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Effects of Solvent Molecular Size on Rates of Topomerization in Organolithium Compounds

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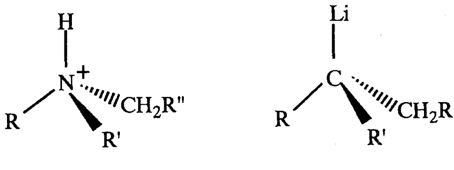
Rates of topomerization of substituted 9-fluorenyllithiums and α-(benzylthio)benzyllithium were determined in various ether-type solvents by the dynamic NMR technique. The rates are small in solvents of bulky molecules in comparison with those of less-bulky molecules. UV-vis spectra of these compounds in the solvents indicate that the compounds tend to exist as solvent-separated ion pairs in solvents of small molecular size, whereas they exist as contact ion pairs in solvents of bulky molecules. ^{1}H NMR spectra did not show signals attributable to two species at the lowest temperature of study. From these results, it is concluded that the observed process is the tumbling of the anion in solvent-separated ion pairs with a rapid pre-equilibrium between contact ion pairs and solvent-separated ion pairs, further intervention of solvent molecule(s) into the observed solvent-separated ion pairs being the rate-limiting step. A term, dimensiosolvatic effect, is proposed for the effects where the solvent molecular size plays important roles in determining rates of reaction or equilibria.

Solvent effects are discussed from various aspects.[1] Of the factors by which solvents affect various phenomena, polarity of the solvent is the most important and has been dealt with since the 1930's.[2] The protic/aprotic nature of the solvent molecules has been recognized as important since the commencement of the use of polar aprotic solvents such as *N,N*-dimethylformamide and dimethyl sulfoxide.[3] However, these aspects have not led to complete understanding of the solvent effects.

There are scattered papers in the literature which imply that molecular size has significance in reaction rates[4] and in equilibria.[5] We have found that the molecular sizes of solvents lead to quite different results in the rates of dissociation of ammonium salts **1** derived from tertiary amines and we published a preliminary paper.[6] The phenomenon is that an ammonium salt in a solvent of bulky molecules dissociates faster than in a solvent of small molecules and the feature of the kinetic parameters is that entropy of activation obtained for a solvent of bulky molecules is a small positive one compared with that for solvents of small molecular sizes, which give rise to a large positive entropy of activation. We have attributed the effects to less effective solvation due to bulky molecules relative to that due to small molecules at the initial state.

We thought it would be worthwhile to examine whether this effect is applicable to other phenomena. As a possible candidate, we chose organolithium compounds **2** because the compounds can be considered as an analog of the ammonium salt, where a lithium cation coordinates with a carbanion (Scheme 1). Since 9-fluorenyllithiums are the most studied series of compounds among organolithiums, a derivative of 9-fluorenyllithium is a natural choice for the starter of this type of investigation. Since the dynamic NMR technique requires a probe for measuring the rates of topomerization, we introduced a methylthiomethyl group, of which methylene protons act as the probe: The chosen substrates are 1-(methylthiomethyl)-9-lithiofluorene (**3a**) and its 9-methyl derivative (**3b**). For further extension, the dynamic behavior of α-(benzylthio)benzyllithium (**4**), of which topomerization in THF was recently reported,[7] in various solvents will be discussed in this paper (Scheme 2).

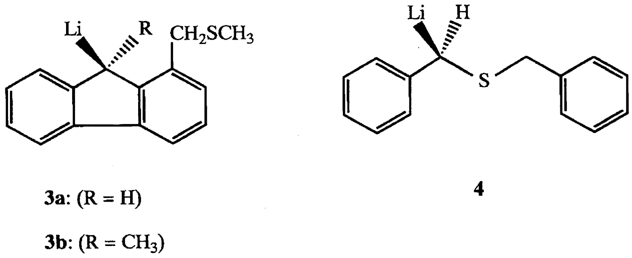


1 **2**

Scheme 1.

Results

Syntheses of Compounds. Synthesis of 1-(methylthiomethyl)fluorene (**5**) was carried out by rearrangement of 9-fluorenyldimethylsulfonium ion, which was caused by base-treatment,[8] and this compound was lithiated in appropriate



3a: (R = H)

3b: (R = CH$_3$)

4

Scheme 2.

solvents with butyllithium to form the lithiated compound **3a** which was directly used for the measurement. The same lithiated compound was treated with methyl iodide to produce 9-methyl-1-(methylthiomethyl)fluorene (**6**) which was lithiated similarly to produce **3b** for submitting to the kinetic measurements (Scheme 3).

A solution of commercially available dibenzyl sulfide in appropriate solvents was treated with *t*-butyllithium and the lithiated compound **4** was submitted for the measurements.

UV-vis Absorption Spectra. These compounds are unstable at room temperature and satisfactory spectra were obtained only below −10 °C. The results for compounds **3** and **4** in various solvents at 180 K are given in Table 1, in which absorptions at relatively long wavelengths only are listed. Clearly absorptions at the region are affected by the solvents used and those at the long wavelengths are recorded for THF and DME solutions, whereas those are missing for diethyl ether and *t*-butyl methyl ether solutions.

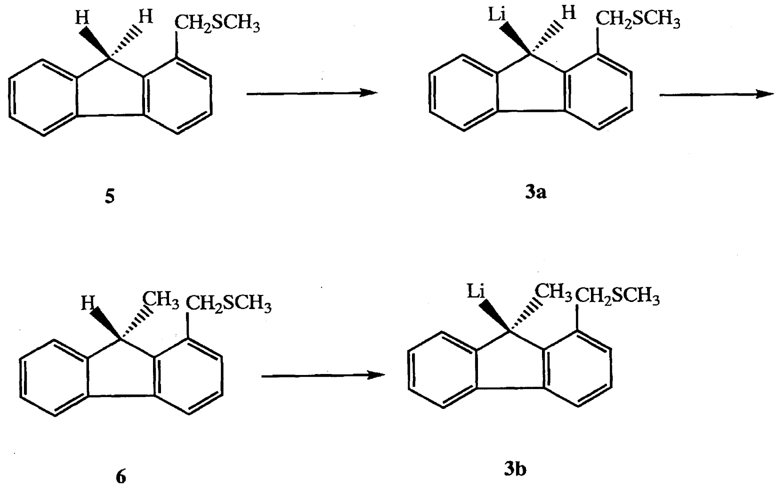
Dynamic NMR Measurements and the Kinetic Data. The ^{1}H NMR spectra of these compounds were recorded at various temperatures with use of the methylene protons of the methylthiomethyl group for compounds **3a** and **3b** and those in the benzyl group for compound **4** as probes. The lineshape analyses of the spectra were performed with the DNMR3K program.[11] The rates of topomerization thus obtained were put into the Eyring equation to produce kinetic parameters. The results are listed in Table 2.

Discussion

Solvents. In this work, we use ethers as solvents. Their polar nature may be an important factor. Therefore, we use Dimroth's $E_T(30)$ values in consideration when appropriate.[1] These values are given in Table 2. For the bulkiness of solvent molecules, we use THF as a solvent of small molecules, *t*-butyl methyl ether as a solvent of bulky molecules, and diethyl ether as an intermediate. The reasons follow.

THF is generally considered to be a solvent of less bulky molecules than diethyl ether. This is because diethyl ether little takes *sc*–*sc* conformation but largely *ap*–*ap* conformation about the C–O bonds due to the steric effects.[13] This stable conformation hinders the solvation sites, lone-pairs on the oxygen atom, to make solvation to cationic species less effective.

t-Butyl methyl ether, having extra methyl groups as com-



Scheme 3.

Table 1. UV-vis Adsorption Spectra of Compounds **3** and **4** at 180 K

Compound	Solvent	Absorption maxima (λ_{max}/nm with log ε in parentheses)
3a	*t*-BuOMe	409.2 (2.94), 431.6 (3.09), 456.8 (3.03)
	Et_2O	409.6 (2.75), 433.4 (2.91), 458.0 (2.87)
	THF	428.2 (3.20), 455.4 (3.21), 487.2 (3.26), 522.2 (3.14)
	DME	426.0 (3.39), 454.4 (3.41), 484.8 (3.50), 520.4 (3.40)
3b	*t*-BuOMe	437.6 (3.17), 465.0 (3.15), 496.8 (2.99)
	Et_2O	437.8 (3.24), 463.4 (3.28), 490.8 (3.15)
	THF	456.4 (2.98), 485.2 (3.18), 519.4 (3.32), 559.8 (3.21)
	DME	449.8 (3.37), 482.6 (3.42), 517.4 (3.54), 557.4 (3.42)
4	*t*-BuOMe	290.8 (2.97), 415.4 (3.31)
	Et_2O	311.8 (3.03), 409.8 (3.02)
	THF	320.8 (3.42), 361.4 (3.48), 458.8 (3.43)
	DME	316.6 (3.25), 369.8 (3.22), 459.2 (3.58)

Table 2. Kinetic Parameters for Topomerization of Compounds **3** and **4**

Compound	Solvent	k_{203}/s^{-1}	$\Delta G^{\ddagger}_{203}/\mathrm{kcal\,mol}^{-1}$	$\Delta H^{\ddagger}/\mathrm{kcal\,mol}^{-1}$	$\Delta S^{\ddagger}/\mathrm{cal\,mol}^{-1}\,\mathrm{K}^{-1}$	$r^{\mathrm{a)}}$	$E_T(30)/\mathrm{kcal\,mol}^{-1\,\mathrm{b)}}$
3a	THF-$d_8$$^{\mathrm{c)}}$	>670	<6.8	—	—	—	37.4
	Et_2O-d_{10}	396	9.3	7.7±0.2	−7.8±0.8	0.9997	34.5
	t-BuOMe	25.3	10.4	7.5±0.3	−14.4±1.5	0.9991	36.0
3b	THF-$d_8$$^{\mathrm{d)}}$	>1100	<6.7	—	—	—	37.4
	Et_2O-d_{10}	8300	8.1	4.7±0.1	−16.7±0.6	0.9995	34.5
	t-BuOMe	57.1	10.1	8.6±0.2	−7.4±1.1	0.9996	36.0
4	THF-d_8	725	9.5	9.1±0.2	−2.0±0.9	0.9996	37.4
	Et_2O-d_{10}	231	10.0	8.9±0.3	−5.2±1.3	0.9992	34.5
	t-$BuOCD_3$	199	10.1	6.6±0.3	−16.3±1.2	0.9992	36.0

a) Correlation coefficient in the statistical treatment. b) Taken from Ref. 1. c) *k*'s and $\Delta G^{\ddagger}$'s at 154 K. d) *k*'s and $\Delta G^{\ddagger}$'s at 213 K.

pared with an ethyl group in diethyl ether, can be classified into a solvent of bulkier molecules than diethyl ether. Although the methyl group on the other side of the ether is smaller than an ethyl group, the steric effects given by the *t*-butyl group should be large enough for *t*-butyl methyl ether to be bulkier than diethyl ether, because the lone pairs on the oxygen atom are sterically protected by the *t*-butyl group.

In this article, we also discuss the bulkiness of molecules when they intervene into the ion pairs. In this case, the bulkiness of the whole molecule should be taken into account. The bulkiness of a *t*-butyl group should play the major role in controlling the intervention of a molecule into ion pairs. Thus the order of the bulkiness of the ethers used in this work should be again: *t*-butyl methyl ether > diethyl ether > THF.

Species Present as Initial State. Since alkyllithiums are known to make various aggregates and to take structures of a wide variety from covalent to fully ionized form as well as to exist as contact ion pairs (CIP) and solvent-separated ion pairs (SSIP) in solution, it will be appropriate to discuss the structures of the lithium compounds we treat with here at the outset. In this section, we present discussions on aggregation and on solvation of ion pairs. The ionic character of the C–Li bond and solvent intervention will be discussed under the headings of the individual compounds.

The aggregation of alkyllithiums is known to be governed by solvents as well as by the structure of the alkyl group.[14—18] Fluorenyllithium exists as a dimer even in hydrocarbons,[19] the fact being attributed to the stability of the fluorenide anion. As expected, the degree of aggregation is dependent on the concentration of the substrate, dimer being favored in a solution of high concentration relative to monomer and vice versa in a dilute solution.[18] The relatively polar solvents such as ethers tend to favor existence of a dimer (and a monomer to some extent) due to stabilization by solvation. These data in the literature imply that compounds we are treating here exist as a mixture of monomer and dimer under our conditions of investigation, the concentration of which favors the dimer.

Fluorenyllithiums. X-Ray structural analysis of 9-fluorenyllithiums reveals that the lithium atom is located close to C(1) and C(9) of the fluorene system, if it is the CIP,[20] whereas it is located far from C(9) of the fluorene if it is the SSIP.[21] Also, extensive sulfur coordination to the lithium atom may occur in the compounds studied in this work. Indeed very large chemical shift differences for the diastereotopic protons in compounds **3** support such structures in the original state. However, topomerization of these compounds should occur through the SSIP. Thus the expression of the lithium compounds as covalent species, as are shown in Scheme 2, is used only for the convenience of drawing.

There is another point which should be discussed before going to the discussion of the initial state of the substrate. That is the presence of CIP and SSIP. Both CIP and SSIP of 9-fluorenyllithium are known to be observable by UV-vis absorption spectra. Smid and co-workers have shown that CIP of 9-fluorenyllithium absorbs at ca. 349 nm with a molar extinction coefficient of ca. 10000, whereas SSIP of the same species does at 374 nm in THF.[22] In the visible region, absorptions due both to CIP and SSIP are observed with some overlaps: The absorption at the longest wavelength, 522 nm, is attributed to the SSIP, whereas the longest wavelength of absorption due to the CIP is 460 nm, the molar extinction coefficients being ca. 1000. Of these, the SSIP is more stable in these compounds than CIP due to stabilization by solvation, low temperature favoring SSIP. The UV-vis absorptions of compounds **3** are in good agreement with the data reported in the literature, indicating that the methylthiomethyl group at the 1-position does not affect the electronic absorption to a significant degree. We also observed the spectra for dilute solutions (ca. 10^{-4} mol L^{-1}) but were not able to find evidence for the existence of free ions. We thus discuss hereafter on the ground that there are only CIP and SSIP in the solutions concerned.

Populations of the ion pairs have been estimated to be ca. 75% CIP in 2-methyltetrahydrofuran and 80% SSIP in THF from spectroscopic studies.[22,23] Steric effects of the solvent molecules on solvation are responsible to the results. Our results shown in Table 1 are in accord with the data reported,[22] and indicate that the lithio compounds **3a** and **3b** exist as mostly SSIP in THF and DME, whereas they are mostly CIP in diethyl ether and in *t*-butyl methyl ether.

Solvent effects favoring SSIP in fluorenyllithiums have been attributed to better solvation of the cations concerned by small molecules relative to large ones. We propose that distances between the cation and the anion in SSIP are also important. Because placement of ion pairs at a large distance should lose Coulombic interactions with respect to that at a small distance, the energy for the former should be higher than that for the latter. This is exactly the case of SSIP with a large molecule versus a small molecule intervening. Polarity of the solvent is also important, because solvation energy should contribute to the stability of both CIP and SSIP.

Solvent effects on the formation of CIP and SSIP are apparent. Although the absorption maximum due to SSIP is not affected by the solvent polarity, that due to CIP is affected.[22] The authors discussed the results, mentioning the better solvation of the cation. We interpret this phenomenon, the placement of the absorption maximum of CIP in polar solvents at a long wavelength relative to that in less polar solvents, to mean that the polar solvent induces the loose CIP with respect to that in the less polar solvents. Absorptions at longer wavelength in UV-vis spectra for polar solvents than those in less polar solvents are keys for this interpretation. This solvation effects are operative not only in CIP but also in SSIP.

Substitution of an alkyl group for a hydrogen at the 9-position of 9-fluorenyllithium is known to shift the UV-vis absorption to a longer wavelength by ca. 2.4 $\mathrm{kcal\,mol^{-1}}$ (1 cal = 4.184 J).[22b] This is also reproduced for compound **3b** with respect to **3a**. In the literature, this is attributed to the difference in the position of the cation due to the steric effects.[22] These authors discussed also that the 9-alkyl group assists formation of SSIP in THF, the results being attributed to the steric effects of the alkyl group again.

α-(Benzylthio)benzyllithium. Earlier calculation of organolithium compounds produced results that imply the C–Li bond was almost covalent[24] but today the general consensus from calculations seems to be that the C–Li bond is almost ionic.[25] However, on the experimental ground, there is evidence that C–Li bond is covalent: C–Li coupling is observed in ^{13}C NMR spectra when ^{6}Li–^{13}C compounds are used: The coupling constant of ca. 16 Hz is observed.[15,26] Therefore, we should discuss the initial state of compound **4** in some detail.

Some X-ray structures of benzyllithium and its derivatives are known.[27] They are close to CIP with some covalent characters: The position of the lithium ion varies from compound to compound and the benzylic carbon is slightly pyramidal. ^{6}Li–^{13}C coupling constant in ^{13}C NMR of benzyllithium is reported to be 3.8 Hz,[28] which is smaller than other coupling constants observed for alkyllithiums. Thus this result is interpreted to mean that the C–Li bond is partially ionic. These results indicate that benzyllithiums are in a delicate balance between the ion pair and the covalent species.

The data in Table 1 show that the absorption maxima of this compound in THF and DME are at the long wavelengths with respect to those in *t*-butyl methyl ether and in diethyl ether. UV-vis absorption spectra of organolithium compounds have been studied by Waack and Doran.[29] They examined substituent effects as well as solvent effects on the electronic spectra of lithium compounds. Their results indicate that the absorption maxima of benzyllithium in THF and in diethyl ether are surprisingly at the same wavelength. Xie and Streitwieser reported that the lithium compound derived from 2-phenyl-1,3-dithiane showed absorption at 322 nm for CIP in THF.[30] They claimed that, although 2-lithio-2-(4-biphenylyl)-1,3-dithiane exhibited absorptions due to SSIP and free ions in addition to CIP, they were not able to detect absorptions due to SSIP of 2-lithio-2-phenyl-1,3-dithiane in THF. The results we obtained are quite different in that the distinct solvent effects were observed.

The absorptions at the long wavelength regions are not expected if these species exist as covalent ones, and we conclude that compound **4** even in *t*-butyl methyl ether and in diethyl ether exists as CIP. It is most likely that SSIP of **4** exists in THF and DME, because the large bathochromic shift of the absorption at the longest wavelength cannot be explained otherwise in addition to the fact that the intensity of the absorption band at the longest wavelength increases at low temperatures. However, comparison of the differences in wavelengths for the THF (or DME) solutions with those for diethyl ether (or *t*-butyl methyl ether) discloses that they are rather small for compound **4** relative to compound **3**. This may be attributed to the less extended π-system for **4** than for **3**.

Close examination of the spectra of **4** indicates that the absorptions in the visible region in diethyl ether are at slightly shorter wavelength than those in *t*-butyl methyl ether. Presumably, the difference in solvation affects the electronic states of the substrates. This kind of discussion was advanced by Smid et al.[22] If this interpretation is correct, *t*-butyl methyl ether is a better solvating molecule than diethyl ether irrespective of the steric effects: This could be caused by its high polarity relative to diethyl ether. Even though the population of the solvated ions is small in *t*-butyl methyl ether relative to that in diethyl ether, the solvated ion pairs absorb at a long wavelength in *t*-butyl methyl ether.

Populations of CIP and SSIP of this compound are not known. However, we believe the ratio, SSIP/CIP, in **4** must be smaller than that of the fluorenyllithiums because the anion in **4** must be less stable than those from **3**. We discuss the solvent effects on topomerization on this standpoint.

Topomerization. Topomerization in lithium compounds has been reported in the literature.[31] Generally, topomerization is a slow process, whereas aggregation/deaggregation and lithium exchange between different aggregates are fast. Thus the rates of these latter two processes are too large to be detected as the lineshape change in NMR spectra.[32] Because, in our system, there is an equilibrium between dimer and monomer, the former predominating, the rates we observe should be the average of the two, from the dimer and from the monomer.

We must identify what is the process which we observe here. Is it a process of solvent intervention to form SSIP from CIP? Or is it occurring in SSIP? After the proposal of the existence of CIP and SSIP in the solvolyses of organic compounds by Winstein and Robinson,[33] Goering et al. showed that, while ^{18}O scrambling occurs at the CIP stage, racemization occurs only at the stage of SSIP, with use of optically active ^{18}O-labeled esters.[34] It is also shown by Monte Carlo calculations that there is an energy barrier, though low, which separates CIP from SSIP.[35] However, it has not been clear which is the rate-limiting step, solvent intervention to CIP or tumbling of an ion in SSIP. The former assumes that the racemization in SSIP is very fast, whereas the latter assumes that the solvent intervention is very fast.

The kinetic data presented in Table 2, the feature of which is negative entropy of activation, seem to support the idea that the rate-limiting step is the solvent intervention to CIP. However, there is a definite drawback in assuming that the process we observe is the solvent intervention to CIP. That is, we do not observe the presence of two species, CIP and SSIP, by ^{1}H NMR spectra, even though we do find one species that gives a distinct set of quartet signals for the methylene protons, which are used as probes. Since UV-vis spectra of these compounds indicate that SSIP is a more stable species than CIP, the barrier to go from SSIP to CIP must be higher than that from CIP to SSIP. The absence of a signal due to one of the two species must mean that there is a rapid equilibrium between CIP and SSIP. The signal we observe is then an average of CIP and SSIP.

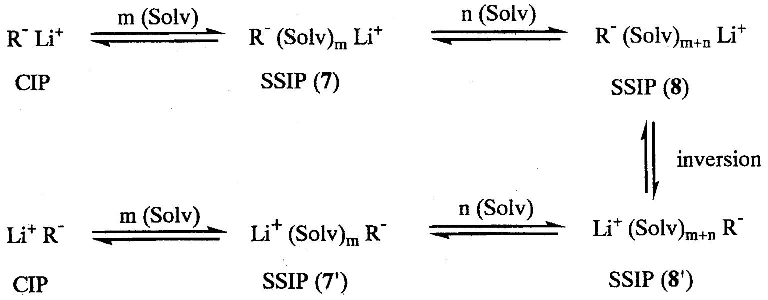
The next problem is the height of the barrier separating topomeric SSIP's. Is it low enough for the SSIP to almost freely and independently tumble or is it so high so that energy is required for the process to occur? We postulate that the latter is the case for diethyl ether and *t*-butyl methyl ether solutions. If the barrier in question were low, we should have observed the average of all the species. This is contradictory to the observation of the diastereotopicity of the methylene protons. We must assume that the independent tumbling of the anionic species in SSIP or moving of the lithium cation from the original site to the topomeric positions of the anion should be the process we observe. This is in accordance with what was found in the racemization, the racemization being slower than ^{18}O exchange by a factor of ca. 2.6 in the reaction of the optically active ester.[34] The SSIP (**7**) we observe in UV-vis spectra is too tight to allow tumbling of the anions independently and further solvent intervention to form a loose SSIP (**8**) is necessary for the tumbling (Scheme 4). The processes which are discussed here thus involve a pre-equilibrium between CIP and SSIP, followed by topomerization. In this context, we postulate that the case of the THF solutions of compounds **3** is the process in which further solvent intervention into SSIP proceeds with ease because of the low barrier.

Because of the nature of a process involving a pre-equilibrium, the activation parameters observed here are difficult to interpret. Dunitz summarized that entropy of freezing a mole of water costs entropy of ca. -10 cal mol^{-1} K^{-1}.[36] Our data in Table 2 are close to this value. Though these might favor solvent intervention be the rate-limiting step, we cannot conclude so until enthalpy and entropy for the pre-equilibrium become known. At any rate, however, further loosening of the SSIP is the key step for topomerization to occur. We assume in the following discussion that the tumbling itself is a facile process, because no extensive line-broadening was observed in NMR spectra, except for the signal due to the methylene protons.

a) Compound 3a. As Table 2 shows, the topomerization in **3a** in THF is too fast to be measured by the dynamic NMR technique, although we measured the spectra at 600 MHz at -110 °C. Using the chemical shift differences in diethyl ether and the coalescence method[37] for determination of the rates, we estimate the maximum free energy of activation to be 6.8 kcal mol^{-1}. We attribute the results to the small size of THF molecules. In further solvation to SSIP, which is necessary for topomerization to occur, the bulkiness of the solvent molecule will affect the distance between positive and negative ions. The longer the distance, the higher the energy needed. Being a small molecule, THF facilitates topomerization relative to solvents of bulky molecules.

The rates of topomerization for diethyl ether solutions are about 15 times larger than those for the *t*-butyl methyl ether solution. We attribute this to the bulkiness of the molecules concerned again. Because *t*-butyl methyl ether is bulkier than diethyl ether, the participation of *t*-butyl methyl ether to further solvation is more energy-requiring than that of diethyl ether. Because *t*-butyl methyl ether is more polar and consequently the SSIP is considered to be looser than diethyl ether, the rates of topomerization is expected to be smaller for diethyl ether than those for *t*-butyl methyl ether solutions if the bulkiness is the same. Thus the bulkiness effects of *t*-butyl methyl ether can be larger than what we see in the apparent rates.

b) Compound 3b. Because the rates of topomerization in **3a** in THF were too large for the measurement by the 600 MHz NMR machine, we tried to reduce the rates by introducing a methyl group. The pK_a values of fluorene and 9-methyl-



Scheme 4.

fluorene are known to be 22.3 and 22.6, respectively.[38)] And this small but distinct difference was hoped to give some measurable effects to our cases of topomerization. Although 9-alkylfluorenyllithium is known to favor SSIP in polar solvents of small molecular size,[22b)] the decrease in the acidity of 9-alkylfluorene should mean less stability of the anion derived from it than that of fluorenide anion. The measurements of the rates of topomerization in compound **3b** were thus performed. The results are shown in Table 2.

Contrary to the expectation from the acidity of the parent compound, the kinetic parameters for **3b** shows that it topomerizes even a little faster than **3a** in the same solvent: Although the rates of topomerization in **3b** in THF cannot be compared with those of **3a** in the same solvent because both topomerize too fast, topomerization in **3b** in diethyl ether and in *t*-butyl methyl ether are definitely faster than the corresponding ones of **3a**. Again, the rates of topomerization in diethyl ether solution are larger than those in *t*-butyl methyl ether, irrespective of the fact that *t*-butyl methyl ether is more polar than diethyl ether. There is one drawback in the data of **3b** in diethyl ether: The chemical shift differences of the methylene protons were so large in this solvent as to make lineshape analysis less reliable than in others. Therefore the kinetic parameters, $\Delta H^\ddagger$ and $\Delta S^\ddagger$, should be used only on the qualitative basis, although correlation factors in the statistical treatment were satisfactory.

The rate enhancement by introduction of the methyl group must be due to the steric effects, which tend to separate ion pairs more distantly than the case where no steric effects are applicable. The looseness of SSIP thus manifested should facilitate the further solvent intervention. That is, the initial state (SSIP) of **3b** is less stable than **3a** in the same solvent due to less Coulombic attraction and the high free energy of the substrate should make the topomerization in **3b** easy relative to **3a**.

c) Compound 4. Although we were able to show that the effect of the molecular size of the solvent can be seen in general, it was not possible to compare the kinetic parameters obtained for solutions of **3** in a solvent of small molecular size, such as THF and DMF, due to the fact that topomerization was too fast for the measurement by the NMR technique. During the course of our work, Hoffmann et al. reported the dynamic NMR study of α-(benzylthio)benzyllithium (**4**) in THF.[7)] We thus used this compound for acquisition and comparison of the kinetic data in solvents of various molecular sizes. The results are listed in Table 2. The rates of topomerization become small as the size of the molecules which comprise the solvent becomes large, but the difference is rather small for this compound.

According to the discussion presented above, in the rate-limiting step for the topomerization, the further intervention of solvent molecule(s) to SSIP plays a decisive role. The results for the THF solution must be attributed to more facile intervention of solvent molecule(s) than solvents of bulky molecules. Probably the original SSIP is already loose due to the effective solvation by THF molecules.

The results for the THF solutions are in agreement with those reported by Hoffmann et al.,[7)] although entropy of activation is a little different. The topomerization rates are almost the same for *t*-butyl methyl ether solutions with those for diethyl ether solutions and they are only about 3.5 times smaller than those obtained for the THF solution. However, the difference may be larger than the apparent value because the high polarity of *t*-butyl methyl ether relative to diethyl ether contributes to enhancing the rates relative to those for diethyl ether solutions. It is also possible that, due to less stability of the benzylic anion than the fluorenyl anion, the energy gap between the SSIP and the transition state becomes small in **4**. Because fluorene is much more acidic than dibenzyl sulfide,[39)] the 9-fluorenyl anion should be more stable than (α-benzylthio)benzyl anion.

Terminology for the Effects of Molecular Size of Solvent. In summary, we have demonstrated that the effects of molecular size of solvents can be an important factor to be considered when we interpret the experimental results, such as rates of reactions and equilibrium constants. Although this aspect of solvent effects has attracted little attention in the past, we should always take into consideration the molecular size of the solvent used when we discuss the solvent effects. Thus it may be convenient to coin a word to express this effect in general. We propose a term, dimensiosolvatic effect. It will also be convenient in discussion, if a term "bulky solvent" is allowed for a solvent composed of bulky molecules and a term "small solvent" for the place of a solvent composed of small molecules.

Experimental

^{1}H and ^{13}C NMR spectra were measured on a Varian Gemini-300 spectrometer operating at 300.1 and 75.0 MHz, respectively. ^{1}H NMR spectra at various temperatures were recorded on a Bruker AMX-R400 spectrometer operating at 400.1 MHz and a Varian Unity-600 spectrometer operating at 599.97 MHz. Elemental analyses were performed with a Perkin–Elmer 240C analyzer. Mass spectra were measured on a JEOL JMS-303HF spectrometer by the fast atom bombardment method. UV-vis spectra at low temperatures were recorded on a Hitachi U-3000 spectrometer equipped with an Oxford Cryostat DN1704 using liquid nitrogen as a coolant. Melting points are uncorrected.

1-(Methylthiomethyl)fluorene (5). To a solution of 12 g (0.050 mol) of 9-bromofluorene[40)] in 40 mL of dry acetone, was added 4.5 mL (0.10 mol) of dimethyl sulfide at room temperature and the mixture was stirred for 5 d at the temperature. During this period precipitates formed. The precipitate was collected by filtration, washed with acetone, and air-dried to give crude (9-fluorenyl)dimethylsulfonium bromide in 81% yield. A part of the product (1.0 g or 3.3 mmol) was dissolved in 25 mL of hot water to remove insoluble impurities and the solution was then cooled to room temperature. To the mixture was added 10% aqueous sodium hydroxide until yellow precipitates no longer appeared. The yellow precipitates were collected on a funnel by filtration and washed with water, with ethanol, and then with ether. A solution of the solid in 25 mL of 5% ethanolic sodium hydroxide was heated under reflux for 5 h and then stirred at room temperature for 12 h. After the solvent was evaporated, the mixture was extracted with benzene and the extract was washed with water. The organic layer was dried over magnesium sulfate and the solvent was evaporated in vacuo.

The residue was submitted to chromatography on silica gel with a hexane eluent. The product was recrystallized from hexane to give colorless crystals, mp 74.0—74.5 °C, in 69% yield. Found: C, 79.60; H, 6.23%. Calcd for $C_{15}H_{14}S$: C, 79.52; H, 6.26%. ^{1}H NMR ($CDCl_3$) $\delta = 2.02$ (3H, s), 3.83 (2H, s), 3.96 (2H, s), 7.19 (1H, d, $J = 7.7$ Hz), 7.31—7.38 (3H, m), 7.55 (1H, d, $J = 7.1$ Hz), 7.69 (1H, d, $J = 7.7$ Hz), 7.77 (1H, d, $J = 7.7$ Hz).

9-Methyl-1-(methylthiomethyl)fluorene (6). To a solution of 0.83 g (3.7 mmol) of **5** in 15 mL of dry tetrahydrofuran was added 2.7 mL (4.4 mmol) of 15% hexane solution of butyllithium at −78 °C under a nitrogen atmosphere. The mixture was stirred for 0.5 h at the temperature. To the solution was added 0.5 mL (7.4 mmol) of iodomethane. The solution was stirred for 2 h at the temperature and then the cooling bath was removed. After room temperature was attained, the mixture was further stirred for 12 h. The mixture was then treated with water and then with 1 mol L^{-1} hydrochloric acid. It was extracted with ether and the organic layer was dried over magnesium sulfate. The solvent was evaporated under a reduced pressure and the residue was distilled with a bulb-to-bulb distillation apparatus (Kugelrohr). The desired compound was obtained as a yellow oil, which distilled at 135—140 °C (bath temperature) under 0.8 mmHg (1 mmHg = 133.322 Pa) pressure, in 0.92 g (88%) yield. HRMS (FAB) Found: *m/z* 241.1084. Calcd for $C_{16}H_{17}S$: (M+1), *m/z* 241.1051. ^{1}H NMR ($CDCl_3$) $\delta = 1.54$ (3H, d, $J = 7.4$ Hz), 2.03 (3H, s), 3.81 and 4.03 (2H, ABq, $J = 13.4$ Hz), 4.21 (1H, q, $J = 7.4$ Hz), 7.23—7.35 (4H, m), 7.49 (1H, d, $J = 6.8$ Hz), 7.69 (2H, dd, $J = 6.2$ and 1.5 Hz). ^{13}C NMR ($CDCl_3$) $\delta = 15.4$, 18.5, 35.7, 41.8, 118.8, 119.8, 123.9, 126.9, 127.1, 127.3, 128.3, 134.3, 140.1, 141.2, 146.8, 149.2.

9-Lithio-1-(methylthiomethyl)fluorene (3a). To a thoroughly dried 5 mm NMR tube was attached a three-way stop-cock and the atmosphere replaced by nitrogen by evacuating and by filling with nitrogen three times. 1-(Methylthiomethyl)fluorene (**5**) (17 mg or 0.073 mmol) was quickly introduced and replacement of the atmosphere was repeated. The tube was closed with a septum and fixed with Parafilm. An appropriate solvent (0.40 mL) was introduced to the tube by a dry gas-tight syringe. The tube was shaken to dissolve the sample and the solution was cooled to −78 °C. After 5 min, 80 μL (0.13 mmol) of a freshly opened 15% solution of butyllithium was injected to the tube. The tube was removed from the bath for about 10 s and shaken to wash all the butyllithium solution into the solution. The solution was kept at −78 °C until the tube was inserted to the NMR probe. It showed the following; ^{1}H NMR spectrum (*t*-BuOMe at −90.6 °C) $\delta = 2.05$ (3H, s), 3.05 and 3.62 (2H, ABq, $J = 13.7$ Hz), 5.01 (1H, s), 6.03 (1H, t, $J = 7.1$ Hz), 6.11 (1H, t, $J = 7.1$ Hz), 6.23 (1H, d, $J = 6.3$ Hz), 6.40 (1H, t, $J = 7.2$ Hz), 6.80 (1H, d, $J = 8.4$ Hz), 7.34 (1H, d, $J = 7.6$ Hz), 7.38 (1H, d, $J = 7.9$ Hz).

9-Lithio-9-methyl-1-(methylthiomethyl)fluorene (3b). This compound was prepared similarly as above by treating 18 mg (0.075 mmol) of the substrate **6** in 0.40 mL of an appropriate solvent with 100 μL (0.15 mmol) of a freshly opened 15% solution of butyllithium in hexane. ^{1}H NMR (THF-d_8, −76.8 °C) $\delta = 1.97$ (3H, s), 2.82 (3H, s), 4.15 (2H, br s), 6.22 (1H, t, $J = 7.3$ Hz), 6.31 (1H, t, $J = 6.6$ Hz), 6.53 (1H, d, $J = 6.1$ Hz), 6.77 (1H, t, $J = 6.8$ Hz), 7.18 (1H, d, $J = 8.1$ Hz), 7.74 (1H, d, $J = 7.6$ Hz), 7.76 (1H, dd, $J = 7.6$ Hz).

Table 3. Temperature Dependence of the Chemical Shift Differences of the Diastereotopic Protons Used as Probes for Dynamic NMR Spectroscopy

Compound	Solvent	$\Delta\nu_{AB}$/Hz[a]	J_{AB}/Hz	T_2/s
3a	Et_2O-d_{10}	$0.257t+294.7$	−12.1	0.035
	t-BuOMe	$-0.510t+177.5$	−13.7	0.045
3b	Et_2O-d_{10}	$0.000t+490.0$	−12.0	0.035
	t-BuOMe	$-1.350t+108.7$	−13.2	0.045
4	THF-d_8	$-1.300t+38.7$	−11.1	0.059
	Et_2O-d_{10}	$-0.750t+120.6$	−11.2	0.040
	t-$BuOCD_3$	$-0.802t+109.9$	−11.2	0.040

a) *t* stands for temperature in Celsius.

Table 4. Rate Constants of Topomerization of Compounds **3** and **4** in Various Solvents

Compound	Solvent	*k*/s^{-1} (*t*/°C)							
3a	Et_2O-d_{10}	28.0	(−93.9),	40.0	(−90.7),	56.0	(−88.1),	86.0	(−84.3),
		128	(−81.3),	180	(−78.1),	240	(−75.0),	340	(−71.9),
		460	(−68.7),	600	(−65.6)				
	t-BuOMe	6.0	(−83.4),	14.0	(−76.3),	28.0	(−69.2),	58.0	(−62.1),
		104	(−54.9),	190	(−47.8),	290	(−40.7),	480	(−33.5)
3b	Et_2O-d_{10}	340	(−111.7),	440	(−108.6),	580	(−105.4),	820	(−102.3),
		1040	(−99.1),	1280	(−96.0),	1700	(−92.8),	2200	(−89.7),
		2800	(−86.5),	3400	(−83.4),	4400	(−80.2)		
	t-BuOMe	10.0	(−84.9),	16.0	(−81.4),	24.0	(−78.0),	34.0	(−74.5),
		52.0	(−71.0),	72.0	(−67.6),	110	(−64.1),	160	(−60.7),
		220	(−57.2)						
4	THF-d_8	26.0	(−87.5),	36.0	(−84.8),	70.0	(−80.3),	90.0	(−78.3),
		160	(−73.3),	220	(−70.6),	320	(−67.6),	440	(−64.8),
		580	(−62.6),	700	(−60.2)	1100	(−55.5)		
	Et_2O-d_{10}	16.0	(−82.7),	24.0	(−79.6),	36.0	(−76.5),	54.0	(−73.4),
		80.0	(−70.3),	116	(−67.2),	186	(−62.0),	320	(−56.9),
		540	(−51.7),	800	(−46.7)				
	t-$BuOCD_3$	24.0	(−83.8),	34.0	(−80.7),	46.0	(−77.6),	70.0	(−73.4),
		94.0	(−69.3),	134	(−64.1),	560	(−46.5),	740	(−41.4)

α-(Benzylthio)benzyllithium (4). This compound was prepared by treatment of 25 mg (0.12 mmol) of dibenzyl sulfide (Tokyo Kasei Co.) in 0.50 mL of an appropriate solvent with 60 μL (0.13 mmol) of 2.1 mol L^{-1} solution of *t*-butyllithium in hexane. The following ^{1}H NMR spectrum was observed at −109.2 °C (THF-d_8) δ = 2.78 (1H, s), 3.03 and 3.44 (2H, ABq, J = 10.9 Hz), 6.00 (1H, d, J = 7.8 Hz), 6.45 (1H, d, J = 7.8 Hz), 6.64 (1H, t, J = 7.4 Hz), 6.82 (1H, t, J = 7.6 Hz), 6.95 (2H, d, J = 7.4 Hz), 7.01 (1H, t, J = 7.4 Hz), 7.14 (2H, t, J = 7.2 Hz), 7.19 (1H, d, J = 7.9 Hz).

Dynamic NMR Measurements and Calculations. The samples prepared in the NMR tubes were placed in the NMR probe which was precooled to −10 °C or below. The temperature was calibrated with use of the chemical shift differences of methanol signals. External acetone-d_6 was used for the D-lock in the case of the *t*-butyl methyl ether solvent. The total lineshape analyses were carried out with use of the DNMR3K[8] program as a coupled two-site exchange. The probes were methylene protons of the methylthiomethyl group for **3** and benzylic methylene protons for **4**. The chemical shift differences were checked at the temperature range where the rates of exchange were negligibly small. The chemical shift differences drifted as the temperature changed and were correlated linearly with temperature at the slow exchange limit. The correlation of the chemical shift differences with temperature in °C together with the coupling constants, which were constant throughout, and T_2's are listed in Table 3. The linear correlation was extrapolated to the temperature range where the site-exchange took place. T_2's were estimated from the line width of the signals due to methylene protons, which were used as probes, at the slow exchange limit and the same value was used for the simulation for the whole range of lineshapes at various temperatures. The rate constants for the topomerization were obtained by visual fitting of the calculated curves with the observed, and multiplied by two to accommodate the fact that enantiomerization takes place after dissociation at a probability of 1/2. The rate constants thus obtained are compiled in Table 4.

UV-vis Spectral Measurements. The solutions of the lithium compounds were prepared similarly for the preparation of those compounds for the NMR measurements. The spectrum was recorded for a solution of **3a** or **3b** of 1.0—2.0×10^{-3} mol L^{-1} concentration in an appropriate solvent. The concentration of **4** was 4.6×10^{-3} mol L^{-1}. A cell of 1.0 mm was used for compound **4**, whereas it was 10 mm for **3a** and **3b**. Changing the temperature of solutions changed the intensities of absorptions. The observed absorptions at 180 K together with intensities are listed in Table 1. For compound **3a**, the spectrum for a ca. 1.0×10^{-4} mol L^{-1} solution was also recorded. The spectrum was identical with those for more concentrated solutions.

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