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Addition of Hydrogen Halides to 1,2-Dialkylpyrrolium Cations

Mark V. SIGALOV,# Shinji TOYOTA, Michinori ŌKI,* and Boris A. TROFIMOV†
Department of Chemistry, Faculty of Science, Okayama University of Science, Ridaicho, Okayama 700
† Institute of Organic Chemistry, Siberian Division of the Russian Academy of Sciences, 664033 Irkutsk, Russia

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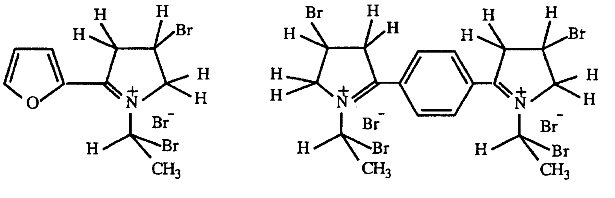
Although it is believed that addition of an acid to 2-substituted pyrroles produces 5-protonated pyrrolium ions and further reaction is prevented by the stability of the product, this work shows that further addition of hydrogen halides takes place to the pyrrolium ion to produce 2-substituted 4-halo-4,5-dihydro-3*H*-pyrrolium ions in general. In the case where the 1-alkyl group is a 1-bromoethyl, addition of hydrogen bromide gives one stereoisomer preferentially, of which conformation was determined by NOE experiments to be two C–Br bonds anti with each other, relative stereochemistry being R^* and S^*. The results are discussed on the thermodynamic stability and/or the kinetic preferences of the products. Generality of the addition of hydrogen bromide to the pyrrolium ion was tested with 1,2-dimethylpyrrole, which gave a kinetically favored isomeric addition product that isomerized to a thermodynamically favored 4-bromo-1,2-dimethyl-4,5-dihydro-3*H*-pyrrolium bromide on standing.

While it had been generally believed that addition of hydrogen halide to the pyrrole ring afforded mainly 2-protonated pyrrolium ions,[1] examples of further addition of hydrogen bromide to produce 2-substituted 4-bromo-4,5-dihydro-3*H*-pyrrolium ions were reported only recently.[2,3] These examples (**1** and **2**) were rather limited and did not give general scope of the formation of the adducts (Scheme 1): There remained several questions to be answered. Although these compounds usually carry an aromatic ring at the 2-position of the pyrrole, is the aromatic ring necessary to form the adduct? Although hydrogen chloride was reported not to add to form the adduct, if the report is true, why is it so? Is the presence of 1-(1-haloalkyl) substituent necessary for the formation of the adducts? What is the stereochemistry of the adducts that carry two chiral centers at the 1-(1-haloalkyl) group and the 4-position? Further study of the phenomenon was needed to get insight into these problems posed on the addition of hydrogen bromide to the pyrrolium ion. This paper is to report the detailed study of the addition of hydrogen halide to the pyrrolium ion to answer the questions.

Results and Discussion

We decided to begin with a compound which carried the same 1-(1-bromoethyl) substituent as compounds **1** and **2** but did an alkyl group at the 2-position instead of the aryl group in **1** and **2**. Thus 2-methyl-1-vinylpyrrole (**3**) was the first example that would produce 1-(1-haloethyl)-2-methylpyrrolium ion (**4**) on treatment with hydrogen halide (Scheme 2).

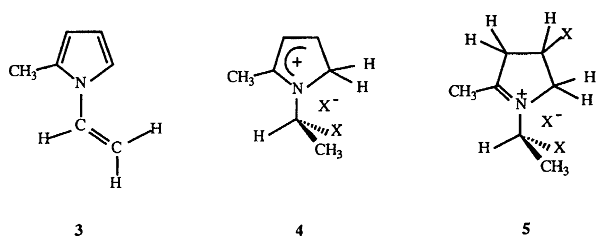


1 **2**

Scheme 1. 2-Aryl-4-bromo-4,5-dihydro-3*H*-pyrrolium ions in the literature.[2,3]

Addition of Hydrogen Bromide to 1-(1-Bromoethyl)-2-methylpyrrolium Bromide (4b). When 2-methyl-1-vinylpyrrole (**3**) was treated with excess of hydrogen bromide at −60 °C, the main product was 1-(1-bromoethyl)-2-methylpyrrolium bromide (**4b**).[3] Upon increase in temperature of the solution to −40 °C, a gradual decrease in the signal intensities due to **4b** and a gradual increase in the signal intensities due to two new specise were observed. The structures of the new species are assigned to **5b** on the basis of spectroscopic data shown in Table 1 together with NOE experimental results and decoupling. The formation ratio of the major isomer to the minor was 9.0 at −5.0 °C.

Structure Assignment. Compound **5b** should have two diastereomers, each of which exists as a racemic mixture, because there are two chiral centers. The structures of these diastereomers are assigned by the spectroscopic evidence shown below: The major compound has stereochemistry of R^* and S^* for the chiral centers in the ring and the side chain, respectively, and the minor has R^* and R^*. The stable conformations of these compounds are also deduced from



3 **4** **5**

a: X = Cl
b: X = Br

Scheme 2. Starting material, intermediates, and products.

#Inoue Fellow (1992—1993). On leave from Siberian Division of the Russian Academy of Sciences.

Table 1. ^{1}H NMR Data of the Hydrogen Halide Adducts (**5** and **9**) at −20 °C

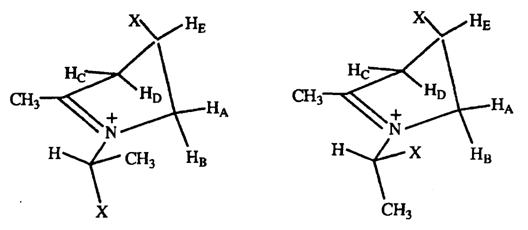
Compound	H_A/δ	H_B/δ	H_C/δ	H_D/δ	H_E/δ	J_{AB}/Hz	J_{CD}/Hz	J_{BE}/Hz	J_{DE}/Hz	J_{AE}/Hz	J_{CE}/Hz
5a (major)	4.65	4.85	3.69	4.22	5.00	14.7	21.3	5.4	6.7	ca. 0	ca. 0
5a (minor)	4.54	4.95	3.77	4.16	5.00	14.7	21.3	5.4	6.7	ca. 0	ca. 0
5b (major)	4.68	5.00	3.78	4.47	4.99	14.7	21.3	5.4	6.7	ca. 0	ca. 0
5b (minor)	4.61	5.12	3.88	4.51	5.00	14.7	21.3	5.4	6.7	ca. 0	ca. 0
9	4.47	5.10	3.70	4.34	4.90	14.9	21.3	5.3	5.6	ca. 0	ca. 0

the spectra: The assignments of the protons are given in Scheme 3 for the convenience of discussions in the assignments which follow. Enantiomeric 1-substituents are drawn for the convenience of drawing and for comparison as *S* and *R* for major and minor isomers, respectively.

The features of the spectral changes are that, while those due to sp^2-protons at δ=7.15 and 8.27 and those at ca. δ=5.3 due to the 5-protons in compound **4b** (see Table 2) disappeared, new signals, a multiplet at ca. δ=5.0 and 2 sets of essentially AB quartet signals at ca. δ=4.8 and ca. δ=4.2 appeared. The methyl signals remained essentially unchanged.

At −20 °C, the signals listed in Table 1 were obtained. Upon irradiation of the 2-methyl signal at δ=2.85 of the major isomer, one proton signal (δ=3.78) of the quartet at the high field exhibited enhancement in differential NOE spectra to show that this should be assigned to one of the 3-protons. The signals due to the 3-protons (H_C and H_D) were actually the AB part of an ABX system. Irradiation of the coupled proton at 3 gave a simpler spectrum of the signal at the lowest field. It will be reasonable to assign the signal at the lowest field to a proton (H_E) which is attached to the carbon with a bromine atom. Fortunately, large temperature dependence of the chemical shifts of the H_C and H_D protons made it possible to assign these signals to respective protons. The A parts of the ABX signals are δ=5.14 and 4.61 and the chemical shift of the X proton (H_E) is at δ=5.01 at +10 °C. Irradiation of H_E at δ=5.01 simplified these coupled signals at δ=5.14 and 4.61 to make them the A parts of AB signals.

Thus the proton at δ=4.99 at −20 °C should be flanked by two methylene proton pairs. The AB quartet signal of **5b** at ca. δ=4.8 in Table 1 was assigned to the 5-protons (H_A and H_B), because they both showed NOE enhancement when the signal at δ=2.21 due to the methyl-protons in the 1-substituent was irradiated as discussed later. Thus the signal at δ=4.99 is due to the 4-proton (H_E), the AB quartet at the high field is due to 3-protons (H_C and H_D) and that at the low field due to 5-protons. Taking these into consideration we assign the structure of this product to **5b**.



major isomer (5) minor isomer (5')

Scheme 3. Conformations and proton assignments of major and minor isomers of **5**.

The NMR data of the minor isomer are quite similar to those of the major. In addition, a double resonance experiment by irradiation at δ=5.00 shows that the signals at ca. δ=4.1 (H_C and H_D) and ca. δ=4.8 (H_A and H_B) are now simple AB's. The results indicate that the connectivities of the protons are the same for the two isomers and the isomers observed are not regioisomers, that could be formed by addition of hydrogen halide in a regiochemically isomeric way, but stereoisomers.

The results confirm that the HBr addition to the pyrrolium ion takes place, even if the 2-substituent is an alkyl group. One of the protons at the 5-position which shows the NMR signal at δ=5.00 in the major isomer exhibits a long range coupling with the 2-methyl protons, the coupling being observed by sharpening the 2-methyl-proton signal when the signal at δ=5.00 was irradiated. This coupling is similar to the case of pyrrolium ions (**4b**)[3] and in agreement with the stereochemical demand for the homoallylic coupling.[4] This point shall be elaborated later.

Interestingly, one of the geminal protons, both at the 3- and 5-positions and both for the major and minor isomers, does not show a measurable coupling with the proton at the 4-position. Examination of a Dreiding model of this cation together with that of the Karplus equation suggests that the ion takes, as an average, an envelope structure with a halogen atom directed to the pseudoaxial position at the tip of the envelope.

Establishing the gross structures of **5b**, we can now discuss the stereostructures of the isomers observed in the system. The problem is which of the structures, **5** and **5′**, corresponds to the major and minor isomers. The relative configuration at the 4-position of the major isomer was determined by combination of results of NOE experiments and those discussed above.

The main conformation of the 1-substituent was considered to be a C–H eclipsing form with the pyrrole moiety, in which the hydrogen directs toward the methyl group. The stable conformation of *s*-alkylbenzenes are known to be either C–H or C–C eclipsing forms with the

Table 2. ^{1}H NMR Data of 1-(1-Haloethyl)-2-methylpyrrolium Ions (**4**)

X	H_3/δ	H_4/δ	H_5/δ	$H_{5'}/\delta$	$C\underline{H}Me/\delta$	$CH\underline{Me}/\delta$	2-Me/δ	J_{34}/Hz	J_{45}/Hz	$J_{55'}$/Hz	$J_{45'}$/Hz	$J_{CH,Me}$/Hz
Cl	7.21	8.21	5.17	5.28	6.38	2.19	2.95	6.0	ca. 0	26.7	ca. 0	6.7
Br	7.15	8.27	5.25	5.35	6.48	2.30	2.90	6.0	ca. 0	26.7	ca. 0	6.7

benzene ring.[5,6] However, if there are 2,6-substituents on the benzene ring, isopropylbenzenes are stable in C–H eclipsing forms due to steric effects.[7] It will be reasonable to assume for compounds **5** and **5′** that they take similar conformations to the substituted isopropylbenzenes (See Scheme 3). Indeed, the NOE experiment that was performed to assign the 3-protons also showed enhancement in the intensity of the 1-hydrogen signal in the 1-substituent by 10%.

Establishing that the 1-(1-bromoethyl) group takes the conformation in which the 1-C–H extends toward the 2-methyl group, one can determine the relative positions of the 5-methylene protons and then stereochemistry at the 4-C by NOE experiments (Scheme 3), though determination of its absolute stereochemistry is not possible. By irradiation of the methyl-protons in the 1-(1-bromoethyl) group of the major product, we have observed enhancement by 3.2% for one (at δ=4.68) of the 5-methylene protons and the same by 1.7% for another proton (at δ=5.00) of the pair. It will be natural to assume that the proton which gives a larger enhancement of the two should be located more closely to the methyl-proton than the other. Thus, if the absolute configuration at the chiral center in the 1-substituent is *S*, the proton that gives the large enhancement is assigned to the pro-*R* proton (H_A), which in turn does not show a measurable coupling with the 4-proton (H_E). These protons should be trans with each other with respect to the ring. The configuration at the 4-C is determined as *R*, if the 1-substituent has the *S* configuration. Likewise, the protons C and D are assigned, the former (H_C) giving negligible coupling with H_E. The assignment is consistent with the fact that H_C shows NOE enhancement when the 2-methyl-protons are irradiated. In this structure, the C–H_B bond is almost perpendicular to the double bond plane in the major isomer and is in conformity with the geometrical requirement for the homoallylic coupling with the 2-methyl-protons.[4]

Now structure **5b** is assigned to the major isomer and **5b′** to the minor isomer. The results indicate that, if the 5-membered ring takes an envelope conformation, the C–Br bond at the 4-position takes an almost anti form to the 1-C–Br bond in the major isomer. In the minor isomer, the C–Br bond at the position 4 is also pseudoaxial, although the absolute configuration at 4-C is R^* if the chiral center in the 1-substituent is R^*. Thus the minor isomer is more polar than the major due to relative directions of two C–Br bonds.

Establishing the stereochemistry of the major product, we can now discuss the stability and/or preference of the formation of the major and the minor isomers. Although the medium is highly polar because of the presence of HBr in excess, the less polar R^*,S^* form is favored. In observing the products of addition of HBr at −40 °C, we noticed that the ratios of **5b** and **5′b** were constant at all the stages of the reaction. Thus it may be argued that it is the kinetic control. However, the proton exchange in the less preferred isomer seemed to be fast, as described below, and the ratio **5b**/**5′b** did not change on standing. Therefore the favored formation of **5b** is due to thermodynamic control, although it might also be favored for kinetic reasons. It is most likely that the less polar form is favored for the electrostatic reasons.

Dynamics Involving Compound 5b. Strictly speaking we must treat the stereoisomers separately. However, because of the complexity as well as the instability of the minor isomers, we should like to discuss the equilibrium by taking the adducts **5** and **5′** together. The ratio **4b**/(**5b**+**5′b**) in **4b**$\rightleftharpoons$(**5b**+**5′b**) is 0.08. Although there were some limitations, the energetics of these equilibria was studied.

The rate-limiting step for the formation of **5b** and **5′b** is reasonably assumed to be the addition of Br^- ion because the pyrrolium ion (**4b**) is a stable species and the addition of proton to the then formed vinylamine should be fast, especially under conditions of excess of hydrogen bromide.[8,9] Another piece of evidence for the assignment of the rate-limiting step is that, while the reaction is measurably slow at low temperatures, we do not observe products due to addition of bromide ion to the pyrrolium ion. If the proton addition to the vinylamine were slow, this compound should have been observed.

The pseudo-first order rate constants of hydrogen bromide addition to pyrrolium ions (**4b**) are shown in Table 3, in which the dependence of the rate constants on the excess of HBr is also given. It will be seen that the addition of HBr to **4b** is rather a slow process at about −40 °C. There are two abnormal points in these data. One is that, contrary to the general belief that the increase in the concentration of a reactant (HBr) should increase the reaction rates, the rates are dimin-

Table 3. Dependence of Rate Constants of HBr Addition to the Pyrrolium Ion **4b** on Excess of HBr at −36 °C

Excess of HBr/mol	3.5	6.0	17
$k\times10^4/s^{-1}M^{-1}$ [a]	9.1	3.1	1.1
$k\times10^4/s^{-1}$	2.6	0.52	0.65

a) M=mol dm^{-3}.

ished when excess of hydrogen bromide is present in the system and become almost constant when the excess is large. Another is that, even in the presence of only 3.5 molar excess of HBr, the reaction obeys the pseudo-first order kinetics. We believe that these abnormalities are explained by assuming that the substrate exists as ion pairs in the solution. Thus the first-order rate constants are also given in Table 3.

For the unimolecularity of the ion-pair collapse, there are ample examples. Because the ion pairs are stabilized in polar media,[10—13] the adduct **5b** is more stabilized in the presence of a large excess of hydrogen bromide than a small excess. Thus the large excess of hydrogen bromide causes the slow collapse of the ion pairs relative to the case of a small excess. The fact that the rates of the addition in the presence of a 3.5 molar excess of HBr obey the first order rate law is in conformity with the presence of ion-pairs.

The rate constants, both pseudo-first order and the first order, of the addition of HBr to **4b** at various temperatures are given in Table 4 together with the enthalpy and entropy of activation for the first order reaction. The feature of the activation parameters is that the entropy of activation is large negative. This might also be unexpected from the experience of deprotonation from the pyrrolium ions,[3] when large positive entropy of activation is obtained. However, this type of change in entropy of activation is also described in the literature for the collapse of ion pairs.

In the collapse of ammonium ions and halide ions in the ion pairs in organic solvent, large positive entropies of activation are observed.[14,15] In contrast, the same reaction of ammonium tosylates gives large negative entropies of activation.[16] The latter entropy of activation is interpreted by the loss of freedom of motion in the transition state. Because of the presence of three equal oxygen atoms, which carry negative charge, in the tosylate, the negative ions can move in the ion pairs in the initial state. This motion is restricted in the transition state of the reaction, because one of the oxygens must be partially bound to the proton in the ammonium ion.

The same situation will take place in the ion pairs of **4b**. This time, the positive ion **4b** has positive charge delocalized over the four atoms and the bromide ion can be close to any of these atoms in the initial state. However, in the transition state of the reaction, the freedom of motion of the anion is restricted because it has to be bound to the 4-C atom. We believe this is the origin of the large negative entropy of activation.

When the temperature of the solution of **5b** was raised, the line shape change due to the minor isomer took place to make it impossible to obtain the signal intensities. Thus the temperature dependence of the equilibrium constant between the two isomers could not be studied. The amount of the pyrrolium ion (**4b**) increased at the expense of the adducts (**5b**) at high temperatures. This observation does indicate that a dynamic process takes place more easily for the minor isomer, which is in agreement with the less population of this isomer. Because the rate constants of isomerization are small for the major isomer, its population is large at equilibrium.

The ratios of the pyrrolium ion to the adducts at various temperatures are shown in Table 5. Clearly the formation of the adducts is disfavored when the temperature is high. Since the entropy should decrease when the adduct is formed and should increase when HBr is detached, favored formation of the adduct **5b** at low temperatures and that of the pyrrolium ion **4b** and HBr at high temperatures are reasonable. Equilibrium is attained too slowly to be measured at −40 °C, whereas the rates of change become observable at 5.0 °C, and are fast when the temperature is 31 °C.

In order to find the site of the dynamics, we observed saturation transfer. Although there was little response in the 5-H signal at $\delta=5.12$ of the minor isomer on irradiation of the HBr signal, irradiation of the signal at $\delta=5.12$ showed a weak response in the HBr signal. This saturation transfer is more clearly observed for the corresponding chlorine compound as described later. Thus we conclude that proton exchange takes place at H_B, although the rates are smaller than the case of the chloro compound (**5′a**). Irradiation of this proton signal did not exhibit any response to the 3-protons to show that the exchange between the 3-H and the 5-H's is also slow, if any, on the time scale of the saturation transfer.

This result apparently violates the principle of microscopic reversibility.[17,18] This will probably mean that the deprotonation at the 3-position is so slow that it is not recognized by the saturation transfer, though the step is followed in dehydrobromination from **5b**. Namely, deprotonation at the 5-position may not be the first step for **5b** to coming back to **4b**.

The results indicate that deprotonation is more facile at the vicinal site to the positive nitrogen than that to a positive carbon in this case. This may be due to the formation of an ammonium ylide that should be stable.[19] It is interesting to note that only one hydrogen at the 5-position, which is cis to the 4-H, is removed as a proton. This may be attributed to the steric effects that prevent approach of anions from the same side of the 4-halogen.

Addition of Hydrogen Chloride. Treatment of 2-methyl-1-vinylpyrrole (**3**) with hydrogen chloride at −40 °C afforded only the corresponding pyrrolium ion (**4a**). However, when temperature was increased to −20 °C, addition of hydrogen chloride became observable. Thus it is a matter of the rates of addition of HCl that led to an erroneous conclusion that HCl did not add to the pyrrolium ion. The ratio of the pyrrolium ion (**4a**) to the adduct (**5a**) was 4.3 at −6 °C and this value did not change in the temperature range of −6 to +4 °C.

It is clearly seen that the addition of HCl is less favored than the case of HBr. By the HSAB theory,[20]

Table 4. Kinetic Data for HBr Addition to the Pyrrolium Ion **4b** at 17 Molar Excess of HBr

Temperature/°C	−42	−36	−31	−21	−18
$k\times 10^4$/s^{-1}M^{-1}	0.71	1.1	1.4	2.9	3.6
$k\times 10^5$/s^{-1}	0.42	0.65	0.82	1.7	2.1
$\Delta H^{\ddagger}$/kcal mol^{-1} 7.3±1.0 [a]					
$\Delta S^{\ddagger}$/cal mol^{-1}K^{-1} −51±4					

a) 1 cal=4.184 J.

Table 5. Ratios of the Pyrrolium Ion (**4b**) to the Adducts (**5b**) in the Presence of 15 Molar Excess of HBr at Various Temperatures

Temperature/°C	−5.0	5.0	15	20	31
4b/(**5b**+**5′b**)	0.08	0.09	0.14	0.16	0.22

it may be attributed to the softness of the Br atom which favors the formation of a bond with a carbon atom rather than with a hydrogen atom. However, if one compares the differences in the bond energies between H–X and C–X, where X is chlorine or bromine, they are about the same. The favored formation of **5b** over **5a** may well be explained by the stability of the aggregates, $(H_nX_{n+1})^-$,[21] which are more stable for the chlorine case than for the bromine case.[3]

Rates of addition are difficult to measure, because the equilibrium is attained at rather a little formation of the adducts but qualitatively it is clear that hydrogen chloride addition is slower than hydrogen bromide. Slow addition of HCl to the pyrrolium ion (**4a**) should be attributed to the decrease in nucleophilicity of the chloride ion.[22] In addition, as it was discussed before,[3] chloride ions form more stable hydrogen bond with HCl than the bromine case to make the chloride ion less nucleophilic than the bromide ion in the presence of HBr.

The two species observed on addition of HCl to the pyrrolium ion are assigned to the adducts (**5a** and **5′a**) because they exhibit very similar ^{1}H NMR spectra with the corresponding bromine compounds. In addition, irradiation at δ=5.00 simplified both AB signals of both isomers. It may be reasonable to conclude from the NMR chemical shift data, which show the same trends both for the ring protons and for the methyl protons in the 1-substituent, as well as the formation ratio, which is now known that **5b** is more abundantly formed than **5′b**, that the major isomer **5a** has the same configuration at 4-C with the major isomer **5b**. This assignment is also supported by the NOE experiments which showed enhancement in the signal intensity of the 3-proton at δ=3.69 on irradiation at the 2-methyl-protons.

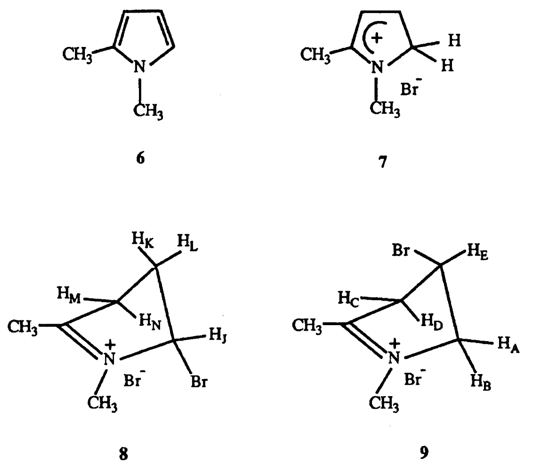
The ratio was 3 : 1 for major and minor isomers at −6 °C and this ratio did not change in the temperature range examined, probably because the range was too narrow to see the change in populations of the isomers. The equilibrium of the two adducts of the chlorine compound is much in favor of the minor with respect to the bromine compounds. The reason for this is not understood at the present time, but it may well be due to the difference in the media containing hydrogen halide and the strength of the hydrogen bond involved.

By irradiation of the HCl signal, saturation transfer to the 5-H signal at δ=4.95 was observed for the minor product, but not at the other protons. Thus this proton is exchanging with the HCl proton relatively fast on the time scale of saturation transfer. However, irradiation of the proton H_B in the minor isomer did not cause any response to the protons at the 3-position. None of the protons in the major isomer **5a** showed this kind of response. These results indicate that the proton exchange in the major isomer as well as that at the 3-position of the minor isomer are slow on the time scale of NMR.

Addition of HBr to 1,2-Dimethylpyrrole (6). Addition of HBr to **6** to form 1,2-dimethylpyrrolium ion (**7**) proceeded with reasonable rates even at −50 °C but further addition to form 4-bromo-1,2-dimethyl-4,5-dihydro-3*H*-pyrrolium ion (**9**) was very slow at −20 °C: No signals due to products were observed after 3 h at this temperature (Scheme 4). However, when the mixture of 1,2-dimethylpyrrole (**6**) and hydrogen bromide in CD_2Cl_2 was allowed to warm up to room temperature and kept at the temperature for 5 d, there formed two new species, the ratio of a main product to a minor being 4 : 1. The major product was assigned to **8** and the minor to **9** from spectroscopic evidence which is discussed below.

The minor product showed a very similar ^{1}H NMR spectrum to the already described adducts (**5** and **5′**) but the main product was different from what was expected to form. However, on standing for further 15 d, the main product (**9**) was the species, which was the expected product described above, and the originally major product (**8**) became minor, the ratio being 7 : 3.

The presence of 1,2-dimethylpyrrolium ion (**7**) was detected to about 10% extent several days after the mixing when formation of the adducts was detected but **7** became almost negligible after a month to indicate that



Scheme 4. 1,2-Dimethylpyrrole and HBr addition products.

the addition products (**8** and **9**) are relatively more stable than the cases of the adducts **5** and **5′**.

The ^{1}H NMR spectrum of the major product (**8**) after several days showed the following signals (δ) at −35 °C: $\delta=2.73$ (3H, s), 2.7 (1H, m), 3.22 (1H, m), 3.50 (2H, br t, J=ca. 8 Hz), 3.70 (3H, s), 6.33 (1H, d, $J=7.5$ Hz). The presence of the ^{1}H signal at $\delta=2.7$, which overlapped with the methyl signal, was confirmed by integration and a double resonance experiment described below.

Upon irradiation of the multiplets at $\delta=3.22$ ($\mathrm{H_K}$), the signal at $\delta=6.33$ ($\mathrm{H_J}$) became a singlet. Irradiation of the signal at $\delta=3.22$ did not give a conclusive result on the coupling with 3-H's because the chemical shifts were too close with each other. However, that at $\delta=3.50$ ($\mathrm{H_M}$ and $\mathrm{H_N}$) simplified the multiplet at $\delta=3.22$ to make the signal the A part of an ABX system, whereas it did not affect the signal at $\delta=6.33$. The difference NOE spectrum with irradiation of the doublet at $\delta=6.33$ showed positive responses at $\delta=3.70$ (1-CH_3), 3.22 ($\mathrm{H_K}$), and 2.7 ($\mathrm{H_L}$). It will be natural to assign the doublet at the lowest field to the proton that is connected to the carbon bearing the bromine atom ($\mathrm{H_J}$). It is also likely that the proton is at the α-position to the nitrogen, if one takes the chemical shift which is at a considerably low field into account. This assignment is supported by the NOE result mentioned above. Then we can draw the structure of the compound as **8**, the complete assignment of the NMR signals of protons being given in the Experimental Part. We draw the C–Br bond pseudoaxial, because the 5-H did not show observable long range coupling with the 2-methyl-protons.

It is interesting to note that only one of the protons at the 4-position shows a observable coupling with the 5-proton. This may also be interpreted that the compound takes an envelope structure, where the 4-C occupies the tip. When the temperature is raised, the spectrum of this compound showed a molecular dynamics by broadened signals at $\delta=3.22$ ($\mathrm{H_K}$) and 3.50 ($\mathrm{H_M}$ and $\mathrm{H_N}$). The signal at $\delta=6.33$ ($\mathrm{H_J}$) became a triplet at 15 °C with a coupling constant of 3.7 Hz. This might mean that either the enantiomerization is taking place or ring flipping is now fast on the time scale of NMR. The details are not known.

Compound **8** must be formed by kinetic control. It is known that 3-protonated pyrroles are formed in a small amount, when pyrroles are treated with acids.[23,24] Indeed, we observed in many cases of 2-substituted pyrrolium ions that the signal broadening took place at the 3-proton and then at the 4-proton when temperature was raised. These will mean that protonation at 3- and 4-positions takes place rather easily. Under these circumstances, bromine can add either at the 2- or 5-position. However, addition of various species to the 2-position of 2-substituted pyrroles is very slow. Thus if a product is to be formed from these species, it should be a derivative of the 4-protonated form. If, in 1,2-dimethyl-4*H*-pyrrolium ion, addition of the bromide ion to the 5-position is fast and the rates of isomerization are small, these will explain the preferential formation of **8** at the beginning of the reaction. It is likely that, because in the 4-protonated form the positive charge is delocalized only over the 5-C and the nitrogen, it is more reactive than the 5-protonated form, in which the positive charge can be delocalized over 1 through 4 positions.

The structure of **9** was determined also by ^{1}H NMR spectral data (Table 1). Two AB type signals were detected. Upon irradiation of the triplet signal at $\delta=4.90$ ($\mathrm{H_E}$), the other signals due to $\mathrm{H_AH_B}$ and $\mathrm{H_CH_D}$ changed to simple AB patterns. Only one of the protons of each AB proton systems ($\mathrm{H_B}$ and $\mathrm{H_D}$) couples with the proton at $\delta=4.90$ ($\mathrm{H_E}$). Thus the structure of **9**, including the major conformation, is similar to those of **5**, except that this compound has no diastereomers. Long range coupling between the 2-methyl-protons and the 5-proton at $\delta=5.10$ ($\mathrm{H_B}$) was also detected by irradiation at the methyl-protons.

Summary. It is found that addition of not only hydrogen bromide but also hydrogen chloride to pyrrolium cations takes place generally. The rates of addition are small when the pyrrolium ions carry only alkyl substituents but are large when there are electronegative substituent(s). The problem in observing the formation of the adducts is the slow addition especially at low temperatures, where observation is generally made. The adducts are less stable at high temperatures due to entropy terms but are more stable than the pyrrolium ion at low temperatures. It should be possible to observe the adducts for many pyrrole derivatives, if one can continue to observe for a long time after mixing them with hydrogen halide at reasonably low temperatures. Failure in observing the adducts in the case of 2-substituted 1-(1-haloalkyl)-3-isopropylpyrrolium ions, of which stereodynamics were reported,[3] should be attributed, at least partly, to the effect of the alkyl sub-

stituent.

Experimental

Materials and Samples for Measurements. 2-Methyl-1-vinylpyrrole was made in Irkutsk Institute of Organic Chemistry according to the published method.[25] 1,2-Dimethylpyrrole was prepared by lithiation of commercially available 1-methylpyrrole with butyllithium followed by methylation with methyl iodide.[26]

The pyrrolium cations were generated by introducing dry HCl or HBr gas into an NMR tube containing 0.6 mL of a 0.5 mol L^{-1} solution of the pyrrole in CD_2Cl_2, which was precooled at −78 °C, for 10—15 min. Under these conditions, hydrogen halide existed in ca. 15 molar excess. For the smaller excess of hydrogen bromide, the time of introduction of hydrogen bromide was adjusted. The NMR tube was then sealed and transferred into an NMR probe precooled at −50 °C. The ^{1}H NMR data of the pyrrolium ions (**4**) are given in Table 2.

The following ^{1}H NMR data (δ) were recorded in addition to those which are listed in Table 1 for **5** and **9**. 4-Chloro-1-(1-chloroethyl)-2-methyl-4,5-dihydro-3*H*-pyrrolium chloride (**5a**): major isomer, 2.06 (3H, d, J=6.2 Hz), 2.88 (3H, br s), 6.33 (1H, q, J=6.2 Hz); minor isomer 2.09 (3H, d, J=6.2 Hz), 2.89 (3H, br s), 6.36 (1H, q, J=6.2 Hz). 4-Bromo-1-(bromoethyl)-2-methyl-4,5-dihydro-3*H*-pyrrolium bromide (**5b**): major isomer 2.21 (3H, d, J=6.7 Hz), 2.85 (3H, br s), 6.40 (1H, q, J=6.7 Hz); minor isomer 2.25 (3H, d, J=6.7 Hz), 2.88 (3H, br s), 6.40 (1H, q, J=6.7 Hz). 4-Bromo-1,2-dimethyl-4,5-dihydro-3*H*-pyrrolium bromide (**9**): 2.72 (3H, s), 3.68 (3H, s).

1,2-Dimethylpyrrolium bromide (**7**) exhibited the following ^{1}H NMR data (δ): 2.77 (3H, s), 3.70 (3H, s), 5.12 (2H, s), 7.00 (1H, d, J=5.8 Hz), 7.90 (1H, d, J=5.8 Hz).

5-Bromo-1,2-dimethyl-4,5-dihydro-3*H*-pyrrolium bromide (**8**) gave the following ^{1}H NMR data (δ and assignment given): δ=ca. 2.7 (H_L, m), 2.73 (2-CH_3, s), 3.22 (H_K, dt, J=14.5 and 7.9 Hz), 3.50 (H_M and H_N, br t, J=ca. 8 Hz), 3.70 (1-CH_3, s), 6.33 (H_J, d, J=7.5 Hz).

NMR Measurements. The ^{1}H NMR spectra were recorded on a JEOL GSX-400 NMR spectrometer, which is installed at Analytical Center and operated at 399.8 MHz. Temperature was read by an equipped thermometer which was calibrated by a methanol sample. The decoupling experiments were carried out using the irradiation power IRATN 130. For the experiments of NOE and saturation transfer, the standard technique NOEDIF, provided with the spectrometer, was used with the following parameters: Irradiation time 5 s, irradiation power IRATN 350, pulse delay 3 s. The protons which are close in space with the irradiated signals gave positive responses, whereas those exchanging with the irradiated gave negative responses.

Kinetic Measurement. Rates of HBr addition to 1-(1-bromoethyl)-2-methylpyrrolium cation were followed by measuring the decrease in its integral intensity of the 2-methyl signal. The use of other signals gave the same results. The observed data were treated as the pseudo-first order kinetics and the obtained rate constants are converted to the first order rate constants. They are given in Tables 3 and 4.

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References

1) M. V. Sigalov, E. Yu. Shmidt, S. E. Korostova, B. A. Trofimov, *Khim. Geterotsikl. Soedin.*, **1991**, 1041; *Chem. Abstr.*, **116**, 194082 (1992).

2) M. V. Sigalov, E. Yu. Shmidt, A. B. Trofimov, and B. A. Trofimov, *J. Org. Chem.*, **57**, 3934 (1992).

3) M. V. Sigalov, S. Toyota, M. Ōki, and B. A. Trofimov, *Bull. Chem. Soc. Jpn.*, **67**, 1161 (1994).

4) M. Barfield and S. Sternhell, *J. Am. Chem. Soc.*, **94**, 1905 (1972).

5) J. Stokr, H. Pivcova, B. Schneider, and S. Dirlikov, *J. Mol. Struct.*, **12**, 45 (1972).

6) L. V. Vilkov, N. I. Sadova, and S. S. Mocalov, *Dokl. Akad. Nauk SSSR.*, **179**, 896 (1968); *Chem. Abstr.*, **69**, 76436 (1968).

7) A. Mannschreck and L. Ernst, *Tetrahedron Lett.*, **1968**, 5939.

8) W. Maas, M. J. Janssen, E. J. Stamhuis, and H. Wynberg, *J. Org. Chem.*, **32**, 1111 (1967).

9) P. Y. Sollenberger and R. B. Martin, *J. Am. Chem. Soc.*, **92**, 4261 (1970).

10) S. Toyota and M. Ōki, *Bull. Chem. Soc. Jpn.*, **63**, 1168 (1990).

11) S. Toyota and M. Ōki, *Bull. Chem. Soc. Jpn.*, **64**, 1554 (1991).

12) S. Toyota and M. Ōki, *Bull. Chem. Soc. Jpn.*, **64**, 1563 (1991).

13) M. Ōki, M. Matsusaka, H. Mishima, and S. Toyota, *Chem. Lett.*, **1993**, 1249.

14) M. Ōki, M. Ohira, Y. Yoshioka, T. Morita, H. Kihara, and N. Nakamura, *Bull. Chem. Soc. Jpn.*, **57**, 2224 (1984).

15) T. Morita and M. Ōki, *Bull. Chem. Soc. Jpn.*, **61**, 1185 (1988).

16) M. Ōki and M. Ohira, *Bull. Chem. Soc. Jpn.*, **57**, 3025 (1984).

17) L. P. Hammett, "Physical Organic Chemistry," 2nd ed, McGraw-Hill, New York (1970), pp. 142—144.

18) J. W. Moore and R. G. Pearson, "Kinetics and Mechanisms," 3rd ed, John-Wiley, New York (1981), pp. 372—378.

19) S. H. Pine, *Org. React.*, **18**, 403 (1970).

20) T. -L. Ho, *Chem. Rev.*, **75**, 1 (1975).

21) F. Y. Fujiwara and J. S. Martin, *J. Chem. Phys.*, **56**, 4091 (1972).

22) P. R. Wells, *Chem. Rev.*, **63**, 171 (1963).

23) E. B. Whipple, Y. Chiang, and R. Hinman, *J. Am. Chem. Soc.*, **85**, 26 (1963).

24) M. V. Sigalov, E. Yu. Shmidt, and B. A. Trofimov, *Khim. Geterotsikl. Soedin.*, **1988**, 334; *Chem. Abstr.*, **110**, 38401 (1989).

25) B. A. Trofimov, in "Pyrroles, Part 2," "The Synthesis, Reactivity, and Physical Properties of Substituted Pyrroles,"ed by R. A. Jones, John Wiley, New York (1992), pp. 131—298.

26) J. M. Brittain, R. A. Jones, J. S. Arques, and T. A. Saliente, *Synth. Commun.*, **12**, 231 (1982).