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Ring–Chain Tautomerism of 2-Aryl-substituted Imidazolidines

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Abstract. *N*-Methyl-, *N*-ethyl-, *N*-(*n*-propyl)-, *N*-(*iso*-propyl)- and *N*-phenyl-2-arylimidazolidines proved to be ring–chain tautomeric mixtures in $CDCl_3$. The ratios of the open and ring forms in the tautomeric equilibria of these compounds is described by the equation $\log K_X = \rho\sigma^+ + \log K_{X=H}$, used earlier for the ring–chain equilibria of saturated 2-aryl-1,3-*O,N*-heterocycles. These are the first examples among 2-arylimidazolidines of ring–chain tautomeric processes characterized by a Hammett-type correlation.

Keywords: imidazolidines; diamines; tautomerism; electronic and steric effects.

The structures and reactivities of numerous five- and six-membered, saturated, *N*-unsubstituted 1,3-*X,N*-heterocycles (*X* = *O, S, NR*) can be characterized by the ring–chain tautomeric equilibria of the 1,3-*X,N*-heterocycles and the corresponding Schiff bases.[1]

The oxazolidines and tetrahydro-1,3-oxazines are groups of saturated 1,3-*X,N*-heterocycles whose ring–chain tautomerism has been studied most thoroughly.[1-3] For 2-aryl-substituted derivatives of these types of compounds, a clear-cut correlation was found between the log K_X values of the equilibria (K_X = [ring]/[chain]) and the Hammett–Brown constants σ^+ of the substituents on the 2-aryl group. The ring–chain tautomerism of these compounds could be described by Equation (1) in both the liquid and gas phases:[2-4]

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

In contrast, ring–chain tautomeric processes in the corresponding 1,3-*N,N*-heterocycles have been observed only in special cases.[1,5-9] Very little is known concerning the effect of the substituents on the tautomeric equilibria of these compounds.[10-15] Therefore, our aim was to investigate the scope and limitations of Equation (1) by studying the ring–chain tautomerism of some 2-aryl-substituted 1-alkyl- and 1-phenyl-imidazolidines.

Model compounds **6-10** were prepared by the reactions of *N*-methyl- (**1**), *N*-ethyl- (**2**), *N*-(*n*-propyl)- (**3**), *N*-(*iso*-propyl)- (**4**) and *N*-phenylethylenediamine (**5**) with equivalent amounts of substituted benzaldehydes (Scheme 1). The ^{1}H NMR spectra of **6-10** revealed that all of these compounds (except **9i**, in which no ring form could be detected) participated in a ring–chain equilibrium in $CDCl_3$ solution.

The ratios of the concentrations of the ring and chain forms for the tautomeric equilibria (log K_X), determined by integration of the well-separated N-C*H*Ar-N (ring) and N=C*H* (chain) proton singlets, seemed

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The equilibria of imidazolidines **6-10** in $CDCl_3$ involve a considerable amount of the ring form, despite the 5-*endo-trig* ring-closure process of the tautomeric forms (**A** → **B**) according to Baldwin's rules.[17] A comparison of the intercepts (the c value is the difference in intercepts of the given 2-arylimidazolidine and the parent unsubstituted 2-aryloxazolidine[3]) reveals that the ratios of the ring forms in the tautomeric equilibria of *N*-methyl-, *N*-ethyl-, *N*-(*n*-propyl)- and *N*-phenylimidazolidines are markedly higher than those for oxazolidines. The steric effect of the α-carbon of the *N*-substituent plays a crucial role in the addition of the NHR group to the C=N bond. An increase in the steric requirement of the *N*-substituent, *i.e.* the number of methyl groups on the carbon adjacent to the nitrogen (*N*-Me → *N*-Et → *N*-*i*Pr), decreased the ratio of the ring forms in the tautomeric equilibria. However, introduction of a methyl group onto the β-carbon of the *N*-substituent (*N*-Et → *N*-*n*Pr) did not significantly influence the intercept values.

The above results indicate that the electronic effect of the substituent on the 2-aryl group definitively determines the ratio of ring and open-chain tautomers in all series of imidazolidines **6-10**. The ring–chain ratios are influenced not only by the substituent *X* on the aromatic ring, but also by the substituent on the *N* atom of the imidazolidine ring. The proportion of the ring form increases in the following sequence of *N*-substituents: *i*Pr < Ph < *n*Pr ≈ Et < Me. Efforts to elucidate the electronic effects of the substituents on the *N*-phenyl group on the tautomeric equilibria of 2-arylimidazolidines 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 $CDCl_3$ or in DMSO-d_6 containing 0.03% TMS as reference. For the equilibria to be established,[18] 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 **6-10** are listed in Table 3.

General method for the synthesis of 2-arylimidazolidines

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 benzene. 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. All of the recrystallized new compounds (**10b,d,g-i**) gave satisfactory data on elemental analysis (C, H, N ±0.3%).

*NMR spectroscopic data on the aliphatic protons of 2-(*p*-bromophenyl) derivatives* **6d-10d** *in* $CDCl_3$

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

6Ad: 8.28 (*s*, 1H, N=C*H*), 3.72 (*t*, 2H, *J* = 6.0, 4-CH_2), 2.91 (*t*, 2H, *J* = 6.0, 5-CH_2), 2.47 (*s*, 3H, NCH_3); **6Bd**: 3.86 (*s*, 1H, 2-C*H*), 3.32 (*ddd*, 1H, *J* = -16.4, 7.7, 2.5, 5-CH_2), 3.24 (*dd*, 1H, *J* = -8.0, 7.7, 4-CH_2), 3.08 (*ddd*, 1H, *J* = -8.0, 8.0, 2.5, 4-CH_2), 2.44 (*dd*, 1H, *J* = 16.4, 8.0, 5-CH_2), 2.20 (*s*, 3H, NCH_3).

7Ad: 8.28 (*s*, 1H, N=C*H*), 3.75 (*t*, 2H, *J* = 5.6, 4-CH_2), 2.96 (*t*, 2H, *J* = 5.6, 5-CH_2), 2.70 (*q*, 2H, *J* = 7.3, CH_2CH$_3$), 1.11 (*t*, 3H, *J* = 7.3, CH$_2$CH_3); **7Bd**: 4.00 (*s*, 1H, 2-C*H*), 3.40 (*dt*, 1H, *J* = -8.2, 3.2, 5-CH_2), 3.25 (*dt*, 1H, *J* = -10.7, 8.2, 4-CH_2), 3.09 (*ddd*, 1H, *J* = -10.7, 8.2, 3.2, 4-CH_2), 2.55 (*dq*, 1H, *J* = -11.8, 7.3, CH_2CH$_3$), 2.38 (*q*, 1H, *J* = 8.2, 5-CH_2), 2.18 (*dq*, 1H, *J* = -11.8, 7.3 CH_2CH$_3$), 1.05 (*t*, 3H, *J* = 7.3 CH$_2$CH_3).

8Ad: 8.28 (*s*, 1H, N=C*H*), 3.75 (*t*, 2H, *J* = 5.8, 4-CH_2), 2.95 (*t*, 2H, *J* = 5.8, 5-CH_2), 2.62 (*t*, 2H, *J* = 7.3, CH_2CH$_2$CH$_3$); 1.5 (*om*, 2H, CH$_2$CH_2CH$_3$), 0.91 (*t*, 3H, *J* = 7.5, CH$_2$CH$_2$CH_3); **8Bd**: 4.00 (*s*, 1H, 2-C*H*), 3.37 (*om*, 1H, 4-CH_2) 3.24 (*om*, 1H, 5-CH_2), 3.09 (*om*, 1H, 4-CH_2), 2.39 (*om*, 2H, CH_2CH$_2$CH$_3$), 2.13 (*om*, 1H, 5-CH_2), 1.45 (*om*, 2H, CH$_2$CH_2CH$_3$), 0.86 (*t*, 3H, *J* = 7.5, CH$_2$CH$_2$CH_3).

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10Ad: 8.23 (*s*, 1H, N=C*H*), 3.83 (*t*, 2H, *J* = 5.5, 4-CH_2), 3.47 (*t*, 2H, *J* = 5.5, 5-CH_2); **10Bd**: 5.35 (*s*, 1H, 2-C*H*), 3.24 (*om*, 2H, 4-CH_2); 3.45 (*m*, 1H, 5-CH_2), 3.63 (*om*, 1H, 5-CH_2).

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Table 3. Physical data on imidazolidines **6-10**

Compd.	M.p. (°C)	Formula	M.W.	δ N=C*H*Ar chain (**A**)	δ N-C*H*Ar-N ring (**B**)
6a	37-39[a,b]	$C_{10}H_{13}N_3O_2$	207.23	8.42	4.07
6b	oil	$C_{10}H_{13}N_3O_2$	207.23	8.41	4.08
6c	oil	$C_{10}H_{13}N_2Br$	241.14	8.26	3.88
6d	oil	$C_{10}H_{13}N_2Br$	241.14	8.28	3.86
6e	oil[c]	$C_{10}H_{13}N_2Cl$	196.68	8.23	3.66
6f	oil	$C_{10}H_{14}N_2$	162.24	8.32	3.87
6g	oil[c]	$C_{11}H_{16}N_2$	176.26	8.29	3.84
6h	oil[c]	$C_{11}H_{16}N_2O$	192.26	8.25	3.89
6i	oil[c]	$C_{12}H_{19}N_3$	205.31	8.17	3.76
7a	oil	$C_{11}H_{15}N_3O_2$	221.26	8.40	4.20
7b	oil	$C_{11}H_{15}N_3O_2$	221.26	8.56	4.22
7c	oil	$C_{11}H_{15}N_2Br$	255.17	8.26	4.02
7d	oil	$C_{11}H_{15}N_2Br$	255.17	8.28	4.00
7e	oil	$C_{11}H_{15}N_2Cl$	210.71	8.28	3.76
7f	oil	$C_{11}H_{16}N_2$	176.26	8.34	4.02
7g	oil	$C_{12}H_{18}N_2$	190.29	8.29	3.96
7h	oil	$C_{12}H_{18}N_2O$	206.29	8.26	3.95
7i	oil	$C_{13}H_{21}N_3$	219.33	8.20	3.69
8a	oil	$C_{12}H_{17}N_3O_2$	235.29	8.42	4.22
8b	oil	$C_{12}H_{17}N_3O_2$	235.29	8.58	4.23
8c	oil	$C_{12}H_{17}N_2Br$	269.19	8.26	4.02
8d	oil	$C_{12}H_{17}N_2Br$	269.19	8.28	4.00
8e	oil	$C_{12}H_{17}N_2Cl$	224.74	8.29	4.01
8f	oil	$C_{12}H_{18}N_2$	190.29	8.33	4.01
8g	oil	$C_{13}H_{20}N_2$	204.32	8.29	3.97
8h	oil	$C_{13}H_{20}N_2O$	220.32	8.26	3.95
8i	oil	$C_{14}H_{23}N_3$	233.36	8.20	3.69
9a	oil	$C_{12}H_{17}N_3O_2$	235.29	8.42	4.62
9b	oil	$C_{12}H_{17}N_3O_2$	235.29	8.58	4.63
9c	oil	$C_{12}H_{17}N_2Br$	269.19	8.26	4.43
9d	oil	$C_{12}H_{17}N_2Br$	269.19	8.28	4.42
9e	oil	$C_{12}H_{17}N_2Cl$	224.74	8.28	4.42
9f	oil	$C_{12}H_{18}N_2$	190.29	8.34	4.43
9g	oil	$C_{13}H_{20}N_2$	204.32	8.30	4.38
9h	oil	$C_{13}H_{20}N_2O$	220.32	8.26	4.36
9i	oil	$C_{14}H_{23}N_3$	233.36	8.20	3.84
10a	oil	$C_{15}H_{15}N_3O_2$	269.31	8.36	5.49
10b	66-71[d]	$C_{15}H_{15}N_3O_2$	269.31	8.35	5.49
10c	oil	$C_{15}H_{15}N_2Br$	303.21	8.19	5.34
10d	64-66[a]	$C_{15}H_{15}N_2Br$	303.21	8.23	5.35
10e	oil	$C_{15}H_{15}N_2Cl$	258.75	8.27	5.41
10f	oil	$C_{15}H_{16}N_2$	224.31	8.28	5.39
10g	60-62[a]	$C_{16}H_{18}N_2$	238.34	8.25	5.37
10h	31-33[a]	$C_{16}H_{18}N_2O$	254.34	8.21	5.35
10i	88-89[a]	$C_{17}H_{21}N_3$	267.38	8.18	5.35

[a]Recrystallized from *n*-hexane. [b]Lit.[13] m.p. 39-40 °C. [c]Lit.[19] oil. [d]Recrystallized from iPr_2O–EtOAc.

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