Substituent Effect on the Enantiomer-Differentiating Reaction of Lithiomethyl *p*-Tolyl Sulfoxide with Meta- or Para-Substituted (*R*)-(−)-Menthyl Benzoates

Norio KUNIEDA,* Takeshi NAKANISHI, and Masayoshi KINOSHITA
Department of Applied Chemistry, Faculty of Engineering, Osaka City University, Sumiyoshi-ku, Osaka 558
(Received February 18, 1989)

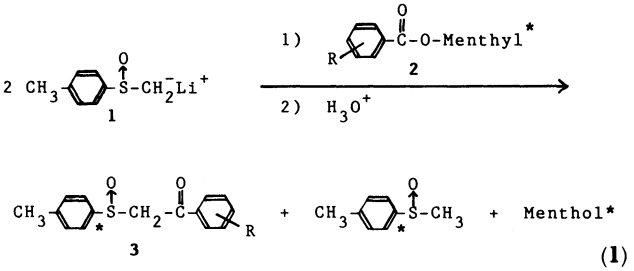
Treatment of (*R*)-(−)-menthyl benzoates, which have a variety of meta- or para-substituents, with 2 equivalents of racemic lithiomethyl *p*-tolyl sulfoxide displays the feature of an enantiomer-differentiating reaction, affording the corresponding optically active β-keto sulfoxides. The degree and the direction of enantioselectivity were affected by the nature of the substituent on benzene ring. The electron-releasing substituents trend to increase the %e.e. value. The reversal in the configuration with the variation in the substituent which has a high electron-withdrawing *p*-CN group was also observed. The *R*/*S* values thus obtained gave a good correlation with Hammett's σ values (r=0.975), affording a negative straight line. Based on these observations, a plausible stereochemical course of this reaction has been discussed.

Electronic effects, in addition to steric bulk, have been evaluated experimentally and theoretically as one of the important factor which controls the direction and the extent of the asymmetric induction in certain asymmetric reactions.[1] On the basis of this concept, the investigation of the substituent effect in asymmetric reactions is considered to afford considerably quantitative informations which may help to clarify the stereochemical course of asymmetric reactions. However, up to now, only a few attentions have been focused on this problem.[2]

During the course of our research concerned with the asymmetric induction by chiral sulfinyl group,[3] we have now found that the reaction of lithiomethyl *p*-tolyl sulfoxide, derived from racemic methyl *p*-tolyl sulfoxide and lithium diethylamide, with a limited amount of substituted (*R*)-(−)-menthyl benzoates displays the feature of an enantiomer-differentiating reaction, affording the corresponding optically active β-keto sulfoxides, and the degree of enantioselectivity of this reaction is markedly affected by the nature of the substituent on benzene ring of the chiral benzoates. In this report, we compile substantial amounts of stereochemical data of the enantiomer-differentiating reaction of racemic α-lithiomethyl *p*-tolyl sulfoxide with (*R*)-(−)-menthyl benzoates possessing a variety of meta- or para-substituents and hence would like to discuss the role of the polar effect of the substituents on the enantioselectivity, as an effort to obtain detailed knowledge for the stereochemistry of this reaction.

Results and Discussion

The reaction of racemic lithiomethyl *p*-tolyl sulfoxide (**1**) with meta- or para-substituted (*R*)-(−)-menthyl benzoates (**2**) was carried out according to a procedure similar to that devised for the reaction of α-lithio sulfoxides with chiral sulfinates or chiral carboxylates described in our previous papers.[3c,f,g] When 2 equivalents of **1**, derived from racemic methyl *p*-tolyl sulfoxide and lithium diethylamide, was allowed to react with **2** in tetrahydrofuran (THF) at −78 °C, the corresponding optically active β-keto sulfoxide (**3**) was produced in a good yield (>92%), together with optically active methyl *p*-tolyl sulfoxide which has the opposite configuration to **3** (Eq. 1). The degree of



(1)

(The star indicates chiral center.)

2 and **3**
a: R=*p*-CH_3O, **b**: R=*p*-*t*-C_4H_9, **c**: R=*p*-CH_3,
d: R=*p*-*i*-C_3H_7, **e**: R=*m*-CH_3, **f**: R=H,
g: R=*p*-Cl, **h**: R=*m*-Cl, **i**: R=*p*-CN.

enantioselectivity of the reaction was estimated by determining the per cent enantiomeric excess (%e.e.) of **3** obtained. That is, the resulting **3** was isolated by a preparative thin-layer chromatography on silica gel and their predominant configuration and the %e.e. value were assigned by direct comparison with the specific rotation of the corresponding authentic (*R*)-(+)-**3**. The authentic (*R*)-(+)-**3** used here was synthesized by the reaction of lithiomethyl *p*-tolyl sulfoxide, derived from optically pure (*R*)-(+)-methyl *p*-tolyl sulfoxide, with the corresponding ethyl benzoates.[3g] Table 1 summarizes the results for the reactions of **1** with nine (*R*)-(−)-menthyl benzoates (**2a—i**) possessing a variety of meta- or para-substituents.

The enantioselectivity of this reaction was sensitive to reaction temperature. The decrease in temperature favored the formation of the predominant enantiomer. The diagram correlating log *R*/*S* against $1/T$ showed

Table 1. Results of the Enantiomer-Differentiating Reaction of α-Lithiomethyl *p*-Tolyl Sulfoxide (**1**) with Chiral Benzoates (**2**)[a]

Benzoates (**2**) R	β-Keto sulfoxides (**3**) $[\alpha]_D^{25}$[b]	$[\alpha]_D^{25}$[c]	%e.e.	*R*/*S*	$\Delta\Delta G^*$ J mol^{-1}	$\Delta\Delta H^*$ kJ mol^{-1}	$\Delta\Delta S^*$ J K^{-1} mol^{-1}
p-CH_3O (**2a**)	**3a** +62.2±2.2°(3)[d]	+253°	24.6	1.65	815		
p-*t*-C_4H_9 (**2b**)	**3b** +53.0±2.2°(2)	+240°	22.1	1.57	729		
p-CH_3 (**2c**)	**3c** +43.8±0.9°(4)	+259°	16.9	1.41	553	−0.70	−0.78
p-*i*-C_3H_7 (**2d**)	**3d** +45.2±3.6°(3)	+248°	18.2	1.45	597		
m-CH_3 (**2e**)	**3e** +37.1±2.1°(3)	+253°	14.7	1.35	480		
H (**2f**)	**3f** +35.5±2.3°(7)	+265.5°	13.4	1.31	438	−0.58	−0.75
p-Cl (**2g**)	**3g** +24.7±3.9°(4)	+269°	9.2	1.20	300	−0.40	−0.43
m-Cl (**2h**)	**3h** +9.7±2.3°(4)	+260°	3.7	1.08	120		
p-CN (**2i**)	**3i** −5.0±0.5°(3)	+315°	1.6	1.03[e]	52		

a) In THF, at −78°C. b) In acetone. c) Specific rotations of the authentic (*R*)-(+)-β-keto sulfoxides (in acetone). d) Average values of 2—7 experiments. The number of experiments is shown in parentheses. e) *S*/*R*.

a linear positive slope over 103° temperature range (from 25 °C to −78 °C). The $\Delta\Delta H^*$ and $\Delta\Delta S^*$ values obtained in the reactions for **2c**, **2f**, and **2g** are listed in Table 1. These exhibited small negative values.

Table 1 clearly reveals that the %e.e. value for **3** obtained markedly affected by the nature of the substituent R. The degree of enantioselectivity varies from 1.6% to 24.6%. As gererally observed, the electron-releasing substituents trend to increase the %e.e. value. The best result has been obtained from the reaction of **1** with **2a** (R=*p*-CH_3O), affording (*R*)-(−)-**3a** of a 24.6% optical purity. Furthermore, the reversal in the configuration with the variation in the substituent R is also observed. Namely, the (*R*)-(−)-menthyl benzoates **2a**, **2b**, **2c**, **2d**, **2e**, **2f**, **2g**, and **2h** preferentially reacted with (*R*)-**1** to yield an excess of (*R*)-**3a—h**, while the ester **2i** which has a high electron-withdrawing *p*-CN group preferentially reacted with (*S*)-**1**, affording (*S*)-**3i** in excess.

When the logarithms of the *R*/*S* values thus obtained were plotted against Hammett's σ values,[4] as shown in Fig. 1, a negative straight line was obtained with the correlation coefficient *r*=0.975. In our previous paper,[3g] we have reported that the reaction of aryl lithiomethyl sulfoxides with (*R*)-(−)-menthyl carboxylates (R′-CO-O-Menthyl) is affected drastically by a steric bulk of the ester moiety R′. However, in the present reaction the demand for the steric effect owing to the substituent R on benzene ring was found to be negligibly small, even where R was bulky *t*-butyl group. Therefore, it can be recognized that the enantioselectivity on the reaction of **1** with **2** should be dependent on the polar effect of the substituent R.

Next the kinetic experiment was conducted on the rate of the reactions using **2a** (R=*p*-CH_3O), **2c** (R=*p*-CH_3), **2f** (R=H), and **2g** (R=*p*-Cl) in THF at −78 °C. The rate was measured by checking the consumption of the starting **1** by means of ^{1}H NMR (see Experimental). The resulting second order rate constants are listed in Table 2, and are found to be in a good correlation with Hammett's σ values[4] with a large positive σ value of

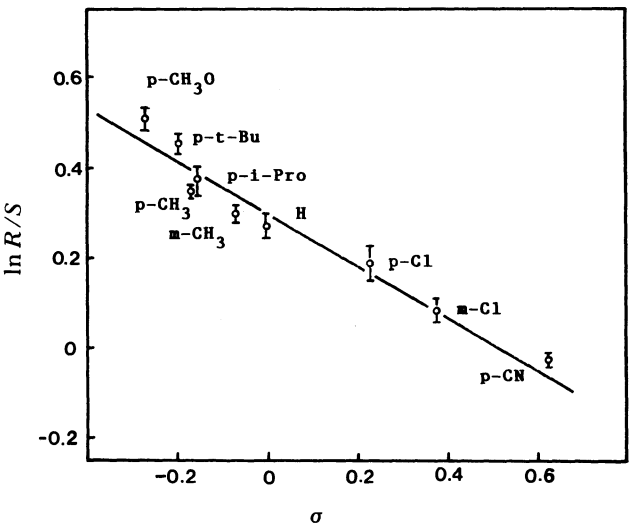


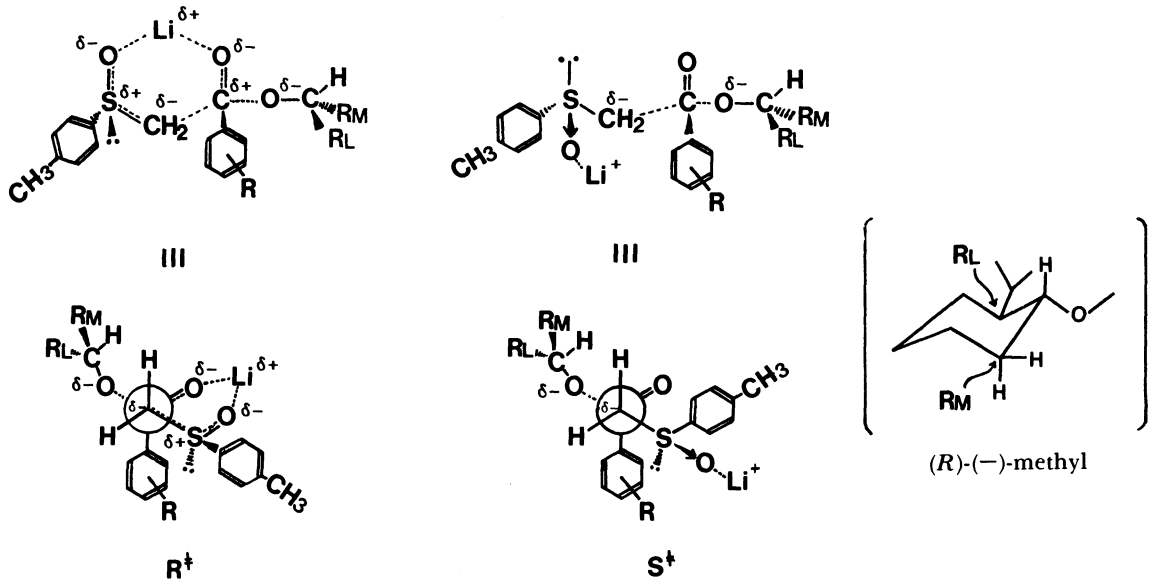
Fig. 1. ln *R*/*S* values of **3** obtained plotted against σ-values.

Table 2. Rate Constants of the Reaction of **1** with Chiral Benzoates (**2**)[a]

Benzoates (**2**) R	k_2 l mol^{-1} s^{-1}
p-CH_3O (**2a**)	4.75±0.55×10^{-4}
p-CH_3 (**2c**)	1.19±0.03×10^{-3}
H (**2f**)	3.67±0.19×10^{-3}
p-Cl (**2g**)	2.45±0.13×10^{-2}

a) In THF, at −78°C (see Experimental).

+3.40 (*r*=0.999). The electron-withdrawing substituent on benzene ring of **2** increases the rate of the reaction. It reveals that the degree of enantioselectivity of the reaction decreases with increasing the reaction rate. This σ correlation and the magnitude of the ρ value of the kinetic data also suggest well that the reaction of **1** with **2** takes place through the B_{AC}-2 type mechanism[5] like in the case of the saponification of (−)-menthyl benzoates (ρ=2.628, at 30 °C).[6]



(The symbols R_M and R_L indicate medium and large groups respectively.)

Scheme 1.

As one of the current of stereochemical studies on the electrophilic substitutions of α-lithio sulfoxides, Marquet et al.[7] and Biellmann et al.[8] have proposed that an electrophilic assistance (a chelation) by the lithium cation on the α-lithio sulfoxides towards the electrophiles plays an important role. On the basis of this evidence together with the B_{AC}-2 mechanism and the prefered configuration for the (*R*)-(−)-menthyl carboxylates,[9] we have proposed[3g] that the reaction of aryl lithiomethyl sulfoxides with (*R*)-(−)-menthyl carboxylates proceeds via a six-membered cyclic transition state.[3b,10] Acoording to this prediction, as well as the steric requirements,[12] the reaction of (*R*)-(−)-menthyl benzoates (**2**) with (*R*)-**1** affording (*R*)-**3** takes a transition state **R*** in Scheme 1 preferentially. Most of the results for the direction of enantioselectivity of this reaction agree fairly well with this prediction. However contrary to our expections, the reaction **2i** with **1** afforded (*S*)-**3i** as described above. The change of the degree of enantioselectivity owing to the substituent R on benzene ring and the reversal in configuration from (*R*) to (*S*) in going from **3h** to **3i** may be attributed to the conformational change of the transition state. The two alternative transition states **R*** and **S*** in Scheme 1 may be postulated according to the polar character of the substituent R. There are differences between the two routes in the degree of bonding of both entering and leaving groups on carbonyl carbon atom at the transition state. Actually, it has been reported that the transition-state geometry is affected by the change of substituents.[13]

The reaction of **1** with (*R*)-(−)-menthyl benzoates which have the electron-releasing substituent proceed through the transition state **R*** which exhibits the formation of tight chelation by lithium cation, since the electron-releasing substituent on benzene ring of **2** should contribute to the formation of a rigid transition state. While (*R*)-(−)-menthyl benzoates which have the electron-withdrawing substituent such as *p*-CN show high reactivity toward **1**, and proceed preferentially through the formation of a loose transition state **S*** which does not participate in the chelate formation by lithium cation. This transition state is less sterically hindered than **R***. Incidentally, the lithium cation in the transition state **S*** is perhaps located at the sulfinyl oxigen, since it has been known that the lithiomethyl phenyl sulfoxide is stabilized by an internal chelation between the metalated carbon and the sulfinyl oxygen.[7]

Table 3. Results of the Reactions of **1** with **2f** and **2i** in the Presence of a Lithium Cation Trapping Agent[a]

Benzoates (**2**)		%e.e. of **3f** and **3i**	
		None	Kryptofix 211[b]
2f	**3f**	13.4(R)[c]	3.8(R)
2i	**3i**	1.6(S)	4.3(S)

a) In THF, at −78°C. b) 1.1 Equivalents based on **1**. c) Predominant configuration.

That is, a gradual change of the transition state from **R*** to **S*** with the increase of the electron-withdrawing character of the substituent R is posturated. In order to get a clue of this, the reactions of **1** with **2f** and **2i** were carried out in the presence of 4,7,13,18-tetraoxa-1,10-diazabicyclo[8.5.5]eicosane (Kryptofix 211)[14] as a trapping agent of the lithium cation. The results are listed in Table 3. To cite the result, the addition of 1.1 equivalents of Kryptofix 211 to the reaction of **1** with **2f** decreases the %e.e. value of (*R*)-**3f** about 3.5 times.

While the addition of 1.1 equivalents of Kryptofix 211 to the reaction of **1** with **2i** increases the %e.e. value of (*S*)-**3i** about 2.7 times.

Inspection of these data indicates that the transition state of the reaction of **1** with (*R*)-(−)-menthyl benzoates (**2**) markedly affected by the nature of the substituent R on benzene ring. We have now considered that the apparent difference in the mode of the transition states between **R*** and **S*** arises from the polar effect exerted by the substituent R.

Experimental

General. The optical rotations were measured with a Jasco DIP-360 type polarimeter. The ^{1}H NMR spectra were determined by using Jeol PS-100 spectrometer; the chemical shifts are reported in δ units, using tetramethylsilane as the internal reference. All the melting points were obtained with a Yanaco MP apparatus and are uncorrected. The IR spectra were taken on a Jasco A-202 type spectrometer.

Starting Materials. Racemic methyl *p*-tolyl sulfoxide was prepared by the periodate oxidation of methyl *p*-tolyl sulfide;[15] bp 99—100 °C/1.5 Torr (1 Torr=133.322 Pa), mp 43 °C (lit,[16] 42—43 °C). (*R*)-(+)-Methyl *p*-tolyl sulfoxide was prepared from (−)-menthyl (*S*)-*p*-toluenesulfinate, mp 107—107.5 °C, $[\alpha]_D^{25}$ −200° (*c* 0.520, acetone), and methylmagnesium iodide according to the method developed by Andersen;[17] mp 74.5 °C, $[\alpha]_D^{20}$ +146° (*c* 0.460, acetone)[lit,[18] mp 73—74.5 °C, $[\alpha]_D$ +145.5° (acetone)]. (−)-Menthol of commercial grade (Hoei Chemicals, Osaka) was used without further purification. (*R*)-(−)-Menthyl benzoates (**2**) were prepared by treating (−)-menthol with the corresponding substituted benzoic acid chlorides in dry ether in the presence of pyridine. $C_{10}H_{19}$-O-CO-C_6H_4-R; [R, mp or bp, specific rotation (*c*, solvent)], *p*-CH_3O (**2a**); 160—161 °C/1 Torr (lit,[19] 229—230 °C/15 Torr), $[\alpha]_D^{20}$ −79.2° (0.671, C_2H_5OH) (lit,[19] $[\alpha]_D^{20}$ −86.5° (neat)), *p*-*t*-C_4H_9 (**2b**); 171—172 °C/1 Torr, $[\alpha]_D^{20}$ −71.1° (1.56, C_2H_5OH), *p*-CH_3 (**2c**); 138—139 °C/1 Torr (lit,[19] 196—198 °C/11 Torr), $[\alpha]_D^{22}$ −85.3° (1.26, C_2H_5OH) (lit,[19] $[\alpha]_D^{20}$ −89.9° (neat)), *p*-*i*-C_3H_7 (**2d**), 166 °C/1—2 Torr, $[\alpha]_D^{20}$ −75.7° (1.37, C_2H_5OH), *m*-CH_3 (**2e**); 140 °C/2 Torr (lit,[6] 109—110 °C/0.1—0.2 Torr), $[\alpha]_D^{20}$ −85.9° (1.18, C_2H_5OH), $[\alpha]_D^{20}$ −89.6° (1.28, C_6H_5) (lit,[20] $[\alpha]_D$ −88.5° (C_6H_5)), H (**2f**); 54.5 °C (lit,[21] 55 °C), $[\alpha]_D^{20}$ −90.5° (1.53, C_2H_5OH) (lit,[21] $[\alpha]_D^{20}$ −83.5° (C_2H_5OH)), *p*-Cl (**2g**); 146 °C/0.5 Torr (lit,[6] 156 °C/1 Torr), $[\alpha]_D^{20}$ −78.3° (1.09, C_2H_5OH) (lit,[22] −80.6° (neat)), *m*-Cl (**2h**); 146—147 °C/1 Torr (lit,[6] 137 °C/0.5 Torr), $[\alpha]_D^{20}$ −80.0° (1.36, C_2H_5OH) (lit,[22] $[\alpha]_D$ −80.45° (neat)), *p*-CN (**2i**); ca. 150 °C/0.5 Torr (lit,[6] ca. 185 °C/1 Torr), $[\alpha]_D^{20}$ −81.0° (2.10, C_2H_5OH). Tetrahydrofuran (THF) was purified by fresh distillation from a solution of sodium benzophenone ketyl before use in all reactions. Butyllithium was obtained as a 1.56 mol dm^{-3} solution in hexane from Mitsuwa Chemical Co., Ltd. (Osaka). Kryptofix 211 was purchased from MERCK and used without further purification.

Reaction of Racemic α-Lithiomethyl *p*-Tolyl Sulfoxide (1) with Substituted (*R*)-(−)-Menthyl Benzoates (2). Into a 50 cm^3 two-necked, round-bottomed flask equipped with a rubber septum, a magnetic stirring bar, and a nitrogen-inlet tube was placed 15 cm^3 of dry THF, 5 mmol of butyllithium in hexane, and 370 mg (5 mmol) of diethylamine through the septum via a syringe at 0 °C under nitrogen. The flask was cooled to −78 °C, a solution of 5 mmol of racemic methyl *p*-tolyl sulfoxide in 2.5 cm^3 of dry THF was added, and the solution was stirred vigorously for 30 min at 0 °C. A solution of a (*R*)-(−)-menthyl benzoate (2.5 mmol) in 2.5 cm^3 of dry THF was then injected via a syringe, drop by drop, into the solution at −78 °C. After being stirred for an adequate time at −78 °C (the progresses of the reaction was monitored by TLC), the mixture was treated with water (10 cm^3), acidified (ca. pH 3) with 10% hydrochloric acid, and extraced with chloroform (3×10 cm^3). The combined chloroform layers were washed with brine, dried (Na_2SO_4), and evaporated in vacuo. Preparative thin-layer chromatography of the residue on silica gel (MERCK 60PF$_{245}$), using ether as the eluent, gave the analytically pure β-keto sulfoxide (**3**) which was subjected to optical rotation measurement.

Preparation of Authentic (*R*)-(+)-β-Keto Sulfoxides (3). The authentic optically pure meta- or para-substituted (*R*)-(+)-α-(*p*-tolylsulfinyl)acetophenones (**3**) were prepared by the same procedure as described in our previous paper.[3g] The treatment of α-lithiomethyl *p*-tolyl sulfoxide, derived from 1.54 g (10 mmol) of (*R*)-(+)-methyl *p*-tolyl sulfoxide and 11 mol of lithium diethylamide, was treated with 5 mmol of an ethyl benzoate in 25 cm^3 of dry THF at 0 °C. By a work-up similar to that used for the reaction of **1** and **2** described above, the corresponding dextrorotatory β-keto sulfoxide was produced. Recrystallization from ether or ethyl acetate yielded the analytically pure β-keto sulfoxide in satisfactory yield (78—93%). The authentic β-keto sulfoxides (**3**) obtained by this procedure exhibited the following properties.

(*R*)-(−)-**3a**: mp 78.5—79 °C. $[\alpha]_D^{25}$ +253° (*c* 0.485, acetone). ^{1}H NMR ($CDCl_3$): δ=2.39 (s, 3H, -CH_3), 3.87 (s, 3H, -O-CH_3), 4.23, 4.49 (dd, *J*=14 Hz, 2H, -CH_2-), 6.85—8.00 (m, 8H, aromatic). IR (KBr): 2900, 1657, 1600, 1570, 1310, 1260, 1175, 1037, 1026, 986, 825 cm^{-1}.

Found: C, 66.38; H, 5.35%. Calcd for $C_{16}H_{16}SO_3$: C, 66.64; H, 5.59%.

(*R*)-(+)-**3b**; mp 88—88.5 °C. $[\alpha]_D^{25}$ +240° (*c* 0.335, acetone). ^{1}H NMR ($CDCl_3$): δ=1.30 (s, 9H, -C(CH_3)$_3$), 2.35 (s, 3H, -CH_3), 4.26, 4.46 (dd, *J*=14 Hz, 2H, -CH_2-), 7.15—7.85 (m, 8H, aromatic). IR (KBr): 2900, 1670, 1602, 1297, 1090, 1043, 1034, 995 cm^{-1}.

Found: C, 72.58; H, 7.15%. Calcd for $C_{19}H_{22}SO_2$: C, 72.57; H, 7.05%.

(*R*)-(+)-**3d**; mp 81.5 °C. $[\alpha]_D^{25}$ +248° (*c* 0.385, acetone). ^{1}H NMR ($CDCl_3$): δ=1.23 (d, *J*=7 Hz, 6H, -CH(C$\underline{H}_3$)$_2$), 2.35 (s, 3H, -CH_3), 2.87 (sept, 1H, -C$\underline{H}$(CH_3)$_2$), 4.25, 4.48 (dd, *J*=14 Hz, 2H, -CH_2-), 7.15—7.85 (m, 8H, aromatic). IR (KBr): 2900, 1675, 1600, 1300, 1040, 1032, 1015, 995, 830 cm^{-1}.

Found: C, 71.33; H, 6.77%. Calcd for $C_{18}H_{20}SO_2$: C, 71.97; H, 6.71%.

(*R*)-(+)-**3e**; mp 92.5 °C. $[\alpha]_D^{25}$ +253° (*c* 0.269, acetone). ^{1}H NMR ($CDCl_3$): δ=2.38 (s, 6H, 2×-CH_3), 4.25, 4.49 (dd, *J*=14 Hz, 2H, -CH_2-), 7.17—7.63 (m, 8H, aromatic). IR (KBr): 2590, 1670, 1603, 1300, 1150, 1050, 1033, 805 cm^{-1}.

Found: C, 70.32; H, 5.99%. Calcd for $C_{16}H_{16}SO_2$: C, 70.56; H, 5.90%.

(*R*)-(+)-**3g**; mp 168—169 °C. $[\alpha]_D^{25}$ +269° (*c* 0.541, acetone). ^{1}H NMR ($CDCl_3$): δ=2.39 (s, 3H, -CH_3), 4.27, 4.44 (dd, *J*=14 Hz, 2H, -CH_2-), 7.18—7.93 (m, 8H, aromatic). IR (KBr): 1674, 1585, 1290, 1085, 1035, 1017, 993, 825 cm^{-1}.

Found: C, 61.26; H, 4.38%. Calcd for $C_{15}H_{13}SO_2Cl$: C, 61.54; H, 4.47%.

(*R*)-(+)-**3h**; mp 105.5 °C. $[\alpha]_D^{25}$ +260° (*c* 0.226, acetone). ^{1}H NMR ($CDCl_3$): δ=2.39 (s, 3H, $-CH_3$), 4.27, 4.47 (dd, *J*=14 Hz, 2H, $-CH_2-$), 7.24—7.86 (m, 8H, aromatic). IR (KBr): 2920, 1675, 1592, 1425, 1300, 1200, 1085, 1039, 1028, 1015, 810 cm^{-1}.

Found: C, 61.54; H, 4.41%. Calcd for $C_{15}H_{13}SO_2Cl$: C, 61.54; H, 4.47%.

(*R*)-(+)-**3i**; mp 171—172 °C. $[\alpha]_D^{25}$ +315° (*c* 0.263, acetone). ^{1}H NMR ($CDCl_3$): δ=2.40 (s, 3H, $-CH_3$), 4.36, 4.43 (dd, *J*=14 Hz, 2H, $-CH_2-$), 7.31, 7.51 (dd, 4H, aromatic), 7.75, 7.96 (dd, 4H, aromatic). IR (KBr): 2900, 1686, 1405, 1356, 1295, 1086, 1034, 1016, 994, 835, 805 cm^{-1}.

Found: C, 67.43; H, 4.60%. Calcd for $C_{16}H_{13}SO_2N$: C, 67.82; H, 4.62%.

The authentic (*R*)-(+)-**3c** and (*R*)-(+)-**3f** have already been prepared in our previous paper.[3g]

Measurement of Enantiomeric Purity. The polarimetric analysis for the mixture of (*R*)- and (*S*)-β-keto sulfoxides (**3**) in acetone indicated that the specific rotation was nicely correlated with the composition of the enantiomeric mixture.[23] A typical experiment using the mixture of optically pure (*R*)-(+)-**3f** and racemic **3f** of various proportions is shown in Fig. 2. Therefore, the per cent enantiomeric excess (%e.e.) for the β-keto sulfoxides (**3**) obtained from the enantiomer-differentiating reaction of **1** and **2** was assigned by direct comparison with the specific rotation of the corresponding authentic **3**, i.e., %e.e.=optical purity=$[\alpha]_{obs}/[\alpha]_{max}\times 100$.[25]

Measurement of the Rate Constant for the Reaction of 1 and 2. The same experimental setup as has been described above was used. A solution of racemic **1** (2 mmol) in 7 cm^3 of dry THF was mixed rapidly with a solution of **2** (1 mmol) in 1 cm^3 of dry THF at −78 °C under nitrogen. From time to time the solution was quenched with water (10 cm^3) to stop the reaction, acidified, and extracted with chloroform (3×30 cm^3). The chloroform layer was washed with brine (3×20 cm^3) and dried (Na_2SO_4). The residue from the organic layer was subjected to the ^{1}H NMR measurement, and the consumption of **1** was measured by checking the methyl proton signal (δ=2.57, $CDCl_3$) of the resulting methyl *p*-tolyl sulfoxide. The second-order rate constant was determined according to the following equation; $kt=1/(C_1-C_2)\cdot\ln C_2(C_1-x)/C_1(C_2-x)$, where C_1 and C_2 represent the molar concentrations of **1** and **2** at time 0, respectively, and x represents the molar concentration that has reacted at time t.

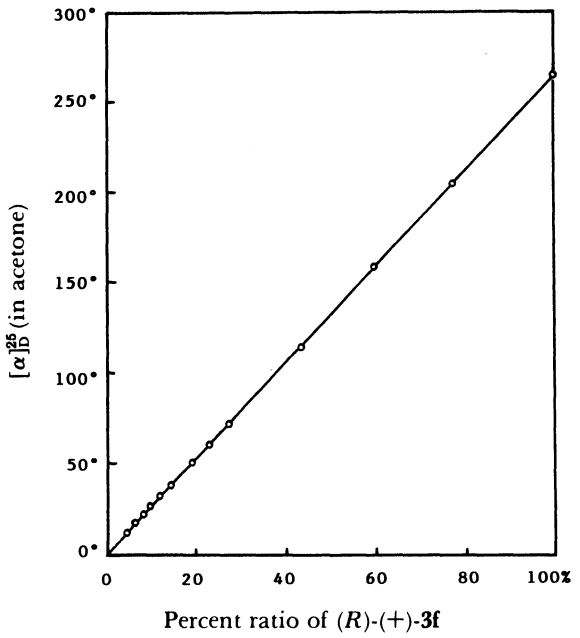


Fig. 2. Relationship between the per cent ratio of (*R*)-(+)-**3f** and the specific rotation.

References

1) H. B. Kagan and J. C. Fiaud, "New Approaches in Asymmetric Synthesis," in "Topics in Stereochemistry," ed by E. L. Eliel and N. Allinger, Interscience Pub., New York, N. Y. (1978), Vol. 10, p. 175; and references cited therein.

2) W. H. Pirkle, M. S. Hockstra, and W. H. Miller, *Tetrahedron Lett.*, **1976**, 2109; J. P. Guetté, J. Capillon, M. Perlet, and M. Guetté, *ibid.*, **1974**, 2409; S. Takenaka and M. Koden, *J. Chem. Soc., Chem. Commun.*, **1978**, 830; J. Capillon and J. P. Guetté, *Tetrahedron*, **35**, 1807, 1817 (1979); L. Duhamel and J. C. Plaquevent, *Bull. Soc. Chim. Fr.*, **1982**, II-75; H. Tomioka, N. Hayashi, Y. Izawa, and M. T. H. Lin, *J. Chem. Soc., Chem. Commun.*, **1984**, 476: B. Alcaide, C. L. Mardomingo, R. Perez-Ossorio, J. Plumet, R. Phan-Tan-Luu, and M. Sargent, *Can. J. Chem.*, **63**, 2241 (1985); F. A. Bottino and P. Finocchiaro, *Polyhedron*, **4**, 1507 (1985); C. K. Cheung, L. T. Tseng, M.-H. Lin, S. Srivastava, and W. J. leNoble, *J. Am. Chem. Soc.*, **108**, 1598 (1986); D. L. Hughes, U. H. Dolling, K. M. Ryan, E. F. Schoenewaldt, and E. J. J. Graboski, *J. Org. Chem.*, **52**, 4745 (1987).

3) a) N. Kunieda, J. Nokami, and M. Kinoshita, *Chem. Lett.*, **1973**, 871; b) N. Kunieda, J. Nokami, and M. Kinoshita, *ibid.*, **1974**, 369; c) N. Kunieda, J. Nokami, and M. Kinoshita, *Bull. Chem. Soc. Jpn.*, **49**, 256 (1976); d) N. Kunieda, J. Nokami, and M. Kinoshita, *Chem. Lett.*, **1977**, 289; e) J. Nokami, N. Kunieda, and M. Kinoshita, *ibid.*, **1977**, 249; f) N. Kunieda, H. Motaki, and M. Kinoshita, *ibid.*, **1978**, 713; g) N. Kunieda, A. Suzuki, and M. Kinoshita, *Bull. Chem. Soc. Jpn.*, **54**, 1143 (1981); h) N. Kunieda and M. Kinoshita, *Phosphorus and Sulfur*, **10**, 383 (1981); i) J. Nokami, T. Mandai, A. Nishimura, T. Takeda, S. Wakabayashi, and N. Kunieda, *Tetrahedron Lett.*, **27**, 5109 (1986); j) N. Kunieda and M. Kinoshita, *Chem. Express*, **3**, 121 (1988).

4) The σ value used here is that reported by Jaffe; H. H. Jaffe, *Chem. Rev.*, **53**, 191 (1953).

5) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca and London (1969), p. 1170.

6) R. W. Taft, Jr., M. S. Newman, and F. H. Verhoek, *J. Am. Chem. Soc.*, **72**, 4511 (1950).

7) G. Chassaing, R. Lett, and A. Marquet, *Tetrahedron Lett.*, **1978**, 471; G. Chassaing and A. Marquet, *Tetrahedron*, **34**, 1399 (1978).

8) J. F. Biellmann and J. J. Vicens, *Tetrahedron Lett.*, **1978**, 467.

9) A. McL. Mathieson, *Tetrahedron Lett.*, **1965**, 4137; R. J. B. Marsden and L. E. Sutton, *J. Chem. Soc.*, **1936**, 1383; M. Legrand and M. J. Rougier, "Application of the Optical Activity to Stereochemical Determination," in "Stereochem-

istry Fundamentals and Methods," ed by H. B. Kagan, Georg Thieme Publishers, Stuttgart (1977), Vol. 2, p. 130.

10) Many six-membered cyclic transition states have been proposed in the asymmetric induction by chiral sulfinyl compounds using organo metallic compounds.[3b,11]

11) For example; R. Annunziata, M. Cinquini, F. Cozzi, F. Montanari, and A. Restelli, *J. Chem. Soc., Chem. Commun.*, **1983**, 1138; M. Cinquini, A. Manfredi, H. Molinari, and A. Restelli, *Tetrahedron*, **41**, 4929 (1985); A. Annunziata, M. Cinquini, F. Cozzi, and A. Restelli, *J. Chem. Soc., Perkin Trans. 1*, **1985**, 2289, 2293; G. Solladie, C. Greck, G. Demailly, and A. Solladié-Cavallo, *Tetrahedron Lett.*, **23**, 5047 (1982); G. H. Posner and E. Asirvatham, *J. Org. Chem.*, **50**, 2589 (1985).

12) V. Prelog, *Helv. Chim. Acta*, **36**, 708 (1953); D. J. Cram and F. A. Abd Elhafez, *J. Am. Chem. Soc.*,**74**, 5828 (1952); T. J. Leitereg and D. J. Cram, *ibid.*, **90**, 4019 (1968).

13) E. R. Thornton, *J. Am. Chem. Soc.*, **89**, 2915 (1967); G. S. Hammond, *ibid.*, **77**, 334 (1955); R. A. More O'Ferrall, *J. Chem. Soc. B*, **1970**, 268, 274.

14) J. M. Lehn and J. P. Sauvage, *J. Chem. Soc., Chem. Commun.*, **1971**, 440.

15) N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, **27**, 282 (1962).

16) A. Cerniani and G. Modena, *Gazz. Chim. Ital.*, **89**, 834 (1959).

17) K. K. Andersen, *Tetrahedron Lett.*, **1962**, 93.

18) K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, **87**, 1958 (1965).

19) J. B. Cohen and H. W. Dudley, *J. Chem. Soc.*, **97**, 1732 (1910).

20) J. Kenyon and B. H. Pickard, *J. Chem. Soc.*, **107**, 35 (1915).

21) H. Rupe, *Justus Liebigs Ann. Chem.*, **327**, 157 (1903).

22) J. B. Cohen and S. H. C. Briggs, *J. Chem. Soc.*, **83**, 1213 (1903).

23) Horeau[24] has been reported that the per cent enantiomeric purity is not always same as the per cent optical purity.

24) A. Horeau, *Tetrahedron Lett.*, **1969**, 3121.

25) M. Raban and K. Mislow, "Topics in Stereochemistry," ed by E. L. Eliel and N. Allinger, Interscience Pub., New York, N. Y. (1967), Vol. 2, pp. 199—230.