Acid-Promoted Reactions of Schiff's Bases with Ketene Dithioacetal, Vinyl Sulfides, and 1,2-Propadienyl Sulfides

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Several types of addition reactions proceed between Schiff's bases and olefinic nucleophiles containing an alkylthio substituent. Ketene dithioacetal or 2-(methylthio)allylsilane reacts with Schiff's bases in the presence of trifluoromethanesulfonic acid to afford β-amino acid equivalents or homoallylic amines, respectively. On the other hand, ene reaction proceeds between 1-alkyl-1,2-propadienyl sulfides and Schiff's bases by treatment with $AlCl_3$, giving 1,3-dienes.

Addition reactions of carbon nucleophiles to Schiff's bases[1] provide efficient methods for the synthesis of nitrogen-containing natural products, e.g., amino acids, β-lactams, and amino sugars. As compared with carbonyl compounds, however, it is not usually an easy task to develop carbon-carbon bond forming reactions by use of Schiff's bases. Strong nucleophiles like alkyllithiums and Grignard reagents can not be utilized in the reaction with Schiff's bases owing to the side reactions, for example, the generation of metallo enamine[2] or the dimerization by reductive coupling.[3]

Various kinds of metal enolates of acetic acid derivatives have been devised for the addition reaction to Schiff's bases.[4] But most of the successful results are restricted to reactions with non-enolizable Schiff's bases, such as aromatic Schiff's bases[5] and imino esters.[6] Enolizable Schiff's bases can be employed only in the reactions with tin(II) enolate-tin(II) triflate,[7] lithium enolate-Me_2AlCl[8] or boron enolate.[9]

Ketene silyl acetals also react with aryl Schiff's bases by the activation with certain Lewis acids, for instance, $TiCl_4$,[10] trimethylsilyl trifluoromethanesulfonate[11] or a phosphonium salt.[12] But aliphatic Schiff's bases are utilizable only in the reaction with β,β-dimethylketene silyl acetals.[10] Accordingly, it is desirable to exploit a general method for the addition reaction of acetic acid equivalents to a wide range of Schiff's bases.

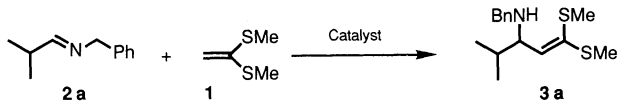
We already disclosed that [2+2] cycloaddition reaction proceeds between electron-deficient olefins and olefins possessing an alkylthio group, such as ketene dithioacetals, vinyl sulfides, and 1,2-propadienyl sulfides,[13] and that ene reaction proceeds between aldehydes and 1,2-propadienyl sulfides.[14] In this paper are reported the acid-catalyzed addition reactions of various Schiff's bases with olefins possessing an alkylthio group.

Results and Discussion

Reaction of Ketene Dithioacetal. At first, 1,1-bis(methylthio)ethylene (**1**), a synthetic equivalent of acetic acid, was chosen as a nucleophile and the reaction with Schiff's bases was investigated.

Reaction of the ketene dithioacetal **1** with an aliphatic Schiff's base, *N*-isobutylidenebenzylamine (**2a**) was tried in the presence of $TiCl_2(OPr^i)_2$ which promoted the [2+2] cycloaddition of **1** with a fumaric acid derivative.[13a] The addition reaction occurred at room temperature but afforded the adduct **3a** only in 21% yield (Table 1, Entry 1). Several catalysts, Lewis acids and protic acids, were screened with the result that trifluoromethanesulfonic acid was a favorable catalyst to give **3a** in high yield (Table 1, Entry 8).

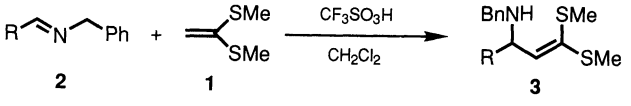
Schiff's base **2b** derived from an aromatic aldehyde also reacted with **1** in the presence of trifluoromethanesulfonic acid, providing the corresponding addition



2a **1** **3a**

Table 1. Effect of Catalyst in the Reaction between Schiff's Base **2a** and **1**

Entry	Catalyst	Solvent	Temp	Yield/%
1	$TiCl_2(OPr^i)_2$	Toluene	0°C	21
2	$TiCl_4$	Toluene	r.t.	0
3	$AlCl_3$	Toluene	r.t.	13
4	Et_2AlCl	CH_2Cl_2	r.t.	31
5	$ZrCl_4$	CH_2Cl_2	0°C	45
6	FSO_3H	CH_2Cl_2	r.t.	27
7	CF_3CO_2H	CH_2Cl_2	r.t.	48
8	CF_3SO_3H	CH_2Cl_2	−22°C	71



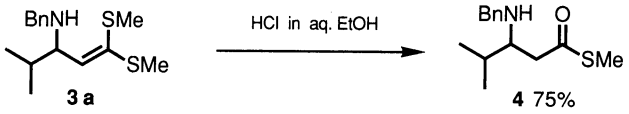
2 **1** **3**

Table 2. The Reaction of Schiff's Bases **2** with Ketene Dithioacetal **1**

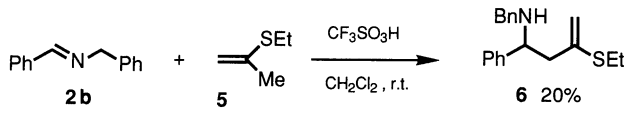
Entry	R	Temp	Yield/%
1	Pr^i (**2a**)	−22°C	71 (**3a**)
2	Ph (**2b**)	−78°C	78 (**3b**)
3	Bu^n (**2c**)	r.t.	40 (**3c**)

product **3b** in good yield. Though Schiff's base **2c** of a primary aldehyde is relatively unstable under the acidic conditions, the product **3c** was obtained in an acceptable yield.

The amino ketene dithioacetal **3a** was easily transformed into the β-amino thioester **4** by hydrolysis in acidic aqueous ethanol,[15] which is known to be readily converted to β-lactam by treatment with copper(I) trifluoromethanesulfonate.[16] The present reaction, therefore, is regarded as a useful method for the preparation of the β-lactam precursors.



Reaction of Vinyl Sulfides. Next a vinyl sulfide, 2-ethylthiopropene (**5**), was submitted to the reaction with Schiff's base instead of ketene dithioacetal **1**. When **5** was treated with the aromatic Schiff's base **2b** employing trifluoromethanesulfonic acid as a catalyst, ene product, *N*-benzyl-3-ethylthio-1-phenyl-3-butenylamine (**6**), was obtained but in an unsatisfactory yield of 20%.



Since the vinyl sulfide **5** exhibited rather low reactivity, reaction of 2-(methylthio)allylsilane (**7**) with the Schiff's base **2a** was investigated with the expectation that the silyl group[17] increases the nucleophilicity of a vinyl sulfide moiety. Allylation reaction[18] proceeded to afford *N*-benzyl-3-methylthio-1-isopropyl-3-butenylamine (**8a**) in moderate yield (65%). Furthermore, the reaction of aromatic and aliphatic Schiff's bases **2b**, **c** yielded the corresponding allylation products **8b**, **c**.

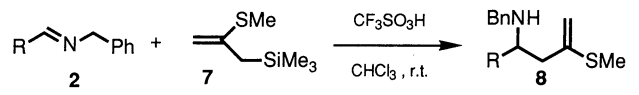
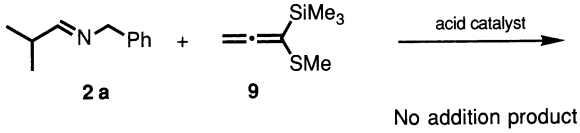


Table 3. The Reaction of Schiff's Bases **2** with **7**

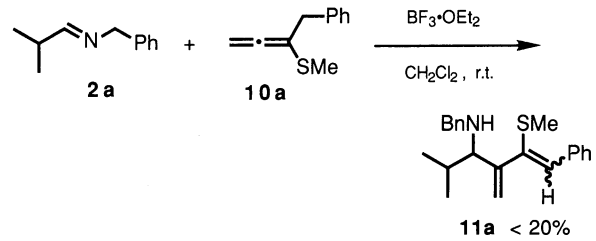
Entry	R	Yield/%
1	Pr^i (**2a**)	65 (**8a**)
2	Ph (**2b**)	78 (**8b**)
3	Bu^n (**2c**)	35 (**8c**)

On the other hand, no addition reaction occurred when 3-trimethylsilylpropene was employed and this result apparently shows that the nucleophilicity of allylsilane is increased by introduction of a methylthio substituent.

Reaction of 1,2-Propadienyl Sulfides. In our previous research, 1-methylthio-1-trimethylsilyl-1,2-propadiene (**9**) was found to readily react with various electron-deficient olefins, affording the [2+2] cycloaddition products.[13b] But when **9** was treated with Schiff's base **2a** in the presence of $AlCl_3$ or trifluoromethanesulfonic acid, no addition product was detected and Schiff's base **2a** was recovered.



In place of the 1-silyl-1,2-propadienyl sulfide **9**, the reaction of 1-alkyl-1,2-propadienyl sulfides was then investigated, because the high reactivity of 1-alkyl-1,2-propadienyl sulfides as an ene component was already revealed in the ene reaction with various aldehydes.[14] Treatment of a mixture of the Schiff's base **2a** and a 1-alkyl-1,2-propadienyl sulfide **10a** with BF_3·OEt_2 afforded the ene product **11a** as expected, though in less than 20% yield.



The yield of this ene reaction was largely dependent upon the Lewis acid employed, and $AlCl_3$ proved to be the suitable catalyst among several Lewis acids ($AlCl_3$, $EtAlCl_2$, $SnCl_4$, $TiCl_4$, and $ZrCl_4$). The reactions between various Schiff's bases **2a**—**c** and 1,2-propadienyl sulfides **10a**—**c** were performed in the presence of $AlCl_3$ and the results are listed in Table 4.

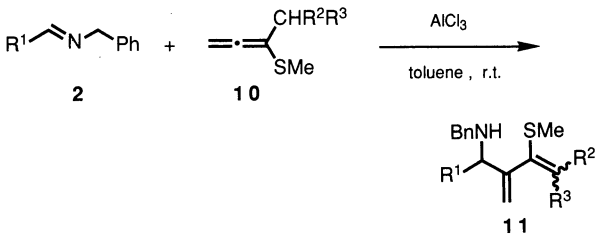


Table 4. The Ene Reaction of Schiff's Bases **2** with 1,2-Propadienyl Sulfides **10**

Entry	Schiff's base R^1	Allene R^2	Allene R^3	Yield/% (*Z*:*E*)
1	Pr^i (**2a**)	Ph	H (**10a**)	83 (2.5:1) (**11a**)
2	Ph (**2b**)	Ph	H (**10a**)	81 (3:1) (**11b**)
3	Bu^n (**2c**)	Ph	H (**10a**)	28 (2:1) (**11c**)
4	Pr^i (**2a**)	Me	Me (**10b**)	88 (**11d**)
5	Ph (**2b**)	Me	Me (**10b**)	80 (**11e**)
6	Bu^n (**2c**)	Me	Me (**10b**)	64 (**11f**)
7	Ph (**2b**)	H	H (**10c**)	53 (**11g**)

The present ene reaction shows a wide generality. That is, not only aromatic Schiff's base **2b**, but also aliphatic ones **2a, c** can be employed as enophiles to react with 1,2-propadienyl sulfides **10a—c**.

Schiff's bases are known as much poorer enophiles than aldehydes, and use of them as enophiles hitherto has been restricted either to the reactions of *N*-sulfonylimines derived from glyoxylate and chloral[19] or to the intramolecular reactions.[20] But by employment of 1,2-propadienyl sulfides as the ene component, ene reaction of various Schiff's bases proceeded smoothly, resulting in the preparation of synthetically useful 1,3-dienes possessing an alkylthio group.[21]

In conclusion, olefinic compounds possessing an alkylthio group react with Schiff's bases by the aid of acids: Addition reaction proceeds with a ketene dithioacetal, allylation reaction with 2-(methylthio)allylsilane, and ene reaction with 1,2-propadienyl sulfides, giving β-lactam precursors, homoallylic amines, and various 1,3-dienes, respectively.

Experimental

General. NMR spectra were measured with Bruker AM500 spectrometer using tetramethylsilane as the internal standard. $CDCl_3$ was used as solvent. IR spectra were recorded with Horiba FT 300-S spectrophotometer. High-resolution mass spectra (HRMS) were obtained with JEOL JMS-D300 mass spectrometer at ionization energy of 70 eV.

Column chromatography was conducted on silica gel (E. Merck, 7734, 70—230 mesh). Preparative thin-layer chromatography (TLC) was performed on a silica gel (Wakogel B-5F).

Dichloromethane was distilled from P_2O_5, then from CaH_2, and dried over Molecular Sieves 4A (MS 4A). Chloroform was freshly distilled from $CaCl_2$. Tetrahydrofuran (THF) was freshly distilled from sodium diphenylketyl. Toluene was distilled and dried over MS 4A. Trifluoromethanesulfonic acid and $AlCl_3$ were reagent grade and were used without further purification. $BF_3{\cdot}OEt_2$ was freshly distilled from CaH_2. Aliphatic Schiff's bases (**2a, c**)[22] and an aromatic one (**2b**)[23] were prepared according to the reported procedures. 1,1-Bis(methylthio)ethylene (**1**)[24] and 2-methylthio-3-trimethylsilyl-1-propene (**7**)[25] were synthesized by the literature methods.

All the operations were carried out under an argon atmosphere.

Typical Procedure for the Reaction between Schiff's Base 2 and Ketene dithioacetal 1 (Table 2). To a dichloromethane solution (3.0 ml) of Schiff's base **2** (0.40 mmol) and 1,1-bis(methylthio)ethylene (**1**) (144.3 mg, 1.2 mmol) was added a dichloromethane solution (2 ml) of trifluoromethanesulfonic acid (72.0 mg, 0.48 mmol) at the temperature indicated in Table 2. After being stirred for 10 h, the reaction mixture was quenched with saturated aqueous sodium hydrogencarbonate. Organic materials were extracted with dichloromethane and the combined extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by TLC to afford the product.

Spectral data of the addition products are as follows.

***N*-Benzyl-1-isopropyl-3,3-bis(methylthio)-2-propenylamine (3a).** IR (neat) 1645, 1581, 1456 cm^{-1}; ^1H NMR δ=0.89 (d, 3H, J=6.8 Hz), 0.95 (d, 3H, J=6.8 Hz), 1.50 (bs, 1H), 1.69—1.76 (m, 1H), 2.28 (s, 3H), 2.29 (s, 3H), 3.63 (d, 1H, J=13.2 Hz), 3.66 (dd, 1H, J=6.1, 9.4 Hz), 3.77 (d, 1H, J=13.2 Hz), 5.69 (d, 1H, J=9.4 Hz), 7.22—7.37 (m, 5H); ^{13}C NMR (125 Hz) δ=16.6, 16.7, 18.5, 19.4, 32.9, 51.5, 62.6, 126.7, 128.0, 128.1, 135.0, 135.2, 140.6. HRMS Found: m/z 281.1251. Calcd for $C_{15}H_{23}NS_2$: M, 281.1273.

***N*-Benzyl-3,3-bis(methylthio)-1-phenyl-2-propenylamine (3b).** IR (neat) 1680, 1577, 1448 cm^{-1}; ^1H NMR δ=1.59 (bs, 1H), 2.22 (s, 3H), 2.28 (s, 3H), 3.70 (d, 1H, J=13.1 Hz), 3.74 (d, 1H, J=13.1 Hz), 5.03 (d, 1H, J=8.8 Hz), 5.86 (d, 1H, J=8.8 Hz), 7.23—7.42 (m, 10H). HRMS Found: m/z 315.1084. Calcd for $C_{18}H_{21}NS_2$: M, 315.1117.

***N*-Benzyl-1-[2,2-bis(methylthio)ethenyl]pentylamine (3c).** IR (neat) 1670, 1579, 1454 cm^{-1}; ^1H NMR δ=0.86 (t, 3H, J=7.0 Hz), 1.27—1.55 (m, 6H), 1.64 (bs, 1H), 2.27 (s, 3H), 2.28 (s, 3H), 3.65 (d, 1H, J=13.1 Hz), 3.75 (d, 1H, J=13.1 Hz), 3.86 (ddd, 1H, J=5.8, 7.9, 9.0 Hz), 5.61 (d, 1H, J=9.0 Hz), 7.20—7.29 (m, 5H). HRMS Found: m/z 295.1409. Calcd for $C_{16}H_{25}NS_2$: M, 295.1430.

Hydrolysis of 3a to *S*-Methyl 3-Benzylamino-4-methylpentanethioate (4). In a mixed solution of concd hydrochloric acid (2.4 ml) and ethanol (10 ml) was dissolved **3a** (112 mg, 0.40 mmol) and stirred for 2 d at room temperature. The resulting solution was neutralized by saturated aqueous sodium hydrogencarbonate, and organic materials were extracted with dichloromethane and the combined extracts were washed with brine and dried over Na_2SO_4. After evaporation of the solvent the crude product was purified by TLC (hexane : ethyl acetate=3 : 1) to afford the thioester **4** (75 mg, 0.30 mmol, 75%). IR (neat) 1685, 1462 cm^{-1}; ^1H NMR δ=0.83 (d, 3H, J=7.1 Hz), 0.85 (d, 3H, J=7.1 Hz), 1.54 (bs, 1H), 1.79—1.84 (m, 1H), 2.24 (s, 3H), 2.55 (dd, 1H, J=7.9, 14.8 Hz), 2.62 (dd, 1H, J=4.7, 14.8 Hz), 2.89 (ddd, 1H, J=4.7, 4.7, 7.9 Hz), 3.68 (d, 1H, J=13.0 Hz), 3.71 (d, 1H, J=13.0 Hz), 7.15—7.26 (m, 5H). HRMS Found: m/z 251.1385. Calcd for $C_{14}H_{21}NOS$: M, 251.1345.

Typical Procedure for the Allylation Reaction between 2-(Methylthio)allylsilane (7) and Schiff's Base 2 (Table 3). The procedure was the same as that of the reaction between ketene dithioacetal **1** and Schiff's bases **2**, except that 2-methylthio-3-trimethylsilyl-1-propene (**7**) was employed in place of ketene dithioacetal **1** and $CHCl_3$ was used as the solvent.

Spectral data of the allylation products are as follows.

***N*-Benzyl-1-isopropyl-3-methylthio-3-butenylamine (8a).** IR (neat) 1627, 1452 cm^{-1}; ^1H NMR δ=0.80 (d, 3H, J=4.6 Hz), 0.81 (d, 3H, J=4.6 Hz), 1.78—1.82 (m, 1H), 1.90 (bs, 1H), 2.10 (s, 3H), 2.17 (dd, 1H, J=9.0, 14.2 Hz), 2.26 (dd, 1H, J=4.5, 14.2 Hz), 2.60 (ddd, 1H, J=4.5, 4.5, 9.0 Hz), 3.64 (d, 1H, J=13.0 Hz), 3.69 (d, 1H, J=13.0 Hz), 4.54 (s, 1H), 4.59 (s, 1H), 7.11—7.22 (m, 5H). HRMS Found: m/z 249.1569. Calcd for $C_{15}H_{23}NS$: M, 249.1553.

***N*-Benzyl-3-methylthio-1-phenyl-3-butenylamine (8b).** IR (neat) 1600, 1454 cm^{-1}; ^1H NMR δ=1.78 (bs, 1H), 2.21 (s, 3H), 2.52 (dd, 1H, J=4.9, 14.1 Hz), 2.58 (dd, 1H, J=9.3, 14.1 Hz), 3.51 (d, 1H, J=13.4 Hz), 3.66 (d, 1H, J=13.4 Hz), 3.93 (dd, 1H, J=4.9, 9.3 Hz), 4.64 (s, 1H), 5.03 (s, 1H), 7.20—7.42 (m, 10H); ^{13}C NMR (125 MHz) δ=14.7, 47.0, 51.6, 60.8, 106.7, 126.7, 127.1, 127.3, 128.0, 128.2, 128.3, 140.5, 143.6, 143.7. HRMS Found: m/z 283.1417. Calcd for $C_{18}H_{21}NS$: M, 283.1396.

***N*-Benzyl-1-(2-methylthio-2-propenyl)pentylamine (8c).** IR (neat) 1601, 1460 cm^{-1}; ^1H NMR δ=0.89 (t, 3H, J=7.0 Hz), 1.23—1.52 (m, 6H), 1.54 (bs, 1H), 2.21 (s, 3H), 2.37 (d, 2H, J=6.5 Hz), 2.81 (tt, 1H, J=6.5, 6.5 Hz), 3.74 (d, 1H, J=13.0 Hz), 3.80 (d, 1H, J=13.0 Hz), 4.65 (s, 1H), 5.04 (s, 1H), 7.20—7.30 (m, 5H); ^{13}C NMR (125 MHz) δ=14.1, 14.9, 22.9, 27.8, 33.6, 42.7, 51.3, 55.8, 105.7, 126.7, 128.1, 140.8, 144.7. HRMS Found: m/z 263.1700. Calcd for $C_{16}H_{25}NS$: M, 263.1710.

Preparation of 1,2-Propadienyl Sulfides (10a—c). 10a was prepared according to the literature procedures.[25] **10b, c** were prepared by the same method for the preparation of **10a**.

4-Methyl-3-methylthio-1,2-pentadiene (10b). To a THF solution (30 ml) of diisopropylamine (3.33 g, 32.9 mmol) was added BuLi (33.2 mmol, 1.62 M hexane solution, 1 M= 1 mol dm^{-3}) dropwise at 0 °C and the mixture was stirred for 10 min. To this reaction mixture was added a THF solution (15 ml) of 1-methylthio-1-propyne (2.74 g, 31.8 mmol) at −78 °C, and after being stirred for 30 min, a THF solution (15 ml) of isopropyl bromide (4.00 g, 32.5 mmol) was added. After being stirred at −78 °C for 1 h, then at −45 °C for 1 h, the reaction was quenched with pH 7 phosphate buffer, and the organic materials were extracted with Et_2O and the extracts were washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the crude materials were purified by distillation. Yield 75%. Bp 100 °C/100 mmHg (1 mmHg= 133.322 Pa). IR (neat) 1945, 1455, 862 cm^{-1}; ^1H NMR δ=1.11 (d, 6H, J=6.9 Hz), 2.11 (s, 3H), 2.22—2.31 (m, 1H), 4.99 (d, 2H, J=2.4 Hz); ^{13}C NMR (125 Hz) δ=15.5, 22.0, 32.1, 81.9, 111.1, 200.8. HRMS Found: m/z 128.0640. Calcd for $C_7H_{12}S$: M, 128.0661.

3-Methylthio-1,2-butadiene (10c). 10c was prepared by the same method for the preparation of **10b** except that methyl iodide was employed in place of isopropyl bromide. Yield 85%. Bp 60 °C/70 mmHg. IR (neat) 1945, 1432, 863 cm^{-1}; ^1H NMR δ=1.91 (t, 3H, J=3.1 Hz), 2.12 (s, 3H), 4.91 (q, 2H, J=3.1 Hz); ^{13}C NMR (125 Hz) δ=15.7, 19.3, 80.1, 99.0, 202.9. HRMS Found: m/z 100.0357. Calcd for C_5H_8S: M, 100.0347.

Typical Procedure for the Ene Reaction between Schiff's Base 2 and 1,2-Propadienyl Sulfide 10 (Table 4). To a toluene solution (5.0 ml) of Schiff's base **2** (0.40 mmol) and 1,2-propadienyl sulfide **10** (0.64 mmol) was added $AlCl_3$ (0.52 mmol) portionwise at ambient temperature. After being stirred for 12 h, the reaction mixture was treated with triethylamine (3 ml) and stirred for 5 min, then pH 7 phosphate buffer was poured into the mixture. Inorganic materials were filtered off and organic materials were extracted with ethyl acetate and the combined extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by column chromatography to give the product. *Z* and *E* isomer of **11a—c** were separated by thin-layer chromatography.

Spectral data of the products are as follows.

(*Z*)-*N*-Benzyl-1-isopropyl-2-methylene-3-methylthio-4-phenyl-3-butenylamine (11a-*Z*). IR (neat) 1599, 1452 cm^{-1}; ^1H NMR δ=0.84 (d, 3H, J=6.9 Hz), 1.03 (d, 3H, J=6.9 Hz), 1.51 (bs, 1H), 1.94—2.08 (m, 1H), 2.14 (s 3H), 3.48 (d, 1H, J=3.9 Hz), 3.68 (d, 1H, J=13.1 Hz), 3.94 (d, 1H, J=13.1 Hz), 5.32 (s, 1H), 5.46 (s, 1H), 6.73 (s, 1H), 7.22—7.57 (m, 10H); ^{13}C NMR (125 MHz) δ=16.1, 16.3, 20.6, 30.2, 52.0, 85.2, 114.8, 126.6, 127.1, 127.9, 128.1, 128.3, 129.5, 130.2, 136.7, 139.4, 141.0, 149.3. HRMS Found: m/z 337.1835. Calcd for $C_{22}H_{27}NS$: M, 337.1886.

(*E*)-*N*-Benzyl-1-isopropyl-2-methylene-3-methylthio-4-phenyl-3-butenylamine (11a-*E*). IR (neat) 1593, 1453 cm^{-1}; ^1H NMR δ=0.73 (d, 3H, J=6.9 Hz), 0.87 (d, 3H, J=6.9 Hz), 1.30 (bs, 1H), 1.88—1.95 (m, 1H), 2.34 (s, 3H), 3.00 (d, 1H, J=1.4 Hz), 3.25 (d, 1H, J=13.0 Hz), 3.73 (d, 1H, J=13.0 Hz), 5.55 (s, 1H), 5.57 (s, 1H), 6.12 (s, 1H), 7.13—7.38 (m, 10H); ^{13}C NMR (125 MHz) δ=15.6, 15.9, 20.8, 30.1, 51.8, 66.0, 117.3, 120.1, 126.4, 126.7, 128.0, 128.1, 128.2, 128.4, 137.5, 140.8, 147.7, 151.9. HRMS Found: m/z 337.1837. Calcd for $C_{22}H_{27}NS$: M, 337.1886.

(*Z*)-*N*-Benzyl-2-methylene-3-methylthio-1,4-diphenyl-3-butenylamine (11b-*Z*). IR (neat) 1601, 1452 cm^{-1}; ^1H NMR δ=1.72 (bs, 1H), 2.00 (s, 3H), 3.74 (d, 1H, J=13.2 Hz), 3.78 (d, 1H, J=13.2 Hz), 4.65 (s, 1H), 5.34 (s, 1H), 5.45 (s, 1H), 6.47 (s, 1H), 7.20—7.44 (m, 15H); ^{13}C NMR (125 MHz) δ=16.1, 52.0, 64.6, 115.2, 126.9, 127.1, 127.3, 127.7, 127.9, 128.2, 128.3, 128.4, 129.4, 130.6, 136.6, 138.0, 140.4, 141.6, 150.8. HRMS Found: m/z 371.1721. Calcd for $C_{25}H_{25}NS$: M, 371.1710.

(*E*)-*N*-Benzyl-2-methylene-3-methylthio-1,4-diphenyl-3-butenylamine (11b-*E*). IR (neat) 1603, 1446 cm^{-1}; ^1H NMR δ=1.24 (bs, 1H), 2.04 (s, 3H), 3.43 (d, 1H, J=13.2 Hz), 3.53 (d, 1H, J=13.2 Hz), 4.24 (s, 1H), 5.35 (s, 1H), 5.54 (s, 1H), 6.31 (s, 1H), 7.14—7.28 (m, 15H). HRMS Found: m/z 371.1720. Calcd for $C_{25}H_{25}NS$: M, 371.1710.

(*Z*)-*N*-Benzyl-1-(1-methylene-2-methylthio-3-phenyl-2-propenyl)pentylamine (11c-*Z*). IR (neat) 1601, 1452 cm^{-1}; ^1H NMR δ=0.86 (t, 3H, J=7.2 Hz), 1.24—1.69 (m, 6H), 1.59 (bs, 1H), 2.11 (s, 3H), 3.55 (t, 1H, J=5.9 Hz), 3.70 (d, 1H, J=12.9 Hz), 3.87 (d, 1H, J=12.9 Hz), 5.33 (s, 1H), 5.36 (s, 1H), 6.73 (s, 1H), 7.21—7.56 (m, 10H). HRMS Found: m/z 351.2012. Calcd for $C_{23}H_{29}NS$: M, 351.2022.

(*E*)-*N*-Benzyl-1-(1-methylene-2-methylthio-3-phenyl-2-propenyl)pentylamine (11c-*E*). IR (neat) 1601, 1456 cm^{-1}; ^1H NMR δ=0.79 (t, 3H, J=6.9 Hz), 0.85—1.45 (m, 6H), 1.56 (bs, 1H), 2.31 (s, 3H), 3.16 (t, 1H, J=5.9 Hz), 3.42 (d, 1H, J=13.1 Hz), 3.69 (d, 1H, J=13.1 Hz), 5.45 (s, 1H), 5.53 (s, 1H), 6.18 (s, 1H), 7.13—7.35 (m, 10H). HRMS Found: m/z 351.2037. Calcd for $C_{23}H_{29}NS$: M, 351.2022.

***N*-Benzyl-1-isopropyl-4-methyl-2-methylene-3-methylthio-3-pentenylamine (11d).** IR (neat) 1610, 1452 cm^{-1}; ^1H NMR δ=0.83 (d, 3H, J=6.9 Hz), 1.01 (d, 3H, J=6.9 Hz), 1.48 (bs, 1H), 1.75—1.80 (m, 1H), 1.82 (s, 3H), 2.01 (s, 3H), 2.05 (s, 3H), 3.41 (d, 1H, J=2.7 Hz), 3.62 (d, 1H, J=13.0 Hz), 3.92 (d, 1H, J=13.0 Hz), 4.93 (d, 1H, J=2.3 Hz), 5.36 (d, 1H, J=2.3 Hz), 7.22—7.40 (m, 5H); ^{13}C NMR (125 MHz) δ=15.8, 16.8, 21.2, 22.4, 22.7, 29.6, 52.1, 65.2, 114.1, 126.7, 128.2, 128.2, 130.6, 137.3, 141.1, 146.2. HRMS Found: m/z 289.1867. Calcd for $C_{18}H_{27}NS$: M, 289.1866.

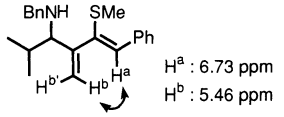
***N*-Benzyl-4-methyl-2-methylene-3-methylthio-1-phenyl-3-pentenylamine (11e).** IR (neat) 1604, 1450 cm^{-1}; ^1H NMR δ=1.31 (s, 3H), 1.81 (bs, 1H), 1.85 (s, 3H), 2.00 (s, 3H), 3.68 (d, 1H, J=13.3 Hz), 3.73 (d, 1H, J=13.3 Hz), 4.52 (s, 1H), 4.79 (s, 1H), 5.45 (s, 1H), 7.21—7.38 (m, 10H); ^{13}C NMR (125 MHz) δ=16.4, 22.8, 23.1, 51.9, 64.8, 114.3, 126.8, 127.0, 128.0, 128.0, 128.0, 128.3, 128.6, 136.5, 140.7, 141.8, 148.0. HRMS Found: m/z 323.1689. Calcd for $C_{21}H_{25}NS$: M, 323.1710.

***N*-Benzyl-1-(3-methyl-1-methylene-2-methylthio-2-butenyl)pentylamine (11f).** IR (neat) 1608, 1454 cm^{-1}; ^1H NMR δ=0.87 (t, 3H, J=7.2 Hz), 1.26—1.42 (m, 6H), 1.59 (bs, 1H), 1.82 (s, 3H), 2.00 (s, 3H), 2.03 (s, 3H), 3.43 (dd, 1H, J=4.3,

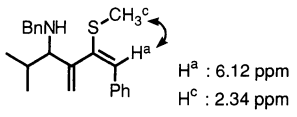
7.0 Hz), 3.68 (d, 1H, J=13.0 Hz), 3.87 (d, 1H, J=13.0 Hz), 4.85 (d, 1H, J=2.2 Hz), 5.39 (d, 1H, J=2.2 Hz), 7.22—7.37 (m, 5H); ^{13}C NMR (125 MHz) δ=14.0, 16.6, 22.2, 22.8, 22.9, 28.3, 33.7, 51.7, 60.4, 114.0, 126.7, 128.1, 128.3, 130.1, 136.8, 141.4, 147.3. HRMS Found: m/z 303.2039. Calcd for $C_{19}H_{29}NS$: M, 303.2023.

***N*-Benzyl-2-methylene-3-methylthio-1-phenyl-3-butenylamine (11g).** IR (neat) 1732, 1601, 1491, 1450 cm^{-1}; ^{1}H NMR δ=1.62 (bs, 1H), 2.16 (s, 3H), 3.09 (d, 1H, J=11.9 Hz), 3.26 (d, 1H, J=11.9 Hz), 4.58 (s, 1H), 4.76 (s, 1H), 5.12 (s, 1H), 5.44 (s, 1H), 5.57 (s, 1H), 7.20—7.48 (m, 5H). HRMS Found: m/z 295.1376. Calcd for $C_{19}H_{21}NS$: M, 295.1396.

Assignment of the Stereochemistry of the Ene Products (11a—c). The relative stereochemistry of the ene product **11a** was determined by the NOESY spectra. In the major isomer, the NOE was observed between H^a and H^b, as shown in the following figure and it was assigned as Z isomer. On the other hand, in the minor isomer, the NOE was observed between H^a and H^c, and it was assigned as E isomer. The singlet signal of H^a proton appeared at 6.73 ppm in Z isomer and it appeared at 6.12 ppm in E isomer.



the major isomer of **11a** (assigned as Z isomer)



the minor isomer of **11a** (assigned as E isomer)

The relative stereochemistry of the other ene products **11b, c** was assigned from the chemical shift of the proton corresponding to H^a. The major isomer, where the singlet signal of H^a appeared at lower field, was determined to be Z isomer and the minor isomer, where it appeared at higher field, was assigned as E isomer.

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