The hydrolysis of 4-amino- and 4-dimethylaminobenzene sulfonyl chlorides: an unprecedented case of independence of reactivity from pH

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General. Starting solvents and reagents were of analytical reagent grade or were redistilled or recrystallized from bench quality materials. Deionized water was distilled from glass and preboiled prior to use to free it from dissolved carbon dioxide. Dioxane (Fluka, UV spectroscopic grade) was dried and freed from peroxides by passage through an activated alumina column, and the absence of peroxides was assessed by the KI test. UV-Vis spectra were recorded with a Kontron Uvikon 941 spectrophotometer.

Materials. Literature methods were followed for the synthesis of 4-aminobenzenesulfonyl chloride **1** and the corresponding hydrochloride **1·HCl**¹, 4-aminobenzenesulfonyl fluoride **2**², and 4-dimethylaminobenzenesulfonyl chloride **4**³. Purity was assessed by measuring their m.p.s: **1·HCl**: m.p. 236-238 °C (decomp.), (lit. 238 °C, decomp.)¹ (compound **1** does not possess a distinct melting point as it undergoes polymerization on heating; its I.R. spectrum, however was identical to that reported by previous authors¹), **2**: m.p. 70-71 °C (lit. 70)², **4**: m.p. 109 – 110 °C (lit. 109.5 – 111.0).³ All compounds gave ¹H N.M.R. spectra fully consistent with their structures. As seen in preliminary experiments, chloride **1** and its hydrochloride **1·HCl**, as expected, at given pH showed the same reactivity. As **1·HCl** is far more stable than **1** (it can be stored unaltered in a dessiccator for long periods of time, and stock dioxane solutions of it are quite stable as well), in most experiments it was employed instead of the free base.

Kinetic measurements. In the case of the least reactive sulfonyl fluoride **2**, kinetic measurements were performed with the Kontron Uvikon 941 spectrophotometer; the same machine equipped with a SFA-11 Rapid Kinetic accessory (HI-TEC SCIENTIFIC Ltd.) was employed to follow the hydrolyses of the more reactive chlorides **1** and **4** in 20% aqueous dioxane; very fast hydrolysis of the chloride **1** in water solvent was followed by means of a stopped-flow apparatus equipped with a parallel diode-array detector.

When the standard kinetic technique was used (as in the case of chloride **2**), the buffered solution (2.5 mL) was equilibrated to the required temperature (± 0.1 °C) in a 1-cm path-length quartz cell placed in the thermostated cell holder of the Kontron Uvikon spectrophotometer. The reaction was initiated by adding 25 or 50 μ L of a stock solution of the substrate ca. 0.01 M in dioxane to the buffer, and automated acquisition of 50-200 data points for each kinetic run was performed. In all cases at least three different buffer concentrations, at constant pH, were employed. The ionic strength was kept at 1.0 M with KCl. The pH of the buffered solutions were measured before and after each kinetic run using a Ross combined electrode, calibrated with standard buffers. All pH values quoted for the dioxane-water solutions are relative values measured directly, no further corrections being applied. The pseudo-first-order rate constants (k_{obs}) were obtained by NLLSQ fitting of absorbance vs time data,⁴ and the values reported in Table S2 are the averages of at least duplicate runs.

Reactions were normally followed over about eight half-lives. The rate constants for the hydrolysis of **2** at pH values below 12 were obtained by initial rates: they were measured for each run up to ca. 10% of

the total reaction and were converted to pseudo-first-order rate constants using infinity values calculated from the known extinction coefficients of the products.

Kinetic experiments for the fast reactions of sulfonyl chlorides **1** and **4** in 20% aqueous dioxane solvent were carried out with the Kontron Uvikon instrument equipped with the SFA-11 Rapid Kinetic accessory. Temperature control was ensured by injecting the pre-thermostatted solutions into the flow cell inserted into the thermostatted cell holder of the spectrophotometer. Rate constants were assessed by following the absorbance decrease at 309 nm, due to the disappearance of the substrates.⁴

Kinetic experiments for the very fast reactions of chloride **1** in water solvent were run on the diode-array stopped-flow apparatus. Reaction course was followed monitoring the disappearance of the substrate absorption band in the 270 - 340 nm interval, whilst rate constants were obtained from the decrease of absorbance at a single, selected wavelength in the range 295.5 – 320.5 nm. Temperature control was assured by the mixing device of the apparatus, consisting of a SF-3L Hi-Tech support unit. Calculations were carried out by means of the SPECFIT program.

References

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- (3) Sukenik, C.N.; Bonapace, J.A.P.; Mandel, N.S.; Pui-Yan Lau, Wood, G.; Bergman, R. G. *J. Am. Chem. Soc.* **1977**, 99, 851 – 858.
- (4) The values of the kinetic parameters, as well as the pK_a values, were obtained from primary kinetic data by iterative nonlinear curve-fitting performed with the Fig.P program (Biosoft, Cambridge, UK).
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Table S1. Hydrolysis of 4-aminobenzenesulfonyl chloride. Solvent water, ionic strength = 1 N (kept constant with KCl); $t = (25.0 \pm 0.1) ^\circ\text{C}$; stopped flow kinetics; analytical wavelength 308.5 nm.

Buffer	pH	$k_{\text{obs}} \text{ (s}^{-1}\text{)}$	$\log k_{\text{obs}}$
KOH 0.1 N	13.00	81.5 ± 6.0	1.91
KOH 0.05 N	12.70	52.1 ± 4.0	1.72
KOH 0.01 N	12.00	9.65 ± 0.50	0.98
KOH 0.005 N	11.70	7.80 ± 0.20	0.89
Carbonate	9.75	5.20 ± 0.20	0.72
Citrate	6.00	6.60 ± 0.20	0.82
HCl 0.001 N	3.00	4.50 ± 0.10	0.65
HCl 0.01 N	2.00	4.50 ± 0.20	0.65
HCl 0.05 N	1.30	4.55 ± 0.20	0.66
HCl 0.1 N	1.00	4.10 ± 0.20	0.61
HCl 1 N	0.00	0.90 ± 0.10	-0.05

Derived parameters (FigP) are: $k_a = (5.17 \pm 0.40) \text{ s}^{-1}$; $k_b = (740 \pm 90) \text{ M}^{-1}\text{s}^{-1}$; $\text{p}K_a = 0.64 \pm 0.10$

Table S2. Hydrolysis of 4-aminobenzenesulfonyl fluoride. Solvent water, ionic strength = 1 N (kept constant with KCl); $t = (25.0 \pm 0.1)^\circ\text{C}$; analytical wavelength: 275 nm.

Buffer	pH	$k_{\text{obs}} (\text{s}^{-1})$	$-\log k_{\text{obs}}$
KOH 0.0984 N	12.99	$3.56 \cdot 10^{-2}$	1.449
KOH 0.0738 N	12.87	$2.84 \cdot 10^{-2}$	1.547
KOH 0.0492 N	12.69	$1.93 \cdot 10^{-2}$	1.714
KOH 0.0246 N	12.39	$1.04 \cdot 10^{-2}$	1.983
KOH 0.01 N	12.00	$3.47 \cdot 10^{-3}$	2.460
carbonate	10.06	$4.42 \cdot 10^{-5}$	4.355
phosphate	8.02	$5.30 \cdot 10^{-7}$	6.278

Derived parameters (FigP) are: $k_{\text{OH}} = (3.67 \pm 0.11) \cdot 10^{-1} \text{ M}^{-1} \text{ s}^{-1}$

Table S3. Hydrolysis of 4-aminobenzenesulfonyl chloride. Solvent 20% aqueous dioxane (v/v), ionic strength = 1 N (kept constant with KCl); $t = (25.0 \pm 0.1) ^\circ\text{C}$; stopped flow kinetics; analytical wavelength range 250 – 330 nm; $\text{p}K_{\text{w}} = 14.51^{\text{a}}$

Buffer	pH	$k_{\text{obs}} \text{ (s}^{-1}\text{)}$	$\log k_{\text{obs}}$
KOH 0.01 N	12.51	2.73 ± 0.10	-0.436
KOH 0.005 N	12.21	1.73 ± 0.03	-0.238
phosphate	11.64	1.15 ± 0.14	-0.061
carbonate	10.38	0.65 ± 0.03	0.194
ammonia	9.38	0.57 ± 0.10	0.244
phosphate	6.96	0.64 ± 0.03	0.194
citrate	5.00	0.67 ± 0.02	0.171
citrate	4.55	0.57 ± 0.05	0.244
HCl 0.01 N	2.10	0.61 ± 0.01	0.218
HCl 0.05 N	1.40	0.58 ± 0.01	0.237
HCl 0.1 N	1.10	0.57 ± 0.01	0.243
HCl 0.5 N	0.40	0.47 ± 0.01	0.327
HCl 1 N	0.10	0.40 ± 0.01	0.402

(a) Value is from Ref. 5.

Derived parameters (FigP) are: $k_{\text{a}} = (0.62 \pm 0.02) \text{ s}^{-1}$; $k_{\text{b}} = (318 \pm 27) \text{ M}^{-1}\text{s}^{-1}$

Table S4. Hydrolysis of 4-dimethyaminobenzenesulfonyl chloride. Solvent 20% aqueous dioxane (v/v), ionic strength = 1 N (kept constant with KCl); $t = (25.0 \pm 0.1)^\circ\text{C}$; stopped flow kinetics; analytical wavelength range 250 – 330 nm; $\text{p}K_w = 14.51^{\text{a}}$

Buffer	pH	$k_{\text{obs}} (\text{s}^{-1})$	$\log k_{\text{obs}}$
KOH 1 N	14.51	2.78 ± 0.09	0.444
KOH 0.1 N	13.51	2.52 ± 0.23	0.401
KOH 0.01 N	12.51	2.47 ± 0.08	0.393
carbonate	10.31	2.39 ± 0.15	0.397
ammonia	9.38	2.37 ± 0.16	0.375
phosphate	6.93	2.36 ± 0.13	0.373
citrate	5.17	2.54 ± 0.09	0.405
HCl 0.001 N	3.10	2.27 ± 0.07	0.356
HCl 0.01 N	2.10	2.36 ± 0.16	0.373
HCl 0.1 N	1.10	2.46 ± 0.26	0.391
HCl 1 N	0.10	2.52 ± 0.16	0.401
HCl 2.4 N ^b	-0.278	1.11 ± 0.02	0.041

(a) Value is from Ref. 5

(b) This value is not shown in Figure 1 because ionic strength was $\neq 1$ M (see text)

Derived parameters (FigP) are: $k_a = (2.46 \pm 0.04) \text{ s}^{-1}$

Table S5. Rate data for calculation of activation parameters^a for the hydrolysis of 4-aminobenzenesulfonyl chloride in 20% aqueous dioxane (v/v); ionic strength = 1 M (KCl); stopped flow kinetics; analytical wavelength range 250 – 330 nm.

pH	t (°C)	k_{obs} (s ⁻¹)	
6.95 ^b	17.1	0.38 ± 0.03	
	25.0	0.64 ± 0.03	$\Delta H^\ddagger = (44.5 \pm 0.2) \text{ kJ mol}^{-1}$;
	34.9	1.17 ± 0.10	$\Delta S^\ddagger = (-99.6 \pm 0.6) \text{ J K}^{-1} \text{ mol}^{-1}$
12.21 ^c	16.9	0.94 ± 0.10	
	25.0	1.73 ± 0.03	$\Delta H^\ddagger = (46.00 \pm 2.22) \text{ kJ mol}^{-1}$
	34.0	2.88 ± 0.30	$\Delta S^\ddagger = (-86.6 \pm 7.5 \text{ J K}^{-1} \text{ mol}^{-1})$

(a) $\Delta S^\ddagger$ values were calculated at 25 °C

(b) phosphate buffer

(c) 0.005 M KOH

Figure S1. Hydrolysis of 4-aminobenzenesulfonyl chloride **1**, initial concentration 2.5×10^{-5} M. Solvent water, pH 11.70 (KOH), ionic strength 1M (KCl), temperature (25 ± 0.1) °C. “Zero time” (upper curve) and “infinity” (lower curve) spectra are shown.

Figure S2. Absorbance vs. time plots (experimental and theoretical) for the hydrolysis of 4-aminobenzenesulfonate **1**. Analytical wavelengths 295.0 and 320.5 nm. Other conditions are the same as those given in Figure S1.

Figure S3. Hydrolysis of 4-aminobenzenesulfonyl chloride **1**, initial concentration 2.5×10^{-5} M. Solvent water, pH 1.30 (HCl), ionic strength 1M (KCl), temperature (25 ± 0.1) °C. “Zero time” (upper curve) and “infinity” (lower curve) spectra are shown.

Figure S4. Absorbance vs. time plots (experimental and theoretical) for the hydrolysis of 4-aminobenzenesulfonate **1**. Analytical wavelength 292.5 nm. Other conditions are the same as those given in Figure S3.

Figure S5. Hydrolysis of 4-aminobenzenesulfonyl chloride **1**, initial concentration 2.5×10^{-5} M. Solvent water, pH 3.00 (HCl), ionic strength 1M (KCl), temperature (25 ± 0.1) °C. “Zero time” (upper curve) and “infinity” (lower curve) spectra are shown.

Figure S6. Absorbance vs. time plots (experimental and theoretical) for the hydrolysis of 4-aminobenzenesulfonyl chloride **1**. Analytical wavelengths 305.0 and 306.5 nm. Other conditions are the same as those given in Figure S5.

Figure S7. Absorbance vs. time plot for the hydrolysis of 4-aminobenzenesulfonyl fluoride **2**. Solvent water, pH = 10.06 (carbonate buffer), ionic strength 1.0 M (KCl), temperature (25 ± 0.1) °C, analytical wavelength 275 nm.

Figure S8. Absorbance vs. time plot for the hydrolysis of 4-aminobenzenesulfonyl chloride **1**. Solvent 20% aqueous dioxane, pH = 12.51 (KOH), ionic strength 1.0 M (KCl), $pK_w = 14.51$, temperature $(25 \pm 0.1)^\circ\text{C}$, analytical wavelength 309 nm.

Figure S9. Absorbance vs. time plot for the hydrolysis of 4-aminobenzenesulfonyl chloride **1**. Solvent 20% aqueous dioxane, pH = 6.96 (phosphate buffer), ionic strength 1.0 M (KCl), $pK_w = 14.51$, temperature $(25 \pm 0.1)^\circ\text{C}$, analytical wavelength 309 nm.

Figure S10. Absorbance vs. time plot for the hydrolysis of 4-aminobenzenesulfonyl chloride **1**. Solvent 20% aqueous dioxane, pH = 11.64 (phosphate buffer), ionic strength 1.0 M (KCl), $pK_w = 14.51$, temperature $(25 \pm 0.1)^\circ\text{C}$, analytical wavelength 309 nm.

Figure S11. Absorbance vs. time plot for the hydrolysis of 4-dimethylaminobenzenesulfonyl chloride **4**. Solvent 20% aqueous dioxane, pH = 13.51 (KOH), ionic strength 1.0 M (KCl), $pK_w = 14.51$, temperature $(25 \pm 0.1)^\circ\text{C}$, analytical wavelength 309 nm.

Figure S12. Absorbance vs. time plot for the hydrolysis of 4-dimethylaminobenzenesulfonyl chloride **4**. Solvent 20% aqueous dioxane, pH = 6.93 (phosphate buffer), ionic strength 1.0 M (KCl), $pK_w = 14.51$, temperature $(25 \pm 0.1)^\circ\text{C}$, analytical wavelength 309 nm.