Asian Journal of Chemistry Vol. 19, No. 3 (2007), 2419-2422

Synthesis and Characterization of 2-Arylbenzimidazoles by Reaction of *o*-Nitroaniline and Aromatic Aldehyde Derivatives *via* Reductive Cyclization

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The synthesis of several 2-substituted benzimidazole derivatives was achieved *via* reduction of *o*-nitroaniline in presence of aromatic aldehydes with sodium dithionite. The derivatives were characterized by physical and spectral analysis.

Key Words: Reductive cyclization, Nitroaniline, Sodium dithionite, Benzimidazoles.

INTRODUCTION

Compounds containing benzimidazole moiety have been known to exhibit a wide range of biological properties[1,2] . They have shown to have interesting biological activities such as bacteriostats, bactericides, insecticides, fungicides and anticarcinogens[3]. Some benzimidazole derivatives with different pharmacological effects are in clinical use[4].

Although there are several routes for the synthesis of benzimidazoles, the traditional methods of 2-arylbenzimidazole preparation involve the condensation and cyclization of benzoic acid derivatives with *o*-diamino-aromatic compounds in the presence of mineral acid[5-7]. Metal catalyzed reaction of *o*-phenylene diamines with aromatic aldehydes is another mean for 2-arylbenzimidazole preparation[8-10].

In connection with these studies, a series of new 2-aryl substituted benzimidazoles was prepared by condensation of the appropriate aldehydes with *o*-nitroaniline in presence of sodium dithionite.

EXPERIMENTAL

All melting points were determined using melting point apparatus and were uncorrected. IR spectra were recorded on a Perkin-Elmer 1800 spectrophotometer as KBr disks. ^{1}H NMR were performed with a Brucker AC 300 NMR spectrometer.

General procedure for the preparation of 2-substituted benzimidazoles[11]:

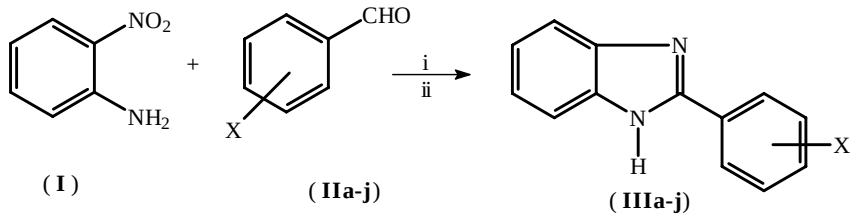
A solution of *o*-nitroaniline (1.0 mmol) and an aromatic aldehyde (1.0 mmol) in ethanol (10 mL) was heated with 1 M aqueous $Na_2S_2O_4$ (3 mmol, 5 mL). After heating the reaction mixture at 70ºC for 5 h, it was cooled to room temperature and treated dropwise with 5 N aqueous NH_4OH (2 mL).

A precipitate was immediately formed which was then filtered , washed with water and dried under reduced pressure to afford the desired products in a satisfactory purity.

RESULTS AND DISCUSSION

The reductive cyclization method represents a viable alternative to the widely used arylidene diamine based synthetic methods. The reaction presumably proceeds *via* arylnitro reduction followed by an intramolecular cyclization[12] to afford 2-arylbenzimidazole.

Reaction scheme



(I) **(IIa-j)** **(IIIa-j)**

i = $Na_2S_2O_4$; ii = 76ºC, 8 h

X = H; *o*-OH; *m*-OH; *p*-OH; *o*-OCH_3; *m*-OCH_3; *p*-OCH_3; *o*-CH_3; *p*-CH_3; *p*-$N(CH_3)_2$

The results obtained showed that when a solution of nitroaniline and aldehyde in EtOH was treated with a freshly prepared aqueous solution of sodium dithionite at 70ºC for 5 h, the desired benzimidazoles with the general structure (**III a-j**) were formed . The products were easily isolated in good yield and their structures were confirmed by physical and spectral analysis (Tables 1 and 2).

IR Spectra: The products showed the usual and expected bands for the different functional groups present on each compound and also showed the bands corresponds to the positions of substituents on the aromatic ring.

^{1}H NMR Spectra: The products showed the signals which corresponds to the different protons which present in each compounds. The chemical shifts for the compounds prepared are given in Table-2.

TABLE-1
PHYSICAL DATA OF 2-SUBSTITUTED BENZIMIDAZOLE DERIVATIVES

Compd. No.	X	m.f.	m.p. (ºC)	Yield (%)	% Found (Calcd.)		
					C	H	N
IIIa	H	$C_{13}H_{10}N_2$	294-6	72	80.56 (80.41)	4.95 (5.15)	14.02 (14.43)
IIIb	*o*-OH	$C_{13}H_{10}N_2O$	176-8	66	74.62 (74.28)	4.23 (4.76)	13.59 (13.33)
IIIc	*m*-OH	$C_{13}H_{10}N_2O$	181-4	63	73.81 (74.28)	4.48 (4.76)	13.78 (13.33)
IIId	*p*-OH	$C_{13}H_{10}N_2O$	166-8	68	74.82 (74.28)	4.52 (4.76)	12.98 (13.33)
IIIe	*o*-OCH_3	$C_{14}H_{12}N_2O$	177-9	65	75.43 (75.00)	4.86 (5.35)	12.31 (12.50)
IIIf	*m*-OCH_3	$C_{14}H_{12}N_2O$	170-2	70	75.28 (75.00)	4.97 (5.35)	12.68 (12.50)
IIIg	*p*-OCH_3	$C_{14}H_{12}N_2O$	182-4	67	75.68 (75.00)	5.65 (5.35)	12.96 (12.50)
IIIh	*o*-CH_3	$C_{14}H_{12}N_2$	211-3	72	80.34 (80.76)	5.42 (5.76)	13.00 (13.46)
IIIi	*p*-CH_3	$C_{14}H_{12}N_2$	242-4	71	80.62 (80.76)	5.93 (5.76)	13.67 (13.46)
IIIj	*p*-$N(CH_3)_2$	$C_{15}H_{15}N_3$	202-4	64	75.54 (75.94)	6.02 (6.32)	17.51 (17.72)

TABLE-2
^{1}H NMR OF 2-SUBSTITUTED BENZIMIDAZOLE DERIVATIVES

Compd. No.	^{1}H NMR (δ ppm) $CDCl_3$ or d_6-DMSO
IIIa	7.28 (d,2H), 7.49 (m,3H), 7.65 (d,2H), 8.06 (m,2H)
IIIb	7.40 (d,2H), 7.66 (m,4H), 7.80 (d,2H), 9.80 (s,1H)
IIIc	7.00 (s,1H), 7.60 (d,2H), 7.70 (m,3H), 7.90 (d,2H), 9.70 (s,1H)
IIId	7.50 (d,2H), 7.60 (d,2H), 7.80 (d,2H), 8.10 (d,2H), 9.80 (s,1H)
IIIe	3.90 (s,3H), 7.50 (d,2H), 7.66 (m,4H), 7.90 (d,2H)
IIIf	3.80 (s,3H), 6.95 (m,3H), 7.00 (s,1H), 7.65 (d,2H), 8.00 (m,2H)
IIIg	3.83 (s,3H), 6.55 (d,2H), 6.95 (d,2H), 7.05 (d,2H), 8.10 (d,2H)
IIIh	2.35 (s,3H), 7.30 (m,4H), 7.50 (d,2H), 8.00 (d,2H)
IIIi	2.37 (s,3H), 7.20 (m,2H), 7.35 (d,2H), 7.56 (b,2H), 8.05 (d,2H)
IIIj	3.00 (s,6H), 6.80 (d,2H), 7.25 (m,2H), 7.38 (m,2H), 7.80 (m,2H)

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(*Received*: 23 August 2006; *Accepted*: 9 November 2006) AJC-5263