$BF_3 \cdot OEt_2$ CATALYZED [4+2] CYCLOADDITION REACTIONS OF N-ARYL SCHIFF'S BASES WITH 1-ALKENYL, 1,2-PROPADIENYL, AND 1-ALKYNYL SULFIDES

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Abstract - [4+2] Cycloaddition reaction proceeds between N-aryl Schiff's bases and 1-alkenyl sulfides, a 1,2-propadienyl sulfide, or 1-alkynyl sulfides in the presence of $BF_3 \cdot OEt_2$ to provide 2-substituted quinoline derivatives. A 2-alkyl-4-quinolone alkaloid, leptomerine, is prepared by applying the present cycloaddition reaction.

In general, Schiff's bases are rather unreactive toward nucleophiles and unstable under acidic conditions. Therefore, it is not an easy task to develop addition reactions of nucleophiles to Schiff's bases as compared with carbonyl compounds. In the previous paper,[1] it is reported that various olefins having an alkylthio group exhibit sufficient reactivity in the nucleophilic addition reaction to N-benzyl Schiff's bases with the aid of acids. For example, the 1,2-addition reaction proceeds by employing a *ketene dithioacetal and* the allylation reaction proceeds by utilizing 2-(methylthio)-allylsilane. It was presumed that the N-aryl Schiff's bases react not only with the ketene dithioacetal but also with less reactive 1-alkenyl and 1-alkynyl sulfides which do not react with N-benzyl Schiff's bases, because their reactivity towards nucleo-

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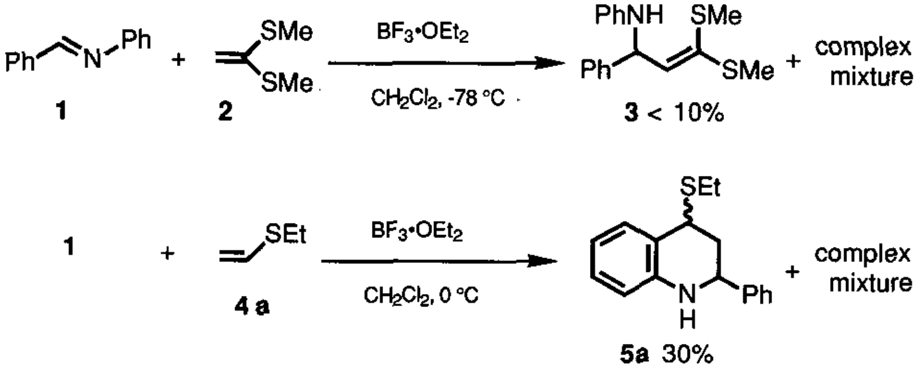
This paper is dedicated to Prof. Edward C. Taylor in celebration of his 70th birthday.

philes might be higher than that of the N-benzyl Schiff's bases by electron-withdrawing effect of an aryl substituent.

When a mixture of a Schiff's base (**1**), prepared from benzaldehyde and aniline, and 1,1-bis(methylthio)ethylene (**2**) was treated with one mole equivalent of $BF_3{\cdot}OEt_2$, the 1,2-addition product (**3**) was obtained yet in low yield (less than 10% yield). In contrast, the reaction between **1** and ethyl vinyl sulfide (**4a**) gave no 1,2-addition product but the [4+2] cycloadduct (**5a**) in 30% yield.[2]



There are some examples of the acid-catalyzed [4+2] cycloaddition reaction in which the N-aryl Schiff's bases are employed as dienes. For instance, Kametani *et al.*[3] made comprehensive research on the [4+2] cycloaddition reaction between N-aryl Schiff's bases and various vinyl ethers and applied the reaction to the synthesis of several natural products containing quinoline skeletons. However, the cycloadducts are afforded generally in low yield. Enamines[4] are also employed as dienophiles, but only the reaction of β-disubstituted enamines gives the cycloadducts in good yield. Thus, it is desirable to develop an alternative dienophile which has wide generality in the [4+2] cycloaddition utilizing N-aryl Schiff's bases as diene components. Formation of the quinoline derivative[5] (**5a**) by the use of the vinyl sulfide (**4a**) prompted us to investigate the cycloaddition reaction of the N-phenyl Schiff's base (**1**) with olefins or acetylenes possessing an alkylthio group.

As a result of screening the reaction conditions, it was found that the yield of the reaction between the Schiff's base (**1**) and the vinyl sulfide (**4a**) was influenced by the amount of Lewis acid. The cycloadduct (**5a**) was afforded in favorable yield (90%) as a mixture of 1:1 diastereomers by the use of a catalytic amount (10 mol%) of $BF_3 \cdot OEt_2$.

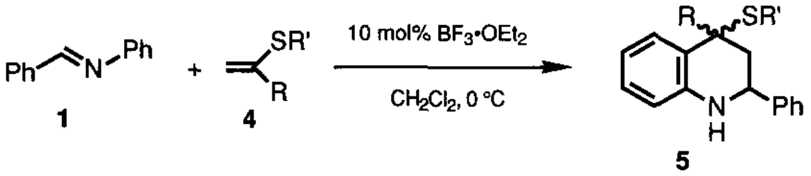
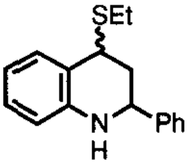
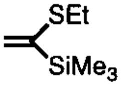
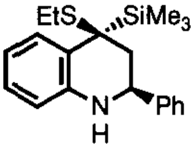
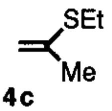
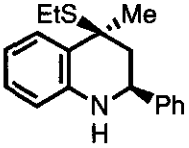
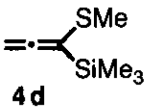
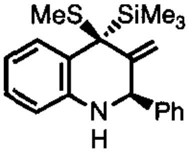


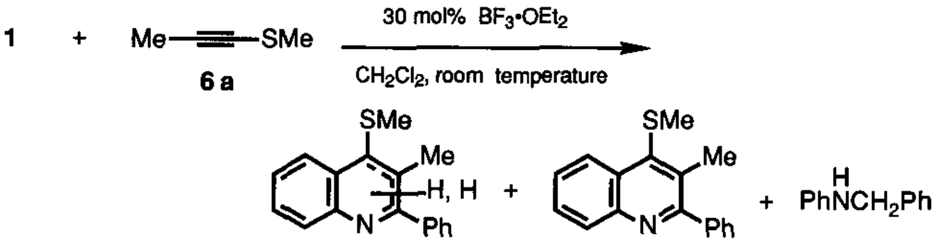
Table 1 The Reaction between Schiff's Base (**1**) and Vinyl Sulfides

Entry	Vinyl Sulfide	Product	
1	 **4 a**		**5a** 90% (1:1)[a]
2	 **4 b**		**5b** 96%[b]
3	 **4 c**		**5c** 78% (10:1)[a]
4	 **4 d**		**5d** 90%[b]

a) Figures in the parenthesis are diasteromer rartios.
b) The other isomer was not detected.

As shown in Table 1, various vinyl sulfides can be utilized as dienophiles in the present [4+2] cycloaddition reaction. For example, when 1-ethylthio-1-trimethylsilylethylene (**4b**) was employed, 4-ethylthio-2-phenyl-4-trimethylsilyl-1,2,3,4-tetrahydroquinoline (**5b**) was obtained in almost quantitative yield as a single stereoisomer (Entry 2). 1-Alkylvinyl sulfides are known to be good ene components in the reaction with aldehydes[6] and Schiff's bases,[1] but the reaction between (**1**) and 2-ethylthiopropene (**4c**) gave only [4+2] cycloaddition product (**5c**) in high yield and no ene product was afforded (Entry 3). Allene compound, 1-methylthio-1-trimethylsilyl-1,2-propadiene (**4d**), can react with **1** to afford 3-methylene-1,2,3,4-tetrahydroquinoline (**5d**) in preferable yield as a single stereoisomer (Entry 4).

[4+2] Cycloaddition also proceeded between 1-alkynyl sulfide (**6a**) and the Schiff's base (**1**) to provide quinoline derivatives (**7**) and (**8**). In this reaction, though the total yield of these cycloadducts was fairly good (77%), the Schiff's base (**1**) was partially consumed as an oxidant to aromatize the dihydroquinoline (**7**). After the isolation, however, **7** was oxidized very slowly to **8** by air and existed as an equilibrium mixture of the possible isomers.



7 45% **8** 32%

(Yields are based on alkynyl sulfide (**6a**))

The present cycloaddition, employing vinyl sulfides as dienophiles, has salient feature which the other cycloadditions using vinyl ethers and enamines do not have. That is, not only aromatic N-aryl Schiff's bases like **1**, but also Schiff's bases prepared from aliphatic aldehydes and aniline (aliphatic N-aryl Schiff's bases) are also utilized as diene components. In general, it is difficult to develop the addition reactions towards aliphatic N-aryl Schiff's bases, becasuse they are easily hydrolyzed and polymerized under acidic conditions. Actually, [4+2] cycloadduct (**10a**) was afforded only in not more than 60% yield, when the isolated aliphatic Schiff's base (**9**) was used (Table 2, Entries 1-4). But the adduct (**10a**) was obtained in better yield by the use of in situ prepared Schiff's base (**9**) (Entries 5, 6).

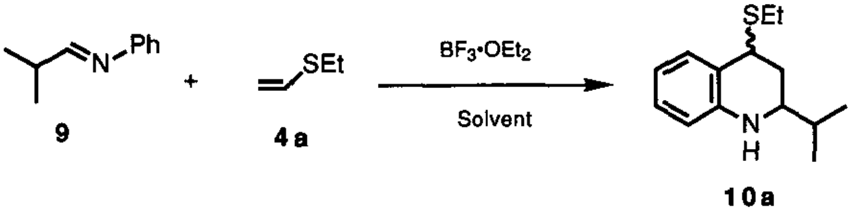


Table 2. Effect of Amount of BF_3•OEt_2 and Solvent

Entry	mol% of BF_3•OEt_2	Solvent	Yield/% of **10a**
1	10	CH_2Cl_2	trace
2	50	CH_2Cl_2	20
3	100	CH_2Cl_2	complex mixture
4	100	Et_2O	60
5*	100	Et_2O	72
6*	100	toluene	83

* Schiff's base (9) was prepared in situ from isobutyraldehyde and aniline in the presence of $MgSO_4$.

As well as the Schiff's base (**9**) prepared from a secondary aldehyde, a Schiff's base (**11**) derived from a primary aldehyde (butanal) can be employed and reacted with the vinyl sulfides (**4a,b**) by the use of one mole equivalent of BF_3•OEt_2 (Table 3).

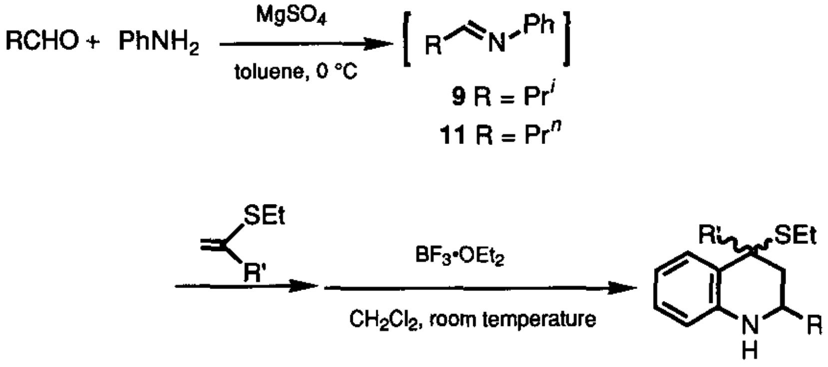
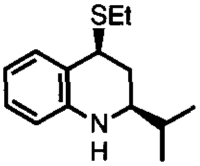
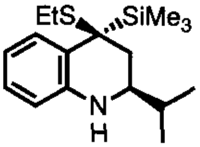
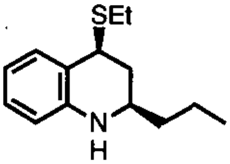
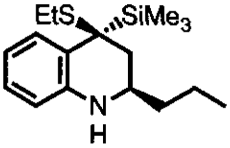


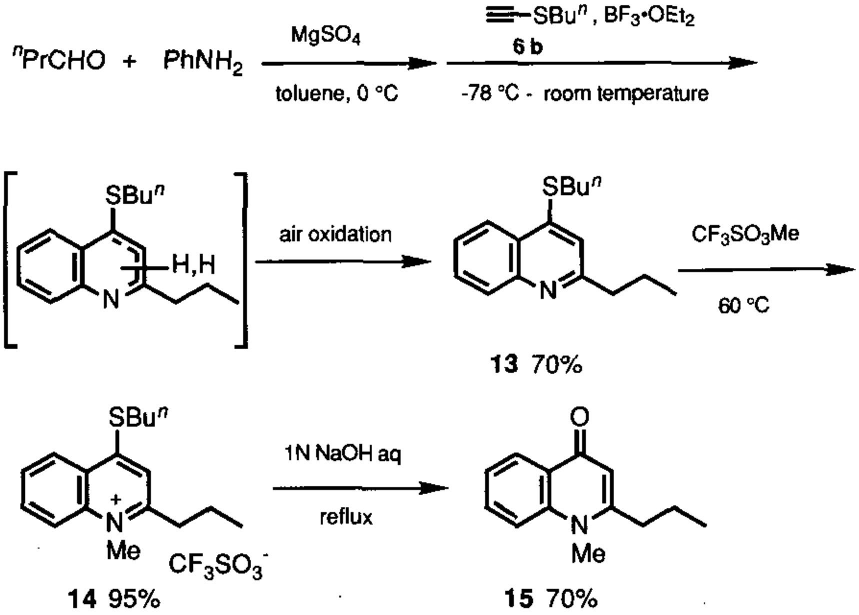
Table 3 The Reaction between Aliphatic Schiff's Bases and Vinyl Sulfides

Entry	R	R'	Product	
1	Pr^i (**9**)	H (**4a**)		**10a** 83% (5:1)[a)]
2	Pr^i (**9**)	$\mathrm{SiMe_3}$ (**4b**)		**10b** 76%[b)]
3	Pr^n (**11**)	H (**4a**)		**12a** 70% (5:1)[a)]
4	Pr^n (**11**)	$\mathrm{SiMe_3}$ (**4b**)		**12b** 79%[b)]

a) Figures in the parenthesis are diasteromer rartios.
b) The other isomer was not detected.

Furthermore, the cycloaddition reaction proceeded between the aliphatic Schiff's base (**11**) and a 1-alkynyl sulfide and was favorably applied to the synthesis of 2-alkyl-4-quinolone alkaloid, leptomerine (**15**).[7] The reaction between the Schiff's base (**11**) prepared in situ and butyl ethynyl sulfide (**6b**) delivered quinoline derivative (**13**) in 70 % yield. N-Methylation of **13** was carried out with methyl trifluoromethanesulfonate[8] in quantitative yield and the subsequent hydrolysis under basic conditions[9] afforded the desired leptomerine (**15**).

In summary, 1-alkenyl, 1-propadienyl, and 1-alkynyl sulfides were found to react with aliphatic N-aryl Schiff's bases as well as aromatic ones to give 2-substituted quinoline derivatives by the [4+2] cycloaddition reaction.



EXPERIMENTAL

General. ^{1}H Nmr spectra (500 MHz) and ^{13}C nmr spectra (125 MHz) 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 operating at 70 eV.

Preparative thin-layer chromatography (tlc) was performed on a silica gel (Wakogel B-5F).

Tetrahydrofuran (THF) was freshly distilled from sodium diphenylketyl. Dichloromethane was distilled from P_2O_5, then from CaH_2, and dried over Molecular Sieves 4A (MS 4A). Toluene was distilled and dried over MS 4A. $BF_3 \cdot OEt_2$ was distilled from CaH_2 and stored in 0.50 M dichloromethane solution (M = mol dm^{-3}) or 1.0 M toluene solution. Methyl trifluoromethanesulfonate was used after distillation. Schiff's base (**1**) was prepared according to the reported procedures.[10] Aldehydes were distilled from $CaCl_2$. 1-Alkenyl sulfides (**4a**)[11] and (**4c**),[12] a 1,2-propadienyl sulfide (**4d**)[12] and alkynyl sulfides (**6a**)[12] and (**6b**)[13] were synthesized by the literature methods.

All the operations were carried out under an argon atmosphere and all the solvents for the [4+2] cycloaddition reaction were degassed before use by irradiating ultrasonic wave under reduced pressure.

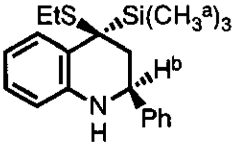
Preparation of 1-Ethylthio-1-trimethylsilylethylene (4b). To a THF solution (40 ml) of ethyl vinyl sulfide (**4a**) (1.76 g, 20.0 mmol) was added t-BuLi (20.4 mmol, 1.7 M pentane solution) dropwise at -78 °C and the mixture was stirred for 1.5 h. To this reaction mixture was added a THF solution (20 ml) of trimethylsilyl chloride (2.39g, 22.0 mmol) at -78 °C. After being stirred for 2 h at -78 °C and for 1 h at -45 °C, the reaction was quenched with pH 7 phosphate buffer, and the organic materials were extracted with pentane 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 2.40 g (75%). bp 85-90 °C/ 70 mmHg (1 mmHg= 133.32 Pa). Ir (neat) 1574, 1450, 1250 cm^{-1}; ^1H nmr δ= 0.16 (9H, s), 1.28 (3H, t, J= 7.4 Hz), 2.73 (2H, q, J= 7.4 Hz), 5.33 (1H, s), 5.41 (1H, s); ^{13}C nmr δ= -1.6, 12.9, 24.2, 114.5, 147.0. Hrms Found m/z 160.0723. Calcd for $C_7H_{16}SSi$: M, 160.0743.

Typical Procedure for the Reaction between the Schiff's Base (1) and 1-Alkenyl Sulfide (4) (Table 1). To a dichloromethane solution (12 ml) of the Schiff's base (**1**) (217.4 mg, 1.20 mmol) and 1-alkenyl sulfide (**4**) (1.32 mmol) was added $BF_3 \cdot OEt_2$ (0.12 mmol, 0.5 M dichloromethane solution) at room temperature. After being stirred for 3-6 h, the reaction was quenched with pH 7 phosphate buffer. Organic materials were extracted with dichloromethane and the combined extracts were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by tlc to afford the product (**5**).

Spectral data of the addition products are as follows.

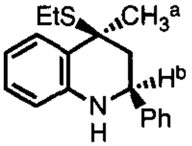
4-Ethylthio-2-phenyl-1,2,3,4-tetrahydroquinoline (5a). **5a** was obtained as a 1:1 diastereomer mixture. Ir (neat) 3373, 1606, 1587, 1486 cm^{-1}; ^1H nmr δ= 1.20 (3H x 0.5, t, J= 7.4 Hz), 1.30 (3H x 0.5, t, J= 7.4 Hz), 2.16 (1H x 0.5, dd, J= 3.2, 7.0), 2.21 (1H x 0.5, dd, J= 11.7, 11.7 Hz), 2.39-2.65 (3H, m), 3.92 (1H x 0.5, brs), 4.05 (1H x 0.5, brs), 4.08 (1H x 0.5, dd, J= 3.2, 3.2 Hz), 4.20 (1H x 0.5, dd, J= 5.9, 11.7 Hz), 4.37 (1H x 0.5, dd, J= 2.4, 11.4 Hz), 4.79 (1H x 0.5, dd, J= 7.1, 7.1 Hz), 6.46 (1H x 0.5, d, J= 7.4 Hz), 6.47 (1H x 0.5, d, J= 7.7 Hz), 6.63 (1H x 0.5, dd, J= 7.4, 7.4 Hz), 6.71 (1H x 0. 5, dd, J= 7.4, 7.4 Hz), 6.99 (1H x 0.5, dd, J= 7.7, 7.7 Hz), 7.15 (1H x 0.5, d, J= 7.4 Hz), 7.26-7.42 (5H + 1H x 0.5, m), 7.63 (1H x 0.5, d, J= 7.7 Hz); ^{13}C nmr δ= 14.6, 14.7, 23.2, 25.3, 36.5, 40.7, 41.3, 41.8, 51.8, 57.1, 114.4, 114.6, 116.9, 117.9, 119.9, 121.0, 126.5, 126.8, 127.6, 127.7, 127.7, 128.1, 128.6, 128.6, 129.2, 130.2, 143.3, 143.8, 144.3, 145.5. Anal. Calcd for $C_{17}H_{19}NS$: C, 75.79; H, 7.11; N, 5.20; S, 11.90. Found: C, 75.61; H, 7.33; N, 5.12; S, 11.97.

4-Ethylthio-2-phenyl-4-trimethylsilyl-1,2,3,4-tetrahydroquinoline (5b). mp 99-100 °C (hexane). Ir (KBr disk) 3398, 1599, 1481 cm^{-1}; ^{1}H nmr δ= 0.15 (9H, s), 1.11 (3H, t, J= 7.6 Hz), 2.23 (1H, dq, J_d= 11.3 Hz, J_q= 7.6 Hz), 2.26-2.43 (3H, m), 3.95 (1H, brs), 4.62 (1H, dd, J= 3.6, 11.3 Hz), 6.48 (1H, dd, J= 0.9, 7.6 Hz), 6.69 (1H, ddd, J= 0.9, 7.6, 7.6 Hz), 6.95 (1H, ddd, J= 1.4, 7.6, 7.6 Hz), 7.28-7.41 (5H, m), 7.57 (1H, dd, J= 1.4, 7.6 Hz); ^{13}C nmr δ= -2.1, 13.9, 20.7, 40.1, 41.6, 55.5, 113.8, 117.3, 122.8, 126.2, 126.3, 127.7, 128.6, 128.7, 144.2, 144.9. Hrms Found m/z 341.1625. Calcd for $C_{20}H_{27}NSSi$: M, 341.1635. Relative stereochemistry was determined by the NOESY spectrum in which NOE between H^a (0.15 ppm) and H^b (4.62 ppm) was observed.



5b

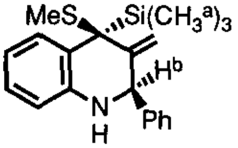
4-Ethylthio-4-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline (5c). 5c was obtained as a 10:1 diastereomer mixture. Ir (neat) 3363, 1581, 1477 cm^{-1}; ^{1}H nmr (major isomer) δ= 1.12 (3H, t, J= 7.5 Hz), 1.68 (3H, s), 2.11 (1H, dd, J= 2.4, 13.3 Hz), 2.18 (1H, dq, J_d= 11.5 Hz, J_q= 7.5 Hz), 2.38-2.45 (2H, m), 4.03 (1H, brs), 4.44 (1H, dd, J= 2.4, 11.9 Hz), 6.54 (1H, dd, J= 0.9, 7.6 Hz), 6.76 (1H, ddd, J= 0.9, 7.6, 7.6 Hz), 7.02 (1H, ddd, J= 1.4, 7.6, 7.6 Hz), 7.30-7.45 (5H, m), 7.68 (1H, dd, J= 1.4, 7.6 Hz); ^{13}C nmr (major isomer) δ= 13.8, 23.1, 32.7, 46.7, 47.1, 54.2, 114.8, 118.2, 125.9, 126.6, 127.5, 127.8, 128.7, 129.1, 143.3, 145.2. Anal. Calcd for $C_{18}H_{21}NS$: C, 76.28; H, 7.47; N, 4.94; S, 11.31. Found: C, 76.32; H, 7.56; N, 4.81; S, 11.64.



5c

Relative stereochemistry of the major isomer was determined by the NOESY spectrum in which NOE between H^a (1.68 ppm) and H^b (4.44 ppm) was observed.

3-Methylene-4-methylthio-2-phenyl-4-trimethylsilyl-1,2,3,4-tetrahydroquinoline (5d). Ir (neat) 3367, 1620, 1595, 1483, 1414 cm^{-1}; ^{1}H nmr δ= 0.15 (9H, s), 1.63 (3H, s), 3.94 (1H, brs), 4.61 (1H, s), 4.98 (1H, s), 5.63 (1H, s), 6.48 (1H, dd, J= 1.0, 7.6 Hz), 6.79 (1H, ddd, J= 1.0, 7.6, 7.6 Hz), 6.96 (1H, ddd, J= 1.3, 7.6, 7.6 Hz), 7.28-7.36 (5H, m), 7.67 (1H, dd, J= 1.3, 7.6 Hz); ^{13}C nmr δ= -1.9, 10.8, 49.1, 60.8, 114.2, 114.4, 118.5, 123.4, 126.1, 127.1, 128.0, 128.5, 129.5, 143.3, 144.6, 145.6. Anal. Calcd for $C_{20}H_{25}NSSi$: C, 70.74; H, 7.42; N, 4.12; S, 9.44. Found: C, 70.53; H, 7.58; N, 4.03; S, 9.41. Relative stereochemistry was determined by the NOESY spectrum in which NOE between H^a (0.15 ppm) and H^b (4.98 ppm) was observed.



5d

The Procedure for the Reaction between the Schiff's Base (1) and 1-Alkynyl Sulfide (6a). The procedure is the same as that for the above reaction between **1** and alkenyl sulfide (**4**) except that the amount of **1** was 1.5 mole equivalent against **6a** and 30 mol% of $BF_3 \cdot OEt_2$ was used.

Equilibrium Mixture of 3-Methyl-4-methylthio-2-phenyl-1,2-dihydroquinoline, 3-Methyl-4-methylthio-2-phenyl-1,4-dihydroquinoline, and 3-Methyl-4-methylthio-2-phenyl-3,4-dihydroquinoline (7). Ir (neat) 1583, 1485 cm^{-1}; distinguishable peaks of ^{1}H nmr (benzene-d_6, 60 °C) δ= 1.62 (3H, brs), 2.31 (3H, brs), 6.88-7.11 (10H, m); ^{13}C nmr δ= 14.1, 16.9, 121.0, 123.6, 127.6, 128.3, 128.5, 129.0, 129.3, 130.0, 134.1, 134.9, 136.2, 136.2, 151.3. Anal. Calcd for $C_{17}H_{17}NS$: C, 76.36; H, 6.41; N, 5.24; S, 11.99. Found: C, 76.42; H, 6.44; N, 5.37; S, 12.10.

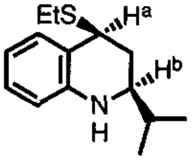
3-Methyl-2-methylthio-2-phenylquinoline (8). mp 96 °C (hexane). Ir (KBr disk) 1554, 1479 cm^{-1}; ^{1}H nmr δ= 2.41 (3H, s), 2.66 (3H, s), 7.41-7.69 (7H, m), 8.13 (1H, d, J= 8.4 Hz), 8.55 (1H, dd, J= 1.0, 8.5 Hz); ^{13}C nmr δ= 18.8, 19.8, 125.9, 127.0, 128.2, 128.3, 128.7, 128.8, 130.1, 133.5, 141.4, 144.4, 146.5, 160.6. Anal. Calcd for $C_{17}H_{15}NS$: C, 76.94; H, 5.70; N, 5.28; S, 12.08. Found: C, 76.74; H, 5.74; N, 5.25; S, 12.14.

Typical Procedure for the Reaction between Aliphatic N-Aryl Schiff's Base and 1-Alkenyl Sulfide (4) (Table 3). To a toluene solution (6 ml) of an aliphatic aldehyde (1.00 mmol) was added a toluene solution (4 ml) of aniline (93.1 mg, 1.00 mmol) dropwise at 0 °C. After being stirred for 10 min, $MgSO_4$ was added and the mixture was stirred for an additional 10 min. To this mixture, a toluene solution (5 ml) of 1-alkenyl sulfide (**4**) (1.20 mmol) was added and, subsequently, $BF_3 \bullet OEt_2$ (1.05 mmol, 1.0 M toluene solution) was added at 0 °C and the temperature of the reaction mixture was raised gradually to room temperature over 3 h. After being stirred for an additional 2-5 h, the reaction was quenched with pH 7 phosphate buffer. Organic materials were extracted with ethyl acetate and the combined extracts were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by tlc to afford the product (**10**) or (**12**).

Spectral data of the addition products are as follows.

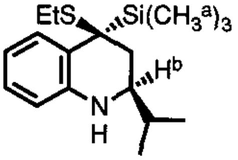
4-Ethylthio-2-isopropyl-1,2,3,4-tetrahydroquinoline (10a). 10a was obtained as a 5:1 diastereomer mixture. Ir (neat) 3392, 1606, 1583, 1483 cm^{-1}; ^{1}H nmr (major isomer) δ= 1.00 (3H, d, J= 5.3 Hz), 1.01 (3H, d, J= 5.3 Hz), 1.23 (3H, t, J= 7.4 Hz), 1.73 (1H, dq, J_d=J_q= 5.3 Hz), 1.88 (1H, ddd, J= 11.5, 12.3, 12.3 Hz), 2.29 (1H, ddd, J= 2.6, 5.6, 12.3 Hz), 2.48 (1H, dq, J_d= 7.4 Hz, J_q= 12.0 Hz), 2.57 (1H, dq, J_d= 7.4 Hz, J_q= 12.0 Hz), 3.13 (1H, ddd, J= 2.6, 5.3, 11.5 Hz), 3.74 (1H, brs), 4.07 (1H, dd, J= 5.6, 12.3 Hz), 6.49 (1H, d, J= 7.6 Hz), 6.68 (1H, dd, J= 7.6, 7.6 Hz), 6.99 (1H, ddd, J= 1.0, 7.6, 7.6 Hz), 7.59 (1H, dd, 1.0, 7.6 Hz); distinguishable peaks of ^{1}H nmr (minor isomer) δ= 1.31 (3H, t, J= 7.4 Hz), 2.03 (1H, dd, J= 2.5, 13.3 Hz), 3.48-3.54 (1H, m), 6.59 (1H, d, J=7.4 Hz), 7.09 (1H, d, J=7.4 Hz); ^{13}C nmr (major isomer) δ= 14.6, 18.0, 18.2, 23.2, 32.6, 34.1, 42.0, 57.5, 114.4, 117.4, 121.3, 127.6, 129.1, 145.8; ^{13}C nmr (minor isomer) δ= 14.6, 18.0, 18.2, 25.2, 29.7, 32.3, 41.4, 52.0, 114.3, 116.4, 120.5, 127.9, 130.0, 144.6. Anal. Calcd for $C_{14}H_{21}NS$: C, 71.44 H, 8.99; N, 5.95; S, 13.62. Found: C, 71.23; H, 8.95; N, 6.01;

S, 13.96. Relative stereochemistry of major isomer was determined by the NOESY spectrum in which NOE between H^a (4.07 ppm) and H^b (3.13 ppm) was observed.



10a

4-Ethylthio-2-isopropyl-4-trimethylsilyl-1,2,3,4-tetrahydroquinoline (10b). Ir (neat) 3396, 1603, 1577, 1483 cm^{-1}; ^{1}H nmr δ= 0.05 (9H, s), 0.97 (3H, d, J= 6.5 Hz), 1.00 (3H, d, J= 6.5 Hz), 1.13 (3H, t, J= 7.5 Hz), 1.62 (1H, dq, J_d=J_q= 6.5 Hz), 2.02 (1H, dd, J= 12.1, 12.5 Hz), 2.19 (1H, dq, J_d= 11.3 Hz, J_q= 7.5 Hz), 2.22 (1H, dd, J= 2.9, 12.5 Hz), 2.40 (1H, dq, J_d= 11.3 Hz, J_q= 7.5 Hz), 3.22 (1H, ddd, J= 2.9, 6.5, 12.1 Hz), 3.71 (1H, brs), 6.41 (1H, d, J= 7.6 Hz), 6.61 (1H, dd, J= 7.6, 7.6 Hz), 6.89 (1H, ddd, J= 1.3, 7.6, 7.6 Hz), 7.49 (1H, dd, J= 1.3, 7.6 Hz); ^{13}C nmr δ= -2.2, 14.0, 17.9, 18.4, 20.6, 33.6, 34.7, 39.7, 55.7, 113.7, 116.9, 123.0, 126.2, 128.5, 145.0. Anal. Calcd for $C_{17}H_{29}NSSi$: C, 66.39; H, 9.50; N, 4.55; S, 10.42. Found: C, 66.83; H, 9.39; N, 4.54; S, 9.96. Relative stereochemistry was determined by the NOESY spectrum in which NOE between H^a (0.05 ppm) and H^b (3.22 ppm) was observed.



10b

4-Ethylthio-2-propyl-1,2,3,4-tetrahydroquinoline (12a). 12a was obtained as a 5:1 diastereomer isomer. Ir (neat) 3379, 1604, 1583, 1487 cm^{-1}; ^{1}H nmr δ= 0.96 (3H, t, J= 7.2 Hz), 1.23 (3H, t, J= 7.4 Hz), 1.38-1.55 (4H, m), 1.84 (1H, ddd, J= 11.1, 11.4, 12.8 Hz), 2.31 (1H, ddd, J= 2.5, 5.9, 12.8 Hz), 2.45 (1H, dq, J_d= 12.1 Hz, J_q= 7.4 Hz), 2.54 (1H, dq, J_d= 12.1 Hz, J_q= 7.4 Hz), 3.30 (1H, ddd, J= 2.5, 6.2, 11.1 Hz), 3.74 (1H, brs), 4.07 (1H, dd, J= 5.9, 11.4 Hz), 6.46 (1H, dd, J= 1.0, 7.8 Hz), 6.67 (1H, ddd, J= 1.0, 7.8, 7.8 Hz), 6.98 (1H, ddd, J= 1.2, 7.8, 7.8 Hz), 7.57 (1H, dd, J= 1.2, 7.8 Hz); distinguishable peaks of ^{1}H nmr (minor isomer) δ= 1.30 (3H, t, J= 7.4 Hz), 2.06 (1H, ddd, J= 2.5, 2.5, 13.4 Hz), 6.58 (1H, ddd, J= 1.0, 7.5, 7.5 Hz), 7.09 (1H, dd, J= 1.4, 7.5 Hz); ^{13}C nmr (major isomer) δ= 14.2, 14.7, 18.8, 25.3, 33.9, 38.6, 41.4, 46.6, 114.4, 116.6, 120.6, 128.0, 130.2, 144.4; ^{13}C nmr (minor isomer) δ= 14.1, 14.7, 18.7, 23.2, 37.8, 38.7, 41.7, 51.8, 114.4, 117.8, 121.5, 127.6, 129.3, 146.0. Hrms Found m/z 235.1419. Calcd for $C_{14}H_{21}NS$: M, 235.1396. Relative stereochemistry of major isomer was determined by the analogy of relative stereochemistry of **10a**.

4-Ethylthio-2-propyl-4-trimethylsilyl-1,2,3,4-tetrahydroquinoline (12b). Ir (neat) 3402, 1577, 1483 cm^{-1}; ^{1}H nmr δ= 0.04 (9H, s), 0.91-0.98 (3H, m), 1.11 (3H, t, J= 7.5 Hz), 1.41-1.49 (4H, m), 1.97 (1H, dd, J= 12.3, 12.7 Hz), 2.17 (1H, dq, J_d= 7.5, J_q= 11.4 Hz), 2.25 (1H, dd, J= 2.9, 12.7 Hz), 3.38 (1H, dq, J_d= 7,5, J_q= 11.4 Hz), 3.39-3.44 (1H, m), 3.69 (1H, brs), 6.39 (1H, d, J= 7.7 Hz), 6.61 (1H, dd, J= 7.7, 7.7 Hz), 6.88 (1H, ddd, 1.3, 7.7, 7.7 Hz), 7.49 (1H, dd, J= 1.3, 7.7 Hz); ^{13}C nmr δ= -2.2, 14.0, 14.2, 18.7, 20.7, 38.4, 39.6, 39.9, 50.0, 113.6, 117.0, 123.1, 126.2, 128.7, 144.7. Hrms Found m/z 307.1773. Calcd for $C_{17}H_{29}NSSi$: M, 307.1792. Relative stereochemistry of **12b** was determined by the analogy of relative stereochemistry of **10b**.

The Synthesis of Leptomerine 15.

4-Butylthio-2-propylquinoline (13). The procedure was the same as that for the reaction of aliphatic N-aryl Schiff's base except that butyl ethynyl sulfide (**6b**) was employed in place of 1-alkenyl sulfide (**4**): Ir (neat) 1572, 1495 cm^{-1}; ^{1}H nmr δ= 0.95 (3H, t, J= 7.4 Hz), 1.00 (3H, t, J= 7.3 Hz), 1.51 (2H, tq, J_t=J_q= 7.4 Hz), 1.71-1.85 (4H, m), 2.88 (2H, t, J= 7.8 Hz), 3.05 (2H, t, J= 7.4 Hz), 7.03 (1H, s), 7.43 (1H, dd, J= 7.6, 8.4 Hz), 7.61 (1H, dd, J= 7.6, 8.4 Hz), 7.99 (1H, d, J= 8.4 Hz), 8.05 (1H, d, J= 8.4 Hz); ^{13}C nmr δ= 13.6, 13.9, 22.1, 23.3, 30.2, 30.7, 41.2, 116.0, 123.3, 125.1, 125.3, 129.1, 129.5, 147.0, 147.7, 161.6. Hrms Found m/z 259.1362. Calcd for $C_{16}H_{21}NS$: M, 259.1396.

4-Butylthio-1-methyl-2-propylquinolinium Trifluoromethanesulfonate (14). A mixture of **13** (260.0 mg, 1.00 mmol) and methyl trifluoromethanesulfonate (328.2 mg, 2.00 mmol) was stirred at 60 °C for 1 h. The crude product was purified by tlc to afford the N-methylated product (**14**) (402.5 mg, 95%): mp 122 °C (H_2O). Ir (KBr disk) 1589, 1566, 1516, 1267, 1157 cm^{-1}; ^{1}H nmr δ= 0.94 (3H, t, J= 7.4 Hz), 1.08 (3H, t, J= 7.3 Hz), 1.53 (2H, tq, J_t=J_q= 7.4 Hz), 1.80 (4H, m), 3.25 (2H, dd, J= 7.9, 7.9 Hz), 3.30 (2H, t, J= 7.4 Hz), 4.32 (3H, s), 7.53 (1H, s), 7.73 (1H, ddd, J= 0.9, 7.2, 8.2 Hz), 8.02 (1H, ddd, J= 1.5, 7.2, 9.1 Hz), 8.24-8.26 (2H, m); ^{13}C nmr δ= 13.5, 13.7, 21.8, 22.1, 29.3, 31.6, 37.2, 38.5, 117.2, 119.2, 125.0, 125.3, 128.2, 128.6, 135.4, 137.8, 159.7, 163.1. Anal. Calcd for $C_{18}H_{24}F_3NO_3S_2$: C, 51.05; H, 5.71; N, 3.31; S, 15.14. Found: C, 50.83; H, 5.54; N, 3.58; S, 15.21.

1-Methyl-2-propyl-4-quinolone (Leptomerine) (15). **14** (425.0 mg, 1.00 mmol) was dissolved in methanol (1 ml) and the solution was poured into 1N NaOH solution (10 ml). The mixture was refluxed for 2 h, then neutralized by 1N HCl. Organic materials were extracted with dichloromethane and the combined extracts were dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by tlc to afford the product (**15**) (140.1 mg, 70%). Melting point and ^1H nmr spectra accorded with those in literature.[7] mp 143-144 °C (AcOEt). Ir (KBr disk) 1630, 1597, 1572 cm^{-1}; ^1H nmr δ= 1.03 (3H, t, J= 7.3 Hz), 1.65-1.73 (2H, m), 2.65 (2H, dd, J=7.8, 7.8 Hz), 3.69 (3H, s), 6.19 (1H, s), 7.32 (1H, dd, J= 8.0, 8.0 Hz), 7.46 (1H, d, J= 8.0 Hz), 7.62 (1H, ddd, 1.7, 8.0, 8.0 Hz), 8.40 (1H, dd, J= 1.7, 8.0 Hz); ^{13}C nmr δ= 13.7, 21.7, 34.0, 36.6, 111.2, 115.3, 123.2, 126.5, 126.6, 132.0, 141.9, 154.4, 177.8. Hrms Found m/z 201.1154. Calcd for $C_{13}H_{15}NO$: M, 201.1155.

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