)7622(2008); Czaun, M. and Norlander, E., Russian J. Org. Chem.., 42, (9), 1420(2006), Al-Messmary,M, Elarfi, M.G. and Mohamed, R. (sent for publication)

8- Leonard, J.T., Rajesh, O.S., Jeyaseeli, L., Murugesh, K., Sivakumar, R. and Gunasekarn, V., Asian J.Chem., 19(1)116(2007)

*****