Effects of Li⁺ and Ag⁺ Ions on the Rotational Barrier in Acetamide and Propionamide System

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The influences of $LiNO_3$ and $AgNO_3$ on the N-C(O) rotational barrier of N,N-dimethylacetamide and N,N-dimethylpropionamide have been investigated. The rotational activation free energy (ΔG^*) for Li⁺-amide complexes is found to increase with increasing salt concentration. On the other hand, that for Ag⁺-amide complexes increases in the presence of Ag⁺ ion up to 0.25 M ion concentration and then decreases as the concentration of Ag⁺ ion is further increased. Such an unusual behavior of Ag⁺-amide complexes has been interpreted in terms of ion-pairing and diluent effect on the amides. However, ¹³C nmr chemical shift data for the amides have shown that both of these ions interact primarily with the carbonyl group in amides.

Introduction

Complexes formed between simple amides and metal cations can be studied by means of various experimental and theoretical techniques, and there have appeared a few papers concerning the rotational barrier about the N-C(O) bond in amides.[1-3] These investigations have mainly been concerned with establishing the nature of substituents and solvent effects on the rotational barrier. It has been found that amide-cation interaction is of importance for understanding the process of conformational transitions in polypeptides and denaturation of proteins.[4,5] Various amides have been employed as model compounds to study the salt effects on the peptide linkage.

More than a decade ago, Temussi and Quadrifoglio[6] have reported that the barriers of internal rotation in the silver-amide complexes were less than that for the pure amide in aqueous system. Recently, Waghorne and Rubalcava[7] obtained the same results from the silver-amide complex in propylene carbonate — N,N-dimethylacetamide system.

This peculiar effect of silver ion on the rotational barrier may be considered to suggest that the binding site of the silver ion to amides may predominantly be the nitrogen atom in the amide at high concentrations. However, according to various spectroscopic studies of the amide complexes with lithium and other metal ions,[8,9] it has been found that the binding site of these metal ions to the amide molecules is the carbonyl oxygen.

In the work presented here it is intended, first, to determine the binding site of the cation to the amide by a systematic investigation of the effect of Ag⁺ ion on the ¹³C chemical shifts of the carbonyl carbon atoms in some amides. This has proven to be a good technique for determining the binding site of the cations in amide systems.[10-13]

Secondly, the rotational barriers about the N-C(O) bond of N,N-dimethylacetamide and N,N-dimethylpropionamide in the presence of $LiNO_3$ and $AgNO_3$ have been measured as a function of electrolyte concentration. For this purpose it is necessary to remove trace of water from the samples to eliminate the possibilities of its participation in the electrolyte-amide interaction.

Finally, mechanisms for the interaction of amides with $AgNO_3$ that results in decreased rotational barrier are proposed.

Experimental

Reagents

N,N-dimethylacetamide(DMA) used in our experiment was Junsei G.R., and N,N-diethylacetamide(DEA) and N,N-dimethylpropionamide(DMP) were both T.C.I. G.R., respectively. These were purified by distillation under reduced

pressure, after refluxing with calcium hydride about 5 to 6 hours. LiNO$_3$ (Baker analyzed reagent) and AgNO$_3$ (Inuisho E.P.) were dried at 60°C under reduced pressure for 24 hours and stored over P$_2$O$_5$ in a glove box. Sampling was done in the glove box filled with dried nitrogen gas.

Instruments

^{13}C nmr spectra were recorded at 25.159 MHz on a Varian XL-100 nmr spectrometer. Samples were put in 12 mm nmr tubes with 5 mm inner tubes containing C$_6$D$_6$+TMS which provides the field locking and external chemical shift standard[14] and eliminates the sample–standard material interaction. Peak positions were referenced to the methyl carbons of TMS. Spectral widths of 5120 Hz were used and errors involved in chemical shift measurements were estimated to be of the order of 0.04 ppm.

Rotational barriers were measured on a Bruker WP-80 CW spectrometer equipped with a variable temperature accessory, and temperatures were measured accurately to ±0.1°C.

Results and Discussion

First of all, it is necessary to decide the principal binding site of cations to amide molecules. Oxygen and nitrogen atoms in amide molecules are the most likely binding sites because of their relatively high electronegativities. However, according to the simple resonace theory, oxygen atom should be the preferred site. The structure of the amide molecule may be described as a hybrid of the following two structures:[15] Each of the above two structures is known to make a significant contribution to the nature of the amide molecule. Clearly, the oxygen atom with negative charge in the structure II is expected to be the favorite site to interact with cations. In
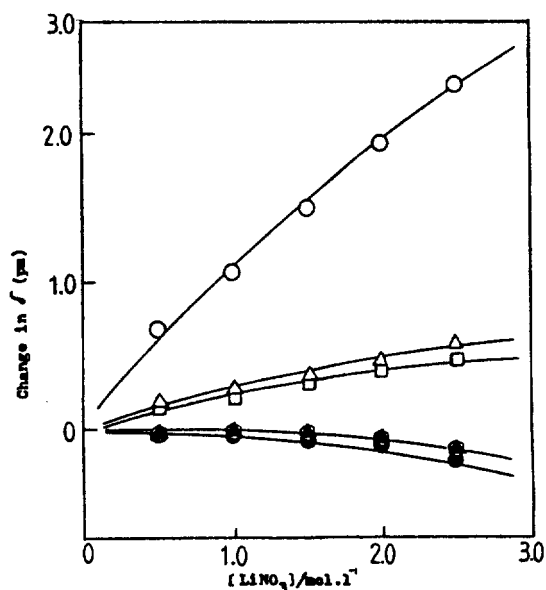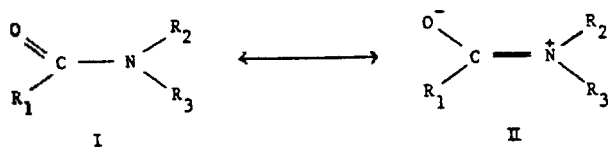
that case, the bond strength of the O-C(N) should decrease and that of the N-C(O) increase. Conversely, complexation at nitrogen site should greatly decrease the relative importance of structure II, thus reducing the N-C(O) bond order and increasing that of the O-C(N) bond, relative to the unperturbed amide molecule.

The effects of increasing concentration of LiNO$_3$ and AgNO$_3$ on the chemical shifts of carbon-13 nuclei in DEA are shown in Figure 1 and 2, respectively. Typical chemical shift data for the effect of LiNO$_3$ and AgNO$_3$ are shown in Table 1 and 2 in case of DEA. From Figure 1 we see that carbonyl carbon and CH$_2$ carbon resonances move downfield with in-

Table 1. Effect of LiNO$_3$ on ^{13}C Chemical Shifts for DEA[a]

Conc.	0.5M	1.0M	1.5M	2.0M	2.5M
C=0	0.68	1.03	1.49	1.91	2.33
anti-CH$_2$	0.13	0.21	0.31	0.38	0.46
syn-CH$_2$	0.17	0.26	0.36	0.40	0.62
acetyl-CH$_3$	-0.05	-0.06	-0.11	-0.16	-0.27
anti-CH$_3$	-0.02	-0.03	-0.03	-0.04	-0.19
syn-CH$_3$	-0.02	-0.03	-0.06	-0.10	-0.17

[a] Expressed in unit of ppm.

Table 2. Effect of AgNO$_3$ on ^{13}C Chemical Shifts for DEA[a]

Conc.	0.5M	1.0M	1.5M	2.0M	2.5M
C=0	0.57	1.24	1.92	2.36	2.96
anti-CH$_3$	0.18	0.43	0.64	0.80	1.03
syn-CH$_2$	0.17	0.40	0.62	0.77	0.98
acetyl-CH$_3$	0.16	0.38	0.50	0.62	0.78
anti-CH$_3$	0.02	0.04	0.03	0.03	0.03
syn-CH$_3$	0.02	0.07	0.08	0.09	0.13

[a] Expressed in unit of ppm.

Figure 1. Effect of LiNO$_3$ on the ^{13}C chemical shifts of DEA C=O, O; anti-CH$_2$, □; syn-CH$_2$, △; anti-CH$_3$, ▲; syn-CH$_3$, O; acetly-CH$_3$, ●.
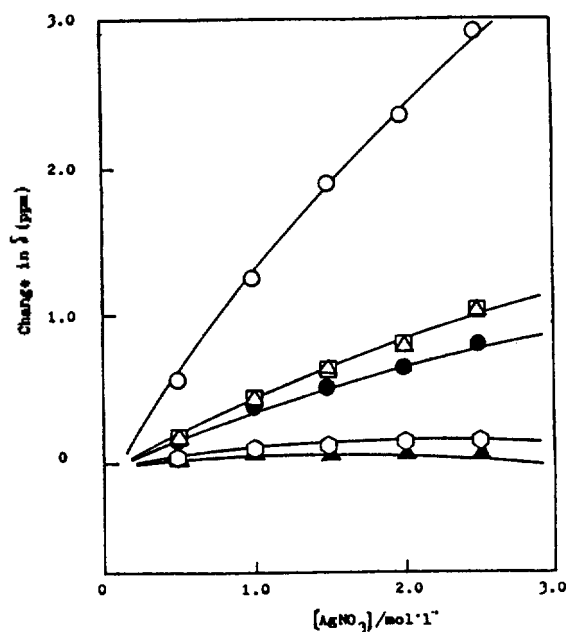
Figure 2. Effect of AgNO$_3$ on the ^{13}C chemical shifts of DEA C=O, □; anti-CH$_3$, □; syn-CH$_2$, △; anti-CH$_3$, ▲; syn-CH$_3$, O; acetyl-CH$_3$, ●.
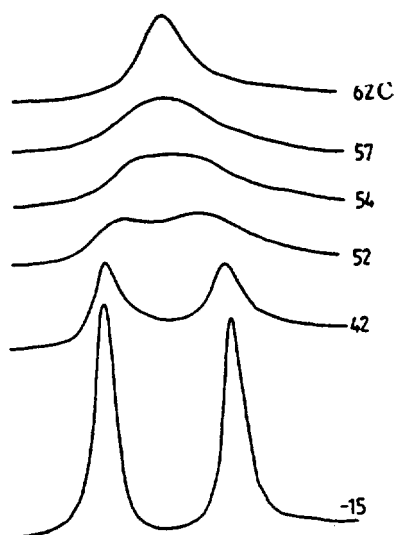
Figure 3. Temperature dependence of NMR spectra of N–methyl groups in 0.5M LiNO₃–DMP system.
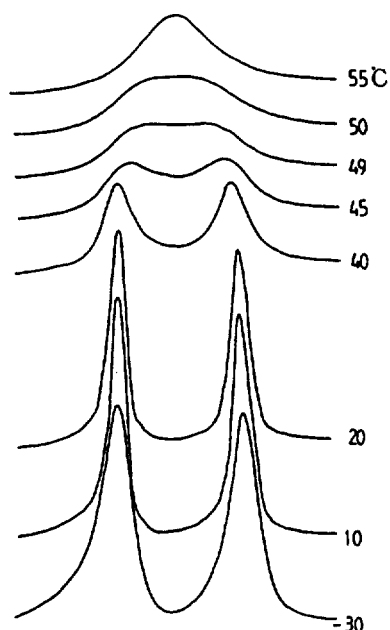
Figure 4. Temperature dependence of NMR spectra of N–methyl groups in 0.5M AgNO₃–DMP system.

Table 3. Effect of LiNO₃ on ¹³C Chemical Shifts for DEA[a]

Conc.	0.5M	1.0M	1.5M	2.0M	2.5M
C = 0	0.40	0.74	1.09	1.39	1.64
anti–CH₃	0.11	0.20	0.26	0.36	0.40
syn–CH₃	0.10	0.19	0.26	0.36	0.41
α–CH₂	0.06	0.15	0.20	0.26	0.30
β–CH₃	0.04	0.05	0.08	0.10	0.10

[a] Expressed in unit of ppm.

Table 4. Effect of AgNO₃ on ¹³C Chemical Shifts for DEA[a]

Conc.	0.5M	1.0M	1.5M	2.0M	2.5M
C = 0	0.41	0.86	1.29	1.94	2.28
anti–CH₃	0.11	0.26	0.40	0.58	0.73
syn–CH₃	0.10	0.21	0.35	0.41	0.64
α–CH₂	0.08	0.24	0.40	0.58	0.74
β–CH₃	0.05	0.11	0.21	0.35	0.41

[a] Expressed in unit of ppm.

Table 5. Effect of LiNO₃ on ¹³C Chemical Shifts for DEA[a]

Conc.	0.5M	1.0M	1.5M	2.0M	2.5M
C = 0	0.52	1.07	1.58	1.97	2.33
anti–CH₃	0.15	0.34	0.46	0.59	0.66
syn–CH₂	0.10	0.24	0.35	0.44	0.53
α–CH₂	0.07	0.16	0.28	0.34	0.37
anti–CH₃	−0.03	−0.03	−0.04	−0.10	−0.16
syn–CH₃	−0.03	−0.03	−0.06	−0.10	−0.16
β–CH₃	0.06	0.18	0.23	0.25	0.25

[a] Expressed in unit of ppm.

creasing LiNO₃ concentration. The carbonyl carbon resonances are affected to much greater extent than those of other carbons in the amide. These results confirm that a direct bonding of Li+ to the carbonyl oxygen in the amide molecule is formed. Since the carbon resonances of the amides shift toward lower field on interaction with cations, one may conclude that metal binding at the carbonyl group results in reduced electron density at the carbonyl carbon and methylene carbon with more significant change in the carbonyl carbon.

From Figure 2 we can also see that similar variations with AgNO₃ concentration are obtained for the carbon resonances in DEA. This behavior can be interpreted in terms of different solvation number of Li+ and Ag+ even though the charge density of Ag+ is less than that of Li+. These results indicate that Ag+ ion also binds to the carbonyl oxygen at high concentration.

Results obtained from the effect of LiNO₃ and AgNO₃ on the ¹³C chemical shifts of DMP and DEP are also shown in Table 3 to 6. All these results support the view that the Ag+ ion interacts directly with the carbonyl oxygen of amides.

In Figure 3 and 4 the nmr spectra of two N–methyl groups in 0.5 M LiNO₃–N,N–dimethylpropionamide and 0.5 M AgNO₃–N,N–dimethylpropionamide are shown as a function of temperature. The nmr spectra for LiNO₃–DEA and AgNO₃–DEA systems are quite similar to those for LiNO₃–DMP and AgNO₃–DMP systems. Two singlets in these spectra observed at room temperature originate from differences in the electronic environment of the proton nuclei in the two methyl groups (anti and syn) and such differences will arise from the fact that the double–bonded form (II) makes a significant contribution to the structure of amide molecules. This double bond character provides a potential barrier to reorientation about the N–C(O) bond and the rate of reorientation about the N–C(O) bond is too slow to average out the small resonance shifts between the two methyl groups. At higher temperatures the rate of reorientation increases and two signals collapse into a broad line. As temperature is lowered, the peak positions of two singlets do not change, but the linewidth of each line becomes narrower.

Barrier heights were determined by substitution of rate constant derived from the nmr coalescence method[16] (Gutowsky–Holm equation) into the Eyring equation, assuming a transmission coefficient of unity. That is,

$$\Delta G^* = 19.14 \ T_c \ (9.97 + \log \ T_c/\Delta \nu) \ J/\text{mol}$$
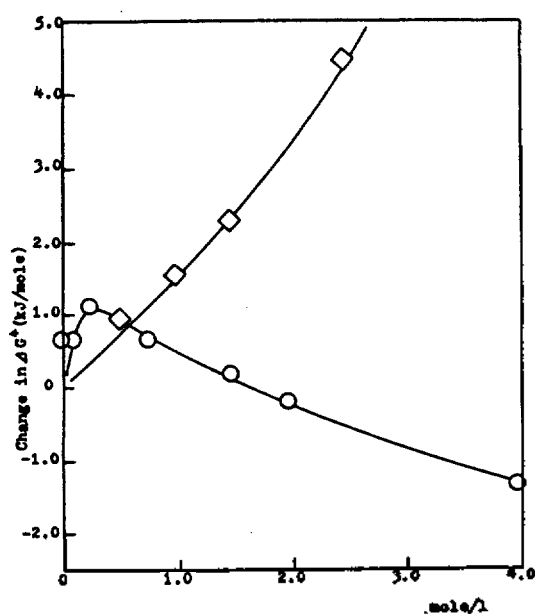
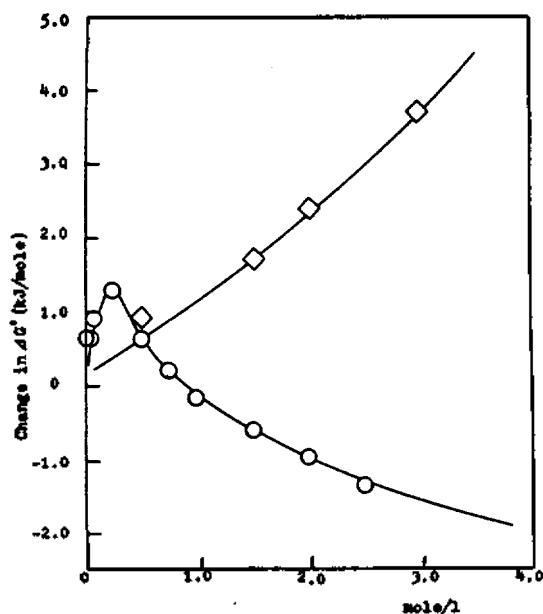**Figure 5.** Effect of salts on the rotational barrier of DMA: LiNO₃, ◇; AgNO₃, ○.

Figure 6. Effect of salts on the rotational barrier of DMP: LiNO₃, ◇; AgNO₃, ○.

where $\Delta v (Hz)$ is the difference between the resonance frequencies of two N-methyl protons in absence of exchange and T_c (°K) is the coalescence temperature.

The effects of increasing concentrations of LiNO₃ on the rotational barrier in DMA are shown in Figure 5. The results show that, as is expected, the observed barrier height (expressed as ΔG^*) to internal rotation in DMA increases as the concentration of LiNO₃ increases. On the other hand, Ag⁺ was found to increase the barrier height until its concentration reaches to 0.25 M, but, unexpectedly, the barrier height was found to decrease markedly as the Ag⁺ concentration is further increased.

Similar trend was observed in the case of DMP for which the barrier height of Li⁺-amide complexes increased with in-

Table 6. Effect of AgNO₃ on ¹³C Chemical Shifts for DEA[a]

Conc.	0.5M	1.0M	1.5M	2.0M	2.5M
C=0	0.65	1.35	1.80	2.10	2.19
anti-CH₂	0.19	0.44	0.56	0.64	0.69
syn-CH₂	0.14	0.32	0.42	0.51	0.54
α-CH₂	0.15	0.32	0.44	0.51	0.57
anti-CH₃	−0.04	−0.07	−0.10	−0.10	−0.11
syn-CH₃	−0.02	−0.03	−0.04	−0.02	−0.02
β-CH₃	0.11	0.21	0.31	0.36	0.47

[a] Expressed in unit of ppm.

Table 7. Spectral Parameters and Free Energy of Activation for Rotation about the N-C(O) Bond in DMA at Various LiNO₃ Concentrations

Concentration(M)	T_c(°C)	Δv(Hz)	ΔG^*(kJ/mol)
0	60	13.8	72.3
0.5	65	14.0	73.4
1.0	67	14.0	73.8
1.5	70	13.8	74.6
2.5	79	13.0	76.8

Table 8. Spectral Parameters and Free Energy of Activation for Rotation about the N-C(O) Bond in DMA at Various AgNO₃ Concentrations

Concentration(M)	T_c(°C)	Δv(Hz)	ΔG^*(kJ/mol)
0	60	13.8	72.3
0.01	63	14.0	72.9
0.1	63	14.0	72.9
0.25	65	14.0	73.4
0.5	64	14.0	73.2
0.75	63	14.0	72.9
1.5	61	13.8	72.5
2.0	59	13.6	72.1
4.0	54	13.6	71.0

creasing salt concentration whereas that of Ag⁺-amide complexes is increased by the presence of Ag⁺ ion up to 0.25 M concentration and decreased at higher concentration. This behavior is shown in Figure 6. These rotational barrier data for the effect of LiNO₃ and AgNO₃ are listed in Table 7 to 10 for DMA and DMP systems.

The increase of the rotational barrier in the dilute concentration region (0 to 0.25 M) was not reported in a previous study[17] in a nonaqueous solvent system in which the most dilute concentration was a mole ratio of amide : Ag⁺ = 2 : 1.

Previously it has been proposed that the decrease in ΔG^* for amides complexed to Ag⁺ ions arises from binding of metal cations to the nitrogen atom[18] or possibly a covalent interaction between the metal d-electrons and the amide carbonyl antibonding orbitals (back-bonding).[19] However, we think that such proposal is hardly acceptable because the results from ¹³C chemical shifts studies in the previous discussions confirmed that the binding site of Ag⁺ ion was the carbonyl oxygen atom in amides. Hence it may be argued that at very low concentration of AgNO₃, Ag⁺ ion breaks the inter-

Table 9. Spectral Parameters and Free Energy of Activation for Rotation about the N–C(O) Bond in DMP at Various LiNO₃ Concentrations

Concentration(M)	T_c(°C)	Δv(Hz)	ΔG^*(kJ/mol)
0	47	11.6	69.8
0.5	52	12.2	70.8
1.5	55	12.2	71.5
2.0	58	12.2	72.2
3.0	63	11.4	73.5

Table 10. Spectral Parameters and Free Energy of Activation for Rotation about the N–C(O) Bond in DMP at Various AgNO₃ Concentrations

Concentration(M)	T_c(°C)	Δv(Hz)	ΔG^*(kJ/mol)
0	47	11.6	69.8
0.01	50	11.8	70.5
0.05	50	11.8	70.5
0.1	51	11.8	70.7
0.25	53	12.0	71.1
0.5	50	11.8	70.5
0.75	48	11.6	70.1
1.0	46	11.4	69.7
1.5	44	11.2	69.3
2.0	42	11.0	68.8
2.5	40	10.8	68.4

molecular association of amides and interacts with the carbonyl oxygen at the same time. At very low concentration of Ag⁺, the latter effect is predominant and increases the rotational barrier of the N–C(O) bond up to 0.25 M concentration. However, the contact ion-pair of Ag⁺–NO₃ forms even at moderate concentrations of AgNO₃ in DMA and DMP which have low dielectric constants. Thus formed ion-pairs will behave as a diluent to break the association of amide molecules causing the observed decrease of the rotational barrier. Such arguments can be supported by some experimental and thermodynamic data.

The rotational barrier height about the N–C(O) bond in DMA was found to decrease markedly as the amount of CCl₄ added to DMA is gradually increased.[20] The result has been interpreted that CCl₄ breaks the self-association of amide molecules, thus acting as a diluent.

According to the conductance data[21] the association constant of AgNO₃ in DMF is about 400. It means that Ag⁺ ion can easily form a contact ion-pair with its counterpart NO₃ ion in the amides with low dielectric constant. Therefore, it is conceivable that Ag⁺–NO₃ ion-pair can behave as a diluent like carbon tetrachloride and thus the rotational barrier can be lowered by this ion-pair even at the moderate concentrations of AgNO₃.

On the other hand, association constant of LiNO₃ in DMF is around 30.[21] In the studied concentration range we have concluded that Li⁺ ion predominantly binds to the carbonyl oxygen of the amide molecule. However, B. M. Rode, et al.[18] have observed that at the concentration of 1:8 of Li⁺: DMF, the activation energy, ΔE^* of N–C(O) rotational barrier of DMF was less than that of pure DMF. Thus it may be thought that

in the case of LiNO₃–DMF system Li⁺–NO₃ ion-pair is formed only at moderately high concentration and again behave as a diluent.

The magnitude of ΔG^* for N–C(O) rotational barrier of DMF is smaller than those of DMA and DMP. We think that it is due to the increased basicity of the carbonyl oxygen in the amide molecule caused by alkyl substitution. The result is in good agreement with the prediction from theoretical calculations.[22,23]

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