Dynamic NMR as a Nondestructive Method for the Determination of Rates of Dissociation. III. Ionic Dissociation of α-Chlorodibenzyl Sulfide[1]

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(Received February 10, 1981)

Rates of dissociation of α-chlorodibenzyl sulfide have been determined by dynamic NMR technique. Examination of the rates at various concentrations of chloroform-*d* solutions has confirmed that the rates are not dependent on concentration, thus establishing that the NMR measurement affords data of unimolecular dissociation. The salt effect seems to be very small since addition of tetraethylammonium bromide hardly affects the rates of dissociation. Rates of dissociation in *o*-dichlorobenzene are smaller than in chloroform-*d*. The main contribution to the decrease in rates is given by the increase in enthalpy of activation, indicating that the hydrogen-bonding ability of chloroform is favorable for ionic dissociation.

Ionization of organic halides is an important process, since it is regarded as the first and rate-determining step in S_N1 type reactions.[2] Winstein *et al.* were able to analyze the dissociation process into at least three steps: formation of intimate ion pair, solvent-separated ion pair, and free ions.[3] In solvolytic reactions, any of the ionic species can produce products depending on concentration,[4] making it difficult to study the earlier stages of ionization by solvolysis.

$$RX \rightleftharpoons R^+X^- \rightleftharpoons R^+ /\!/ X^- \rightleftharpoons R^+ + X^-$$

products products products

Various methods have been worked out in order to clarify the early stages. One is the exchange of a halogen (or a sulfonyloxyl) group which is labeled by an isotope.[5,6] However, it has a handicap intrinsically in that the rates are measured in the presence of salts, giving rise to the salt effect. Other methods involve racemization of an optically active halide (or sulfonate)[7] or scrambling or retention of oxygen-18 isotopes in carboxylates[8] and sulfonates.[9] These techniques apparently require optical resolution of the substrate and preparation of the isotopically labeled compounds. If a facile method is available, it would help clarify the initial stages of ionization of organic halide to a considerable extent.

We have found that easily ionizable compounds such as 2-chloro-1,3,5-trithiane exhibit a drastic change in line shapes of their NMR spectra, indicating the ionization process of the compounds.[10] The method has been applied to substituted α-chlorodibenzyl sulfide to show that it is possible to extend the method to ionic dissociation if the compound in question carries diastereotopic protons and a chiral center which is lost on ionization.[11]

Since the process was followed by the coalescence temperature method[12] of NMR spectroscopy, only the free energies of activation have been available. Kinetic data at various temperatures would enable us to get further insight into the early stages of ionization; most of earlier works provided kinetic data only at a certain temperature. The concentration *ca.* 0.5 mol L^{-1} utilized in the routine measurements of ^1H NMR spectroscopy might be too high to observe S_N1 type ionization; in the classical methods a lower concentration was used. It is necessary to examine the usual concentration in NMR measurements as regards S_N1 reactions.

We have carried out dynamic NMR measurements of α-chlorodibenzyl sulfide solutions in various concentrations. The line shapes were simulated and activation parameters, ΔH^* and ΔS^*, were obtained. This paper reports the results. The effects of the salts added as well as the solvents on ionic dissociation are discussed.

Experimental

Materials and Solutions. α-Chlorodibenzyl sulfide was prepared by the chlorination of dibenzyl sulfide with *N*-chlorosuccinimide.[11] Chloroform-*d* or *o*-dichlorobenzene was dried over Molecular Sieves 4A and solutions were prepared in a dry box desiccated with diphosphorus pentaoxide. The solutions were made directly by weighing the sample and the solvent. The concentrations were calculated by using the density of the solvent. Substance to be added to chloroform-*d* solutions was carefully dried either in a vacuum or by means of Molecular Sieves.

^1H NMR Measurements. The spectra were obtained on a Hitachi R-20B spectrometer equipped with a temperature variation accessory for solutions with high concentration, and on a JEOL FX-60 spectrometer equipped with a temperature variation accessory and FT-facilities for solutions with low concentration. Both instruments were operated at 60 MHz. The temperature of the solution was determined by the chemical shift differences of methanol and ethylene glycol protons, at low and high temperatures, respectively, when not directly read by a thermocouple.

Acquisition and Processing of Data. The ^1H NMR spectral line shapes were simulated with a modified Binsch program,[13] the process being treated as an AB⇌BA exchange. $\Delta\delta_{AB}$ and J_{AB} were obtained by simulating the spectra at temperatures low enough where the rate of exchange is considered to be zero. They were treated as constant throughout the temperature range examined. The T_2 values were obtained from the half band widths of the methine proton signals at given temperatures. The calculated spectra were compared with the observed by visual fitting. The rates of proton spin exchange thus obtained were put into the Eyring equation and activation parameters, ΔH^* and ΔS^*, were obtained.

The free energies of activation for the spin exchange at the coalescence temperatures were obtained by putting the observed data into[14]

$$k_c = \frac{\pi}{\sqrt{2}}\sqrt{6J_{AB}^2 + \Delta\delta_{AB}^2}. \quad (1)$$

Table 1. AB proton exchange in α-chlorodibenzyl sulfide in chloroform-*d*: ^{1}H NMR spectral data at 60 MHz and kinetic parameters

	Run 1	Run 2	Run 3	Run 4
Concentration/mol L^{-1}	0.267	0.195	0.116	0.0190
$\Delta\delta_{AB}$/Hz	9.49	9.39	8.97	9.26
J_{AB}/Hz	13.80	13.20	13.20	13.66
ΔH^*/kcal mol^{-1}	6.8±1.0	6.8±0.6	6.8±0.1	6.8±0.6
ΔS^*/e.u.	−29.8±3.2	−28.9±2.0	−29.7±0.3	−30.1±2.0
ΔG_c^*/kcal mol^{-1} a)	15.5	15.3	15.4	15.4
ΔG_c^*/kcal mol^{-1} b)	16.0	15.6	15.9	16.1
T_c/°C	37	32	34	36
k_c/s^{-1} a)	78.0	74.8	74.5	77.1

a) Obtained by the coalescence temperature method. b) Calculated from the enthalpy and the entropy of activation.

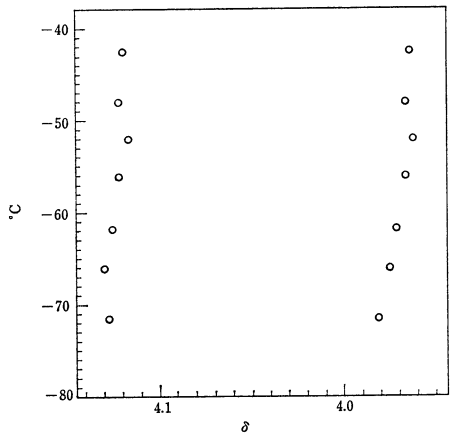


Fig. 1. Chemical shifts of A and B protons of α-chlorodibenzyl sulfide in chloroform-*d* at various temperatures.

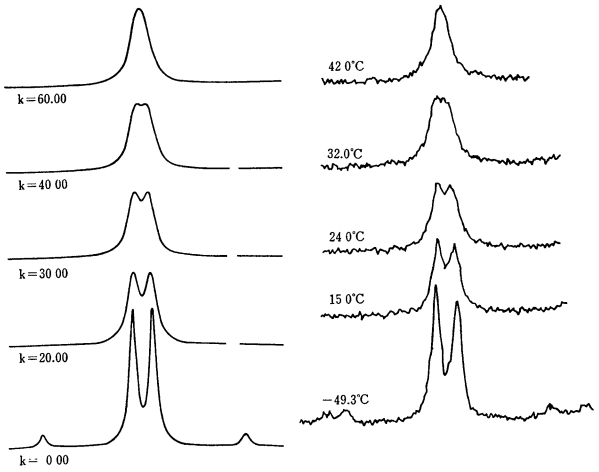


Fig. 2. Calculated and observed AB parts of the spectra of α-chlorodibenzyl sulfide in chloroform-*d* at the concentration of 0.195 mol L^{-1}. The signals outside of the AB are due to impurities.

Results and Discussion

Since the diastereotopic protons in α-chlorodibenzyl sulfide is connected to the chiral center *via* two single bonds, there are various conformations possible in solution. The distribution of the conformations and consequently chemical shift difference might change with temperature. This is serious in total line shape analysis, since the chemical shift difference cannot be directly read from the line shapes at near-by coalescence temperatures. The difficulty is usually overcome by assuming the linearity of the change in the chemical shift difference due to temperature. We have measured the chemical shift differences at various temperature by observing the spectra at a temperature where the exchange of proton spins is slow, and also at several lower temperatures. The results are shown in Fig. 1. We see that the chemical shifts change with temperature. The difference in chemical shifts between protons A and B remains almost constant, enabling us to assume that the chemical shift differences are constant througout the temperature range examined. Coupling constants of the AB protons were invariant as well.

The agreement between the calculated and the observed spectra is satisfactory. A set of typical data is given in Fig. 2. The data obtained with chloroform-*d* solutions are summarized in Table 1. The kinetic parameters obtained with various concentrations agree within the error limit, although the concentrations have been changed by an order of magnitude. The calculated free energies of activation from the enthalpies and entropies of activation, obtained by line shape analyses, are in good agreement with those obtained by the coalescence temperature method. This may be taken as evidence that the line shape analysis affords reliable data since the principles of the two methods differ.

The activation parameters are independent of concentration. It is assumed in the NMR theory of exchange of proton spins that the process is unimolecular. If the reaction is multimolecular, its treatment would be as follows. If the actual reaction is of *n*-th order, the rates of the reaction is expressed by

$$v = k[x]^n. \quad (2)$$

Since, in the NMR treatment, the reaction is taken to be of the first order, the rate expression becomes

$$v = k[x]^{n-1}[x] = k'[x]. \quad (3)$$

Putting the k' value into the Eyring equation, we obtain

Table 2. AB proton exchange in α-chlorodibenzyl sulfide in *o*-dichlorobenzene: ^{1}H NMR spectral data at 60 MHz and kinetic parameters

	Run 5	Run 6	Run 7
Concentration/mol L^{-1}	0.214	0.197	0.167
$\Delta\delta_{AB}$/Hz	10.15	10.39	10.15
J_{AB}/Hz	13.2	13.2	13.2
ΔH^*/kcal mol^{-1}	10.6±1.0	8.1±0.4	9.1±0.9
ΔS^*/e.u.	−22.0±2.7	−29.8±1.1	−24.4±4.7
ΔG_c^*/kcal mol^{-1} a)	18.4	19.1	17.4
ΔG_c^*/kcal mol^{-1} b)	18.7	19.4	17.4
T_c/°C	92.5	105.3	96.0
k_c/s^{-1}	75.3	75.4	75.3

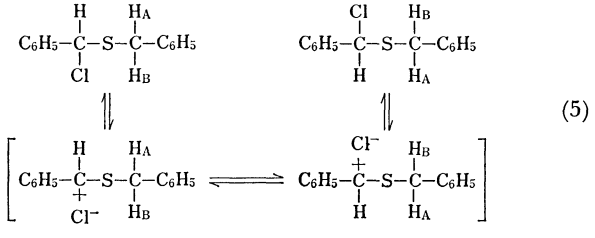
a) Obtained by the coalescence temperature method. b) Calculated from the enthalpy and the entropy of activation.

$$\ln\frac{k'}{T} = \frac{\Delta H^*}{R}\times\frac{1}{T} + \ln[x]^{n-1} + \frac{\Delta S^*}{R} + \ln\frac{k_B}{h}. \quad (4)$$

Thus correct ΔH^* can be obtained from the slope of the straight line by the plot. However, the intercept contains a $\ln[x]^{n-1}$ term, indicating that if the reaction is not unimolecular but multimolecular, the apparent ΔS^* should change with concentration. Since the actual values of ΔS^* are invariant throughout the concentration range examined, the constancy assures that we are measuring the unimolecular dissociation process of the α-halo sulfide.

The enthalpy of activation is very small whereas the entropy of activation is very large negative (Table 1). Easily ionizable organic halides give very large negative entropy of activation for solvolysis. For example, triphenylmethyl chloride gives ΔH^* 12.5 kcal mol^{-1} (1 cal=4.18 J) and ΔS^* −17 e.u. (1 e.u.= 4.18 J K^{-1} mol^{-1}) in aqueous acetone.[15] The entropy of activation for the exchange of chloride ion between an ammonium salt and triphenylmethyl chloride is even larger: ΔH^* and ΔS^* are 12.4 kcal mol^{-1} and −39 e.u. at 50 °C, respectively.[6] It is suggested that a large negative entropy of activation is associated with an ionization process in a medium of low dielectric constant.[16] The loss of freedom in motion of solvent molecules by ionization should cause the phenomenon.

The present results are the consequence of racemization of the compound which should be derived by the motion of ionic species. If the ion pair collapses from the side where the chloride ion departs, it does not cause racemization: it is not observed as the exchange of proton spins and the situation is apparent from Eq. 5.



(5)

Instead, either the rotation of the planar cation or the motion of chloride ion from one side to another of the cation plane is necessary to cause racemization, *i.e.* exchange of AB proton spins. This motion requires some freedom of the ionic species. This process does not seem possible in the intimate ion pair as suggested by Winstein and Robinson[17] for the attack by a solvent molecule, but it is possible in a loose, solvent-separated ion pair. It is not clear whether the formation of the intimate ion pair is the rate determining step of the observed change: the second step, intervention of solvent molecule(s), might be the rate determining as well. However, the above discussion indicates that the solvent-separated ion pairs are formed in nonpolar solvents like chloroform.

As a preliminary test of the salt effect on the ionization in this system, tetraethylammonium bromide was added. A solution containing 0.115 mol L^{-1} of α-chlorodibenzyl sulfide and 0.112 mol L^{-1} of the salt in chloroform-*d* showed the coalescence of the signals AB due to the methylene protons at 32.2 °C which differ little from those in Table 1. Since lowering in solution temperature caused precipitation of the salt, it was not possible to obtain the chemical shift difference and the coupling constant of the AB protons for calculation of the free energy of activation at the coalescence temperature. By using the data of Run 2, Table 1, which are not considered to be affected much by the salt added, the rate constant at 32.2 °C is calculated to be 74.8 s^{-1}. The presence or absence of the salt effect should be discussed carefully,[4] but the results suggest that the salt effect[18] is practically absent, since high concentration of the salt should affect the rates of ionization to some extent.[19] The salt effect is larger in less polar media.[20] Winstein *et al.* suggested that it is mostly caused by ion pairs in less polar media because the concentration of free ions is too low.[21] Although sodium tetraethylaluminate becomes solvent-separated ion pairs in benzene on addition of polar solvents,[22] it is not possible to utilize this in our case. However, it is almost certain that there are solvent-separated ion pairs in our system because of the low polarity of the medium. Further elaboration to fill the gap between the solvents, such as acetone and diethyl ether used by Winstein *et al.*,[20] and chloroform is apparently needed.

Pyridine reacts almost instantaneously with chloride to form a salt on addition to a solution in chloroform, but we could detect no ^{1}H NMR signals attributable

to α-bromodibenzyl sulfide which could be formed by exchange of the anion, after leaving a solution of tetraethylammonium bromide and α-chlorodibenzyl sulfide in chloroform to stand overnight. Swain and Kreevoy[6] found that the chloride-exchange could occur in benzene with measurable rates.

In order to examine the solvent effect on the enthalpy and entropy of activation for ionization, *o*-dichlorobenzene was used as a solvent. The results are given in Table 2. The dissociation of the halide in *o*-dichlorobenzene is slower in this solvent than in chloroform.[11] The main factor which decreases the rates of dissociation is the enthalpy term. Entropy of activation is large negative, the absolute value decreasing to some extent.

The larger enthalpy of activation indicates that the ionic species are less stabilized by the solvation of *o*-dichlorobenzene than by that of chloroform. This is contrary to expectation from the dielectric constants; 4.81 and 9.93 for chloroform and *o*-dichlorobenzene, respectively. Donor numbers and acceptor numbers are often used for the ionic species,[23] but they are unknown for these solvents except for the acceptor number of chloroform. *Z* values[24] may be useful because they are obtained from the UV spectra of salts (ion pairs) in various solvents; 63.2 and 60.0 for chloroform and *o*-dichlorobenzene, respectively. The Z values correspond to energy (kcal mol^{-1}) of the light absorbed by the ion pairs and ions and the difference is correlated with the difference in energy of the ground and the excited states,[25] not being directly connected with the freedom of ion pairs. Nonetheless, among other solvent parameters the *Z* values give best results for correlating the rates of dissociation of α-chlorodibenzyl sulfide in the two solvents. From the microscopic stand point, chloroform, which is capable of forming hydrogen bond,[26] can stabilize anions[27] and this ability is responsible for the observed results. The observed decrease in the enthalpy of activation should include this stabilization.

Conclusion. Dynamic NMR technique has been used for the investigation of ionic dissociation of α-chlorodibenzyl sulfide, which has a pair of diastereotopic protons; their diastereotopicity is lost on ionization. The process involves the ionization of the halide into intimate ion pairs and then solvent-separated ion pairs. Racemization may take place at this stage and the racemized solvent-separated ion pairs lose the solvent molecule(s) to give racemized intimate ion pairs which then collapse into the inverted covalent species.

$$RX \rightleftharpoons R^+X^- \rightleftharpoons R^+ /\!/ X^- \rightleftharpoons X^- /\!/ R^+ \rightleftharpoons X^-R^+ \rightleftharpoons XR$$

In this technique we do not have to see the presence of ionic species. The usual dynamic NMR technique makes use of the coalescence of the two signals ascribable to the respective species to estimate the rates of exchange. Kessler *et al.* investigated the rates of ionization of triarylmethyl derivatives by observing both the covalent and ionic species.[28] The rates of dissociation are obtained in relatively nonpolar solvents. The rates of ionization can be obtained at various temperatures without prior optical resolution of the substrate, affording activation parameters of ionization. The technique affords information on unimolecular dissociation at concentration of *ca.* 0.2 mol L^{-1}, which gives insight into the early stages of the S_N1 reactions.

The only shortcoming of this technique is that the substrate should possess diastereotopic protons whose diastereotopicity is lost on ionization. This may limit utilization of the technique to some extent and may require modification of a molecule which is conveniently studied by the classical method. The rates of exchange of proton spins should be 10^0—10^{-5} s^{-1} as in the usual dynamic NMR technique.[29] This will not hamper the usefulness of the technique because this kind of limitation is always present for other techniques as well. It is difficult to obtain reliable data by the classical method if the rates exceed 10^{-3} s^{-1}. The compound we used is very easily ionizable, thus reacting with atmospheric moisture. Although this may cause some errors, but it is the main reason why we were able to carry out the studies in relatively nonpolar aprotic solvents.

It is not possible to identify by this method how much of the solvent-separated ion pairs return to the covalent species without racemization, but this is unavoidable in the ionization of organic halides. Combination with isotopic labeling and subsequent observation of scrambling will afford useful data in this context.

The work was carried out with a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture.

References

1) Preceding paper: M. Ōki, Y. Yoshioka, H. Kihara, and N. Nakamura, *Chem. Lett.*, **1980**, 1625.

2) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca (1953), pp. 306—418.

3) S. Winstein, E. Clippinger, A. H. Fainberg, and G. C. Robinson, *J. Am. Chem. Soc.*, **76**, 2597 (1954); S. Winstein, B. Appel, R. Baker, and A. Diaz, *Chem. Soc. (London), Spec. Publ.*, **19**, 109 (1965).

4) D. J. Raber, J. M. Harris, and P. v. R. Schleyer, "Ions and Ion Pairs in Solvolytic Reactions," in "Ions and Ion Pairs in Organic Reactions," ed by M. Szwarc, John-Wiley, New York (1974), Vol. 2, pp. 247—374.

5) S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck, and G. C. Robinson, *J. Am. Chem. Soc.*, **78**, 328 (1956); P. B. D. de la Mare, D. M. Hall and E. Maugher, *Recl. Trav. Chim. Pay-Bas*, **87**, 1394 (1968).

6) C. G. Swain and M. M. Kreevoy, *J. Am. Chem. Soc.*, **77**, 1122 (1955).

7) S. Winstein, A. Ledwith, and M. Hojo, *Tetrahedron Lett.*, **1961**, 341; Ref. 5b.

8) H. L. Goering and J. F. Levy, *Tetrahedron Lett.*, **1961**, 644; *J. Am. Chem. Soc.*, **84**, 3853 (1962).

9) H. L. Goering and B. E. Jones, *J. Am. Chem. Soc.*, **102**, 1628 (1980) and papers cited therein.

10) K. Arai and M. Ōki, *Tetrahedron Lett.*, **1975**, 2183; *Bull. Chem. Soc. Jpn.*, **49**, 553 (1976).

11) K. Arai and M. Ōki, *Bull. Chem. Soc. Jpn.*, **50**, 175 (1977).
12) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York (1959), p. 218; J. W. Emsley, J. Feeney, and C. H. Sutcliff, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, Oxford (1965), p. 481.
13) G. Binsch, *Topics Stereochem.*, **3**, 87 (1970).
14) M. Ōki, H. Iwamura, and N. Hayakawa, *Bull. Chem. Soc. Jpn.*, **36**, 1542 (1963); **37**, 1865 (1964); R. J. Kurland, M. B. Rubin, and W. B. Wise, *J. Chem. Phys.*, **40**, 2426 (1964).
15) C. G. Swain and C. B. Scott, *J. Am. Chem. Soc.*, **75**, 246 (1953).
16) A. A. Frost and R. G. Pearson, "Kinetics and Mechanisms," John-Wiley, New York (1953), p. 127.
17) S. Winstein and G. C. Robinson, *J. Am. Chem. Soc.*, **80**, 169 (1958).
18) L. C. Bateman, M. G. Church, E. D. Hughes, C. K. Ingold, and N. A. Taher, *J. Chem. Soc.*, **1940**, 979.
19) A. H. Fainberg and S. Winstein, *J. Am. Chem. Soc.*, **78**, 2763 (1956).
20) S. Winstein, S. Smith, and D. Darwish, *J. Am. Chem. Soc.*, **81**, 5511 (1959).
21) S. Winstein, P. E. Klinediensk, and G. C. Robinson, *J. Am. Chem. Soc.*, **83**, 885 (1961).
22) N. Ahmad and M. C. Day, *J. Am. Chem. Soc.*, **99**, 941 (1977).
23) V. Gutman, "The Donor-Acceptor Approach to Molecular Interactions," Plenum Press, New York (1978), pp. 17—33.
24) C. Reichardt, "Solvent Effects in Organic Chemistry," Verlag Chemie, Weinheim (1979), pp. 237—250.
25) E. M. Kosower, "An Introduction to Physical Organic Chemistry," John-Wiley, New York (1968), pp. 260—263 and pp. 293—302. See also J. W. Larsen, A. G. Edwards, and P. Dobi, *J. Am. Chem. Soc.*, **102**, 6780 (1980).
26) G. C. Pimentel and A. L. McCllelan, "The Hydrogen Bond," W. H. Freeman, San Francisco (1960), p. 197.
27) S. Y. Lam, C. Louis, and R. L. Benoit, *J. Am. Chem. Soc.*, **98**, 1156 (1976).
28) M. Feigel, H. Kessler, and A. Walter, *Chem. Ber.*, **111**, 2947 (1978) and earlier papers.
29) L. M. Jackman and A. Cotton, "Dynamic Nuclear Magnetic Resonance Spectroscopy," Academic Press, New York (1975).