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Dynamic NMR as a Nondestructive Method for Determination of Rates of Dissociation. XXI. Dissociation in 1-(1-Haloethyl)pyrrolium Cations[1)]

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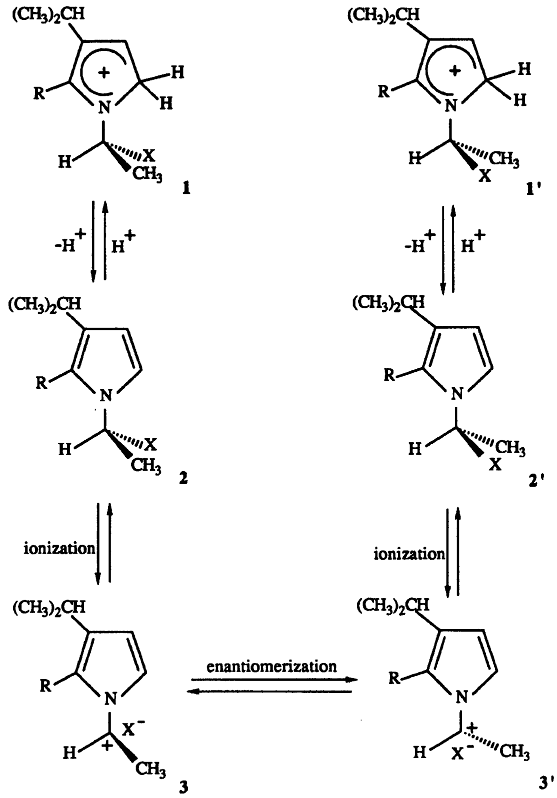
Topomerization observed for the isopropyl-methyls in the title compounds was reinvestigated with use of the total line shape analysis of NMR spectra. It was found that deprotonation from the pyrrolium cation preceded and was an independent step from the topomerization but the former strongly affects kinetic parameters for the latter process in the presence of excessive hydrogen halide. The extent of the excessiveness of hydrogen halide in the system also affects the reaction rates and the effects were discussed on the standpoint of activation parameters. The rates of topomerization of the isopropyl-methyls were found to be identical with the rates of enantiomerization at the 1-substituent in 1-(1-bromopropyl)-3-isopropyl-2-phenylpyrrolium ion to suggest that the topomerization in other compounds was also attributed to the ionization at the 1-substituent. The results suggest that a 1-pyrrolyl group assists ionization of 1-pyrrolylmethyl halide more effectively than a phenyl group in benzyl halide. This was reproduced by ab initio calculations.

Site exchange of the two methyl-protons in the isopropyl group in 1-(1-haloethyl)-3-isopropylpyrrolium halide (**1**) had been reported.[2)] The phenomenon was attributed to the ionic dissociation of the C–Hal bond followed by enantiomerization in the haloethyl group (Scheme 1). There remained ambiguity, however, in the conclusion for the following reasons.

Firstly, the rates of ionic dissociation of (1-chloroethyl)benzene are known to be much smaller than the time scale that is required for the observation of the line-shape change in the dynamic NMR.[3)] Although 1-(chloromethyl)pyrrole is described in the literature,[4)] the ease of ionization is not known. There may not be any reason to believe that pyrroles should enhance ionization of the 1-chloroethyl group attached to it relative to the role of a phenyl group in ionization of (1-chloroethyl)benzene. Secondly, although only the coalescence phenomena of the isopropyl-methyl signals were observed, there are a variety of possibilities that explain the topomerization of the isopropyl-methyls in compounds in question because the process is a complex one and should involve at least the following steps: 1) Deprotonation to form free pyrrole derivatives **2**, 2) ionization at the C–Hal bond to form ion pairs **3**, 3) enantiomerization at the ionization site, 4) C–Hal bond formation, and 5) protonation. The protonation–deprotonation process of the pyrrole ring at positions other than the 5-position might explain the results observed, if the protonation-deprotonation corresponds to the creation and erasure of a chiral center in the pyrrole ring such as addition of a proton to the 2-position.

Thus we felt that it would be worthwhile to measure the NMR spectra at various temperatures to analyze the line shapes and to get further insight into the phenomena observed. Activation parameters obtained by the line shape analysis should afford information about the transition state of the reaction which will enable us to discuss the process in more detail. This paper is a report of the reinvestigation of the phenomena in detail together with investigations on related compounds.



Scheme 1. Proposed mechanisms of topomerization.

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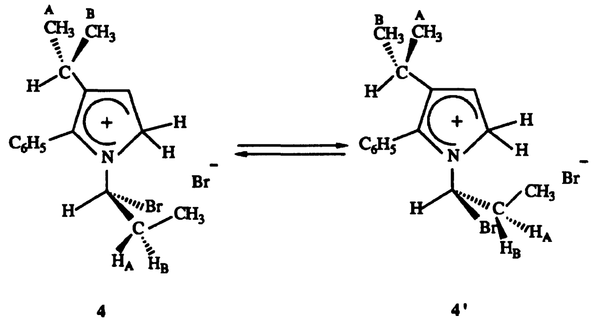
Results

The measurements of the ^{1}H NMR spectra were carried out at various temperatures and the observed line shapes were analyzed with use of the DNMR3K program.[5] Attempted analysis of the deprotonation processes by simulating the line shapes of the 5-methylene protons which were formed by protonation of the pyrrole ring failed because the line shapes were not reproduced by the simulation, probably because one of the protons dissociates and the process is not a simple A-B site exchange. The following two probes were used to obtain kinetic parameters for deprotonation. 1) The line shapes of the methyl-protons at the 2-position which showed long-range coupling with the 5-protons that disappeared on enhancement of the rates of deprotonation were simulated with the program as the case of dissociation of methylamine hydrochloride.[7] 2) In the cases where the compounds carried a 2-aryl group, loss of coupling was observed in the ^{13}C NMR spectra of C_5 and the line shapes were simulated similarly.

For topomerization of the isopropyl group, the line shapes were simulated as the 2-site exchange. The rates of ionization at the C–Hal bond were obtained by multiplying the observed rates of topomerization of the isopropyl-signals by two, because the probability of return of the ionized species to the covalent species, when the stereochemistry is retained or enantiomerization takes place, should be 50 : 50. The results are shown in Tables 1 and 2.

Similarly, the rates of topomerization in 1-(1-bromopropyl)-3-isopropyl-2-phenylpyrrolium bromide (**4**), which is shown in Scheme 2, were obtained with use of two probes, isopropyl-methyls and methylene-protons in the 1-bromopropyl group, to see whether these probes gave identical rates. The results are shown in Table 3.



Scheme 2. Topomerization in 1-(1-bromopropyl)-3-isopropyl-2-phenylpyrrolium ion.

Careful examination of the observed spectra confirmed that no other species ascribable to the origin of the creation of a new chiral center was existent. This proves that we can concentrate our discussion on the mechanisms of the topomerization as were proposed earlier and are depicted in Scheme 1.

The rate constants of the dynamic processes are given at 273 K because this temperature is within or close to the range of actual observation of line shapes in the extreme cases, fast and slow, because large entropies of activation might cause a large error if the values are extrapolated far outside of the observation range. Because of the very small chemical shift differences, the data for 1-(1-bromoethyl)-3-isopropyl-2-methylpyrrolium bromide (**1**: R=CH_3, X=Br) are given only at the coalescence temperature (282 K).

Because it is very difficult to set a defined excess of hydrogen halide in practice, we examined the effects of the degree of excess of hydrogen halide on the kinetic parameters. The results obtained for the compounds with 2-aryl substituents are shown in Tables 4 and 5. Excess of hydrogen halide tends to stabilize the pyrrolium ions and the rates are small compared to the case of less excess of hydrogen bromide. The rates of topomerization of the isopropyl-methyls can be assumed that they are almost constant when the excess of hydrogen bromide is more than 20, whereas they are increased as the excess of hydrogen halide is decreased, attain maximum at about 3—5 moles of hydrogen halide, and decrease again when the excess of hydrogen bromide becomes negligible. These results are in conformity with the results published earlier.[2]

Discussion

The results in Tables 4 and 5 assure that the effects of excess of hydrogen halide are saturated when the excess becomes 20 molar or more as reported earlier.[2] Thus we can discuss the results obtained with 20 or more excess of hydrogen halide together.

The rates of deprotonation processes obtained by the different probes of a substrate in a given solution, Entries 5 and 6 in Table 1, prove that both ^{13}C and ^{1}H dynamic NMR give the same results within experimental errors and confirm that we can discuss the results obtained with different probes together. Reproducibility of the data is limited, as is seen from Entries 1 and 6 in Table 1, because of the simple line shapes[8] and small coupling constants. The reliability of the kinetic data obtained by simulations of complex line shapes, e.g. topomerization, should be more reliable[8] than the deprotonation. However, discussions of various factors are possible with these deprotonation data if we allow some reservations.

Comparison of the results obtained under similar conditions in Tables 1 and 2, e.g. Entry 4 in Table 1 and Entry 6 in Table 2, clearly shows that the deprotonation and topomerization are independent steps in the reaction observed and deprotonation is faster than topomerization of the isopropyl-methyls, though their rate constants are not far apart from each other. Thus deprotonation precedes topomerization as was assumed earlier.[2]

Deprotonation at Large Excess of Hydrogen Halide. It is appropriate to discuss the results of

Table 1. Activation Parameters for Deprotonation in 2-Substituted 1-(1-Haloethyl)-3-isopropylpyrrolium Halides (**1**)

Entry	X	R	Excess of HX	Probe	$\Delta H^{\ddagger}$/kcal mol^{-1} [a)]	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}	$\Delta G^{\ddagger}{}_{273}$/kcal mol^{-1}	k_{273}/s^{-1}
1	Br	CH_3	25	2-$C\underline{H}_3$	23.9±1.1	31.1±3.8	15.3	4.5
2	Cl	CH_3	20	2-$C\underline{H}_3$	29.4±1.5	54.4±5.6	14.5	14
3	Br	C_6H_5	25	5-$\underline{C}$	22.2±1.4	32.8±5.1	13.2	140
4	Br	p-$CH_3OC_6H_4$	25	5-$\underline{C}$	25.0±2.1	39.2±8.0	14.3	20
5[b)]	Br	CH_3	25	5-$\underline{C}$	27.7±2.2	45.6±7.9	15.3	3.4
6[b)]	Br	CH_3	25	2-$C\underline{H}_3$	26.5±2.7	40.5±9.7	15.4	2.6
7	Cl	CH_3	10	2-$C\underline{H}_3$	23.1±1.2	40.8±5.0	12.0	1500
8	Br	CH_3	1.0	2-$C\underline{H}_3$	17.9±1.2	21.8±5.2	12.0	1400

a) 1 cal=4.184 J. b) These data were obtained for the same solution.

Table 2. Activation Parameters for Topomerization of Isopropyl-Methyls in 2-Substituted 1-(1-Haloethyl)-3-isopropylpyrrolium Halides (**1**)

Entry	X	R	Excess of HX	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}	$\Delta G^{\ddagger}{}_{273}$/kcal mol^{-1}	k_{273}/s^{-1}
1	Cl	CH_3	20	24.9±1.7	36.4±6.2	15.0	5.5
2	Br	CH_3	25			15.9[a)]	2[a)]
3	Cl	p-$CH_3OC_6H_4$	30	30.1±2.5	56.3±9.0	14.7	10
4	Cl	C_6H_5	30	28.8±1.4	55.2±6.1	13.7	60
5	Cl	p-ClC_6H_4	25	18.7±1.2	21.5±5.0	12.4	620
6	Br	p-$CH_3OC_6H_4$	25	21.0±1.4	23.0±5.0	14.8	8.8
7	Br	C_6H_5	25	18.9±0.4	18.5±1.6	13.9	45
8	Br	p-ClC_6H_4	25	17.4±0.5	15.8±2.2	13.0	210
9	Br	CH_3	1.0	20.4±1.5	26.8±6.1	13.0	215

a) At 282 K.

Table 3. Activation Parameters for Topomerization in 1-(1-Bromopropyl)-3-isopropyl-2-phenylpyrrolium Bromide (**4**) in the Presence of a 25 Molar Excess of Hydrogen Bromide

Entry	Probe	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}	$\Delta G^{\ddagger}{}_{273}$/kcal mol^{-1}	k_{273}/s^{-1}
1	$CH(C\underline{H}_3)_2$	19.2±0.9	19.6±3.6	13.8	48
2	$CHBrC\underline{H}_2CH_3$	18.6±1.2	16.7±4.9	13.9	42

Table 4. Dependence of Kinetic Parameters for Topomerization in Compound **1** (X=Br, R=C_6H_4Cl-p) on the Degree of Excess of Hydrogen Bromide

HBr Excess	3.4	9.0	25	50
$\Delta H^{\ddagger}$/kcal mol^{-1}	11.2±0.8	13.4±0.7	17.3±0.6	17.7±0.5
$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}	−3.0±3.5	4.9±3.0	15.8±2.2	16.6±1.9
$\Delta G^{\ddagger}{}_{273}$/kcal mol^{-1}	12.0	12.0	13.0	13.2
k_{273}/s^{-1}	13×10^2	13×10^2	21×10	16×10

Table 5. Dependence of Kinetic Parameters for Topomerization in Compound **1** (X=Br, R=$C_6H_4OCH_3$-p) on the Degree of Excess of Hydrogen Bromide

HBr Excess	0	2.5	8.0	25
$\Delta H^{\ddagger}$/kcal mol^{-1}	8.6±0.5	12.6±1.0	15.9±0.5	21.0±1.4
$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}	−14.2±2.2	2.1±4.5	11.4±2.0	23.0±5.0
$\Delta G^{\ddagger}{}_{273}$/kcal mol^{-1}	12.4	12.1	12.8	14.8
k_{273}/s^{-1}	62×10	13×10^2	33×10	8.8

the deprotonation–protonation process first. Our results are consistent with the observation that the rates of protonation of pyrroles are about three magnitude of ten faster than the deprotonation,[9)] because at the equilibrium of deprotonation–protonation we observe, we do not see any deprotonated species present in the system. The features of the activation parameters are that the entropy of activation is large positive, the rates tend to be larger when hydrogen chloride is added than the case of hydrogen bromide, e.g. Entries 1 and 2 in Table 1, and hydrogen bromide tends to give smaller enthalpy of activation and smaller entropy of activation than the case of hydrogen chloride.

The entropy of activation is expected to be positive because the ionic species tend to lose the electric charge, which restrict the motion of solvent molecules, at the transition state. However, this factor is common for every case examined, we may neglect this in comparison of the data.

At the first glance, it may be attracting to conclude that, because bromide anion has less proton-affinity than chloride anion,[10)] the process is slow for the hydrogen bromide case. However, this explanation does not accommodate the enthalpy and the entropy change from the chloride to the bromide, because entropy of activation as well as enthalpy of activation are different between the two halogen cases.

In the literature, the presence of hydrogen chloride–chloride anion complex, HCl_2^-, and the bromine counterpart, HBr_2^-, is postulated to account for the dependence of chemical shifts of protons in hydrogen halide on the concentration of tetrabutylammonium halide[11)] and the results of nuclear quadrupole resonance.[12)] The authors of the former paper observed that HCl_2^- is much more stable than HBr_2^-. The presence of HCl_2^- anion was postulated in HCl-catalyzed racemization of 1-phenylethyl chloride as well.[13)] It is also known that hydrogen fluoride forms a very stable complex with a fluoride anion.[14)] These may support discussion assuming the presence of HX_2^- in our system. However, because the HX_2^- complex is anionic in its nature, it will form hydrogen bond with HX which is present in the system in excess. Indeed the presence of a polymeric $[H_n(Hal)_{n+1}]^-$ ion in the presence of a large excess of hydrogen halide is reported.[15)]

We believe our data can be accommodated if we assume that the polymeric association of $[H_n(Hal)_{n+1}]^-$ is more stable if the halogen belongs to the earlier row of the periodic table but becomes less stable when we descend the periodic table. This is reasonable because, when we descend the periodic table the polarizability of the atom becomes large and hence the hydrogen-bonding energy becomes small. At the transition state for deprotonation, the strongly bound complex is freed to increase the entropy of the system, thus making the entropy of activation more positive in the case of hydrogen chloride than that of hydrogen bromide. Because of the formation of stronger aggregation, $(H_nCl_{n+1})^-$ is less basic than $(H_nBr_{n+1})^-$, though it is known that Cl^- is more basic than Br^- in nonaqueous solution.[10)] These account for the low activation enthalpy and smaller positive entropy of activation for the case of hydrogen bromide than that of hydrogen chloride.

Substitution of an aryl group for the 2-methyl group in 3-isopropyl-2-methylpyrrolium bromide (**1**: X=Br, $R=CH_3$) enhances the rates of deprotonation (Entries 3 and 4 in Table 1). The more electron-withdrawing the aryl group, the larger the rates of deprotonation. This may well be attributed to the electronic effects of the substituent on the stabilization of the cation and the transition state by the electron-withdrawing nature of the aryl group.

In the initial state of the reaction, the cation is stabilized if a substituent is electron-donating by either inductive or mesomeric effects. The aryl group is more electron-withdrawing than an alkyl group if the acidity[16)] of the corresponding carboxylic acid can be used as a measure, and the electron-withdrawing character of the *p*-methoxyphenyl group is weaker than that of the phenyl group. Thus, as far as the initial state of the reaction concerns, the methyl should give the lowest rates of deprotonation followed by the *p*-methoxyphenyl and the phenyl compounds.

This expectation is materialized, because the rates are $2\text{-}CH_3 < 2\text{-}(p\text{-}CH_3OC_6H_4) < 2\text{-}C_6H_5$. However, the differences are rather large. This may well include the energy of the transition state. Because the transition state more or less exhibits the character of 2-arylpyrrole, it is more stabilized by the 2-aryl substituent than by the 2-methyl and the rates should be enhanced in the aryl compounds.

Deprotonation at Small Excess of Hydrogen Halide. The effects of the excess of hydrogen halide are remarkable. Although, due to instability of the hydrogen chloride case, a small excess of hydrogen chloride is not practical for the study, it is still clear that, if the excess of hydrogen halide is limited, the rates of deprotonation are much larger than the case of a large excess of hydrogen halide (Compare Entries 1 and 8 or 2 and 7 in Table 1). This will mean that association discussed above exists in the presence of excess of hydrogen halide, reducing the proton-abstracting ability of the complex anion. Entropy of activation, which increases to a small extent in the case of small excess of hydrogen halide relative to the case of a large excess, supports the idea.

Although hydrogen bromide seems to give higher rates of deprotonation than the hydrogen chloride case (Table 8), this is due to the difference in excess of hydrogen halide. In this small excess of hydrogen halide, $(H_nBr_{n+1})^-$ species seems to have more proton-affinity than the chlorine case and the large excess of HBr case in which aggregation is more extensive.

It is also noteworthy that the entropy of activation is rather large positive for the small excess of hydrogen bromide (Entry 8 in Table 1), although it seems to be decreased relative to the case of large excess of hydrogen halide (Entry 1 in Table 1). This contrasts the data for topomerization in compound **1** with a 2-aryl substituent in the presence of a small excess of hydrogen halide discussed later in this paper. They are small positive or even small negative.

Topomerization of Isopropyl-Methyls at Large Excess of Hydrogen Halide. The rates of topomerization shown in Table 2 reveal similar tendency to those in Table 1, exhibiting the changes according to the substrate and conditions which follow. The rates are larger when halogen is chlorine than the case of bromine, e.g. Entries 5 and 8 in Table 2, and electron-withdrawing substituents enhance the rates, e.g. Entries 6 and 8. This means that, although deprotonation and topomerization are independent steps, their rates as well as activation parameters are mainly controlled by the first deprotonation step. Thus it will be appropriate to discuss the data on the standpoint of deprotonation when hydrogen halides are present in large excess.

When one compares entropy of activation obtained for the chlorine and the bromine cases, one notices that the chlorine case gives larger entropy of activation, e.g. Entries 3 and 6 in Table 2. This result must again be attributed to the stronger association of hydrogen chloride than hydrogen bromide to the corresponding halide anion. Release of the strong association at the transition state of the reaction should result in a large positive entropy of activation.

It is also noted that the compound that carries a chlorophenyl group gives a significantly smaller entropy of activation than other aryl compounds, especially in the case of hydrogen chloride (Entry 5). This may be attributed to the earliness of the transition state in the reaction coordinate, where the aggregation of hydrogen chloride is not completely released. The earliness of the transition state is plausible because this compound carries the most electron-attracting substituent. The small enthalpy of activation of this reaction is in agreement with the idea of the early transition state.

The topomerization of the isopropyl-methyls may now be assumed that ionization of the 1-haloethyl group is the cause for the phenomenon, because the deprotonation and the topomerization are independent processes. However, there is one point which should be cleared to come to this conclusion. That is, whereas entropy of activation is usually large negative for this type of ionization because ionization of a covalent molecule causes restriction of the freedom of motion of solvent molecules,[17,18] the system under investigation affords rather large positive entropy of activation in all the cases. We have examined two factors which would justify the assumption that the topomerization is really caused by ionization in the 1-substituent. They are examination of topomerization with use of two probes, the 3-isopropyl-methyls and protons that are incorporated in the 1-substituent where ionization should take place, and that of the effects of excess of hydrogen bromide.

The first is the case of 1-(1-bromopropyl)-3-isopropyl-2-phenylpyrrolium bromide (**4**), in which the 2-methylene-protons of the 1-substituent serve as probes for detecting ionization of the C–Br bond, to see whether the ionization of the 1-bromopropyl group and the topomerization of the isopropyl-methyl groups give the same kinetic parameters, when large excess of hydrogen bromide is present. The results shown in Table 3 clearly indicate that both topomerization of the methylene-protons in the 1-bromopropyl group and that of the isopropyl-methyl groups give the same kinetic parameters within the experimental errors. This strongly suggests that the topomerization of the isopropyl-methyls in compounds **1** is really due to enantiomerization at the 1-bromoethyl group.

It is also interesting to note that the rates of topomerization in compound **4** are the same with the corresponding compound **1** (R=C_6H_5, X=Br). Because the inductive effect of a methyl group is small when a bond intervenes, the results are reasonable.

Effects of Excess of Hydrogen Bromide on Topomerization. The data in Tables 4 and 5 give some interesting points with respect to the effects of the extent of excess of hydrogen bromide. The rates are not affected by the degree of excess of hydrogen bromide, if the excess is more than 25, but become large when the excess becomes small and attain a maximum at about 3 molar excess. This result is in conformity with the results published earlier that were derived by the coalescence method.[2)]

The entropy of activation is large positive when hydrogen bromide is present in large excess, while it decreases as the extent of excess of hydrogen bromide decreases, and is negative when only 2 moles of hydrogen bromide is used for 1 mole of the substrate, i.e. no excess of hydrogen bromide is present but to form the pyrrolium bromide (**1**). The last entropy of activation is typical for ionization of the neutral organic compounds.[17,18)] The results will mean that, although topomerization itself should give negative entropy of activation, the process is so strongly affected by the presence of excess of hydrogen halide that it exhibits the activation parameters which are similar to the deprotonation.

This will mean that these steps, deprotonation and topomerization, are independent, being far apart from each other, under the conditions of small excess of hydrogen halide and the kinetic parameters of the deprotonation affect those of the topomerization to a lesser extent.

The reasons for the presence of maximum rates of topomerization, when one goes from a large excess of hydrogen bromide to no excess, are not well understood at the present time but may well be a reflection of the following factors. On going from a large excess of hydrogen bromide to a small excess, one observes that both enthalpy and entropy of activation decrease. Because the topomerization process is strongly affected by the deprotonation process in the presence of a large excess of hydrogen halide, the decrease in enthalpy of activation is reasonable because less association of hydrogen bromide with the ionic species should make the anionic species more effective to the deprotonation, rendering the activation energy smaller. The decrease in the entropy of activation can be interpreted in the same way, because the aggregate is partially deaggregated in the transition state. When no excess of hydrogen bromide is present, the effect of the first step, deprotonation, will become minimum to make the observation closer to the real ionization in the 1-substituent. The combination of these factors could produce the observed trends.

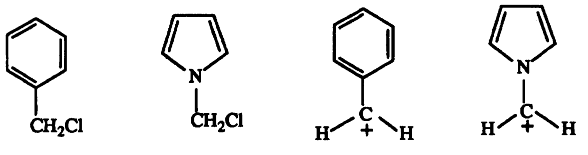
There is one exception for the above-mentioned excess effect of hydrogen halide on the entropy of activation. That is the case of 1-(1-bromoethyl)-3-isopropyl-2-methylpyrrolium bromide (**1**: R=CH_3, X=Br): This compound gives still a large positive entropy of activation for the topomerization (Entry 9 in Table 2). The exact reason for this is not known at present.

Nature of Topomerization. Coming back to the problem of ionization in the 1-haloethyl group, we can now discuss the nature of the reaction observed. The ionization itself should not be an exception from other compounds: It should give negative entropy of activation, if excess of hydrogen halide does not exist. Thus we must assume that the presence of excess of hydrogen halides causes the large positive entropy of activation for the ionization of the C–Hal bond. It is then natural to assume that, although the ionization of the C–Hal bond is the rate-limiting step in the topomerization of the isopropyl-methyls, the process is strongly affected by the deprotonation as the preceding step, rendering the activation parameters for enantiomerization dependent on those for the first deprotonation step.

This means that the free form **2** is at a rather high energy state in the presence of excessive hydrogen halide and the energy minimum is shallow to make the backward reaction to **1** fast under the conditions. Yet the free form must be present to complete the topomerization reaction.

This type of reactions is called to involve a pre-equilibrium[19] or a preliminary equilibrium.[20] In these reactions, the observed rates involve the equilibrium constants as well as the rate constant of the second slow reaction. Accordingly, the activation parameters include the difference in thermodynamic parameters between the intermediate and the initial state. Our results are in conformity with the theoretical considerations. When hydrogen bromide is present in large excess, the backward reaction in the equilibrium becomes important. Eventually, this type of examples was reported with use of the dynamic NMR technique for inversion of amines in aqueous solutions.[21]

The decrease in entropy of activation for topomerization, as the excess of hydrogen halide is decreased, may be the results of combination of weak association of hydrogen halide with a halide anion and gradual transition to observing the independent topomerization. When the deprotonation controls the topomerization, aggregation–deaggregation of hydrogen halide with halide ion is important. Aggregation is weaker in the case of bromine, rendering the entropy of activation smaller than the case of chlorine. It is also true that presence of more excess of hydrogen halide molecules would result in more restriction of the motion of the molecules due to association which is freed in the transition state of the reaction. As the ionic dissociation in the 1-substituent becomes important, the activation parameters tend to become similar to those observed for other covalent species.



5 **6** **7** **8**

Scheme 3. Arylmethyl chlorides and arylmethyl cations.

Table 6. Final Energies, as Calculated by ab initio Molecular Orbital Methods, of Compounds **5**—**8** and Their Difference between Related Compounds (Hartrees[a)])

Basis Set	3-21G	6-31G*
Compound **5**	−724.95812	−728.64004
Compound **7**	−267.38045	−268.88673
ΔE(**7**−**5**)	457.57767	459.75331
Compound **6**	−703.18055	−706.74044
Compound **8**	−245.61717	−246.99796
ΔE(**8**−**6**)	457.56338	459.74248
$\Delta\Delta E$/Hartree[b)]	0.01428	0.01082
$\Delta\Delta E$/kcal mol^{-1} [b)]	9.0	6.8

a) 1 Hartree = 2625.5 kJ mol^{-1} = 627.50 kcal mol^{-1}.
b) $\Delta\Delta E$=ΔE(**7**−**5**)−ΔE(**8**−**6**).

Ease of Formation of 1-Pyrrolylmethyl Cation. Although the above results strongly suggest that 1-pyrrolylmethyl cation is more easily formed than benzyl cation, one might argue that, because of the presence of a large excess of hydrogen halide, even benzyl halide derivatives would ionize under the conditions. To erase this possibility, we observed the NMR spectra of (1-bromopropyl)benzene which was dissolved in CD_2Cl_2 and excess of hydrogen bromide. No sign of ionization of the substrate was observed even at room temperature.

Establishing that 1-(1-haloethyl)pyrroles ionize at the C–Hal bond more easily than the case of (1-haloethyl)benzene, we may conclude that the pyrrole ring is more stabilizing the cation attached to it than a phenyl ring. In order to support this conclusion, we have also calculated the total energies of the corresponding chlorides (**5** and **6**) and of arylmethyl cations (**7** and **8**). We performed this calculation because the difference between the heat of formation of the chloride and that

Table 7. Dependence of Chemical Shift Differences in Compounds **1** and **4** on Temperature

R	X	Probe	Excess of HX	$\Delta\nu$/Hz=$A-BT$/K A	 B
CH_3	Cl	$(C\underline{H}_3)_2CH$	20	59.2	0.194
CH_3	Br	$(C\underline{H}_3)_2CH$	1.0	51.2	0.195
p-$CH_3OC_6H_4$	Cl	$(C\underline{H}_3)_2CH$	30	206.1	0.524
C_6H_5	Cl	$(C\underline{H}_3)_2CH$	30	160.6	0.426
p-ClC_6H_4	Cl	$(C\underline{H}_3)_2CH$	30	188.1	0.519
p-$CH_3OC_6H_4$	Br	$(C\underline{H}_3)_2CH$	25	149.1	0.428
p-$CH_3OC_6H_4$	Br	$(C\underline{H}_3)_2CH$	8.0	141.2	0.421
p-$CH_3OC_6H_4$	Br	$(C\underline{H}_3)_2CH$	2.5	130.2	0.398
p-$CH_3OC_6H_4$	Br	$(C\underline{H}_3)_2CH$	0	142.1	0.500
C_6H_5	Br	$(C\underline{H}_3)_2CH$	25	126.5	0.382
p-ClC_6H_4	Br	$(C\underline{H}_3)_2CH$	50	125.8	0.360
p-ClC_6H_4	Br	$(C\underline{H}_3)_2CH$	25	131.3	0.381
p-ClC_6H_4	Br	$(C\underline{H}_3)_2CH$	9.0	122.4	0.377
p-ClC_6H_4	Br	$(C\underline{H}_3)_2CH$	3.4	114.1	0.360
C_6H_5[a)]	Br	$(C\underline{H}_3)_2CH$	25	139.2	0.351
C_6H_5[a,b)]	Br	$CHBrC\underline{H}_2$	25	−122.6	−0.796

a) Compound **4**. b) Negative values are given by taking into account the negative coupling constants for geminal protons.

Table 8. Rate Constants of Deprotonation

R	X	Excess of HX	Probe	k/s^{-1}(t/ °C)
CH_3	Br	25	2-CH_3	1.0(−4.5),1.6(−2.5),2.6(0),4.0(1.5),5.6(4),9.2(7),13(10),18(13)
CH_3	Br	25	5-C	1.5(−3),3.0(0),5.0(2),7.5(4),10.0(7),19.0(10),24(13)
CH_3	Cl	20	2-CH_3	2.0(−9),6.0(−4),10(−2),18(1),32(4),40(5),46(6),58(8)
C_6H_5	Br	25	5-C	4.0(−21),8.0(−18),12(−15),28(−12),40(−8),64(−6),84(−4),100(−2.5)
p-$CH_3OC_6H_4$	Br	25	5-C	1.0(−17),2.0(−12),6.0(−7),10(−3.5),18(−1),30(2),38(3.5)
CH_3	Cl	10	2-CH_3	0.4(−42),1.0(−39),2.4(−36),3.2(−34),4.8(−32),6.8(−30),10.4(−28),14(−26)
CH_3	Br	1.0	2-CH_3	1.2(−45),3.0(−42),4.0(−40),6.8(−37),10.0(−35),15(−32)

Table 9. Rate Constants of Topomerization

R	X	Excess of HX	Probe	k/s^{-1}(t/ °C)
CH_3	Cl	20	$(C\underline{H}_3)_2H$	4.0(−2),6.0(1),11(4),13(5),16(6),22(8),32(11)
C_6H_5	Cl	30	$(C\underline{H}_3)_2H$	1.0(−19),3.0(−4),5.5(−12),8.0(−10),12(−8),19(−6),23(−4),40(−2)
p-$CH_3OC_6H_4$	Cl	30	$(C\underline{H}_3)_2H$	2.0(−7),4.0(−4),10(0),14(2),20(4),34(6),46(8)
p-ClC_6H_4	Cl	30	$(C\underline{H}_3)_2H$	4.0(−35),8.0(−30),14(−27),19(−25),30(−22),42(−20),82(−15)
C_6H_5	Br	25	$(C\underline{H}_3)_2H$	2.0(−22),3.0(−19),6.3(−14),12(−10),16(−8),20(−6),28(−4),35(−2),46(0),55(2)
p-$CH_3OC_6H_4$	Br	25	$(C\underline{H}_3)_2H$	6.0(−2),9.0(0),12(2),16(4),23(6),33(9),38(11),60(14)
p-$CH_3OC_6H_4$	Br	8.0	$(C\underline{H}_3)_2H$	2.0(−42),3.0(−37),6.0(−32),8.0(−30),10(−28),14(−26),19(−24),24(−22) 31(−20),44(−17)
p-$CH_3OC_6H_4$	Br	2.5	$(C\underline{H}_3)_2H$	4.5(−53),7.0(−48),10.0(−44),18(−42),21(−40),28(−37),40(−34),52(−32)
p-$CH_3OC_6H_4$	Br	0	$(C\underline{H}_3)_2H$	6.0(−59),11(−53),18(−48),23(−45),30(−42),38(−39),50(−35)
p-ClC_6H_4	Br	50	$(C\underline{H}_3)_2H$	1.0(−36),2.0(−31),5.0(−26),10(−21),14(−19),20(−16),24(−14),32(−12),60(−8)
p-ClC_6H_4	Br	25	$(C\underline{H}_3)_2H$	2.0(−34),4.0(−29),9.0(−24),12(−22),17(−20),22(−18),27(−16),35(−14),45(−12)
p-ClC_6H_4	Br	9.0	$(C\underline{H}_3)_2H$	3.0(−52.5),6.0(−48),8.5(−45),11(−42),18(−39),27(−36),41(−33)
p-ClC_6H_4	Br	3.4	$(C\underline{H}_3)_2H$	4.0(−58),8.0(−53),10.5(−51),14(−48),18(−45),27(−42),39(−39)
C_6H_5[a)]	Br	25	$(C\underline{H}_3)_2H$	1.0(−26),2.5(−21),3.5(−18),6.0(−15),8.0(−13),12(−9.5),23(−5.5)
C_6H_5[a)]	Br	25	$C\underline{H}_2$	1.1(−26),2.2(−21),3.6(−18),4.4(−15),5.0(−13),11(−9.5),22(−5.5)
CH_3	Br	1.0	$(C\underline{H}_3)_2H$	0.5(−37),0.8(−35),1.7(−32),2.3(−29),3.8(−26),4.7(−24),8.0(−22)

a) Compound **4**.

of the cation should be the true measure of the ease of ionization of the chloride (Scheme 3).

The results are shown in Table 6. The conformation of benzyl chloride is known to be stable, when the C–Cl bond is orthogonal to the benzene ring.[22)] Thus we adopted this conformation in calculation. For the conformation of 1-(chloromethyl)pyrrole (**6**), three conformations, C–Cl bond eclipsing the aromatic ring, C–Cl bond forming a dihedral angle of 60° with the ring, and C–Cl bond orthogonal to the ring, were calculated and it was found that the last conformation was the most stable of the three as the case of benzyl chloride. Thus the results shown in the table are for this conformation only. The plane of the cationic part of the arylmethyl cations was rotated and was found to be coplanar with the aromatic ring at their most stable conformations, as expected. The differences between the heat of formation of the chloride and that of the arylmethyl cation are dependent on the basis sets used for the calculations. We have calculated with the basis sets of STO-3G, 3-21G, 6-31G, and 6-31G*. Because the difference is always larger for phenylmethyl cation than 1-pyrrolylmethyl cation, we list only the results of 3-21G and 6-31G*. The results support that 1-(chloromethyl)pyrrole is more easily ionizing than benzyl chloride.

In conclusion, this work confirms that the topomerization of the isopropyl-methyls in compound **1** is caused by enantiomerization in the 1-haloethyl group, although its kinetic parameters are strongly affected by the preceding deprotonation step. It is also proved that the assistance for ionization of the 1-chloroethyl group provided by the 1-pyrrolyl group is much more efficient than the phenyl group.

Experimental

Materials and Generation of Cations. All vinylpyrroles used in this work were synthesized following the published methods[23] in Irkutsk Institute of Organic Chemistry. The pyrrolium cations (**1** and **4**) were generated by introducing dry hydrogen chloride or hydrogen bromide gas into 0.6 cm^3 of a 0.5 mol dm^{-3} solution of a 1-vinylpyrrole derivative in CD_2Cl_2 placed in an NMR tube, which was cooled to −78 °C, for 10—15 min. This low temperature treatment was necessary to prevent decomposition of the cation, which was rather unstable when the amount of hydrogen halide was limited. The excess of hydrogen halide was estimated by the duration of the introduction of hydrogen halide and was calculated by the NMR intensities. The NMR tube was sealed and transferred into an NMR probe precooled to −50 °C.

1-(Bromopropyl)benzene was prepared by a standard method[24] and treated in the same way as the vinylpyrroles.

Dynamic NMR. The spectra were measured on a JEOL GSX-400 NMR spectrometer which operated at 399.8 MHz for ^{1}H and 100.5 MHz for ^{13}C. Temperature was read by an equipped thermometer which was calibrated by a methanol sample.

Chemical shift differences of the diastereotopic methyl-protons in the isopropyl group drifted as temperature was changed. The chemical shift differences were determined at five temperatures in the slow exchange limit and they were correlated with a straight line. The temperature dependence is summarized in Table 7. These equations were used for estimating the chemical shift differences by extrapolation to temperatures where the line shape change was observed.

The coupling constants were constant in the temperature ranges where observation was made and thus used for simulation as observed. T_2 was evaluated from the band width at slow exchange limits and was used as such to get the best fit spectra. The typical values were 0.15, 0.24, 0.07, and 0.05 s for isopropyl-methyl protons, 2-methyl-protons, methylene-protons in **4**, and 5-C, respectively.

For the simulation of the carbon spectra of 2-arylpyrrolium cations, ^{1}H off-resonance decoupling method was employed, because the direct spin-spin coupling constants (^1J) were too large, ca. 150 Hz, to require observation at high temperatures which was not practicable. By applying the ^{1}H off-resonance decoupling technique, the coupling constants of 20—25 Hz were observed, which were convenient to observe line shape changes at around 0 °C. The reliability of this method was checked by comparing the rate constants obtained by using the loss of coupling of 2-methyl signals of compound **1** ($R=CH_3$, $X=Br$).

In the case of compound **4**, the line shapes were simplified by irradiating the 1-methine proton. This method is known to not affect the rate constants obtained.[25] The dependence of chemical shift differences of the methylene protons on temperature is given in Table 7.

These data were put into DNMR3K[5] program and the best fit spectra were determined by visual fitting. The rate constants thus obtained, typical data of which are listed in Tables 8 and 9, were put into the Eyring equation to afford kinetic parameters.

Calculations. ab initio calculations were performed on a CONVEX computer using the GAUSSIAN 92 program.[26] The optimized structures of the arylmethyl chloride were those possessing the C–Cl bond orthogonal to the aromatic plane, whereas those of the cations were coplanar with respect to the cationic moiety and the aromatic ring.

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