# Kinetic Evidence for Hypervalent Intermediate in Acid Hydrolysis of N-Arylbenzenesulfinamides

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Nucleophilic substitution reactions of sulfinic acid derivatives occur with predominent inversion of configuration at sulfur.[1] These results are mainly interpreted by an addition elimination mechanism with a trigonal bipyramidal reaction intermediate (sulfurane) and a concerted $S_N2$ displacement mechanism.[1,2]

The isolation of stabilized bicyclic sulfuranes suggests that these species may form as intermediates in nucleophilic substitution reactions of sulfinic acid derivatives.[3] However, despite continuing efforts, there are very rare definitive experiments to demonstrate the formation of these intermediates.

Some years ago,[4] we reported acid catalyzed hydrolysis of some simple sulfinamides. In this report, we found downward breaks in the pH-rate profile for acid catalyzed hydrolysis of sulfinamides having electron donating group in the leaving group, aniline. These data provided the first unequivocal evidence that nucleophilic substitution reaction at sulfinyl sulfur may proceed by a two-step mechanism through a hypervalent reaction intermediate.

In this study, we have extended our study to identify the hypervalent intermediate in acid catalyzed reactions of sulfinamides having halide or more stronger electron donating group in the leaving group or the sulfinyl group. So, we have performed the acid catalyzed hydrolyses of N-(3-methyl-5-methoxyphenyl)-benzenesulfinamide (**1-a**), N-(tolyl)-toluenesulfinamide (**1-b**), N-(4-fluorophenyl)-toluenesulfinamide (**1-c**), N-(4-ethylphenyl)-benzenesulfinamide (**1-d**) and N-(4-fluorophenyl)-benzenesulfinamide (**1-e**).

## Experimental Section

**Materials.** All materials and solvents for synthesis of the substrates were purchased from Aldrich or Tokyo Kasei. Acid solution were prepared from concentrated acid (60% $HClO_4$) and titrated with standard NaOH solution. Water used for acidic solutions was freed from $CO_2$ by boiling deionized water under a nitrogen gas. All organic solvents were purified by the well known methods.[5]

N-arylbezenesulfinamides were prepared by addition of sulfinyl chloride to appropriate amines as previously described.[6] Benzenesulfinyl chloride was obtained by purging chlorine gas to reaction mixtures of 0.1mol diphenyldisulfide and 0.2 mol acetic anhydride at 0 °C ~ −10 °C. Byproducts, acetylchloride and excess chlorine were removed by heating to 50 °C under reduced pressure (15 mmHg). N-arylbezenesulfinamides synthesized were purified by the method of either a silica gel column chromatography or recrystallization and identified by spectral data as follows.

**N-(3-Methyl-5-methoxyphenyl)-benzenesulfinamide (1-a):** pale green solid; m.p. 89-91 °C; Rf = 0.1 (hexane/ethylacetate/2/1); FT-IR (KBr, cm⁻¹), 3438 (N-H), 1305 (S=O); ¹H NMR (200 MHz, CDCl₃), δ 2.27 (s, 3H), 3.77 (s, 3H), 5.89 (s, 1H), 6.56 (d, 1H), 6.93 (s, 1H), 7.03 (d, 1H), 7.56-7.40 (m, 3H), 7.69-7.71 (m, 2H); Mass (m/z), 259 (M⁺).

**N-(Tolyl)-toluenesulfinamide (1-b):** white solid (recrystallization from ether); m.p. 117-119 °C (lit.,[7] 118-120 °C); Mass (m/z), 245 (M⁺).

**N-(4-Fluorophenyl)-toluenesulfinamide (1-c):** yellow solid; m.p. 115-117 °C; Rf = 0.4 (hexane/ethylacetate/2/1); FT-IR (KBr, cm⁻¹), 3220 (N-H), 1325 (S=O); ¹H NMR (200 MHz, CDCl₃), δ 2.43 (s, 3H), 5.90 (s, 1H), 6.93-6.97 (m, 2H), 7.02-7.06 (m, 2H), 7.31-7.35 (m, 2H), 7.36-7.67 (m, 2H); Mass (m/z): 249 (M⁺).

**N-(4-Ethylphenyl)-benzenesulfinamide (1-d):** pale yellow solid; m.p. 116-118 °C; Rf = 0.5 (hexane/ethylacetate/2/1); FT-IR (KBr, cm⁻¹), 3434 (N-H), 1290 (S=O); ¹H NMR (200 MHz, CDCl₃), δ 1.19 (t, J = 4.3, 3H), 2.60 (q, J = 7.5, 2H), 6.21 (s, 1H), 7.05-7.10 (m, 2H), 7.30-7.33 (m, 3H), 7.52-7.56 (m, 2H), 7.71-7.76 (m, 2H); Mass (m/z), 245 (M⁺).

**N-(4-Fluorophenyl)-benzenesulfinamide (1-e):** brown solid; m.p. 103-105 °C; Rf = 0.4 (hexane/ethylacetate/2/1); FT-IR (KBr, cm⁻¹), 3446 (N-H), 1375 (S=O); ¹H NMR (200 MHz, CDCl₃), δ 6.02 (s, 1H), 6.97-7.01 (m, 2H), 7.02-7.05 (m, 2H), 7.52-7.55 (m, 3H), 7.75-7.77 (m, 2H); Mass (m/z), 234 (M⁺-H).

**Kinetics.** The rates for acid catalyzed hydrolysis were measured spectrophotometerically in aqueous perchloric acid at the constant ionic strength of 0.1 M with NaClO₄ in the concentration range from $5.0 \times 10^{-2}$ to $1.0 \times 10^{-4}$ mol dm⁻³ at 25 ± 0.1 °C by following the decrease in absorbance due to disappearance of the substrates at wavelengths in the range of 246-254 nm.

**Table 1**. Catalytic rate constants for acid catalyzed hydrolysis of the various *N*-arylbenzenesulfinamides ($XC_6H_4S(O)NHAr$) at 25 °C and ionic strength 0.1 M with $NaClO_4$

| | Substrates | | $k_H$ ($M^{-1}s^{-1}$) | |
|---|---|---|---|---|
| No. | X | Ar | pH > 3 | pH < 3 |
| **1-a** | H | 2-CH$_3$, 5-CH$_3$OC$_6$H$_3$ | 2.77 (r = 0.9962) | 1.84 (r = 0.9996) |
| **1-b** | *p*-CH$_3$ | *p*-CH$_3$C$_6$H$_4$ | 1.49 (r = 0.9994) | 0.712 (r = 0.9988) |
| **1-c** | *p*-CH$_3$ | *p*-FC$_6$H$_4$ | 3.33 (r = 0.9965) | 1.63 (r = 0.9969) |
| **1-d** | H | *p*-C$_2$H$_5$C$_6$H$_4$ | 1.29$^a$ (r = 0.9992) | |
| **1-e** | H | *p*-FC$_6$H$_4$ | 0.958$^a$ (r = 0.9994) | |

$^a$The values were calculated at the whole pH range (pH 1.3-4.0). Standard deviations of all $k_H$ values are between $9.29 \times 10^{-3}$ and $4.25 \times 10^{-2}$.

The rate measurements were carried out using a Hewlett Packard 8452 Diode Array Spectrophotometer equipped with a Shimadzu TB-85 thermo bath to keep the temperature of the reaction mixture at 25 °C ± 0.1 °C. Typically, kinetic run was initiated by injecting 30 $\mu$L of $1.0 \times 10^{-2}$ M stock solution of the substrate dissolving in acetonitrile into 3.0 mL of aqueous perchloric acid solution.

The catalytic rate constants were obtained from plot of rate constant versus concentration of acid. pH values of reaction mixtures were measured at 25 °C with a DP-215M Dong-Woo meter.

### Results and Discussion

The acid catalyzed hydrolysis reactions were carried out under pseudo first order conditions. The observed rate constants ($k_{obs}$) were obtained from 89532 K Kinetic Software (serial No. 325 G00380) of the Hewlett Packard company which was based on the slope value of the plot of $\ln(A_o-A_t)$ vs. time. The observed rate constants for the acid
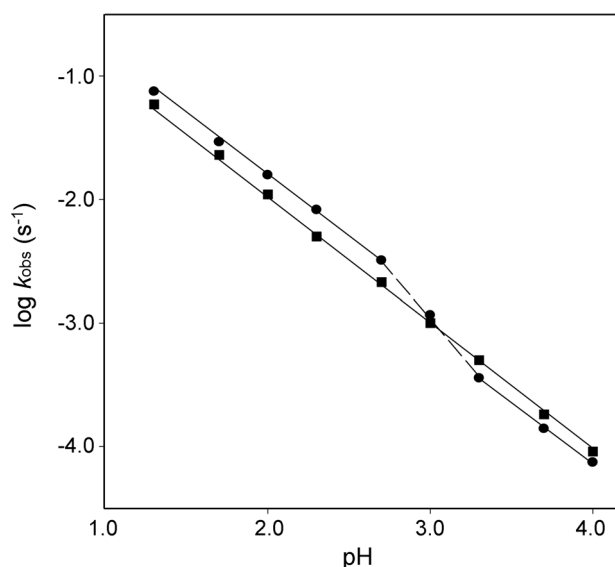


**Figure 1**. pH-rate profiles for acid catalyzed hydrolyses of *N*-(tolyl)-toluenesulfinamide (1-b: ● ) and *N*-(4-fluorophenyl)-benzenesulfinamide (1-e: ■ ) at 25 °C and the ionic strength of 0.1 M with $NaClO_4$.

catalyzed reaction of all compounds are proportional to acid concentration with a slope of −1.0 in the pH range 1.3-4.0. Therefore, the observed rate constant ($k_{obs}$) is given by equation (1), where $k_H$ is the catalytic rate constant of hydronium ion.

$$k_{obs}= k_H [H_3O^+] \tag{1}$$

The catalytic rate constants are listed in Table and the pH-rate profiles are presented in Figure.

The pH rate profile of the compound (**1-e**) shows a straight line with increasing concentration of acid, while that for the substrate (**1-b**) having electron donating group in benzene-sulfinyl group and leaving group appears a break at around pH 3.0. A similar break was also observed for the substrates (**1-a**) and (**1-c**) but not for the substrate (**1-d**).

These results are accommodated with reaction mechanism
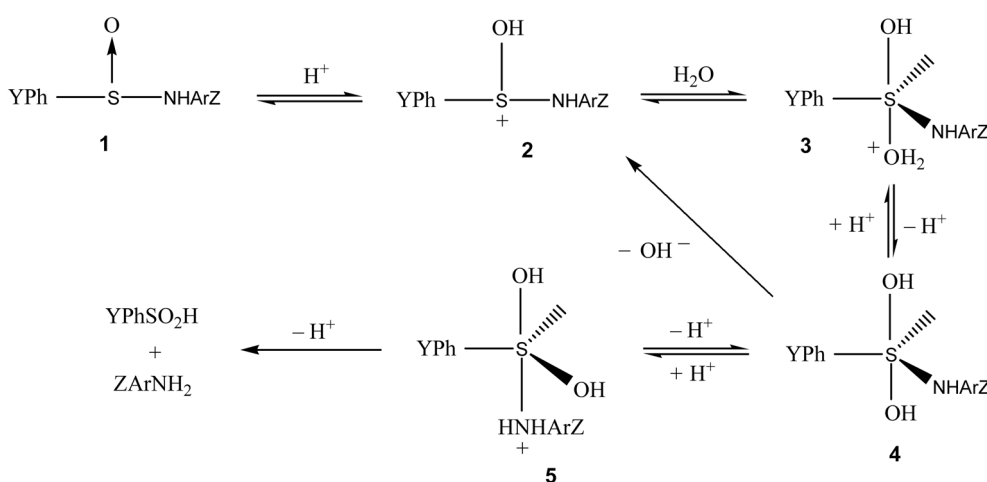


**Scheme 1**

involving hypervalent intermediates as shown in Scheme 1; *i.e.*, a change over of the rate determining step occurs at around pH 3 for the substrates (**1-a**), (**1-b**) and (**1-c**). In Scheme **1**, the first protonation to the substrate occurs at sulfinyl oxygen atom from the previous observation for which the substrate undergoes [18]O isotope exchange during hydrolysis.[4] And then, the intermediates are in various forms of configuration and of protonation. Among the protonated forms, **3** returns to the reactant, **2** by giving away $H_2O$, while the *N*-protonated form, **5** goes to the product by expelling aniline.

In the hydrolyses of (**1-a**), (**1-b**) and (**1-c**), the rate determining step at the lower pH should be the formation of the intermediate, since the greater fraction of the protonated intermediate is in the form of **5** because of higher basicity of the amine fraction as compared with the case of the substrates, (**1-d**) and (**1-e**), having ethyl and fluoro substituents and thus the decay of the intermediate is more facilitated.[4]

With increasing pH, the contribution from the neutral intermediate **4**, which returns to the reactant form, becomes greater and the decay of the intermediate becomes rate determining step. In the case of the substrates (**1-d**) and (**1-e**) having less basic aniline group, the contribution from **5** is smaller and then the rate determining step must be the decay of the intermediate in the whole pH range.

Finally, a significant aspect of this study is to observe kinetic evidence for the hypervalent intermediate in acid hydrolysis of sulfinamides having more stronger electron donating group in the sulfinyl group or in the leaving group.

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