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Dynamic NMR Technique Can Detect the Difference in Proton Affinities of 9-[2-(Diethylamino)methyl-6-methylphenyl]fluorene Rotamers[1)]

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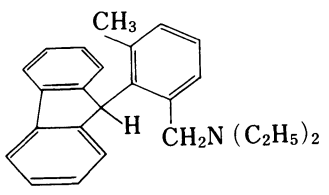
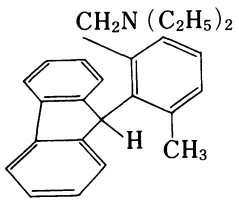
The proton exchange processes in the trifluoroacetates of the title compound were detected by the NMR method: whereas the free energy of activation for the exchange process in the ap rotamer in $CDCl_3$ was 16.4 kcal/mol at 298 K, that in THF-d_8 was 13.7 kcal/mol. In contrast, the sp rotamer exhibited the free energy of activation for the same process of 14.1 and 13.4 kcal/mol in $CDCl_3$ and THF-d_8, respectively. The presence of NH-π interactions in the ap rotamer and the absence of it in the sp are concluded to be responsible to the difference in $CDCl_3$.

During the course of investigation on the difference in basicities of rotational isomers of 9-[2-(dialkylamino)methyl-6-methylphenyl]fluorenes,[2)] we noticed that in the ^1H NMR spectra of the trifluoroacetate salts of the diethyl compound (1), the ap rotamer showed a broad doublet for the benzylic CH_2N protons at room temperature, while the sp-rotamer showed only a singlet for the corresponding protons. The facts imply that there is a rate process taking place, the most probable candidate of the phenomenon being the proton exchange between the ammonium ion and the trifluoroacetate anion. This finding allured us to further study of the phenomenon and the purpose of this paper is to present the results of the investigation and to discuss the implications therefrom.



sp-1



ap-1

Treatment of a mixture of rotameric 9-(2-bromomethyl-6-methylphenyl)fluorene with diethylamine afforded a mixture of rotamers of 1, which is rich in the sp. Chromatography followed by recrystallization afforded the pure sp-form easily. Equilibration of the trifluoroacetate salts of the compound was overwhelmingly in favor of the ap form which could be purified by recrystallization from ether. The dynamic NMR measurement was carried out with the use of a JEOL FX-90Q instrument. The solvents were either chloroform-d or tetrahydrofuran-d_8. The total line shape analysis was performed by the use of the DNMR3 program.[3] The obtained rate constants were taken as half of the real rate constants,[4] which were put into the Eyring equation together with temperatures to produce kinetic parameters. The results are shown in Table 1.

Table 1. Kinetic Parameters for the Proton Exchange Processes in Compound 1 Trifluoroacetates

Solvent	Rotamer	$\Delta H^{\ddagger}$ / kcal mol^{-1}	$\Delta S^{\ddagger}$ / cal mol^{-1} K^{-1}	$\Delta G^{\ddagger}_{298}$ / kcal mol^{-1}
$CDCl_3$	sp-1	10.7 ± 0.2	-11.4 ± 0.9	14.1
	ap-1	18.6 ± 0.8	7.3 ± 2.8	16.4
THF-d_8	sp-1	10.3 ± 0.6	-10.5 ± 2.1	13.4
	ap-1	10.2 ± 0.4	-11.9 ± 1.7	13.7

Before discussing the probable cause for the difference in kinetic parameters, it will be necessary to mention on the mechanisms of the proton exchange. There are two possible mechanisms that can explain the observed NMR phenomena, Eqs. 1 and 2.[5,6] Equation 1 is the mere exchange of proton between the ammonium ion and the trifluoroacetate anion, whereas Eq. 2 represents the role of free amine which is formed in a minute amount in the system. The second can be called the chain mechanism of the proton exchange.

$$ArCH_2NH^+Et_2 + CF_3COO^- \rightleftharpoons ArCH_2NEt_2 + CF_3COOH \quad (1)$$

$$ArCH_2NEt_2 + ArCH_2NH^+Et_2 \rightleftharpoons ArCH_2NH^+Et_2 + ArCH_2NEt_2 \quad (2)$$

The line shape of the NMR spectra at 40 °C did not change until the added amount of trifluoroacetic acid reached 0.12 equivalent to the dissolved salt of ap-1. The absence of the effect of added trifluoroacetic acid up to 0.12 equivalent definitely rules out the possibility of Eq. 2 as the mechanism of the exchange of proton, because, if it were the case, the addition should lower the rates of exchange by virtue of diminishing the concentration of the free amine. As to the effect of trifluoroacetic acid in excess of 0.12 equivalent, we should like to ascribe it to the formation of hydrogen bond between the acid and the trifluoroacetate anion, which should result in the weakening of the proton-

accepting ability of the anion. We conclude therefore that the mechanism of the proton exchange we are observing is shown by Eq. 1.

If one looks at the data in Table 1, it is apparent that the ap-1 salt in $CDCl_3$ gives a very large free energy of activation for the process relative to the sp-1 salt and even to the ap-1 salt in tetrahydrofuran. This may be attributed to the presence of the NH-π interaction in the ap form,[2] which is absent in the sp form, to the first approximation. However, since the free energy of activation contains entropy of activation which has contributions of solvent molecules involved, it will give much better insight, if we divide the free energy into enthalpy and entropy. Although the division of free energies of activation obtained by the dynamic NMR technique is controversial, it is also true that data obtained by careful total line shape analysis are reproducible when the line shape is complex.[7,8] Since the line shapes are rather simple in this case, we may have to discuss enthalpies and entropies of activation with some reservations. However, the large differences seen in Table 1 should be significant and thus deserve discussion on the enthalpies and entropies of activation described below.

The enthalpy of activation for the exchange process in the ap-1 salt in chloroform-d is larger than that of the sp-1 salt by 8 kcal/mol. This may be a little too large to attribute wholly to the NH-π hydrogen bond in the ap form, because even the strongest OH-O hydrogen bonding has the enthalpy of ca. 10 kcal/mol[9] and, if one considers the weak basicity of the π-system, the enthalpy of formation of the NH-π bond should be less than the OH-O hydrogen bond: the OH-π hydrogen bond is known to have the enthalpy of formation of 2 kcal/mol at the largest.[10] It is possible either that the experimental value of 8 kcal/mol difference contains some error and/or that the ap form is stabilized relative to the sp due to solvation effects by chloroform.[11]

In THF-d_8, on the contrary, both salts of ap-1 and sp-1 give very similar results, which are close to that of the sp-1 salt in chloroform-d. The results will strongly indicate that the solvation by THF which bears an oxygen atom is important relative to the NH-π hydrogen bond even in the ap form. Thus we conclude that the NH-π interaction in the ap form is important in only solvents which do not form the hydrogen bond with the NH group.

The entropies of activation are also interesting: it is positive for the exchange process in the ap form in chloroform-d, whereas others are all negative. The entropies of activation for proton exchange in an ammonium ion with chloride ion in ion pairs are known to be very large positive,[12] This is attributed to the increase in the freedom of motion of solvent molecules. However, in a similar proton exchange process between an ammonium ion and sulfonate anions, the entropy of activation becomes small negative or close to zero.[13] This has been attributed to the decrease in the freedom of motion of the anion: the anion bears three equivalent oxygen atoms with which it can have interactions with the cation in the ground state but in the transition state one of the oxygens must be bound to form a partial bond with the proton on the ammonium ion. If this explanation is applied to the case examined here, a small negative or near zero entropy of activation can be expected because the carboxylate anion has two equivalent oxygen atoms. We should like to suggest that the entropy of activation of ca. -10 cal

mol^{-1} K^{-1} is normal for the process of the proton exchange examined here. Then the positive entropy of activation for the exchange in the ap-1 salt in $CDCl_3$ is abnormal. This must be caused by the presence of the NH-π hydrogen bond: by the formation of the bond in the ground state, the freedom of motion in the side chain of the ap form is restricted but the freedom increases in the transition state of the proton exchange, because the NH-π hydrogen bond is partially broken.

In summary, we were able to show for the first time that the proton exchange process was detectecd by the dynamic NMR technique in an ammonium carboxylate and the rates of the exchange could be different to a large extent for respective rotamers. The rates are governed by intramolecular interactions as well as the solute-solvent interactions. The method may be applied to wide variety of amines and will contribute to the knowledge of basicity of amines in various aprotic solvents as well as the basicity of rotational isomers.

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