

Stability of Sodium Diethyldithiocarbamate in Aqueous Solution

by Proton Magnetic Resonance Spectroscopy

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The stability of sodium diethyldithiocarbamate (SDDC) has been investigated previously using spectrophotometric, polarographic, potentiometric, and gas evolution techniques. In the present study the stability of SDDC in aqueous media has been investigated by proton magnetic resonance (pmr) spectroscopy. The decomposition of $\sim 0.073M$ SDDC in deuterated $1.0M$ solutions of pD 4.8 to 7.9 buffers was followed at temperatures between 28° and 60° C. The rate data thus obtained were used to calculate the Arrhenius activation energy

(ΔE_a) and the activation thermodynamic parameters (ΔG^\ddagger , ΔH^\ddagger , ΔS^\ddagger) for the decomposition process. The results of the present pmr study agree with published data obtained by other methods at relatively low SDDC concentrations (0.001 to $0.003M$) and temperatures (1° to 30° C). This agreement indicates that the decomposition reaction proceeds in essentially the same manner in deuterated systems at relatively high temperature and concentration as it does in dilute, nondeuterated solutions at lower temperatures.

Sodium diethyldithiocarbamate (SDDC) has been shown to be an effective chelating agent in the treatment of nickel carbonyl poisoning (Sunderman, 1966) and in the mobilization of nickel and copper in hepatolenticular degeneration. It has also been found to lower the noradrenaline level in rat brain by inhibiting the action of dopamine- β -oxidase (Carlsson *et al.*, 1966; Collins, 1965). Dithiocarbamates in general have powerful fungicidal properties, and after absorption into cucumber seedling roots, SDDC has been shown to give rise to various derivatives which are fungitoxic (Dekhujzen, 1964). The diethyldithiocarbamate moiety is itself a reduction product of tetraethylthiuram disulfide whose broad spectrum of utility includes use as seed disinfectant, fungicide, rubber accelerator and vulcanizer, and medicinal agent for the treatment of alcoholism. Because of their widespread usage and the importance of their reactions, the stabilities of SDDC and other dithiocarbamates are of much interest.

The decomposition of sodium diethyldithiocarbamate (SDDC) has previously been studied under various conditions of pH, concentration, and temperature. The techniques utilized in these studies include spectrophotometry (Aspila *et al.*, 1969; Bode, 1954), gas evolution measurements (Hallaway, 1959; James and Garton, 1952; Lopatecki and Newton, 1952), polarography and potentiometric titration (Joris *et al.*, 1969; Zahradnik and Zuman, 1959). In the present investigation the techniques of proton magnetic resonance (pmr) spectroscopy were used to study the decomposition of SDDC under conditions of concentration, temperature, and isotopic substitution (deuteration) which differ from those

used in previously published work. The reaction half-life values, which are in agreement with data in the literature, are used to calculate the specific rate constants (k_{sp}) for the decomposition process at four temperatures. The temperature dependence of k_{sp} was then used to calculate the Arrhenius activation energy (ΔE_a) and the activation thermodynamic parameters (ΔG^\ddagger , ΔH^\ddagger , ΔS^\ddagger) for the reaction.

EXPERIMENTAL

Apparatus. A standard Varian HA-100 nmr spectrometer was used in the investigation. The instrument was operated in the frequency-sweep mode locked on the water protons present in the deuterated buffer solvents. Rate measurements were made at elevated temperatures (40° , 50° , and 60° C) maintained within $\pm 2^\circ$ C using a Varian variable temperature controller. Measurements at $28 \pm 1^\circ$ C were made at the ambient probe temperature.

Reagents. Reagent grade SDDC in the trihydrate form $(CH_3CH_2)_2NCS_2Na \cdot 3H_2O$ from the J. T. Baker Chemical Co. was used without further purification for all of the rate measurements. Deuterated $1.0M$ acetate and $1.0M$ phosphate buffer solutions were prepared with Mallinckrodt reagent grade glacial acetic acid or Fisher primary standard KH_2PO_4 in D_2O obtained from Diaprep, Inc. The pD values of aliquots of these solutions were adjusted by adding Diaprep NaOD (40% in D_2O) until the desired pD was reached. The pD values were determined using a Beckman Zeromatic II pH meter standardized with protonated buffers. A correction factor of 0.4 units (Covington *et al.*, 1968) was added to the observed meter reading to get the pD of the deuterated solutions.

Procedure. The mechanism by which SDDC decomposes in aqueous media is thought to be via rapid attack by H^+ (or D^+) at the nitrogen of the dithiocarbamate anion followed by dissociation of the zwitterion into diethylamine and carbon disulfide (Aspila *et al.*, 1969; Zahradnik and Zuman,

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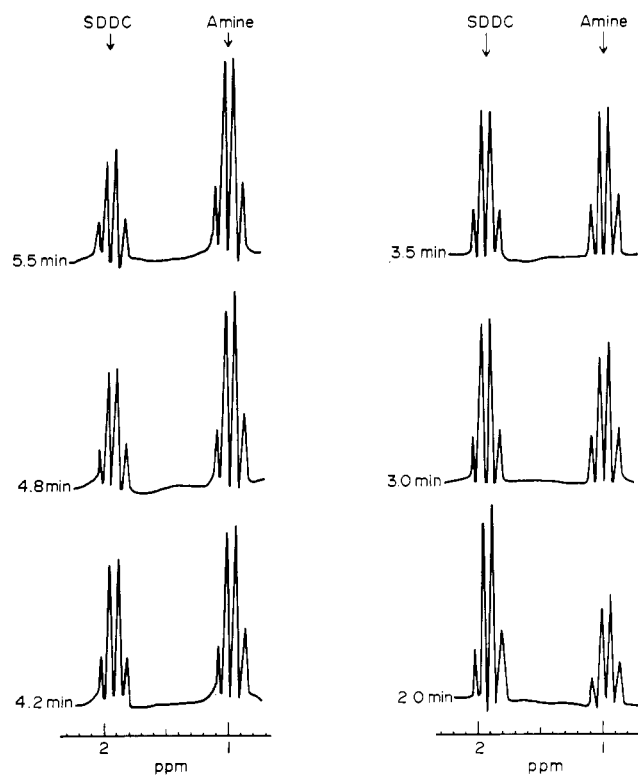
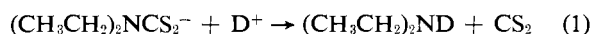


Figure 1. Tracings of the methylene region of pmr spectra showing the extent of decomposition of SDDC at various times after mixing

The initial concentration of SDDC in the 1.0M acetate buffer solution was 0.073M. The half-life of this reaction at 28° C and pD 5.6 is 3.5 min

1959). It has been demonstrated that the net decomposition reaction for SDDC above pH 3 is well represented by Equation 1. The half-life of this reaction at a given pD and tempera-



ture was determined in the present study by observing the methylene region of the pmr spectrum of a sample at various times during the reaction. The $-\text{CH}_2-$ quartet from the reactant SDDC appears about 0.95 ppm downfield from the $-\text{CH}_2-$ quartet which corresponds to the product diethylamine. As a reaction progressed, therefore, a decrease in size in the downfield quartet and an increase in size of the highfield quartet were observed as illustrated in Figure 1. Since the pmr line shapes of both quartets are similar, comparison of the heights of the peaks gives essentially the same measure of relative concentrations as does comparison of the integrated peak areas. Thus the half-life ($t_{1/2}$) of a reaction was taken to be that time at which the average heights of the two center peaks of each quarter were equal. For reactions with half-life values less than 1 min, allowance was made for the difference in times at which the two quartets were recorded. In these cases plots of peak height vs. time were made for each quartet, and the reaction half-life was taken as the time at which the curves crossed. For the pD range of the buffer solutions used in this study, integration of the pmr signals indicated that loss of the amine into the sample tube above the solution was negligible.

The time of reaction was measured from the point of mixing of the solid SDDC with the deuterated buffer, which had previously been thermally equilibrated in the sample tube in a water bath. Quantities of SDDC $\cdot 3\text{H}_2\text{O}$ weighing from 6.4 to 6.7 mg were added to 0.4 cc of the appropriate buffer

Table I. Reaction Half-Life Dependence on pD and Temperature

pD	T (°C)	$t_{1/2}$ (min)	pD	T (°C)	$t_{1/2}$ (min)
4.8	28	0.5	7.4	40	51
5.3	28	1.3			
5.6	28	3.5	5.9	50	0.8
5.9	28	7.2	6.4	50	2.0
6.1	28	13	6.9	50	5.3
6.5	28	30	7.4	50	17
6.8	28	57	7.9	50	65
7.1	28	110			
7.5	28	285	7.4	60	7.7
7.7	28	480			
7.9	28	780			

making solutions that were $\sim 0.073M$ in SDDC. All measurements at less than pD 6.0 and the one measurement at pD 6.4 and 50° C were made using acetate buffers. Phosphate buffers were used for all of the other rate determinations.

RESULTS AND DISCUSSION

The reaction half-lives measured in this study are given in Table I. The temperature range (28° to 60° C) covered by these data is higher than that (1° to 30° C) used in the studies in the literature mentioned above, and the rate constants determined in the present work are accordingly larger.

The concentrations of SDDC and the buffers in this study are greater (by a factor of at least 10) than in the solutions reported in the other investigations. The result of the higher ionic strength used in the present work is an increase in the value of the rate constant observed. The magnitude of this increase can be estimated from the Brønsted relation given in Eq 2.

$$\log k = \log k^0 + z_a z_b 1.02 \sqrt{I} / (1 + 2\sqrt{I}) \quad (2)$$

There k is the rate constant measured at ionic strength I , and k^0 is the rate constant at infinite dilution. The symbols z_a and z_b represent the charges on the reacting ions. Although Equation 2 can be rigorously applied only at low values of I , it indicates the values of the rate constants measured in the experiment at $I = 1.75$ are perhaps $10^{0.3}$ (or ~ 2) times larger than those measured by others at $I = 0.01$.

The first order dependence of the SDDC decomposition rate on both the hydrogen ion concentration and the SDDC concentration has been established previously for dilute solutions at low temperatures. The linear curves in Figure 2 show that the decomposition reaction is also first order with respect to deuterium ion concentration in more concentrated solutions at elevated temperatures. It is assumed in the following treatment that the reaction also remains first order in SDDC at the relatively high concentrations and temperatures used in this study. Preliminary measurements in the authors' laboratory supported this assumption.

The rate expression given in Eq 3 defines the specific rate constant (k_{sp}) as it is discussed in the present work. The integrated form of Eq 3 can be rearranged to give Eq 4 which applies when half of the SDDC has decomposed and the time, t , equals the half-life $t_{1/2}$. Figure 3 shows plots of Eq 4 using the data at 28° and 50° C from Table I. The slopes of the two curves in Figure 3 are proportional to k_{sp} at those temperatures and were used to calculate the rate constants shown in Table II. The values of k_{sp} at 40° and 60° C in

$$-d[\text{SDDC}]/dt = k_{sp}[\text{D}^+][\text{SDDC}] \quad (3)$$

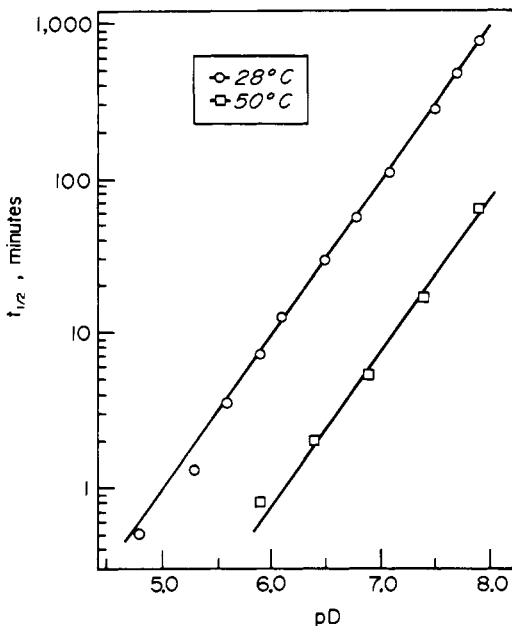


Figure 2. Dependence of reaction half-lives on pD

$$1/t_{1/2} = k_{sp}[D^+]/\ln 2 \quad (4)$$

this table were calculated directly from Eq 4, using pD and $t_{1/2}$ data from Table I.

The values of the specific rate constants measured in this study may reflect an isotope effect. It has been reported (Aspila *et al.*, 1969) that the apparent rate constant for the decomposition of pyrrolidine dithiocarbamate is about two times greater in D_2O than in H_2O , depending upon the acidity of the solution. Assuming that a similar situation exists with SDDC, the values of k_{sp} given in Table II may be higher than they would be in protonated solutions.

The temperature dependence of k_{sp} is indicated by the upper curve in Figure 4. The linear relationship between $\log k_{sp}$ and the reciprocal absolute temperature may be

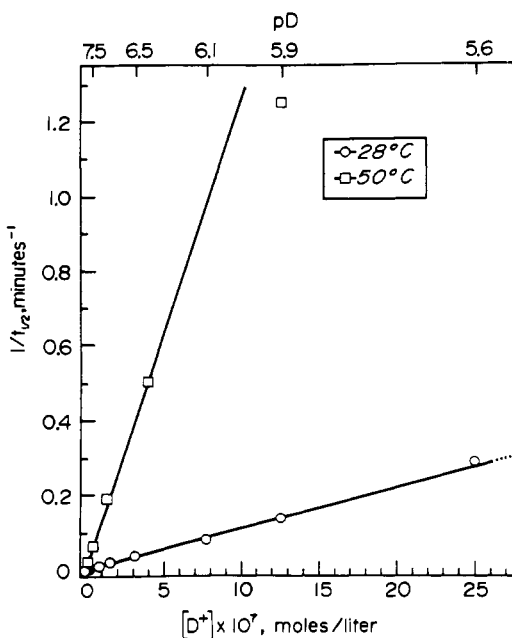


Figure 3. Graphs for determining k_{sp} at 28° and 50° C

Table II. Specific Rate Constant at Various Temperatures

T (°C)	k_{sp} (liters/mole/min)
28	7.76×10^4
40	3.41×10^5
50	8.76×10^5
60	2.26×10^6

explained by the Arrhenius rate theory wherein the rate constant (k) for a process is related to the activation energy (ΔE_a) for that process, as in Eq 5.

$$k = Ae^{-\Delta E_a/(RT)} \quad (5)$$

There A is the preexponential or frequency factor, R is the gas constant in terms of cal/(mole deg), and T is the absolute temperature. The slope of a semilogarithmic plot of k vs. $1/T$ equals $-\Delta E_a/(2.303 R)$, and from the slope of the upper curve in Figure 4 the activation energy for the decomposition of SDDC under the conditions used in the present investigation is calculated to be 21.1 kcal/mole. This value is 1.7 kcal lower than a previously reported value (Zahradnik and Zuman, 1959) determined at a lower concentration in a non-deuterated buffer system. This difference of approximately 8% indicates the importance of the ionic strength and isotope effects.

A second way of explaining the influence of temperature on k_{sp} follows from consideration of the absolute reaction rate theory. In this theory a rate constant (k) is related to the thermodynamic free energy of activation (ΔG^\ddagger) according to Eq 6.

$$k = (\kappa k_B T/h) e^{-\Delta G^\ddagger/(RT)} \quad (6)$$

There k_B and h are, respectively, the Boltzmann and Planck constants, κ is a transmission coefficient here taken as unity, and R , T , and ΔG^\ddagger have the meanings previously assigned. Making the substitution $\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$ introduces the enthalpy (ΔH^\ddagger) and entropy (ΔS^\ddagger) of activation and allows Eq 6 to be rearranged to the form given in Eq 7. So the lower curve plotted in Figure 4 follows the form of

$$k/T = \left(\frac{k_B}{h} e^{-\Delta S^\ddagger/R} \right) e^{\Delta H^\ddagger/(RT)} \quad (7)$$

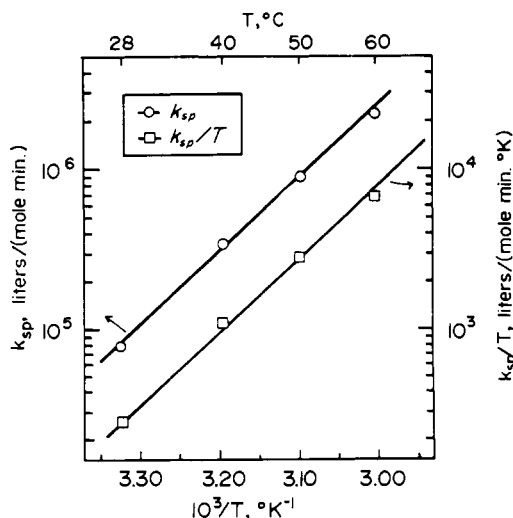


Figure 4. Graphs for determining ΔE_a and ΔH^\ddagger

Table III. Activation Parameters for the Decomposition of SDDC

ΔE_a	21.1 kcal/mole
ΔH^\ddagger	20.5 kcal/mole
ΔG^\ddagger (28° C)	13.3 kcal/mole
ΔG^\ddagger (50° C)	12.8 kcal/mole
ΔS^\ddagger (28° C)	23.9 cal/(mole deg)
ΔS^\ddagger (50° C)	23.8 cal/(mole deg)

Eq 7, and from its slope ΔH^\ddagger is evaluated to be 20.5 kcal/mole. The values of ΔE_a and ΔH^\ddagger derived from the graphs in Figure 4 conform in magnitude to the theoretical relationship that $\Delta E_a = \Delta H^\ddagger + RT$.

The free energy of activation (ΔG^\ddagger) was calculated using Eq 6 and values of k_{sp} expressed in terms of seconds at 28° and 50° C. The results of the computations are given in Table III. Also given there are values of ΔS^\ddagger which were calculated at 28° and 50° C from the above relationship between ΔG^\ddagger and ΔH^\ddagger . The close agreement between ΔS^\ddagger values at 28° and 50° C is an indication that the enthalpy of activation is relatively independent of temperature over the temperature range investigated. The large positive values of ΔS^\ddagger result from the loss of order in the solution which accompanies the reaction of two solvated ions to form a neutral species in an aqueous system.

The specific rate constants determined in the present investigation are probably several times greater than they would be in nondeuterated media of lower ionic strength at comparable temperatures. However, because of the logarithmic

relationship involved, the activation energy for SDDC determined under these different conditions would be expected to agree within 10%. This indicates that the deuteration and concentration requirements of the pmr experiment are not severe limitations, and the data obtained from such a system can be related to the more common nondeuterated, dilute systems. The main advantage of the pmr technique in a study such as this is that data can be obtained easily in a rapid and direct manner.

By comparison of the activation parameters for SDDC obtained in the present investigation with similar parameters for other metallic dithiocarbamates, it is hoped that information will be obtained which can help to explain the relative reactivities of these compounds in certain biological systems.

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