April, 1987] © 1987 The Chemical Society of Japan NOTES Bull. Chem. Soc. Jpn., 60, 1555—1557 (1987) 1555

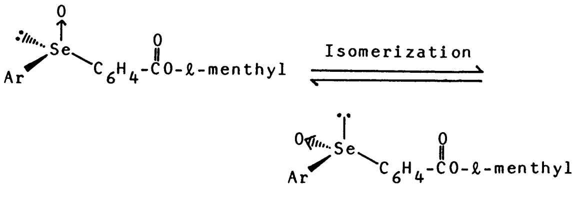
# An Estimation of the Configurational Stability of Diaryl Selenoxides by Means of $^{77}$Se NMR Spectroscopy

Toshio Shimizu, Masato Yoshida, and Michio Kobayashi*
Department of Chemistry, Faculty of Science, Tokyo Metropolitan University, Fukazawa, Setagaya-ku, Tokyo 158

(Received September 25, 1986)

**Synopsis.** The activation energies for the racemization of the optically active diaryl selenoxides were estimated by the use of the $^{77}$Se NMR spectra of the diastereomeric diaryl selenoxides.

Many optically active sulfoxides have been prepared. On the contrary, though, despite repeated attempts,[1)] there has been no example of the isolation of the enantiomerically pure selenoxide until recently. The difficulty of the optical resolution of selenoxide has been attributed to its facile racemization through an achiral hydrate ($RSe(OH)_2R'$) formed by the addition of water to seleninyl group.[2)] A few years ago, the synthesis of the partly optically active alkyl aryl selenoxides was reported by Davis et al.[3,4)] In these alkyl aryl selenoxides, bulky ortho substituents were found to be effective for retarding the racemization via an achiral hydrate.[3)] We succeeded previously in preparing the optically active diaryl selenoxides, which had bulky ortho substituents by using asymmetric oxidation[5)] or optical resolution.[6)] The attempt to resolve optically the diaryl selenoxides which did not possess bulky ortho substituents was unsuccessful as well as in the case of the alkyl aryl selenoxides. Therefore, it seemed that it would be very interesting to study the configurational stabilities of the diaryl selenoxides which have ortho substituents with different bulkiness. The activation energies for the racemization of the optically active diaryl selenoxides have not been studied. When we measured the selenium-77 NMR spectra of diastereomeric mixture of the diaryl selenoxides with the *p*-(*l*-menthoxycarbonyl) group, we noticed the existence of two signals of $^{77}$Se assignable to each isomers.



This finding suggested that the measurement of selenium-77 resonance at various temperatures may make it possible to estimate Gibbs' free energies of activation for the racemization of optically active diaryl selenoxides. We will report here the results of one study of the racemization of diastereomeric diaryl selenoxides obtained from selenium-77 NMR.

## Results and Discussion

Firstly, the $^{77}$Se NMR spectrum of 2,4,6-tri-*t*-butylphenyl 4′-(*l*-menthoxycarbonyl)phenyl selenoxide (**5**) was observed in $CDCl_3$; Compound **5** is a mixture of the diastereomers of d,l- and l,l-form. The chemical shifts of $^{77}$Se NMR for organic selenium compounds spread over a range of the order of 3000 ppm, and the half widths of the signals are usually narrow ($\Delta\nu_{1/2} \lesssim 1$ Hz).[7)] These features of $^{77}$Se resonance allow us to expect that a small difference between two diastereomers may give two well-resolved signals. In fact, the two selenium atoms of the diastereomers of **5** resonated at different frequencies in $^{77}$Se NMR; $\Delta\nu_{ab}$=8.79 Hz (Fig. 1). In the $^1$H NMR (60 MHz) and $^{13}$C NMR (22.5 MHz) spectra of **5**, the assignment of signals to each diastereomer was difficult because of their complexity. Similarly, other diastereomeric selenoxides (**1**—**4**), which had less bulky ortho substituents than the *t*-butyl group, were subjected to $^{77}$Se NMR measurements. The results are summarized in Table 1. Two signals for the diastereomeric selenoxides were observed for **2**, **3**, and **4**. In the case of **1**, which had no ortho substituent, only one signal was observed at 20 °C; at −40 °C, however, the signals were separated.

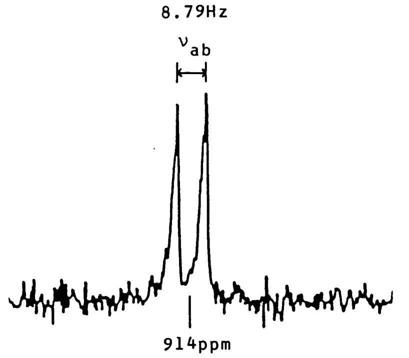
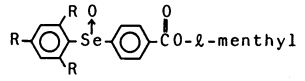


Fig. 1. Resolution of $^{77}$Se signals for diastereomeric selenoxide (**5**) in $CDCl_3$ at room temperature.

Table 1. $^{77}$Se NMR Chemical Shifts and Separations of Signals for Diastereomeric Selenoxides (**1**—**5**)[a)]



| | R | Chemical shift[b)] ppm | $\nu_{ab}$ Hz |
|---|---|---|---|
| **1** | H | 873 | —[c)] |
| **2** | Me | 888 | 7.08 |
| **3** | Et | 886<br>891 d) | 6.10<br>13.67 d) |
| **4** | *i*-Pr | 881 | 4.15 |
| **5** | *t*-Bu | 914 | 8.79 |

a) The spectra were measured in $CDCl_3$ at 20 °C. b) The chemical shifts from MeSeMe were calculated based on PhSeSePh[8)] as the external standard. c) The signals for this selenoxide could not be separated at 20 °C. d) In $C_6D_6$.

Table 2. Coalescence Temperatures ($T_c$) and Gibbs' Free Energies of Activation ($\Delta G^{\neq}$) for Isomerization of Diastereomeric Selenoxides (**1**—**5**)

| Selenoxide | Solvent | Chemical shift[a] | $\nu$ab[a] | $T_c$ | $\Delta G^{\neq}$ |
|---|---|---|---|---|---|
| | | ppm | Hz | K | (kJ mol$^{-1}$) |
| **1** | $CDCl_3$ | 873 | 11.35[b] | 283 | 61.6 |
| **2** | $CHCl_2CHCl_2$ | 892 | 5.86 | 333 | 74.8 |
| **3** | $CHCl_2CHCl_2$ | 929 | 5.62 | 343 | 77.2 |
| **4** | $CHCl_2CHCl_2$ | 886 | 3.42[c] | >373 | >85.8 |
| **5** | $CHCl_2CHCl_2$ | 919 | 12.70 | >353[d] | >77.1 |

a) At 20 °C. b) At −40 °C. c) At 70 °C. d) This selenoxide decomposed slowly during the measurement at 80 °C to give di-[4-(*l*-menthoxycarbonyl)phenyl] diselenide as the major decomposition product.

This observation suggested that the isomerization between two diastereomers of **1** is too fast compared to the $^{77}$Se NMR time scale at 20 °C. The signals of selenoxide (**1**) coalesced at 10 °C. Gibbs' free energy of the activation for the isomerization of diastereomeric **1** was estimated to be 61.6 kJ mol$^{-1}$ in chloroform-*d* from the following equation[9]:

$$\pi\nu_{ab}/\sqrt{2} = (kT/h)\exp(-\Delta G^{\neq}/RT).$$

The two signals for **2**—**5** showed little indication to coalesce at 40 °C in the same solvent. Therefore, in the cases of **2**—**5**, the $^{77}$Se NMR were examined in high-boiling solvents such as *p*-xylene (in the case of **5**), chlorobenzene (in the cases of **2** and **5**), or 1,1,2,2-tetrachloroethane. Interestingly, the isomers of **2**—**5** resonated at the same frequencies in the aromatic solvents, even at 20 °C (in the case of chlorobenzene) or at 20—60 °C (in the case of *p*-xylene). The lack of the separation of the $^{77}$Se signals may be attributed to the specific aromatic solvent-induced shifts, not to the rapid racemization. The measurement of the coalescence temperature was successful in 1,1,2,2-tetrachloroethane. The coalescence temperatures and the free energies of activation for the isomerization are summarized in Table 2. These results indicate that the rate of the isomerization of the selenoxides is strongly dependent on the bulkiness of the ortho substituents. The free energy of the activation for the isomerization obtained from the coalescence temperature of $^{77}$Se signals is, because of the inversion of the configuration around selenium atom in the optically active selenoxides, considered to correspond to the free energy of activation for the racemization. The above results suggest that the optical resolution of the diaryl selenoxides which possess no ortho substituent may be difficult at room temperature because of the facile racemization. For the racemization of the optically active selenoxide, there are two plausible mechanisms. One is the racemization through the formation of the achiral hydrate, and the other is the pyramidal inversion of the configuration around the selenium atom. The values of Gibbs' free energies of activation for the racemization obtained in the present study can reasonably be explained by the pyramidal inversion.

## Experimental

All the melting points were determined on a Yamato MP-21 apparatus. The IR spectra were recorded on a Hitachi 260-10 Spectrometer, the $^1$H NMR spectra, with TMS as an internal standard, on a JEOL-JNM-PMX 60SI apparatus, and the mass spectra, on a JEOL JMS-DX300 Mass Spectrometer. The optical rotations were measured on a JASCO DIP-140 digital polarimeter.

**Measurement of $^{77}$Se NMR spectra.** The $^{77}$Se NMR spectra were recorded at 17.03 MHz on a JEOL FX90Q NMR instrument. About 0.2 mol dm$^{-3}$ solutions of the selenoxides were prepared in solvents well-dried with molecular sieves. The external rocks with DMSO-$d_6$ were used except in the cases using $CDCl_3$ and $C_6D_6$ as solvents. The chemical shifts were measured with complete proton decoupling at room temperature. The separations of the two signals were observed with 0.24 Hz per data point (data points: 8192, sampling time: 4.09s, pulse-flipping angle: 45°).

**Materials.** The diastereomeric 2,4,6-trisubstituted-phenyl 4′-(*l*-menthoxycarbonyl)phenyl selenoxides (**1**—**5**) were synthesized by means of the oxidation[5] of the corresponding selenides, which themselves been prepared by the esterification of 2,4,6-trisubstituted phenyl 4′-carboxyphenyl selenides.[6] For the preparation of latter, two synthetic routes were possible. The phenyl and triisopropylphenyl derivatives were prepared by means of reactions of potassium areneselenolates with 4-iodobenzoic acid in the presence of copper powder.[10] For the preparation of mesityl, triethylphenyl, and tri-*t*-butylphenyl derivatives, the reactions[11] of aryllithiums with *p*-ethoxycarbonylphenyl selenocyanate,[12] followed by hydrolysis, were applied. The physical properties of the selenoxides (**1**—**5**) were measured as a mixture of the diastereomeric isomers. The preparation of **4** was previously reported.[6]

**Phenyl 4-(*l*-Menthoxycarbonyl)phenyl Selenoxide (1):** Mp 164—170 °C; $[\alpha]_D^{24}$—41.1°(*c* 1.12, $CHCl_3$); IR (KBr) $\nu$=825 (Se=O) and 1700 (C=O) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$=0.6—2.3 (18H, m, *l*-menthyl except O-methine H), 4.91 (1H, dt, *J*=5.6, 9.8 Hz, O-methine), 7.3—7.9 (5H, m, aromatic protons of phenyl), 7.73 and 8.09 (4H, ABq, *J*=8.0 Hz, aromatic protons of *p*-substituted phenyl); Exact Mass. Found: *m/z* 432.1146 ($^{80}$Se), Calcd for $C_{23}H_{28}O_3Se$: 432.1204.

**Mesityl 4-(*l*-Menthoxycarbonyl)phenyl Selenoxide (2):** Mp 49.5—53 °C; $[\alpha]_D^{24}$—36.9° (*c* 1.03, $CHCl_3$); IR (KBr) $\nu$=825 (Se=O) and 1710 (C=O) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$=0.6—2.2 (18 H, m, *l*-menthyl except O-methine H), 2.24 (3H, s, para methyl), 2.43 (6H, s, ortho methyl), 4.91 (1H, dt, *J*=4.4, 10.0 Hz, O-methine), 6.79 (2H, s, aromatic protons of mesityl), 7.59 and 8.04 (4H, ABq, *J*=8.0 Hz, aromatic protons of *p*-substituted phenyl); Exact Mass. Found: *m/z* 474.1638 ($^{80}$Se), Calcd for $C_{26}H_{34}O_3Se$: 474.1673.

**2,4,6-Triethylphenyl 4′-(*l*-Menthoxycarbonyl)phenyl Selenoxide (3):** Viscous oil; $[\alpha]_D^{24}$—32.0° (*c* 1.06, $CHCl_3$); IR (liquid film) $\nu$=820 (Se=O) and 1705 (C=O) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$=0.6—2.3 (27H, m, methyl of triethylphenyl and *l*-menthyl except O-methine H), 2.4—3.2 (6H, m, methylene of triethylphenyl), 4.93 (1H, dt, *J*=4.2, 9.9 Hz, O-methine), 6.93 (2H, s, aromatic protons of triethylphenyl), 7.63 and 8.07 (4H, ABq, $J$=8.6 Hz, aromatic protons of *p*-substituted phenyl); Mass: 516 ($^{80}$Se) (M$^+$). Exact Mass. Found: *m/z* 500.2228 ($^{80}$Se) (lack of one oxygen), Calcd for $C_{29}H_{40}O_2Se$: 500.2193.

**2,4,6-Tri-*t*-butylphenyl 4′-(*l*-Menthoxycarbonyl)phenyl Selenoxide (5):** Mp 145—146 °C; $[\alpha]_D^{21}$−23.2° (*c* 1.25, $CHCl_3$); IR (KBr) $\nu$=830 (Se=O) and 1710 (C=O) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$=0.6—2.4 (18H, m, *l*-menthyl except O-methine H), 1.37 (9H, s, methyl of para *t*-butyl), 1.48 (18H, s, methyl of ortho *t*-butyl), 4.89 (1H, dt, $J$=5.6, 10.0 Hz, O-methine), 7.52 (2H, s, aromatic protons of tri-*t*-butylphenyl), 7.01 and 7.91 (4H, ABq, $J$=8.0 Hz, aromatic protons of *p*-substituted phenyl); Mass: 600 ($^{80}$Se) (M$^+$); Exact Mass. Found: *m/z* 584.3182 ($^{80}$Se) (lack of one oxygen), Calcd for $C_{35}H_{52}O_2Se$: 584.3133.

## References

1) For example: W. R. Gaythewaite, J. Kenyon, and H. Phillips, *J. Chem. Soc.*, **1928**, 2280, 2287.

2) M. Oki and H. Iwamura, *Tetrahedron Lett.*, **1966**, 2917; K. B. Sharpless, M. W. Young, and R. F. Lauer, *ibid.*, **1973**, 1979.

3) F. A. Davis, J. M. Billmers, and O. D. Stringer, *Tetrahedron Lett.*, **24**, 3191 (1983).

4) F. A. Davis, O. D. Stringer, and J. P. McCauley, Jr., *Tetrahedron*, **41**, 4747 (1985).

5) M. Kobayashi, H. Ohkubo, and T. Shimizu, *Bull. Chem. Soc. Jpn.*, **59**, 503 (1986).

6) T. Shimizu and M. Kobayashi, *Chem. Lett.*, **1986**, 161.

7) I. Johannsen, L. Henriksen, and H. Eggert, *J. Org. Chem.*, **51**, 1657 (1986).

8) J. D. Odom, W. H. Dawson, and P. D. Ellis, *J. Am. Chem. Soc.*, **101**, 5815 (1979).

9) D. K. Dalling, D. M. Grant, and L. F. Johnson, *J. Am. Chem. Soc.*, **93**, 3678 (1971).

10) K. Šindelář, E. Svátek, J. Metyšová, J. Metyš, and M. Protiva, *Collect. Czech. Chem. Commun.*, **34**, 3792 (1969).

11) B. Greenberg, E. S. Gould, and W. Burlant, *J. Am. Chem. Soc.*, **78**, 4028 (1956).

12) H. Bauer, *Ber.*, **46**, 92 (1913).