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Dynamic NMR as a Nondestructive Method for the Determination of Rates of Dissociation. X. Rates of Dissociation of the C–N Bond in Substituted 1-(1,3-Dithiolan-2-yl)pyridinium Perchlorates[1,2)]

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Rates of dissociation of the C–N bond in substituted 1-(1,3-dithiolan-2-yl)pyridinium ions in the perchlorate forms were obtained by the dynamic NMR technique in nitromethane-d_3 and for one case in acetonitrile-d_3. The study of the substituent effects on the rates of dissociation revealed that the rates were linearly correlated with the pK_a values of the substituted pyridines. The mechanism of the dissociation was postulated to be of S_N2 type, the perchlorate ion acting as a nucleophile, from the kinetic data.

Dynamic NMR techniques are unique in that the rates of dissociation of molecular species can be studied in nonpolar aprotic solvents without destruction of the molecule. The so-called topomerization[3)] is the key step in this methodology. The method had been originally applied to organometallic compounds[4)] and then the method has now been extended to the dissociation of organic halides,[5)] ammonium ions derived from tertiary amines and acids,[6)] and amine ligands of some coordination compounds.[7)] The method is capable of producing the rates of dissociation which exceed the limit obtainable by the classical kinetic method.

Since quaternary ammonium salts can be considered as composed of a tertiary amine and a carbocation, the dissociation of this group of compounds must be on an extrapolation map of the above-mentioned ammonium salts or coordination compounds. From the standpoint of organic chemistry, there are varieties of reactions of quaternary ammonium salts which involve dissociation of the C–N bond in them.[8)] Hence it will be interesting to find examples of ammonium salts which give suitable rates of dissociation for the dynamic NMR technique. This will also give information which is useful in understanding the dissociation processes in aprotic solvents.

The crucial point is that we must search a group of compounds which give suitable rate constants of dissociation for the dynamic NMR technique. Our experience showed that the pyridinium salt which was derived from benzyl α-chlorobenzyl sulfide and pyridine exhibited too low rates of dissociation for the dynamic NMR. Thus we explored compounds which could produce more stable carbocation than the α-(benzylthio) benzyl cation. The natural choice was to introduce two sulfur atoms alpha to the cation.

1,3-Dithiolan-2-yl cation was expected to be a good candidate for the system in question. Various attempts to identify the suitable compounds, including the pyridinium compounds derived from 2-chloro-1,3-dithiolane, led to a finding that 1-(1,3-dithiolan-2-yl)pyridinium salts were suitable for the investigation. Perchlorate salts were selected because of their stability and the ease of syntheses.

The compounds were prepared by treating 1,3-dithiolane with triphenylmethyl perchlorate and then with substituted pyridines in acetonitrile. The compounds were rather unstable and were especially moisture-sensitive, if the substituent was electron-withdrawing. In spite of the easy deterioration in the air, they could be purified by recrystallization from acetonitrile-ether, if we handled them carefully, under dry conditions.

The 400 MHz NMR spectra of the compounds were determined as nitromethane-d_3 solutions except for one case, when acetonitrile-d_3 was used. The use of the polar solvent was necessary because their solubilities in nonpolar aprotic solvents were very low. The compounds exhibited either complex AA′BB′ patterns or a broad signal for the ring protons of the 1,3-dithiolane, the former giving broadening of the signals at high temperatures and the latter showing AA′BB′ signals at low temperatures. The rate process becomes slow as the 4-substituent on the pyridine ring becomes electron-donating. Although we have made various pyridinium salts of this type, which carry electron-withdrawing substituents, their rates of hydrolysis were too large to obtain pure samples. Thus, although the trend in the rate processes mentioned above is apparent, we wish to present the results with the samples only which gave correct elemental analyses in this paper.

The change in the line shapes of the NMR spectra is indicative of the presence of a dynamic process. The site exchange is most reasonably explained by assuming the dissociation of the C–N bond of the pyridinium salts followed by association to the covalent species, when topomerization takes place (Eq. 1). If the basicity of a pyridine compound is high, the C–N bond in question must be stronger than the case of a weak base, because it is the acid-base combination. The above results conform to this expectation, if we assume the dissociation of the C–N bond in the pyridinium ions.

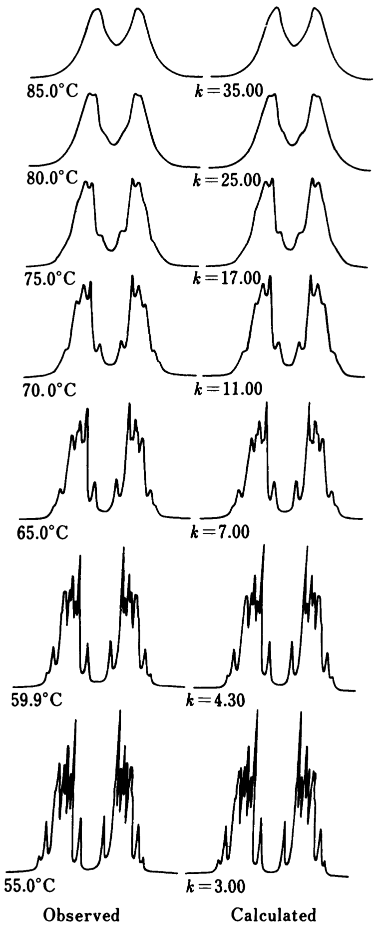


Fig. 1. Observed and calculated AA′BB′ ^{1}H NMR spectra of 4-methoxy-1-(1,3-dithiolan-2-yl)pyridinium perchlorate at various temperatures.

Table 1. Equations Correlating the Chemical Shift Differences and Temperature and Coupling Constants of AA′BB′ Systems in Substituted 1-(1,3-Dithiolan-2-yl)pyridinium Perchlorates

Substituent	$f(T)$[a]	J_{gem}/Hz	J_{cis}/Hz	J_{trans}/Hz
4-CH_3O	106.12—0.18T	−11.9	5.2	6.8
4-CH_3	100.02—0.18T	−11.9	5.3	6.8
H	88.13—0.15T	−11.9	5.3	6.8
3-CH_3O	88.32—0.16T	−11.9	5.3	6.8

a) $f(T)$ for $\Delta\nu$/Hz=$f(T)$/K.

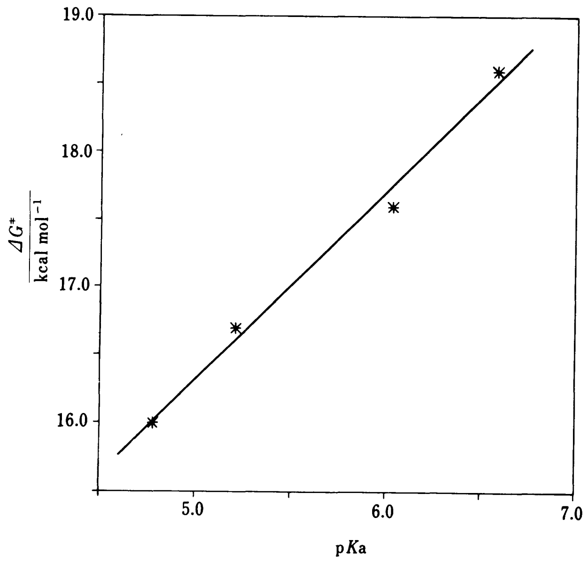


Fig. 2. Relationship between the pK_a values of pyridine bases and the free energy of activation for dissociation of the C–N bond in 1-(1,3-dithiolan-2-yl)-pyridinium perchlorates.

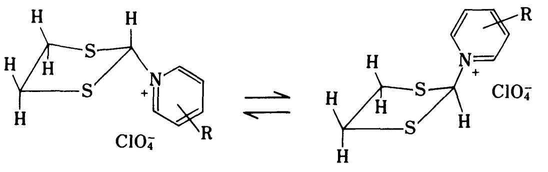
Table 2. Rate Constants (k) and Transverse Relaxation Times (T_2) at Various Temperatures as Obtained by Simulation of the NMR Line Shapes

Substituent	k/s^{-1} (T_2/s, Temperature/°C)
4-CH_3O	3.0 (0.47, 55.0), 4.3 (0.45, 59.9), 7.0 (0.47, 65.0), 11.0 (0.41, 70.0), 17.0 (0.45, 75.0), 25.0 (0.41, 80.0), 35.0 (0.45, 85.0)
4-CH_3	3.7 (0.57, 40.0), 5.5 (0.66, 45.0), 8.8 (0.65, 50.0), 14.0 (0.52, 55.0), 21.5 (0.50, 60.0), 32.5 (0.49, 65.1)
H	3.7 (0.22, 25.1), 6.4 (0.32, 30.7), 9.1 (0.24, 35.0), 13.4 (0.18, 40.0), 19.5 (0.13, 45.0), 29.0 (0.15, 50.0)
3-CH_3O	2.6 (0.36, 10.2), 4.3 (0.36, 14.8), 6.8 (0.35, 20.0), 11.0 (0.36, 24.9), 18.0 (0.31, 30.1), 28.0 (0.29, 35.0)

Table 3. Activation Parameters for the Dissociation of the C–N Bond in Substituted 1-(1,3-Dithiolan-2-yl)pyridinium Perchlorates

Substituent	Correlation[a] Coecfficient	$\Delta H^{\neq}$ [b] / kcal mol^{-1}	$\Delta S^{\neq}$ / cal mol^{-1} K^{-1}	$\Delta G^{\neq}_{298}$ / kcal mol^{-1}	k_{298} / s^{-1}	pK_a[c]
4-CH_3O	0.9993	19.0±0.8	1.2±2.4	18.6	0.142	6.58
4-CH_3	0.9995	17.8±0.8	0.9±2.3	17.6	0.804	6.03
H	0.9995	15.0±0.7	−5.6±1.7	16.7	3.79	5.21
3-CH_3O	0.9998	15.9±0.5	−0.3±1.6	16.0	11.2	4.78

a) In the least squares treatment. b) 1 cal=4.184 J. c) Ref. 10.



(1)

1a **1b**

Typical line shapes at various temperatures together with the simulated spectra of 4-methoxy-1-(1,3-dithiolan-2-yl)pyridinium perchlorate are given in Fig. 1. The spectral parameters of the AA′BB′ patterns were obtained by simulation with the use of the LAOCN III program stored in the Computer Center of this University. The simulation was performed for the spectra at various temperatures where the rates of the exchange were negligibly small. This operation confirmed that the coupling constants were temperature-independent, while chemical shift differences for the A and B protons were temperature-dependent. The drift of the chemical shift differences could be linearly correlated with temperature. The correlation of the chemical shift differences with temperature together with coupling constants are compiled in Table 1 for the nitromethane-d_3 solutions. Thus the chemical shift differences at a given temperature could be calculated by these equations and were used for the simulation.

The rate constants of topomerization at various temperatures were obtained by simulation of the line shapes with the use of DNMR3 program.[9] The rate constant k and the transverse relaxation time T_2 were treated as variables. In spite of this practice, thanks to the complicated line shapes, the variation of k gives a different trend in modification of the line shape from that in T_2, thus enabling us to determine unique values of k and T_2. The values k and T_2 are given in Table 2. The agreement of the calculated spectra with the observed was satisfactory, as is shown in Fig. 1.

Putting the rate constants and temperatures into the Eyring equation, we obtained the kinetic parameters which are shown in Table 3. A trend is apparent: The more basic is the pyridine derivative, the higher is the enthalpy of activation. Indeed, the pK_a values of the pyridine bases and the free energy of activation for the dissociation gives a good straight line, as is shown in Fig. 2, the slope and the correlation coefficient being 4.8 and 0.995, respectively. The linearity is not necessarily held between the base strengths toward the proton and carbon acids,[11] but the increase in the hardness of the carbocation in this case due to the presence of two alpha sulfur atoms will be the key factor for this linearity between the proton and carbocation acids. The results clearly indicate that the bond dissociation is the key step in the observed topomerization processes. Thus we are able to show examples of self dissociation of ammonium salts which can be observed by the dynamic NMR technique. Further application of this technique in this area will certainly contribute to the understanding of the S_N1 type substitution reactions of the ammonium salts which have been known for some time.

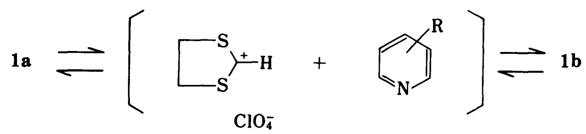
The entropies of activation are interesting: They are all close to zero. Although the reliability of entropy of activation obtained by the dynamic NMR method had been questioned, a concensus has now been established that it is reproducible and reliable, when the total line shape analyses are performed on complex line shapes.[4b,12] The observed entropies of activation make a striking contrast with the other cases we have examined so far. It has been shown that, if a covalent species dissociates to form ion pairs, the entropy of activation is large negative, whereas it is large positive, if an ion pair colapses to form a covalent species on dissociation.[5,6] Since the case studied here is the dissociation of an ion pair to covalent species, the simple application of the above generalization to the present case tells that entropy of activation should be large positive because the disorderedness of solvent molecules should increase at the transition state of the reaction.[13] Yet the observed entropy of activation is close to zero.

We should like to take this fact as indicative of the reaction mechanism and the rate determining step. In principle, the bond dissociation of the C–N can occur either in S_N1 (Eq. 2) or in S_N2 (Eq. 3) fashion.

If the dissociation is of S_N1 type, 1, 3-dithiolan-2-yl cation and a pyridine molecule are partially formed at the transition state. The net electric charge is invariant, whereas a new particle is being formed. This transition state should give positive entropy of activation. The results in Table 3 are not in conformity with this expectation.

In the S_N2 type reactions, the perchlorate anion must be the nucleophile. This is unusual but not without precedence. Perchlorate esters are known[14] and perchlorate anion shows nucleophilic nature in some instances.[15] It is possible, therefore, that the reaction proceeds in the S_N2 fashion. However, in the S_N2 type reactions, the electric charges are to be extinguishing and this contributes to the increase in the entropy of activation. Thus there must be good reasons why the observed entropy of activation is close to zero, if we postulate the rate-determining step of the reaction to be of S_N2 type.[16,17]

We believe the followings are the explanations for the observation. In the ground state of the reaction, perchlorate anion will be rotating freely with having interactions through its four equivalent oxygens, bearing the negative charge, with the cationic center. In the transition state, a partial covalent bond is to be formed, thereby losing the freedom of motion of the perchlorate ion. This should contribute to the



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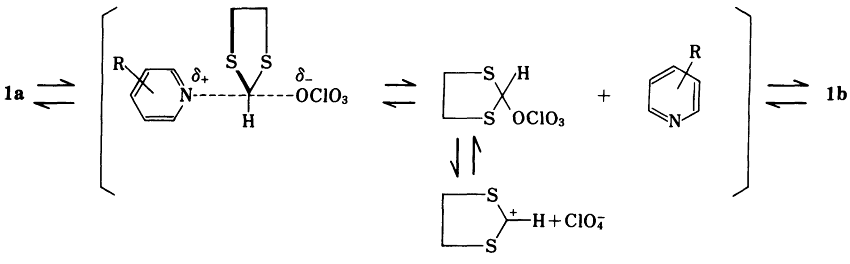

(3)

decrease in entropy. The decrease in entropy due to the loss of freedom of motion of the anion and the increase in entropy due to the increase in the freedom of motion of the solvent molecules may compensate to make the absolute values of the entropy of activation very small. There are examples of this sort: Whereas proton transfer reactions from an ammonium ion to chloride ion exhibits a large positive entropy of activation, that between an ammonium ion and sulfonate anion proceeds with nearly zero entropy of activation.[19] Therefore, we conclude that the bond dissociation reaction in the 1-(1,3-dithiolan-2-yl)-pyridinium ions takes place with the S_N2 type mechanisms.

Table 4. ^{1}H NMR Data and Kinetic Parameters for the Dissociation of 1-(1,3-Dithiolan-2-yl)pyridinium Perchlorates in CD_3CN

$\Delta\nu$/Hz vs. Temperature/K Correlation	$\Delta\nu = 66.46 - 0.10T$
J_{gem}/Hz, J_{cis}/Hz, J_{trans}/Hz	−11.9, 5.4, 6.8
k/s^{-1} (T_2/s, Temperature/°C)	4.0 (0.30, 25.1), 6.4 (0.33, 30.3), 9.2 (0.30, 35.4), 13.3 (0.25, 40.0), 19.3 (0.18, 45.0), 28.0 (0.17, 50.0)
Correlation Coefficient	0.9997
$\Delta H^{\ddagger}$/kcal mol^{-1}	14.2±0.5
$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}	−8.1±1.6
$\Delta G^{\ddagger}_{298}$/kcal mol^{-1}	16.4

Since the perchlorate ester which is transiently formed is very unstable due to the fact that the cation is stabilized by the presence of two alpha sulfur atoms, it rapidly dissociates to an ion pair which subsequently topomerizes and then recombines to form the topomer of the starting material. This series of reactions completes the observed process.

The dissociation reaction of 1-(1,3-dithiolan-2-yl)-pyridinium perchlorate can also be detected in acetonitrile-d_3. The NMR data as well as kinetic parameters are listed in Table 4. The chemical shift differences are small in acetonitrile relative to those in nitromethane. This causes coalescence of the signals at lower temperature in acetonitrile than in nitromethane. However, the kinetic parameters for the dissociation in the two solvents are very close with each other. This may be rationalized by the fact that the polarity of the solvents is similar. Because of the similarity of the results, no further measurements were carried out for other compounds in acetonitrile.

Table 5. Melting Points and Elemental Analyses of Substituted 1-(1,3-Dithiolan-2-yl)pyridinium Perchlorates

Substituent	Mp (θ_m/°C)	Analysis					
		C/%		H/%		N/%	
		Calcd	Found	Calcd	Found	Calcd	Found
4-CH_3O	96—114[a]	34.45	34.21	3.86	3.83	4.47	4.32
4-CH_3	64—66	36.30	36.05	4.06	4.25	4.71	4.68
H	140—149[a]	33.86	33.74	3.55	3.46	4.94	4.80
3-CH_3O	86—87	34.45	34.14	3.86	4.27	4.47	4.34

a) With decomposition.

Table 6. ^{1}H NMR Data of Substituted 1-(1,3-Dithiolan-2-yl)pyridinium Perchlorates in CD$_3$NO$_2$ at 400 MHz

Substituent	Temperature °C	Chemical Shifts (δ)				
		1,3-Dithiolane		Pyridine		Others
		3,4-H	1-H	3,5-H	2,6-H	
4-CH$_3$O	10	3.68 (m)	7.25 (s)	7.52 (dd)	8.97 (dd)	4.27 (s)
4-CH$_3$	10	3.72 (m)	7.34 (s)	7.06 (dd)	9.04 (dd)	2.75 (s)
H	10	3.73 (m)	7.43 (s)	8.18 (td)	9.26 (dd)	8.67 (td)[a]
3-CH$_3$O	0	3.73 (m)	7.40 (s)	b)	9.83[c]	4.14 (s)[d]

a) 4-H of the pyridine ring. b) 5-H gives a signal at δ 8.08 (q). c) Apparent triplet for 2-H. d) 4-H and 6-H give signals at δ 8.18 (q) and 8.90 (apparent d), respectively.

Experimental

The compounds examined here are easily hydrolyzable with water in the air or in solvents. Special care was exercised to remove trace of water from the solvents and to avoid contact with air. Nitromethane-d_3 and acetonitrile-d_3 were dried over Molecular Sieves 3A, the method being recommended by a literature for acetonitrile.[20] Acetonitrile for the syntheses of the compounds was distilled from its mixture with phosphorus pentaoxide and dried over Molecular Sieves 3A. Ether was distilled from its mixture with lithium tetrahydridoaluminate.

Substituted 1-(1,3-Dithiolan-2-yl)pyridinium Perchlorates. The whole operations were carried out under dry argon. Triphenylmethyl perchlorate[21] (0.44 g or 1.3 mmol) was dissolved in 5 mL of acetonitrile. To this solution was added 0.15 g (1.4 mmol) of 1,3-dithiolane[22] in one portion and the mixture was stirred for 10 min at room temperature, and then 30 mL of dry ether was added to form yellow precipitates. The solvent was removed by filtration and the solid was washed with ether for several times. The solid was then dissolved in acetonitrile and mixed with 1.3 mmol of an appropriate pyridine derivative. Ether was added to the mixture until slight turbidity was observed at room temperature and the whole was cooled to −40~−50 °C. The precipitate was collected by filtration and recrystallized from acetonitrile–ether. The melting points and analytical data are given in Table 5 and the ^{1}H NMR data in Table 6.

Dynamic NMR Spectral Study. The spectral measurement was carried out with either a JEOL GX400 machine installed in Nippon Kayaku Company, Ltd., or that in Institute for Molecular Science. Samples were dissolved in nitromethane-d_3 or in acetonitrile-d_3 to make up a solution of ca. 200 mmol L^{-1}. Temperature was read by a thermocouple. For measurements of the dependence of the chemical shift differences on temperature, the spectra were obtained at 4—5 points of temperatures where the exchange of sites of magnetic spins was negligibly slow. The straight line was drawn by the least squares method. Fitting of the calculated spectra with the observed was carried out visually.

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16) Ordinary S$_\text{N}$2 reactions are known to proceed with negative entropy of activation.[18] However, this is due to the fact that the reaction occurs from a free nucleophile and a substrate in solution and is different from the case discussed here, where the reaction occurs from tight ion pairs or solvent-separated ion pairs. This assumption is consistent

with the fact that ammonium chlorides and a bromide give large positive entropy of activation for their dissociation.[6,19]

17) In Eq. 3, it is not meant that the reaction to afford the topomerized product proceeds with S_N2 mechanism between the perchlorate ester and the pyridine, but that a reaction between the pyridine and the perchlorate ester and/or the ion pair takes place. The necessary information for the diagnosis of the contribution of the two possible routes cannot be obtained because this step is not rate-determining. At any rate, a simple S_N2 reaction between the formed perchlorate ester and the pyridine does not account for the topomerization: It gives back the original topomer. The ester must dissociate to the ion pair in which topomerization takes place.

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