

Reactions of some Unsaturated Carboxylic Acids with *o*-Phenylenediamine in Acid Medium-I

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Summary: Vinyl acetic acid and crotonic acid when separately condensed with orthophenylenediamine in the presence of 4N hydrochloric acid gave 2,3-propene-2 benzimidazole 1 and 7-methyl, 2,3-benzo, 1:4-diazocyclo-heptene-5-one 2 respectively. These results indicate that the migration of double bond to adjacent carbon in the formation of 1 occurs after the formation of benzimidazole ring.

Introduction

The programme [1-4] of synthesis of new 2-substituted benzimidazoles by the condensation of ortho-phenylenediamine with different carboxylic acids has been extended to the preparation of benzimidazoles having an unsaturated side chain. When isomeric unsaturated acids, vinyl acetic and crotonic acids were used, it was found that the former yielded 2,3-propene-2 benzimidazole 1 (Fig.1), whereas the latter gave the already reported [5], 7-methyl, 2:3 benzo, 1:4-diazocyclo-heptene-5-one 2 (Fig.2). These results indicate that the migration of double bond to the adjacent carbon in the formation of 1 takes place only after the ring closure to benzimidazole (route b Fig. 1). If this was not the case, then crotonic acid and vinyl acetic acid would have yielded the same product through the same intermediate [1] (3, Fig. 1 and 2).

Physical properties, R_f values and retention time in thin-layer and high pressure liquid chromatograph respectively are listed in Table 1.

Structure elucidation of 1 and 2 has been achieved by nuclear magnetic resonance and mass -spectral studies of these compounds. Nuclear magnetic

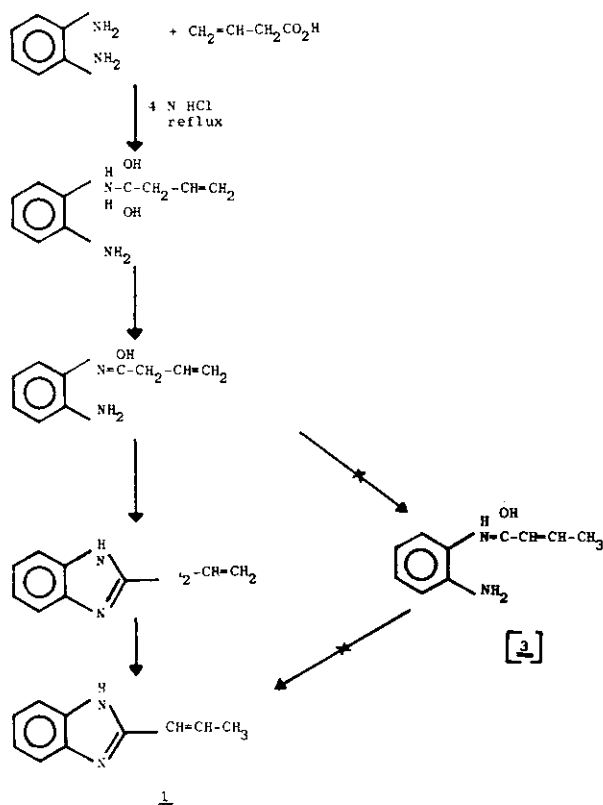


FIG. 1

resonance data of 1 shown in Tables II (^1H) and III (^{13}C), and those of 2 in Tables IV (^1H) and V (^{13}C) respectively. It has been found that aromatic

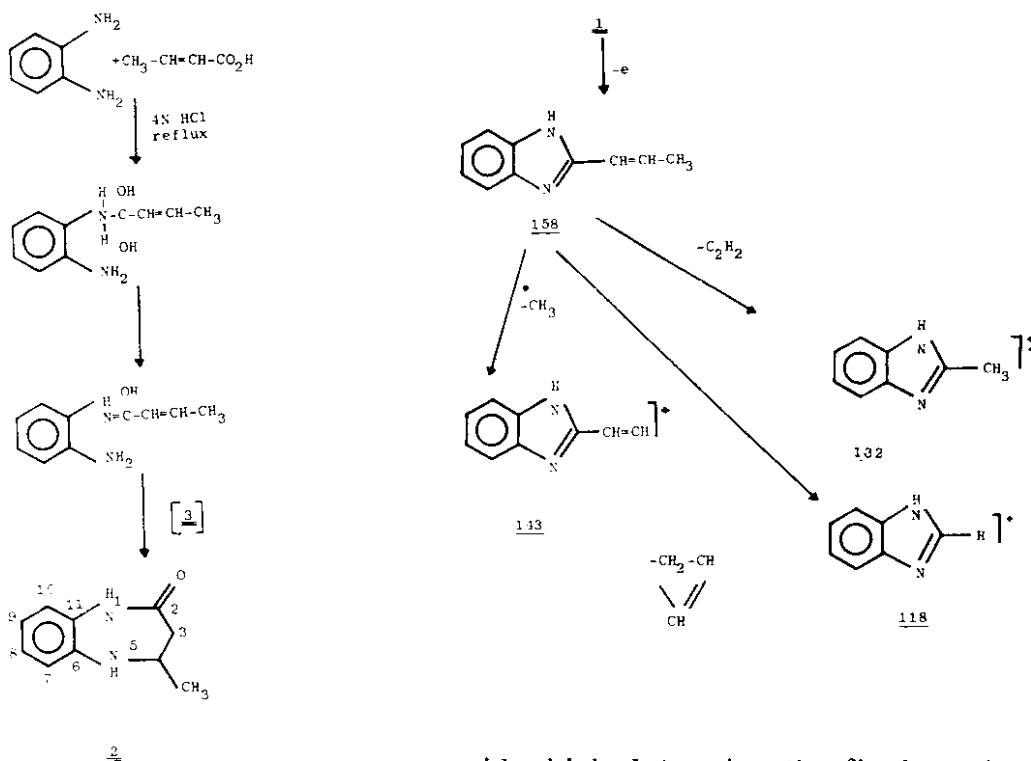


FIG. 2

protons in **1** appear at a lower field as compared to those of **2**, and the symmetric peak pattern in **1** is changed to complex pattern in **2**, indicating that all aromatic protons (e,f,f¹,e¹ Table IV) become nonequivalent due to the unsymmetric substitution of aromatic ring.

Major peaks in the mass-spectrum of **1** appear at *m/e* 158, 143, 132 and 118, the base peak being the molecular ion at 158. The base peak in the mass-spectrum of **2** is at *m/e* 119, and the major peaks are at *m/e* 176 (molecular ion), 161, 144, 133 and 108. The mass-spectral fragmentation patterns of **1** and **2** are shown in Fig. 3 and 4 respectively.

It is now being planned to make a systematic study of the structural features present in the unsaturated

acid which determine the final product (a diazepine or a benzimidazole) in this condensation reaction. Moreover, a series of diazepines having different groups attached to carbon 4 (Fig. 2), will be prepared, in order to study the stereochemistry of seven membered diazepine ring with the help of ¹H and ¹³C nuclear magnetic resonance spectroscopy.

Experimental

Preparation of 1: A mixture of 4.3 g (0.05 mole) of vinyl acetic acid and 5.4 g (0.05 mole) of *o*-phenylenediamine was refluxed in 25 ml of 4N hydrochloric acid with good stirring for eight hours. The reaction mixture on cooling and neutralization with sodium carbonate gave light brown solid, which on recrystallization from ethyl acetate afforded 3.9g colourless needles, melting at 158-60°.

Compound **2** was prepared using 0.05 mole (4.3 g) of crotonic acid with the same procedure as used for the

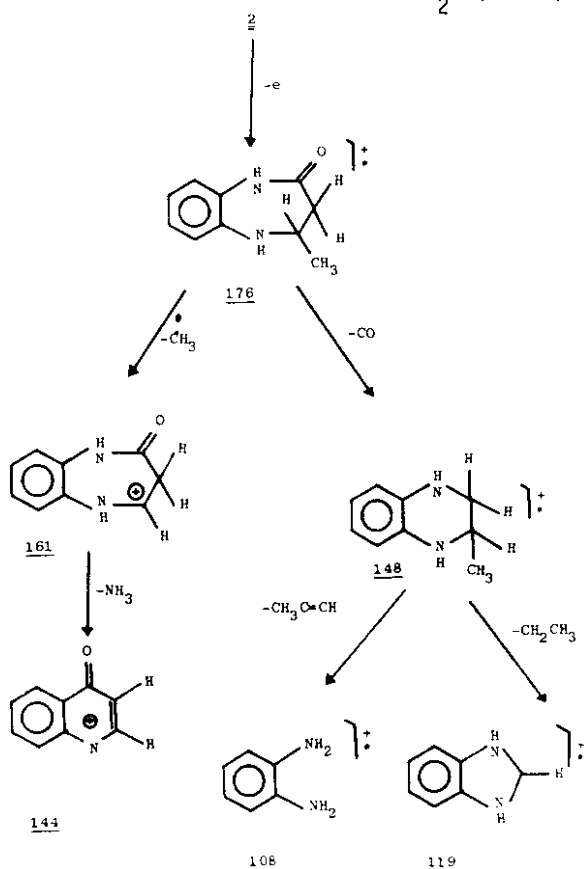
Table-1: Physical Constants and Chromatographic Data for 1 and 2

Compound	Molecular Formula [Molecular Weight]	m.p. °C* [Solvent for crystallization]	Yield %	R _f values x 10 ² (TLC)					Retention Time (HPLC)	
				1**	2**	3**	4**	5**	1***	2***
<u>1</u>	C ₁₀ H ₁₀ H ₂ [158]	158-60° [Ethylacetate]	50	12	91	71	75	33	12.30	22
<u>2</u>	C ₁₀ H ₁₄ N ₂ [176]	180-182° [Chloroform]	70	10	85	56	67	63	5.06	9

* Melting points have been recorded in open capillaries and are uncorrected.

** Solvent systems: 1 = Acetone: Pet. ether. (1:4); 2 = Acetone : Pet. ether (4 : 1),
3 = Ethylacetate; 4 = Ethylacetate:Methanol (19 : 1);
5 = Methanol : H₂O(1 : 10);

*** Solvent systems: 1 = Chloroform
2 = MeOH : H₂O (1 : 1)

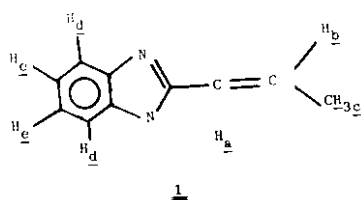


preparation of 1. It was recrystallized from chloroform to yield 6.1 g of colourless shining needles melting at 184-85°.

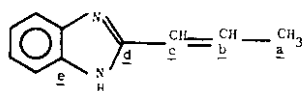
Chromatography

Thin-layer chromatography was carried out on 0.25 mm. thick 20 x 20 cm. chromoplates of silica gel HF 254 (Fluka) in a series of solvents as listed in Table 1.

High performance liquid chromatography was done on 25 x 46 mm 1D ultrasphere ODS (C₁₈) reversed phase prepacked column using isocratic liquid chromatograph (Altex model 330 A). Column effluent was monitored with an analytical UV detector (Altex model 110 A) at 254 nm. for the detection of benzimidazoles. Solvents used (Fluka HPLC grade) for chromatography are shown in Table 1. Attenuation was 0.16 AUFS during all measu-

Table-2: Types of protons and proton magnetic resonance spectral data of 11

Proton	Chemical Shifts (ppm)	Peak Pattern	Coupling Constants (Hz)
1 <u>H_a</u>	6.54	doublet of quartet	$J_{c,a} = 1.6$ $J_{a,b} = 15.9$
1 <u>H_b</u>	6.81	doublet of quartet	$J_{a,b} = 15.9$ $J_{bc} = 6.7$
3 <u>H_c</u>	1.92	double doublet	$J_{c,a} = 1.6$ $J_{c,b} = 6.7$
2 <u>H_d</u>	7.5	double doublet	$J_{ortho} = 6$
2 <u>H_e</u>	7.22	double doublet	$J_{meta} = 3.1$

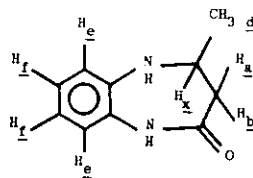
Table-3: Types of Carbon atoms and ¹³C nuclear magnetic resonance spectral data of 1.

Carbon Atoms	Chemical Shifts (ppm)
1 <u>a</u>	18.43
1 <u>b</u>	120.56
1 <u>c</u>	134.06
1 <u>d</u>	150.84
2 <u>e</u>	138.56
2 <u>f</u>	114.75
2 <u>g</u>	122.61

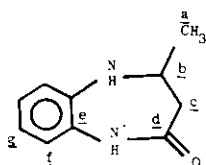
rements. Chart speed was 1 mm min⁻¹ on XY recorder (Kipp and Zonnen BD 40). Pressure varied from 800-900 psi when chloroform was used as solvent, and 1,000 - 1,200 psi with MeOH: H₂O (1:1) Flow rate was 0.5 ml. min⁻¹ during all measurements. All measurements were made at ambient temperature. Retention time recorded for 1 and 2 are listed in Table 1.

Acknowledgement

The authors are grateful to Dr. Alan Boyd, Department of Chemistry, Edinburgh University, Scotland for the measurement of proton and ¹³C nuclear magnetic resonance spectra of 1 and 2. Proton magnetic resonance spectrum of 1 was recorded at 300 MHz and that of 2 at 200 MHz. ¹³C nuclear magnetic resonance spectra were

Table-4: Types of protons and proton magnetic resonance data of 2.2

Protons	Chemical Shifts (ppm)	Peaks Pattern	Coupling Constants (Hz)
1 H _a	2.42	quartet	$J_{a,b} = 13.6$ $J_{a,x} = 7.79$
1 H _b	2.63	quartet	$J_{a,b} = 13.6$ $J_{b,x} = 4.17$
1 H _x	4.01	multiplet (14 lines)	$J_{d,x} = 6.32$ $J_{a,x} = 7.79$ $J_{b,x} = 4.17$
3 H _d	1.32	doublet	$J_{d,x} = 6.32$
Aromatic Protons (H _e , H _e ¹ , H _f , H _f ¹)	6.74-7.0	Complex multiplet	

Table-5: Types of carbon atoms and ¹³C nuclear magnetic resonance spectral data of 2.

Carbon Atoms	Chemical Shifts (ppm)
1a	23.54
1b	41.47
1c	53.70
1d	172.43
2e	138.27
2f	121.18
2g	125.54

We also wish to express our grateful thanks to H.E.J. Research Institute of Chemistry, Karachi University for the measurement of mass-spectra of 1 and 2.

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recorded at 75 MHz.