Preferential Association of 7-Azaindole Dimer in Acetonitrile Studied by Mass Spectrometry

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The preferential association of 7-azaindole (Az) dimer was observed by the mass spectrometric analysis of clusters isolated from liquid droplets containing Az and acetonitrile. In the mass spectrum, the peaks corresponding to the even-numbered Az clusters, $(Az)_{2, 4, 6, 8 \cdots}$, were observed much more prominently than those neighboring odd-numbered Az clusters, $(Az)_{3, 5, 7, 9 \cdots}$.

Molecular self-assembling is one of the most attractive research subjects in correlation with self-organization in biological systems and a new strategy in chemical synthesis. In biological systems, the balance of various non-covalent interactions, such as hydrogen-bonding, hydrophobic, electrostatic interactions etc., controls molecular self-assembling processes efficiently.

In order to understand how such non-covalent interactions control molecular self-assembling, molecular clusters composed of acid and base molecules were studied by mass spectrometry.[1] In the acid-base systems, e.g., phenol-pyridine, phenol-aniline, and phenol-pyrazine, a hydrogen bond is formed between the acid and the base molecule, and a dipole moment is induced along the hydrogen bond by the acid-base interaction. When a large dipole moment is induced, that is, in case of relatively strong acid-base pairs, multilayer stacking structures were found to be formed by the dipole-dipole interactions.

Here we report on the observation of a very unique clustering of 7-azaindole(Az) in comparison with the acid-base clustering investigated previously. Az forms a stable dimer through double hydrogen bonding as shown in Figure 1, and the association of Az dimers was found to be much more favorable than that of Az monomers through the mass spectrometric analysis of the clusters.

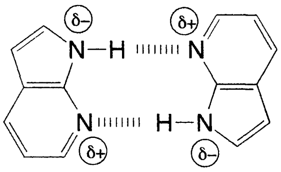

Figure 1. Schematic picture of 7-azaindole dimer.

The experimental setup has already been described elsewhere;[1-3] therefore, only a brief outline of the method is given here. The mass spectrometer was composed of a four-stage differentially pumped vacuum system, a quadrupole mass filter, and a liquid injector nozzle. A sample solution was injected into the vacuum chamber through the heated nozzle with a flow rate of 0.08 ml/min, and liquid droplets were generated. The liquid droplets were exploded by the vacuum adiabatic expansion. At the explosion of droplets, strongly interacting molecules remain as clusters, but weakly interacting molecules are vaporized as monomeric molecules. The resulting monomers and clusters were ionized and analyzed by the mass spectrometer.

Figure 2 shows typical mass spectra of clusters generated from the solution containing Az and acetonitrile (molar ratio of Az : acetonitrile = 1 : 80) at the nozzle temperatures 190 °C (Figure 2-a) and 170°C (Figure 2-b). In Figure 2-a, it is clearly shown that the distribution of Az clusters with an even number of Az molecules is much more prominent than those with odd numbers. Clusters with Az_n : n = 2, 4, 6, 8, 10, and 12 are found to be more stable than their neighboring odd-numbered clusters. With decreasing the nozzle temperature, as shown in Figure 2-b, larger Az clusters with an even number of Az molecules become difficult to form, that is, disintegrate into smaller clusters through solvation by acetonitrile. The clusters composed of Az and acetonitrile molecules, $(Az)_m(CH_3CN)_n$, are remarkably increased instead. Even-numbered Az clusters without CH_3CN are still observed as prominent species; however, for $(Az)_m(CH_3CN)_n$ clusters, the odd-even rule is not conserved. For example, the insert in Figure 2-b shows that the signal intensities for the series of clusters including three Az molecules [the peaks 3-6, 3-7, etc. (m-n represents $(Az)_m(CH_3CN)_n$)] are found to be stronger than those including four Az molecules (the peaks 4-6, 4-7, etc.). The clusters including an odd number of Az molecules are probable the only ones solvated by acetonitrile. When the solvating acetonitrile is vaporized at higher temperatures, the even-numbered Az clusters increase remarkably. This indicates that even in the solvated species, the Az dimer is stabilized as to behave like an unimolecule, and it easy to associates to form even-numbered clusters. In other words, the solvated Az clusters include not only the Az dimer but also the Az monomer; however, at higher temperatures, the preferential association of the Az dimer is promoted to form the even-numbered Az cluster. This is confirmed by the effect of methanol on this clustering as described below.

After addition of methanol to the acetonitrile solution, the mass peaks of Az clusters become smaller. In pure methanol, Az does not exist as a dimer or in higher aggregated forms. This indicates that the self-association of Az is diminished by hydrogen bonding interaction of Az with methanol, and Az exists as monomeric form solvated by methanol. Since N-H and N of Az will be blocked by the hydrogen bond with a methanol molecule, an Az dimer would be difficult to form. It is interesting that the Az clustering is strongly dependent on the used solvents: acetonitrile and methanol. When the Az dimer is formed in acetonitrile, a kind of quadrupole may be induced as shown in Figure 1. A quadrupole-quadrupole interaction can promote the association of Az dimers to afford the even-numbered Az clusters. Therefore, the association of Az dimers

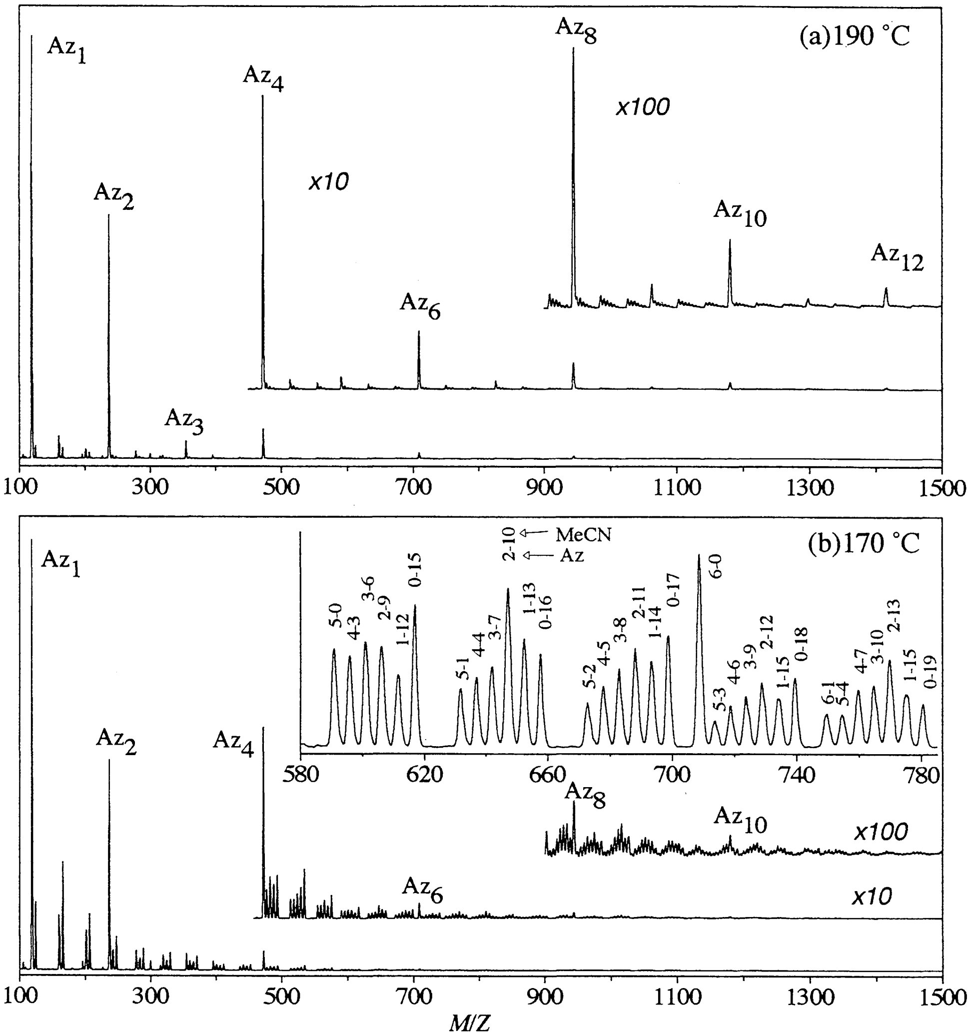

Figure 2. Mass spectra of clusters generated from a 7-azaindole in acetonitrile solution at nozzle temperature of 170 (a) and 190 °C (b). Insert in (b) represents expanded spectrum from M/Z=580 to 786, and paired numbers represent m-n for $(Az)_m(CH_3CN)_n$ clusters.[4]

is more favorable than that of Az monomers. On the other hand, in methanol, each Az molecule is solvated to be isolated, which restrains to have Az-Az interaction even at the vaporization of the methanol. In order to know the influence of Az-Az dimer formation on the clustering, we investigated also the clustering of indole in acetonitrile. It has only a N-H group and is not capable of double hydrogen bonding in its dimer. Indole clusters were observed by mass spectrometry. The intensity of the clusters decreases monotonically with the increase of the number of association and even-numbered clusters do not become preferable. The present novel findings, that is, the even-number association of Az in acetonitrile prevails over the odd numbered association, indicate that Az dimers stabilized by the double hydrogen bonding associate spontaneously further to give larger even-numbered Az clusters.

References and Notes

1 A.Wakisaka, Yoshikatsu Akiyama, Yoshitaka Yamamoto, Theo Engst, Harutoshi Takeo, Fujio Mizukami, Kengo Sakaguchi and Harold Jones, *J. Chem. Soc. Faraday Trans.*, **92,** 3539 (1996).
2 A. Wakisaka, S. Takahashi, and N. Nishi, *J. Chem. Soc., Faraday Trans.*, **91,** 4063 (1995).
3 N. Nishi and K. Yamamoto, *J. Am. Chem. Soc.*, **109,** 7353 (1987).
4 The clustering is very much sensitive to the temperature and concentration. At the nozzle temperatures between 170 and 190 °C, the acetonitrile in the liquid droplets is completely vaporized. At much higher temperatures, the resulting Az larger clusters were broken due to the excess thermal energy; on the other hand, at much lower temperatures, clustering of acetonitriles become more predominant.