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Diastereoselective Heteroconjugate Addition of Acetylenic Derivatives

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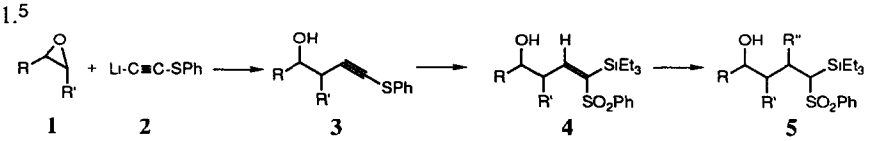
Abstract *Phenylthioacetylene, as its lithium acetylide, was used for opening of epoxides to afford homopropargyl alcohols. Hydrosilylation of these acetylenes were followed by oxidation to afford the corresponding silylvinyl sulfones, the electrophile in the heteroconjugate addition, which showed very high selectivity. The stereocontrolled processes are discussed.*

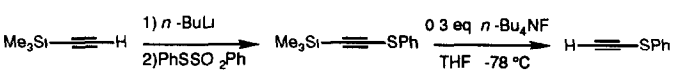
Introduction Asymmetric synthesis *via* heteroconjugate addition has been an important methodology for the synthesis of stereochemically complex molecules.[1] The first diastereoselective heteroconjugate addition, leading to a *syn*-oriented product through an α-chelation effect, was described in 1979.[2] Efforts have continued since then to give *anti*-isomers preferentially.[3] The methodology has recently allowed the introduction of alkynyl groups[4] (R in eq 1) in the heteroatom group conjugated olefin (**4** heteroolefin) which carries a template for the diastereotopic induction. We have preliminary reported that phenylthioacetylene can act as nucleophile to give an adduct **3**, which is further used as the precursor of the heteroolefin **4** through hydrosilylation as shown in eq. 1.[5]



1 **2** **3** **4** **5** (eq. 1)

The investigation for diastereoselective carbon-carbon bond forming process *via* heteroconjugate addition strategy is described.

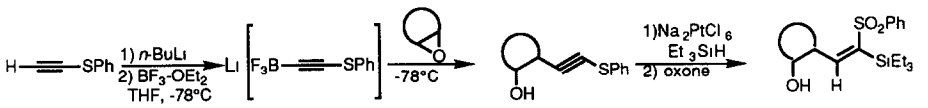
Heteroolefin Synthesis Phenylthioacetylene **2** can be the precursor to β-oxyheteroolefin **4** as shown in eq. 1 through opening of epoxides **1**. This procedure involves a hydrosilylation of **3** with triethylsilane catalyzed by platinum derivative as the key step.[6] The acetylenic sulfide **8** was difficult to prepare and thus no practical method had been reported until Magriotis[7] recently reported two-step synthesis involving bromination followed by dehydrobromination from phenyl vinyl sulfide. We have selected **6** as the starting material for **8** (eq. 2).



6 **7** **8** (eq. 2)

Lithium salt of **6** was sulfenylated by trapping with S-phenyl benzenethiosulfonate[8] ($PhSSO_2Ph$) to give us the sulfide **7** in 83% yield. We found desilylation of **7** with TBAF (tetrabutylammonium fluoride) afforded **8** only

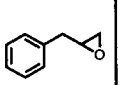
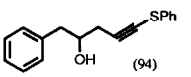
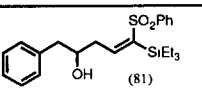
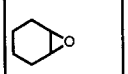
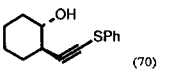
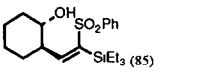
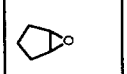
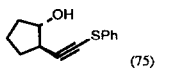
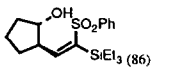
at low temperatures. Since phenylthioacetylene **8** was unstable under basic conditions and polymerized at higher temperatures, ^{1}H-NMR appeared only aromatic region, δ 7.38-7.56 ppm. The desilylation of **7** was best conducted at -78°C with 0.3 equiv. of TBAF in THF to give **8** in 83% yield. Phenylthioacetylene **8** was stockable as a stock solution in ether (*ca.* 20 % w/v) at -20°C: even after six month-storage, the acetylenic signal was observed at δ 3.24 ppm (1H, s) by ^{1}H-NMR.



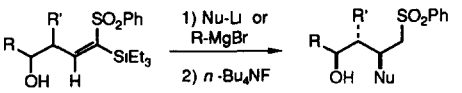
8 **9** **3** **4** (eq. 3)

Opening of an epoxide with phenylthioacetylene **8** was investigated as eq. 3. The lithium acetylide of **8** generated by treatment with *n*-BuLi at -78°C was mixed with BF_3-OEt_2 (0.8 equiv.).[9] In case of mono-substituted epoxide, phenylthioalkynyl group was introduced regioselectively at the less hindered site. The reaction of the phenylthioacetylide **9** with cycloalkene oxides gave alkynylated products with *trans*-configuration as *trans*-alkynylcycloalkanols. All of the β-hydroxy phenylthioacetylenic derivatives **3** were obtained in satisfactory yield. The characteristic CMR of C≡C-S were δ 95-101 and 66-68 ppm, respectively.[10] Three examples were chosen for demonstration of heteroolefin precursors, involving hydrosilylation[6] with triethylsilane in the presence of platinum catalyst and further oxidation with OXONE[11] ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) of the β-hydroxy phenylthioacetylenes. The results are summarized in Table 1

Table 1 . The Synthesis of β-Hydroxy Phenylthioacetylenes and Corresponding β-Hydroxy Heteroolefins

oxirane	β-hydroxy phenylthioacetylene (% yield)	heteroolefin (% yield)
 **10**	 **11** (94)	 **16** (81)
 **12**	 **13** (70)	 **17** (85)
 **14**	 **15** (75)	 **18** (86)

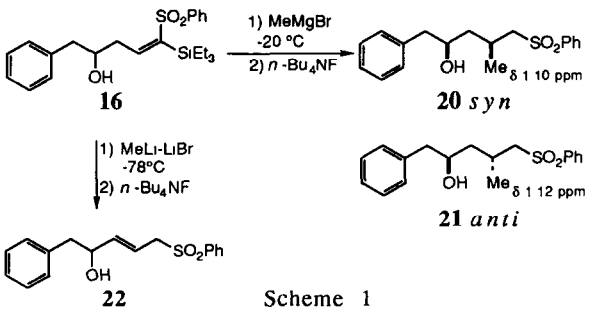
Addition of nucleophile to the heteroolefin In the previous studies, the principle of *syn*-diastereoselective addition through chelation between the nucleophile and an α-oxygen atom suggested that *anti*-diastereoselectivity could be achieved through a β-chelation effect.[3] On the eletrophilic olefin **16**, **17** and **18** were examined addition of nucleophile which produced the adduct **19** with high stereospecificity through β-chelation effect (eq. 4). The heteroolefin **16** carrying a free hydroxyl group on the β-carbon was treated with MeMgBr in Et_2O at -20°C and the product was desilylated with 0.5 equiv. of TBAF to afford the adducts **20** and **21** (Me signals at δ 1.10ppm, d, J=7Hz and 1.12ppm, d, J=7Hz, respectively) in ratio of 3:2 as shown in Scheme 1.



R, R' alkyl or H (eq. 4)

4 **19**

Addition of MeLi-LiBr to **16**, however, did not give the adduct but gave **22**. This may be due to the strong basicity of MeLi. Grignard reagent might be less basic or strongly coordinated with the dissociated alkoxide in **16**. The results of solvent effects in this addition are summarized in Table 2. The solvent effects in the diastereoselection were striking. The addition afforded *only* the *syn*-adduct **20** in 56% yield when carried out in THF or a mixture of THF and *n*-hexane as solvent; none of the trace amount of *anti*-isomer **21** being detected.

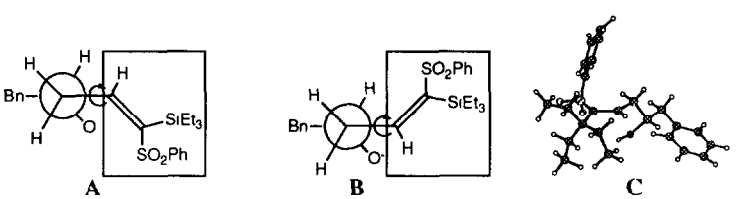


16 **20** *syn* **21** *anti* **22**

Scheme 1

Table 2 Effect of solvent in the addition of Grignard reagent to heteroolefin **16**

solvent	**20** *syn*- %	**21** *anti*- %	%yield of Me adduct	**22** %yield
Et_2O	60	40	51	30
THF	100	0	56	39
THF-Hex (1 1)	100	0	49	19
THF-Hex (1 2)	100	0	48	33

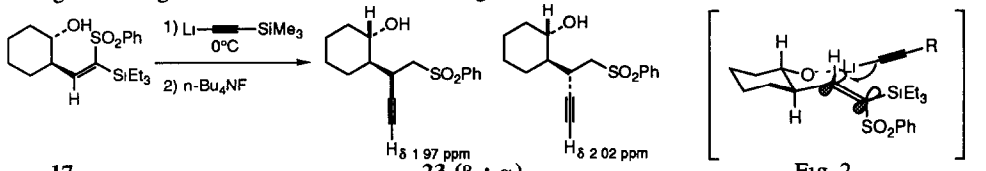


A **B** **C** Fig 1

Diastereoselective formation of *syn* -Me adduct **20** was the first successful example of the high 1,3-asymmetric induction in heteroconjugate addition. The reaction mechanism is speculated through the Newman projection of **16** illustrated in Fig 1 (**A** and **B**), in which two conformers with opposite sp^2 faces of the electrophilic olefin are indicated Therefore, the actual conformation at the transition state may be similar to **C** as one of the possible conformations, which brings the alkoxide group right over the sp^2 face.

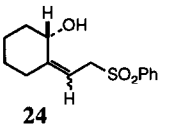
The heteroolefin **17** was treated with 6 equiv. of lithium trimethylsilylethynylide, which was obtained by the addition of MeLi-LiBr to **6** in THF. After treatment of the product with TBAF, a mixture of β- and α-

alkynylated adducts **23** (74% yield) was obtained in *ca.* 2.1:1 ratio judging from the nmr data (δ 1.97ppm, d, J=2.7Hz and δ 2.02ppm, d, J=2.7Hz, respectively) (Scheme 2). The stereochemistry of alkynylated product was assigned through the mechanism as shown in Fig 2.



17 **23** (β : α) Fig 2

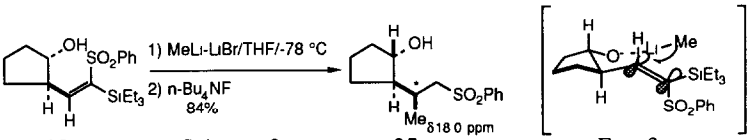
condition	adduct 23			24
	β-%	α-%	%yield	%yield
MeLi-LiBr in THF	68	32	74	6
MeLi in 30%HEX-THF	80	20	82	5



24 Scheme 2

In this conformation, alkynyllithium should coordinate with the alkoxide to attack from the back side and the β-adduct **23** was produced. The alkynylated products **23** were enhanced (82% yield) when LiBr free MeLi was employed in 30% *n*-hexane/THF. In this case, the enhancement of selectivity was observed. The alkynyllithium addition to heteroolefin **17** afforded an essentially 4:1 mixture of β- and α-adducts **23**. It was noticed that heteroconjugate addition was basically in competition with double bond migration of heteroolefin itself. This migration was due to the basicity of the alkynyllithium nucleophile and gave rise to product **24**.

The stereoselective addition to five membered heteroolefin analog **18** was excellent. Addition of 5 equiv. of MeLi-LiBr to **18** in THF at -78°C and desilylation afforded **25** in 84% yield (Scheme 3). No double bond migration was observed. The diastereoselectivity was extremely high, leading to the *single* methyl adduct **25** (δ 1.12ppm, d, J=7Hz). Its stereochemistry was assigned through a similar mechanism (Fig 3).

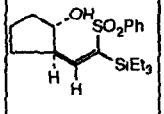
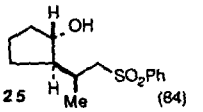
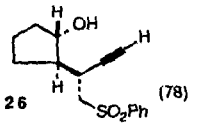
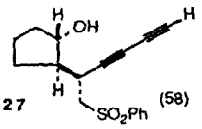
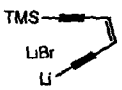
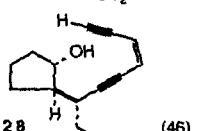


18 Scheme 3 **25** Fig 3

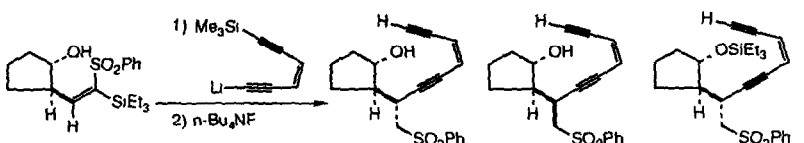
Addition of several acetylenic derivatives were examined and the results are summarized in Table 3. The first trial was lithium trimethylsilylethynylide nucleophile. Addition of MeLi-LiBr to ethynyltrimethylsilane, which gave the single alkynylated adduct **26** in 78% yield. The acetylenic signals of proton and carbons of **26** appeared at δ 2 00ppm (d, J=2.5Hz) and δ 72 1 and 82.4ppm, respectively.

In entry 3 (Table 3), the lithium 4-(trimethylsilyl)buta-1,3-diynylide generated from MeLi and Me3Si-C≡C-C≡C-SiMe3 in a mixture of 30% *n*-hexane and THF was reacted at 0°C with **18.** Desilylation of this mixture with TBAF afforded the alkynylated adduct **27**. It should be noticed that appropriate desilylation was done at 0°C. The characteristic CMR of diyne functional group, HC≡C-C≡C-, appeared at δ 66 1, 67.7, 68.3 and 75 5ppm (assignment being interconvertible).

Table 3 : Heteroconjugate addition of nucleophiles to heteroolefin **18**

heteroolefin	entry	nucleophile	condition of conjugate addition	product (% yield)
 **18**	1	MeLi-LiBr	THF , -78°C	 **25** (84)
	2	Li-≡-TMS-LiBr	THF , -23°C	 **26** (78)
	3	Li-≡-≡-TMS	30% *n* -HEX-THF *0°C*	 **27** (58)
	4		THF , -42°C	 **28** (46)

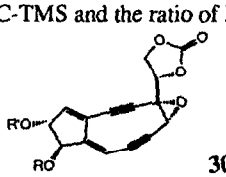
In entry 4, lithium 6-(trimethylsilyl)hex(*cis*)-3-ene-1,5-diynylide nucleophile was generated in THF with MeLi-LiBr at -42°C. The adduct **28a** was obtained as the single stereoisomer (β-adduct). Desilylation step was best carried at 0°C. If desilylation was carried at -78°C, the silyl ether **29** was obtained due to the incompletion of reaction. Acetylenic proton of the silyl ether β-adduct **29** appeared at δ 3.22ppm (d, J=2Hz). The CMR of sp-carbons, HC≡C-C≈C-C≡C- were δ 84.0, 75.8, 81.9 and 96.2ppm while sp^2-carbons, -CH=CH- were δ 118.0 and 121.3ppm (interconvertible assignments). The lithium alkynylide (6 equiv. generated with MeLi at -30°C) was added to **18** and afforded the adduct **28** after desilylation (Scheme 4, Table 4). A mixture of β and α adducts in *ca.* 4:1 ratio was obtained judging from nmr data of acetylenic proton (δ 3.30ppm, d, J=2Hz and δ 3.12ppm, d, J=2Hz, respectively). The diastereoselectivity of this reaction became worse when the lithium acetylide was employed at -30°C.



18 **28a** (β-) **28b** (α-) **29** Scheme 4

Table 4 Generation of Li-C≡C-CH=CH-C≡C-TMS and the ratio of Product **28**

condition	adduct 2 8		
	β-%	α-%	%yield
MeLi , at -30°C	80	20	66
MeLi-LiBr , at -42°C	100	0	46



30 part of neocarzinostatin chromophore

The enediynylated adduct **28** was of particular interest because of the related natural product synthesis, *e g* neocarzinostatin chromophore **30**.

The β-chelation effects in heteroconjugate addition of various nucleophiles to heteroolefin **18** have been demonstrated to have great synthetic utility for the carbon-carbon bond formation in a highly diastereoselective manner as described above.

Experimental

Phenylthioacetylene (**8**) Trimethysilylethyne **6** (5.6 g, 56.7 mmol) was dissolved in anhydrous THF (200 ml) at 0°C. *n*-BuLi soln. (1.7M, 34 ml, 57.2 mmol) was added dropwise with stirring under N_2 atmosphere. After 45 min, a soln. of $PhSSO_2Ph$ (13 g, 52 mmol) in THF (100 ml) was introduced at 0°C. The stirring was continued for 5 hr and the reaction mixture was mixed with sat. NH_4Cl soln The mixture was extracted with ether and the organic layer was washed with water and sat. NaCl soln The ether solution was passed through a column containing sodium sulfate and silica gel, and the eluate was evaporated *in vacuo* and the residue was purified by bulb-to-bulb distillation (70°C, 0.03 tor) with Kugelrohr to produce **7** (8.83 g, 83% yield) This oil was dissolved in THF (450 ml) and cooled to -78°C and then mixed with *n*-Bu_4NF (1.1 M, 11.7 ml, 12.9 mmol) for 3 hr at this temp Sat. NH_4Cl was added to this mixture and the product was extracted with ether. Organic layer was washed with water and sat. NaCl soln , passed through a column containing sodium sulfate and silica gel, and the eluate was kept as a stock solution in ether (*ca* 20 % w/v) at -20°C Almost no decomposition of **8** was observed after 6 months. ^{1}H-NMR (200 MHz,$CDCl_3$) δ 3 24 (1H, s) ppm

General Method for Opening of Epoxides (**10**) Phenylthioacetylene (**8**, 1.3 g, 9.7 mmol) was dissolved in dry THF (125 ml) at -78°C. *n*-BuLi soln. (1.7M, 5.1 ml, 8.7 mmol) was added dropwise with stirring under N_2. After 1 hr, BF_3-OEt_2 (0.85 ml, 6.93 mmol) was added and the mixture was stirred for 15 min. To this mixture was added dropwise a solution of (±)-(2,3-epoxypropyl)benzene **10** (1 g, 7 46 mmol) in THF (25 ml) and the stirring was continued for 3 hr at -78°C The reaction mixture was poured into sat. $NaHCO_3$ and extracted with ether. After work-up, the crude mixture was subjected to silica gel chromatography (1:1 Et_2O-*n*-hexane) to afford the phenylthioacetylene **11** (1.9 g, 94% yield). ^{1}H-NMR (200 MHz, $CDCl_3$) · δ 2 66 (1H, dd, J=17, 6 Hz), 2 74 (1H, dd, J=17, 5 5 Hz) , 2 88 (1H, dd, J=13.5, 7 5 Hz), 3 00 (1H, dd, J=13 5, 5 5 Hz), 4 00-4 20 (1H, m) ppm ^{13}C-NMR ($CDCl_3$) . δ 28.2, 42 6, 67 9 70 8, 95 7 125.8, 126 1,126 4, 128.3, 128 9, 129 2, 132 9, 137 5 ppm EI-MS m/z : 268 (M^+), 148, 147 (100), 121, 103 Anal. calcd. for $C_{17}H_{16}OS$: C 76.08% ; H 6.01% Found C 75 95% ; H 6 04%

Opening of Epoxides (**12**) The reaction was performed as described for **10.** Phenylthioacetylene (**8**, 534 mg, 3.98 mmol) in dry THF (30 ml) was cooled to -78°C. *n*-BuLi soln (1 7M, 2 1 ml, 3 6 mmol) was added After 1 hr, BF_3-OEt_2 (0.35 ml, 2.85 mmol) was added and stirred for 15 min To this mixture was added a soln. of cyclohexene oxide **12** (300 mg, 3.06 mmol) in THF (10 ml) After 3 hr at -78°C, work-up as **10** was performed to yield the phenylthioacetylene product **13** (499 mg) in 70% yield as an oil. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.46 (1H, ddd, J=11 5, 9 5, 4.0 Hz), 3 50 (1H, td, J=9.5, 4 2 Hz) ppm ^{13}C-NMR ($CDCl_3$) . δ 23 9, 24 6, 30 9, 33 3, 40 2, 67.4, 73.2, 100.7, 125 8, 126.2, 129.0, 133.2 ppm. EI-MS m/z 232 (M^+), 147, 121, 115, 77 (100), 69, 57 Anal calcd for $C_{14}H_{16}OS$: C 72.37% ; H 6 94%. Found · C 72 40% ; H 7.20%.

Opening of Epoxides (**14**) The reaction was performed as described for **10.** Phenylthioacetylene (**8**, 574 mg, 4 26 mmol), *n*-BuLi (1.7M, 2.3 ml, 3.93 mmol) and BF_3-OEt_2 (0 39 ml, 3.14 mmol)] was reacted

with cyclopentene oxide **14** (300 mg, 3.6 mmol) in THF (40 ml) to give the phenylthioacetylene product **15** (580 mg) in 75% yield as an oil. ^{1}H-NMR (200 MHz, CDCl3) : δ 2.76-2.91 (1H, m), 4.28 (1H, q, J=5.5 Hz) ppm. ^{13}C-NMR (CDCl3) . δ 21.8, 30.9, 33.6, 41.0, 66.6, 79.1, 101.1, 125 8, 126.1, 129.0, 133.4 ppm. EI-MS m/z : 218 (M^+), 149, 81, 79, 77, 71, 69, 57 (100), 55 Anal. calcd. for C13H14OS : C 71.52% ; H 6.46%. Found C 71 66% ; H 6 78%.

General Method for Heteroolefin Synthesis (**16**) In the presence of Na2PtCl6 (IV) (0.021 M, 0.1 ml, 0.0019 mmol) a soln. of the phenylthioacetylene **11** (500 mg, 1.87 mmol) and triethylsilane (3 ml) in 1,2-dichloroethane (10 ml) was heated at refluxing temp. under Ar atmosphere for 10 hr The mixture was diluted with *n*-hexane (10 ml) at room temp. and filtered through Hyflo Super-cel. The filtrate was evaporated *in vacuo* to dryness and further oxidized. An aqueous soln. of OXONE (3.74 g, 6.08 mmol in 15 ml of water) was added to a soln of crude hydrosilylated product in MeOH (15 ml) at room temp. To this mixture was added a soln. of sodium potassium tartrate (1.3 g, 4.6 mmol in 10 ml of 1·1 MeOH-water) to keep pH *ca.* 4 during the reaction. After stirring overnight, the mixture was decanted and then concentrated The aqueous mixture was extracted with CH_2Cl_2. Organic layer was dried over anh. Na_2SO_4 and evaporated. The heteroolefin **16** (627 mg) was purified by column chromatography (silica gel, 1:1 Et2O/*n*-hexane) to give colorless oil in 81% overall yield (2 steps). ^{1}H-NMR (200 MHz, CDCl3) . δ 2.56-2.80 (4H, m), 3.78-3 94 (1H, m), 6 70 (1H, t, J=7.5 Hz) ppm. ^{13}C-NMR (CDCl3) δ 3.4, 7.0, 37.5, 43.9, 71.2, 126.5, 126.8, 128.4, 128.8, 129.3, 132 6, 137.6, 143.2, 145.4 , 155.4 ppm. EI-MS m/z. 387 (M^+-Et), 91 (100), 77. Anal. calcd for C23H32O3SSi : C 66.30% , H 7.74%. Found : C 66.35%; H 7 87%.

Heteroolefin Synthesis (**17**) A mixture of Na2PtCl6 (IV) (0.021 M, 0.06 ml, 0.0013 mmol), phenylthioacetylene **13** (300 mg, 1.29 mmol) and triethylsilane (3 ml) in 1,2-dichloroethane (10 ml) was heated for 6 hr. After work-up, the product was oxidized with OXONE (3 11 g, 5.06 mmol in 10 ml of water) to the heteroolefin **17** (447 mg), which was purified with silica gel (2:1 Et2O-*n*-hexane) to obtain colorless oil in 85% overall yield (2 steps). ^{1}H-NMR (200 MHz, CDCl3) : δ 2.98-3.32 (2H, m), 6 32 (1H, d, J=10 5 Hz) ppm ^{13}C-NMR (CDCl3) δ 3 4 , 6.9, 24 3, 24.6, 30.4, 35 3, 47.7, 73.3, 126.7, 128.7, 132.6, 143.9, 161 4 ppm. EI-MS m/z : 351 (M^+-Et), 77, 69, 57 (100) Anal. calcd for C20H32O3SSi C 63.11% ; H 8.49% Found : C 62.90% , H 8 64%

Heteroolefin Synthesis (**18**) Compound **15** (994 mg, 4.56 mmol) was similarly converted into **18** (1.6 g) which was obtained after purification (silica gel, 3:1 Et2O-*n*-hexane) as colorless oil in 86% overall yield (2 steps) ^{1}H-NMR (200 MHz, CDCl3) · δ 3 30-3 50 (1H, m), 3.84-4.00 (1H, m), 6.36 (1H, d, J=10 5 Hz) ppm ^{13}C-NMR (CDCl3) δ 3 5, 7 1, 22 5, 31 3, 34 7, 49 9, 79.2, 126 8, 129 0, 132.8, 143.5, 161.6 ppm. EI-MS m/z 337 (M^+-Et), 163, 133, 125, 107, 97, 77 (100), 59, 57, 55. Anal. calcd for C19H30O3SSi · C 62 25% , H 8 25% Found · C 62 12% , H 8.56%.

Nucleophilic Addition to Heteroolefin **16** *Method A* : The heteroolefin **16** (30 mg, 0.07 mmol) was dissolved in dry THF (2 ml) and the soln. was cooled to -78°C To this soln was added MeMgBr soln. (3M, 0.07 ml, 0.22 mmol). The mixture was stirred for 4 hr at -20°C to -10°C under N_2 The reaction medium was quenched with sat. NH_4Cl and extracted with Et_2O. After work-up, the residue was dissolved in THF (2 ml) and mixed with *n*-Bu4NF (1.1 M, 0.02 ml, 0.02 mmol). The mixture was stirred for 3.5 hr at room temp. Sat. NH_4Cl was added to this mixture and the product was extracted with ether. After drying and concentration *in vacuo*, the residue was purified by PLC (silica gel, 3 times 3:1 Et2O/*n*-hexane) to yield **20** (*syn*-, 9 mg, 56% yield) and the double bond migration product **22** (7 mg, 39% yield). *Method B* : In stead of dry THF, 2 ml of dry 1:1THF/*n*-hexane was used in this addition. The reaction was carried in the same manner as described in *method A* by using 27 mg (0.06 mmol) of heteroolefin **16**. The adduct **20** (*syn*-, 8 mg, 49%

yield) and the product **22** (4mg, 19% yield) were obtained from this method. *Method C* : In stead of dry THF, 2 ml of dry Et2O was used in heteroconjugate addition step. The reaction was carried in the same as *method A*. The ^{1}H-NMR studying of product indicated that the mixture of adduct **20** and **21** in ratio 3 : 2 (*syn-anti-*) and the product **22** were occurred. Data of adduct **20** : ^{1}H-NMR (200 MHz, CDCl3) : δ 1.10 (3H, d, J=7 Hz), 1.52-1.70 (2H, m), 2.28-2.50 (1H, m), 2.64 (1H, dd, J=13.5, 8 Hz), 2.76 (1H, dd, J=13.5, 5 Hz), 2 96 (1H, dd,J=19, 7 Hz), 3.28 (1H, dd, J=19, 5 Hz), 3.78- 3.98 (1H, m) ppm. ^{13}C-NMR (CDCl3) : δ 21.1, 25.8, 43 1, 44.5, 61.9, 69.9, 126.5, 127.8 128.5, 129 2, 129.3, 133.4, 138.0, 140.0) ppm. Anal. calcd. for C18H22O3S : C 67.89% ; H 6.96%. Found : C 67.84% ; H 7.02 %. ^{1}H-NMR (200 MHz, CDCl3) of Me group which was differentiated between adduct **20** and **21** · Me of **20** : δ 1.10 ppm (d, J=7 Hz); Me of **21** : δ 1.12 ppm (d, J=7Hz). Data of product **22** : ^{1}H-NMR (200 MHz, CDCl3) : δ 2.66 (1H, dd, J=13.5, 8 Hz), 2 76 (1H, dd, J=13.5, 5.5 Hz), 3.70-3.88 (2H, m), 4.22-4.40 (1H, m), 5.60-5 80 (2H, m) ppm. ^{13}C-NMR (CDCl3) : δ 43.6, 59 6, 72.3, 116.5, 126.5, 128.3, 128.4, 128.9, 129.3, 133.6, 137 0, 138.2, 142.3 ppm. EI-MS m/z : 302 (M+), 233 (100), 211, 143, 142, 141, 125, 115, 92, 91, 90, 77, 51. Anal. calcd. for C17H18O3S : C 67.52% ; H 6.00%. Found: C 67.37% ; H 6.14 %.

Heteroconjugate Addition to Heteroolefin **17** *Method A* : Trimethylsilylethynyllithium was generated by addition of MeLi-LiBr (1.5M, 0.53 ml, 0.79 mmol) to the soln of ethynyltrimethylsilane (85 mg, 0.87 mmol) in dry THF (3 ml) at -23°C under N2 atmosphere. After 1 hr, to this soln was added **17** (50 mg, 0.13 mmol) in 2 ml of dry THF. The mixture was allowed to warm to 0°C with stirring for 6 hr. The reaction was quenched with sat. NH4Cl and extracted with Et2O. After work-up, the residue was dissolved in THF (5 ml) and mixed with *n*-Bu4NF (1.1 M, 0.06 ml, 0.07 mmol). The mixture was stirred for 4 hr at room temp. Sat. NH4Cl was added to this mixture and the product was extracted with ether. Purification was effected by PLC (silica gel, 3 times 2:1 Et2O/*n*-hexane) and mixture of β and α adducts **23** (27mg, 74% yield) were obtained in *ca.* 2.1:1 ratio judging from the nmr data. The resultant double bond migration product **24** (2 mg, 6% yield) was obtained. *Method B* : MeLi (1.2M, 0.39ml, 0.47 mmol) and ethynyltrimethylsilane (51 mg, 0.52 mmol) were used for generation of trimethylsilylethynyllithium in 30% *n*-hexane/THF (4 ml). In this method, 30 mg (0.08 mmol) of heteroolefin **17** and 0.04 ml (1.1M, 0.04 mmol) of TBAF were used in heteroconjugate addition and desilylation steps, respectively. The reaction yielded a mixture of β and α adduct **23** (19 mg, 82% yield) in *ca.* 4:1 ratio and product **24** (2 mg) in 5% yield. Data of β-adduct **23** : ^{1}H-NMR (200 MHz, CDCl3) δ 1 97 (1H, d, J=2 7 Hz), 3.14-3.26 (1H, m), 3.48 (1H, dd, J=14.5, 7.5 Hz), 3.52-3 60 (1H, m), 3.62 (1H, dd, J=14.5,5.5 Hz) ppm. ^{13}C-NMR (CDCl3) : δ 24.7, 25.5, 29 4, 30 4, 36.3, 47.8, 59.5, 71.7, 71.9, 82.4, 128 2, 129.1, 133.6, 139.4 ppm. EI-MS m/z · 292 (M+), 290, 152, 151, 150, 125, 95, 91, 77, 55 (100), 51 Anal. calcd. for C16H20O3S : C 65 72% ; H 6 89% Found : C 65.57%, H 6.99% Data of α-adduct **23** : ^{1}H-NMR (200 MHz, CDCl3) δ 2.02 (1H, d J=2.7 Hz), 2 32-3.04 (1H, m), 3.32 (1H, dd, J=14, 9 Hz), 3 50 (1H, dd, J=14, 3 5 Hz), 4.24 (1H, brs) ppm. Data of product **24** : ^{1}H-NMR (200 MHz, CDCl3) · δ 3 87 (2H, d, J=8 Hz), 3 98-4.10 (1H, m), 5 49 (1H, td, J=8, 1 2 Hz) ppm. EI-MS m/z 266 (M+), 125, 105 (100), 77, 69, 57.

Heteroconjugate Addition of MeLi *to* **18** Heteroolefin **18** (35 mg,0.09 mmol) was dissolved in dry THF (3 ml) and cooled to -78°C. To this soln. was added MeLi-LiBr (1.5M, 0.32 ml, 0.47 mmol) under N2 atmosphere. After stirring for 5 hr at -78°C, the mixture was quenched with sat. NH4Cl and extracted with Et2O The product, after the work-up, was dissolved in THF (3 ml) and mixed with *n*-Bu4NF (1 1M, 0.04 ml, 0.04 mmol). After stirring for 1 hr at room temp., the reaction mixture was mixed with sat.NH4Cl and extracted with Et2O. The product was purified by PLC (silica gel, 3 times, 3:1 Et2O/*n*-hexane) to afford **25** (21 mg, 84% yield) as pure stereoisomer. ^{1}H-NMR (200 MHz, CDCl3) . δ 1.12 (3H, d, J=7 Hz), 2.97 (1H, dd, J=14 5, 8 Hz),

3 26 (1H, dd, J=14.5, 4 Hz), 3.86-4.00 (1H, m) ppm. ^{13}C-NMR (CDCl3) : δ 18.0, 21.9, 27.6, 30.0, 35.4, 52.4, 60.7, 75.0, 127 9, 129.3, 133.6,140.1 ppm. Anal. calcd. for C14H20O3S : C 62.66% ; H 7.51% Found · C 62 59% ; H 7.62%.

Heteroconjugate Addition of Li-C≡C-SiMe3 *to* **18** Trimethylsilylethynyllithium was generated by addition of MeLi-LiBr soln. (1.5M, 0.33 ml, 0.49 mmol) to the soln. of ethynyltrimethylsilane (53 mg, 0.54 mmol) in dry THF (2 ml) at -23°C under N2 atmosphere. After 1 hr, **18** (30 mg, 0.08 mmol) in dry THF (1 ml) was introduced to this mixture, which was stirred further 6.5 hr at -23°C. The mixture was quenched with sat NH4Cl soln. and extracted with Et2O. The product was dissolved in 2 ml of THF and *n*-Bu4NF (1.1M, 0.04 ml, 0.04 mmol) was added. Stirring at room temp. for 2.5 hr, the mixture was mixed with sat. NH4Cl soln. and followed by extraction with Et2O. The product was purified by PLC (silica gel, 3 times 3:1 Et2O/*n*-hexane) to give **26** (18 mg, 78% yield) as a colorless oil. ^{1}H-NMR (200 MHz, CDCl3) : δ 2.00 (1H, d, J=2.5 Hz), 3.02-3.16 (1H, m), 3 44 (1H, dd, J=14, 7 Hz), 3.50 (1H, dd, J=14, 6 Hz), 4.06-4.22 (1H, m) ppm. ^{13}C-NMR (CDCl3) : δ 21 9, 29.3, 29.9, 35.5, 50.2, 59.3, 72.1, 75.9, 82.4, 128.2, 129.2, 133.8, 139.6 ppm. EI-MS m/z : 278 (M+), 194, 137, 136, 125, 91, 77, 55 (100). Anal. calcd. for C15H18O3S : C 64.72% ; H 6.52% Found : C 64.58% ; H 6.81%

Heteroconjugate Addition of Li-C≡C-C≡C-SiMe3 *to* **18** 4-(Trimethylsilyl)buta-1,3-diynyllithium was generated by addition of MeLi (1.2M, 0.41 ml, 0.49 mmol) to the soln. of 1,4-bis(trimethylsilyl)-1,3-butadiyne (104 mg, 0.54 mmol) in dry 30% *n*-hexane/THF (4 ml) at 0°C under N2 atmosphere. After 45 min of stirring, **18** (30 mg,0.08 mmol) in 1 ml of dry THF was added dropwise to this mixture. The stirring was continued for 4 hr at 0°C. Sat. NH4Cl was added to the mixture and the product was extracted with Et2O. The product was dissolved in 5 ml of THF and cooled to -20°C. *n*-Bu4NF (1.1M, 0.04 ml, 0.04 mmol) was added. The reaction was allowed to warm to 0°C with stirring for 4 hr. The mixture was mixed with sat. NH4Cl soln. and followed by extraction with Et2O. The ethereal layer yielded an oil which was purified by PLC (silica gel, 3:1 Et2O/*n*-hexane) to give **27** (15 mg, 58% yield) as an oil.^{1}H-NMR (200 MHz, CDCl3) : δ 1 97 (1H, d, J=1 2 Hz), 3.22 (1H, qd, J=6.5,1.2 Hz), 3.43 (1H, dd, J=14.5, 7.5 Hz), 3.52 (1H, dd, J=14.5, 6.5 Hz), 4 12 (1H, q, J=6 5 Hz) ppm. Data of silylether derivative* of the adduct **27** : ^{1}H-NMR (200 MHz, CDCl3) : δ 1.97 (1H, d, J=1.2 Hz), 3.08-3.20 (1H, m), 3.40 (1H, dd, J=14 5, 5 Hz), 3.48 (1H, dd, J=14.5, 8 Hz), 4.05 (1H, q, J=7 Hz) ppm. ^{13}C-NMR (CDCl3) : δ 5 2, 7.0, 21 1, 27.7, 30 1, 35 0, 50.9, 59.1, 66.1, 67.7, 68.3, 75.5, 75.9, 128.2, 129.1, 133.9, 139.2 ppm. EI-MS m/z · 387 (100, M+-CH2CH3), 161, 160, 148, 77, 57, 55. Anal. calcd. for C23H32O3SSi C 66.30% ; H 7.74%. Found : C 66.31%; H 8.03% * This silyl ether derivative was obtained when desilylation step was carried at -78°C for 30 min and the desilylation was not complete in such a low temp. By contrast, desilylation was completed at room temp. but it seemed to be too drastic to obtain product The appropriate temperature of this reaction was 0°C.

Heteroconjugate Addition of Li-C≡C-CH=CH-C≡C-SiMe3 *to* **18** *Method A* . To the solution of 1,6-bis(trimethylsilyl)hex(*cis*)-3-ene-1,5-diyne (119 mg, 0.54 mmol) in dry THF (4 ml) was introduced MeLi-LiBr (1.5M, 0.33 ml, 0.49 mmol) at -42°C under N2 atmosphere and 6-(trimethylsilyl)hex(*cis*)-3-ene-1,5-diynyllithium was generated. After 1 hr of stirring, the heteroolefin **18** (30 mg, 0.08 mmol) in 1 ml of dry THF was added dropwise to the mixture and stirring was continued for 7 hr at -42°C. The mixture was quenched with sat. NH4Cl soln. and extracted with Et2O. After the work-up, the product was dissolved in 5 ml of THF and cooled to -20°C and mixed with *n*-Bu4NF (1.1M, 0.08 ml, 0.08 mmol). The reaction was allowed to warm to 0°C with stirring for 4 hr. The mixture was mixed with sat. NH4Cl soln. and followed by extraction with Et2O. The work-up oil was purified by PLC (silica gel, 2 times 3:1 Et2O/*n*-hexane) to afford the single stereoisomer, β-adduct **28a** (13 mg, 46% yield). *Method B* : 6-(Trimethylsilyl)hex(*cis*)-3-ene-1,5-diynllithium was generated similar to *method A* by using MeLi (1.2M, 0.41 ml, 0.49 mmol) in stead of MeLi-

LiBr at -30°C. After desilylation and purification, the mixture of β and α adducts **28a** and **b** (18 mg, 66% yield) was obtained in *ca.* 4:1 ratio (from nmr data). Data of β-adduct **28a** : ^{1}H-NMR (200 MHz, CDCl3) : δ 3.12-3 30 (1H, m), 3.30 (1H, d, J=2 Hz), 3 46 (1H, dd, J=14.5, 7 Hz), 3.52 (1H, dd, J=14.5, 6 Hz), 4.20 (1H, q, J=6 5 Hz), 5.60 (1H, dd, J=11, 2 Hz), 5 72 (1H, dd, J=11, 2.5 Hz) ppm. EI-MS (high resolution) m/z : 328.1152 (calcd for M^+ 328.1133), 279, 187, 186, 185 (100), 158, 157, 115, 102, 77, 67, 51. ^{1}H-NMR (200 MHz, CDCl3) of mixture of β and α adducts **28a** and **b** (method B, not isolated) which could be differentiated : β-adduct : δ 4.20 (1H, q, J=6.5 Hz), 3.30 (1H, d, J=2 Hz) ppm. α-adduct : δ 4.08 (1H, q, J=6.5 Hz), 3.12 (1H, d, J=2 Hz) ppm. Data of silylether derivative* of the β-adduct **29** : ^{1}H-NMR (200 MHz, CDCl3) : δ 3.22 (1H, d, J=2 Hz), 3.26-3.38 (1H, m), 3.48 (1H, dd, J=14.5, 7.5 Hz), 3.56 (1H, dd, J =14.5, 7 5 Hz), 4.18 (1H, q, J=7 Hz), 5 58 (1H, dd, J=10.5 Hz), 5 68 (1H, dd, J=10.5, 2 Hz) ppm. ^{13}C-NMR (CDCl3) · δ 5.2, 7.0, 21.4, 27.7, 30.6, 35.2, 50.9, 59.7, 75 6, 84.0, 75.8, 81.9, 96 2, 118.0, 121.3, 128.3, 129.0, 133.5, 139.6ppm. *This silylether derivative was obtained when desilylation step was treated with TBAF (1.1M, 0.04 ml, 0.04 mmol) at -78°C for 1 hr and the desilylation was not complete in this such condition. The suitable condition was found to be 1 equivalent of TBAF at 0°C for 4 hr to complete desilylation.

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