

SUBSTITUENT EFFECTS IN THE RING-CHAIN TAUTOMERISM OF 1,2-DIARYLIMIDAZOLIDINES

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Abstract – 1,2-Diaryl-substituted imidazolidines proved to be ring-chain tautomeric mixtures in CDCl₃ at 300 K. Both 1- and 2-aryl groups exerted significant electronic effect on the tautomeric equilibria, which could be described by the equation $\log K_X = \rho\sigma^+ + \log K_{X=H}$.

Physical and chemical properties of disubstituted organic compounds are influenced significantly by the electronic or steric effects of both substituents.¹⁻³ This phenomenon plays a crucial role in the ring-chain tautomerism of saturated 1,3-*N,N*-heterocycles.⁴⁻⁶ For 1-alkyl- or 1-phenyl-substituted 2-arylimidazolidines, tautomeric equilibria were determined not only by the electronic effects of the substituents on the 2-aryl group, but also by the steric effects of the *N*-alkyl group, which could be described by Equation (1):⁶

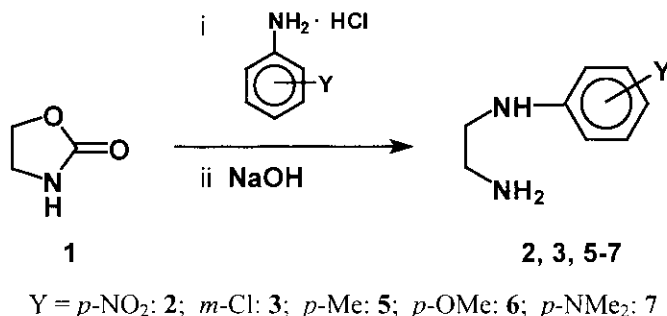
$$\log K_X = \rho\sigma^+ + \log K_{X=H} \quad (\text{Eq. 1})$$

As a continuation of our previous studies⁶ on the ring-chain tautomerism of imidazolidines, our present aim was to study the electronic effects of aryl groups in positions 1 and 2. Studies on the electronic effects of aryl groups on the tautomeric equilibria of 1,3-*X,N*-heterocycles (*X* = O, N, S) are restricted mostly to 2-aryl derivatives;⁷ the effects of aryl substituents at other positions have been investigated in only a few cases. For 4-aryl-2,2-dialkyl-substituted 1,3,4-oxadiazines, electron-withdrawing groups on the phenyl ring increased the ratios of the ring-closed tautomers.⁸ An aryl substituent at position 4 or 6 did not exert

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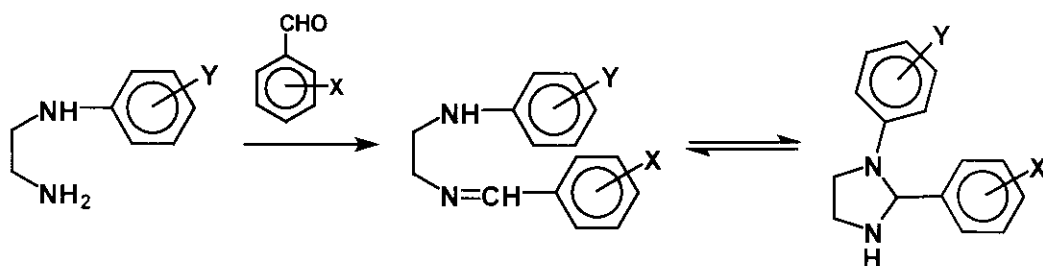
observable electronic effects on the ring-chain tautomeric ratios of 2,4- or 2,6-diaryl-substituted tetrahydro-1,3-oxazines.⁹

N-Arylethylenediamines, the starting materials for the synthesis of 1,2-diarylimidazolidines, were prepared according to the convenient method of Poindexter *et al.* by reacting equivalent amounts of 2-oxazolidinone (**1**) with the appropriate substituted aromatic amine hydrochlorides (Scheme 1).¹⁰ To provide large differences in electronic properties, *p*-nitro (**2**), *m*-chloro (**3**), *p*-methyl (**5**), *p*-methoxy (**6**) and *p*-dimethylamino (**7**) derivatives were chosen besides the unsubstituted *N*-phenylethylenediamine (**4**).



Scheme 1

The ring-closures of ethylenediamines (**2**, **3**, **5-7**) with equivalent amounts of substituted benzaldehydes were carried out under mild reaction conditions (ambient temperature, 1 h) to give imidazolidines (**8**, **9**, **11-13a-i**) in good yields (Scheme 2). Compounds (**10a-i**) were prepared earlier.⁶



Y = <i>p</i> -NO ₂ :	2	8Aa-i	8Ba-i
Y = <i>m</i> -Cl:	3	9Aa-i	9Ba-i
Y = H:	4	10Aa-i	10Ba-i
Y = <i>p</i> -Me:	5	11Aa-i	11Ba-i
Y = <i>p</i> -OMe:	6	12Aa-i	12Ba-i
Y = <i>p</i> -NMe ₂ :	7	13Aa-i	13Ba-i

X = *p*-NO₂: **a**; *m*-NO₂: **b**; *m*-Br: **c**; *p*-Br: **d**; *p*-Cl: **e**; H: **f**; *p*-Me: **g**; *p*-OMe: **h**; *p*-NMe₂: **i**

Scheme 2

The ^1H NMR spectra of imidazolidines (**8-13 a-i**) unequivocally proved that these compounds exist as ring-chain tautomeric mixtures in CDCl_3 at 300 K. Data on (**11a**) was chosen to demonstrate the ^1H NMR spectra of the prepared 1,2-diaryl-imidazolidines. The chemical shifts and multiplicities of the aliphatic protons in the spectra of (**11a**) correspond to the values for 2-(*p*-bromophenyl)-1-phenylimidazolidine (**10d**).⁶ The ratios at equilibrium were determined by integration of the well-separated N-CHAr-N (ring) and N=CH (chain) singlets (Table 1).

Table 1 Ring (B) percentages at tautomeric equilibrium for compounds (**8-13**) in CDCl_3 at 300K

Compd.			8	9	10 ^a	11	12	13
		Y	<i>p</i> -NO ₂	<i>m</i> -Cl	H	<i>p</i> -Me	<i>p</i> -OMe	<i>p</i> -NMe ₂
	X	σ^+	0.79	0.4	0	-0.311	-0.778	-1.7
a	<i>p</i> -NO ₂	0.79	57.4	62.2	68.6	71.9	69.4	73.3
b	<i>m</i> -NO ₂	0.73	49.9	62.2	68.0	70.5	62.2	66.4
c	<i>m</i> -Br	0.405	45.6	49.5	52.6	56.2	63.9	55.8
d	<i>p</i> -Br	0.15	39.4	41.6	46.1	48.1	46.0	46.6
e	<i>p</i> -Cl	0.114	37.0	39.9	42.4	45.0	42.6	45.4
f	H	0	37.7	35.2	35.7	37.1	33.3	34.5
g	<i>p</i> -Me	-0.311	30.8	26.9	27.5	28.4	25.6	26.9
h	<i>p</i> -OMe	-0.778	18.5	16.5	15.8	18.1	16.7	16.1
i	<i>p</i> -NMe ₂	-1.7	6.2	5.6	4.6	5.2	4.3	2.7

^aLiterature⁶ data.

When Equation (1) was applied to the log K_X values, good linear correlations were obtained versus the Hammett-Brown parameter σ^+ of the substituent X on the 2-phenyl group for all five new sets of imidazolidines (**8, 9, 11-13**) (Figure 1, Table 2).

According to the data in Table 2, the value of ρ in Equation (1) is markedly influenced by the electronic character of substituent Y on the 1-phenyl group. A more electron-donating substituent Y produces a higher ρ value. This means that differences in the ring-chain tautomeric ratios in a set of 2-aryl-substituted imidazolidines are decreased by introducing an electron-withdrawing substituent on the nitrogen. Our efforts to find a mathematical relationship between the electronic parameters of substituent Y and the value of ρ have not resulted in an acceptable correlation. The electronic character of Y did not have any significant effect on the log $K_{X=H}$ values of Equation (1).

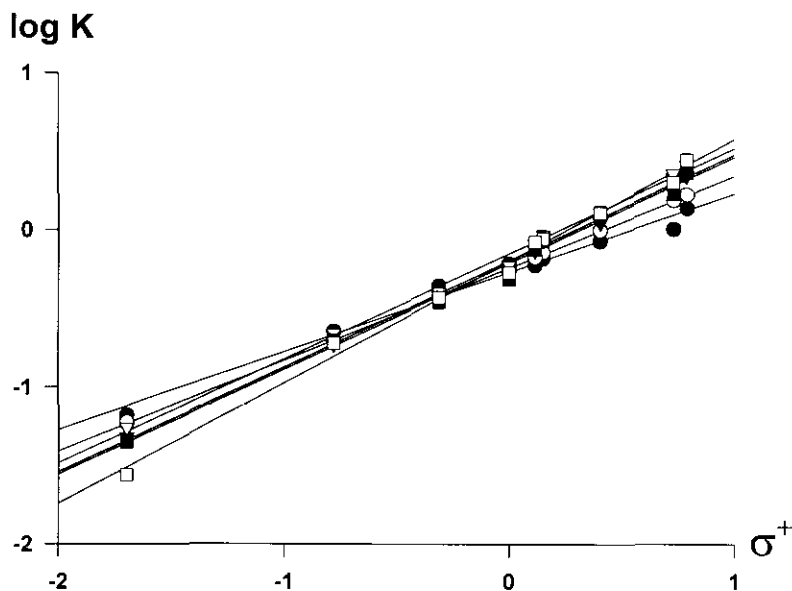


Figure 1 Plots of log K for (8): ●, (9): ○, (10): ▼, (11): ▽, (12): ■ and (13): □ vs Hammett-brown parameter σ^+

Table 2 Linear regression analysis data on compounds (8-13)

Compd	Y	No. of points	Slope (ρ) ^a	Intercept ^a	Correlation coefficient
8	<i>p</i> -NO ₂	9	0.49(3)	-0.27(6)	0.991
9	<i>m</i> -Cl	9	0.58(0)	-0.25(1)	0.999
10 ^b	H	9	0.67(1)	-0.20(3)	0.997
11	<i>p</i> -Me	9	0.67(2)	-0.15(4)	0.997
12	<i>p</i> -OMe	8	0.68(4)	-0.20(9)	0.989
13	<i>p</i> -NMe ₂	7	0.77(3)	-0.20(6)	0.996

^aStandard deviations are given in parentheses. ^bLiterature⁶ data.

The above results demonstrate that the ring-chain tautomeric equilibria of 1,2-diaryl-substituted imidazolidines are significantly influenced by the electronic characters of both the aryl group at position 2 and (to a lesser extent) the aryl group at position 1. Efforts to explain the above results on the basis of electron densities at amine (NHC₆H₄Y) and imine (N=CHC₆H₄X) moieties are in progress.

EXPERIMENTAL

^1H NMR spectra were recorded on a Bruker AVANCE DRX 400 spectrometer at 300 K. using a "5 mm inverse Z gradient" probehead. The samples were dissolved in CDCl_3 containing 0.03% TMS as a reference. For the equilibria to be established,¹¹ the solutions were left to stand at ambient temperature for 1 day before the ^1H NMR spectra were run. The number of scans was usually 64.

Melting points were determined on a Kofler micro melting point apparatus and are not corrected. The physical data on compounds (**8**, **9**, **11-13**) are listed in Table 3. *N*-(*m*-Chlorophenyl)- (**3**), *N*-(*p*-tolyl)- (**5**), *N*-(*p*-methoxyphenyl)- (**6**) and *N*-(*p*-dimethylaminophenyl)ethylenediamine (**7**) were prepared by known procedures.¹⁰

N-(*p*-Nitrophenyl)ethylenediamine (**2**)

Equimolar quantities (0.2 mol) of 2-oxazolidone and *p*-nitroaniline were heated neat in a 160-170 °C oil bath under nitrogen until all CO_2 evolution had ceased. The dark reaction mixture was allowed to cool to rt. It was then dissolved in 150 mL of 10% NaOH and extracted with CHCl_3 . The combined organic extracts were washed with brine and then dried over anhydrous Na_2SO_4 . The solvent was distilled off *in vacuo* and the resulting crystalline substance was purified by column chromatography on silica gel (eluent: methanol). Yield: 5.41 g (17.3%). mp 135-137 °C (lit.,¹² mp 139-141 °C). The NMR and IR spectra of compound (**2**) correspond to the literature¹² data.

General method for the synthesis of 2-arylimidazolidines (**8**, **9**, **11-13a-i**)

To a solution of the appropriate diamine (3 mmol) in 20 mL of absolute methanol, an equivalent amount of aromatic aldehyde was added (in the case of liquid aldehydes, a freshly distilled sample was used), and the mixture was left to stand at ambient temperature for 1 h. The solvent was evaporated off and the evaporation was repeated after the addition of 10 mL of toluene. The oily products were dried in a vacuum desiccator for 24 h. The NMR spectra proved that the purities of these compounds were greater than 95%. Crystalline products were filtered off and recrystallized.

^1H NMR spectroscopic data on 2-(*p*-nitrophenyl)-1-(*p*-tolyl)imidazolidine (**11a**)

The protons of the open form (**A**) are numbered according to the corresponding protons of the ring form (**B**) (δ in ppm; in brackets the multiplicity, couplings in Hz and assignment, respectively).

(**11Aa**): 8.35 (s, 1H, $\text{N}=\text{CH}$), 8.25 (d, 2H, $J = 8.8$, $\text{C}_6\text{H}_5\text{NO}_2$), 7.88 (d, 2H, $J = 8.8$, $\text{C}_6\text{H}_5\text{NO}_2$), 6.99 (d, 2H, $J = 8.5$, $\text{C}_6\text{H}_5\text{Me}$), 6.58 (d, 2H, $J = 8.5$, $\text{C}_6\text{H}_5\text{Me}$), 3.88 (dt, 2H, $J = 5.8$, 1.3, 4- CH_2), 3.49 (t, 2H, $J = 5.7$, 5- CH_2), 2.24 (s, 3H, CH_3); (**11Ba**): 8.17 (d, 2H, $J = 8.8$, $\text{C}_6\text{H}_5\text{NO}_2$), 7.58 (d, 2H, $J = 8.8$, $\text{C}_6\text{H}_5\text{NO}_2$).

Table 3 Physical and analytical data on imidazolidines (**8**, **9**, **11-13 a-i**)^a

Compd	mp (°C)	Yield (%)	Formula	Analysis			δ N=CHAr (s) chain (A)	δ N-CHAr-N (s) ring (B)
				Calculated/Found (%)				
				C	H	N		
8a	179-181 ^b	72	C ₁₅ H ₁₄ N ₄ O ₄	57.32 57.07	4.49 4.38	17.83 17.65	8.33	5.61
8b	oil	~100	C ₁₅ H ₁₄ N ₄ O ₄	57.32 —	4.49 —	17.83 —	8.32	5.62
8c	oil	~100	C ₁₅ H ₁₄ N ₃ O ₂ Br	51.74 —	4.05 —	12.07 —	8.18	5.48
8d	128-133 ^c	69	C ₁₅ H ₁₄ N ₃ O ₂ Br	51.74 51.69	4.05 4.84	12.07 11.90	8.20	5.48
8e	140-143 ^c	76	C ₁₅ H ₁₄ N ₃ O ₂ Cl	59.31 59.18	4.65 4.72	13.83 13.77	8.21	5.49
8f	oil	~100	C ₁₅ H ₁₅ N ₃ O ₂	66.90 —	5.61 —	15.60 —	8.25	5.51
8g	109-110 ^c	64	C ₁₆ H ₁₇ N ₃ O ₂	67.83 67.94	6.05 7.82	14.83 14.69	8.21	5.47
8h	oil	~100	C ₁₆ H ₁₇ N ₃ O ₃	64.20 —	5.72 —	14.04 —	8.17	5.46
8i	oil	~100	C ₁₇ H ₂₀ N ₄ O ₂	65.37 —	6.45 —	17.94 —	8.08	5.39
9a	oil	~100	C ₁₅ H ₁₄ N ₃ O ₂ Cl	59.31 —	4.65 —	13.83 —	8.37	5.49
9b	oil	~100	C ₁₅ H ₁₄ N ₃ O ₂ Cl	59.31 —	4.65 —	13.83 —	8.36	5.49
9c	oil	~100	C ₁₅ H ₁₄ N ₂ BrCl	53.36 —	4.18 —	8.30 —	8.21	5.35
9d	oil	~100	C ₁₅ H ₁₄ N ₂ BrCl	53.36 —	4.18 —	8.30 —	8.23	5.35
9e	oil	~100	C ₁₅ H ₁₄ N ₂ Cl ₂	61.45 —	4.81 —	9.55 —	8.24	5.36
9f	oil	~100	C ₁₅ H ₁₅ N ₂ Cl	69.63 —	5.84 —	10.83 —	8.29	5.39
9g	oil	~100	C ₁₆ H ₁₇ N ₂ Cl	70.45 —	6.28 —	10.27 —	8.25	5.36
9h	oil	~100	C ₁₆ H ₁₇ N ₂ OCl	66.55 —	5.93 —	9.70 —	8.22	5.35
9i	oil	~100	C ₁₇ H ₂₀ N ₃ Cl	67.65 —	6.68 —	13.92 —	8.16	5.32
11a	69-71 ^c	55	C ₁₆ H ₁₇ N ₃ O ₂	67.83 67.59	6.05 5.81	14.83 14.66	8.35	5.44
11b	74-75 ^d	49	C ₁₆ H ₁₇ N ₃ O ₂	67.83 67.95	6.05 6.10	14.83 14.79	8.35	5.44
11c	oil	~100	C ₁₆ H ₁₇ N ₂ Br	60.58 —	5.40 —	8.83 —	8.19	5.30
11d	72-74 ^c	64	C ₁₆ H ₁₇ N ₂ Br	60.58 60.71	5.40 5.27	8.83 8.79	8.22	5.31

Table 3 (continued)

11e	58-61 ^d	52	C ₁₆ H ₁₇ N ₂ Cl	70.45 70.18	6.28 6.07	10.27 10.33	8.23	5.32
11f	oil	~100	C ₁₆ H ₁₈ N ₂	80.63 —	7.61 —	11.75 —	8.28	5.35
11g	68-70 ^d	49	C ₁₇ H ₂₀ N ₂	80.91 81.03	7.99 8.16	11.10 10.95	8.24	5.32
11h	51-53 ^d	45	C ₁₇ H ₂₀ N ₂ O	76.09 75.84	7.51 7.35	10.44 10.28	8.21	5.31
11i	52-54 ^d	52	C ₁₈ H ₂₃ N ₃	76.83 76.62	8.24 8.17	14.93 14.80	8.20	5.27
12a	oil	~100	C ₁₆ H ₁₇ N ₃ O ₃	64.20 —	5.72 —	14.04 —	8.36	5.39
12b	oil	~100	C ₁₆ H ₁₇ N ₃ O ₃	64.20 —	5.72 —	14.04 —	8.28	5.39
12c	oil	~100	C ₁₆ H ₁₇ N ₂ OBr	57.67 —	5.14 —	8.41 —	8.21	5.26
12d	62-64 ^d	48	C ₁₆ H ₁₇ N ₂ OBr	57.67 57.40	5.14 4.93	8.41 8.26	8.23	5.26
12e	51-53 ^d	51	C ₁₆ H ₁₇ N ₂ OCl	66.55 66.34	5.93 5.86	9.70 9.71	8.24	5.27
12f	oil	~100	C ₁₆ H ₁₈ N ₂ O	75.56 —	7.13 —	11.01 —	8.28	5.28
12g	81-83 ^d	55	C ₁₇ H ₂₀ N ₂ O	76.09 76.18	7.51 7.43	10.44 10.38	8.25	5.26
12h	58-60 ^d	58	C ₁₇ H ₂₀ N ₂ O ₂	71.81 71.64	7.09 6.81	9.85 9.78	8.21	5.25
12i	80-82 ^c	60	C ₁₈ H ₂₃ N ₃ O	72.70 72.56	7.80 7.67	14.13 14.14	8.15	5.21
13a	79-81 ^d	47	C ₁₇ H ₂₀ N ₄ O ₂	65.37 —	6.45 —	17.94 —	8.35	5.37
13b	oil	~100	C ₁₇ H ₂₀ N ₄ O ₂	65.37 —	6.45 —	17.94 —	8.34	5.37
13c	oil	~100	C ₁₇ H ₂₀ N ₃ Br	58.97 —	5.82 —	12.13 —	8.19	5.24
13d	89-91 ^d	49	C ₁₇ H ₂₀ N ₃ Br	58.97 58.71	5.82 5.58	12.13 12.04	8.23	5.24
13e	82-85 ^c	52	C ₁₇ H ₂₀ N ₃ Cl	67.65 67.49	6.68 6.38	13.92 13.75	8.24	5.25
13f	oil	~100	C ₁₇ H ₂₁ N ₃	76.37 —	7.92 —	15.72 —	8.22	5.28
13g	60-62 ^d	52	C ₁₈ H ₂₃ N ₃	76.83 76.70	8.24 7.99	14.93 15.08	8.25	5.25
13h	78-79 ^c	48	C ₁₈ H ₂₃ N ₃ O	72.70 72.58	7.80 7.63	14.13 14.01	8.21	5.23
13i	oil	~100	C ₁₉ H ₂₆ N ₄	73.51 —	8.44 —	18.05 —	8.14	5.19

^a Analytical data were determined only for recrystallized new compounds. ^b Recrystallized from *i*-Pr₂O--EtOAc.^c Recrystallized from *n*-hexane-*i*-Pr₂O. ^d Recrystallized from *n*-hexane.

6.99 (*d*, 2H, $J = 8.5$, C_6H_5Me), 6.38 (*d*, 2H, $J = 8.5$, C_6H_5Me), 5.44 (*s*, 1H, 2-CH), 3.68 (*ddd*, 1H, $J = -8.5$, 6.9, 3.8, 5-CH₂), 3.41 (*q*, 1H, $J = 7.5$, 5-CH₂), 3.29 (*ddd*, 1H, $J = -11.6$, 6.6, 3.5, 4-CH₂), 3.16 (*ddd*, 1H, $J = -11.6$, 7.5, 6.6, 4-CH₂), 2.23 (*s*, 3H, CH₃).

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