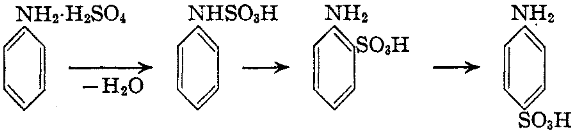
[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY, HARVARD UNIVERSITY, AND THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Mechanism of the Sulfonation of Aromatic Amines. II. Sulfonation at Elevated Temperatures with Sulfuric Acid

BY ELLIOT R. ALEXANDER

In an earlier communication[1] it was shown that while dimethylaniline may be sulfonated at low temperatures with fuming sulfuric acid in the *meta* position, aniline yields a mixture of products in which the *ortho* and *para* isomers predominate. At 180–200°, however, both aniline[2] and dimethylaniline[3] may be sulfonated selectively in the *para* position by "baking" with sulfuric acid.

The mechanism of the *para* sulfonation of aromatic amines has received considerable attention[4] and has been studied in some detail by Bamberger and his associates.[4] These investigators have suggested that, at least in the case of aniline, phenylsulfamic acid (II) is formed as an intermediate and that the over-all transformation can be pictured as a molecular rearrangement proceeding through the steps I–IV.



I II III IV

Neither II nor III was isolated from the reaction, but their experiments showed that both the salts of phenylsulfamic acid (II) and orthanilic acid (III) could be transformed into IV.

Clearly, however, this mechanism cannot be a general one for the *para* sulfonation of aromatic amines because intermediates such as II cannot be written for tertiary amines.

At low temperatures it was shown that aniline and dimethylaniline are sulfonated with fuming sulfuric acid by different mechanisms[1] and it therefore seemed plausible that different mechanisms were also in operation at high temperatures in spite of the fact that *para* isomers were obtained in each case. Accordingly the effect of sulfuric acid on the sulfonation of aniline and dimethylaniline was studied in an attempt to gain further insight into the mechanisms of these reactions.

Experimental

Sulfonation of Aniline *in vacuo*.—Aniline acid sulfate[2] (4.00 g., 0.0209 mole) and the appropriate amount of 100% sulfuric acid[5] were placed in a clean, dry, 500-ml. round-bottomed flask. After adding a boiling stone, the flask was attached to an oil pump and evacuated to a pressure of 1 to 3 mm. As soon as some bubbling subsided, the flask was immersed in a metal-bath maintained at 183–185° for exactly five minutes. During this time the flask was swirled continuously so as to distribute the melt in a thin layer over the bottom and sides of the flask. As the reaction proceeded water was evolved, the mixture became somewhat discolored, and in the case of the runs in which the large amounts of sulfuric acid were used, a ring of acid could be observed refluxing about one-half of the way up on the sides of the flask. When the flask was removed from the bath, it was quickly wiped free of adhering metal with a dry cloth and allowed to cool to room temperature.

After cooling, 100 ml. of distilled water was added, the melt was dissolved with warming, and the contents were rinsed thoroughly into an 800-ml. beaker with about 400 ml. of distilled water. The solution was then made basic with 10% sodium hydroxide solution, further diluted with distilled water to about 750 ml. and evaporated to dryness on the steam-bath. This removed the unreacted aniline by steam distillation. The amount of sulfanilic acid formed in each run was determined by dissolving the residue in 400 ml. of distilled water, acidifying, and titrating with standard sodium nitrite solution.[6] The results of the runs are summarized in Fig. 1.

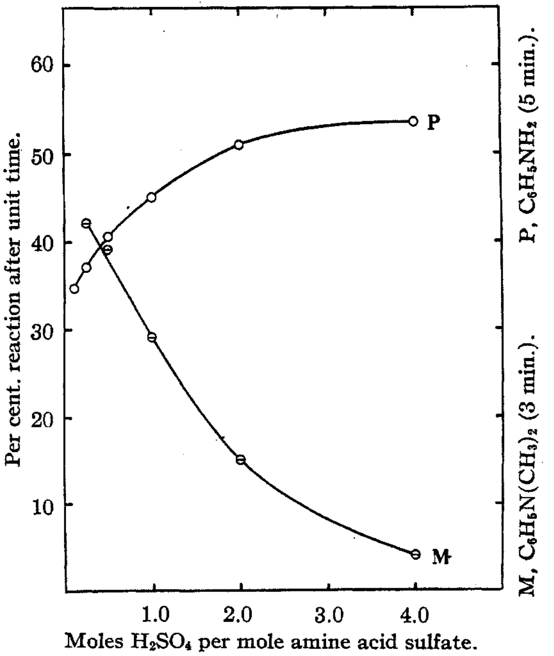


Fig. 1.—Effect of sulfuric acid upon rate of sulfonation of aniline and dimethylaniline at 185°.

Sulfonation of Dimethylaniline *in vacuo*.—Dimethylaniline acid sulfate[7] (2.00 g., 0.00913 mole) and the appropriate amount of 100% sulfuric acid were allowed to react in the manner already described for exactly three

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(1) Alexander, THIS JOURNAL, **68**, 969 (1946).

(2) Huber, *Helv. Chim. Acta*, **15**, 1379 (1932).

(3) Evans, *Chem. News*, **73**, 54 (1896).

(4) C. M. Suter, "Organic Chemistry of Sulfur," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 247.

(5) Prepared by adding 25% fuming sulfuric acid to concd. sulfuric acid until the maximum freezing point was obtained. One hundred per cent. sulfuric acid melts at about 10.5°.

(6) Kolthoff and Stenger, "Volumetric Analysis," Interscience Publishers, Inc., New York, N. Y., 1942, p. 240.

(7) Sugden and Wilkins, *J. Chem. Soc.*, 1297 (1929).

TABLE I

SULFONATION OF ANILINE AT 140° IN A CLOSED SYSTEM

Time, min.	Ml. NaNO$_3$ soln. required[a]	x[b]	$(a - x)$	$(b - x)$	$\left(\frac{1}{b-a}\left[\frac{2.303^a}{b-a}\log\left(\frac{b-x}{a-x}\right)-\frac{b}{b-x}\right]\right)$	$\left(\frac{c}{b-a}\left[\frac{2.303}{b-a}\log\left(\frac{b-x}{a-x}\right)-\frac{1}{b-x}\right]\right)$	Sum, cols. 6 and 7
Run A[c] $a = 1.058$[d]; $b = 5.392$[e]; $c = 1.893$[f]							
15	1.55	0.047	1.011	5.345	−0.1392	0.0859	−0.0533
30	2.96	.091	0.967	5.301	− .1390	.0890	− .0500
60	5.20	.159	.899	5.233	− .1388	.0939	− .0449
90	7.16	.219	.840	5.173	− .1386	.0986	− .0400
120	9.16	.280	.777	5.112	− .1375	.1043	− .0332
150	11.32	.346	.711	5.046	− .1365	.1105	− .0260
181	12.90	.395	.663	4.997	− .1355	.1160	− .0190
210	13.81	.426	.634	4.996	− .1349	.1193	− .0156
258	15.83	.485	.573	4.907	− .1329	.1272	− .0057
332	18.52	.567	.490	4.825	− .1294	.1398	+ .0104
Run B[g] $a = 1.610$[d]; $b = 4.219$[e]; $c = 1.714$[f]							
30	1.25	0.040	1.570	4.179	−0.4056	0.0893	−0.0662
90	6.54	.208	1.402	4.011	− .4032	.1016	− .0529
122	9.02	.287	1.323	3.932	− .4009	.1072	− .0465
150	10.39	.330	1.279	3.889	− .3986	.1112	− .0416
180	11.40	.362	1.247	3.857	− .3972	.1140	− .0382
213	12.58	.400	1.210	3.819	− .3954	.1175	− .0340
258	14.95	.475	1.134	3.744	− .3899	.1253	− .0241
306	16.50	.525	1.084	3.694	− .3856	.1309	− .0169
358	18.83	.599	1.011	3.620	− .3784	.1397	− .0053
Run C[h] $a = 0.7090$[d]; $b = 5.904$[e]; $c = 1.942$[f]							
15	1.68	0.352	0.674	5.869	−0.1368	0.0921	−0.0447
30	3.75	.785	.631	5.826	− .1367	.0958	− .0409
60	7.88	.165	.544	5.739	− .1361	.1044	− .0317
90	10.48	.220	.490	5.685	− .1356	.1107	− .0249
120	12.94	.271	.438	5.663	− .1332	.1182	− .0150
154	15.04	.315	.394	5.589	− .1336	.1240	− .0096
184	17.28	.362	.347	5.542	− .1322	.1319	− .0003
214	18.38	.385	.324	5.519	− .1314	.1363	+ .0049
258	21.90	.459	.250	5.445	− .1277	.1530	+ .0253
310	23.68	.496	.213	5.408	− .1252	.1636	+ .0384

[a] 0.520 molar. [b] Change in concentration of anilinium ion, sulfuric acid and oxonium ion after time t. [c] Prepared from 30.00 g. of aniline sulfate and 170.4 g. of 96% sulfuric acid. Each sample weighed 16.958 g. [d] Initial concentration of anilinium ion in moles per 1000 g. of solution. [e] Initial concentration of sulfuric acid in moles per 1000 g. of solution. [f] Initial concentration of oxonium ion in moles per 1000 g. of solution. [g] Prepared from 51.00 g. of aniline sulfate and 171.9 g. of 96% sulfuric acid. Each sample weighed 16.337 g. [h] Prepared from 30.00 g. of aniline sulfate and 267.9 g. of 96% sulfuric acid. Each sample weighed 26.284 g.

minutes. When the reaction mixture had cooled to room temperature, the flask was connected to a Kjeldahl apparatus, excess 10% sodium hydroxide solution was added, and the liberated free base was quantitatively steam distilled into 100 ml. of 0.5 molar hydrochloric acid contained in a 1-liter volumetric flask. After appropriate dilution, the unreacted dimethylaniline in solution was determined colorimetrically by the method of Haslam and Hearn[8] which is based upon the fact that solutions of dimethylaniline develop an intense yellow color on treatment with nitrous acid. The results of these runs are also summarized in Fig. 1.

Sulfonation of Aniline in a Sealed Tube.—From a solution prepared by dissolving an accurately weighed amount of aniline sulfate[9] in a weighed amount of 96% sulfuric acid, samples were withdrawn by means of a pipet calibrated in terms of the particular mixture being used. The samples were introduced into clean, dry, Pyrex test-tubes and sealed at once in such a way that as little air as possible was enclosed in the vial.

The reaction was carried out by immersing the tubes in a vapor thermostat of boiling n-butyl ether (140°) and the reaction was followed by withdrawing the vials after various time intervals. After cooling, the vials were opened and rinsed thoroughly into a 500-ml., round-bottomed flask. The solution was then made basic with 50% sodium hydroxide solution and steam distilled until the distillate showed no turbidity when tested with bromine water. The apparatus was then rinsed down carefully with distilled water and the amount of sulfanilic acid formed in each run was determined as before with standard sodium nitrite solution.[6]

Three runs were carried out using different concentra-

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(8) Haslam and Hearn, *Analyst*, **69**, 141 (1944).

(9) Schröder, *Ber.*, **12**, 1613 (1879).

tions of aniline sulfate and sulfuric acid. The results are summarized in Table I.

Attempted Sulfonation of Dimethylaniline in a Sealed Tube.—The sulfonation of dimethylaniline was attempted in the manner described above and the reaction was followed by the steam distillation–colorimetric analysis technique. It was found, however, that either no appreciable reaction took place (at 140 and 179°) or that decomposition occurred together with sulfonation (at 220°) so as to make the runs unsuitable for kinetic analysis. Thus after two hours at 220°, when the mole ratio of sulfuric acid to dimethylaniline was 5.380, the reaction mixture became very black, the odor of sulfur dioxide could be observed, and the reaction was found to have proceeded to the extent of 41%. In another run under the same conditions but when the ratio of sulfuric acid to dimethylaniline was increased to 17.65 the reaction was found to have proceeded to the extent of 86%. These results are in sharp contrast to the experiments carried out *in vacuo* in which it was found that an *increase* in the amount of sulfuric acid used caused a *decrease* in the extent of reaction with dimethylaniline (Fig. 1).

Discussion

In Fig. 1 is summarized the effect of varying the concentration of sulfuric acid upon the rate of sulfonation of aniline and dimethylaniline when the reaction was carried out *in vacuo*. From these curves it is quite clear that the mechanism of the *para* sulfonation of aniline is different from that of dimethylaniline since an excess of sulfuric acid *increased* the rate of reaction of aniline but *decreased* the rate of reaction of dimethylaniline. Another series of experiments was therefore undertaken to sulfonate aniline and dimethylaniline in a closed system so as to prevent the escape of water from the reaction mixture.

As can be seen from the data of Table I, aniline was sulfonated readily in a sealed tube with 96% sulfuric acid at 140°. Dimethylaniline, however, could not be clearly sulfonated in this way. Essentially no reaction occurred at 140 or 179° and at 220° decomposition began to occur. Thus for the successful *para* sulfonation of dimethylaniline it appears that water must be removed from the reaction mixture.

Unfortunately it is impossible to analyze the curves of Fig. 1 mathematically since a certain amount of water distilled as the reaction proceeded and this prevented an exact knowledge of the concentrations of the reactants in the reaction mixture. Qualitatively, however, it is interesting to observe that a mechanism based upon the preliminary dissociation of dimethylaniline acid sulfate into dimethylaniline and sulfuric acid would be expected to give these effects in the right direction. Thus if the over-all reaction were represented as

$$[C_6H_5NH(CH_3)_2^+]\,HSO_4^- \rightleftarrows C_6H_5N(CH_3)_2 + H_2SO_4 \quad (I)$$

$$C_6H_5N(CH_3)_2 + H_2SO_4 \rightleftarrows p\text{-}(CH_3)_2NC_6H_4SO_3H + H_2O \quad (II)$$

the rate of reaction, d*P*/d*t*, can be expressed by the equation

$$\frac{dP}{dt} = k[C_6H_5N(CH_3)_2][H_2SO_4] = k_1[C_6H_5NH(CH_3)_2^+][HSO_4^-] \quad (III)$$

from which it can be seen that when the reaction mixture is diluted with sulfuric acid, the concentration of dimethylanilinium ion and bisulfate ion would be lowered and therefore the rate of reaction would be decreased.[10]

In Table I is shown the kinetic data obtained from the study of the sulfonation of aniline with 96% sulfuric acid at 140° in a closed system. From these data the lines in Fig. 2 were obtained by plotting the function

$$\frac{c}{b-a}\left[\frac{2.303}{b-a}\log\left(\frac{b-x}{a-x}\right) - \frac{1}{b-x}\right] + \frac{1}{b-a}\left[\frac{2.303a}{b-a}\log\left(\frac{b-x}{a-x}\right) - \frac{b}{b-x}\right]$$

against time in minutes. In this expression *a* is the initial concentration of anilinium ion, *b* is the initial concentration of undissociated sulfuric acid,[11] *c* is the initial concentration of oxonium ion,[12] and *x* is the change in concentration of anilinium ion, sulfuric acid, or oxonium ion, after time *t*. It is one way of testing the integrated form of the rate equation

$$\frac{dP}{dt} = k_2\,\frac{[C_6H_5NH_3^+][H_2SO_4]^2}{[OH_3^+]} \quad (IV)$$

which will be derived later. Thus after making the appropriate substitutions

$$\frac{dx}{dt} = k\,\frac{[a-x][b-x]^2}{[c+x]} \quad (V)$$

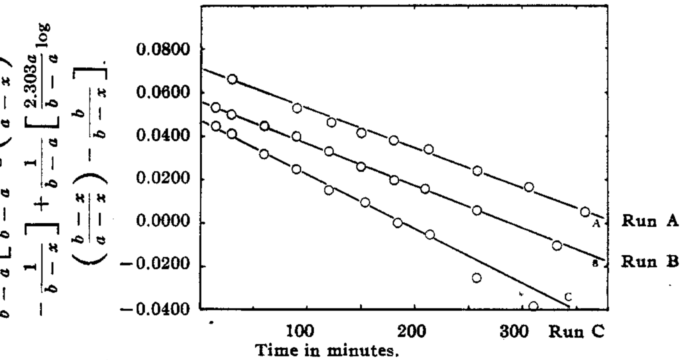

Fig. 2.—Plot showing that the sulfonation of aniline at 140° follows the equation: $\frac{dP}{dt} = k\,\frac{[C_6H_5NH_3^+][H_2SO_4]^2}{[OH_3^+]}$: Run A, λ = 1.85; Run B, λ = 1.92; Run C, λ = 2.20.

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[10] A calculation of the rate constants for this sulfonation from the data in Fig. 1 shows that the rate of reaction is indeed proportional to the product of the dimethylanilinium and bisulfate ions as these equations require. This agreement may be simply fortuitous, however, because of the difficulties already mentioned.

[11] Approximated as being equal to the stoichiometric concentration of sulfuric acid minus the concentration of water present.

[12] Approximated as being equal to the concentration of water present.

and

$$\int \frac{c\,\mathrm{d}x}{[a + x][b + x]^2} + \int \frac{x\,\mathrm{d}x}{[a + x][b + x]^2} = kt + C \qquad \text{(VI)}$$

whence a straight line should be obtained by plotting the sum of the integrals on the left side of the equation against time. In Fig. 2 it will be observed that reasonably straight lines were obtained throughout at least 54% of reaction[13] and that the rate constants of the different runs are in fair agreement in spite of the fact that no correction could be made for the change in the nature of the reaction medium brought about by a fourfold change in anilinium ion concentration.[14]

While there may be other mechanisms which could be postulated to fit the data, it is interesting that a mechanism based upon the intermediate formation of a sulfur trioxide addition complex with aniline[1] is in agreement with equation IV. Thus, if the over-all transformation of aniline to sulfanilic acid can be represented by the equations VII to IX

$$2H_2SO_4 \overset{K_1}{\rightleftarrows} SO_3 + OH_3^+ + HSO_4^- \qquad \text{(VII)}$$

$$SO_3 + C_6H_5NH_3^+ \overset{K_2}{\rightleftarrows} C_6H_5NHSO_3H + H^+ \qquad \text{(VIII)}$$

$$\begin{array}{l} C_6H_5NHSO_3H + H_2SO_4 \xrightarrow{k_3} \\ \qquad [HO_3SC_6H_4NHSO_3H + H_2O] \\ \qquad\qquad \downarrow \\ \qquad HO_3SC_6H_4NH_2 + H_2SO_4 \qquad \text{(IX)} \end{array}$$

it can be seen that

$$\frac{\mathrm{d}P}{\mathrm{d}t} = k_3[C_6H_5NHSO_3H][H_2SO_4]$$

whence

$$\frac{\mathrm{d}P}{\mathrm{d}t} = k_3K_2\frac{[SO_3][C_6H_5NH_3^+][H_2SO_4]}{[H^+]} = k_3K_1K_2\frac{[C_6H_5NH_3^+][H_2SO_4]^3}{[H^+][HSO_4^-][OH_3^+]} \qquad \text{(XI)}$$

and since

$$K_{H_2SO_4} = \frac{[H^+][HSO_4^-]}{H_2SO_4} \qquad \text{(XII)}$$

$$\frac{\mathrm{d}P}{\mathrm{d}t} = \frac{k_3K_1K_2}{K_{H_2SO_4}}\frac{[C_6H_5NH_3^+][H_2SO_4]^2}{[OH_3^+]} \qquad \text{(XIII)}$$

Acknowledgment.—The author wishes to express his appreciation to the trustees of the Frank B. Jewett Fellowships for a fellowship which made part of this investigation possible.

Summary

A study of the influence of sulfuric acid on the sulfonation of aniline and dimethylaniline at 140 and 185° has shown that in spite of the similarity of the starting materials, the conditions for reaction, and the isomers obtained, the mechanisms of the reactions are different. At 185° when the reaction is carried out *in vacuo* the rate of reaction is increased in the case of aniline and decreased in the case of dimethylaniline by the addition of excess sulfuric acid. At 140° when the reaction is carried out in a closed system the rate of sulfonation of aniline appears to follow the equation

$$\frac{\mathrm{d}P}{\mathrm{d}t} = \frac{k[C_6H_5NH_3^+][H_2SO_4]^2}{[OH_3^+]}$$

Reaction mechanisms have been proposed which are compatible with these facts.

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[13] The last two points of run c in Fig. 2 represent 65 and 70% reaction, respectively.

[14] Neither anhydrous sodium sulfate nor anhydrous potassium sulfate were found to be soluble enough in 96% sulfuric acid to be used to maintain a constant ionic strength.

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY AND BIOLOGICAL CHEMISTRY OF WASHINGTON UNIVERSITY]

Zein Solutions as Association–Dissociation Systems[1]

BY BARRETT L. SCALLET[2]

Sørensen[3] in 1930 advanced the hypothesis that the molecules of soluble proteins consist of a number of components comparatively loosely held together by means of secondary valences. The amino acid residues within these components are of course linked together by principal valences, but the secondary linkages are so much weaker that changes in the salt content, hydrogen ion activity, alcohol content, or temperature of a protein solution may give rise to reversible dissociation.

Sørensen's conclusions were based on solubility relationships, amino acid analyses, osmotic pressure measurements, acid and base titrations and optical rotation measurements on various proteins, especially serum albumin. Eriksson-Quensel and Svedberg[4] showed clearly by means of the ultracentrifuge that the hemocyanins dissociate reversibly within certain *p*H ranges.

Sinclair and Gortner[5] demonstrated that gliadin must be considered to be a reversible association–dissociation system, since fractionation followed by reworking of the fractions yielded two products identical in physical properties with the original gliadin preparation.

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[1] From a dissertation presented to the Board of Graduate Studies of Washington University in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1946.

[2] Present address: Corn Products Division, Anheuser-Busch, Inc., St. Louis, Missouri.

[3] Sørensen, *Compt. rend. trav. lab. Carlsberg*, **18**, (no. 5), 1 (1930).

[4] Eriksson-Quensel and Svedberg, *Biol. Bull.*, **71**, 498 (1936).

[5] Sinclair and Gortner, *Cereal Chem.*, **10**, 171 (1933).