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

Anikó Göblyös, László Lázár, Ferenc Evanics,[‡] and Ferenc Fülöp*

Institute of Pharmaceutical Chemistry, Albert Szent-Györgyi Medical University, H-6701 Szeged, POB 121, Hungary

[‡]Institute of Pharmaceutical Analysis, Albert Szent-Györgyi Medical University, H-6701 Szeged, POB 121, Hungary

Abstract – 1,2-Diaryl-substituted imidazolidines proved to be ring-chain tautomeric mixtures in $CDCl_3$ 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]

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

As a continuation of our previous studies[6] 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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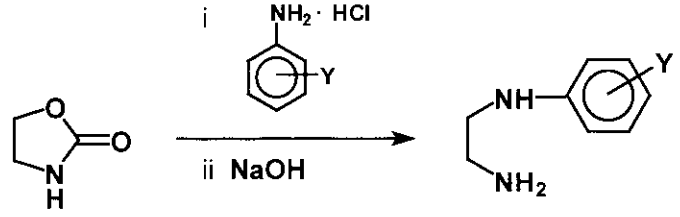
*e-mail: fulop@pharma.szote.u-szeged.hu

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**).

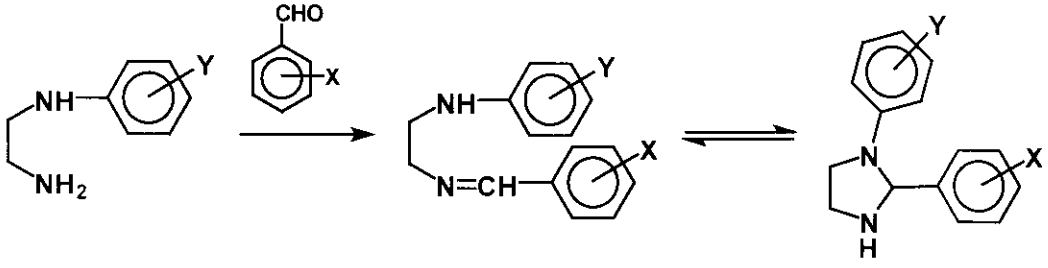


1 **2, 3, 5-7**

Y = *p*-NO_2: **2**; *m*-Cl: **3**; *p*-Me: **5**; *p*-OMe: **6**; *p*-NMe_2: **7**

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 = *p*-NO_2:	**2**	**8Aa-i**	**8Ba-i**
Y = *m*-Cl:	**3**	**9Aa-i**	**9Ba-i**
Y = H:	**4**	**10Aa-i**	**10Ba-i**
Y = *p*-Me:	**5**	**11Aa-i**	**11Ba-i**
Y = *p*-OMe:	**6**	**12Aa-i**	**12Ba-i**
Y = *p*-NMe_2:	**7**	**13Aa-i**	**13Ba-i**

X = *p*-NO_2: **a**; *m*-NO_2: **b**; *m*-Br: **c**; *p*-Br: **d**; *p*-Cl: **e**; H: **f**; *p*-Me: **g**; *p*-OMe: **h**; *p*-NMe_2: **i**

Scheme 2

The ^{1}H 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 ^{1}H NMR spectra of the prepared 1,2-diarylimidazolidines. 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-C*H*Ar-N (ring) and N=C*H* (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	*p*-NO_2	*m*-Cl	H	*p*-Me	*p*-OMe	*p*-NMe_2
	X	σ^+	0.79	0.4	0	-0.311	-0.778	-1.7
a	*p*-NO_2	0.79	57.4	62.2	68.6	71.9	69.4	73.3
b	*m*-NO_2	0.73	49.9	62.2	68.0	70.5	62.2	66.4
c	*m*-Br	0.405	45.6	49.5	52.6	56.2	63.9	55.8
d	*p*-Br	0.15	39.4	41.6	46.1	48.1	46.0	46.6
e	*p*-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	*p*-Me	-0.311	30.8	26.9	27.5	28.4	25.6	26.9
h	*p*-OMe	-0.778	18.5	16.5	15.8	18.1	16.7	16.1
i	*p*-NMe_2	-1.7	6.2	5.6	4.6	5.2	4.3	2.7

[a]Literature[6] 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).

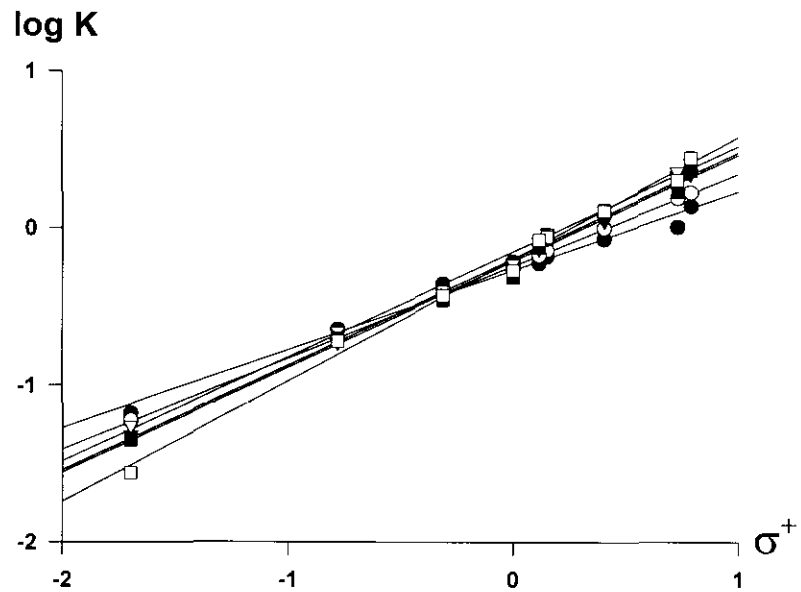


Figure 1 Plots of log K for (**8**): ●, (**9**): ○, (**10**): ▼, (**11**): ▽, (**12**): ■ and (**13**): □ *vs* Hammett-brown parameter σ^+

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

Compd	Y	No. of points	Slope (ρ)[a]	Intercept[a]	Correlation coefficient
8	*p*-NO_2	9	0.49(3)	-0.27(6)	0.991
9	*m*-Cl	9	0.58(0)	-0.25(1)	0.999
10[b]	H	9	0.67(1)	-0.20(3)	0.997
11	*p*-Me	9	0.67(2)	-0.15(4)	0.997
12	*p*-OMe	8	0.68(4)	-0.20(9)	0.989
13	*p*-NMe_2	7	0.77(3)	-0.20(6)	0.996

[a]Standard deviations are given in parentheses. [b]Literature[6] 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 electon densities at amine (NHC_6H_4Y) and imine ($N{=}CHC_6H_4X$) moieties are in progress.

EXPERIMENTAL

^{1}H 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 ^{1}H 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 literature[12] 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.

^{1}H 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, N=C*H*), 8.25 (*d*, 2H, *J* = 8.8, $C_6H_5NO_2$), 7.88 (*d*, 2H, *J* = 8.8, $C_6H_5NO_2$), 6.99 (*d*, 2H, *J* = 8.5, C_6H_5Me), 6.58 (*d*, 2H, *J* = 8.5, C_6H_5Me), 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, $C_6H_5NO_2$), 7.58 (*d*, 2H, *J* = 8.8, $C_6H_5NO_2$),

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

Compd	mp (°C)	Yield (%)	Formula	Analysis Calculated/Found (%) C	H	N	δ N=C*H*Ar (*s*) chain (**A**)	δ N-C*H*Ar-N (*s*) ring (**B**)
8a	179-181[b]	72	$C_{15}H_{14}N_4O_4$	57.32 57.07	4.49 4.38	17.83 17.65	8.33	5.61
8b	oil	~100	$C_{15}H_{14}N_4O_4$	57.32 –	4.49 –	17.83 –	8.32	5.62
8c	oil	~100	$C_{15}H_{14}N_3O_2Br$	51.74 –	4.05 –	12.07 –	8.18	5.48
8d	128-133[c]	69	$C_{15}H_{14}N_3O_2Br$	51.74 51.69	4.05 4.84	12.07 11.90	8.20	5.48
8e	140-143[c]	76	$C_{15}H_{14}N_3O_2Cl$	59.31 59.18	4.65 4.72	13.83 13.77	8.21	5.49
8f	oil	~100	$C_{15}H_{15}N_3O_2$	66.90 –	5.61 –	15.60 –	8.25	5.51
8g	109-110[c]	64	$C_{16}H_{17}N_3O_2$	67.83 67.94	6.05 7.82	14.83 14.69	8.21	5.47
8h	oil	~100	$C_{16}H_{17}N_3O_3$	64.20 –	5.72 –	14.04 –	8.17	5.46
8i	oil	~100	$C_{17}H_{20}N_4O_2$	65.37 –	6.45 –	17.94 –	8.08	5.39
9a	oil	~100	$C_{15}H_{14}N_3O_2Cl$	59.31 –	4.65 –	13.83 –	8.37	5.49
9b	oil	~100	$C_{15}H_{14}N_3O_2Cl$	59.31 –	4.65 –	13.83 –	8.36	5.49
9c	oil	~100	$C_{15}H_{14}N_2BrCl$	53.36 –	4.18 –	8.30 –	8.21	5.35
9d	oil	~100	$C_{15}H_{14}N_2BrCl$	53.36 –	4.18 –	8.30 –	8.23	5.35
9e	oil	~100	$C_{15}H_{14}N_2Cl_2$	61.45 –	4.81 –	9.55 –	8.24	5.36
9f	oil	~100	$C_{15}H_{15}N_2Cl$	69.63 –	5.84 –	10.83 –	8.29	5.39
9g	oil	~100	$C_{16}H_{17}N_2Cl$	70.45 –	6.28 –	10.27 –	8.25	5.36
9h	oil	~100	$C_{16}H_{17}N_2OCl$	66.55 –	5.93 –	9.70 –	8.22	5.35
9i	oil	~100	$C_{17}H_{20}N_3Cl$	67.65 –	6.68 –	13.92 –	8.16	5.32
11a	69-71[c]	55	$C_{16}H_{17}N_3O_2$	67.83 67.59	6.05 5.81	14.83 14.66	8.35	5.44
11b	74-75[d]	49	$C_{16}H_{17}N_3O_2$	67.83 67.95	6.05 6.10	14.83 14.79	8.35	5.44
11c	oil	~100	$C_{16}H_{17}N_2Br$	60.58 –	5.40 –	8.83 –	8.19	5.30
11d	72-74[c]	64	$C_{16}H_{17}N_2Br$	60.58 60.71	5.40 5.27	8.83 8.79	8.22	5.31

Table 3 (continued)

11e	58-61[d]	52	$C_{16}H_{17}N_2Cl$	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	$C_{17}H_{20}N_2O$	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	$C_{16}H_{17}N_3O_3$	64.20 –	5.72 –	14.04 –	8.36	5.39
12b	oil	~100	$C_{16}H_{17}N_3O_3$	64.20 –	5.72 –	14.04 –	8.28	5.39
12c	oil	~100	$C_{16}H_{17}N_2OBr$	57.67 –	5.14 –	8.41 –	8.21	5.26
12d	62-64[d]	48	$C_{16}H_{17}N_2OBr$	57.67 57.40	5.14 4.93	8.41 8.26	8.23	5.26
12e	51-53[d]	51	$C_{16}H_{17}N_2OCl$	66.55 66.34	5.93 5.86	9.70 9.71	8.24	5.27
12f	oil	~100	$C_{16}H_{18}N_2O$	75.56 –	7.13 –	11.01 –	8.28	5.28
12g	81-83[d]	55	$C_{17}H_{20}N_2O$	76.09 76.18	7.51 7.43	10.44 10.38	8.25	5.26
12h	58-60[d]	58	$C_{17}H_{20}N_2O_2$	71.81 71.64	7.09 6.81	9.85 9.78	8.21	5.25
12i	80-82[c]	60	$C_{18}H_{23}N_3O$	72.70 72.56	7.80 7.67	14.13 14.14	8.15	5.21
13a	79-81[d]	47	$C_{17}H_{20}N_4O_2$	65.37 –	6.45 –	17.94 –	8.35	5.37
13b	oil	~100	$C_{17}H_{20}N_4O_2$	65.37 –	6.45 –	17.94 –	8.34	5.37
13c	oil	~100	$C_{17}H_{20}N_3Br$	58.97 –	5.82 –	12.13 –	8.19	5.24
13d	89-91[d]	49	$C_{17}H_{20}N_3Br$	58.97 58.71	5.82 5.58	12.13 12.04	8.23	5.24
13e	82-85[c]	52	$C_{17}H_{20}N_3Cl$	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	$C_{18}H_{23}N_3O$	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]Analitical data were determined only for recrystallized new compounds. [b]Recrystallized from iPr_2O– EtOAc. [c]Recrystallized from *n*-hexane–iPr_2O. [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-C*H*), 3.68 (*ddd*, 1H, J = -8.5, 6.9, 3.8, 5-CH_2), 3.41 (*q*, 1H, J = 7.5, 5-CH_2), 3.29 (*ddd*, 1H, J = -11.6, 6.6, 3.5, 4-CH_2), 3.16 (*ddd*, 1H, J = -11.6, 7.5, 6.6, 4-CH_2), 2.23 (*s*, 3H, CH_3).

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