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Asymmetric Induction Reactions. I. Asymmetric [2,3] Sigmatropic Rearrangements of Sulfur Ylides Derived from Chiral Ketenimines and Trimethylsulfonium Ylide[1,2]

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The asymmetric [2,3] sigmatropic rearrangements of 2-alkylamino-3-phenyl-2-pentenylmethylsulfonium methylides were accomplished by the reaction of ethylphenylketenimines **3** having a chiral carbon next to the nitrogen atom with trimethylsulfonium ylide, and acidic hydrolysis of the imines **4** thus obtained led to optically active 3-methylthiomethyl-3-phenyl-2-pentanone (**5**). The reaction of ethylphenylketene (−)-menthylimine (**3g**) with trimethylsulfonium ylide at −78 °C resulted in the highest optical yield of (*R*)-(−)-**5** in the above sequence.

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

Creation of asymmetric quaternary carbon atoms[3] is generally required for the synthesis of optically active natural products such as steroids, terpenoids, and alkaloids. Many methods have been developed for the asymmetric formation of carbon–carbon bonds.[4] Among them, one of the most efficient methods is intramolecular transfer of chirality by means of asymmetric [2,3][5] and [3,3] sigmatropic rearrangements[6] and intramolecular substitution reactions.[7]

Only a few reports have been published on asymmetric [2,3] sigmatropic rearrangements of sulfur ylides[5d] involving chirality at the sulfur atoms. Apparently, these chiral sulfonium salts have not been easily accessible, and therefore these methods are not practically useful for the introduction of asymmetry into a molecule.

We wish to report herein a potentially useful method for the creation of a new asymmetric carbon by [2,3] sigmatropic rearrangements *via* sulfur ylides, which are easily derived from readily obtainable ketenimines[8] having chirality next to the nitrogen atoms, and a sulfur ylide. To our knowledge no report has been published hitherto on asymmetric induction with chiral ketenimines, except for a recent report on asymmetric cycloaddition to chiral ketene iminium salts.[9]

Chiral ketenimines having an asymmetric carbon next to the nitrogen atom were prepared from the corresponding amides derived from optically active primary amines in the following way. Reaction of *N*-(*S*)-*sec*-butylphenylacetamide (**1a**) and *N*-(*S*)-*sec*-butyl-2-phenylbutyramide (**1b**) with an equivalent amount of phosphorus pentachloride were carried out by refluxing in benzene for 2 h to produce *N*-(*S*)-*sec*-butylphenylacetimidoyl chloride (**2a**) and *N*-(*S*)-*sec*-butyl-2-phenylbutyrimidoyl chloride (**2b**), respectively. Refluxing of **2a** and **2b** in benzene in the presence of triethylamine (10 eq) resulted in dehydrochlorination to afford phenylketene (*S*)-*sec*-butylimine (**3a**) and ethylphenylketene (*S*)-*sec*-butylimine (**3b**) in 72 and 83% yields from the corresponding amides, respectively. The ketenimines **3a** and **3b** each showed a strong absorption band at 2010—2020 cm^{-1} characteristic of a ketenimine function. The ketenimines **3a** and **3b** were purified by distillation under high vacuum, and the physical

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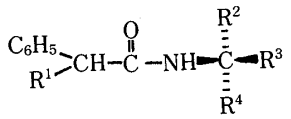
TABLE I. Synthesis of the Chiral Ketenimines **3a, b** from the Amides **1a, b** *via* the Imino Chlorides **2a, b**

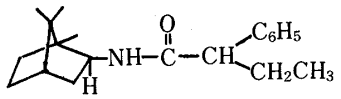
	1		2[a]		3[b]				Recovered 1 from 3[c]
	$[\alpha]_D^{20}$ ($CHCl_3$)	bp (°C) (1 mmHg)	Yield (%)	$[\alpha]_D^{27}$ ($CHCl_3$)	bp (°C) (4—5 mmHg)	Yield (%)	IR (cm^{-1}) (C=C=N)	$[\alpha]_D^{20}$ (THF)	$[\alpha]_D^{20}$ ($CHCl_3$)
a	+21.9° (c=1.60)	85	80	+8.5° (c=4.35)	90	90	2010	+19.4° (c=2.79)	+21.9° (c=1.60)
b	+17.1° (c=6.66)	85—95	90	+14.8° (c=3.59)	90—100	92	2020	+33.0° (c=4.33)	+14.8° (c=1.69)

a) The imino chlorides **2a, b** were prepared by heating the amides **1a, b** and phosphorus pentachloride in refluxing benzene for 2 h. *b*) The ketenimines **3a, b** were prepared by treating the imino chlorides **2a, b** with triethylamine in refluxing benzene for 12—17 h. *c*) The amides **1a, b** recovered by hydrolysis of the (+)-**3a, b** obtained with 4 N aqueous hydrochloric acid–acetone (1 : 10) (at room temperature).

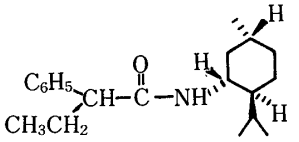


1a–e

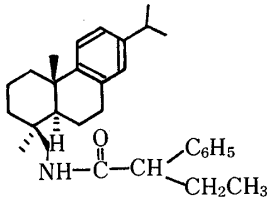
	R^1	R^2	R^3	R^4
1a :	H	CH_3	CH_2CH_3	H
1b :	CH_2CH_3	CH_3	CH_2CH_3	H
1c :	CH_2CH_3	$CH_2C_6H_5$	CH_2OCH_3	H
1d :	CH_2CH_3	$CH(CH_3)_2$	CH_2OCH_3	H
1e :	CH_2CH_3	CH_3	CH_2OCH_3	H



1f

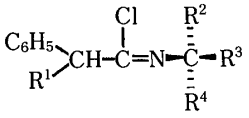


1g



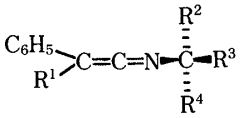
1h

Chart 1

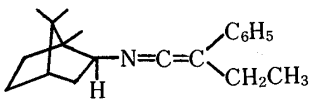


2a–e

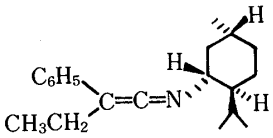
	R^1	R^2	R^3	R^4
a :	H	CH_3	CH_2CH_3	H
b :	CH_2CH_3	CH_3	CH_2CH_3	H
c :	CH_2CH_3	$CH_2C_6H_5$	CH_2OCH_3	H
d :	CH_2CH_3	$CH(CH_3)_2$	CH_2OCH_3	H
e :	CH_2CH_3	CH_3	CH_2OCH_3	H



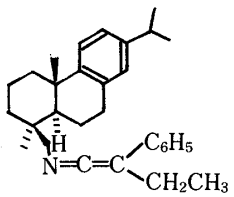
3a–e



3f



3g



3h

Chart 2

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Table II. Effects of Reaction Temperature and Solvent on Asymmetric Induction in the Reaction of **3b** with Trimethylsulfonium Ylide[a]

Solvent	Reaction conditions Reaction temp. (°C)	Reaction time (h)	Yield[b] (%)	Product **5** $[\alpha]_D$ (EtOH) (*c*, °C)	e.e. (%)[c]
THF	0	21.0	20	+6.5° (6.90, 22)	9.0
THF	−20	21.0	40	+10.2° (1.27, 25)	14.1
THF	−78	11.0	33	+9.3° (1.40, 16)	13.0
Et_2O	r.t.	19.5	19	+8.3° (3.24, 22)	11.5
THF–HMPA (10:1)	−20	19.0	20	+4.7° (3.00, 22)	6.5
THF–DMSO (7:1)	0	19.0	25	+3.5° (1.70, 23)	4.8
Et_2O–DMSO (7:1)	r.t.	13.5	20	+0.7° (1.40, 23)	1.0

a) The ketenimine **1b** (2.23 mmol) was reacted with trimethylsulfonium ylide (4.46 mmol) in 25 ml of the solvent under the conditions given in this table. *b*) Yields based on the amide **1b**, the starting material for the ketenimine **3b**. *c*) The enantiomeric excess was determined by NMR analysis with a shift reagent, $[Eu(hfc)_3]$.

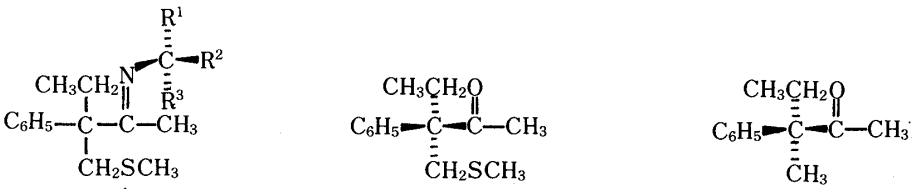
properties are listed in Table I.

Complete maintenance of chirality during these procedures was confirmed by comparison of the optical rotations of the starting amides used with those of the amides recovered by hydrolysis of the ketenimines **3a** and **3b** with 4 N aqueous hydrochloric acid–acetone (1 : 10) (at room temperature).

Other chiral ketenimines **3c**—**h** having higher boiling points were prepared by using the same sequence *via* imidoyl chlorides **2** from the corresponding diastereomeric amides **1c**—**h**, but they were thermally converted partially or wholly into nitriles[10] during distillation under high vacuum. Therefore the ketenimines were subjected directly to the next reactions without distillation or further purification by other methods because of their lability.

A solution of trimethylsulfonium ylide[11] [prepared by treating trimethylsulfonium iodide (2.0 eq) with butyllithium (1.5 N hexane solution, 2.4 eq) at −20 °C for 1 h] in tetrahydrofuran (THF) was reacted with (*S*)-(+)-**3b** at −20 °C for 21 h to give an imine **4**. The imine **4** was hydrolyzed by refluxing it in 10% aqueous hydrochloric acid–benzene (2 : 1) for 2 h, affording finally (*S*)-(+)-3-methylthiomethyl-3-phenyl-2-pentanone (**5**) with 14.1% enantiomeric excess in 40% yield [based on the starting amide **1b** used and corrected for the recovered amide **1b** (22%)]. The effects of reaction temperature and solvent on the asymmetric induction are summarized in Table II. As shown in Table II, the addition of hexamethylphosphoramide (HMPA) and dimethyl sulfoxide (DMSO) were not effective in this asymmetric induction.

The enantiomeric purity of the newly created asymmetric carbon of **5** was determined by nuclear magnetic resonance (NMR) analysis using a shift reagent, tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]europium (III) $[Eu(hfc)_3]$. The absolute configuration of **5** was determined to be (*S*)-(+) by the hydrogenetic conversion of **5** with Raney Ni into 3-methyl-3-phenyl-2-pentanone (**6**) of known configuration.[12]



4 (*S*)-(+)-**5** (*R*)-(−)-**6**

Chart 3

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The formation of **5** was rationalized in the following way. Nucleophilic addition of trimethylsulfonium ylide to a carbon–nitrogen double bond of the chiral ketenimine, followed by a [2,3] sigmatropic rearrangement of the sulfur ylide (**7B**) obtained by proton transfer from the C_1 carbon to the nitrogen atom in **7A**, produced an imine **4**, which was smoothly converted into an optically active ketone **5** by hydrolysis with 10% aqueous hydrochloric acid.

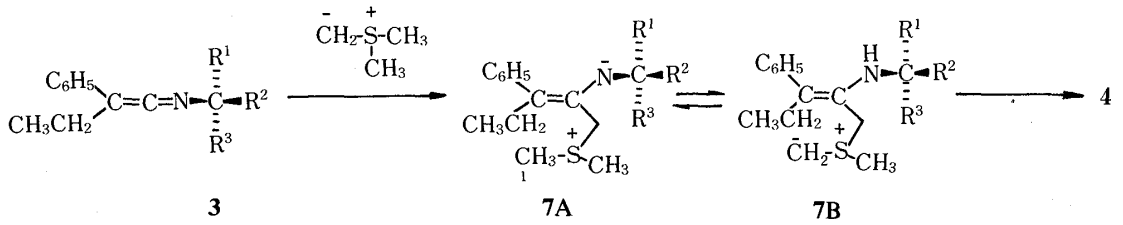

Chart 4

The effects of other amino components on this asymmetric induction were studied in the same way, using readily available optically active primary amines, and the results are summarized in Table III.

As indicated in Table III, with decreasing reaction temperature, the enantiomeric excess of the product (**5**) increased. The reaction of ethylphenylketene (−)-menthylimine (**3g**), prepared from a readily obtainable amide **1g**, with trimethylsulfonium ylide at −78 °C resulted in the highest optical yield of (*R*)-(−)-**5**. Since ethylphenylketene (+)-dehydroabiethylimine (**3h**) has an asymmetric center at the β position, the steric effect on the asymmetric induction was very low. Among the ketenimines **3b**—**h** employed herein, **3b**, **3e**, and **3f** have the same configuration and the other ketenimines **3c**, **3d**, **3g**, and **3h** have the same steric environment.

Therefore, (*S*)-(+)-**5** was obtained from **3b**, **3e**, and **3f**, while (*R*)-(−)-**5** was prepared from **3c**, **3d**, **3g**, and **3h**. Based on the absolute configuration of the product **5** obtained in each case, the most plausible mechanistic pathway for this asymmetric induction may be as follows.[8c,d] Initial addition of trimethylsulfonium ylide to the carbon–nitrogen double bond in the ketenimines **3b**—**h** would be preferred from the less-hindered side, namely from the

TABLE III. Asymmetric Induction in the [2, 3] Sigmatropic Rearrangement of Sulfur Ylides Derived from Chiral Ketenimines **3c**—**h** and Trimethylsulfonium Ylide[a]

Ketenimines	Reaction conditions: Reaction temp. (°C)	Reaction time (h)	Yield[b] (%)	Product **5**: $[\alpha]_D$ (EtOH) (*c*, °C)	Absolute confign.	e.e. (%)[c]
3c	−20	24.0	37	−3.2° (1.58, 22)	*R*	4.4
3d	−20	18.5	20	−11.1° (0.82, 15)	*R*	15.3
3e	−20	21.5	21	+4.0° (1.26, 21)	*S*	5.6
3f	−20	22.0	46	+10.3° (6.62, 20)	*S*	14.3
3f	−78	11.0	6	+28.1° (0.82, 20)	*S*	39.0
3g	0	22.0	34	−22.3° (3.81, 22)	*R*	30.9
3g	−20	23.5	47	−27.3° (2.56, 21)	*R*	37.8
3g	−78	12.5	36	−40.0° (1.00, 17)	*R*	55.6
3h	−20	19.0	75	−2.8° (1.82, 23)	*R*	3.9

a) The ketenimines **3c**—**h** (2.23 mmol) were reacted with trimethylsulfonium ylide (4.46 mmol) in 25 ml of THF under the conditions given in this table. *b*) Yields based on the corresponding amides **1c**—**h** used for the preparation of the ketenimines **3c**—**h**. *c*) The enantiomeric excess was determined by NMR analysis with a shift reagent, [Eu(hfc)$_3$].

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same direction as the ethyl group in this case. After proton transfer from the C_1 carbon to the nitrogen atom in **7A**, approach of the sulfur ylide group to the π-bond in **7B** would occur from the less-hindered upside, as indicated by the thick arrow in **8**, because of the energetic difference due to steric interference between the small (S) or medium (M) groups and the sulfur ylide moiety in the most preferred conformation (**8**) of **7B**, in which the large group (L) might be oriented on the same extended plane as the carbon–carbon double bond–nitrogen line in *anti* conformation to the functionality.

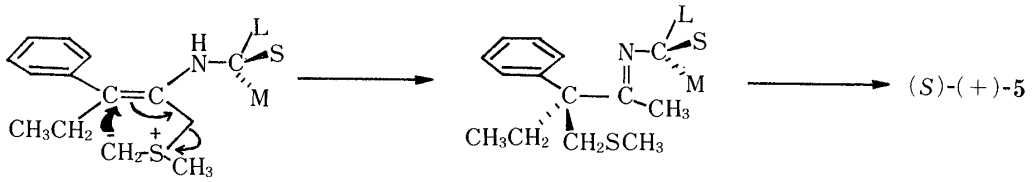

Chart 5

Thus, the readily obtainable ketenimines **3** affording consistently rather high enantioselectivity should represent a valuable synthetic tool for the preparation of optically active α'-substituted methyl ketones, which have a wide utility in organic synthesis.

Experimental

Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. Thin-layer or preparative thick layer plates were made of 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 were taken on a Hitachi RMU-6MG or RMU-7M spectrometer. Optical rotations were measured on a Union-Giken PM-101 polarimeter.

Synthesis of Amides 1a—h——(*S*)-*N*-*sec*-Butylphenylacetamide (**1a**): Phenylacetyl chloride (0.90 ml) was added to a mixture of 500 mg (6.84 mmol) of (*S*)-*sec*-butylamine and 0.95 ml (6.84 mmol) of triethylamine in 13 ml of THF at 0 °C, and the reaction mixture was stirred at room temperature for 25 h, then quenched with 10% aqueous hydrochloric acid and extracted with ether. The ethereal extracts were combined, washed 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 crude product was recrystallized from ligroin to afford 900 mg (69% yield) of **1a** as colorless needles of mp 67—69 °C. $[\alpha]_D^{25}$ +21.9° (c=3.74, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3300 (NH), 1630 (C(=O)–NH). NMR (CCl_4) δ: 0.80 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 1.00 (3H, d, J=7 Hz, $C\underline{H}_3CH$–N), 1.27 (2H, q, J=7 Hz, $C\underline{H}_2CH_3$), 3.33 (2H, s, $C\underline{H}_2C_6H_5$), 3.40—4.00 (1H, m, CH–N), 7.00—7.20 (5H, m, C_6H_5), 7.40 (1H, d, J=9 Hz, NH). *Anal.* Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.52; H, 8.99, N, 7.28.

The amides, *N*-(*S*)-*sec*-butyl-2-phenylbutyramide (**1b**), *N*-(+)-bornyl-2-phenylbutyramide (**1f**), *N*-(−)-menthyl-2-phenylbutyramide (**1g**), and *N*-dehydroabietyl-2-phenylbutyramide, (**1h**) were prepared in the same way as described above, by reaction of 2-phenylbutyryl chloride with commercially available optically active primary amines, (*S*)-(+)-*sec*-butylamine, (+)-bornylamine,[13] (−)-menthylamine, and (+)-dehydroabietylamine.

1b: IR ν_{max}^{film} cm^{-1}: 3300 (NH), 1640 (C(=O)–NH). NMR (CCl_4) δ: 0.93 (6H, t, J=7 Hz, $2C\underline{H}_3CH_2$), 1.00 (3H, d, J=7 Hz, $C\underline{H}_3CH$–N), 1.20—2.50 (4H, m, $2C\underline{H}_2CH_3$), 3.40 (1H, t, J=8 Hz, CH–C(=O)–), 3.53—4.10 (1H, m, CH–N), 7.00—7.40 (5H, m, C_6H_5), 7.65 (1H, br s, NH). MS m/e: 219 (M^+). Exact mass determination: 219.1611 (Calcd for $C_{14}H_{21}NO$: 219.1620).

1f: Colorless needles of mp 160 °C (recryst. from hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3320 (NH), 1640 (C(=O)–NH). NMR (CCl_4) δ: 0.60 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 0.73 (3H, s, CH_3), 0.83 (3H, s, CH_3), 0.97 (3H, s, CH_3), 1.10—2.30 (9H, m),

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2.90—3.90 (2H, m, CH–N and CH–$\overset{O}{\overset{\|}{C}}$), 5.50 (1H, br s, NH), 7.00—7.40 (5H, m, C_6H_5). MS *m/e*: 299 (M^+). Exact mass determination: 299.2217 (Calcd for $C_{20}H_{29}NO$: 299.4400). *Anal.* Calcd for $C_{20}H_{29}NO$: C, 80.22; H, 9.76; N, 4.64. Found: C, 80.23; H, 9.81; N, 4.59.

1g: Colorless needles of mp 183—185 °C (recryst. from hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (NH), 1655 ($\overset{O}{\overset{\|}{C}}$–NH). NMR ($CDCl_3$) δ: 0.60—1.20 (12H, m, $4CH_3$), 1.30—2.10 (11H, m), 3.05—4.00 (2H, m, $C\underline{H}$–N and CH–$\overset{O}{\overset{\|}{C}}$), 5.00 (1H, br s, NH), 7.16—7.50 (5H, m, C_6H_5). *Anal.* Calcd for $C_{20}H_{31}NO$: C, 79.67; H, 10.37; N, 4.65. Found: C, 79.73; H, 10.27; N, 4.71.

1h: IR ν_{max}^{film} cm^{-1}: 3350 (NH), 1650 ($\overset{O}{\overset{\|}{C}}$–NH). NMR ($CCl_4$) δ: 0.80 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 0.90 (3H, s, CH_3), 1.10 (3H, s, CH_3), 1.20 (6H, d, J=7 Hz, $(C\underline{H}_3)_2CH$), 1.40—2.30 (11H, m), 2.53—3.56 (6H, m, $C\underline{H}(CH_3)_2$, $C\underline{H}CH_2CH_3$, $C\underline{H}_2C{=}C$, and CH_2–N), 6.30 (1H, br s, NH), 6.70—7.23 (8H, m, aromatic H). MS *m/e*: 431 (M^+). Exact mass determination: 431.3176 (Calcd for $C_{30}H_{41}NO$, 431.3186).

N-(*S*)-(1-Methoxy-3-phenyl-2-propyl)-2-phenylbutyramide (**1c**): (*S*)-2-Amino-3-phenylpropanol (1.208 g, 8.00 mmol), obtained by $LiAlH_4$ reduction of (*S*)-phenylalanine ethyl ester, was reacted with 848 mg (8.00 mmol) of benzaldehyde under reflux in 40 ml of benzene with a Dean–Stark's apparatus to give 1.912 g of (*S*)-2-benzylidene-imino-3-phenylpropanol [IR ν_{max}^{film} cm^{-1}: 1640 (C=N)]. A solution of this imine in 10 ml of THF was added to a suspension of 460 mg (9.60 mmol) of sodium hydride (50% oily, washed with hexane before use) in 5 ml of THF at 0 °C, and the mixture was stirred at room temperature for 1 h. Methyl iodide (1.704 g, 12.00 mmol) was added to the above mixture at 0 °C and the reaction mixture was stirred at 0 °C for 16 h, and at room temperature for 18 h. Then 10% aqueous hydrochloric acid (4 ml) was added to the above mixture and the whole was heated under reflux for 2 h. After cooling, the mixture was washed with ether. The aqueous layer was made basic by saturation with K_2CO_3 and extracted with ether. The ethereal extracts were combined, dried over anhydrous K_2CO_3, and concentrated to dryness under reduced pressure to give 788 mg of (*S*)-1-methoxy-3-phenyl-2-propylamine. A solution of 959 mg of 2-phenylbutyryl chloride in 10 ml of THF was added to a mixture of 2.00 ml (14.33 mmol) of triethylamine and the (*S*)-1-methoxy-3-phenyl-2-propylamine obtained above, 0 °C, and the reaction mixture was stirred at room temperature for 17 h, then quenched with 10% aqueous hydrochloric acid and extracted with ether. The ethereal extracts were combined, washed 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 crude product was subjected to preparative thin-layer chromatography (TLC, ether–hexane, 1 : 1) to give 1.680 g of **1c** as colorless prisms of mp 67—70 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300 (NH), 1640 ($\overset{O}{\overset{\|}{C}}$–NH). NMR ($CDCl_3$) δ: 0.80 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 1.40—2.30 (2H, m, $C\underline{H}_2CH_3$), 2.70 (2H, t, J=7 Hz, $CH_2C_6H_5$), 3.17 (2H, s, CH_2O), 3.20 (3H, s, OCH_3), 3.30—4.40 (2H, m, CH–N and CH–$\overset{O}{\overset{\|}{C}}$), 5.98 (1H, br s, NH), 6.80—7.30 (10H, m, $2C_6H_5$). *Anal.* Calcd for $C_{20}H_{25}NO_2$: C, 77.13; H, 8.07; N, 4.50. Found: C, 77.08; H, 8.12; N, 4.46.

N-((*S*)-1-Methoxy-3-methyl-2-butyl)-2-phenylbutyramide (**1d**) and *N*-((*S*)-1-methoxy-2-propyl)-2-phenylbutyramide (**1e**) were prepared in the same way starting from (*S*)-valine ethyl ester and (*S*)-alanine ethyl ester, respectively.

1d: IR ν_{max}^{film} cm^{-1}: 3310 (NH), 1640 ($\overset{O}{\overset{\|}{C}}$–NH). NMR ($CCl_4$) δ: 0.56—1.10 (9H, m, $C\underline{H}_3CH_2$ and $CH(C\underline{H}_3)_2$), 1.46—2.13 (3H, m, $C\underline{H}(CH_3)_2$ and $C\underline{H}_2CH_3$), 3.06 (3H, s, OCH_3), 2.70—3.90 (4H, m, CH–N, CH_2O, and CH–$\overset{O}{\overset{\|}{C}}$), 5.50 (1H, br s, NH), 7.00—7.50 (5H, m, C_6H_5). MS *m/e*: 263 (M^+). Exact mass determination: 263.1886 (Calcd for $C_{16}H_{25}NO_2$, 263.3700).

1e: IR ν_{max}^{film} cm^{-1}: 3300 (NH), 1620 ($\overset{O}{\overset{\|}{C}}$–NH). NMR ($CCl_4$) δ: 0.85 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 1.10 (3H, d, J=6 Hz, $C\underline{H}_3CH$–N), 1.55—2.35 (2H, m, $C\underline{H}_2CH_3$), 3.10 (3H, s, OCH_3), 3.20—4.20 (4H, m, $\overset{O}{\overset{\|}{C}}$–CH, CH–N, and CH_2O), 6.03 (1H, d, J=8 Hz, NH), 7.00—7.40 (5H, m, C_6H_5). MS *m/e*: 235 (M^+). Exact mass determination: 235.1572 (Calcd for $C_{14}H_{21}NO_2$, 235.3200).

Synthesis of Chiral Ketenimines 3a, b——*N*-(*S*)-*sec*-Butylphenylacetimidoyl Chloride (**2a**): The amide **1a** (751 mg, 3.93 mmol) was reacted with 819 mg (3.93 mmol) of phosphorus pentachloride in 12 ml of refluxing benzene for 2 h. After cooling, the reaction mixture was concentrated under reduced pressure and the residue was distilled under high vacuum to give 613 mg (80% yield) of **2a**: IR ν_{max}^{film} cm^{-1}: 1650 (C=N), 1600, (C_6H_5). NMR (CCl_4) δ: 0.87

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(3H, t, $J=7$ Hz, $C\underline{H}_3CH_2$), 1.10, 1.20 (3H, d, d, $J=3$, 3 Hz, $C\underline{H}_3CH$–N), 1.50 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 3.60—3.90 (3H, m, CH_2–C=N and CH–N), 7.10—7.50 (5H, m, C_6H_5). The boiling point and the optical rotation of **2a** obtained are given in Table I.

Phenylketene (*S*)-*sec*-Butylimine (**3a**): A solution of 506 mg (2.42 mmol) of **2a** and 3.40 ml (24.20 mmol) of triethylamine in 18 ml of anhydrous benzene was refluxed for 12 h. The separated white precipitates were filtered off and the filtrate was concentrated *in vacuo*. The residue was distilled under high vacuum to give 376 mg (90% yield) of **3a**. The boiling point, the IR spectrum (C=C=N), and the optical rotation of **3a** thus obtained are given in Table I.

N-(*S*)-*sec*-Butyl-2-phenylbutyrimidoyl Chloride (**2b**): The amide **1b** (1.038 g, 4.74 mmol) was reacted with 987 mg (4.74 mmol) of phosphorus pentachloride in 12 ml of refluxing benzene for 2 h. After cooling, the mixture was concentrated under reduced pressure and the residue was distilled under high vacuum to give 953 mg (90% yield) of **2b**: IR ν_{max}^{film} cm^{-1}: 1640 (C=N), 1600 (C_6H_5). NMR (CCl_4) δ: 0.90 (6H, t, $J=7$ Hz, $2CH_3$), 1.10, 1.15 (3H, d, d, $J=6$ Hz, $C\underline{H}_3CHN$), 1.30—2.20 (4H, m, $2C\underline{H}_2CH_3$), 3.40—3.90 (2H, m, CH–C=N and CH–N), 7.00—7.40 (5H, m, C_6H_5). The boiling point and the optical rotation of **2b** thus obtained are given in Table I.

Ethylphenylketene (*S*)-*sec*-Butylimine (**3b**): A mixture of 879 mg (3.70 mmol) of **2b** and 5.15 ml (37.00 mmol) of triethylamine in 20 ml of anhydrous benzene was refluxed for 17 h. The separated white precipitates were filtered off and the filtrate was concentrated *in vacuo*. The residue was distilled under high vacuum to give 681 mg (92% yield) of **3b**. The boiling point, the IR spectrum (C=C=N), and the optical rotation of **3b** thus obtained are listed in Table I.

Hydrolysis of Ketenimines 3a, b——A solution of 53 mg of **3a** and 0.3 ml of 4 N aqueous hydrochloric acid in 3 ml of acetone was stirred at room temperature for 24 h. The mixture was concentrated *in vacuo* and the residue was diluted with chloroform. The solution was washed sequentially with saturated aqueous NaCl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl, then dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to preparative TLC (hexane–ether 2 : 3) to give 43 mg (73% yield) of **1a**.

The hydrolysis of **3b** (49 mg) was carried out in the same way to give 37 mg (70% yield) of **1b**.

The spectral data of the products were identical with those of the authentic amides **1a** and **1b**. The optical rotations of the starting materials and the recovered amides are listed in Table II.

Synthesis of Other Chiral Ketenimines 3c—h——General Procedure: A mixture of one of the amides **1c—h** (2.26 mmol) and phosphorus pentachloride (470 mg, 2.26 mmol) in 10 ml of benzene was refluxed for 3 h. After cooling, 3.10 ml (22.6 mmol) of triethylamine was added and the mixture 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 **3c—h**. The C=C=N absorption in the IR spectrum (cm^{-1}) and the yields (%) based on the corresponding amides are as follows. **3c**: 2020, 96; **3d**: 2025, 94; **3e**: 2020, quantitative; **3f**: 2020, 95; **3g**: 2020, 99; **3h**: 2030, quantitative.

Reaction of Ketenimines 3b—h with Trimethylsulfonium Ylide——A 1.5 N hexane solution of butyllithium (3.60 ml, 5.35 mmol) was added to a suspension of trimethylsulfonium iodide (910 mg, 4.46 mmol) in 15 ml of THF at −20 °C, and the mixture was stirred at −20 °C for 1 h. A solution of a ketenimine **3b—h** (2.23 mmol) in 10 ml of THF was added to the above mixture and the reaction solution was stirred under the conditions given in Tables II and III. The reaction mixture was quenched with saturated aqueous NaCl and extracted with ether. The ethereal layers were combined, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product, the imine **4**, was hydrolyzed by refluxing it in 10% aqueous hydrochloric acid (6 ml)–benzene (3 ml) for 2 or 3 h. 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 3-methylthiomethyl-3-phenyl-2-pentanone (**5**): IR ν_{max}^{film} cm^{-1}: 1710 ($-\overset{O}{\overset{\|}{C}}-$). NMR ($CCl_4$) δ: 0.76 (3H, t, $J=7$ Hz, $C\underline{H}_3CH_2$), 1.66 (3H, s, SCH_3), 1.80 (3H, s, $\overset{O}{\overset{\|}{C}}-CH_3$), 2.06 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 2.80—3.06 (2H, m, CH_2S), 6.90—7.40 (5H, m, C_6H_5). MS *m/e*: 222 (M^+). Exact mass determination: 222.1093 (Calcd for $C_{13}H_{18}OS$, 222.1078).

The yields, the optical rotations, and the enantiomeric excess of the product (**5**) derived from various kinds of chiral ketenimines **3b—h** are summarized in Tables II and III.

Hydrogenetic Desulfenylation of 5 with Raney Ni——A solution of 91 mg of **5** ($[\alpha]_D$ +10.3° ($c=4.95$, EtOH)) in 6 ml of ethyl alcohol was refluxed for 12 h with deactivated Raney Ni (0.80 ml in ethyl alcohol).[14] After removal of the catalyst by filtration, the filtrate was concentrated *in vacuo*. The residual oil was subjected to preparative TLC (hexane–isopropyl ether 8 : 1) to give 46 mg (63% yield) of 3-methyl-3-phenyl-2-pentanone (**6**):[12] IR ν_{max}^{film} cm^{-1}: 1710 ($-\overset{O}{\overset{\|}{C}}-$). NMR ($CCl_4$) δ: 0.73 (3H, t, $J=7$ Hz, $C\underline{H}_3CH_2$), 1.40 (3H, s, CH_3), 1.80 (3H, s, $CH_3-\overset{O}{\overset{\|}{C}}$), 1.92 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 7.00—7.40 (5H, m, C_6H_5). MS *m/e*: 176 (M^+). $[\alpha]_D^{21}$ +1.6° ($c=1.28$, cyclohexane).

References and Notes

1) This paper is dedicated to Professor Shun-ichi Yamada on the occasion of his 70th birthday.

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