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Dynamic NMR as a Nondestructive Method for the Determination of Rates of Dissociation. XIII. Sulfur Inversion in 9,9-Dialkyl-10-mesitylthioxanthenium Salts[1)]

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The sulfur-inversion in the title compound (alkyl=ethyl) was found to take place with the following activation parameters by dynamic NMR spectroscopy: $\Delta H^{\neq}=23.8\pm0.2$ kcal mol^{-1}, $\Delta S^{\neq}=2.6\pm0.4$ cal mol^{-1} K^{-1}. The significance of the near zero entropy of activation is discussed. The mesityl group in the title compounds also showed restricted rotation of which barrier to rotation was estimated to be 14 kcal mol^{-1} at 318 K for the compound where the alkyl is a methyl.

During the course of investigation by the dynamic NMR spectroscopy on the dissociation of a chemical bond, it has become clear that the entropy of activation is large positive if the ground state is ionic and the transition state is losing the electric charge, whereas it is large negative if the ground state is covalent and the transition state is of ionic character.[2)] Thus this technique may be used as a diagnostic means for the mechanism of a dynamic process of a molecule.

Sulfur-inversion in sulfonium ions is known to take place with a free energy of activation of ca. 25—30 kcal mol^{-1} (1 cal=4.184 J).[3)] In contrast to this fact, the sulfur ligand in platinum complexes inverts with much less free energy of activation,[4)] which might be an implication that the mechanism of the sulfur-inversion in the complexes is different from the true inversion: inversion after dissociation is one of the alternative possibilities.

In tackling this problem, we expected that the dynamic NMR technique would give valuable information. However, literature search indicated that the number of literatures that treated with this problem by dynamic NMR is very limited: to our knowledge, there is only one paper that reports the kinetic parameters of sulfur-inversion in sulfonium ions, this paper giving only free energy of activation.[5)] Therefore, some basic data should be accumulated in order to prove that the dynamic NMR technique is useful in discussing the mechanism of inversion of sulfur. As one of the contributions to this end, we have reported that the sulfur-inversion in a sulfonium ion, in which the C–S bond dissociation is unlikely to occur, exhibits near-zero entropy of activation by a classical method.[6)] A next problem is to prove that the dynamic NMR technique affords in fact a near-zero entropy of activation, if the mechanism of the sulfur-inversion does not involve the C–S bond dissociation followed by inversion.

The only one literature we found reported that the sulfur-inversion in 9,9-dimethyl-10-phenylthioxanthenium perchlorate takes place to show coalescence of the two methyl signals at ca. 200 °C at 60 MHz.[5)] In this compound, the C–S bonds involved are aromatic carbon-to-sulfur ones only: the involvement of the bond dissociation is unlikely in the sulfur-inversion. Since the coalescence temperature of the key signals of the reported compound would be too high for the instrument we possess (270 MHz), we decided to modify the molecule to lower the coalescence temperature.

There are two techniques to lower the coalescence temperature: one is to reduce the difference in chemical shifts of the exchanging nuclei, and the other is to raise the ground state energy so that the energy gap between the ground state and the transition state for inversion becomes small. We chose the latter method firstly. The former will be accomplished by selecting the chain length of the alkyl groups at the 9-position.

The syntheses of the compounds used in this study were carried out by the known methods. 9,9-Dialkylthioxanthene (**1**) was oxidized to the corresponding sulfoxide **2** which was treated with sulfuric acid after dissolving in mesitylene.[5)] For the synthesis of 9,9-dibenzyl compound, this method failed probably because of the presence of the phenyl ring in the benzyl group. Therefore, only the 10-phenyl derivative **5** was prepared by phenylation[7)] of 9,9-dibenzylthioxanthene (**4**).

Although it was hoped that the introduction of a mesityl group into the 10-position of the thioxanthenium ion would lower the barrier to inversion, the change in the observed line shapes of 10-mesityl-9,9-dimethylthioxanthenium perchlorate (**3**: $R=CH_3$, $X=ClO_4$) at high temperatures was not good enough for the total line shape analysis. Introduction of two benzyl groups in the 9-position of thioxanthenium ion was not satisfactory either: 9,9-dibenzyl-10-phenylthioxanthenium perchlorate (**5**) possessed a too high barrier to inversion for the measurement with our instrument, although we hoped that the steric effects of the benzyl groups would lower the barrier.

Finally we synthesized 9,9-diethyl-10-mesitylthioxanthenium tetrafluoroborate (**3**: $R=C_2H_5$, $X=BF_4$) and found the compound to be suitable for the

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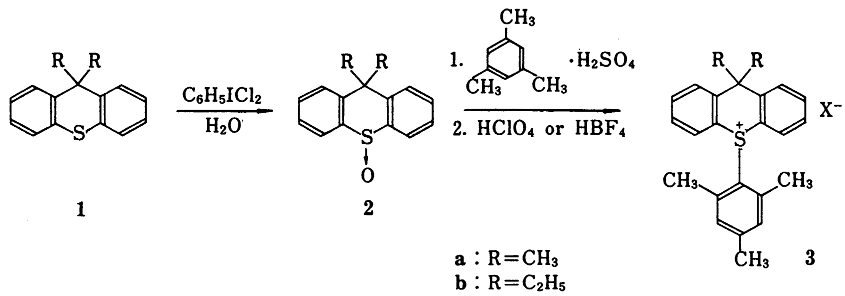
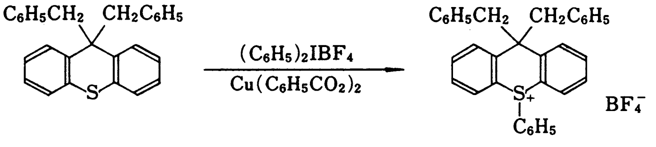


1 2 3

a : R=CH_3
b : R=C_2H_5



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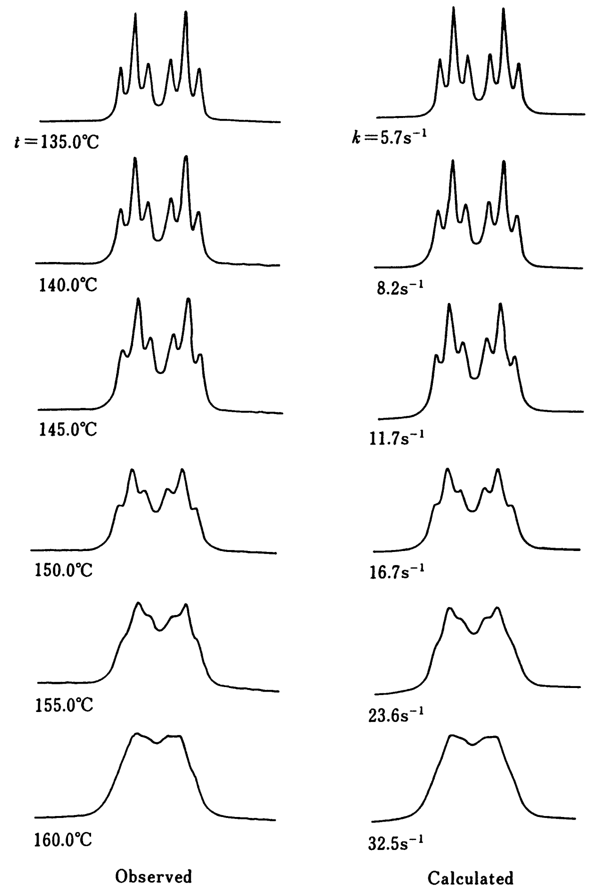

Fig. 1. Observed and calculated line shapes of the methyl protons of 9,9-diethyl-10-mesitylthioxanthenium tetrafluoroborate.

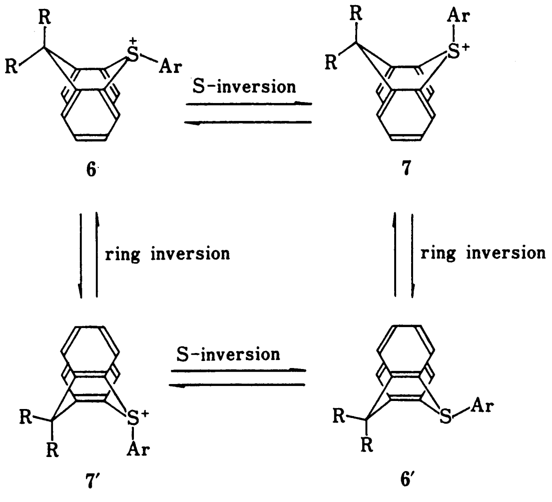

Fig. 2. Isomerization circuit.

dynamic NMR work, thanks to the steric effects given by the mesityl group and probably by the ethyl groups, in addition to the small chemical shift differences of the methyl protons in the ethyl groups. The kinetic data obtained by the total line shape analysis are given in Fig. 1, taking typical examples, together with observed and calculated line shapes for the methyl protons of the ethyl groups. The enthalpy of activation, 23.8±0.2 kcal mol^{-1}, and entropy of activation, 2.6±0.4 cal mol^{-1} K^{-1}, were obtained by putting these results into the Eyring equation. The correlation coefficient was excellent.

The feature of the kinetic parameters is the near-zero entropy of activation. Since the C-S bonds in this compound can be assumed to not dissociate under the conditions of the investigation, the sulfur-inversion must be a single step process. In such processes, the entropy of activation is near-zero in agreement with the results obtained by a classical method applied to other sulfonium compounds that do not easily dissociate at the C-S bonds. We may conclude that in those cases the dynamic NMR technique gives reliable data as was the case of internal rotation in molecules.[8]

It may be argued that, since the 9,10-dihydroanthracene and its analogs take a boat conformation in the ground state,[9] the process we observe here may not be the sulfur-inversion. We believe, however, that the process observed here is indeed the sulfur-inversion for the following reasons. The isomerization circuit is shown in Fig. 2. Firstly, the rates of ring inversion in this type of compounds are known to be very large at room temperature.[10] Therefore, the ring inversion cannot be the rate-determining step of the observed process. Secondly, if the mesityl group is axial **7** or **7′**, then the steric interaction of the mesityl group with the alkyl group in the 9-position that opposes the mesityl group is great: the mesityl-axial conformation **7** or **7′** will be too unstable to be observed. Therefore, the ground state for the compounds in question must be the mesityl-equatorial conformation **6** and **6′**. When sulfur-inversion takes place from the stable conformation, the mesityl-axial conformation is assumed transiently but the ring inversion follows very rapidly. It also means that, if the ring inversion takes place to form the mesityl-axial conformation, the reverse process follows rapidly.

The molecular ion of 9,9-dialkyl-10-mesitylthioxanthenium showed broad peaks for the methyl protons of the mesityl group as well as the aromatic protons which are directly bonded to the mesityl-phenyl group at room temperature to indicate that the rotation of the mesityl group is fairly slow. By lowering the temperature of the solution of 9,9-dimethyl-10-mesitylthioxanthenium perchlorate (**3**: R=CH_3, X=ClO_4), we found the two methyl signals were separated (1.14 and 2.96) as well as the meta protons of the mesityl group (7.14 and 7.38). The coalescence of the methyl proton signals took place at 318 K. Because of the presence of other proton signals in the region where the coalescence of the signals took place, we abandoned the total line shape analysis and the free energy of activation for rotation was obtained as 14 kcal mol^{-1} at the coalescence temperature by assuming that the chemical shift difference is constant throughout the temperature range examined.

This barrier to rotation may be compared with that for the mesityl or 2,6-dimethylphenyl group in 9,9-dimethyl-10-(2,6-dimethylphenyl)-9,10-dihydroanthracene, 19.6 kcal mol^{-1} at 399 K,[11] and 9,9-dimethyl-10-mesitylxanthene , 17.6 kcal mol^{-1} at 298 K.[12] The lowering of the barrier to rotation in the sulfur compound (**3**: RCH_3, X=ClO_4) is undoubtedly caused by the large bond-lengths of the C–S bonds relative to the C–C bonds.

Experimental

NMR Measurement. The NMR data including the dynamic NMR were collected with the use of a JEOL GX-270 spectrometer unless otherwise mentioned. The temperature was calibrated by a thermometer. For the dynamic NMR measurements, a solution of ca. 40 mmol L^{-1} was used. Dimethyl-d_6 sulfoxide and chloroform-*d* were used for high and low temperature measurements, respectively.

Calculation of Rate Constants. The exchange of spins observed here is in principle $A_3X_2B_3Y_2 \rightleftarrows B_3Y_2A_3X_2$. We approximated the process to be $AX_2 \rightleftarrows BY_2$ for the convenience of calculation which was carried out by the use of DNMR3 program.[13] The coupling constants were found to be constant at several temperatures, where the exchange was negligibly slow. Thus we assumed $J_{AX}=J_{BY}=7.3$ Hz at the temperature range examined. Since the transverse relaxation time (T_2) could not be obtained from a signal within the molecule, the relaxation time was obtained by calculation that gave the best fit with the observed signals at temperatures in the slow exchange limit. T_2 was thus obtained as 0.12 s and this value was used throughout the calculation of the line shapes at various temperatures. The chemical shifts drifted as the temperature was changed. At the slow exchange limit, we observed the chemical shifts of the A, B, X, and Y protons at various temperatures to obtain the correlations between the temperature and the chemical shift. The results are shown in Table 1. These relations were extrapolated to the temperatures where the line shapes changed. The agreement between the observed and the calculated spectra was excellent, as is seen in Fig. 1. The following rate constants (s^{-1}) were obtained (temperature in °C given in parentheses): 5.7 (135.0), 6.8 (137.5), 8.2 (140.0), 9.7 (142.5), 11.7 (145.0), 13.9 (147.5), 16.7 (150.0), 19.6 (152.0), 23.6 (155.0), 28.0 (157.5), 32.5 (160.0), 38.5 (162.5). These data were put into the Eyring equation to obtain the enthalpy of activation, 23.8±0.2 kcal mol^{-1}, and entropy of activation, 2.6±0.4 cal mol^{-1} K^{-1}. The correlation coefficient was 0.999.

Table 1. Correlation between Temperature and Chemical Shifts of the Protons Involved in the Exchange

Nuclei[a]	$f(t)$[b]
A	$0.179t + 151.41$
B	$0.234t + 170.22$
X	$0.144t + 489.97$
Y	$0.0510t + 735.89$

a) For A, B, X, and Y, see the text. b) $\nu=f(t)$, t being temperature in °C.

For the calculation of the free energy of activation for rotation of the mesityl group, the equation

$$k_c = \frac{\pi \Delta \nu}{\sqrt{2}}$$ [14]

was used, where $\Delta\nu$ is the chemical shift difference of the exchanging proton signals and k_c the rate constant at the coalescence temperature. The value of the rate constant was put into the Eyring equation.

9,9-Dibenzylthioxanthene (4). To a solution of 5.32 g (17.5 mmol) of 9-benzylthioxanthen-9-ol[15] in 100 mL of ether was added 30 mL of 70% perchloric acid at −78 °C with stirring. The mixture was allowed to warm up to the room temperature and the red precipitates were collected. Recrystallization from hot acetic acid gave 4.91 g of 9-benzylthioxanthylium perchlorate. To a Grignard solution prepared from 4.8 g (38 mmol) of benzyl chloride, 0.92 g (38 mmol) of magnesium and 100 mL of ether, was added 4.90 g (12.7 mmol) of the perchlorate and the mixture was refluxed for 2 h. The mixture was decomposed with aqueous ammonium chloride and the ether layer was separated. After drying over sodium sulfate, ether was removed and the residue was submitted to chromatography on silica gel with hexane as an eluent to afford 2.44 g (50.8%) of the desired product and 1.00 g of 9-benzylidenethioxanthene, identified by its melting point, 119.0—120.0 °C (lit,[15] mp 121—122 °C), and its ^{1}H NMR spectra ($CDCl_3$, δ): 6.87 (1H, s), 6.9—7.8 (13H, m). The desired product was purified by recrystallization from dichloromethane-hexane, mp 160.0—161.0 °C. Found: C, 85.39; H, 5.80; S, 8.27%. Calcd for $C_{27}H_{22}S$: C, 85.67; H, 5.86; S, 8.47%. ^{1}H NMR ($CDCl_3$) δ=3.52 (4H, s), 6.6—7.4 (18H, m).

9,9-Dibenzyl-10-phenylthioxanthenium Tetrafluoroborate (5). A mixture of 0.55 g (1.5 mmol) of 9,9-dibenzylthioxanthene in 15 mL of chlorobenzene, 0.55 g (1.5 mmol) of diphenyliodonium tetrafluoroborate[7] and 10 mg of copper(II) benzoate was heated at 120—125 °C under a nitrogen atmosphere for 3 h. The mixture was cooled and ether was added to induce precipitation. Recrystallization of the precipitate from ethanol afforded 0.33 g (42%) of the desired product, mp 296—297 °C (decomp). Found: C, 72.79; H, 4.75; S, 6.16%. Calcd for $C_{33}H_{27}BF_4S$: C, 73.07; H, 5.02; S, 5.91%. ^{1}H NMR ($CDCl_3$) δ=3.60 (2H, s), 4.08 (2H, s), 6.02 (2H, d, J=7.2 Hz), 6.6—7.6 (17H, m), 7.96 (2H, t, J=7.2 Hz), 8.42 (2H, d, J=7.2 Hz).

10-Mesityl-9,9-dimethylthioxanthenium Perchlorate (3a: X=ClO$_4$). To a solution of 0.44 g (1.8 mmol) of 9,9-dimethylthioxanthene 10-oxide (**2a**)[5] in 5 mL of mesitylene, was added 1 mL of concentrated sulfuric acid at 0 °C with stirring. The stirring was continued for 10 d. The mixture was poured into water and shaken with ether. To the aqueous layer cooled at 0 °C, was added 2 mL of 70% perchloric acid. After stirring for 1h, the precipitates were collected and washed with water and then with ether. Recrystallization from acetone-ether afforded 0.60 g of the desired product, mp 262.0—263.5 °C. Found: C, 64.56; H, 5.90; S, 7.56; Cl, 8.08%. Calcd for $C_{24}H_{25}ClO_4S$: C, 64.78; H, 5.66; S, 7.20; Cl, 7.97%. ^{1}H NMR ($CDCl_3$, −50 °C) δ=1.14 (3H, s), 1.52 (3H, s), 2.18 (3H, s), 2.46 (3H, s), 2.96 (3H, s), 7.14 (1H, s), 7.25 (2H, d, J=7.5 Hz), 7.38 (1H, s), 7.51 (2H, d, J=7.5 Hz), 7.78 (2H, t, J=7.5 Hz), 7.91 (2H, d, J=7.5 Hz).

9,9-Diethylthioxanthene 10-Oxide (2b). To a solution of ethylmagnesium iodide prepared from 1.0 mL (13 mmol) of ethyl iodide, 0.3 g (13 mmol) of magnesium and 50 mL of ether, was added 1.85 g (5.70 mmol) of 9-ethylthioxanthylium perchlorate[16] and the mixture was heated for 2 h. The mixture was decomposed with aqueous ammonium chloride and the ether layer was separated. The ether solution was washed with water and dried over magnesium sulfate. Evaporation of the solvent afforded practically pure 9,9-diethylthioxanthene (**1b**) in 99% yield. ^{1}H NMR ($CDCl_3$) δ=0.68 (6H, t, J=7.3 Hz), 2.07 (4H, q, J=7.3 Hz), 7.1—7.5 (8H, m).

The practically pure thioxanthene **1b** was dissolved in 10 mL of pyridine and 1 mL of water. To the solution was added 1.70 g (6.18 mmol) of phenyliodonium dichloride in 7 mL of pyridine in 10 min at −40 °C and the mixture was stirred overnight. Dilute sulfuric acid was added with cooling to neutralize and the mixture was extracted with chloroform. The chloroform layer was washed with water and dried over sodium sulfate. Evaporation of the solvent and addition of hexane afforded crystals in 87.5% yield. Recrystallization of the product from hexane gave the pure sample, mp 125.0—125.5 °C. Found: C, 75.46; H, 6.84; S, 11.84%. Calcd for $C_{17}H_{18}OS$: C, 75.52; H, 6.71; S, 11.86%. ^{1}H NMR ($CDCl_3$) δ=0.61 (3H, t, J=7.5 Hz), 0.84 (3H, t, J=7.5 Hz), 1.62 (2H, q, J=7.5 Hz), 2.47 (2H, q, J=7.5 Hz), 7.4—7.6 (6H, m), 8.0—8.2 (2H, m).

9,9-Diethyl-10-mesitylthioxanthenium Tetrafluoroborate (3b: X=BF$_4$). A mixture of 0.38 g of the sulfoxide **2b**, 5 mL of mesitylene and 1 mL of concentrated sulfuric acid was stirred at room temperature for 4 d. The mixture was poured into ice-water and ether-soluble materials were removed by shaking with ether. To the aqueous layer was added 2 mL of 40% tetrafluoroboric acid with cooling and the mixture was stirred for 1 h at 0 °C. The precipitate was collected by filtration, washed with water and then with ether, and recrystallized from ethanol to afford 0.17 g of the desired product, mp 202.0—203.0 °C. Found: C, 67.83; H, 6.53; S, 6.96%. Calcd for $C_{26}H_{29}BF_4S$: C, 67.53; H, 6.40; S, 7.16%. ^{1}H NMR (DMSO-d_6) δ=0.57 (3H, t, J=7.3 Hz), 0.64 (3H, t, J=7.3 Hz), 1.38 (3H, br s), 1.86 (2H, q, J=7.3 Hz), 2.40 (3H, s), 2.73 (2H, q, J=7.3 Hz), 2.94 (3H, br s), 7.21 (1H, br s), 7.38 (2H, d, J=7.8 Hz), 7.49 (1H, br s), 7.60 (2H, t, J=7.8 Hz), 7.86 (2H, t, J=7.8 Hz), 8.09 (2H, d, J=7.8 Hz).

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