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Asymmetric Induction Reactions. II.[1] Stereochemical Studies on Asymmetric [2,3] Sigmatropic Rearrangements Using Chiral Ketenimines

KUNIO HIROI* and SHUKO SATO

Synthetic Chemistry Laboratory, Tohoku College of Pharmacy, 4-4-1, Komatsushima, Sendai, Miyagi 983, Japan

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Stereochemical studies were performed on asymmetric [2,3] sigmatropic rearrangements of sulfur ylides derived from chiral ketenimines possessing various kinds of substituents and prochiral sulfur ylides.

A mechanistic pathway for these rearrangements is proposed on the basis of the stereochemical results obtained. New asymmetric centers are induced on the sulfur atoms of the ylides during the reactions.

Keywords——chiral ketenimine; sulfur ylide; prochiral sulfur ylide; [2,3] sigmatropic rearrangement; asymmetric induction

Asymmetric sigmatropic rearrangements have received much attention in recent years as a means for the efficient creation of new asymmetric carbons.[2-6] We have reported a useful method for the creation of an asymmetric carbon by a [2,3] sigmatropic rearrangement using chiral ketenimines and trimethylsulfonium ylide.[1,7] Reaction of chiral ketenimines with trimethylsulfonium ylide resulted in a [2,3] sigmatropic rearrangement of the intermediary sulfur ylides followed by acid hydrolysis of the resulting imines to give an optically active α′-substituted methyl ketone. We wish to report herein further stereochemical studies on this

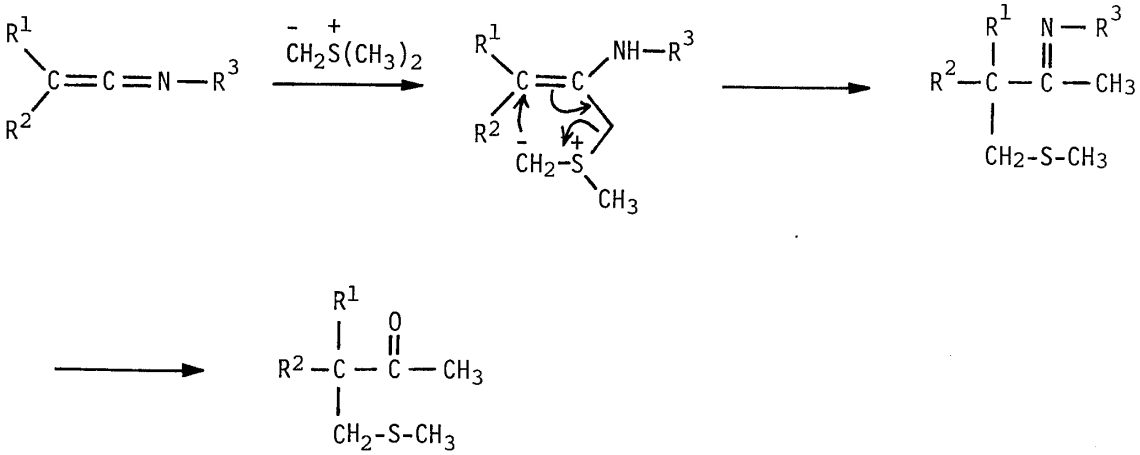
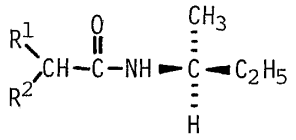


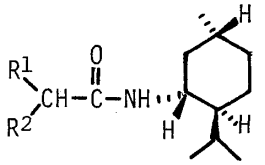
Chart 1

asymmetric [2,3] sigmatropic rearrangement by using chiral ketenimines possessing various kinds of substituents and prochiral sulfur ylides.

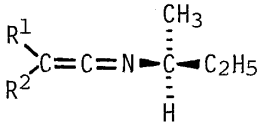
The ketenimines **3** and **4** were prepared from the corresponding amides **1** and **2** by chlorination of the amides with phosphorus pentachloride followed by dehydrochlorination of the imidoyl chlorides with triethylamine.[1,8] Steric effects on this asymmetric induction were



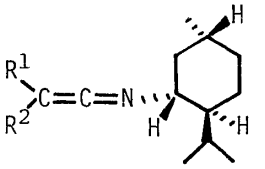
1a–d



2a–d



3a–d

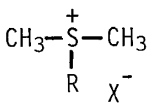


4a–d

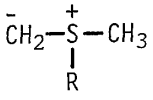
a: $R^1 = C_6H_5$, $R^2 = CH_3$
b: $R^1 = C_6H_5$, $R^2 = CH_2CH_3$
c: $R^1 = C_6H_5$, $R^2 = CH_2CH{=}CH_2$
d: $R^1 = o\text{-}CH_3OC_6H_4$, $R^2 = CH_2CH_3$

Chart 2

studied by using these ketenimines possessing various substituents as R^1 and R^2, such as a phenyl or *o*-methoxyphenyl group, and a methyl, ethyl, or allyl group, respectively. Reaction of the ketenimines **3** and **4** with **6a** followed by acidic hydrolysis gave optically active α′-substituted methyl ketones **7**—**10**. The results are summarized in Table I.

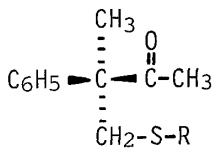


5a: $R = CH_3$, $X = I$
5b: $R = C_6H_5$, $X = ClO_4$
5c: $R = o\text{-}CH_3C_6H_4$, $X = ClO_4$
5d: $R = C_{10}H_7(\beta)$, $X = ClO_4$
5e: $R = C_{10}H_7(\alpha)$, $X = ClO_4$

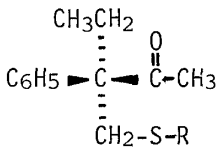


6a: $R = CH_3$
6b: $R = C_6H_5$
6c: $R = o\text{-}CH_3C_6H_4$
6d: $R = C_{10}H_7(\beta)$
6e: $R = C_{10}H_7(\alpha)$

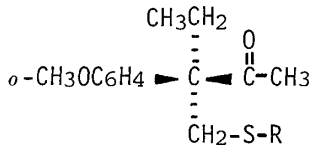
Chart 3



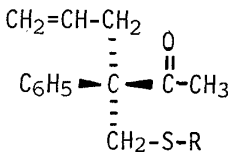
7a: $R = CH_3$
7b: $R = C_6H_5$
7c: $R = o\text{-}CH_3C_6H_4$
7d: $R = C_{10}H_7(\beta)$
7e: $R = C_{10}H_7(\alpha)$



8a: $R = CH_3$
8b: $R = C_6H_5$



9: $R = CH_3$



10: $R = CH_3$

Chart 4

As shown in Table I, with increasing steric bulkiness of R^2, (methyl, ethyl, and allyl groups), the degree of the asymmetric induction decreased. Namely, a greater difference of steric bulkiness between R^1 and R^2 led to a higher optical yield of the products. However,

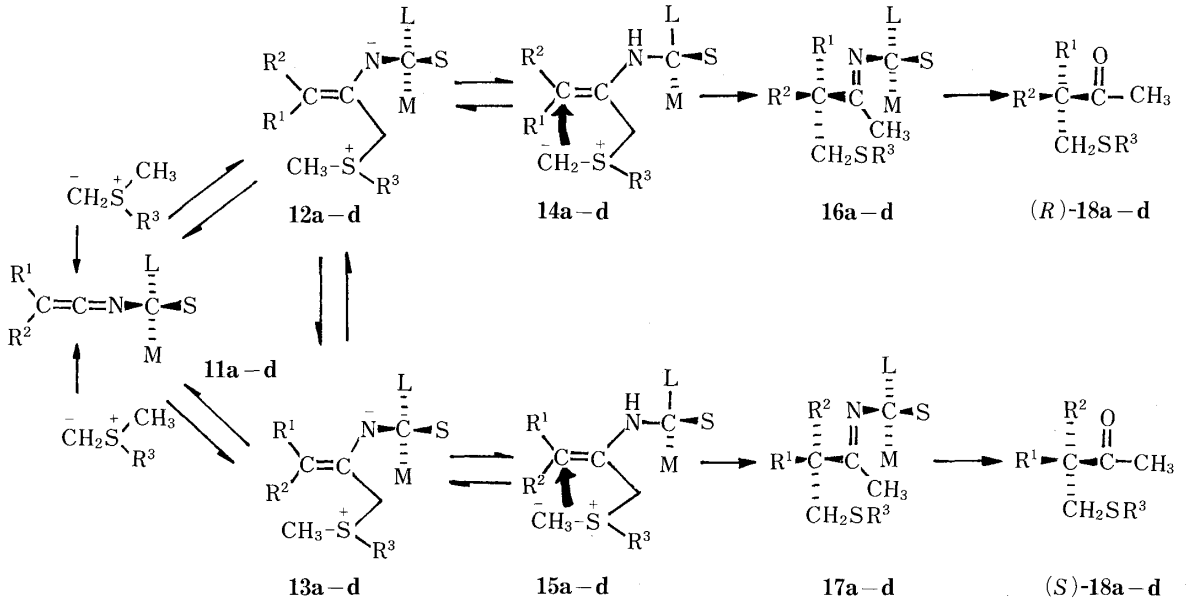
TABLE I. Steric Effects on Asymmetric Induction in the Reaction of the Ketenimines **3a—d** and **4a—d** with the Sulfur Ylide **6a**

Ketenimines	Reaction conditions		Products	Yield of **7—10** (%)	Product **7—10** $[\alpha]_D$ (EtOH)	ee (%)[a]
	Reaction temp. (°C)	Reaction time (h)				
3a	−20	9.0	**7a**	79	+8.2° (c=29.0, 17 °C)	10.4
	0	12.5				
3b	−20	21.0	**8a**	40	+10.2° (c=1.27, 25 °C)	14.1
3c	−20	22.0	**10**	32	+3.6° (c=6.16, 23 °C)	2.9
3d	−20	22.0	**9**	5	+4.8° (c=0.42, 23 °C)	1.9
4a	−20	21.5	**7a**	45	−31.4° (c=11.3, 25 °C)	40.0
4b	−20	23.5	**8a**	47	−27.3° (c=2.56, 21 °C)	37.8
4c	−20	22.5	**10**	18	−20.9° (c=1.29, 23 °C)	17.0
4d	−20	22.0	**9**	23	−17.4° (c=2.47, 20 °C)	7.0

a) The enantiomeric excess (%) was determined by NMR analysis with a shift reagent [Eu(hfc)$_3$].

unexpectedly, replacement of the phenyl group (R^1) in the ketenimines **3b** and **4b** with an *o*-methoxyphenyl group provided 3-(2-methoxyphenyl)-3-methylthiomethyl-2-pentanone (**9**) in very poor optical yields.

These results can be rationalized in terms of the following mechanistic pathway. The sulfur ylide **6a** would attack the ketenimine **11** preferentially from the much less hindered side (R^2), forming mainly **13**. Proton transfer from the methyl group to the nitrogen atom would yield the sulfur ylide **15**. A [2,3] sigmatropic rearrangement of the sulfur ylide would occur from the less hindered top side of the most preferred conformation (**15**) in which the largest group (L) is orientated in the *anti*-coplanar conformation to the olefin. Hydrolysis of the imine **17** would yield (*S*)-**18**. In the reaction of **3d** and **4d** with **6a**, very severe steric interference would occur between R^1 and the aminoalkyl groups in **13d**, and therefore **13d** would be partially equilibrated to **12d**, consequently producing **9** in a much lower optical yield.



12a—d **14a—d** **16a—d** (*R*)-**18a—d**

11a—d

13a—d **15a—d** **17a—d** (*S*)-**18a—d**

a : R^1=C_6H_5, R^2=CH_3; **b** : R^1=C_6H_5, R^2=C_2H_5; **c** : R^1=C_6H_5, R^2=CH_2CH=CH_2; **d** : R^1=*o*-$CH_3OC_6H_4$, R^2=C_2H_5

Chart 5

TABLE II. Steric Effect of the Sulfur Ylides **6a**—**e** on Asymmetric Induction with the Ketenimine **3a**

Sulfur ylides **6**	Reaction conditions		Yield of **7a**—**e** (%)	Product **7a**—**e** $[\alpha]_D$ (EtOH)	ee (%)[a]
	Reaction temp. (°C)	Reaction time (h)			
6a	−20	9.0	79	+8.2° (c=29.0, 17 °C)	10.4
	0	12.5			
6b	0	20.0	79	+12.2° (c=34.5, 18 °C)	30.7
6c	0	20.0	75	+11.5° (c=7.63, 21 °C)	27.2
6d	0	20.0	81	+13.5° (c=5.33, 19 °C)	38.4
6e	0	16.0	60	+7.2° (c=8.70, 17 °C)	39.1

a) The enantiomeric excess (%) was determined by NMR analysis with a shift reagent [Eu(hfc)$_3$].

TABLE III. Steric Effect of the Sulfur Ylides **6a, b** on Asymmetric Induction with the Ketenimines **4a, b**

Ketenimines	Sulfur ylides	Reaction conditions		Product	Yield (%)	Product **7a, b** and **8a, b** $[\alpha]_D$ (EtOH)	ee (%)[a]
		Reaction temp. (°C)	Reaction time (h)				
4a	**6a**	−20	21.5	**7a**	45	−31.4° (c=11.3, 25 °C)	40.0
4a	**6a**	−78	12.0	**7a**	21	−42.1° (c=1.26, 23 °C)	53.6
4a	**6b**	0	21.5	**7b**	55	+23.2° (c=7.38, 24 °C)	58.4
4b	**6a**	0	22.0	**8a**	34[1)]	−22.3° (c=3.81, 22 °C)	30.9
4b	**6b**	0	18.0	**8b**	29	−10.1° (c=1.59, 22 °C)	45.9

a) The enantiomeric excess (%) was determined by NMR analysis with a shift reagent [Eu(hfc)$_3$].

The use of prochiral sulfur ylides **6b**—**e** in this reaction should generate sulfonium ylides **14** or **15** as intermediates, in which a new asymmetric center has been induced on the sulfur atoms. Thus, several kinds of sulfur ylides **6b**—**e** were used in order to investigate the steric effects of the sulfur ylide moieties on the asymmetric induction.

Reaction of methylphenylketene (*S*)-*sec*-butylimine (**3a**), methylphenylketene (−)-menthylimine (**4a**), and ethylphenylketene (−)-menthylimine (**4b**) with sulfur ylides **6a**—**e** followed by acidic hydrolysis produced (*S*)- or (*R*)-3-arylthiomethyl-3-phenyl-2-butanone (**7**) and (*R*)-3-phenyl-3-phenylthiomethyl-2-pentanone (**8b**), respectively. The enantiomeric excess of the products was determined by nuclear magnetic resonance (NMR) analysis with a shift reagent, tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]europium (III) [Eu(hfc)$_3$]. The results are summarized in Tables II and III.

As shown in Tables II and III, the optical yields of the products increased with increasing steric bulkiness of the substituents R on the sulfur ylides **6**, without any serious decrease of the product yields. This means that a new asymmetric center is created on the sulfur atoms of the ylides **14** and **15** during the reaction of chiral ketenimines **11** with prochiral sulfur ylides **6b**—**e**.

The absolute configurations of the products **7b**—**d** were determined by chemical correlation of **7b**—**d** to 3-methyl-3-phenyl-2-pentanone (**25**) of known configuration[9)] as follows. Ketalization of (+)-**7b**—**d** with ethylene glycol followed by oxidation of the sulfides **19a**—**c** with $NaIO_4$ produced diastereomeric sulfoxides **20a**—**c**. Heating of the sulfoxides **20a**—**c** in acetic anhydride resulted in Pummerer rearrangements, yielding thiohemiacetal acetates **21a**—**c**. Hydrolysis of the acetates **21a**—**c** with methanolic KOH gave (+)-3,3-ethylenedioxy-2-methyl-2-phenylbutyraldehyde (**22**). The Witting condensation of the al-

dehyde **22** with triphenylphosphonium methylide provided (+)-4,4-ethylenedioxy-3-methyl-3-phenyl-1-pentene (**23**), which was subjected to catalytic hydrogenation with palladium–carbon followed by deprotection of the ethylene ketal with *p*-toluenesulfonic acid–acetone to give (*S*)-(+)-3-methyl-3-phenyl-2-pentanone (**25**) of known configuration.[9] Thus, the absolute configurations of **7b—d** were determined to be (*S*)-(+)-**7b—d**.

The four stereoisomers **26a—d** could be considered as cyclic transition states for the [2,3]

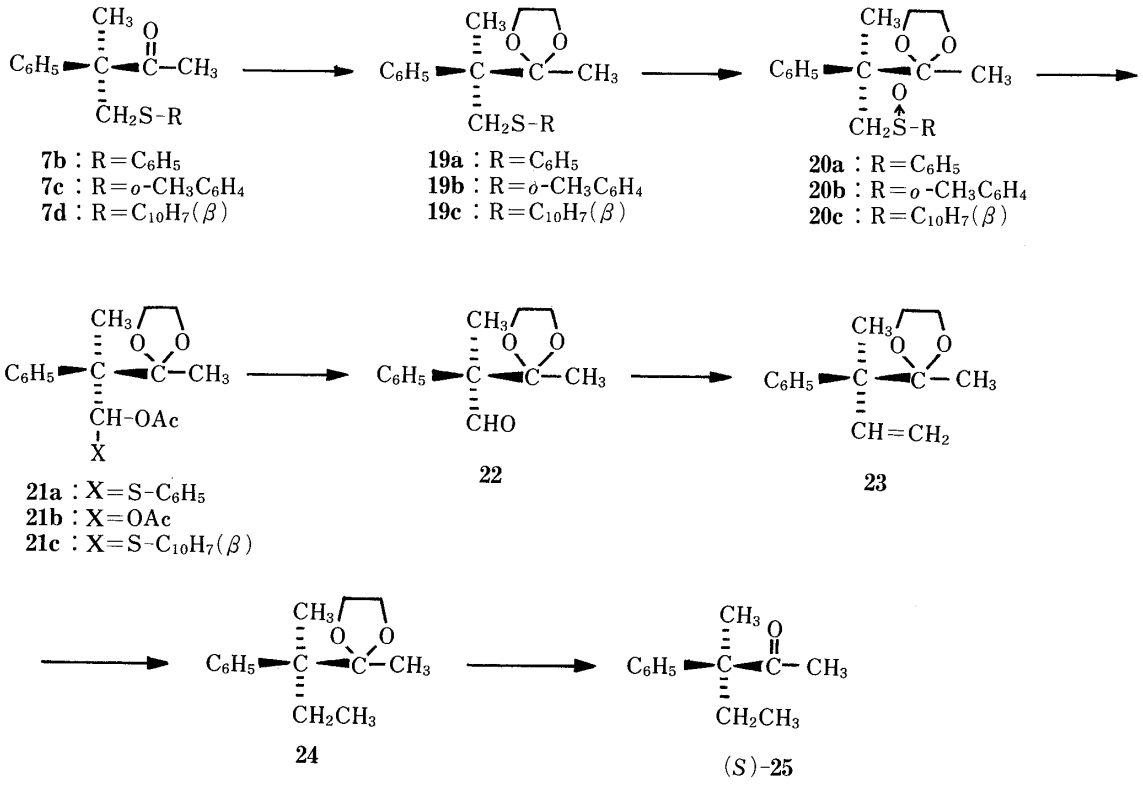


Chart 6

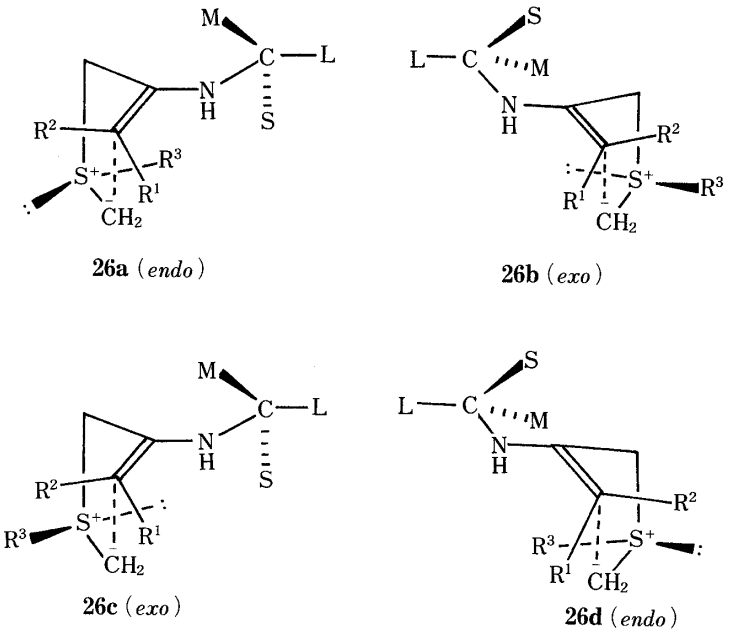


Chart 7

sigmatropic rearrangement of the sulfur ylides **15** having asymmetric sulfur atoms. Among these conformers **26a—d**, severe steric interference should occur between R^3 and the amino substituents at the C_2 position in the *endo* forms **26a** and **26d**. Therefore, the rearrangement would occur preferentially from the direction of the small group (S) in the conformationally preferred *exo* form and proceed *via* a transition state **26c**, resulting in high optical yields.

Experimental

Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. Thin-layer or preparative thick layer plates were made of E. Merck Silica gel 60PF-254 activated by drying at 140 °C for 3.5 h. Infrared (IR) spectra were obtained in the indicated state with a Hitachi 215 spectrometer. NMR spectra were determined in the indicated solvent with a Hitachi R-24B high-resolution NMR spectrometer; chemical shifts are given in ppm from tetramethylsilane. Splitting patterns are designated as s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Mass spectra (MS) were taken on a Hitachi RMU-6MG or RMU-7M or a JEOL JMS-DX300 spectrometer. Optical rotations were measured on a Union-Giken PM-101 polarimeter.

Synthesis of Amides 1 and 2 General Procedure——A solution of 2-phenylpropionyl chloride, 2-phenyl-4-pentenoyl chloride, or 2-(2-methoxyphenyl)butyryl chloride (6.96 mmol) in 10 ml of tetrahydrofuran (THF) was added to a mixture of (*S*)-*sec*-butylamine or (−)-menthylamine (6.96 mmol) and triethylamine (20.88 mmol) in 10 ml of THF cooled at 0 °C. The reaction mixture was stirred at room temperature overnight, then quenched with 10% aqueous hydrochloric acid, and extracted with chloroform. The organic layers were combined, washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residual oil was subjected to preparative thin-layer chromatography (TLC) (ether–hexane 1 : 1).

N-(*S*)-*sec*-Butyl-2-phenylpropionamide (**1a**): Colorless needles of mp 70—72 °C (Recryst. from hexane). $[\alpha]_D^{25}$ +20.8° (*c*=2.02, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3400 (NH), 1640 (CONH). NMR (CCl_4) δ: 0.83 (3H, t, *J*=8 Hz, $C\underline{H}_3CH_2$), 0.98, 1.02 (3H, d, d, *J*=8, 8 Hz, $C\underline{H}_3CH$), 1.00—1.70 (2H, m, $C\underline{H}_2CH_3$), 1.40 (3H, d, *J*=7 Hz, $C\underline{H}_3CH$), 3.46 (1H, d, *J*=8 Hz, $C\underline{H}CH_3$), 3.83 (1H, q, *J*=8 Hz, $C\underline{H}CH_3$), 5.83—6.00 (1H, br s, NH), 7.10—7.30 (5H, m, C_6H_5). *Anal.* Calcd for $C_{13}H_{19}NO$: C, 76.05; H, 9.33; N, 6.82. Found: C, 76.11; H, 9.30; N, 6.91.

N-(*S*)-*sec*-Butyl-2-phenyl-4-pentenamide (**1c**): $[\alpha]_D^{25}$ +17.4° (*c*=2.58, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450 (NH), 1640 (CONH). NMR (CCl_4) δ: 0.70 (3H, t, *J*=7 Hz, $C\underline{H}_3CH_2$), 1.06 (3H, d, *J*=6 Hz, $C\underline{H}_3CHN$), 1.10—1.70 (2H, m, $C\underline{H}_2CH_3$), 2.20—3.20 (2H, m, $C\underline{H}_2CH{=}C$), 3.40—4.00 (2H, m, CH–N, $CH–\overset{O}{\overset{\|}{C}}$), 4.80—5.10 (2H, m, $C\underline{H}_2{=}CH$), 5.38—6.03 (1H, m, $C\underline{H}{=}CH_2$), 7.00—7.30 (6H, m, C_6H_5, NH). MS *m/e*: 231 (M^+). Exact mass determination: 231.1596 (Calcd for $C_{15}H_{21}NO$: 231.1621).

N-(*S*)-*sec*-Butyl-2-(2-methoxyphenyl)butyramide (**1d**): $[\alpha]_D^{25}$ +16.0° (*c*=2.31, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450 (NH), 1660 (CONH). NMR (CCl_4) δ: 0.90 (6H, t, *J*=7 Hz, $2C\underline{H}_3CH_2$), 1.28 (3H, d, *J*=7 Hz, $C\underline{H}_3CHN$), 1.40—2.66 (4H, m, $2C\underline{H}_2CH_3$), 3.36—3.80 (2H, m, $CH–\overset{O}{\overset{\|}{C}}$, CH–N), 3.73 (3H, s, OCH_3), 4.93—5.40 (1H, br s, NH), 6.50—7.26 (4H, m, C_6H_4). MS *m/e*: 249 (M^+). Exact mass determination: 249.1710 (Calcd for $C_{15}H_{23}O_2N$: 249.1727).

N-(−)-Menthyl-2-phenylpropionamide (**2a**): Colorless needles of mp 157—159 °C (recryst. from hexane). $[\alpha]_D^{22}$ −54.8° (*c*=3.72, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450 (NH), 1660 (CONH). NMR ($CDCl_3$) δ: 0.70—1.10 (12H, m, $4CH_3$), 1.13—2.00 (9H, m), 3.20—4.00 (2H, m, CHN, $CH–\overset{O}{\overset{\|}{C}}$), 4.96—5.46 (1H, m, NH), 7.00—7.36 (5H, m, C_6H_5). *Anal.* Calcd for $C_{19}H_{29}NO$: C, 79.39; H, 10.17; N, 4.87. Found: C, 79.28; H, 10.13; N, 4.62.

N-(−)-Menthyl-2-phenyl-4-pentenamide (**2c**): $[\alpha]_D^{22}$ −53.6° (*c*=3.32, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450 (NH), 1660 (CONH). NMR ($CDCl_3$) δ: 0.68 (3H, d, *J*=7 Hz, $C\underline{H}_3CH$), 0.83 (6H, d, *J*=5 Hz, $(C\underline{H}_3)_2CH$), 1.00—2.00 (9H, m), 2.10—3.10 (2H, m, $CH_2C{=}C$), 3.20—4.00 (4H, m, $CH–\overset{O}{\overset{\|}{C}}$, CHN), 4.73—5.20 (2H, m, $CH_2{=}C$), 5.30—6.00 (1H, m, $CH{=}C$), 6.70 (1H, d, *J*=10 Hz, NH), 7.00—7.40 (5H, m, C_6H_5). MS *m/e*: 313 (M^+). Exact mass determination: 313.2404 (Calcd for $C_{21}H_{31}NO$: 313.2404).

N-(−)-Menthyl-2-(2-methoxyphenyl)butyramide (**2d**): Colorless pillars of 107—110 °C (recryst. from hexane). $[\alpha]_D^{22}$ −55.1° (*c*=3.34, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3430 (NH), 1655 (CONH). NMR ($CDCl_3$) δ: 0.46—2.56 (23H, m), 3.30—3.90 (2H, m, $C\underline{H}CH_2$, CHN), 3.76 (3H, s, OCH_3), 5.36—5.63 (1H, m, NH), 6.70—7.30 (4H, m, C_6H_4). *Anal.* Calcd for $C_{21}H_{33}NO_2$: C, 76.09; H, 10.03; N, 4.23. Found: C, 76.11; H, 10.13; N, 4.32.

Synthesis of Chiral Ketenimines 3a—d and 4a—d General Procedure——A mixture of one of the amides **1a—d** and **2a—d** (2.26 mmol) and phosphorus pentachloride (470 mg, 2.26 mmol) in 10 ml of benzene was refluxed for 3 h. After the above mixture had cooled, 3.10 ml (22.6 mmol) of triethylamine was added, and the whole was further refluxed for 18 h. The separated white precipitates were filtered off and the filtrate was concentrated under reduced

pressure to give the corresponding chiral ketenimines **3a—d** and **4a—d**. The C=C=N absorptions in the IR spectrum (cm^{-1}) and the yields (%) based on the corresponding amides were as follows. Methylphenylketene (*S*)-*sec*-butylimine (**3a**): 2020, quantitative. Allylphenylketene (*S*)-*sec*-butylimine (**3c**): 2010, quantitative. Ethyl(2-methoxyphenyl)ketene (*S*)-*sec*-butylimine (**3d**): 2010, quantitative. Methylphenylketene (−)-menthylimine (**4a**): 2020, quantitative. Allylphenylketene (−)-menthylimine (**4c**): 2020, quantitative. Ethyl(2-methoxyphenyl)ketene (−)-menthylimine (**4d**): 2020, 85%.

Ethylphenylketene (*S*)-*sec*-butylimine (**3b**) and (−)-menthylimine (**4b**) were prepared from the corresponding amides **1b** and **2b**[1] according to the reported procedure.[1]

Reaction of Chiral Ketenimines 3a—d and 4a—d with Sulfur Ylides 6a—e General Procedure——A dry 50 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar, and containing a sulfonium salt **5a—e** (4.31 mmol), was flushed with nitrogen and maintained under a positive pressure of nitrogen. Freshly distilled anhydrous THF (12 ml) was added, followed by addition of a 1.5 N hexane solution of butyllithium (4.3 ml, 6.46 mmol) at −20 °C. The mixture was stirred at −20 °C for 1 h, then a solution of ketenimine **3** or **4** (2.16 mmol) in 10 ml of THF was added at −20 °C. The reaction mixture was stirred under the conditions given in Tables I—III. The reaction was quenched with saturated aqueous NaCl and the mixture was extracted with ether. The ethereal layers were combined, washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure.

A mixture of the crude product obtained, 4 ml of 10% aqueous hydrochloric acid, and 1 ml of benzene was refluxed for 3 h. After cooling, the mixture was extracted with ether. The organic layers were combined, washed sequentially with 10% aqueous hydrochloric acid, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residual oil was subjected to preparative TLC (hexane–ether 8 : 1) to give a 3-arylthiomethyl-3-phenyl-2-alkanone (**7—10**).

The yields, the optical rotations of the ketones obtained, and the reaction conditions employed are summarized in Tables I—III. The values of enantiomeric excess of the products were determined by NMR analysis with a shift reagent [Eu(hfc)$_3$], and are summarized in Tables I—III.

3-Methylthiomethyl-3-phenyl-2-butanone (**7a**): IR ν_{max}^{film} cm^{-1}: 1710 (–C(=O)–), 1600 (C_6H_5). NMR δ: 1.60 (3H, s, CH_3), 1.73 (3H, s, SCH_3), 1.86 (3H, s, C(=O)–CH_3), 2.90 (2H, s, CH_2S), 7.00—7.36 (5H, m, C_6H_5). MS *m/e*: 208 (M^+). Exact mass determination: 208.0912 (Calcd for $C_{12}H_{16}OS$: 208.0922).

3-Phenyl-3-phenylthiomethyl-2-butanone (**7b**): IR ν_{max}^{film} cm^{-1}: 1705 (–C(=O)–), 1600 (C_6H_5). NMR δ: 1.63 (3H, s, CH_3), 1.86 (3H, s, C(=O)–CH_3), 3.40 (2H, s, CH_2S), 7.10—7.20 (10H, m, C_6H_5, SC_6H_5). MS *m/e*: 270 (M^+). Exact mass determination: 270.1106 (Calcd for $C_{17}H_{18}OS$: 270.1019).

3-(*o*-Tolylthiomethyl)-3-phenyl-2-butanone (**7c**): IR ν_{max}^{film} cm^{-1}: 1710 (–C(=O)–), 1600 (aromatic). NMR δ: 1.60 (3H, s, CH_3), 1.82 (3H, s, C(=O)–CH_3), 2.23 (3H, s, $C_6H_4C\underline{H}_3$), 3.30 (2H, s, CH_2S), 6.86—7.03 (4H, m, C_6H_4), 7.10—7.30 (5H, m, C_6H_5). MS *m/e*: 284 (M^+). Exact mass determination: 284.1240 (Calcd for $C_{18}H_{20}OS$: 284.1235).

3-(2-Naphthylthiomethyl)-3-phenyl-2-butanone (**7d**): IR ν_{max}^{film} cm^{-1}: 1705 (–C(=O)–), 1600 (aromatic). NMR (CCl_4) δ: 1.65 (3H, s, CH_3), 1.86 (3H, s, C(=O)–CH_3), 3.46 (2H, s, CH_2S), 7.00—8.00 (12H, m, C_6H_5, $C_{10}H_7$). MS *m/e*: 320 (M^+). Exact mass determination: 320.1232 (Calcd for $C_{21}H_{20}OS$: 320.1233).

3-(1-Naphthylthiomethyl)-3-phenyl-2-butanone (**7e**): IR ν_{max}^{film} cm^{-1}: 1705 (–C(=O)–), 1600 (aromatic). NMR (CCl_4) δ: 1.63 (3H, s, CH_3), 1.80 (3H, s, C(=O)–CH_3), 3.36 (2H, s, CH_2S), 6.96—8.36 (12H, m, C_6H_5, $C_{10}H_7$). MS *m/e*: 320 (M^+). Exact mass determination: 320.1195 (Calcd for $C_{21}H_{20}OS$: 320.1233).

3-Phenyl-3-phenylthiomethyl-2-pentanone (**8b**): IR ν_{max}^{film} cm^{-1}: 1710 (–C(=O)–), 1600 (phenyl). NMR (CCl_4) δ: 0.75 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 1.80 (3H, s, CH_3–C(=O)), 2.26 (2H, q, J=7 Hz, $C\underline{H}_2CH_3$), 3.30—3.53 (2H, m, CH_2S), 7.05—7.25 (10H, m, $2C_6H_5$). MS *m/e*: 284 (M^+). Exact mass determination: 284.1233 (Calcd for $C_{18}H_{22}OS$: 284.1233).

3-(2-Methoxyphenyl)-3-methylthiomethyl-2-pentanone (**9**): IR ν_{max}^{film} cm^{-1}: 1710 (–C(=O)–), 1600 (aromatic). NMR (CCl_4) δ: 0.77 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 0.90 (3H, s, CH_3S), 1.55 (2H, q, J=7 Hz, $C\underline{H}_2CH_3$), 1.90 (3H, s, CH_3–C(=O)), 2.40—2.95 (2H, m, CH_2S), 3.80 (3H, s, OCH_3), 6.60—7.30 (4H, m, C_6H_4). MS *m/e*: 252 (M^+). Exact mass

determination: 252.1195 (Calcd for $C_{14}H_{20}O_2S$: 252.1185).

3-Methylthiomethyl-3-phenyl-5-hexen-2-one (**10**): IR ν_{max}^{film} cm^{-1}: 1715 (–C(=O)–), 1600 (phenyl). NMR (CCl_4) δ: 1.73 (3H, s, SCH_3), 1.83 (3H, s, CH_3–C(=O)), 2.30—3.00 (2H, m, $CH_2C=C$), 2.96 (2H, s, CH_2S), 4.66—5.70 (3H, m, $CH_2=CH$), 6.76—7.46 (5H, m, C_6H_5). MS *m/e*: 234 (M^+). Exact mass determination: 234.1072 (Calcd for $C_{14}H_{18}OS$: 234.1077).

Synthesis of Sulfonium Salts 5c—e Dimethyl(*o*-tolyl)sulfonium Perchlorate (5c)——Methyl iodide (7.5 ml, 120.8 mmol) was added to a solution of 5.56 g (40.26 mmol) of methyl *o*-tolyl sulfide and 9.18 g (44.29 mmol) of silver perchlorate in 27 ml of acetonitrile. The mixture was stirred at room temperature for 72 h. The yellowish precipitates were filtered off and the filtrate was concentrated *in vacuo*. The residue was recrystallized from ethanol to give 9.17 g (90% yield) of **5c** as colorless needles of mp 98—99 °C. IR ν_{max}^{film} cm^{-1}: 1590 (tolyl). NMR (D_2O) δ: 2.53 (3H, s, $C_6H_4CH_3$), 3.13 (6H, s, $2CH_3$), 7.30—7.80 (4H, m, C_6H_4). *Anal.* Calcd for $C_8H_{11}ClO_4S$: C, 40. 26; H, 4.65; Cl, 14.85; S, 13.43. Found: C, 40.01; H, 4.46; Cl, 14.99; S, 13.02.

Other sulfonium salts **5d**,**e** were prepared in the same way as described above. The sulfonium salts **5a**[10] and **5b**[11] were obtained according to the reported methods.

Dimethyl(2-naphthyl)sulfonium Perchlorate (**5d**): Colorless pillars of mp 147—149 °C (recryst. from ethanol). IR ν_{max}^{Nujol} cm^{-1}: 1585 (naphthyl). NMR (D_2O) δ: 3.23 (6H, s, $2CH_3$), 7.36—8.00 (7H, m, $C_{10}H_7$). *Anal.* Calcd for $C_{12}H_{13}ClO_4S$: C, 49.92; H, 4.54; Cl, 12.28; S, 11.10. Found: C, 49.72; H, 4.53; Cl, 12.62; S, 11.20.

Dimethyl(1-naphthyl)sulfonium Perchlorate (**5e**): Colorless needles of mp 147.5—149 °C (recryst. from ethanol). IR ν_{max}^{Nujol} cm^{-1}: 1600 (naphthyl). NMR (D_2O) δ: 3.20 (6H, s, $2CH_3$), 7.50—8.06 (7H, m, $C_{10}H_7$). *Anal.* Calcd for $C_{12}H_{13}ClO_4S$: C, 49.92; H, 4.54; Cl, 12.28; S, 11.10. Found: C, 50.02; H, 4.46; Cl, 12.34; S, 11.21.

Transformation of 3-Arylthiomethyl-3-phenyl-2-butanone (7b—d) into 3-Methyl-3-phenyl-2-pentanone (25) 2,2-Ethylenedioxy-3-phenyl-3-phenylthiomethylbutane (19a)——A mixture of 1.03 g (3.82 mmol) of (+)-**7b** ($[\alpha]_D^{16}$ +12.1 ° (*c*=11.7, EtOH)) and 3.67 g (57.4 mmol) of ethylene glycol in 35 ml of benzene was refluxed with a Dean–Stark apparatus for 24—27 h in the presence of catalytic amount of *p*-toluenesulfonic acid. After cooling, the mixture was diluted with ether and the solution was washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give 1.09 g (91% yield) of **19a**: $[\alpha]_D^{18}$ −0.3 ° (*c*=6.71, EtOH). IR ν_{max}^{film} cm^{-1}: 1600, 1580 (phenyl). NMR (CCl_4) δ: 1.05 (3H, s, CH_3), 1.55 (3H, s, CH_3), 3.20—4.00 (6H, m, OCH_2CH_2O, CH_2S), 6.80—7.40 (10H, m, $2C_6H_5$). MS *m/e*: 314 (M^+). Exact mass determination: 314.1338 (Calcd for $C_{19}H_{22}SO_2$: 314.1339). Treatment of **7c** and **7d** as described above afforded the corresponding ethylene ketals.

2,2-Ethylenedioxy-3-phenyl-3-(*o*-tolylthiomethyl)butane (**19b**): 97% yield. $[\alpha]_D^{16}$ −0.9 ° (*c*=9.25, EtOH) (using **7c** with a rotation of $[\alpha]_D^{16}$ +11.0 ° (*c*=11.0, EtOH). IR ν_{max}^{film} cm^{-1}: 1595 (phenyl). NMR (CCl_4) δ: 1.06 (3H, s, CH_3), 1.56 (3H, s, CH_3), 2.16 (3H, s, $C_6H_4CH_3$), 3.00—4.00 (6H, m, CH_2S, OCH_2CH_2O), 6.76—7.56 (9H, m, C_6H_5, C_6H_4). MS *m/e*: 328 (M^+). Exact mass determination: 328.1492 (Calcd for $C_{20}H_{24}O_2S$: 328.1497).

2,2-Ethylenedioxy-3-(1-naphthylthiomethyl)-3-phenylbutane (**19c**): 89% yield. $[\alpha]_D^{18}$ −4.7 ° (*c*=7.75, EtOH) (using **7d** with a rotation of $[\alpha]_D^{16}$ +13.1 ° (*c*=9.52, EtOH)). IR ν_{max}^{film} cm^{-1}: 1595 (phenyl). NMR (CCl_4) δ: 1.06 (3H, s, CH_3), 1.60 (3H, s, CH_3), 3.30—4.00 (6H, m, OCH_2CH_2O, CH_2S), 6.90—7.80 (12H, m, C_6H_5, $C_{10}H_7$). MS *m/e*: 364 (M^+). Exact mass determination: 364.1472 (Calcd for $C_{23}H_{24}O_2S$: 364.1495).

2,2-Ethylenedioxy-3-phenyl-3-phenylsulfinylmethylbutane (20a)——A suspension of 593 mg (1.89 mmol) of **19a** ($[\alpha]_D^{18}$ −0.3 ° (*c*=6.71, EtOH)) and 444 mg (2.08 mmol) of sodium metaperiodate in aqueous methanol (4.5 ml of methanol and 0.1 ml of H_2O) was stirred at room temperature for 45 h. The mixture was concentrated under reduced pressure and the residue was diluted with chloroform. The white precipitates were filtered off and the filtrate was concentrated to dryness under reduced pressure. The residual oil was subjected to preparative TLC (hexane–ether 8 : 1) to give 623 mg (quantitative yield) of **20a**: $[\alpha]_D^{14}$ +6.1 ° (*c*=4.91, EtOH). IR ν_{max}^{film} cm^{-1}: 1600, 1580 (phenyl), 1040 (sulfoxide). NMR (CCl_4) δ: 1.00 (3H, s, CH_3), 1.47, 1.60 (3H, s, s, CH_3), 3.02, 3.12 (2H, s, s, CH_2S), 3.40—3.90 (4H, m, OCH_2CH_2O), 6.80—7.50 (10H, m, $2C_6H_5$). MS *m/e*: 330 (M^+). Exact mass determination: 205.1211 (Calcd for $C_{13}H_{17}O_2$($M^+ - C_6H_5SO$), 205.1228).

Treatment of **19b** and **19c** as described above afforded the corresponding sulfoxides.

2,2-Ethylenedioxy-3-phenyl-3-(*o*-toluenesulfinylmethyl)butane (**20b**): 84% yield. $[\alpha]_D^{19}$ +9.7 ° (*c*=6.62, EtOH) (using **19b** with a rotation of $[\alpha]_D^{16}$ −0.9 ° (*c*=9.25, EtOH)). IR ν_{max}^{film} cm^{-1}: 1600, 1580 (aromatic), 1030 (sulfoxide). NMR (CCl_4) δ: 1.00 (3H, s, CH_3), 1.70, 1.82 (3H, s, s, CH_3), 2.30, 2.20 (3H, s, s, CH_3), 2.83—3.23 (2H, m, CH_2S), 3.33—4.00 (4H, m, OCH_2CH_2O), 6.83—8.00 (9H, m, C_6H_5 and C_6H_4). MS *m/e*: 344 (M^+). Exact mass determination: 344.1505 (Calcd for $C_{20}H_{24}O_3S$: 344.1446).

2,2-Ethylenedioxy-3-(2-naphthylsulfinylmethyl)-3-phenylbutane (**20c**): 95% yield. $[\alpha]_D^{18}$ −0.8 ° (*c*=6.25, EtOH) (using **19c** with a rotation of $[\alpha]_D^{18}$ −4.7 ° (*c*=7.75, EtOH)). IR ν_{max}^{film} cm^{-1}: 1595 (aromatic), 1040, 1070 (sulfoxide). NMR (CCl_4) δ: 1.03 (3H, s, CH_3), 1.70, 1.86 (3H, s, s, CH_3), 3.06—3.46 (2H, m, CH_2S), 3.56—4.06 (4H, m, OCH_2CH_2O), 7.00—8.10 (12H, m, C_6H_5, $C_{10}H_7$). MS *m/e*: 381 (M^+ +1). Exact mass determination: 381.1519 (Calcd for $C_{23}H_{25}O_3S$ [$(M+H)^+$], 381.1523).

1-Acetoxy-3,3-ethylenedioxy-2-methyl-2-phenyl-1-phenylthiobutane (21a)——A solution of 336 mg (1.02 mmol) of **20a** obtained above in 1 ml of acetic anhydride was refluxed for 4.5 h. The reaction mixture was concentrated under reduced pressure and the residual oil was subjected to preparative TLC (ether–hexane 1 : 1) to give 243 mg (64% yield) of **21a**: $[\alpha]_D^{16}$ −1.3° (c=7.81, EtOH). IR ν_{max}^{film} cm^{-1}: 1740 (ester), 1585 (phenyl). NMR (CCl_4) δ: 0.95, 1.00 (3H, s, s, CH_3), 1.50, 1.68 (3H, s, s, CH_3), 1.85, 1.97 (3H, s, s, $O-\overset{O}{\overset{\|}{C}}-CH_3$), 3.50—3.90 (4H, m, OCH_2CH_2O), 4.10 (1H, s, OCHS), 6.80—7.50 (10H, m, $2C_6H_5$). MS m/e: 373 (M^+ + 1). Exact mass determination: 373.1459 (Calcd for $C_{21}H_{25}O_4S$ [$(M+H)^+$], 373.1473).

Heating of **20b** and **20c** obtained above in refluxing acetic anhydride followed by the same work-up gave 1,1-diacetoxy-3,3-ethylenedioxy-2-methyl-2-phenylbutane (**21b**) and 1-acetoxy-3,3-ethylenedioxy-2-methyl-1-naphthylthio-2-phenylbutane (**21c**), respectively.

21b: 28% yield. $[\alpha]_D^{19}$ +0.1° (c=8.14, EtOH). IR ν_{max}^{film} cm^{-1}: 1750 (ester), 1600, 1590 (phenyl). NMR (CCl_4) δ: 1.63—2.26 (12H, m, $2CH_3$, $2CH_3\overset{O}{\overset{\|}{C}}-O$), 4.13 (4H, s, OCH_2CH_2O), 6.83—7.56 (5H, m, C_6H_5).

21c: 38% yield. $[\alpha]_D^{17}$ −6.2° (c=6.00, EtOH). IR ν_{max}^{film} cm^{-1}: 1745 (ester), 1590 (aromatic). NMR (CCl_4) δ: 0.92, 1.00 (3H, s, s, CH_3), 1.65, 1.82 (3H, s, s, CH_3), 1.93 (3H, s, $CH_3\overset{O}{\overset{\|}{C}}-O$), 3.43—3.90 (4H, m, OCH_2CH_2O), 4.06 (1H, s, OCHS), 6.73—7.83 (12H, m, C_6H_5, $C_{10}H_7$). MS m/e: 422 (M^+). Exact mass determination: 422.1536 (Calcd for $C_{25}H_{26}O_4S$: 422.1551).

3,3-Ethylenedioxy-2-methyl-2-phenylbutyraldehyde (22)——A solution of 158 mg (0.42 mmol) of **21a** obtained above ($[\alpha]_D^{16}$ −1.3° (c=7.81, EtOH)) in 2 ml of 8% KOH-methanol solution was stirred at room temperature for 12 h and then refluxed for 3 h. The mixture was concentrated under reduced pressure. The residue was extracted with ether. The ethereal layers were combined, washed with 10% aqueous NaOH and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residual oil was subjected to preparative TLC (ether–hexane 1 : 1) to give 52 mg (56% yield) of **22**: bp 170 °C (oil bath) (4 mmHg). $[\alpha]_D^{17}$ +11.9° (c=12.7, EtOH). IR ν_{max}^{film} cm^{-1}: 1720 (aldehyde), 1600, 1580 (phenyl). NMR (CCl_4) δ: 1.13 (3H, s, CH_3), 1.50 (3H, s, CH_3), 3.60—4.00 (4H, m, OCH_2CH_2O), 7.00—7.50 (5H, m, C_6H_5), 9.90 (1H, s, $\overset{O}{\overset{\|}{C}}-H$). MS m/e: 220 (M^+). *Anal.* Calcd for $C_{13}H_{16}O_3$: C, 70.87; H, 7.32. Found: C, 70.91; H, 7.42.

Hydrolysis of **21b** ($[\alpha]_D^{19}$ +0.1° (c=8.14, EtOH), prepared from **21b**) and **21c** ($[\alpha]_D^{17}$ −6.2° (c=6.00, EtOH), prepared from **20c**) was carried out with methanolic KOH under the same conditions as described above to give **22** possessing a rotation of $[\alpha]_D^{17}$ +10.3° (c=0.58, EtOH) or $[\alpha]_D^{19}$ +14.5° (c=2.48, EtOH), respectively.

4,4-Ethylenedioxy-3-methyl-3-phenyl-1-pentene (23)——A solution of triphenylphosphonium methylide [prepared from 195 mg (0.48 mmol) of methyltriphenylphosphonium iodide and 58 mg (1.20 mmol) of sodium hydride (washed with hexane before use)] in 1 ml of THF was added to a solution of 53 mg (0.24 mmol) of **22** ($[\alpha]_D^{17}$ +11.9° (c=12.7, EtOH)) in 4 ml of THF. The reaction mixture was stirred at room temperature for 25 min and refluxed for 13 h. After cooling, the mixture was quenched with saturated aqueous NaCl and extracted with ether. The ethereal layers were combined, washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residual oil was subjected to preparative TLC (hexane–ether 3 : 2) to give 48 mg (92% yield) of **23**: bp 125 °C (oil bath) (0.2 mmHg). $[\alpha]_D^{18}$ +9.6° (c=1.46, EtOH). IR ν_{max}^{film} cm^{-1}: 1640 (C=C), 1600 (phenyl). NMR (CCl_4) δ: 1.12 (3H, s, CH_3), 1.50 (3H, s, CH_3), 3.20—3.80 (4H, m, OCH_2CH_2O), 4.90, 5.13 (1H, d, d, J=9.2 Hz, CH=C), 6.20—6.70 (1H, m, CH=C), 6.90—7.50 (5H, m, C_6H_5). MS m/e: 218 (M^+). *Anal.* Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.10; H, 8.36.

2,2-Ethylenedioxy-3-methyl-3-phenylpentane (24)——A solution of 15 mg (0.68 mmol) of **23** ($[\alpha]_D^{18}$ +9.6° (c=1.46, EtOH) in 1 ml of dioxane was added to a mixture of 103 mg (2.05 mmol) of hydrazine hydrate, 0.05 ml of 1% aqueous cupric sulfate, and 0.05 ml of acetic acid. A suspension of 146 mg (0.68 mmol) of sodium metaperiodate in 2 ml of H_2O was added at 0 °C to the above mixture. The whole was stirred at room temperature for 21.5 h and then diluted with ether. The ethereal solution was washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give 15 mg (quantitative yield) of **24**: bp 120 °C (oil bath) (0.15 mmHg). $[\alpha]_D^{20}$ +6.5° (c=1.23, EtOH). IR ν_{max}^{film} cm^{-1}: 1600 (phenyl). NMR (CCl_4) δ: 0.60 (3H, t, J=7 Hz, $CH_2\underline{CH_3}$), 1.00 (3H, s, CH_3), 1.32 (3H, s, CH_3), 1.63 (2H, q, J=7 Hz, CH_2), 3.30—3.70 (4H, m, OCH_2CH_2O), 6.70—7.20 (5H, m, C_6H_5). *Anal.* Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.41; H, 9.26.

(*S*)-3-Methyl-3-phenyl-2-pentanone (25)——A solution of 10 mg (0.045 mmol) of **24** ($[\alpha]_D^{20}$ +6.5° (c=1.23, EtOH)) in 3 ml of acetone was stirred at room temperature for 70 h in the presence of a catalytic amount of *p*-toluenesulfonic acid. The mixture was concentrated under reduced pressure and the residue was dissolved in benzene. The solution was washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give 8 mg (quantitative yield) of (*S*)-**25**:[9] $[\alpha]_D^{19}$ +23.9° (c=1.34, cyclohexane). IR ν_{max}^{film} cm^{-1}: 1710 (ketone), 1600 (phenyl). NMR (CCl_4) δ: 0.73 (3H, t, J=7 Hz, $C\underline{H_3}CH_2$), 1.40 (3H, s, CH_3), 1.80 (3H, s, $CH_3\overset{O}{\overset{\|}{C}}$), 1.92 (2H, q, J=7 Hz, $C\underline{H_2}CH_3$), 7.00—7.40 (5H, m, C_6H_5). MS m/e: 176 (M^+).

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