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Effects of Solvent Molecular Size on Dissociation Rates of the N–H Bond in Ammonium Salts Derived from Tertiary Amines

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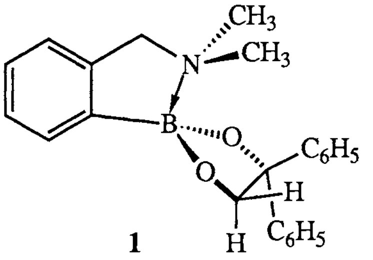
Rates of dissociation of the N–H bond in ammonium salts derived from tertiary amines were found to be enhanced in solvents of which molecular size is large with respect to those in solvents of small molecular size, if polarities of the solvents are about the same. The effects are attributed to the weak solvation by the solvents of large molecular size which is associated with small positive entropy of activation. Thus the third aspect of solvent effects, bulkiness of solvent molecules, is proposed.

Rates of dissociation of the B–N bond in an intramolecular boron-amine complex (**1**) have been reported from our laboratory.[1] The rates are enhanced, generally speaking, in nonpolar solvents and are reduced in polar solvents with some exceptions for solvents of which molecules carry an atom with lone pairs of electrons. The general tendency is ascribed to the better stabilization of the original state of the solute by polar solvents than the less polar solvents, because the compound is partially ionic. The exceptions were attributed to the S_N2-type assistance for the dissociation by the atom that carries lone pairs of electrons.



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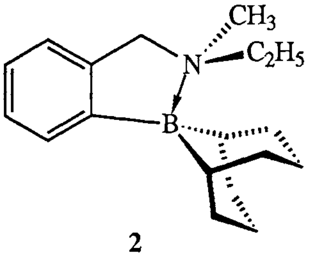

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In order to examine the assumption, we have determined the rates of dissociation of the same type of boron compounds that prevent S_N2-type participation of the solvent molecules. Namely a 9-borabicyclo[3.3.1]nonane derivative (**2**), in which the boron occupies the steric situation similar to the central carbon in a *tert*-butyl group, has been submitted to the rate study.[2] As expected, this compound shows the general tendency of the rates of dissociation in various solvents, as can be summarized that the dissociation is slower in polar solvents than in the nonpolar.

We thought that the S_N2-type assistance of solvent molecules could be also blocked by using a solvent of which molecules are bulky. Thus the rates of dissociation of the B–N bond in compound **1** were examined in *tert*-butyl methyl ether and *tert*-butyl methyl ketone. Although the detailed line-shape analysis was not possible for the system because of masking by solvent signals, the coalescence points of the probe signals gave, to our surprise, rather low barrier to dissociation of the B–N bond in compound **1**, as are shown in Table 1. Here, the

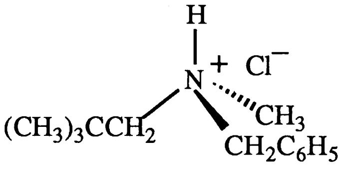
Table 1. Rates of Dissociation of the B–N Bond in Compound **1** in Various Solvents as Measured by Dynamic NMR Method

Solvent	$\Delta H^\ddagger$/kcal mol^{-1}	$\Delta S^\ddagger$/cal mol^{-1} K^{-1}	$\Delta G^\ddagger$/kcal mol^{-1}	k/s^{-1}	$E_T(30)$
$CDCl_3$	15.2±0.4	16.1±1.9	11.7 (219 K)	9.8 (219 K)	39.0
$(CH_3)_3CCOCH_3$			10.9 (219 K)	67.4 (219 K)	39.0
$C_4D_{10}O$[a]	14.1±0.3	13.4±1.3	11.3 (208 K)	5.9 (208 K)	34.5
$(CH_3)_3COCH_3$			10.3 (208 K)	65.5 (208 K)	35.5

a) diethyl-d_{10} ether.

polarity of the solvents is compared with use of $E_T(30)$ values.3) It is clear that, if we compare the rates obtained for solutions of **1** in solvents with similar polarities, the rates are enhanced in solvents of which molecules are bulky.

In order to see the generality of the phenomenon, we decided to measure the rates of dissociation of various compounds in solvents of various molecular size. We selected, as the most fundamental models, ammonium salts derived from tertiary amines. Although we had had some experience of measuring the rates of dissociation in tertiary amine hydrochlorides,4,5) these amine hydrochlorides were not soluble enough in solvents of bulky molecules and thus more soluble ammonium salts had to be sought.



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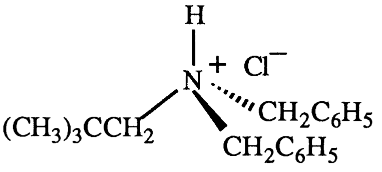

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Since it is known that introduction of a *tert*-butyl group to a molecule increases the solubility of the parent compound in nonpolar solvents, a neopentyl group was introduced to increase the solubility of ammonium salts. Indeed, benzylmethylneopentylammonium chloride (**3**) and dibenzylneopentylammonium chloride (**4**) were soluble enough in trimethylacetonitrile and in 2-methyl-2-nitropropane for the measurements, but they were not soluble enough in other solvents of bulky molecules. The benzyl-methylene protons were used as probes and the measurement was carried out by irradiating the ammonium proton for simplifying the analysis. This method is known to yield reliable data for the N–H bond dissociation.6) The obtained line shapes were simulated with use of DNMR3K program7) and the kinetic parameters thus obtained are summarized in Table 2.

From the data in Table 2, dissociation rates in compound **4** are much larger than those in compound **3**. This is reasonable because of the inductive effect of the phenyl group; the basicity of compound **4** must be lower than compound **3**. For this reason together with solubility problems, it was difficult to use the same reference solvent for the two compounds. Thus 1,1,2,2-tetrachloroethane-d_2 and acetone-d_6 were used as reference solvents for compounds **3** and **4**, respectively.

Table 2. Rates of Dissociation of the N–H Bond in Compounds **3** and **4** in Various Solvents as Measured by Dynamic NMR Method

Solvent	$\Delta H^\ddagger$/kcal mol^{-1}	$\Delta S^\ddagger$/cal mol^{-1} K^{-1}	$\Delta G^\ddagger$/kcal mol^{-1} a)	k/s^{-1} a)	$E_\mathrm{T}(30)$
		Compound **3**			
CD_3CN	36.5±0.1	50.7±0.4	18.7	14.9	45.6
$(CH_3)_3CCN$	31.4±0.1	44.9±0.3	15.7	1210	41.3
CD_3NO_2	36.3±0.4	48.1±1.1	19.5	5.1	46.3
$(CH_3)_3CNO_2$	31.9±0.2	44.1±0.4	16.7	370	41.6
$(CDCl_2)_2$	36.5±0.2	48.8±0.5	19.4	5.7	39.4
		Compound **4**			
CD_3CN	26.4±0.1	28.2±0.4	17.1	33.1	45.6
$(CH_3)_3CCN$	22.0±0.1	21.7±0.3	14.8	1080	41.3
CD_3NO_2	26.5±0.1	28.2±0.3	17.2	27.5	46.3
$(CH_3)_3CNO_2$	22.0±0.1	21.4±0.4	14.9	889	41.6
$(CD_3)_2CO$	24.9±0.1	24.9±0.4	16.6	67.9	42.2

a) Free energies of activation and rate constants are at 350 K and 330 K for compounds **3** and **4**, respectively.

Comparing the results of compound **3**, obtained for the tetrachloroethane-d_2 solvent, with those obtained for trimethylacetonitrile and for 2-methyl-2-nitropropane solutions, one notices that the rates of dissociation for the tetrachloroethane solution were much smaller than those in the trimethylacetonitrile and 2-methyl-2-nitropropane solutions, irrespective of the fact that the polarity of the solvent is higher for the latter two compounds than that of tetrachloroethane. This tendency is contradictory to the general belief that the dissociation of ionic compounds to covalent species is slow in polar solvents due to stabilization of the original system by solvation. By contrast, comparison of the rates in acetonitrile with those in trimethylacetonitrile and the same for nitromethane and 2-methyl-2-nitropropane reveals that the tendency is as expected from the polarity of solvents. The difference in rates of dissociation in acetonitrile-d_3 and nitromethane-d_3 may be attributed to a microscopic difference in the solvation state and indicates that comparisons are safer, if possible, when they are made in a same series of functional groups.

Compound **4** showed similar tendency. Dissociation in acetone-d_6 is much slower than those in trimethylacetonitrile and in 2-methyl-2-nitropropane, irrespective of a small difference in polarity of the solvent as judged by E_T values. It is especially noteworthy that the difference in polarities between acetonitrile and acetone or nitromethane and acetone causes a little difference in the rates of dissociation irrespective of a rather large difference in polarities, whereas the difference becomes very large, if the molecular size becomes large.

The rates of dissociation of compound **3** in trimethylacetonitrile or 2-methyl-2-nitropropane are ca. 70—80 times larger than those in acetonitrile or nitromethane. The difference is less, ca. 30 times, for compound **4**. These data clearly indicate that there is a factor which affects the rates of dissociation of the N–H bonds in the amine salts but had not been considered in the past. We postulate that the factor is the bulkiness of the solvent molecules: This means that when we discuss the solvent effect, bulkiness effect of solvent molecules must be considered in addition to the two factors, polar and protic.

The solvent bulkiness effect is caused by the effectiveness of solvation by solvent molecules. If a solvent molecule is bulky, the solvation should be completed by a less number of solvent molecules and be of less stabilization because of steric effects on solvation than the case of small solvent molecules. Thus stabilization due to solvation by bulky molecules provides less lowering the energy of the original system. This discussion necessarily leads to an expectation that the entropy of activation should be less positive in the case of bulky molecules than that of small molecules, although generally the entropy of activation must be positive for the N-H bond breaking in the ammonium salts, because the freedom of solvent molecules should increase in the transition state due to the change from an ionic original state to covalent-like transition state. And indeed, we observe that the entropy of activation is less positive in solvents like trimethylacetonitrile and 2-methyl-2-nitropropane.

The bulkiness effect of the solvent molecules seems to be affected by the size of solute: The effect is larger for the small molecules as is evidenced by comparison of the data of compounds **3** and **4** and the lesser effect observed for compound **1** is in conformity with the generalization. Irrespective of these variations, the present results do show that the third aspect of solvent effects, bulkiness effect of the solvent molecules, must be taken into account when one discusses the solvent effects in general. If a covalent substrate ionizes in solvents, we expect that the entropy of activation must be less negative when the solvent molecules are bulky than that in solvents of small molecules, though it must be always negative in any solvent.9,10)

In the literature, there are not many but a small number of papers which mention that the effect of solvent molecular size is important in reactions or in equilibrium.11—16) However, because the effects of polarity and those of the bulkiness are not generally separated, we may have to reexamine the data on these view points before coming to a solid conclusion on the reported solvent effects.

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