Application of Linear Free Energy Relationships (LFER) to pK_{aH+} of Benzimidazolium Cations: Chemical Education Perspective

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Abstract:

Application of Linear Free Energy Relationships (LFER) to pK_{aH+} data in water at 25º C of deprotonation of protonated fused ring systems like benzimidazolium cations is carried out in the present work. With a good comparison of the sites of substituents with reference to a functional group in benzene ring and the imidazolium ring, an excellent Hammett correlation is observed for the deprotonation of (pK_{aH+}) of protonated fused ring systems like benzimidazolium cations. For the three substituents OH, MeO and Me at position 4 in the benzimidazole satisfy the correlation with σ_I values. A positive Hammet ρ values of 1.93 indicates that electron withdrawing substituents facilitate the deprotonation. Under the same conditions a Taft ρ^* value of 1.11 is obtained for the deprotonation of 2-substituted-benzimidazolium cations. The available pK_{aH+} data in 5% aq. ethanol at 30º C of 2-methyl benzimidazolium cations and 2-(hydroxyethyl) benzimidazolium cations also followed Hammett correlation. The lower Hammett ρ value of 0.89 for 2-(hydroxyethyl) benzimidazolium cation series than that of 1.78 of 2-methyl benzimidazolium cation series is explained in terms of strong intramolecular hydrogen bonding in 2-(hydroxyethyl) benzimidazolium cation which resists the easy deprotonation. Deprotonation of 1-substituted-benzimidazolium cations did not follow Hammett relation.

Keywords:

LFER; Benzimidazolium cations; Hammett Equation; Taft Equation

Introduction:

It is needless to mention that Hammett equation is ever glowing tool in Physical-Organic Chemistry [1]. Hammett equation has emerged from the study of dissociation equilibriums of benzoic acids in water at 25º C [1]. There were reports on the application of Hammett equation to five membered heterocycles [2, 3]. Several studies appeared on the application of Hammett equation to benzimidazoles [4-10]. In these studies [4-10] different versions of arguments presented. In halogenated benzimidazolium cations [4], 5(6)-halogen substituted compounds did not follow Hammett equation which is attributed to the tautomeric nature of the ring, but a

satisfactory correlation is shown with 4(7)-halogenated derivatives. In the rest of the studies [5-10] a brief introduction is given on the application of Hammett equation to these derivatives. The present study is a little further detailed extension of the application of both Hammett and Taft equations to fused ring systems like benzimidazolium cations. In the present study we brought a total of nineteen substituted benzimidazolium cations on one platform. We have applied Hammett and Taft equations to the dissociation equilibriums of deprotonation of these benzimidazolium cations. An excellent Hammett correlation is obtained using σ_I values for 4 substituted compounds and normal σ values for 5/6 substituted compounds. And Taft correlations are obtained in the case of 2-substituted benzimidazolium cations.

Methods:

All correlations were done using KaleidaGraph software, Reading, PA, USA. All the chemical structures were drawn using chemdraw. The pK_{aH+} data is from different sources [4-10]. All reaction constants (Hammett ρ and Taft ρ^*) are to be understood as positive values. All the loci of the plots in this article are with negative slope because the pK_{aH+} data is plotted against the substituent constants (Hammett σ and Taft σ^*).
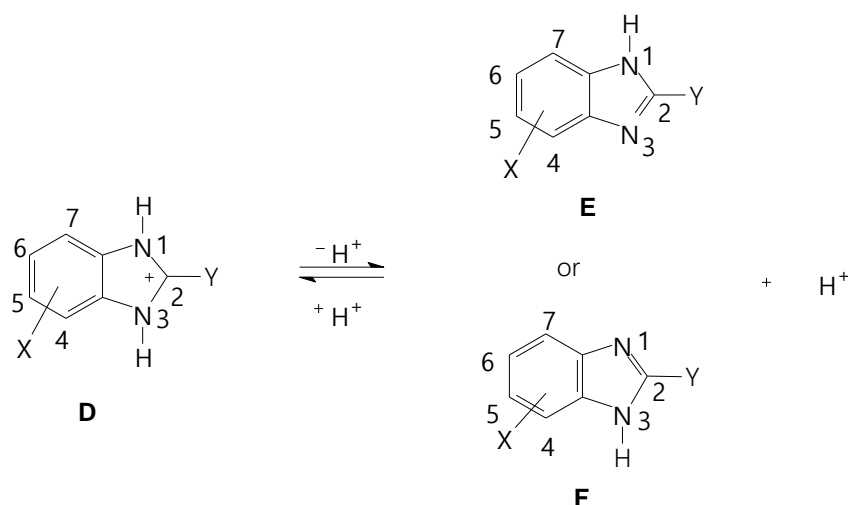
Discussion:

Table 1 summarizes the pK_{aH+} data of different substituted benzimidazolium cations. Different resonance structures of benzimidazolium cation are as shown in Scheme 1 (structures **A, B, C**). The most stable structure of benzimidazolium cation is as shown in **D** due to its C-2 symmetry.
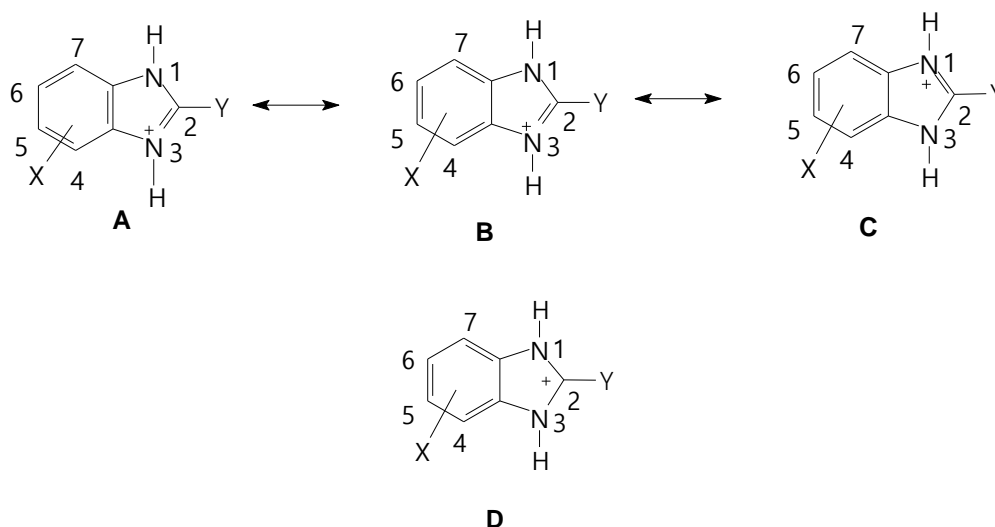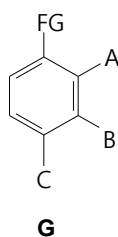

Scheme 1

The deprotonation equilibrium is shown in Scheme 2.

Scheme 2

In scheme 3, structure **G** is the depiction of the benzene derivative with substituents at *ortho*, *meta* and *para* positions to FG.


Scheme 3

In **G**, FG = functional group, A, B and C are substituents at *ortho*, *meta* and *para* positions respectively. Comparing either structure **D** with the structure **G**, the substituent X either at 5 or 6 position in benzimidazolium cation with respect to depronatable site of N(1) or N(3) would be *para* to either N(1)-H or N(3)-H and similarly either at 4 or 7 position would be *meta* to either N(1)-H or N(3)-H. The substituent Y will be ortho to either N(1)-H or N(3)-H.

With fourteen substituents a Hammett plot is constructed and shown in figure 1. A relatively more than 1 positive value of Hammett ρ of 1.93 (R = 0.9565) indicates that the deprotonation is strongly enhanced by electron withdrawing substituents and retarded by electron donating substituents. The serial numbers labeled for points in the plot refer to the substituents under column ii in the Table 1.

Figure 1: Plot of pK_{aH+} versus Hammett σ_I and σ_p

Hammett ρ = 1.93
R = 0.9565
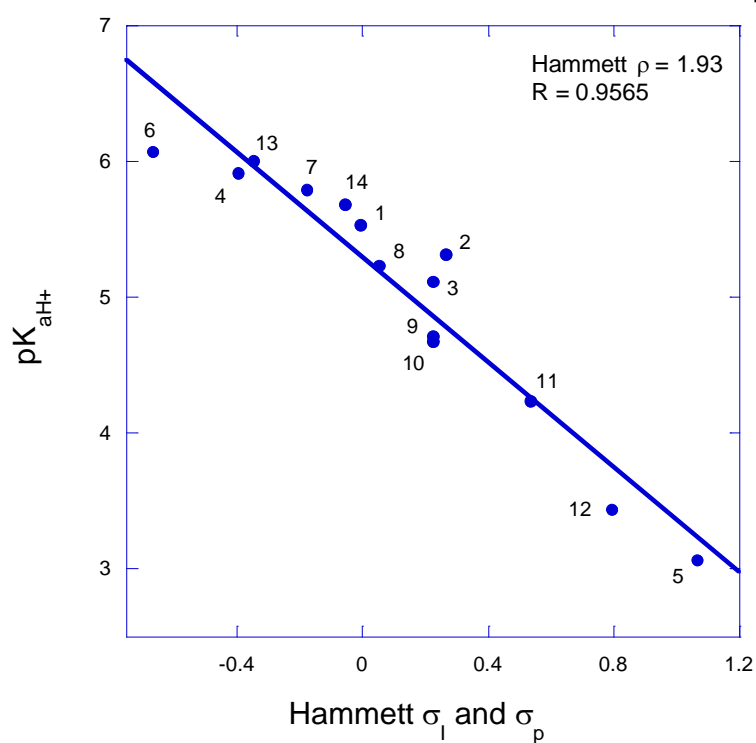
With four substituents a Taft plot is constructed and shown in figure 2.

Figure 2: Plot of pK_{aH+} versus Taft $\sigma*$

Taft $\rho*$ = 1.11
R = 0.9776
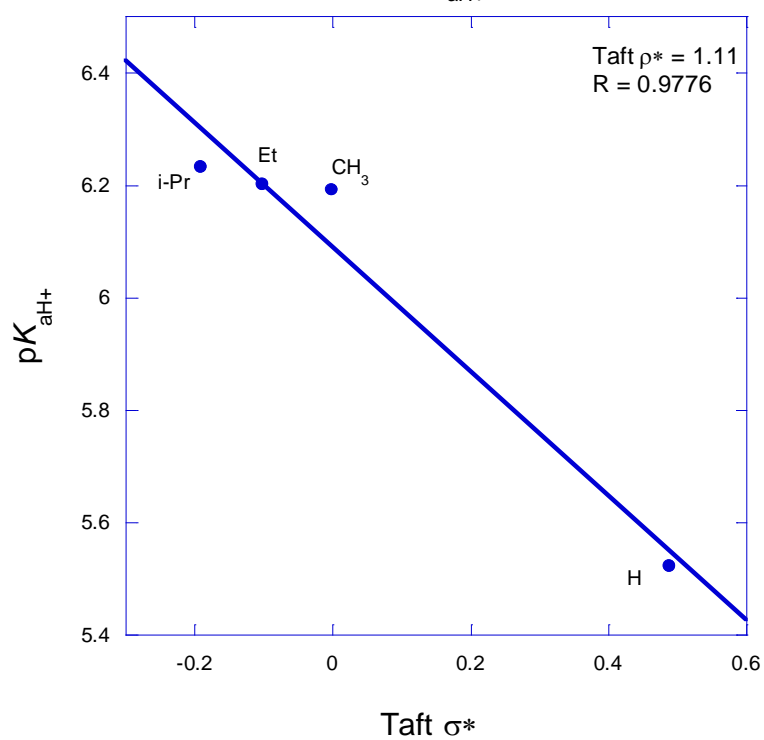
Again, relatively moderate value of Taft ρ^* of 1.11 (R = 0.9776) indicates that the deprotonation is enhanced by electron withdrawing substituents and retarded by electron donating substituents. The serial numbers labeled for points in the plot refer to the substituents under column v in the Table 1.

The pK_{aH+} data is available in 5% aqueous ethanol at 30° C for six substituted benzimidazolium cations with five substituents at *meta* and one substituent at *para* position (columns viii, ix, and x, Table 1). With this data an excellent Hammett plot is obtained (figure 3).

Figure 3: Plot of pK_{aH+} versus Hammett σ
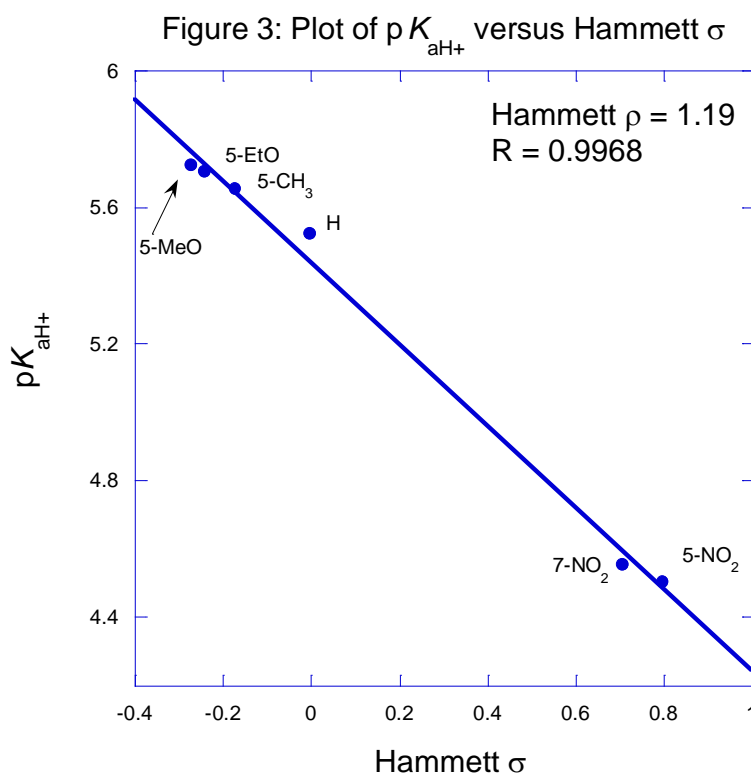
Neglecting very small effect of temperature on Hammett ρ [11], comparing the Hammett ρ values in pure water at 25° C (figure 1) and in 5% aqueous ethanol at 30° C (figure 3), the value in pure water (1.91) is higher than in 5% aqueous ethanol (1.19). This may be since the proton on nitrogen in benzimidazolium cation (scheme 1, structure **D**) becomes less susceptible for deprotonation in less nucleophilic 5% aqueous ethanol than more nucleophilic pure water.

The pK_{aH+} data is available in 5% aqueous ethanol at 30° C for six substituted benzimidazolium cations with CH_3 and $CH(OH)CH_3$ groups at position 2 (columns xi and xii of table 1). Different substituents for these two compounds are in column ii. The corresponding Hammett plots are given in figure 4 and figure 5.
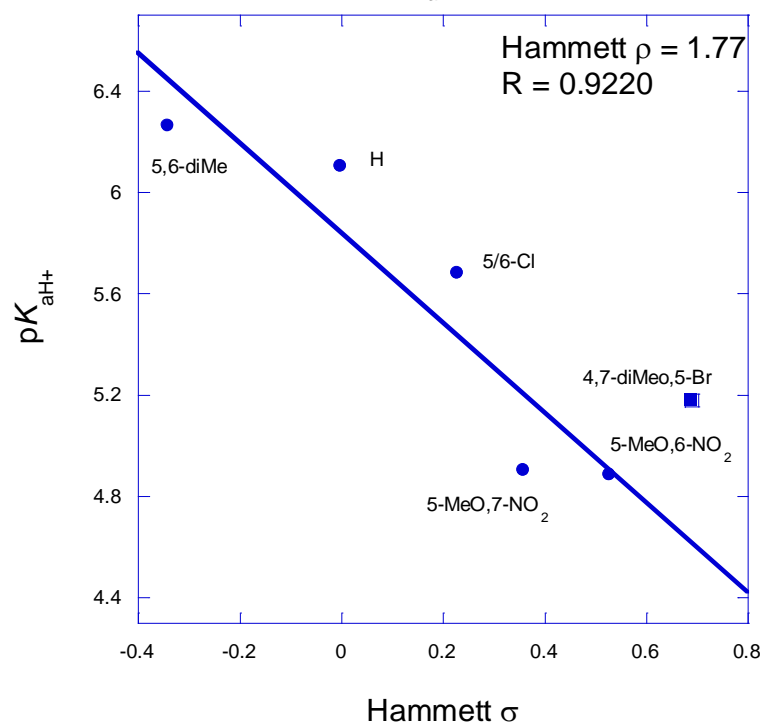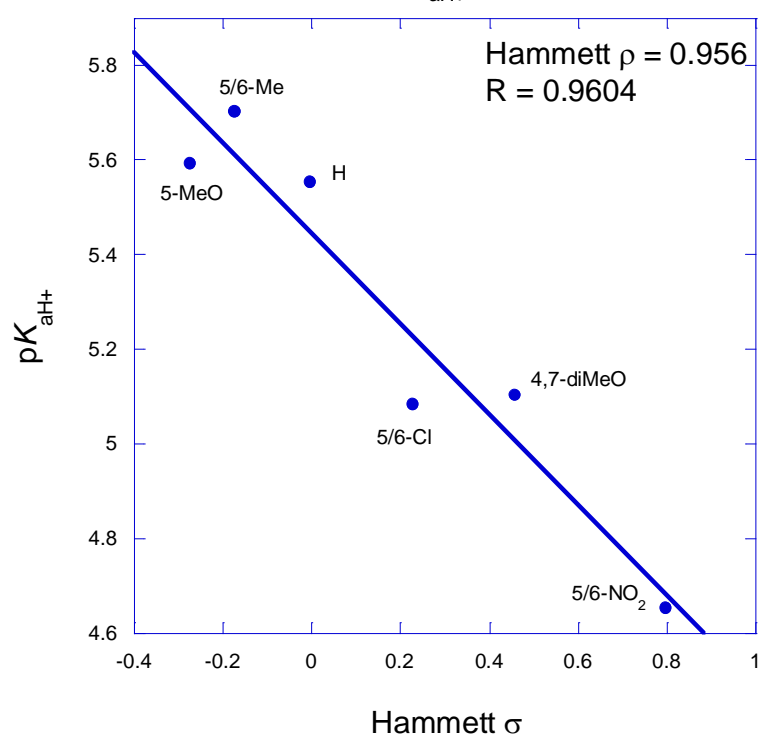
Figure 4: Plot of pK_{aH+} versus Hammett σ

Hammett ρ = 1.77
R = 0.9220

5,6-diMe
H
5/6-Cl
4,7-diMeo,5-Br
5-MeO,6-NO$_2$
5-MeO,7-NO$_2$

pK_{aH+}

Hammett σ

Figure 5: Plot of pK_{aH+} versus Hammett σ

Hammett ρ = 0.956
R = 0.9604

5/6-Me
5-MeO
H
4,7-diMeO
5/6-Cl
5/6-NO$_2$

pK_{aH+}

Hammett σ

The lower Hammett ρ value of 0.956 for the deprotonation of the cation with α-hydroxyethyl (-CH(OH)CH$_3$) group at position 2 of than that of 1.77 of the cation with CH$_3$ group at the

same position may be due to the formation of a strong intramolecular hydrogen bonding as shown in scheme 4.
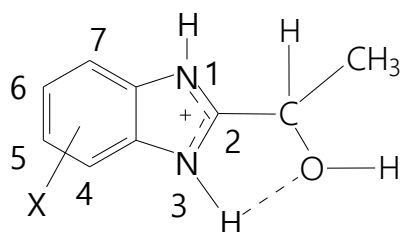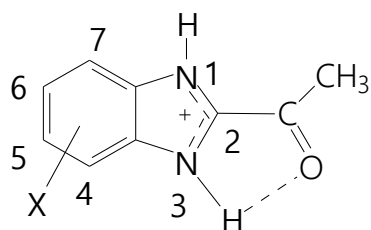

Scheme 4

The structure shown in scheme 4 strongly resists the deprotonation of the cation results in lower Hammett ρ value.

The pK_{aH+} data is available in 5% aqueous ethanol at 30° C for nine substituted benzimidazolium cations at position 2. A Taft plot is presented in figure 6. The data corresponds to the columns xiii, xiv and xv of table 1.


Figure 6: Plot of pK_{aH+} versus Taft σ^*
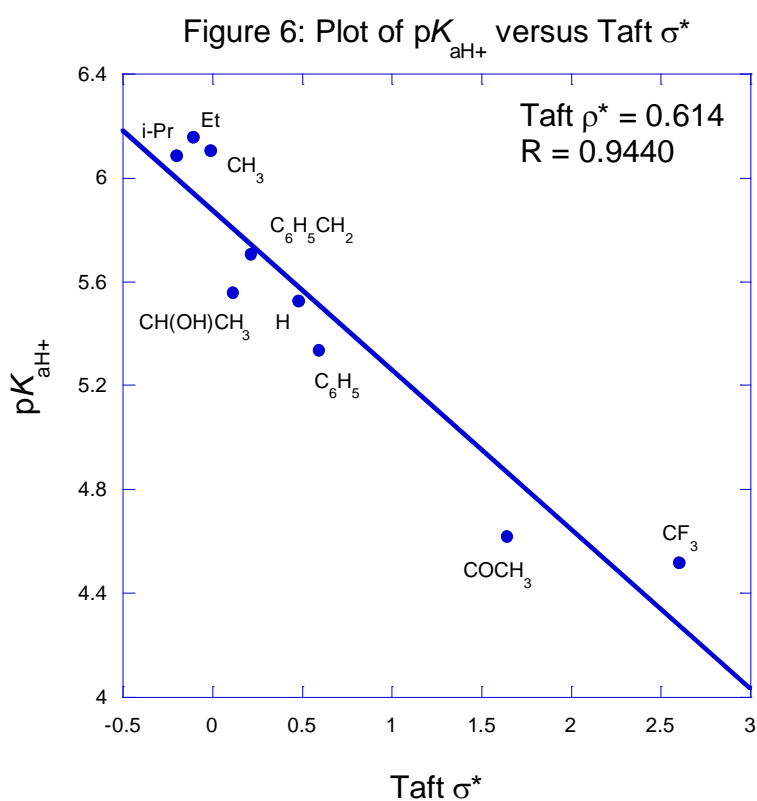
The point of the branched chain substituent i-Pr which may cause steric effect and the points of the substituents $CH(OH)CH_3$, $COCH_3$, and CF_3 capable of forming hydrogen bonding as shown in scheme 4, scheme 5, and scheme 6 are deviating from the Taft correlation (figure 6).
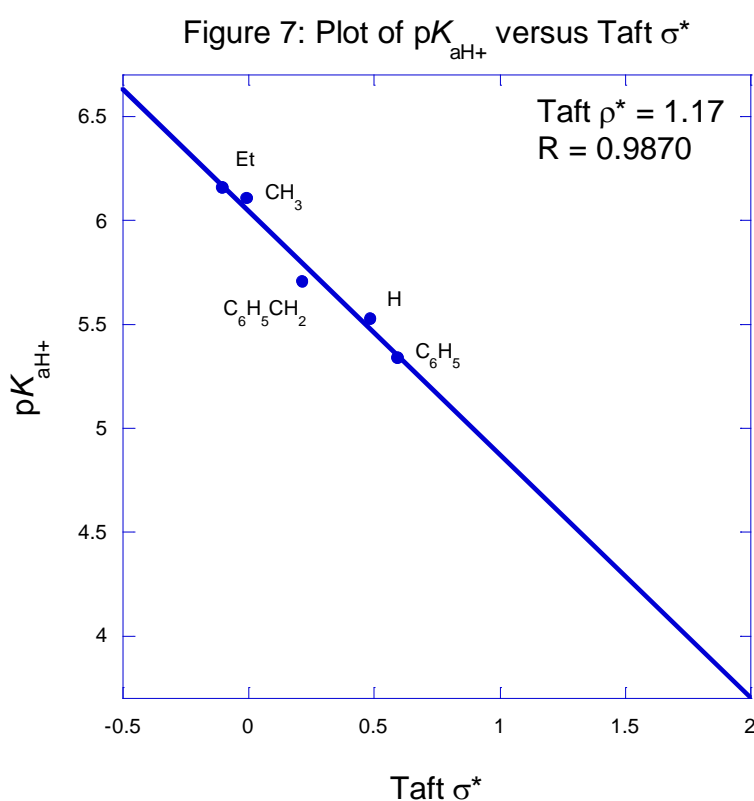
Replotting without these substituents improved the correlation form R = 0.9440 to R = 0.9870. The replot is shown in figure 7.

Scheme 5   Scheme 6

Figure 7: Plot of pK_{aH+} versus Taft σ^*

Taft $\rho^* = 1.17$
R = 0.9870
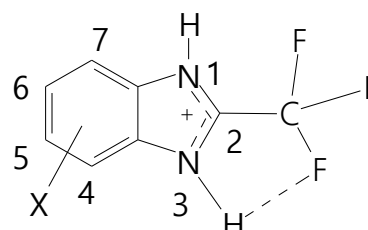
Lastly a Hammett plot is given in figure 8 with the substituents at position 1 with X = Y = H of the benzimidazolium cation at 25° C in water like the conditions for figure 1. The points correspond to the data given in columns xvi and xvii of table 1. But no correlation is observed. This may be due to fact that the C-2 symmetry of structure **D** of scheme 1 is lost by the substitution at N(1) position by a substituent [8] and this leads to the reduction in resonance stability.
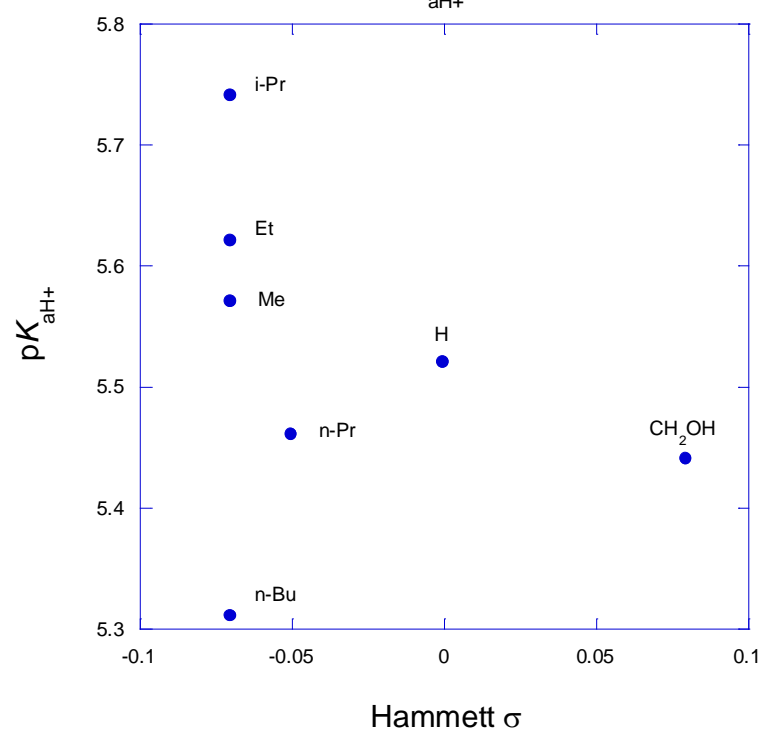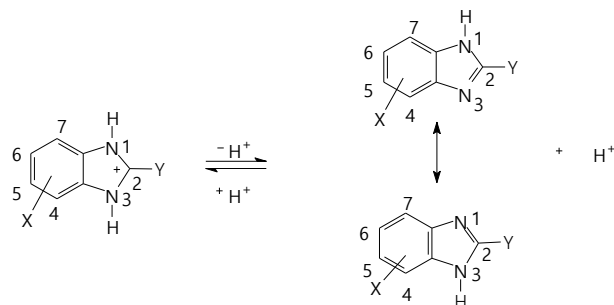
Figure 8: Plot of pK_{aH+} versus Hammett σ

Table 1: pK$_{aH+}$ data of different substituted benzimidazolium cations

Sl. No.	with Y = H X	Hammett σ$_p$ and σ$_I$	pK$_{aH+}$	X = H Y	Taft σ*	pK$_{aH+}$	Y = H X	Hammett σ	pK$_{aH+}$	pK$_{aH+}$ Y = Me	pK$_{aH+}$ Y = CH(OH)CH$_3$	X = H Y	Taft σ*	pK$_{aH+}$	X =Y = H with substituents at 1-position Hammett σ		pK$_{aH+}$
									at 30°C in 5% aqueous EtOH						at 25°C in H$_2$O		
i	ii	iii	iv	v	vi	vii	viii	ix	x	xi	xii	xiii	xiv	xv	xvi		xv
1	H	0.00	5.48	H	0.49	5.48	H	0.00	5.52	6.10	5.55	H	0.49	5.48	H	0.00	5.48
2	4-OH	0.27	5.30	Me	0.00	6.19	5-Me	-0.17	5.65			Me	0.00	6.10	Me	-0.07	5.57
3	4-MeO	0.23	5.10	Et	-0.10	6.20	5-MeO	-0.27	5.72			Et	-0.10	6.15	Et	-0.07	5.62
4	4-OH-6-NH$_2$	-0.39	5.90	i-Pr	-0.19	6.23	5-OEt	-0.24	5.70			i-Pr	-0.19	6.08	i-Pr	-0.07	5.74
5	4-OH-6-NO$_2$	1.07	3.05				5-NO$_2$	0.80	4.50			CH(OH)CH$_3$	0.12	5.55	n-Pr	-0.05	5.46
6	5/6-NH$_2$	-0.66	6.06				7-NO$_2$	0.71	4.55			C$_6$H$_5$CH$_2$	0.22	5.70	n-Bu	-0.07	5.31
7	5/6-CH$_3$	-0.17	5.78								5.70	C$_6$H$_5$	0.60	5.33	CH$_3$OH	0.08	5.44
8	5/6-F	0.06	5.22									COCH$_3$	1.65	4.61			
9	5/6-Cl	0.23	4.70							5.68	5.08	CF$_3$	2.61	4.51			
10	5/6-Br	0.23	4.66														
11	5/6-CF$_3$	0.54	4.22														
12	5/6-NO$_2$	0.80	3.42								4.65						
13	5,6-diMe	-0.34	5.99							6.26							
14	4-Me	-0.05	5.67														
15	5-MeO,6-NO$_2$	0.53								4.88							
16	5-MeO,7-NO$_2$	0.36								4.90							
17	4,7-diMeO,5-Br	0.69								5.18							
18	5-MeO	-0.27									5.59						
19	4,7-diMeO	0.46									5.10						

Note: Columns iv–vii at 25°C in H$_2$O; columns viii–xii at 30°C in 5% aqueous EtOH; columns xvi at 25°C in H$_2$O.

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