Direct Measurement of the Rates of Ionic Dissociation by Dynamic NMR Technique. Dissociation of α-Chlorodibenzyl Sulfides

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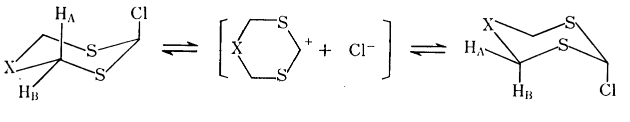
Exchange processes of diastereotopic protons of α-chlorodibenzyl sulfides were observed by means of dynamic nuclear magnetic resonance. Polar effects of solvents and substituent effects on the ease of the exchange process of protons in *p,p'*-disubstituted α-chlorodibenzyl sulfides indicate that the process occurs with the dissociation of the compounds into benzylic cations and chloride ion. It is possible to measure the rates of ionic dissocation by observing the change in the line shape of signals in ^{1}H NMR spectra. The scope of the method is discussed.

In a previous paper a report was given on the observation of ionic dissociation of 2-chloropolythianes (**1**) by dynamic nuclear magnetic resonance technique.[1] In this case, inversion of the six-membered ring is the required process to average the chemical shifts of the protons in question. Thus, the energetics of the ring inversion might be included in the energetics of ionic dissociation, when the compound requires small energy for the dissociation.



(*1*) (*1'*)

We have undertaken an extension of the above technique in order to generalize the method for determination of the rates and/or energetics for ionic dissociation of certain organic compounds. Since the ionic dissociation is a crucial step in S_N1 reactions, a knowledge of the rates of ionization would help understand such reactions.

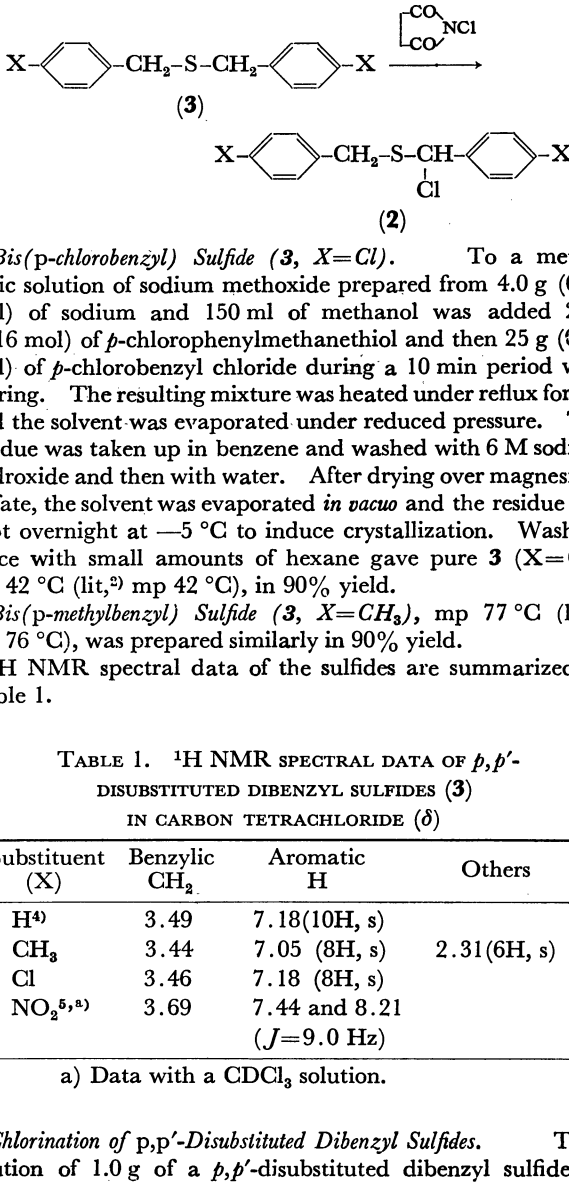
For application of dynamic NMR technique, the compound should satisfy the following three conditions. a) It can produce a stable cation since NMR technique can detect neither very slow nor very fast exchange processes. b) It possesses a pair of diastereotopic protons. c) It is desirably an acyclic compound, direct measurement of the rates of ionization being possible, since ring inversion is not necessary for the averaging of protons.

Suitable samples are α-chloro sulfides since they produce stable cations due to the presence of sulfur atoms, as confirmed for chloropolythianes. After several trials we found that α-chlorodibenzyl sulfides (**2**) satisfy the conditions: the cation produced receives additional stabilization due to the presence of a benzene ring. This paper describes the determination of free energies for ionic dissociation of these compounds and discusses the effects of substituents and solvents on ionic dissociation.

(**2**)

Experimental

Syntheses. The compounds required for the measurements were prepared by chlorination of substituted dibenzyl sulfides (**3**) with *N*-chlorosuccinimide. All the sulfides were known compounds but two were prepared by modified methods.



(**2**)

Bis(p-*chlorobenzyl) Sulfide* (**3**, *X=Cl*). To a methanolic solution of sodium methoxide prepared from 4.0 g (0.17 mol) of sodium and 150 ml of methanol was added 25 g (0.16 mol) of *p*-chlorophenylmethanethiol and then 25 g (0.16 mol) of *p*-chlorobenzyl chloride during a 10 min period with stirring. The resulting mixture was heated under reflux for 3 h and the solvent was evaporated under reduced pressure. The residue was taken up in benzene and washed with 6 M sodium hydroxide and then with water. After drying over magnesium sulfate, the solvent was evaporated *in vacuo* and the residue was kept overnight at −5 °C to induce crystallization. Washing twice with small amounts of hexane gave pure **3** (X=Cl), mp 42 °C (lit,[2] mp 42 °C), in 90% yield.

Bis(p-*methylbenzyl) Sulfide* (**3**, *X*=CH_3), mp 77 °C (lit,[3] mp 76 °C), was prepared similarly in 90% yield.

^{1}H NMR spectral data of the sulfides are summarized in Table 1.

Table 1. ^{1}H NMR spectral data of *p,p'*-disubstituted dibenzyl sulfides (**3**) in carbon tetrachloride (δ)

Substituent (X)	Benzylic CH_2	Aromatic H	Others
H[4]	3.49	7.18(10H, s)	
CH_3	3.44	7.05 (8H, s)	2.31(6H, s)
Cl	3.46	7.18 (8H, s)	
NO_2[5,a]	3.69	7.44 and 8.21 (J=9.0 Hz)	

a) Data with a $CDCl_3$ solution.

Chlorination of p,p'*-Disubstituted Dibenzyl Sulfides.* To a solution of 1.0 g of a *p,p'*-disubstituted dibenzyl sulfide in 10 ml of carbon tetrachloride was added 1.1 equivalents of powdered *N*-chlorosuccinimide at 35 °C with stirring during a 5 min period under nitrogen atmosphere. Stirring was continued for 1—2 h after completion of the addition. The reaction mixture was filtered in order to remove insoluble materials, contact with moisture being avoided as completely as possible. From ^{1}H NMR spectral data of the filtrate, the purity and yield of *p,p'*-disubstituted α-chlorodibenzyl sulfides were estimated to be 90—95% and 85—90%, respectively.

The nitro compound, being sparingly soluble in carbon tetrachloride, was chlorinated in benzene by essentially the same procedure.

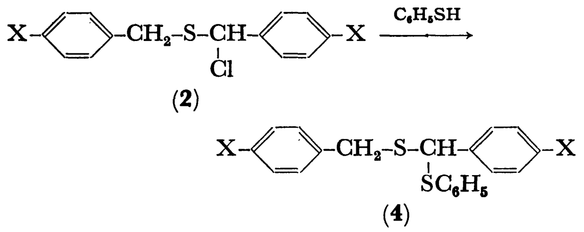
^{1}H NMR spectral data of the *p,p'*-disubstituted α-chlorodibenzyl sulfides are given in Table 2.

TABLE 2. ^{1}H NMR SPECTRAL DATA OF *p,p'*-DISUBSTITUTED α-CHLORODIBENZYL SULFIDES (**2**) IN CARBON TETRACHLORIDE (δ)

Substituent (X)	Benzylic δ	CH_2 J	Methine H	Aromatic H	Others
H[6]	3.88 3.98	15	5.69	7.30 (10H, m)	
CH_3	3.79 3.93	*ca.* 13	5.67	6.9—7.4 (8H, m)	2.39(3H, s) 2.32(3H, s)
Cl	3.80 3.99	13.5	5.63	7.29 (8H, s)	
NO_2[a]	4.07 4.20	13.5	5.87	7.50—7.70[b] 8.15—8.35 (8H, double q)	

a) Data with a $CDCl_3$ solution. b) It was impossible to determine which of the two pairs at the higher field forms the AB quartet with a pair of signals at the lower field. The coupling constants for the two AB quartets were 9.0 Hz.

Benzenethiolyses of p,p'*-Disubstituted α-Chlorodibenzyl Sulfides.* The solutions of *p,p'*-disubstituted α-chlorodibenzyl sulfides obtained above were treated with 2—3 equivalents of benzenethiol at room temperature for 8—10 h and the resulting mixture was evaporated *in vacuo* Chromatography of the residue on silica gel afforded pure *p,p'*-disubstituted α-phenylthiodibenzyl sulfides (**4**). The pertinent data are summarized in Table 3.



^{1}H NMR Measurement. ^{1}H NMR spectra were recorded on a Hitachi R 20B spectrometer, operating at 60 MHz, with a temperature variation accessory. The temperature reading was calibrated by measuring the chemical shift difference between methylene and hydroxy protons of ethylene glycol for the higher temperatures and that between methyl and hydroxy protons of methanol for the lower temperatures.

Kinetic Parameters. The rate constants of the exchange processes at the coalescence temperature were obtained by application of the following equation,[7] where J_{AB} is the coupling constant of the diastereotopic protons and $\Delta\nu_{AB}$ the chemical shift difference of these protons.

$$k_c = \frac{\pi}{\sqrt{2}}\sqrt{6J_{AB}^2+\Delta\nu_{AB}^2} \tag{1}$$

Free enrgies of activation at the coalescence temperature were obtained by substituting k_c into the following equation.

$$\Delta G_c^\ddagger = 4.57T_c\left\{10.319+\log\frac{T_c}{k_c}\right\} \tag{2}$$

Results and Discussion

Confirmation of the Structure of p,p'*-Disubstituted α-Chlorodibenzyl Sulfides.* Since the *p,p'*-disubstituted α-chlorodibenzyl sulfides (**2**), key compounds in this paper, are reactive toward moisture, their structures must be confirmed by other means. This is accomplished by a) the chemical method and b) ^{1}H NMR spectral data. In a), since the method of preparation is generally applied to α-chlorination of sulfides,[8] a chlorine atom is expected to enter at a benzylic position. The ease of reaction of these compounds with benzenethiol is supporting evidence for the structure, since other normal halides would not be so reactive as these compounds. The substituted α-phenylthiodibenzyl sulfides (**4**) are analyzed correctly. In b) the two benzylic protons turn to a methine proton

TABLE 3. MELTING POINTS, ^{1}H NMR DATA (CCl_4, δ), AND ANALYTICAL DATA OF *p,p'*-DISUBSTITUTED α-PHENYLTHIODIBENZYL SULFIDES (**4**)

Substituent (X)	Mp (°C)		Found (%)	Calcd (%)	^{1}H NMR data CH_2	CH	Arom. H	Others
H	Oil	C	74.56	74.49			7.11(5H, s)	
		H	5.62	5.63	3.66	4.74	7.15(5H, bs)	
		S	19.99	19.88	3.85		7.21(5H, bs)	
					(J=13.0)			
CH_3	Oil	C	75.08	75.38	3.67			2.28(3H, s)
		H	6.25	6.33	3.83	4.75	7.0 —7.3	2.30(3H, s)
		S	18.00	18.29	(J=13.0)		(13H, m)	
Cl	61 — 62	C	61.16	61.38				
		H	4.03	4.12	3.65	4.70	7.15—7.25	
		Cl	18.17	18.12	3.83		(13H, m)	
		S	16.27	16.38	(J=13.0)			
NO_2	136.5—137	C	57.97	58.24			7.24(5H, s)	
		H	4.17	3.91	3.89	4.88	7.30—7.55[a]	
		N	6.87	6.79	4.08		8.05—8.30[a]	
		S	15.45	15.55	(J=13.5)		(8H, double q)	

a) See Table 2, footnote b. The coupling constants for the two AB quartets were 9.0 Hz.

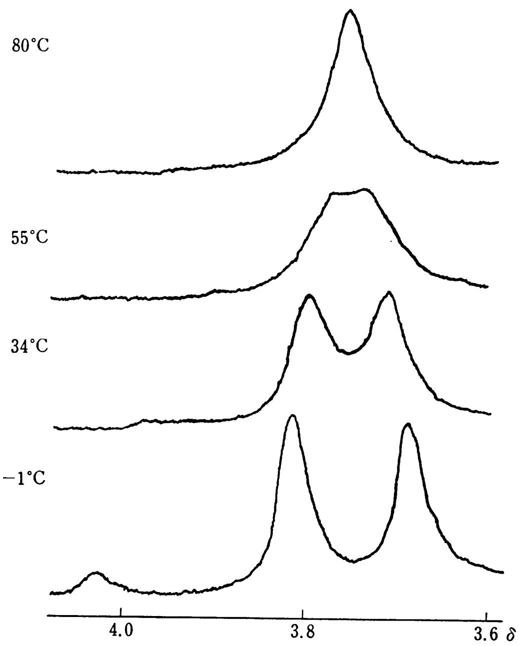


Fig. 1. Temperature dependence of the signals at δ *ca.* 4 in the spectrum of α-chlorodibenzyl sulfide in 1-chloronaphthalene.

which gives a signal at a low field. In addition, the benzylic protons in the chloro compounds **2** and in phenylthio compounds **4** give AB quartets: it would not be possible to explain if a chiral center were not present in the proximity of these protons.

Dynamic NMR and the Rate Process. The ^{1}H NMR spectra of the chlorides **2** were found to be dependent on solvents and temperature. Typical examples of temperature-dependence of the spectra are shown in Fig. 1. Since a quartet signal of a diastereotopic pair of protons does not usually coalesce below 200 °C, the temperature-dependent spectra suggest that a certain exchange process involving bond breaking takes place under these conditions. The process should be such that chirality due to asymmetric carbon is lost.

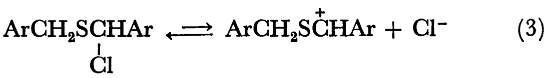
Survey of solvent and substituent effects on the coalescence temperature and free energies of activation will shed light on the nature of the process. The temperature dependence of the spectra of α-chlorodibenzyl sulfide was investigated in various solvents. The results are given in Table 4. Nitrobenzene showed no tendency of line broadening even at 0 °C. The coalescence temperature is lower when the solvent is more polar, the free energies of activation being lower. The cases of chloroform and deuteriochloroform are exceptions. We wish to attribute this anomaly to the hydrogen bond effect. Chloroform is known to form hydrogen bond[9] which should stabilize an anion.[10] No such stabilization is expected in the other solvents used. Deuteriochloroform would stabilize the anion to a greater extent, since deuterium compounds are known to form a stronger hydrogen bond than the corresponding ^{1}H compounds.[11]

Table 4. Solvent effects on the exchange process of protons in α-chlorodibenzyl sulfide (**2**, X=H)

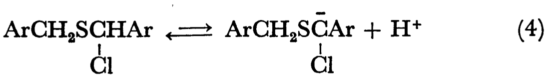
Solvent	ε	T_C (°C)	J_AB (Hz)	$\Delta\nu_\mathrm{AB}$ (Hz)	$\Delta G^{\ne}_\mathrm{C}$ (kcal/mol)
CCl_4	2.24	>80	13.5	5.5	>17.8
C_6H_6	2.27	>70	13.5	16	>17.2
$CHCl_3$	4.81	37	14	6	15.5
$CDCl_3$	—	17	14	6	14.5
m-$Cl_2C_6H_4$	5.04	82	14	7	17.8
$C_{10}H_7Cl$[a)]	5.04	55	13	10	16.5
C_6H_5Cl	5.62	55	13	8	16.5
o-$Cl_2C_6H_4$	9.93	42	13.5	5	15.8
$C_6H_5NO_2$	34.8	<0	(13)	(8)	(<13.6)[b)]

a) 1-Chloronaphthalene. b) J_AB and $\Delta\nu_\mathrm{AB}$ in chlorobenzene are diverted.

The results obtained by changing the solvent are consistent with the idea that the loss of the chiral center is of polar nature. Heterolysis of the C–S bond requires much energy. Then, in principle, the following two modes of dissociation are possible.



$$\mathrm{ArCH_2S}\underset{\mathrm{Cl}}{\mathrm{C}}\mathrm{HAr} \rightleftharpoons \mathrm{ArCH_2S}\overset{+}{\mathrm{C}}\mathrm{HAr} + \mathrm{Cl^-} \qquad (3)$$



$$\mathrm{ArCH_2S}\underset{\mathrm{Cl}}{\mathrm{C}}\mathrm{HAr} \rightleftharpoons \mathrm{ArCH_2S}\underset{\mathrm{Cl}}{\overset{-}{\mathrm{C}}}\mathrm{Ar} + \mathrm{H^+} \qquad (4)$$

Although it may seem that Eq. 3 is a more plausible process, Eq. 4 may not be ruled out without convincing evidence. Such evidence should be provided when the substituent effect is examined: if the process is represented by Eq. 3, electron-releasing groups should facilitate the exchange, and the reverse is true if the process is represented by Eq. 4.

The results of changing the substituent are given in Table 5, in which σ_m values are included as a measure of electron-donating or electron-withdrawing ability. The results are in line with the idea that the electron-donating substituent facilitates the process. Thus the exchange of proton spins occurs following Eq. 3.

Rate Constants of the Ionic Dissociation. Although the planar cation itself erases the non-equivalency of the CH_2 protons due to its planar structure, we observe no NMR spectra of the cation because of its transient nature. Thus the equivalency of the methylene protons at a higher temperature is caused by the rapid mixing of one stereoisomer with another. The mixing or interconversion of one stereoisomer with another can occur in one or more of the following steps. If the compound dissociates into a free cation and a free anion, recombination to produce the mother compound would proceed from either side of the plane of the cation, thus producing a 1:1 mixture of the enantiomers. If the cation undergoes internal rotation about the S–C$^+$ axis while the anion remains immobile, the stereoisomer is formed, or else, the anion will recombine with the cation from the other side than that where the former departed. These cases are possible when the ions form a loose ion pair. If the ions form a tight ion pair, it is not possible to invert the stereochemistry directly. However, we might consider the cation to be of pyramidal shape and inversion of the pyramid followed by recombination with an anion derived from another molecule leads to the formation of a stereoisomer.

It is difficult to determine to what extent the above

TABLE 5. FREE ENERGY OF ACTIVATION FOR THE EXCHANGE PROCESS AND FOR THE IONIC DISSOCIATION OF *p,p'*-DISUBSTITUTED α-CHLORODIBENZYL SULFIDES (**2**)

	o-$Cl_2C_6H_4$ solution				$C_6H_5NO_2$ solution		
Substituent	σ_m	T_C (°C)	$\Delta G^{\neq}_C$ (kcal/mol) (Eachange)	$\Delta G^{\neq}_C$ (kcal/mol) (Ionic dissociation)	T_C (°C)	$\Delta G^{\neq}_C$ (kcal/mol) (Exchange)	$\Delta G^{\neq}_C$ (kcal/mol) (Ionic dissociation)
CH_3	−0.07	−21	12.5	12.2	≪0[a]	≪13.6[a]	≪13.4
H	0.00	42	15.8	15.4	<0[a]	<13.6[a]	<13.4
Cl	0.37	101	18.8	18.3	40	15.7	15.3
NO_2	0.71	—	—	—	100	18.8	18.3

a) The signal due to benzyl protons of *p,p'*-dimethyl-α-chlorodibenzyl sulfide was sharper than that of α-chlorodibenzyl sulfide.

factors are responsible. To a first approximation, however, we may take a model in which the probability of the ion pairs returning to the original stereochemistry and forming the other stereochemistry are 50: 50 as a result of many factors. The rate of the dissociation of the chloride **2** must then be twice the rate of the exchange process. The results are included in Table 5.

It is of interest that the barriers to the ionic dissociation of these compounds are comparable to or smaller than that of triphenylmethyl chloride. The enthalpy and the entropy of activation for the reaction of triphenylmethyl chloride in aqueous acetone were reported to be 12.5 kcal/mol and −17 e.u. at temperatures between −34 °C and −14 °C.[12] The free energy of activation is then calculated to be *ca.* 17 kcal/mol at about −20 °C. If we assume this to be the pure S_N1 reaction, the energy should correspond to that for ionic dissociation. Since the polarity of the solvent is high in this case, the ionic dissociation of the chloro compound **2** may be taken as an easy one. The enthalpy and entropy of activation for the exchange process of chloride ion in benzene are reported to be 12.4 kcal/mol and −39 e.u. respectively, at 50 °C for triphenylmethyl chloride[13] and the free energy is calculated as 25 kcal/mol at that temperature.

Conclusion. The method described here for determining the rates of ionic dissociation seems to be of value in kinetic studies. For the tranditional chemical method, racemization or isotope exchange had to be used. This necessitates an optically active compound or isotopically enriched ions. As an example, the rate of ionization of triphenylmethyl chloride was estimated from the exchange of the chloro group with isotopically labelled tetraalkylammonium chloride,[13] but the method is hampered by the fact that the concentration of the ammonium chloride affects the rates. The method described here needs no expensive isotopes, optical isomers nor a nucleophile to react. Thus the rate of ionization can be obtained without perturbation of the excess of other materials. Since the ionization of an organic compound into a stable cation and an anion is an important step in S_N1 reactions and many stable cations show substantial barriers for reaction with another anion,[14] dynamic NMR method provides an important means for understanding such a reaction.

If a compound possesses a good leaving group at a chiral or prochiral center and diastereotopic protons close to the center, and produces a fairly stable carbonium ion, then the rates of the dissociation can be determined by dynamic NMR technique.[15] As one example, the case of α-chlorodibenzyl sulfides is presented.

References

1) K. Arai and M. Ōki, *Bull. Chem. Soc. Jpn.*, **49**, 553 (1976).

2) Z. Martynowicz, *Chem. Z.*, **1910, II**, 1048.

3) C. L. Jackson and J. F. White, *J. Am. Chem. Soc.*, **2**, 166 (1880).

4) Preparation of this compound was reported previously: C. Märcker, *Ann. Chem. Pharm*, **136**, 75 (1865).

5) Preparation of this compound was reported previously: O. Fischer, *Ber.*, **28**, 1338 (1895); T. S. Price and D. F. Twiss, *J. Chem. Soc.*, **95**, 1728 (1909).

6) Preparation of this compound by other methods was briefly reported as an intermediate: H. Böhme, *Ann. Chem.*, **563**, 54 (1949); K. C. Schreiber and V. P. Fernandez, *J. Org. Chem.*, **26**, 2910 (1961).

7) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co. Inc., 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.

8) D. L. Tuleen R. H. Bennett, *J. Heterocycl. Chem.*, **6**, 115 (1969).

9) G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman and Co., San Francisco (1960), p. 197.

10) S. Y. Lam, C. Louis, and R. L. Benoit, *J. Am. Chem. Soc.*, **98**, 1156 (1976).

11) L. N. Ferguson, "The Modern Structural Theory of Organic Chemistry," Prentice-Hall, Inc., Englewoods Cliff, New Jersey (1963), p. 128; G. Dahlgren, Jr. and F. A. Lay, *J. Am. Chem. Soc.*, **82**, 1303 (1960).

12) C. G. Swain and C. B. Scott, *J. Am. Chem. Soc.*, **75**, 246 (1953).

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

14) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y. (1953), p. 360.

15) For references of DNMR spectroscopy, see for example, L. M. Jackman and A. Cotton, "Dynamic Nuclear Magnetic Resonance Spectroscopy," Academic Press, Inc., New York (1975).