CHEMISTRY LETTERS, pp. 161-164, 1986.

SYNTHESIS OF OPTICALLY ACTIVE SELENOXIDE

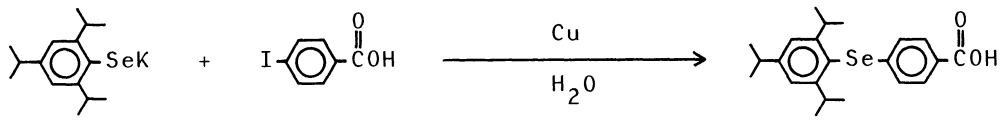
Toshio SHIMIZU and Michio KOBAYASHI*

Department of Chemistry, Faculty of Science,
Tokyo Metropolitan University, Fukazawa,
Setagaya, Tokyo 158

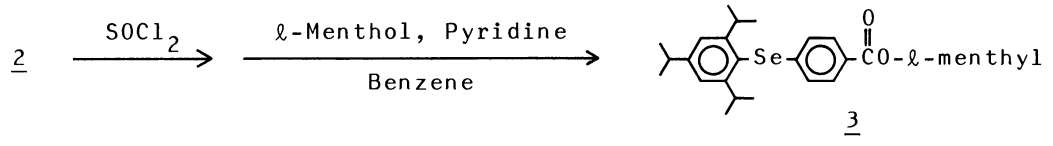
Fractional recrystallization of diastereomeric 2,4,6-triisopropylphenyl 4'-(ℓ-menthyloxycarbonyl)phenyl selenoxide gave optically pure (-)-selenoxide. Transesterification of this diastereomerically pure (-)-selenoxide with methanol gave enantiomeric (-)-2,4,6-triisopropylphenyl 4'-(methoxycarbonyl)-phenyl selenoxide in 88.1% optical purity.

Since optically active sulfoxides were resolved for the first time in 1926[1] many optically active sulfoxides had been isolated up to the present. On the contrary, despite of the repeated attempts,[2] there had been no example of the optically active selenoxide for a long time. Difficulty of optical resolution of selenoxide is attributed the facile racemization due to the formation of achiral hydrates.[2,3] In 1970, two optically active diastereomeric steroidal selenoxides were isolated for the first time.[4] Recently partially active enantiomeric selenoxides were prepared by using bulky substituents to prevent racemization via achiral hydrate by Davis et al.[5] However their optical purities were only 5-11%. We report here the synthesis of diastereomeric optically pure selenoxide and enantiomeric selenoxide with high optical activity.

Diastereomeric 2,4,6-triisopropylphenyl 4'-(ℓ-menthyloxycarbonyl)phenyl selenoxide (dia.-1) was prepared by the following scheme. Reaction of potassium 2,4,6-triisopropylbenzeneselenolate with 4-iodobenzoic acid in water in the



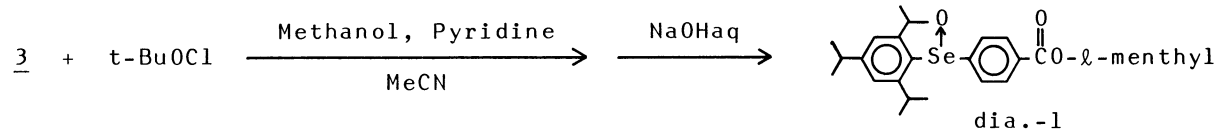
2



3

$[\alpha]_D^{22}$ -30.8° (c 1.16, $CHCl_3$)

mp 120-121 °C (MeOH)



dia.-1

$[\alpha]_D^{19}$ -30.5° (c 1.00, $CHCl_3$)

mp 149-150.5 °C

presence of copper powder gave 2,4,6-triisopropylphenyl 4'-carboxyphenyl selenide (2) in 47% yield after a day of reflux.[6] 2,4,6-Triisopropylphenyl 4'-(ℓ-menthyloxycarbonyl)phenyl selenide (3) was prepared in 84% yield via acid chloride from 2. Oxidation of selenide 3 was achieved with t-butyl hypochlorite in the presence of methanol and pyridine in 91% yield.[7] The $[\alpha]_D$ of resulting selenoxide 1 was -30.5° in chloroform. No asymmetric oxidation of selenide group was observed by HPLC using optically active column.[8] Therefore, this optical rotation must be due to ℓ-menthyl moiety. Fractional recrystallization was repeated from methanol. Optically pure diastereomeric selenoxide (-)-1[9] (1.00 g) was obtained after five recrystallization from 7.30 g of the diastereomeric selenoxide pair dia.-1 (Table 1). The CD spectrum of (-)-1 shows the negative Cotton effect at 290 nm in methanol. Furthermore, 1.45 g of (+)-selenoxide (+)-1

Table 1. Fractional recrystallization of dia.-1

	(-) crystal	(+) from mother liquid
Optical purity[a]	100%	75.3%
$[\alpha]_D$ ($CDCl_3$)[b]	-99.0°	+17.7°
$CD[\theta]_{290}$ (MeOH)	-2.80×10^4	$+1.86\times10^4$
Mp θm/°C	186.5-187.5	147-151

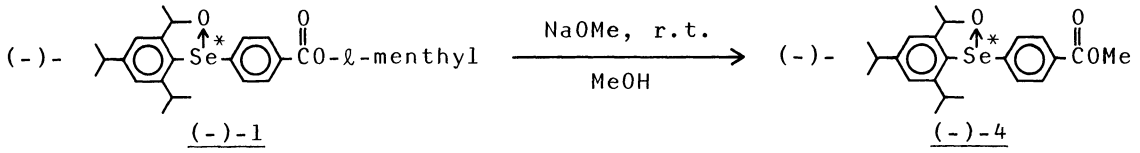
a) Optical purities were determined by HPLC using optically active column.[8]

b) Optical rotations were taken in chloroform at 26 °C ((-)-1) and 19 °C ((+)-1).

was obtained from mother liquid in 75.3% optical purity. This selenoxide (+)-1 has the positive Cotton effect.

Thermal stabilities of optically active selenoxide (-)-1 toward racemization were preliminary examined. Optically active selenoxide (-)-1 is stable in crystalline state at room temperature. Its solution in dry methanol showed no loss of optical activity after 3 h at room temperature. In boiling methanol, however, selenoxide (-)-1 was converted slowly to dia.-1. Optical purity of (-)-1 was decreased from 100% to 50% after about 40 h in boiling methanol. No racemization was detected after 3 h by vigorous stirring in dichloromethane-water in the presence of sodium hydroxide. According to Davis et al.,[5] addition of a trace of p-toluenesulfonic acid monohydrate to (+)-methyl 2,4,6-triisopropylphenyl selenoxide resulted in complete racemization in less than 10 seconds.

Accordingly, we attempted transesterification of (-)-1 under basic conditions, namely with methanol in the presence of sodium methoxide at room temperature.



(-)-1

Optically pure

(-)-4

O.P. 88.1%

$[\alpha]_D^{27}$ -66.3° (c 1.01, $CHCl_3$)

$CD[\theta]_{293}$ -1.57×10^4 (MeOH)

mp 206.5-208 °C

When reaction was followed by HPLC, transesterification was shown to be completed after 4 d. The product was extracted with dichloromethane after addition of water. Removal of the solvent gave a solid product, which was washed with hexane several times. Enantiomeric selenoxide (-)-4[10] was obtained in 66% chemical yield. The structure and chemical purity were confirmed by ^{1}H-NMR and HPLC. Optical purity of (-)-4 was estimated to be 88.1% by HPLC using optically active column.[8] Studies on its absolute configration are under way.

References

1) P. W. B. Harrison, J. Kenyon, and H. Phillips, J. Chem. Soc., 1926, 2079.

2) For example: W. R. Gaythwaite, J. Kenyon, and H. Phillips, J. Chem. Soc., 1928, 2280, 2287.

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

4) D. N. Jones, D. Mundy, and R. D. Whitehouse, J. Chem. Soc., Chem. Commun., 1970, 86.

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

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

7) M. Kobayashi, H. Ohkubo, and T. Shimizu, in press.

8) Bakerbond chiral phase HPLC column DNBPG/Aminopropylsilica; 25 cm × 4.6 mm; using hexane : 2-propanol = 95 : 5 as eluent.

9) Compound (-)-1: Mp 186.5-187.5 °C. $[\alpha]_D^{26}$ -99.0° (c 1.25, $CHCl_3$). $CD[\theta]_{290}$ -2.80×10^4 (MeOH). IR (KBr) ν = 820(Se=O) and 1710(C=O) cm^{-1}. UV (MeOH) 220 (ε 2.24×10^4), 240(2.24×10^4), and 275(1.03×10^4) nm. ^{1}H-NMR (60 MHz, $CDCl_3$) δ= 0.92, 1.24, 1.30 (18H, d, J=6.6 Hz, CH_3 of triisopropylphenyl), 0.6-2.2 (18H, m, ℓ-menthyl except O-methine), 2.89 (1H, hep., J=6.6 Hz, methine of para isopropyl), 3.73 (2H, hep., J=6.6 Hz, methine of ortho isopropyl), 4.93 (1H, dt, J=4.2, 9.9 Hz, O-methine), 7.03 (2H, s, aromatic protons of triisopropylphenyl), 7.61 and 8.07 (4H, ABq, J=8.4 Hz, aromatic protons of p-substituted aromatic ring). Mass M^+ 558(^{80}Se). Found: m/e 542.2661 (^{80}Se)(lack of one oxygen). Calcd for $C_{32}H_{46}O_3{}^{80}Se$: 542.2662.

10) Compound (-)-4: Mp 206.5-208 °C. $[\alpha]_D^{27}$ -66.3° (c 1.01, $CHCl_3$). $CD[\theta]_{293}$ -1.57×10^4 (MeOH). IR (KBr) ν = 820(Se=O) and 1720(C=O) cm^{-1}. UV (MeOH) 214 (ε 2.27×10^4), 237(2.03×10^4), and 275(9.28×10^3) nm. ^{1}H-NMR (60 MHz, $CDCl_3$) δ = 0.92, 1.24, 1.30 (18H, d, J=6.6 Hz, CH_3 of triisopropyl), 2.91 (1H, hep., J=6.6Hz, para methine), 3.73 (2H, hep., J=6.6 Hz, ortho methine), 3.91 (3H, s, methoxy), 7.06 (2H, s, aromatic protons of triisopropylphenyl), 7.65 and 8.10 (4H, ABq, J=7.2 Hz, aromatic protons of p-substituted aromatic ring). Found: m/e 434.1390 (^{80}Se). Calcd for $C_{23}H_{30}O_3{}^{80}Se$: 434.1359.

(Received October 28, 1985)