Asymmetric Induction Reactions. I. Asymmetric [2,3] Sigmatropic Rearrangements of Sulfur Ylides Derived from Chiral Ketamines and Trimethylsulfonium Ylide$^{1,2}$

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The asymmetric [2,3] sigmatropic rearrangements of 2-alkylamino-3-phenyl-2-pentenyilmethylsulfonium methylides were accomplished by the reaction of ethylphenylketenimes 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 $-78^\circ$C resulted in the highest optical yield of (R)(−)-5 in the above sequence.

Keywords — asymmetric induction; [2,3] sigmatropic rearrangement; chiral ketenimine; sulfur ylides; 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$^8$ 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$^9$ 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 cycloadition 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-buty1phenylacetamido (1a) and N-(S)-sec-buty1-2-phenylbutyramide (1b) with an equivalent amount of phosphorus pentachloride were carried out by refluxing in benzene for 2 h to produce N-(S)-sec-buty1phenylacetimidoyl chloride (2a) and N-(S)-sec-buty1-2-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-buty1limine (3a) and ethylphenylketene (S)-sec-buty1limine (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
Table I. Synthesis of the Chiral Ketenimines 3a, b from the Amides 1a, b via the Imino Chlorides 2a, b

<table>
<thead>
<tr>
<th></th>
<th>1a</th>
<th>2a</th>
<th>3a</th>
<th>Recovered 1 from 3a</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$[a]_{D}^{20}$ (CHCl$_3$)</td>
<td>bp (%)</td>
<td>Yield (%)</td>
<td>$[a]_{D}^{20}$ (4 mmHg)</td>
</tr>
<tr>
<td>a</td>
<td>+21.9°</td>
<td>85</td>
<td>80</td>
<td>+8.5°</td>
</tr>
<tr>
<td></td>
<td>(c=1.60)</td>
<td>(c=4.35) &amp;</td>
<td></td>
<td>(c=3.59) &amp;</td>
</tr>
<tr>
<td>b</td>
<td>+17.1°</td>
<td>85—95</td>
<td>90</td>
<td>+14.8°</td>
</tr>
<tr>
<td></td>
<td>(c=6.66)</td>
<td>(c=3.59) &amp;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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.

![Chemical Structures](chart1.png)

![Chemical Structures](chart2.png)

Chart 1

Chart 2
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 trimethylsulfonylum ylide\(^{11}\) [prepared by treating trimethylsulfonylum iodide (2.0 eq) with butyllithium (1.5 N hexane solution, 2.4 eq) at \(-20^\circ C\) for 1 h] in tetrahydrofuran (THF) was reacted with (S)-(+)–3b at \(-20^\circ C\) 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)-(+)–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 hexamethylphosphoramidite (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-(heptfluoropropylhydroxymethylene)-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.\(^{12}\)

\[\text{Table II. Effects of Reaction Temperature and Solvent on Asymmetric Induction in the Reaction of 3b with Trimethylsulfonylum Ylide}\]

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Reaction conditions</th>
<th>Product 5</th>
<th>e.e. (%)(^{\text{a}})</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reaction temp. (°C)</td>
<td><a href="EtOH">(\varepsilon)</a> (°C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reaction time (h)</td>
<td>Yield (%)</td>
<td></td>
</tr>
<tr>
<td>THF</td>
<td>0</td>
<td>21.0</td>
<td>20</td>
</tr>
<tr>
<td>THF</td>
<td>-20</td>
<td>21.0</td>
<td>40</td>
</tr>
<tr>
<td>THF</td>
<td>-78</td>
<td>11.0</td>
<td>33</td>
</tr>
<tr>
<td>Et(_2)O</td>
<td>r.t.</td>
<td>19.5</td>
<td>19</td>
</tr>
<tr>
<td>THF–HMPA</td>
<td>-20</td>
<td>19.0</td>
<td>20</td>
</tr>
<tr>
<td>THF–DMSO</td>
<td>(7:1)</td>
<td>0</td>
<td>19.0</td>
</tr>
<tr>
<td>Et(_2)O–DMSO</td>
<td>(7:1)</td>
<td>r.t.</td>
<td>13.5</td>
</tr>
</tbody>
</table>

\(^{a}\) The ketenimine 1b (2.23 mmol) was reacted with trimethylsulfonylum 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].

\[\text{Chart 3}\]
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 C₁ 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.

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 ethynylphenylketene (−)-methyllylimine (3g), prepared from a readily obtainable amide 1g, with trimethylsulfonium ylide at −78 °C resulted in the highest optical yield of (R)-(−)-5. Since ethynylphenylketene (+)-dehydroabietylimine (3b) 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, 3c, 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, 3c, 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: 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* |
|----------------------------------|--------------|----------------|----------------|----------------|
| Ketenimines | Reaction conditions | 5 | Reaction conditions | 5 | Absolute e.e. (٪) |
| Reaction temp. (°C) | Reaction time (h) | Yield(%) | [α]D (EtOH) (e, °C) | Absolute config. |
| 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 |
| 3g | −78 | 11.0 | 6 | +28.1° (0.82, 20) | S | 39.0 |
| 3h | 0 | 22.0 | 34 | −22.3° (3.81, 22) | R | 30.9 |
| 3g | −20 | 23.5 | 47 | −23.7° (2.56, 21) | R | 37.8 |
| 3h | −78 | 12.5 | 36 | −40.0° (1.00, 17) | R | 55.6 |
| 3h | −20 | 19.0 | 75 | −28° (1.82, 23) | R | 3.9 |

* 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 amines 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].
same direction as the ethyl group in this case. After proton transfer from the C₁ 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 mixture reaction 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 NaHCO₃, and saturated aqueous NaCl, dried over anhydrous Na₂SO₄, 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. [α]D₂O 21.9° (c = 3.74, CHCl₃). IR νmax cm⁻¹: 3300 (NH), 1630 (C–NH). NMR (CDCl₃) δ: 0.80 (3H, t, J = 7 Hz, CH₂CH₃), 1.00 (3H, d, J = 7 Hz, CH₂CH₂–N), 1.27 (2H, q, J = 7 Hz, CH₂CH₂), 3.35 (2H, s, OCH₂CH₂), 3.40—4.00 (1H, m, CH–N), 7.00—7.20 (5H, m, C₆H₅), 7.40 (1H, d, J = 9 Hz, NH). Anal. Caled for C₁₂H₁₄N: 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(--)methyl-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, and (−)-dehydroabietylamine.

1b: IR νmax cm⁻¹: 3300 (NH), 1640 (C–NH). NMR (CDCl₃) δ: 0.93 (6H, t, J = 7 Hz, 2CH₃CH₂), 1.00 (3H, d, J = 7 Hz, CH₂CH₂–N), 1.20—2.50 (4H, m, 2CH₂CH₂), 3.40 (1H, t, J = 8 Hz, CH–C–), 3.53—4.10 (1H, m, CH–N), 7.00—7.40 (5H, m, C₆H₅), 7.65 (1H, brs, NH). MS m/z: 219 (M⁺). Exact mass determination: 219.1611 (Caled for C₁₄H₁₃N: 219.1620).

If: Colorless needles of mp 160 °C (recryst. from hexane). IR νmax cm⁻¹: 3320 (NH), 1640 (C–NH). NMR (CDCl₃) δ: 0.60 (3H, t, J = 7 Hz, CH₂CH₂), 0.73 (3H, s, CH₃), 0.83 (3H, s, CH₂), 0.97 (3H, s, CH₃), 1.10—2.30 (9H, m),
2.90—3.90 (2H, m, CH-N and CH-C), 5.50 (1H, br s, NH), 7.00—7.40 (5H, m, C6H5). MS m/e: 299 (M+). Exact mass determination: 299.2217 (Caled for C26H20NO: 299.4400). Anal. Caled for C26H20NO: 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 νCHCl3 cm⁻¹: 3400 (NH), 1655 (C=NH).

NMR (CDCl3) δ: 0.60—1.20 (12H, m, 4CH3), 1.30—2.10 (11H, m), 3.05—4.00 (2H, m, CH-N and CH-C), 5.00 (1H, brs, NH), 7.16—7.50 (5H, m, C6H5). Anal. Caled for C25H21NO: C, 79.67; H, 10.37; N, 4.65. Found: C, 79.73; H, 10.27; N, 4.71.

1h: IR νfilm cm⁻¹: 3350 (NH), 1650 (C=NH). NMR (CDCl3) δ: 0.80 (3H, t, J = 7 Hz, CH3CH2), 0.90 (3H, s, CH3), 1.10 (3H, s, CH3), 1.20 (6H, d, J = 7 Hz, CH2CH3), 1.40—2.30 (11H, m), 2.53—3.56 (6H, m, CH(CH3)2, CH2CH2CH3, CH2C=CH, and CH-N), 6.30 (1H, brs, NH), 6.70—7.23 (8H, m, aromatic H). MS m/e: 431 (M+).

Exact mass determination: 431.3176 (Caled for C24H24N2O, 431.3186).

N-(S)-(1-Methoxy-3-phenyl-2-propyl)-2-phenylbutyramide (1e): (S)-2-Amino-3-phenylpropanol (1.208 g, 8.00 mmol), obtained by LiAlH4 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-benzylidenemino-3-phenylpropanol [IR νmax 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 basic by saturation with K2CO3 and extracted with ether. The ethereal extracts were combined, dried over anhydrous K2CO3, 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-phenylbutyl 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 NaHCO3 and saturated aqueous NaCl, dried over anhydrous Na2SO4, 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 1e as colorless prisms of mp 67—70 °C. IR νmax cm⁻¹: 3300 (NH), 1640 (C=NH). NMR (CDCl3) δ: 0.80 (3H, t, J = 7 Hz, CH3CH2), 1.40—2.30 (2H, m, CH2CH3), 2.70 (2H, t, J = 7 Hz, CH2C6H5), 3.17 (2H, s, CH2O), 3.20 (3H, s, OCH3), 3.30—4.40 (2H, m, CH-N and CH-C), 5.98 (1H, brs, NH), 6.80—7.30 (10H, m, 2C6H5). Anal. Caled for C20H22N2O2: 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 νmax cm⁻¹: 3310 (NH), 1640 (C=NH). NMR (CDCl3) δ: 0.56—1.10 (9H, m, CH3CH2 and CH(CH3)2), 1.46—2.13 (3H, m, CH(CH3)2 and CH2CH3), 3.06 (3H, s, OCH3), 2.70—3.90 (4H, m, CH-N, CH2O, and CH-C), 5.50 (1H, br s, NH), 7.00—7.50 (5H, m, C6H5). MS m/e: 263 (M+). Exact mass determination: 263.1886 (Caled for C16H22N2O2, 263.3700).

1e: IR νmax cm⁻¹: 3300 (NH), 1620 (C=NH). NMR (CDCl3) δ: 0.85 (3H, t, J = 7 Hz, CH3CH2), 1.10 (3H, d, J = 6 Hz, CH3CH-N), 1.55—2.35 (2H, m, CH2CH3), 3.10 (3H, s, OCH3), 3.20—4.20 (4H, m, C=CH, CH-N, and CH2O), 6.03 (1H, d, J = 8 Hz, NH), 7.00—7.40 (5H, m, C6H5). MS m/e: 235 (M+). Exact mass determination: 235.1572 (Caled for C14H17N2O2, 235.3200).

Synthesis of Chiral Ketenimines 3a, b——N-(S)-sec-Butylphenacetimidoyl 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 νmax cm⁻¹: 1650 (C=N), 1600, (C=H). NMR (CDCl3) δ: 0.87
Phenyketone (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-phenylbutyrimidyl 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 νmax cm⁻¹: 1640 (C = N), 1600 (C = H). NMR (CCl₄) δ: 0.90 (6H, t, J = 7 Hz, 2CH₃), 1.10, 1.15 (3H, d, d, J = 6 Hz, CH₂CN), 1.30—2.20 (4H, m, 2CH₂CH₃), 3.40—3.90 (2H, m, CH = C = N and CH = N), 7.00—7.40 (5H, m, C₆H₅). The boiling point and the optical rotation of 2b thus obtained are given in Table I.

Ethylphenyketone (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 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 NaHCO₃, and saturated aqueous NaCl, then dried over anhydrous Na₂SO₄, and concentrated in vacuo. The residue was subjected to preparative TLC (hexane–ether 2:3) to give 43 mg (73% yield) of 3a.

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; 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 ether layers were combined, dried over anhydrous Na₂SO₄, 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 NaHCO₃, and saturated aqueous NaCl, dried over anhydrous Na₂SO₄, 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 νmax cm⁻¹: 1710 (−C=O). NMR (CCl₄) δ: 0.76 (3H, t, J = 7 Hz, CH₂CH₃), 1.66 (3H, s, SCH₃), 1.80 (3H, s, C–CH₃), 2.06 (2H, q, J = 7 Hz, CH₂CH₃), 2.80—3.06 (2H, m, CH₂S), 6.90—7.40 (5H, m, C₆H₅). MS m/e: 222 (M⁺). Exact mass determination: 222.1093 (Calcd for C₁₅H₁₉OS₂, 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 ([α]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 of ethyl alcohol). 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): IR νmax cm⁻¹: 1710 (−C=O). NMR (CCl₄) δ: 0.73 (3H, t, J = 7 Hz, CH₂CH₃), 1.40 (3H, s, CH₃), 1.80 (3H, s, CH₃–C), 1.92 (2H, q, J = 7 Hz, CH₂CH₃), 7.00—7.40 (5H, m, C₆H₅). MS m/e: 176 (M⁺). [α]D + 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.