

**Preparation, Physical Properties,  
Mass and Nuclear Magnetic Resonance Spectra  
of Some 2-Alkyl Benzimidazoles**

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**Summary:** Preparation, physical properties, mass and proton magnetic resonance spectral data of 2-alkyl ( $\text{CH}_3/\text{C}_2\text{H}_5$ )-5-nitro-benzimidazoles (1) and (2) and their p-toluene sulfonyl derivatives (3) and (4) have been described. Two benzimidazoles (5) and (6) having same alkyl substituents but no nitro group in 5-position and their p-toluene sulfonyl derivatives (7) and (8) were prepared and studied for the sake of comparison of their n.m.r spectral properties with (3) and (4). In addition (1) and (2) were reduced to 5-amino-benzimidazoles (9) and (10).

Aim of the present work is to study the proton magnetic resonance spectral peak pattern of benzimidazoles substituted unsymmetrically [1] in the aromatic region as compared to that of those benzimidazoles which do not have such substitution. For this purpose 2-methyl-5-nitro-(1) (prepared by another route previously [2]), 2-ethyl-5-nitro- (2) benzimidazoles, p-toluene sulfonyl derivatives of (1) and (2), i.e. (3) (a, b) and (4) (a, b), 2-methyl- (5), 2-ethyl- (6) benzimidazoles, p-toluene sulfonyl derivatives of (5) and (6), i.e. (7) and (8) were prepared according to the methods described in the experimental. Table I shows physicals properties and mass-spectral fragmentation pattern of these compounds. Nitro groups in (1) and (2) could be successfully reduced to amino-groups by zinc dust and hydrochloric acid yielding 2-methyl, 5-amino-(9) and 2-ethyl-5-amino (10) benzimidazoles respectively (Table I).

Compounds (9) and (10) were nicely crystalline but due to their very low solubility in all possible solvents, their proton magnetic resonance spectra

could not be recorded. They were characterized by the formation of azo-dyes and their structures were confirmed [5-10] by their mass spectral fragmentation patterns (Scheme IV). Mass spectral fragmentation pattern of compounds (1) and (2), (3) and (4), (7) and (8) have been shown in schemes I [8], II [8] and III respectively.

Proton magnetic resonance spectral data of (1), (2), (3) (a and b); (4) (a and b); (5), (6) and (7), (8) are shown in Tables II, III, IV, V and VI respectively. Table VII shows chemical shifts of similar protons in different compounds.

As is evident from Tables V and II, benzene proton of (5) and (6) show the usual  $A_2B_2$  pattern [7-9], whereas those in (1) and (2) show a more complex ABC pattern due to the presence of nitro group in position 5 of the benzimidazole system.

Aliphatic and aromatic protons show splitting of each peak in (3) and (4),

Table-I

Benzimidazole	Molecular Formula	Molecular Weight	M.P°C Solvent for crystal- lization	Acetone:Pet.ether 1: 1 R <sub>f</sub> Silica gel	Yield	Mass-spectral Fragmentation.
(1) 2-Methyl,5-nitro-	C <sub>8</sub> H <sub>7</sub> N <sub>3</sub> O <sub>2</sub>	177	220/H <sub>2</sub> O	0.4	44	177 (base peak), 161,147 131,130,129,119, 118, 117, 104,103,91,90,65,64.
(2) 2-Ethyl,5-nitro-	C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O <sub>2</sub>	191	165/H <sub>2</sub> O	0.7	48	191 (base peak) 190, 177, 161, 147,145,144,143,131,130, 129,119,118, 117, 104,103, 91,90,65,64.
(3) 2-Methyl, 5-nitro 1-p-toluene sulfonyl	C <sub>15</sub> H <sub>13</sub> N <sub>3</sub> O <sub>4</sub> S	331	151/EtOH	0.83	64	331,267,177,157,155,147 131,130,129,119,118,117, 105,104,91(base peak),90, 65,64,63.
(4) 2-Ethyl, 5-nitro, 1-p-toluene sulfonyl	C <sub>16</sub> H <sub>15</sub> N <sub>3</sub> O <sub>4</sub> S	345	145/EtOH	0.87	65	345,281,190,157,155,147, 145,144,143,131,130,129, 119,118,117,105,104,91, (base peak), 90,65,64.
(5) 2-Methyl-	C <sub>8</sub> H <sub>8</sub> N <sub>2</sub>	132	175-6/H <sub>2</sub> O	0.21	54	* Ref.No.3
(6) 2-Ethyl-	C <sub>9</sub> H <sub>10</sub> N <sub>2</sub>	146	175/H <sub>2</sub> O	0.33	60	* Ref.No.3
(7) 2-Methyl,1-p-toluene sulfonyl	C <sub>15</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub> S	286	115/MeOH/H <sub>2</sub> O	0.61	39	286,221,180,157,155,131, 123,105,103,91(base peak) 65,63.
(8) 2-Ethyl-1-p-toluene sulfonyl	C <sub>16</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub> S	300	136/MeOH/H <sub>2</sub> O	0.65	60	300,235,180,157,147,143 131,123,105,103,91 (base- peak) 65,63.
(9) 2-Methyl,5-amino-	C <sub>8</sub> H <sub>9</sub> N <sub>3</sub>	147	230/H <sub>2</sub> O	0.7	23	147(base peak) 146,133, 119,107,105,92,91,80, 79,65,64.
(10)2-Ethyl-5-amino-	C <sub>9</sub> H <sub>11</sub> N <sub>3</sub>	161	230/H <sub>2</sub> O	0.75	34	161(base peak), 147,146, 133,119,107,105,97,91, 80,79,65,64.

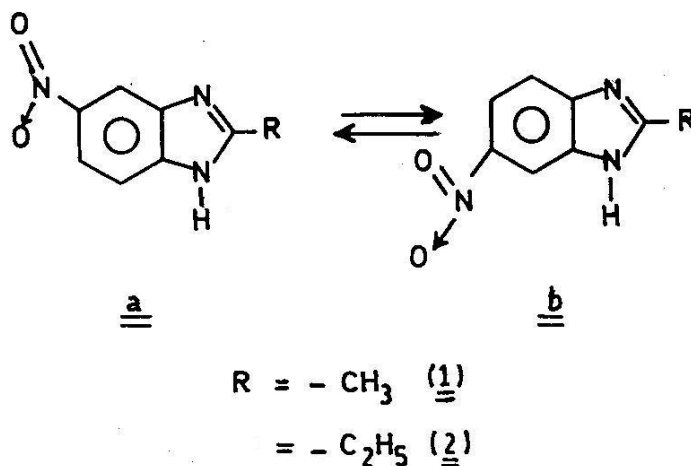


Fig. 1

whereas no such splitting is observed in (7) and (8).

Peak assignments to isomer of (3) and (4) could be made by considering the position of nitro group relative to p-toluene sulfonyl group in these isomers. In "cis" isomers (3b) and (4b) aliphatic protons (3d, 3h and 2d) are shifted to slightly lower field as compared to those in the "trans" isomers (3a) and (4a), reason being enhanced electron withdrawing effect exerted by the nitro and p-toluene sulfonyl groups which are present on the same side of the ring system (3b) and (4b).

Aromatic protons  $\text{H}_a$  and  $\text{H}_c$  also exhibit similar influence. In (3b) and (4b) (cis-isomers)  $\text{H}_a$  is shifted to lower field as compared to the same proton in (3a) and (4a) because of the close vicinity to the two electron withdrawing groups. By the same token,  $\text{H}_c$  is found at lower field in "trans" isomers as compared to that in "cis" isomers.

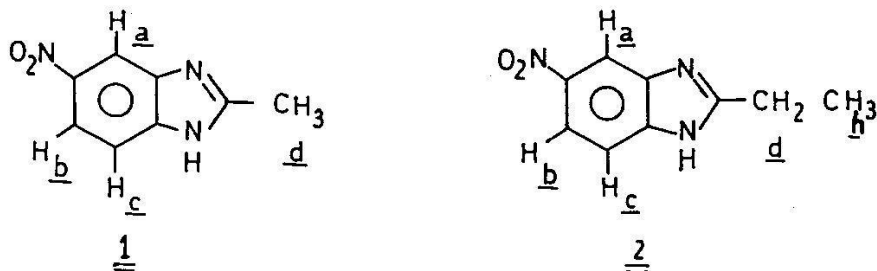
Although the peak pattern in the aromatic region is less extended in (7) and (8) and exhibits lesser number

of peaks, it is extremely complicated and it is not possible to assign chemical shifts and coupling constants to different atoms or groups.

It has also been found on the basis of integration that the proportion of "trans" isomers (3a) and (4a) is lightly more than that of "cis" isomers (3b) and (4b). On the basis of field effect it would be expected that the "cis" tautomers (b) of (1) and (2) shown in Fig. 1 should exhibit stronger acidic properties and should also react at a faster rate in the replacement of imine proton of (1) and (2) with p-toluene-sulfonyl group. However the presence of nitro-group on the same side as imino group in tautomer b hinders the attack and tautomer a therefore reacts at a faster rate, leading to the formation of slightly higher amount of (3a) and (4a).

The chemical shifts of aliphatic protons in (3-8) are in conformity with the expected electron withdrawing effects of nitro - and p-toluene sulfonyl groups. Aliphatic protons (3h), (3d) and (2d) (Table VII) appear at the lowest field where two electron withdrawing groups (in (3)

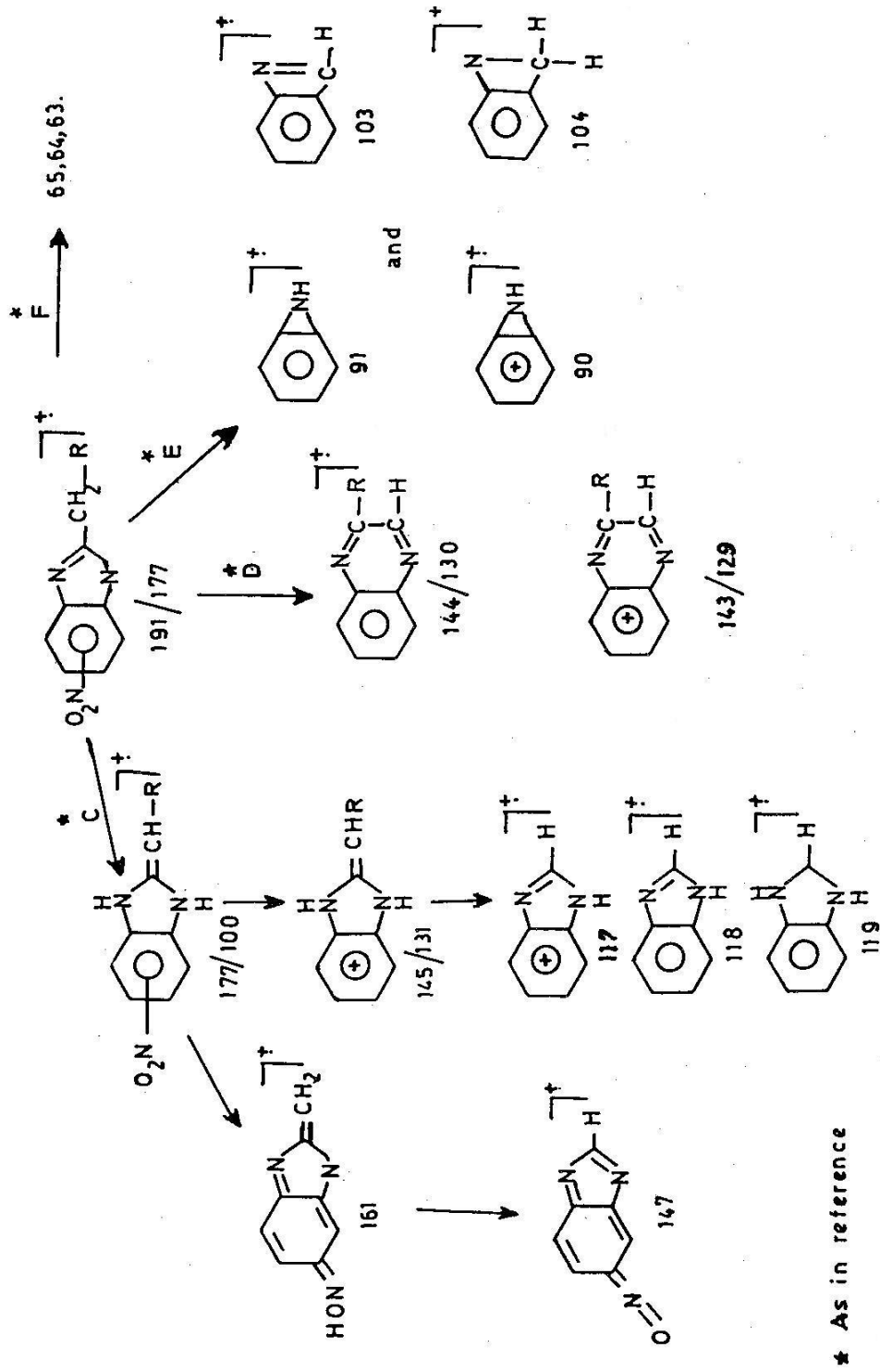
Table-II Types of Protons and Proton Magnetic Resonance Data of (1) and (2)



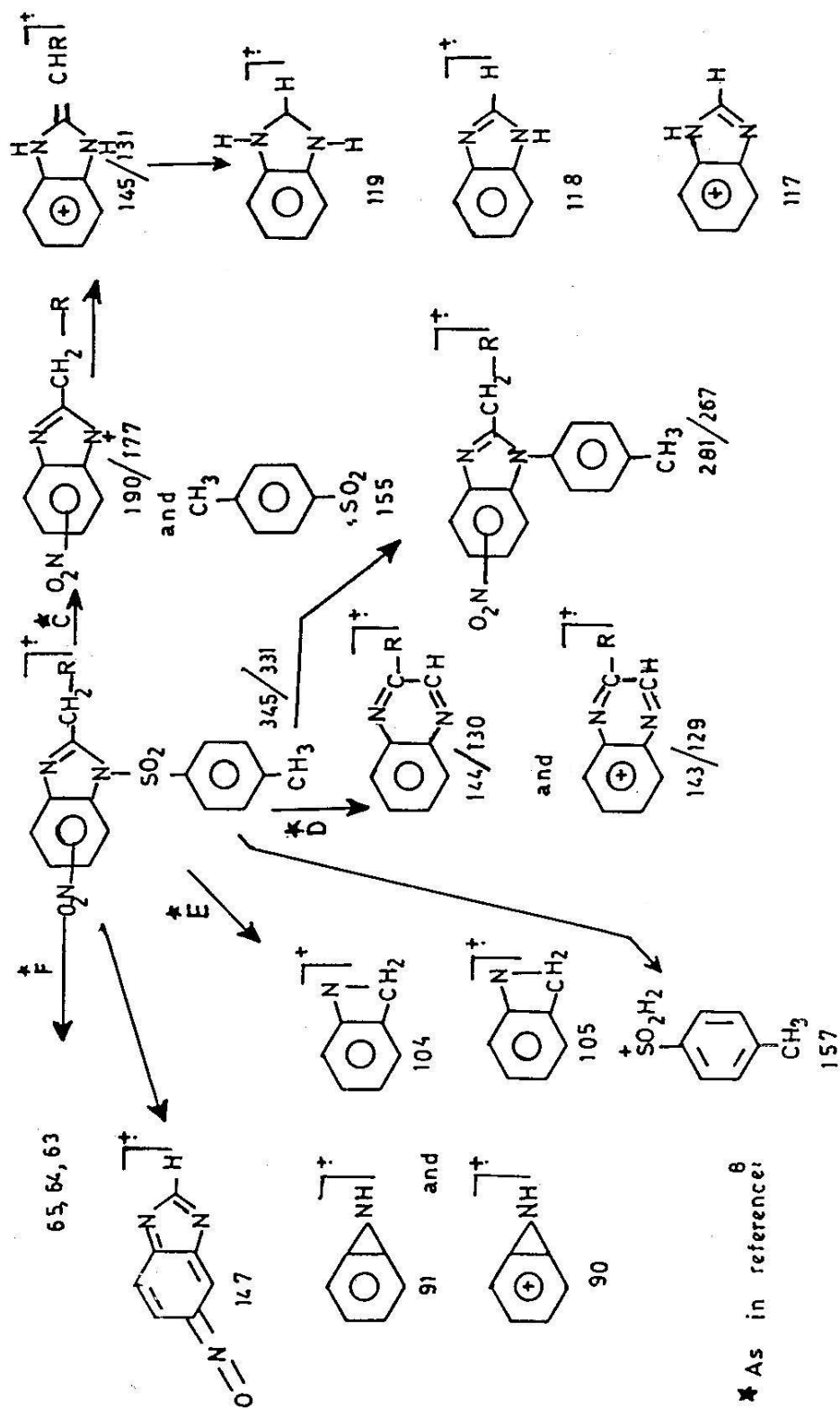
Compound	Protons	Chemical Shifts and Peak Pattern (ppm)	Coupling Constant (Hz)
(1)	3 Hd	2.63 s	-
	1Ha	8.4 d	$J_{a,b} = 1.9$
	1Hb	8.1 dd	$J_{a,b} = 1.9$ $J_{b,c} = 8.7$
	1Hc	7.6 dd	$J_{c,b} = 8.7$ $J_{a,c} = \text{v. small}$
	3 Hh	1.42 t	$J_{d,h} = 7.5$
(2)	2 Hd	3.0 q	$J_{d,h} = 7.5$
	1 Ha	8.4 d	$J_{a,b} = 2$
	1 Hb	8.1 dd	$J_{a,b} = 2$ $J_{b,c} = 8.8$
	1 Hc	7.62 dd	$J_{c,b} = 8.8$ $J_{c,a} = \text{v. small}$ (Ca 0.5)

and (4)) nitro and p-toluene sulfonyl are present. Compounds (7) and (8) show chemical shifts of these protons at a lower field as compared to the corresponding protons in (5) and (6) where none of these electron withdrawing groups is present.

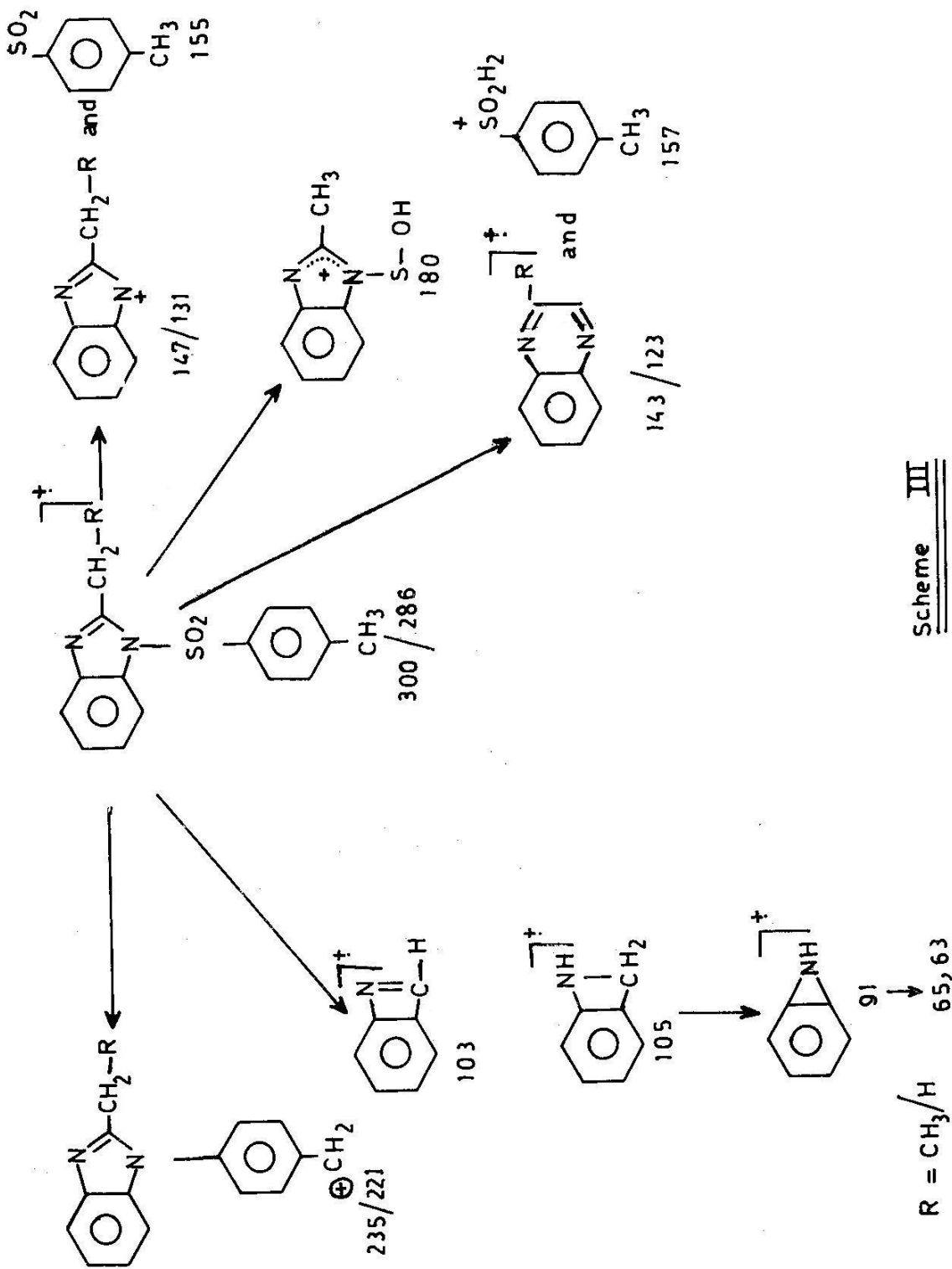
Coupling constants  $J_{h,d}$  increases in the order (4b), (8), (2) to (6) showing values of 7.3, 7.33, 7.5 and 7.57 Hz respectively as expected [11] on the basis of the electron withdrawing effects of nitro and p-toluene sulfonyl groups.



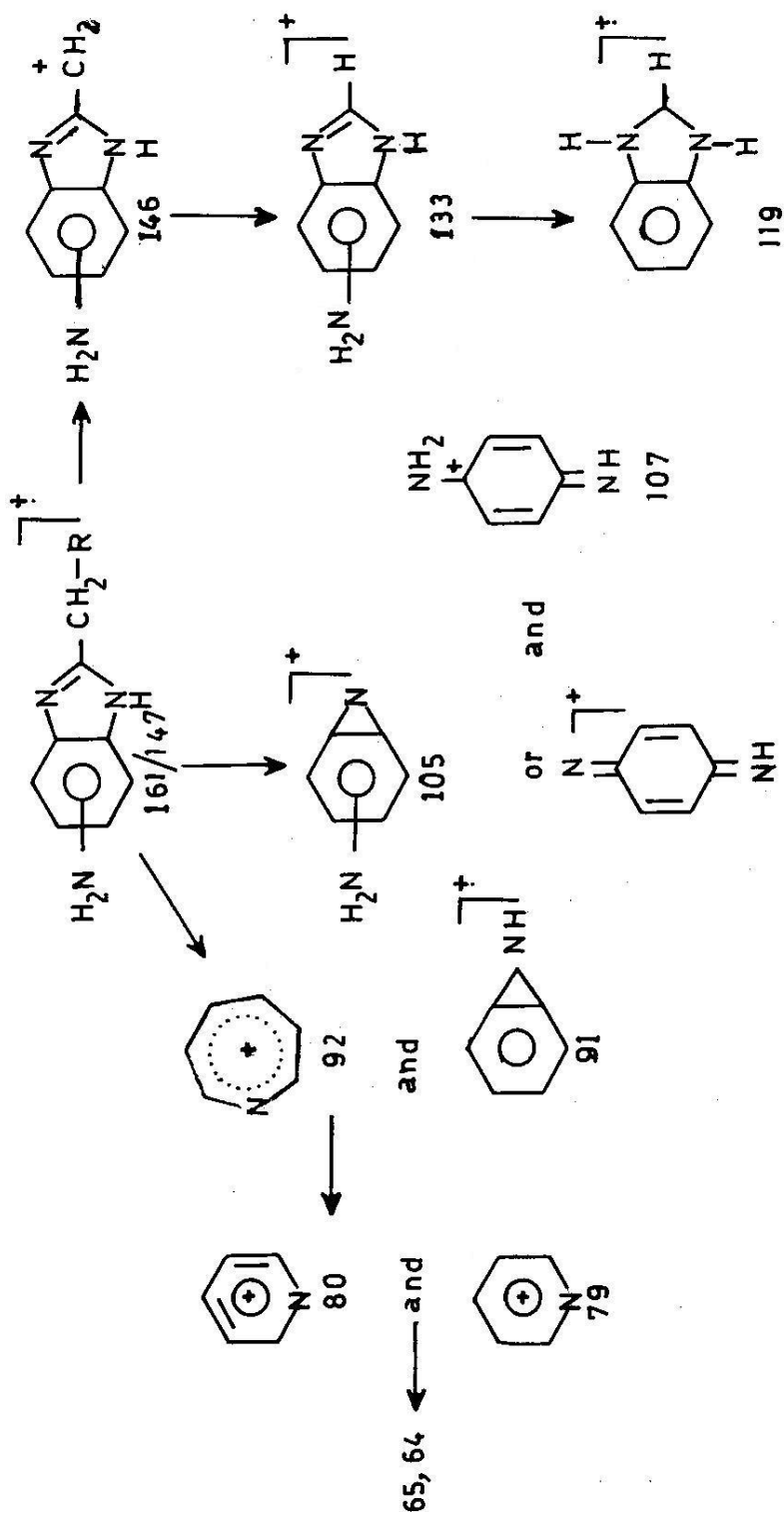
Scheme I



Scheme II



Scheme III



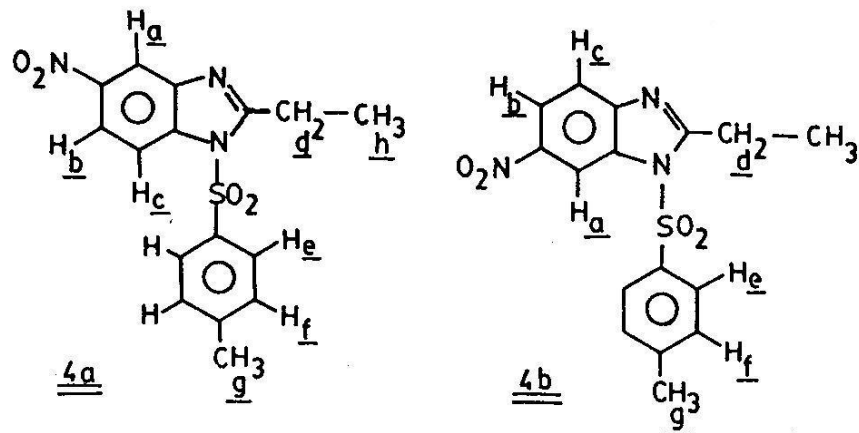
R = CH<sub>3</sub>/H

Scheme IV





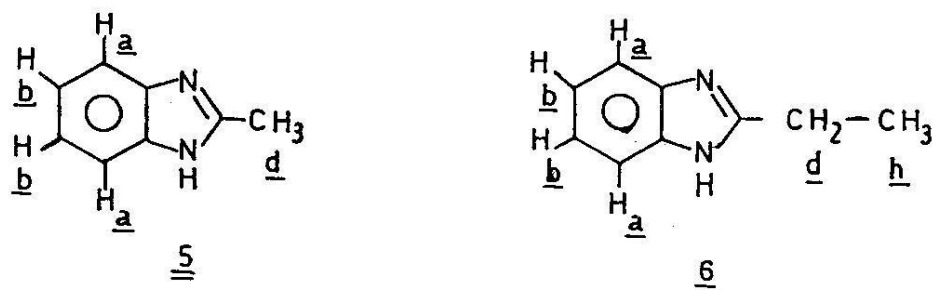
Table-IV Types of Protons and Proton Magnetic Resonance Spectral Data of (4) (a and b)



Compound	Protons	Chemical Shifts and Peak Pattern (ppm)	Coupling Constants (Hz)
(4a)	3 Hh	1.46 (t)	$J_{h,d} = 7.3$
	2 Hd	3.20 (q)	$J_{h,d} = 7.3$
	3 Hg	2.42 (s)	-
	1 Ha	8.54 (d)	$J_{a,b} = 1.47$
	1 Hb	Cannot be read	-
	1 Hc	8.15 d	$J_{c,d} = 9.04$
	2 He	7.35 (broad d) (for 4b also)	-
	2 Hf	* 7.85 d	$J_{e,f} = 8.54$
(4b)	3 Hh	1.46 t	$J_{h,d} = 7.3$
	2 Hd	3.26 q	$J_{h,d} = 7.3$
	3 Hg	2.42s	-
	1 Ha	8.96 d	$J_{a,b} = 7.81$
	1 Hb	Cannot be read	-
	1 Hc	7.74 d	$J_{c,d} = 2.2$
	2 He	7.35 (broad d) (for 4a also)	-
	2 Hf	* 7.82 d	$J_{e,f} = 8.3$

\*Can be interchanged.

Table-V: Types of Protons and Proton Magnetic Resonance Data of (5) and (6).



Compound	Protons	Chemical Shifts and Peaks Pattern (ppm)	Coupling Constant (Hz)
(5)	3 Hd	2.64 (s)	-
	2 Ha	7.55 dd	$J_{ortho} = 5.9$
	2 Hb	7.21 dd $A_2B_2$	$J_{meta} = 3.2$
(6)	3 Hh	1.45 (t)	$J_{d,h} = 7.57$
	2 Hd	3.02 q	$J_{d,h} = 7.57$
	2 Ha	7.56(dd) $A_2B_2$	$J_{ortho} = 5.9$
	2 Hb	7.21(dd)	$J_{meta} = 3.4$

Alkyl protons (3d), (2d) and (3h) in (1) and (2) however exhibit chemical shifts at a higher field than the corresponding protons in (5) and (6) where no nitro group is present for which a plausible explanation could not be found.

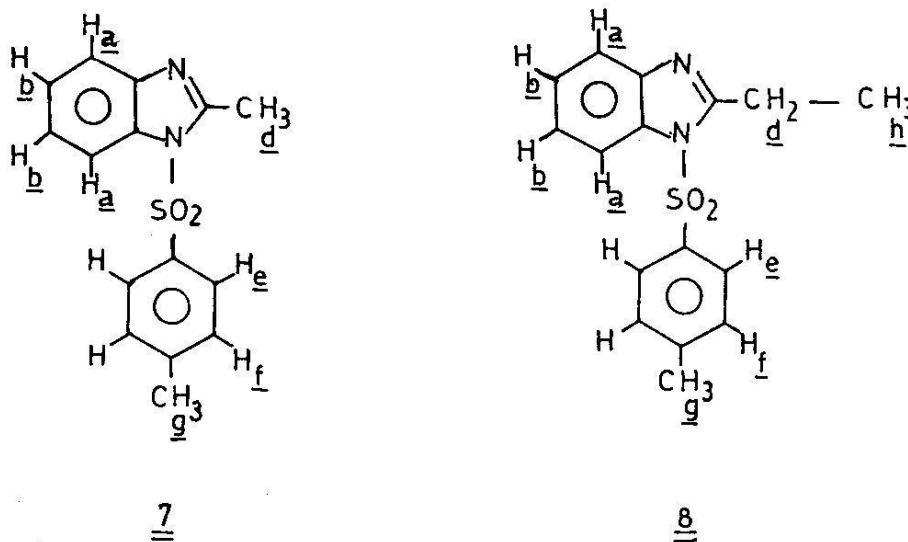
Chemical shifts of methyl protons  $3H_g$  present in p-toluene sulfonyl region of (3) and (4) (2.42 ppm) as compared to those of the same protons in (7) and (8) (2.37 ppm) show the electron withdrawing influence of nitro-group in this far removed position also perhaps due to the continuous linkage through conjugated system.

### Experimental

Compounds (1) and (2) were prepared by condensing acetic acid and propionic acid separately with 4-nitro-ortho-phenylenediamine in a Philip's reaction. Similarly (5) and (6) could be prepared by condensing acetic acid and propionic acid separately with ortho-phenylenediamine.

Percentage yields, solvents used for crystallization, melting points and  $R_f$  values of these compounds are listed in Table 1. Usual procedures for the preparation of p-toluene sulfonyl derivatives was adopted for conversion of

Table-VI: Types of Protons and Proton Magnetic Resonance Spectral Data (7) and (8).



Compound	Protons	Chemical Shifts and Peak Pattern (ppm)	Coupling Constants (Hz)
(7)	3 Hd	2.81 (s) (Slightly split)	-
	3 Hg	2.37 (s)	-
	Aromatic Protons	7.24-8.03 Complex	-
(8)	3 Hh	1.448 (t)	$J_{d,h}$ 7.33
	2 Hd	3.181 (q)	$J_{d,h}$ 7.33
	3 Hg	2.377 s	-
	Aromatic Protons	7.228-8.088 Complex	-

Table-VII Chemical Shifts and Coupling Constants of Protons in Different Compounds

Number of Compound	Aliphatic Protons	3h	3d	1Ha	1Hb	1Hc	3Hg	2Hc	2HF	2Ha	2Hb
(1)	-	2.63(s)	-	8.4(d) J <sub>a,b</sub> =1.9	8.1(d,d) J <sub>a,b</sub> =1.9 J <sub>c,b</sub> =8.7	7.6(d) J <sub>c,b</sub> =8.7	-	-	-	-	--
(2)	1.42(t) J <sub>d,h</sub> =7.57	-	3.0(q)	8.4(d) J <sub>a,b</sub> =2	8.1(d,d) J <sub>a,b</sub> =2 J <sub>c,b</sub> =8.8	7.62(d,d) J <sub>c,b</sub> =8.8	-	-	-	-	--
a)	-	2.85(s)	-	8.51(d) J <sub>a,b</sub> =1.95	Cannot be read	8.14(d) J <sub>c,b</sub> =9.03	2.42	7.83 d J <sub>e,f</sub> =8.84	7.35 (d)	-	-
(3)	-	2.87(s)	-	8.95(d)	-do-	7.71(d) J <sub>b,c</sub> =8.8 J <sub>c,a</sub> =v.small	2.42	7.87 d	7.35(d)	-	-
b)	1.46(t) J <sub>d,h</sub> =7.4	-	3.20(q)	8.54(d) J <sub>a,b</sub> =1.47	-do-	8.15(d) J <sub>c,b</sub> =9.04	2.42	7.35(b,d)	7.85(d)	-	-
(4)	1.46(t) J <sub>d,h</sub> =7.3	-	3.26(q)	8.96(d) J <sub>a,b</sub> =2.2	-do-	7.74(d) J <sub>c,b</sub> =7.8	2.42	7.35(b,d)	7.82(d)	-	-
(5)	-	2.64(s)	-	-	-	-	-	-	-	7.55 (dd)	-
(6)	1.45(t)	-	3.02(q)	-	-	-	-	-	-	J <sub>ortho</sub> =5.9 J <sub>meta</sub> =7.56 7.56 (dd) J <sub>ortho</sub> =5.9	-
(7)	-	2.8(s)	-	-	-	-	2.37	-	-	J <sub>meta</sub> =3.4 7.212 (dd)	-
(8)	1.448(t)	-	3.181(q)	-	-	-	2.377	-	-	-	7.21(dd)

(1), (2), (5) and (6 into (3), (4), (7), and (8) respectively using p-toluene sulfonyl chloride in presence of sodium hydroxide.

#### Preparation of (9)

A mixture of 8 g (0.045 mole) of (1) and 24 g zinc dust were refluxed in 130 ml of 6N hydrochloric acid for one hour. Contents were poured into 80 ml of water after cooling and neutralized with sodium carbonate. The precipitated dark reddish black compound was collected, washed, dried and recrystallized. Percentage yield and physical properties are listed in Table 1.

#### Preparation of (10)

This compound was prepared using 5 g 0.026 mole of (2) and 15 g of zinc dust in 80 ml 6N hydrochloric acid by the procedure described for (9). Percentage yield and physical properties of the compound obtained in the form of light brown needles are described in Table 1.

#### Diazotization of (9)

A cooled solution of 2-naphthol in excess of sodium hydroxide solution was added to a cooled solution of 0.2g of (9) dissolved in 1.0 ml of conc. hydrochloric acid and diluted with 3.0ml water, and few drops of sodium nitrate solution. A scarlet dye was formed.

#### Diazotization of (10)

0.2g of (10) was diazotized in the same manner as described for (9). A scarlet dye was obtained.

Mass spectra of the new compounds (1-4) and (7-10) (Table 2 and Scheme I-V) were measured in HEJ Research

Institute of Chemistry, University of Karachi. Proton magnetic resonance spectra of compounds (1-8) were measured in chloroform using Jeol 100 MHz nuclear magnetic resonance spectrometer and TMS as internal reference (Table II-VII).

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