

Summary

A calorimeter which operates near 60° has been devised and used to measure the heat taken up by a sample when transferred to the calorimeter from a thermostat at some lower temperature. Measurements of the changes in heat content have been made on dry glucose glass, and on samples containing up to 3% of water. When the glass is cooled only a few degrees below its congealing temperature, which is between 25 and 30° for the dry glass, it was found that equilibrium heat content was not reached even after three weeks of storage. For equilibrium heat capacity measurements, the contribution of any water present in the glass was

found to be additive. One per cent. of water in the glass lowered the congealing temperature about 8°. Equilibrium heat capacity values have been obtained for glucose glass between 5 and 60°.

The heat capacities of crystalline glucose and of 1,2,3-trichloropropane were also measured between 0 and 60°.

Since glassy substances are so extremely slow to reach equilibrium with respect to heat content, it is not permissible to use the heat capacity of glasses obtained by the Nernst method in entropy calculations or in discussions concerning the third law of thermodynamics.

LAFAYETTE, INDIANA

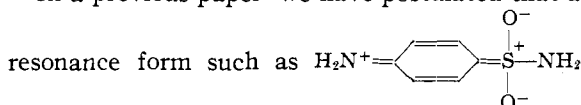
RECEIVED APRIL 26, 1941

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY OF THE UNIVERSITY OF CALIFORNIA]

The Dipole Moment of Sulfanilamide and Related Compounds^{1,2}

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In a previous paper⁴ we have postulated that a



may contribute somewhat to the structure of sulfanilamide. Although it has been stated⁵ that forms of this same type are not possible with a sulfonic acid we see no reason for such an assumption since sulfur is a second row element and is not necessarily limited to a maximum of four covalent bonds as is the case with first row elements like nitrogen or oxygen.^{6,7} In this paper we have measured the dipole moment of sulfanilamide and some related compounds to obtain evidence on the possible existence of such resonance forms.

Results

The symbols used in the equations and tables are: ω , the weight fraction of solute; d , the density of the solution; ϵ , the dielectric constant; P_2 , the polarization of the solute; P_{20} , the polariza-

tion of the solute at infinite dilution; P_{E_2} , the electronic polarization of the solute; μ , the dipole moment; T , the absolute temperature; p_1 , the specific polarization of the solvent; p_2 , the specific polarization of the solute; and p_{12} , the specific polarization of the solution. The P_{E_2} values were calculated from the refractive indices of the solutions using the D sodium line. The P_{20} values were obtained by plotting P_2 against ω and extrapolating to zero concentration. The polarization and dipole moments were calculated by means of the equations

$$p_1 = \frac{\epsilon - 1}{\epsilon + 2} \frac{1}{d}$$

$$p_{12} = \frac{\epsilon - 1}{\epsilon + 2} \frac{1}{d} = (1 - \omega) p_1 + \omega p_2$$

$$P_2 = M_2 \left(p_1 + \frac{p_{12} - p_1}{\omega} \right)$$

$$\mu = 0.0127 \sqrt{(P_{20} - P_{E_2})T}$$

TABLE I
MEASUREMENTS IN DIOXANE AT 25°

ω	d	ϵ	P_2
Aniline			
0.004758	1.0269	2.2332	102
.007211	1.0269	2.2434	98
.012450	1.0270	2.2670	95
Xenylamine			
.004209	1.0272	2.2268	147
.008937	1.0277	2.2443	150
.012436	1.0280	2.2565	147
.017020	1.0284	2.2755	149

(1) Supported in part by a grant from the Research Board of the University of California.

(2) Presented at the meeting of the American Chemical Society held in conjunction with the A. A. A. S. meeting at Pasadena, June 20, 1941.

(3) James M. Goewey Fellow in Pharmaceutical Chemistry, 1940-41.

(4) Halverstadt and Kumler, *THIS JOURNAL*, **63**, 624 (1941).

(5) Armstrong, James and Weissberger, *ibid.*, **63**, 182 (1941).

(6) Branch and Calvin, "The Theory of Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1941.

(7) Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1940, p. 221.

TABLE I (Concluded)

ω	d	e	P_2
Xenylamine (in Benzene)			
0.005561	0.8736	2.2887	118
.009370	.8743	2.2987	122
.013784	.8753	2.3099	123
.018806	.8763	2.3226	123
Benzenesulfonamide			
.004210	1.0280	2.2987	567
.008237	1.0292	2.3856	562
.012069	1.0303	2.4697	556
.015631	1.0313	2.5460	547
<i>p</i> -Phenylbenzenesulfonamide			
.004831	1.0280	2.2834	625
.008125	1.0287	2.3338	620
.011312	1.0295	2.3835	616
.016929	1.0311	2.4697	604
Sulfanilamide			
.004368	1.0284	2.3496	929
.007848	1.0296	2.4635	905
.010880	1.0305	2.5629	886
.017019	1.0327	2.7681	853
Metanilamide			
.003896	1.0282	2.3035	695
.007654	1.0295	2.3919	676
.011599	1.0307	2.4909	674
.015514	1.0320	2.5871	662
<i>p</i> -(<i>p</i> -Aminophenyl)-benzenesulfonamide			
.002465	1.0276	2.2692	1022
.003828	1.0281	2.3020	1010
.006156	1.0284	2.3597	1006
.007888	1.0291	2.4035	1010

TABLE II
IN DIOXANE AT 25°

	P_{20}	P_{E_2}	μ
Aniline	106	31	1.90
Xenylamine	148	59	2.07
Xenylamine (in benzene)	122	59	1.74
Benzenesulfonamide	577	39	5.09
<i>p</i> -Phenylbenzenesulfonamide	630	68	5.20
Sulfanilamide	960	45	6.63
Metanilamide	705	45	5.63
<i>p</i> -(<i>p</i> -Aminophenyl)- benzenesulfonamide	1012	75	6.71

Discussion

By comparing the moments of sulfanilamide with those of aniline and benzenesulfonamide it should be possible to find out if a form with a separation of charge makes a contribution to the structure of the molecule. This case is not as simple as that of *p*-nitroaniline, aniline and nitrobenzene where the moment of the nitro group is in the plane of the ring and the moment of *p*-nitroaniline is considerably larger than the sum of the moments of aniline and nitrobenzene. In

the sulfanilamide case the large moment of the sulfonamide group is directed at some angle to the plane of the benzene ring, and the moment of sulfanilamide is not greater than the sum of the moments of aniline and benzenesulfonamide.

The only suitable solvent we have found for the measurement of sulfanilamide is dioxane and therefore it seemed desirable to measure the comparison compounds, aniline and benzenesulfonamide, in the same solvent. When we did so we obtained a value of 5.09 for benzenesulfonamide which seems a reasonable value compared with the value of 5.05 for diphenyl sulfone⁸ (measured in benzene) since in both compounds the two sulfur-oxygen semi-polar double bonds must contribute the major part of the moment. The measurement of aniline in dioxane, however, resulted in a moment which was abnormally high, 1.90 in comparison with the values 1.53, 1.48 reported for this compound in benzene and hexane.⁹ This difference of 0.37–0.42 unit is greater than differences usually associated with a simple solvent effect.

The measurement of xenylamine (4-aminobiphenyl) in dioxane resulted in a value for its moment of 2.07 which is 0.31–0.34 unit greater than its moment in benzene, 1.73 and 1.76 as reported in the literature.¹⁰ We measured xenylamine in benzene and obtained a value of 1.74 in excellent agreement with the published values. It is evident that these amines give values that are 0.3 to 0.4 unit higher in dioxane than in other solvents. This effect is to be studied further to see if it is shown by amines other than primary aromatic amines.

The question arises as to whether the amine group in sulfanilamide shows this same abnormal effect. This cannot be determined directly because sulfanilamide is not sufficiently soluble in benzene or other suitable solvents to make an accurate measurement. However, we shall use the values for the amines as determined in dioxane, which amounts to assuming that the amine group in sulfanilamide shows the abnormal effect. If resonance is evident in this case it would be more apparent if the values for the moments of the amines in benzene were used in the calculations.

The moment of *p*-nitroaniline in dioxane shows this same abnormal effect. Several years ago Kumler and Porter measured this compound in

(8) DeVries and Rodebush, *THIS JOURNAL*, **53**, 2888 (1931).(9) Cowley and Partington, *J. Chem. Soc.*, 1598 (1938).(10) LeFèvre and LeFèvre, *ibid.*, 1130 (1936).

dioxane¹¹ and obtained a value of 6.68 which is 0.36 unit higher than LeFèvre and LeFèvre's value¹⁰ 6.32 in benzene, an abnormality about the same as that found for aniline and xenylamine in dioxane. It seems not unreasonable then to assume that sulfanilamide would show a like effect.

To arrive at the moment sulfanilamide would have if no resonance such as has been postulated were present, the moment of metanilamide has been measured and used as a standard of reference. In metanilamide we have a compound with the same groups as sulfanilamide but the resonance form postulated for sulfanilamide is not possible for the meta compound. Hence the moment sulfanilamide would have without any contribution from this resonance form can be calculated from the moment of metanilamide. Any increase in dipole moment due to an inductive effect is included in the value thus calculated since the inductive effect in case of metanilamide would be virtually the same as in the case of sulfanilamide.

To calculate the moment sulfanilamide would have assuming free rotation we developed the formula

$$\mu_{f.r.} = \sqrt{\mu_1^2 + \mu_2^2 + 2\mu_1\mu_2 \cos \sigma \cos c_1 \cos c_2}$$

where μ_1 is the moment of the amine group, μ_2 the moment of the sulfonamide group, σ the angle between the axes of rotation and c_1 and c_2 the angles which the two moments make with their respective axes of rotation. This formula is apparently a special case of the general formula developed by Eyring.¹²

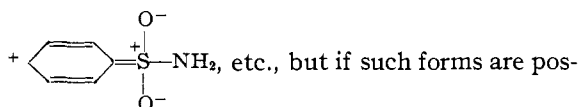
We have adopted the following conventions in applying the formula. The axes of rotation are assumed to be directed from the ring to the group. Thus σ for the meta position is 120° and taking 70° for the angle the resultant dipole of the amino group makes with the N-C bond, c_1 for the amino group in metanilamide is 110° .

Any hindrance to free rotation in the meta compound would arise from resonance between the amine group and the ring or between the sulfonamide group and the ring and it would be no greater than in aniline and benzenesulfonamide. If the amino group is fixed in aniline due to the contribution of the forms $-\langle \text{C}_6\text{H}_5 \rangle = \overset{+}{\text{N}}\text{H}_2$, etc., with a double bond between nitrogen and carbon, it is to be supposed that the hydrogen atoms lie in or near the plane of the ring. However, the

value of the Kerr constant indicates that the angle between the resultant dipole in aniline and the axis of maximum polarizability is about 70° ($c_1 = 180 - 70 = 110^\circ$). Since the axis of maximum polarizability lies in the plane of the benzene ring the hydrogen atoms are outside this plane and the hydrogen-nitrogen bonds are at some large angle to the plane of the ring, hence there is perhaps some doubt that the amino group is fixed in aniline. There would probably be less tendency for the sulfonamide group to be fixed in benzenesulfonamide since sulfur is a second row element and second row elements show less tendency than first row elements to form double bonds.

In calculating the moment sulfanilamide would have if no more resonance were present in it than is present in the meta compound we first calculate the value of $\cos c_1 \cos c_2$ by substituting 120° for σ and the measured moments of metanilamide, aniline and benzenesulfonamide for μ free rotation, μ_1 and μ_2 , respectively, in the above formula. Using this calculated value of -0.225 for $\cos c_1 \cos c_2$ we calculate the moment of sulfanilamide to be 5.82. The calculated moment has this same value if the amino group is fixed in the plane of the ring, and the benzenesulfonamide group has free rotation.

If free rotation is not present in the sulfonamide group it is most likely to be excluded due either to steric effects or to resonance. From a study of the Stuart models there is no indication of any steric effects being involved in the rotation about the carbon-sulfur bond. Resonance could stop rotation due to contributions from such forms as



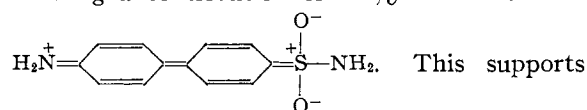
in benzenesulfonamide or metanilamide their contribution would be greatly increased by having a group that can accept a positive charge in the para position, as is the case with sulfanilamide. Also if the sulfonamide group is fixed there appear to be at least six symmetrical positions for it and the calculated moment is virtually the same as for free rotation.⁶ Thus whether the groups are rotating or fixed the fact that the observed moment 6.63 is considerably higher than the calculated moment gives evidence that a contribution of about 3% is made to sulfanilamide by forms with a separation of charge.

(11) Kumler and Porter, *THIS JOURNAL*, **56**, 2549 (1934).

(12) Eyring, *Phys. Rev.*, **39**, 746 (1932).

The biphenyl analogs of aniline, benzenesulfonamide and sulfanilamide have moments 0.17, 0.11 and 0.08 unit higher than the corresponding benzene compounds. The slightly larger moments for the biphenyl compounds can be largely attributed to induction. The magnitudes of the excess moments for the biphenyl compounds are about the same as those found for the bromo, nitro and aminonitro compounds where the differences are 0.09, 0.14 and 0.14, respectively.¹⁰

A calculation of the dipole moment of *p*-(*p*-aminophenyl)-benzenesulfonamide can be made in a fashion analogous to that for sulfanilamide. The product $\cos c_1 \times \cos c_2$ is assumed to be the same as in metanilamide and the values of μ_1 and μ_2 are taken from xenylamine and *p*-phenylbenzenesulfonamide, measured in dioxane. The value of the calculated moment is 6.02, which is 0.69 unit below the observed moment 6.71, indicating a contribution of 1.5% from the form



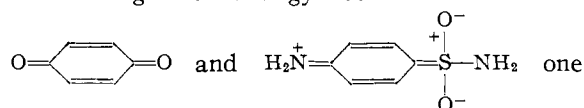
the evidence obtained by others that resonance effects can take place across both rings and that the two benzene rings in biphenyl derivatives are not independently conjugated.¹⁰ The amount of the contribution of the resonating form in *p*-(*p*-aminophenyl)-benzenesulfonamide is considerably less than it is in sulfanilamide. This results from the separation of charge in the case of the biphenyl compound being about twice as great as in the case of sulfanilamide.

It is interesting to make this same calculation on the esters of *m*- and *p*-aminobenzoic acids, because from other sources there is evidence that the para compound has contributions from the

form while the meta compound cannot have such a form. It would then be expected that the meta compound would have an observed moment very near the calculated moment while the para compound would have an observed moment somewhat in excess of the calculated moment. Taking the moments of 1.5 for the amino and 1.8 for the ester, a value of 110° for the angle the resultant dipole in the amino group makes with the directed ring—N bond, and 55° for the angle the resultant of the ester group makes with the directed ring—C bond, the meta compound has a calculated moment of 2.45 in good

agreement with the observed moment of 2.40,¹³ while the para compound has a calculated moment of 2.56 which is 0.74 unit less than the observed moment of 3.30.¹³ This corresponds to a contribution of 2.5% from the form with a separation of charge. Although this percentage contribution is small it has a very great effect on the rate of hydrolysis of the compound as is indicated in a recent paper by Westheimer and Metcalf.¹⁴ Somewhat analogous is the Mills-Nixon effect where the predominance of one Kekulé form over the other by a few per cent. is enough to dominate a substitution reaction.¹⁵

If a quinone-hydroquinone system has a high potential the quinone is a good oxidizing agent and the quinone form relatively unstable. Considering the analogy between the forms



would expect the forms with a separation of charge to contribute less to those compounds in which the analogous quinones have a higher potential. Diphenoquinone has a potential of 0.954 and *p*-benzoquinone a potential of 0.715,¹⁶ therefore one would expect the form with a separation of charge to contribute less with *p*-(*p*-aminophenyl)-benzenesulfonamide than with sulfanilamide. The dipole moment evidence indicates that this is the case.

A theory in regard to the action of sulfanilamide is that the active agent is an oxidized form of the compound. Since we do not know the structure of the oxidized form we cannot say how the oxidation-reduction potential might vary with structural changes. However, it has been concluded¹⁷ that the first step in the oxidation of primary arylamines is the removal of one hydrogen atom from the nitrogen. Forms with a positive charge on the nitrogen would inhibit the removal of a hydrogen atom while aiding the liberation of a hydrogen ion. Assuming this mechanism of oxidation applies to sulfanilamide type compounds it is expected that *p*-(*p*-aminophenyl)-benzenesulfonamide will be more readily oxidized than sulfanilamide and qualitative observations on hot aerated solutions of the two compounds confirm this.

(13) Estermann, *Z. physik. Chem.*, **1B**, 134 (1928).

(14) Westheimer and Metcalf, *THIS JOURNAL*, **63**, 1339 (1941).

(15) Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., p. 136.

(16) Fieser, *THIS JOURNAL*, **52**, 4915 (1930).

(17) Fieser, *ibid.*, **52**, 5204 (1930).

p-(*p*-Aminophenyl)-benzenesulfonamide has been tested in the laboratories of Parke, Davis and Company, for activity against streptococcal infected mice. It was found to be inactive. Blood level studies showed adequate absorption of the compound.

It is possible that the therapeutic effects of sulfanilamide and related compounds are associated with the contributions made by the forms with a separation of charge. At least this is one of the more attractive hypotheses to account for the inactivity of compounds such as metanilamide and *p*-(*p*-aminophenyl)-benzenesulfonamide. Other compounds are being investigated in this connection.

Experimental

Apparatus.—The dielectric constants were measured with an oscillating circuit containing a gold plated condenser of 113.43 μmf capacity which was connected in parallel with a 1500 μmf General Radio calibrated variable condenser. A commercial broadcasting station KPO operating at a frequency of 680 kilocycles was used as a source of constant frequency oscillations. Densities were measured with a pycnometer of approximately 10 ml. capacity. Refractive indices were taken with a Pulfrich refractometer. Temperatures were controlled to within $\pm 0.1^\circ$ by electrically regulated thermostats. The capacity of the gold-plated condenser was determined using thiophene free benzene which had been dried over sodium and distilled through a 1-m. column packed with glass helices. The benzene was assumed to have a dielectric constant of 2.2760. If the lower value 2.2725 for benzene reported in the literature had been used our dioxane would have a correspondingly lower dielectric constant.

Materials

Dioxane.—Commercial 1,4-dioxane was purified as described previously.¹⁸ It had a boiling point of 101.0–101.2°, cor., at 753 mm. and a dielectric constant of 2.2095 at 25°.

Aniline.—The *c. p.* aniline was distilled from zinc dust in the presence of nitrogen. The colorless product boiled at 184.65–184.70°, uncorr.

Xenylamine.—The Eastman Kodak Co. practical grade was distilled from zinc dust in the presence of nitrogen. A colorless product resulted with a melting point of 50.5–51.5°, corr.

Benzenesulfonamide.—The Eastman Kodak Co. product was dissolved in 95% alcohol, treated twice with Norite and then crystallized from alcohol. The colorless compound which resulted had a melting point of 156–157°, corr.

***p*-Phenylbenzenesulfonamide.**—Biphenyl was sulfonated using a modified form of the procedure of U. S. Patent 1,865,776, July 5, 1932, and the copper salt was precipitated according to Latschinow.¹⁹ One hundred

grams of Eastman practical grade biphenyl was added to 45 ml. of concentrated sulfuric acid. The mixture was stirred thoroughly and heated in a steam-bath. At the end of twenty minutes it was poured into 300 ml. of hot water, 500 ml. of cold water was added and cooled to room temperature. The mixture was then extracted with three 100-ml. portions of ether and 36 g. of biphenyl was recovered from the ether extracts. The aqueous solution was warmed to 60° to drive out the ether dissolved therein and cupric oxide powder was added and stirred until it no longer reacted, 40 g. being required. The mixture was cooled to room temperature, the copper salt which contains 6H₂O filtered off and washed twice with water and once with ether. The salt was dried overnight in an oven at 100°. The product weighed 81 g., 61% yield based on the biphenyl actually used, 100 – 36 = 64 g.

***p*-Phenylbenzenesulfonyl chloride** was prepared directly from the above copper salt. Fifty grams of the salt was ground fine and mixed with 150 g. of phosphorus pentachloride in a 250-ml. Erlenmeyer flask. Much heat and hydrogen chloride were evolved and the contents became dark brown and partially liquefied. The flask was heated under reflux in an oil-bath at 150° for about ten minutes until the contents completely liquefied, then cooled and 200 ml. of water added with due care. Much hydrogen chloride and heat were again evolved. The precipitate was ground fine and boiled several times with water until the filtrate was colorless. The precipitate was then dried in an oven for twenty minutes at 70°. Some of the chloride was recrystallized from glacial acetic acid and there resulted white prisms which melted at 114–115°, cor.

For the preparation of *p*-phenylbenzenesulfonamide the above crude chloride was placed in a stainless steel bomb together with 250 ml. of a 15% solution of dry ammonia in absolute alcohol. The bomb and contents were then heated at 120° for seven hours, cooled and opened. The white precipitate which was present was boiled two times with water, ground fine, washed with water and dried overnight in an oven at 150°. There resulted 27 g. of the crude amide which melted at 220–224°. This was dissolved in 450 ml. of hot 50% dioxane–water which was then cooled to 40° and the first crop of crystals was filtered off, pressed out with a rubber sheet, washed with a little pure dioxane and dried overnight in a vacuum desiccator over sulfuric acid. There resulted 14 g. of white crystals which melted at 225.0–226.5°, cor. No elevation in melting point resulted on additional recrystallizations. From the mother liquor an additional 6 g. of the amide was obtained of about the same purity.

Sulfanilamide.—Commercial sulfanilamide was recrystallized twice from 95% alcohol. The product melted at 165–166°.

***p*-(*p*-Aminophenyl)-benzenesulfonamide.**—This compound was prepared as described previously.^{4,20} It exhibited the double melting point at 259–260° and 266–267°, cor.

Metanilamide.—Sixty-five grams of nitrobenzene was added slowly to 250 g. of 20% fuming sulfuric acid at 50°, then heated at 115° for forty minutes, after which the solution was cooled to 40°, 140 g. of chlorosulfonic acid

(18) Kumler, *THIS JOURNAL*, **62**, 3292 (1940).

(19) Latschinow, *Ber.*, **6**, 194 (1873).

(20) Van Meter, Bianculli and Lowy, *THIS JOURNAL*, **62**, 3146 (1940).

added slowly, and heated at 115° for two hours. After cooling to room temperature the mixture was poured onto 1500 g. of crushed ice with stirring. The chloride was filtered off and weighed 68 g. while wet. This chloride was placed in 500 ml. of cold concentrated ammonium hydroxide and stirred for nine hours. The precipitate was filtered off, washed three times with water and dried in an oven at 130°. The crude *m*-nitrobenzenesulfonamide weighed 42 g. and melted at 152–157°; 2.3 g. of this was recrystallized from 70 ml. of water and the 2.1 g. of crystals had a melting point of 162–163°, cor.

Forty grams of the crude *m*-nitrobenzenesulfonamide was placed in 600 ml. of 12% hydrochloric acid together with 80 g. of granulated tin, and refluxed for six hours. On cooling and filtering, 50 g. of nearly white crystals was obtained that contained much tin, presumably a complex tin salt. Thirty-five grams of this salt was dissolved in 250 ml. of 0.4 *N* hydrochloric acid and hydrogen sulfide bubbled through the solution for six hours until all the tin was converted to the sulfide. The tin sulfide was then filtered off and the filtrate made strongly basic to phenolphthalein. A small amount of a slightly bluish precipitate formed and was filtered through charcoal. The colorless filtrate was then brought to a *pH* of about 9 with concentrated hydrochloric acid. White crystals formed which were filtered off, washed twice with a little ice water and then dried overnight in a desiccator over sulfuric acid. There resulted 5.9 g. of metanilamide which was recrystallized from water and melted at 139.4–140.2° cor. Since the previously reported melting point of metanilamide was 142 and 143°^{21,22} we recrystallized some of this metanilamide two more times from water and found no change in the melting point.

As a test of its purity we determined the time-temperature cooling curve²³ of the metanilamide. A small unsilvered Dewar test-tube was fitted with a thermometer, heated to about 150° and 2 g. of the melted compound poured into it. The Dewar was placed in a larger test-tube which was immersed in a well-stirred oil-bath maintained at a temperature about 20° below the temperature registered by the thermometer in the Dewar tube. The cooling curve shown in Fig. 1 clearly shows that the melting point is 140.2°, cor. Furthermore, it indicates that our compound is a pure substance since the temperature at the midpoint when half the solvent has solidified is exactly the same as the initial freezing point.

Summary

Dipole moments of the following compounds were measured in dioxane and found to be: sulfanilamide 6.63, aniline 1.90, benzenesulfonamide 5.09, *p*-(*p*-aminophenyl)-benzenesulfonamide 6.71, xenylamine 2.07, *p*-phenylbenzenesulfonamide 5.20, metanilamide 5.63.

(21) Hypheneth, *Ann.*, **221**, 204 (1883).

(22) Dyke, *Quart. J. Pharm. Pharmacol.*, **10**, 319 (1937).

(23) Norton, "Laboratory Technique in Organic Chemistry," McGraw-Hill Book Company, Inc., New York, N. Y., 1938, p. 40.

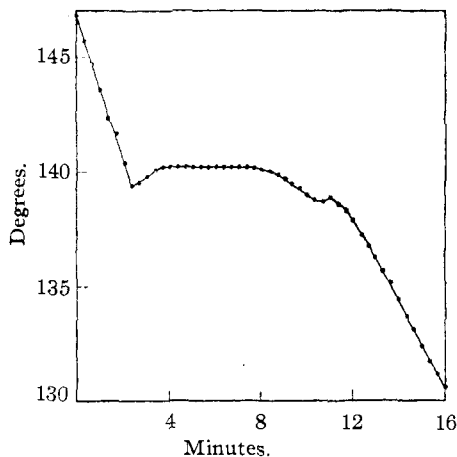


Fig. 1.—Time-temperature curve for metanilamide; solidification began at 2.3 min.; liquid was all gone at 11.3 min.

Aniline and xenylamine have moments 0.3–0.4 unit higher in dioxane than in benzene.

The moments sulfanilamide and *p*-(*p*-aminophenyl)-benzenesulfonamide would have without any resonance between the amino and sulfonamide groups have been calculated. The observed moments for sulfanilamide and *p*-(*p*-aminophenyl)-benzenesulfonamide were higher than the calculated moments by 0.81 and 0.69 unit, respectively. This is interpreted as evidence that a form with a separation of charge contributes appreciably to the structure of the molecules. The contribution of the form in case of sulfanilamide is about 3%, or more than twice that of the analogous form in the biphenyl derivative. The connection between the contribution of these forms, the therapeutic effect, the rate of oxidation and the stability of the corresponding quinones is discussed.

The moment of methyl *m*-aminobenzoate has been calculated and a value of 2.45 obtained in good agreement with the observed value of 2.40. The calculated moment for methyl *p*-aminobenzoate, 2.56, is 0.74 unit below the observed moment, 3.30, indicating that the contribution of the form with a separation of charge is about the same in this case as in the case of sulfanilamide.

A cooling curve for metanilamide was run and it gave evidence that our sample was of high purity and had a melting point of 140.2°, cor., as compared with the literature values of 142 and 143°.