

*Anal.* Calcd for  $C_{10}H_8N_2O_2$ : C, 58.76; H, 3.91; N, 13.71. Found: C, 58.84; H, 3.97; N, 13.59.

**3-Amidylphthalides (5).** Oxidation of 1-Hydroxy-3-amidylphthalans.—All oxidations were carried out using the procedure described above for oxidation of compounds of structure 1. Ice bath conditions were employed. Products were recrystallized from acetonitrile. Yields ranged from 50–60%.

**Oxidation of 2a and 2b.**—The product in both cases was 5b: mp 175–176°; ir ( $cm^{-1}$ ) 3257 (NH), 1748 (phthalide C=O), 1626 (amide C=O), 755, 688, 745 (CH out-of-plane deformation); nmr (DMSO- $d_6$ )  $\tau$  2.68 (d, 1,  $J = 9$  Hz, CHN), 1.90–2.08 (2 m's, 9, ArH), 0.42 (d, 1,  $J = 9$  Hz, NH).

*Anal.* Calcd for  $C_{15}H_{11}NO_3$ : C, 71.14; H, 4.34; N, 5.53. Found: C, 71.02; H, 4.40; N, 5.58.

**Oxidation of 2c.**—The product, 5c, had mp 162–163°; ir ( $cm^{-1}$ ) 3250 (NH), 1755 (phthalide C=O), 1630 (amide I CO), 750, 840 (CH out-of-plane deformation); nmr (DMSO- $d_6$ )  $\tau$  7.1–8.1 (m's, 9, ArH, CHN), 0.15 (d, 1,  $J = 9$  Hz, NH).

*Anal.* Calcd for  $C_{15}H_{11}NO_3Cl$ : C, 62.50; H, 3.47; N, 4.86. Found: C, 62.25; H, 3.66; N, 4.81.

**Oxidation of 2d.**—Use of the general procedure with 2d led to formation of 5d, mp 180–182° from acetonitrile: ir ( $cm^{-1}$ ) 3257 (NH), 1757 (phthalide C=O), 1630 (amide I C=O), 747 840, (CH out-of-plane deformation); nmr (DMSO- $d_6$ )  $\tau$  6.16 (s, 3, OCH<sub>3</sub>), 2.68 (d, 1,  $J = 10$  Hz, CHN), 2.95 and 2.06 (2 d's, 4,  $J = 9$  Hz, ArH on *para*-substituted ring), 2.50–2.00 (m, partially superimposed on down field ArH of *para*-substituted ring, 4, ArH in *ortho*-substituted ring), 0.48 (d, 1,  $J = 10$  Hz, NH).

*Anal.* Calcd for  $C_{15}H_{13}NO_3$ : C, 67.84; H, 4.59; N, 4.95. Found: C, 67.84; H, 4.59; N, 4.90.

**Oxidation of 2e.**—The product of this oxidation was 5e: mp 179–180°; ir ( $cm^{-1}$ ) 3256 (NH), 2959 (CH<sub>3</sub>), 1754 (phthalide C=O), 1653 (amide I C=O), 745 (CH out-of-plane deformation); nmr (DMSO- $d_6$ )  $\tau$  8.85 (s, 9, CH<sub>3</sub>), 2.94 (d, 1,  $J = 9$  Hz, CHN), 2.30 (m, 4, ArH), 1.25 (d, 1,  $J = 9$  Hz, NH).

*Anal.* Calcd for  $C_{15}H_{15}NO_3$ : C, 66.93; H, 6.48; N, 6.00. Found: C, 67.05; H, 6.40; N, 5.95.

**Acid-Catalyzed Hydrolysis of 2.**—Acid-catalyzed hydrolysis of the phthalans *via* the method described in ref 1 led to formation

of benzoic acid from 2a and 2b, *p*-chlorobenzoic acid from 2c, *p*-methoxybenzoic acid from 2d, and trimethylacetic acid from 2e. Products were identified *via* undepressed mixture melting points when applicable and ir spectra which were identical with those of authentic samples.

**Base-Catalyzed Hydrolysis of 2.**—The procedure used for base-catalyzed hydrolysis of the phthalans was that described in ref 1; however, all reactions except one were carried out at room temperature. Such reactions resulted in formation of benzamide from 2b, *p*-chlorobenzamide from 2c, *p*-methoxybenzamide from 2d, and trimethylacetamide from 2e. No identified products were isolated from base-catalyzed hydrolysis of 2a.

All products isolated were identified by undepressed mixture melting points and infrared spectra which were identical with those of authentic samples.

**Conversion of 2b to 2a.**—Compound 2b (0.51 g, 0.002 mol) was dissolved in 20 ml of absolute ethanol; 1 ml of 1 M HCl was added, and the mixture was allowed to stir overnight. Removal of solvent on the rotary evaporator and recrystallization from acetonitrile yielded 0.46 g (80%) of 2a identical with that prepared by reaction of *o*-phthalaldehyde with benzamide in ethanolic sodium ethoxide.

**Registry No.**—1a, 26268-85-9; 1b, 1968-04-3; 1c, 26268-87-1; 1d, 26268-88-2; 1e, 26268-89-3; 1f, 26268-90-6; 2a, 26268-91-7; 2b, 26322-33-8; 2c, 26268-92-8; 2d, 26268-93-9; 2e, 26322-34-9; 3c, 26268-94-0; 3d, 26322-35-0; 3f, 26322-36-1; 4c, 26268-95-1; 4f, 26268-96-2; 5b, 26268-97-3; 5c, 26322-37-2; 5d, 26322-38-3; 5e, 26268-98-4.

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## Rate and Equilibrium in Carbanion Formation<sup>1a</sup> by Bis(methylsulfonyl)methane

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Bis(methylsulfonyl)methane has been found to have a  $pK_a$  of 12.54 in water at 25°. The rate constant for exchange of its methylene hydrogen atoms in deuterium oxide at 25° is  $(8 \pm 2) \times 10^{-4} \text{ sec}^{-1}$  per hydrogen atom, and the Arrhenius activation energy is  $8 \pm 3 \text{ kcal/mol}$ . Between one tenth and one half of the ion pairs formed by donation of a proton from the sulfone to water are estimated to recombine with exchange instead of dissociating.

A number of studies of the kinetics and stereochemistry of the formation of carbanions stabilized by  $\alpha$ -sulfone substituents have been made.<sup>2</sup> Several of these studies provide evidence that the pyramidal form of the carbanion is not as unstable relative to the planar form as is the case for carbanions stabilized by  $\alpha$ -carbonyl,  $\alpha$ -aryl, and certain other substituents, and it is not even clear that the most stable form of  $\alpha$ -sulfonyl carbanions is necessarily the planar one. According to the principle of least motion,<sup>3,4</sup> if  $\alpha$ -sulfonyl carbanions are not preferentially planar or if the difference in stabilities be-

tween their planar and pyramidal forms is particularly small, then, other things being equal, they should be formed more rapidly than equally basic carbanions whose planar forms are much more stable than their pyramidal forms.

The data available in 1953 were sufficient to convince Pearson and Dillon that "sulfones are characterized by high rates of ionization for a given acid strength."<sup>5</sup> However, these data included only five observations on sulfones, and there was no sulfone for which both the rate and equilibrium constants for carbanion formation had been determined. We therefore decided to make such a determination, using bis(methylsulfonyl)methane, a sulfone for which both constants seemed likely to be measurable.

The  $pK_a$  of this bissulfone was found by potenti-

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(1) (a) This investigation was supported in part by Grant GP-7629 from the National Science Foundation. (b) National Science Foundation Undergraduate Research Participant, summer, 1969.

(2) Cf. D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965.

(3) F. O. Rice and E. Teller, *J. Chem. Phys.*, **6**, 489 (1938); **7**, 199 (1939).

(4) J. Hine, *J. Org. Chem.*, **31**, 1236 (1966).

(5) R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, **75**, 2439 (1953).

metric titration to be 12.54, in good agreement with the value 12.5 reported without experimental details<sup>6</sup> and in moderate agreement with the admittedly rough value 14.<sup>7</sup>

Although  $(\text{MeSO}_2)_2\text{CD}_2$  was easily prepared from the bissulfone and deuterium oxide, its deuterium exchange with protium oxide could not be studied conveniently because the proton magnetic resonance (pmr) peak due to the methylene group is so near the protium oxide peak. Therefore, the reaction studied kinetically was the exchange between deuterium oxide and the protiated bissulfone. When the bissulfone was dissolved in pure deuterium oxide, the peak due to the methylene group had disappeared before the pmr spectrum could be run. In view of the possibility that this exchange reaction was catalyzed largely by the deuterioxide ions in the solution, the experiment was repeated using acidified deuterium oxide. The methylene peak was then found to disappear at an observable rate, the half-life of the reaction being about 7 min at 42°. The reaction kinetics had to be studied at bissulfone concentrations of only a few hundredths molar, because the solubility of the bissulfone in water is low and the rapidity of exchange made it impractical to take the time to saturate the water with bissulfone. In these solutions the methylene peak is so small that peak area measurements are not very reproducible. In our rate constant determination we tried to compensate somewhat for this poor reproducibility by making a large number of measurements.

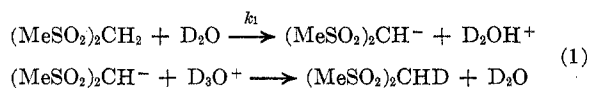
From the results shown in Table I, it is seen that

TABLE I  
RATE CONSTANTS FOR DEPROTONATION OF THE  
METHYLENE GROUP OF BIS(METHYLSULFONYL)-  
METHANE IN DEUTERIUM OXIDE SOLUTION

[Acid] <sup>a</sup>	Temp, °C	No. of runs	10 <sup>4</sup> $k_1$ , <sup>b</sup> sec <sup>-1</sup>	Mean correln coefficient
0.108	25	5	8.7 ± 3.5	0.93
0.0108	25	5	7.7 ± 1.2	0.93
0.0011	25	5	9.5 ± 1.1	0.95
0.108	42	9	16.5 ± 3.2	0.96
0.0108	42	6	17.2 ± 2.7	0.95
0.0011	42	3	20.7 ± 1.4	0.94

<sup>a</sup> Hydrochloric acid. <sup>b</sup> Means and standard deviations.

rate constants obtained in the presence of 0.108, 0.0108, and 0.0011 *M* hydrochloric acid are all within the experimental uncertainty of each other. From this and the fact that  $\alpha$ -hydrogen exchange by sulfones has not been found to be acid catalyzed, it was concluded that the proton removal was being accomplished by solvent molecules, possibly by mechanism 1 (eq 1). The



method of calculating rate constants employed, in which the removal of all the equivalent protons is treated as a single reaction, gives the rate constant *per* proton, *i.e.*, the statistically corrected rate constant,<sup>8</sup> which in the

present case is equal to one half the rate constant for carbanion formation. Since those carbon acids that have been studied (nitromethane<sup>9</sup> and 3-methyl-2,4-pentanedione<sup>10</sup>) ionize 37–69% faster in protium oxide than in deuterium oxide solution, the first-order rate constant for the ionization of bis(methylsulfonyl)methane in protium oxide at 25° is estimated to be  $(2.6 \pm 0.6) \times 10^{-3} \text{ sec}^{-1}$ , assuming that mechanism 1 is the only reaction path. From this value and the ionization constant, the value  $(9 \pm 3) \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}$  may be calculated for  $k_p$ , the rate constant for protonation of bis(methylsulfonyl)methide ions by hydrogen ions in water at 25°. This value is so near the rate constant ( $k_d$ ) that would be expected for the diffusion of the two ions together<sup>11</sup> as to suggest that a significant fraction of the ion pairs formed by diffusion together undergo proton transfer. This fraction, which will be denoted  $f$ , may be expressed in terms of rate constants that are known or can be rather reliably estimated, by the following derivation. The rate constant  $k_1$  for exchange *via* the formation of dissociated ions must equal  $(1 - f)k_c$ , where  $k_c$  is the rate constant for the formation of carbanions involved in exchange, including those carbanions that are formed only as part of ion pairs that collapse without dissociation. The value for  $k_p$  stated above was calculated from  $k_c$ , but it should have been calculated from  $k_1$ . It follows that  $k_p$  is really equal to  $(1 - f)(9 \pm 3) \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}$ . It may also be seen that  $k_p$  must be equal to the rate constant  $k_d$  for formation of ion pairs from the dissociated ions multiplied by the fraction of those ion pairs that undergo proton transfer. If these two expressions for  $k_p$  are equated, eq 2 results,

$$\begin{aligned} k_d f &= (1 - f)(9 \pm 3) \times 10^9 \text{ M}^{-1} \text{ sec}^{-1} \\ f &= \frac{(9 \pm 3) \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}}{k_d + (9 \pm 3) \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}} \end{aligned} \quad (2)$$

which may be solved for  $f$  with the result shown. Since  $k_d$  may be estimated<sup>11</sup> to be in the range  $1\text{--}4 \times 10^{10} \text{ M}^{-1} \text{ sec}^{-1}$ ,  $f$  is probably between 0.1 and 0.5.

From the kinetics of exchange at 42°, an Arrhenius activation energy of  $8 \pm 3 \text{ kcal/mol}$  may be calculated.

When the acid concentration was decreased further to  $8 \times 10^{-4}$ ,  $4 \times 10^{-4}$ , and  $2 \times 10^{-4} \text{ M}$ , the rate constants observed for exchange at 25°,  $(11.8 \pm 1.2) \times 10^{-4}$ ,  $(61 \pm 22) \times 10^{-4}$ , and  $(300 \pm 40) \times 10^{-4} \text{ sec}^{-1}$ , respectively, seemed to increase more rapidly than  $1/[\text{D}^+]$ . We have no explanation for this observation, which was not investigated thoroughly, but it cannot arise simply from attack of deuterioxide ions on the bissulfone. An upper limit on the rate constant for attack of deuterioxide ions on the bissulfone may be obtained from the data in Table I. It seems assured that this reaction is contributing less than  $4 \times 10^{-4} \text{ sec}^{-1}$  to the total rate constant obtained in the presence of 0.0011 *M* acid. Since the deuterioxide ion concentration in this solution was about  $1.4 \times 10^{-12} \text{ M}$ , the second-order rate constant for attack by  $\text{OD}^-$  is less than  $3 \times 10^8 \text{ M}^{-1} \text{ sec}^{-1}$ . Thus, when bis(methylsulfonyl)methane is involved in a proton-transfer reaction in which the equilibrium constant is considerably smaller than in the protonation of the bis(methylsulfonyl)methide ion, the rate constant in the exergonic direction falls short of the

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(7) G. Schwarzenbach and E. Felder, *Helv. Chim. Acta*, **27**, 1701 (1944).

(8) Cf. J. Hine, L. G. Mahone, and C. L. Liotta, *J. Amer. Chem. Soc.*, **89**, 5911 (1967).

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(10) F. A. Long and D. Watson, *J. Chem. Soc.*, 2019 (1958).

(11) M. Eigen, *Angew. Chem., Int. Ed. Engl.*, **3**, 1 (1964).

diffusion-controlled rate constant by at least two powers of ten. In contrast, glucose and guanidinium ions [each of which has an acidity constant within a factor of two of that for bis(methylsulfonyl)methane] are deprotonated by hydroxide ions with rate constants larger than  $10^{10} M^{-1} \text{sec}^{-1}$ .<sup>11</sup> Thus, although Pearson and Dillon's generalization is supported by the present work, the proton-transfer reactions of bis(methylsulfonyl)methane are slower than those of an oxygen or nitrogen acid (in which the acidic proton is not internally hydrogen bonded) of the same strength.

### Experimental Section

**Reagents.**—The method of Backer<sup>12</sup> was used for the preparation of bis(methylsulfonyl)methane: mp 147–148.5° (lit.<sup>12</sup> mp 148°); pmr ( $\text{CD}_3\text{SOCD}_3$ )  $\tau$  4.58 (m, 2,  $J = 0.6$  Hz,  $\text{CH}_2$ ) and 6.78 ppm (t, 6,  $J = 0.6$  Hz,  $\text{CH}_3$ ); mass spectrum (70 eV)  $m/e$  (rel intensity) 172 (14), 94 (100), 79 (54), 78 (33), 63 (86).

When bis(methylsulfonyl)methane was recrystallized from deuterium oxide solution, the product was bis(methylsulfonyl)methane- $d_2$ : mass spectrum (70 eV)  $m/e$  (rel intensity) 174 (10), 96 (65), 80 (25), 79 (55), 63 (100).

Solvent solutions for kinetic runs were prepared by dissolving gaseous hydrogen chloride in 99.8% deuterium oxide, titrating, diluting with deuterium oxide, and retitrating. In the most concentrated solutions used (0.1  $M$ ), this increased the protium content of the solvent by 50%.

**Determination of  $pK_a$ .**—A Radiometer automatic titrator (ABU1, PHM26c, SBR2c, and type C electrode) was used manually to titrate 25-ml samples of 0.00653 and 0.02317  $M$  bis(methylsulfonyl)methane with 0.1326  $M$  sodium hydroxide solution at 25°. From the pH values recorded at intervals of about 0.2 ml from 0.4–2.5 ml of added base, values of the ionization constant were calculated from the equation

$$K_a = \frac{[\text{H}^+]^2 + [\text{H}^+][\text{Na}^+] - K_w}{[(\text{MeSO}_2)_2\text{CH}_2]_t + (K_w/[\text{H}^+]) - [\text{H}^+] - [\text{Na}^+]}$$

where  $[(\text{MeSO}_2)_2\text{CH}_2]_t$  is the "total" concentration of bissulfone (including its conjugate base), pH was assumed to be equal to  $-\log [\text{H}^+]$ , and  $K_w$  is the value for the autoprotolysis constant of water calculated (by averaging several determinations) from the pH measured when the given volume of sodium hydroxide solution was added to pure water in the absence of sulfone. This method of calculation may be considered to be a way of calibrating the system at the high pH's encountered in the titration. The reliability of the method is supported by the values of  $pK_w$  obtained, ranging from 13.90 to 13.98, none of which differed by more than 0.02 from the value at the given ionic strength that may be obtained from a plot of the data listed by Harned and Owen.<sup>13</sup> The runs using 0.00653  $M$  bissulfone gave  $pK_a$  values around 12.6, but these were based on measured pH values that differed from those in the absence of sulfone by only about 0.05. The values obtained using 0.02317  $M$  bissulfone, where the pH differed by about 0.18 from that observed using no sulfone, are believed to be more reliable. Application of the Debye-Hückel limiting law to 11 observations between ionic strengths 0.0021

(12) H. J. Backer, *Recl. Trav. Chim. Pays-Bas*, **65**, 53 (1946).

(13) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," 3rd ed, Reinhold, New York, N. Y., 1958, pp 752–754.

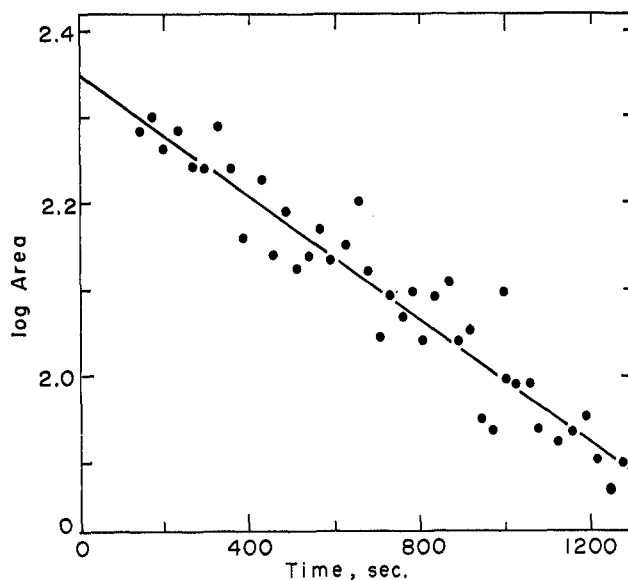


Figure 1.—Kinetic plot for the deuteration of bis(methylsulfonyl)methane in deuterium oxide containing 0.0108  $M$  hydrochloric acid.

and 0.0120  $M$  gave the average value  $12.536 \pm 0.008$  for  $pK_a$  at infinite dilution.

**Kinetics of Deuterium Exchange.**—In a typical run, about 1 ml of a solution of hydrochloric acid in deuterium oxide was added to more finely powdered bis(methylsulfonyl)methane than would readily dissolve, and the mixture was shaken vigorously for about 30 sec and filtered through a disposable pipet containing glass wool into a nmr tube. The nmr tube was inserted into the Varian A60-A nmr spectrometer, which had already been tuned for a solution of the bissulfone in deuterium oxide, taking care that no spinning side bands from the nearby peak due to the residual protons in the deuterium oxide fell too near the methylene peak of the bissulfone. The methylene peak was scanned repeatedly (the solution was too dilute for reliable results to be obtained from the integrator on the spectrometer) and the time noted at the midpoint of each scan. The peak areas were measured, some by planimetry and some by cutting out and weighing, before the method of counting squares was settled on. Rate constants were calculated from the slopes of the best lines, determined by the method of least squares, through plots of the logarithm of the area of the peaks vs. time. In a few runs the area of the methyl peaks was used as an internal standard and  $\log (A_{\text{CH}_2}/A_{\text{CH}_3})$  was plotted against time, but it was not clear that this resulted in any more reliable rate constants. Correlation coefficients for the plots ranged from 0.83 to 1.00 with a median of 0.95. The runs were followed to about 75% completion. Some of the runs were carried out at  $42 \pm 1^\circ$ , the temperature attained when the variable temperature controller was not used, and some at  $25 \pm 1^\circ$ . The average number of points taken was 37 at 25° and 17 at 42°. A kinetic plot for a typical run (correlation coefficient 0.95) is shown in Figure 1. The rate constants obtained are summarized in Table I.

**Registry No.**—Bis(methylsulfonyl)methane, 1750-62-5.