BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 45, 271—274(1972)

The Kinetics and Mechanism of the Reactions of *N*-Sulfinylanilines with Formic Acid

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(Received August 9, 1971)

We have examined the kinetics of the reactions between *N*-sulfinylanilines and formic acid. The reactions follow this rate equation; rate$=k[\text{R-C}_6\text{H}_4\text{-NSO}][\text{HCOOH}]$. The kinetic runs were made over a wide temperature range (40—90°C) in order to obtain the values of the activation energy. The values for the reactions of *N*-sulfinylaniline, *N*-sulfinyl-*p*-toluidine, and *N*-sulfinyl-*p*-chloroaniline with formic acid are 14.6, 15.1, and 10.1 kcal/mol respectively. The reaction mechanism is discussed by means of their NMR spectral data.

In 1932, Carré and Libermann reported that carboxylic acids react with *N*-sulfinylaniline to form the corresponding anilides:[1)]

$$C_6H_5NSO + RCOOH \longrightarrow C_6H_5NHCOR + SO_2$$

Recently, Smith and King re-examined the above reaction.[2)] They presented the possibility that a trace of either thionyl chloride, or hydrogen chloride, or traces of both, might be present as an impurity in *N*-sulfinylaniline and that one of these impurities might have been acting as the catalyst. In consequence, the following mechanism was postulated by them;

$$C_6H_5NSO + 3HCl \longrightarrow C_6H_5NH_2\cdot HCl + SOCl_2$$

$$RCOOH + SOCl_2 \longrightarrow RCOCl + SO_2 + HCl$$

$$C_6H_5NH_2\cdot HCl + RCOCl \longrightarrow C_6H_5NHCOR + 2HCl$$

They concluded that the steps involved in the reaction of *N*-sulfinylaniline with carboxylic acids are correctly described by the above sequence, in which both aniline hydrochloride and thionyl chloride are intermediates. The reaction was shown to require the presence of hydrogen chloride.

On the other hand, some recent reports from this laboratory have described the reactions of *N*-sulfinylanilines with alkene oxides[3,4)] and the general structures of the reaction products, the oxathiazolidines, as determined by means of their NMR[4)] and mass spec-

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[1)] P. Carre' and D. Libermann, *C. R. Acad. Sci. Paris.*, **194**, 2218 (1932).

[2)] W. T. Smith and G. G. King, *J. Org. Chem.*, **24**, 976 (1959).

[3)] F. Yamada, T. Nishiyama, M. Kinugasa, and M. Nakatani, This Bulletin, **43**, 3611 (1970).

[4)] T. Nishiyama and F. Yamada, *ibid.*, **44**, 3073 (1971).

tra.[5] In these circumstances, it became of interest to study the reactivity of *N*-sulfinylanilines in relation to formic acid. The present paper is concerned with the kinetics of the reactions of *N*-sulfinylanilines with formic acid carried out in the absence of the catalysts, that is, in the absence of both hydrogen chloride and thionyl chloride. The reaction mechanism is also discussed.

Experimental

Measurements. All the melting points are uncorrected. The NMR spectra were obtained at 60 MHz with a Japan Electron Optics Model JNM 3H-60 spectrometer at room temperature. The chemical shifts are reported in ppm downfield from the internal TMS (δ). A constant-temperature bath was employed; it was equipped with an immersion heating element that afforded a temperature control of ±0.1°C.

Materials. *N*-Sulfinylaniline, *N*-sulfinyl-*p*-toluidine, and *N*-sulfinyl-*p*-chloroaniline were prepared and purified by the reported method.[6] No hydrogen chloride or thionyl chloride was left in the *N*-sulfinylanilines. These facts were confirmed by using both gas chromatography and the NMR method. The formic acid was of an analytical grade and was dried for several days over anhydrous copper sulfate and filtered, after which the filtrate was distilled under reduced pressure.

Kinetic Procedure. In a 3-necked, 30-m*l* flask equipped with a gas inlet and output tubes and an addition funnel, we placed *N*-sulfinylaniline (0.05 mol). In a typical second-order run, about a twofold excess of formic acid was added rapidly to start the reaction. The flask was swirled in order to mix the reactants and was then kept at a constant temperature. A constant flow of dry nitrogen gas was introduced into the reaction mixture throughout the reaction (2.0—4.5 *l*/hr). Nitrogen was passed through the reaction flask to sweep the sulfur dioxide evolved into 80 m*l* of water in the absorption bulbs; at the end of a sufficient period, 5 or 10 min, the bulbs were disconnected and exchanged for other bulbs using a three-way stopcock. In each run, a 10-m*l* portion was withdrawn from the aqueous solution; we then added a known excess of an iodine solution (0.1 N) and determined the amount of the excess by back titration with standard sodium thiosulfate. The rate of sulfur dioxide's release was obtained by this method. The conversion of *N*-sulfinylaniline based on the initial concentration can, therefore, be obtained by means of the measurement of the sulfur dioxide evolved. The rate constants given in the table are the averages of two or more determinations.

Reaction-products Criterion. The crystals were obtained in almost quantitative yields by the reactions of *N*-sulfinylanilines with formic acid and did not show any melting-point depression when the products were mixed with authentic samples of the corresponding *p*-substituted formanilides; formanilide, mp and mmp 46.0—47.5°C; *N*-*p*-tolylformamide, 50.0—50.4°C, and *N*-*p*-chlorophenylformamide, 99.0—99.8°C. The analytical results of these compounds coincided with those of the authentic compounds.

Results and Discussion

The rate of the reaction of *N*-sulfinylanilines with formic acid was followed by the iodine titration of the sulfur dioxide evolved. The results gave good second-order rate constants for all the runs, and the points obtained fell on good straight lines (Fig. 1):

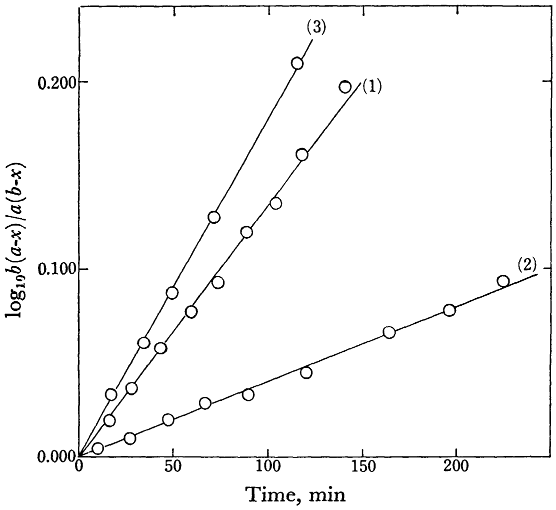

Fig. 1. The second-order plots for the reaction of *N*-sulfinylanilines with formic acid at 60°C. *a* and *b* are the initial concentrations of formic acid and *N*-sulfinylanilines, respectively.
(1) *N*-sulfinylaniline, 5.03 mol/*l*; formic acid, 13.03 mol/*l*. conversion 48.4%.
(2) *N*-sulfinyl-*p*-toluidine, 5.98 mol/*l*; formic acid, 10.86 mol/*l*. conversion 34.7%.
(3) *N*-sulfinyl-*p*-chloroaniline, 5.17 mol/*l*; formic acid, 10.92 mol/*l*. conversion 54.0%.

Table 1. THE RATE CONSTANTS AND THE VALUES OF THE ACTIVATION ENERGY FOR THE REACTION OF *N*-SULFINYLANILINES WITH FORMIC ACID

Temp. C°	*N*-Sulfinylaniline $k \times 10^4$, *l*/mol·min	*N*-Sulfinyl-*p*-toluidine $k \times 10^4$, *l*/mol·min	*N*-Sulfinyl-*p*-chloroaniline $k \times 10^4$, *l*/mol·min
40	—	—	2.9
50	1.5	0.9	4.8
60	3.6	1.8	7.2
70	7.3	4.0	12.3
80	12.2	6.6	—
90	16.1	9.4	—
E, kcal/mol	14.6	15.1	10.1

$$\text{rate} = k[\text{R-C}_6\text{H}_4\text{-NSO}][\text{HCOOH}]$$

Table 1 shows the rate constants of the reactions of *N*-sulfinylanilines with formic acid at various temperatures, along with the values of the activation energy as evaluated from the slopes of the Arrhenius plots. The data given in Table 1 clearly indicate that *N*-sulfinyl-*p*-chloroaniline reacted faster with formic acid than did *N*-sulfinylaniline, as expected, and also faster than *N*-sulfinyl-*p*-toluidine. The reaction is facilitated by the introduction of an electron-attracting substituent into the phenyl group, but is retarded by that of an electron-releasing substituent.

Observation of the Reaction Process using NMR. The spectrum of *N*-sulfinylaniline in carbon tetrachloride exhibits the two-proton and three-proton multiplets due to the ring proton in the regions of 7.93—8.10 and 7.45—7.58 ppm respectively (Fig. 2). In the reaction

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[5] F. Yamada, T. Nishiyama, Y. Fujimoto, and M. Kinugasa, *ibid.*, **44**, 1152 (1971).

[6] A. Michaelis and R. Herz, *Ber.*, **23**, 3480 (1890).

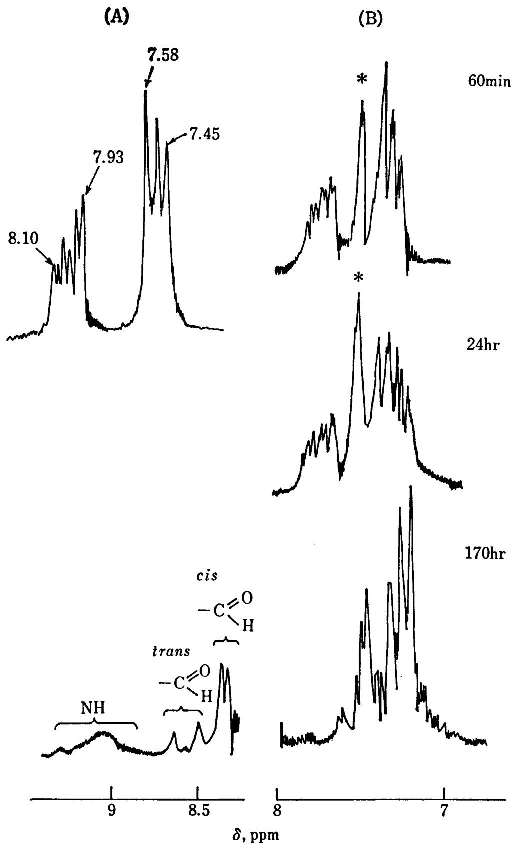


Fig. 2. The NMR spectrum of *N*-sulfinylaniline in CCl_4 (A) and changes of the NMR spectra with reaction time (B). Asterisks indicate the peak at 7.73 ppm.

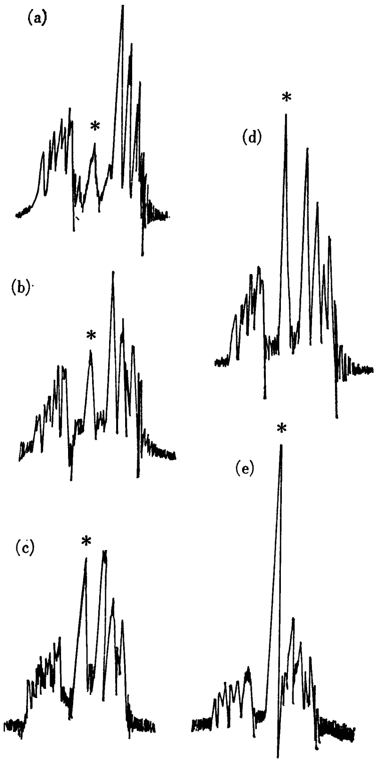


Fig. 3. The NMR signals of the ring protons of the reaction mixtures of *N*-sulfinylaniline with formic acid under various concentrations at 40°C for 60 min, molar ratios of *N*-sulfinylaniline to formic acid; (a) 1:4.3, (b) 1:5.5, (c) 1:7.6, (d) 1:11.1, and (e) 1:17.6. The spectra are not necessarily on exactly the same scale. Asterisks indicate the peak at 7.73 ppm.

of a fivefold excess of formic acid with *N*-sulfinylaniline at 25°C, a new single peak immediately appears at 7.73 ppm (60 min). After the mixture has stood 24 hr, the peak was intensified. These signals changed with the reaction time. Of these signals, the three-proton signal changed most remarkably as a result of the overlapping of the ring-proton signal of the reaction product. The peak at 7.73 ppm increased and then decreased gradually. When the reaction was over, the two-proton signal disappeared; these NMR signals were changed to those of formanilide (170 hr).

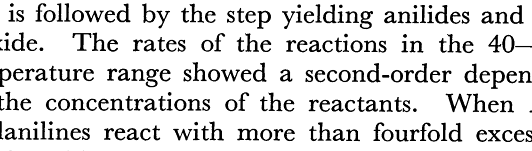
Figure 3 shows the NMR spectra of the reaction mixtures at different concentrations. After a mixture has stood for 60 min at 40°C, the peak at 7.73 ppm shows various intensities. This fact indicates that the intensive changes at the 7.73 ppm peak depend on the molar ratios of *N*-sulfinylaniline to formic acid under these experimental conditions.

Table 2. Chemical shifts in different solvents (1.70 mmol/m*l*)

Compound	Solvent	Chemical shifts, δ, ppm		
		Ring proton	New peak	Methyl
N-Sulfinylaniline	HCOOH	7.49—8.08	7.73	—
	CCl_4	7.45—8.10	—	—
N-Sulfinyl-*p*-toluidine	HCOOH	7.28 7.41 7.80 7.93	7.54	2.47
	CCl_4	7.22 7.35 7.84 7.97	—	2.62
N-Sulfinyl-*p*-chloroaniline	HCOOH	7.41 7.57 7.84 8.00	7.70	—
	CCl_4	7.40 7.55 7.87 8.02	—	—

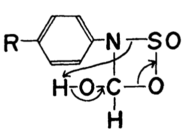
The chemical shifts of *N*-sulfinylanilines in both formic acid and carbon tetrachloride are shown in Table 2. No new peak, such as the peak at 7.73 ppm, was observed in the carbon tetrachloride solutions. Peaks at 7.73, 7.54, and 7.70 ppm could, however, be observed in the formic acid solutions.

Probable Mechanism. The results presented above indicate that the reactions proceed by the following pathway:

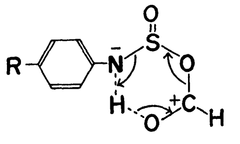


The reaction is initiated by the interaction between a sulfur atom of the –N=S=O group and a carbonyl oxygen of formic acid. Thus, the molecules can form a 1: 1 complex; this step is probably rate-determining and is followed by the step yielding anilides and sulfur dioxide. The rates of the reactions in the 40—90°C temperature range showed a second-order dependence on the concentrations of the reactants. When *N*-sulfinylanilines react with more than fourfold excesses of formic acid or at low temperatures, below 40°C, new peaks were observed in their NMR spectra (in Table 2). It can, therefore, be suggested that the peaks indicate the existence of the intermediate in each reaction, The new chemical shifts appeared as a result of the formation of the intermediates. The NMR spectrum of aniline formate in formic acid shows a single peak at 7.53 ppm, a slightly higher shift than that of the above intermediates. Aniline formate is also well-known as an intermediate of the reaction of aniline with formic acid.

There are ample examples in the literature to show that *N*-sulfinyl compounds form four-membered intermediates *via* the cycloaddition of the reactants. For example, Kresze and Albrecht[7,8] reported that the reactions of *N*-sulfinyl compounds with carbonyl compounds were transformations analogous to a Wittig reaction in which the carbonyl oxygen is replaced by the R–N= or RSO$_2$–N= group and the sulfur dioxide is eliminated. On the other hand, we have easily prepared the 2-oxo-3-aryl-1,2,3-oxathiazolidines, that is, five-membered heterocyclic compounds, by the cycloadditions of *N*-sulfinylanilines to alkene oxides.[3,4] From these facts, the four-membered ring structure seems to be less stable than the five-membered ring structure. In these circumstances, we propose a four or six-membered heterocyclic structure as an intermediate as follows:



four-membered intermediate



six-membered intermediate

At the present time, the four-membered ring-activated complex and the six-membered ring-activated complex are entirely compatible with the above experimental data.

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7) R. Albrecht, G. Kresze, and B. Mlakar, *Chem. Ber.*, **97**, 483 (1964).

8) G. Kresze and R. Albrecht, *Angew. Chem.*, **74**, 782 (1962).