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# Stereoselective Synthesis of 1,4-Disubstituted 1,3-Diene from Aldehyde Using Organotitanium Reagent[1]

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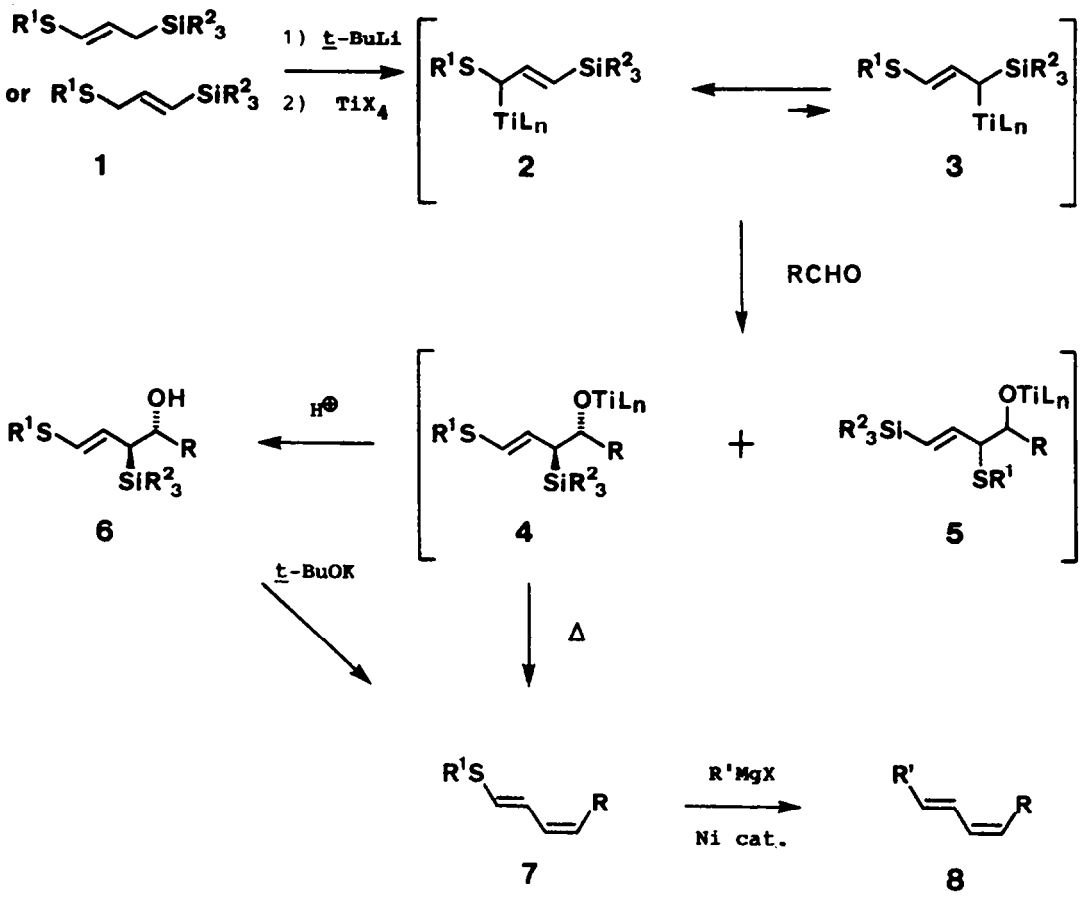
**Abstract** - Organotitanium reagent generated from 1-t-butylthio-3-trimethylsilyl-1-propene condenses with aldehydes to give 1-t-butylthio-(E,Z)-1,3-alkadienes in a single step via (E)-erythro-β-hydroxysilane in a highly regio- and stereoselective manner. 1,4-Dialkyl-1,3-diene is obtaind from the diene sulfide by cross coupling reaction with Grignard reagent in the presence of nickel catalyst. The utility of the method is illustrated by application to the synthesis of **Spilanthol**, a naturally occurring insecticide from Spilanthese olerancae in five steps.

## Introduction

The need for the stereoselective synthetic method of polyenes has become increasingly apparent in recent years, in part because of the intermediary nature of polyene function in the olefinic natural products synthesis, and also in part because of the possibility of applying the methodology to the construction of numerous biologically and biogenetically interesting structures having acyclic polyenes. We have recently described stereoselective syntheses of 1,3-dienes from aldehydes using allyltitanium reagents from allylphosphine,[2] allylsulfides,[3] and allylsilane.[4] Further, a new synthetic route to 2-alkylthio-1,3-diene was now available.[2] We have also revealed an excellent potentiallity of alkylthio group for further elaboration of carbon chain using the nickel catalyzed alkylation process.[3] The high stereoselectivity of allyltitanium reagent[5] made it apparent that routes to 1-alkylthio-1,3-diene would be highly desirable. One of the most important processes among them would be a route for the transformation of aldehydes to 1-alkylthio-1,3-dienes from which 1,4-disubstituted 1,3-dienes[6,7,8] would be prepared stereoselectively (Scheme 1). We now describe a method which responds to this scheme.

The stereochemical control and the flexibility inherent in our approach to the construction of the 1,3-diene system suggested the application of the method to the synthesis of a number of acyclic polyenes.[9] The utility of the method is illustrated by application to the synthesis of **Spilanthol** (10), which was first isolated from Heliopsis longipes (A. Gray) Blake,[10] a member of the Compositae, and was shown to be insecticidally active.[11] In later work, the compound was found to be identical with naturally occurring insecticide from Spilanthese olerancae.[10]

**Scheme 1.**




## Results and Discussion.

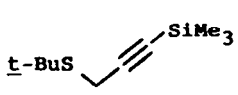
Starting materials were prepared by the silylation of the corresponding lithiated allylsulfide: 1a and 1e (from allyl t-butyl sulfide) in 60% and 77% yields, respectively, 1c (from allyl n-propyl sulfide) in 60% yield, and 1d (from allyl isopropyl sulfide) in 78% yield. The sulfide 1b was also prepared by the hydroalumination of 3-t-butylthio-1-trimethylsilyl-1-propyne (19) in 67% yield.


1a


1b


R= n-Pr: 1c
i-Pr: 1d
t-Bu: 1e


18

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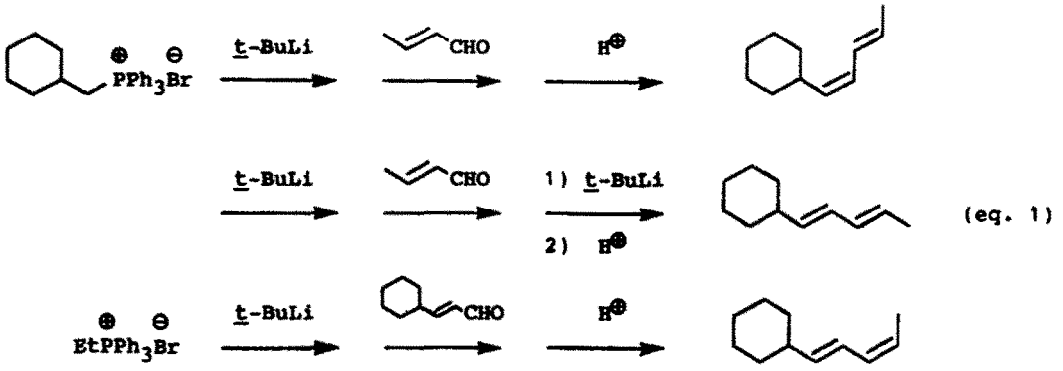
**Stereoselective Synthesis of 1,4-Disubstituted-1,3-butadienes.** Reaction of titanium reagent of type 2, with aldehydes gave (E)-erythro-β-oxidosilanes 4 exclusively which were smoothly transformed into the 1-alkylthio-(E,Z)-1,3-alkadienes 7 via the cycloelimination of the sort already established for the Peterson reaction[12] (Scheme 1). The diene sulfide 7 was further converted into 1,4-dialkyl-(E,Z)-1,3-butadiene derivatives 8 with Grignard reagent by nickel-catalyzed cross coupling reaction.[13] The stereoselectivity of 8 was determined by gc analysis by comparison with authentic samples synthesized independently.[14]

The results of several experiments are summarized in Table 1. It is clear that because of the significant steric effect of alkylthio group, a greater measure of stereochemical control and regioselectivity in carbon-carbon bond forming processes might result from the use of t-butylthio group rather than the more common methylthio group. Hence larger alkylthio group gave better erythro selectivity (entry 1,2,3 in Table 1). Although the triphenylsilyl derivative ($R^2$= Ph; entry 1-6) underwent clean metallation with n-butyllithium at 0°C to form lithiated 1, the condensation with aldehyde gave rise to a mixture of stereoisomers with low selectivities. Nickel(II) 1,3-bis(diphenylphosphinopropane) chloride, Ni(dppp)$Cl_2$, was found to be the most effective catalyst for the cross coupling reaction of 7 with Grignard reagent.[13]

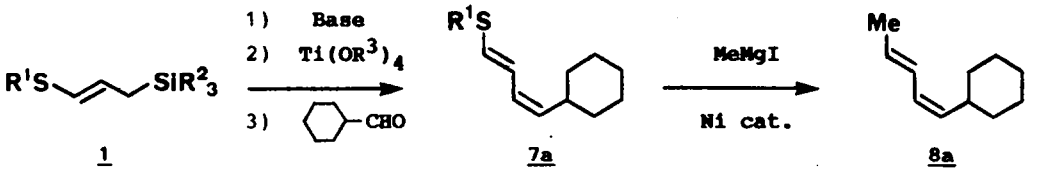
Authentic samples for gc analysis were synthesized as follows: 1-cyclohexyl-(E,Z)-1,3-pentadiene was synthesized from crotonaldehyde with cyclohexylmethylidenetriphenylphosphorane, the (E,E)-isomer from crotonaldehyde with cyclohexylmethylidenetriphenylphosphorane using the β-oxido ylide procedure and, the (Z,E)-isomer from 3-cyclohexyl-2-propenal with ethylidenetriphenylphosphorane, respectively (eq. 1).[14]




(eq. 1)

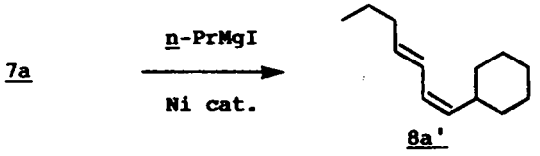
The possible explanation[3b] of these selectivities is as follows. The reaction of the allylic organometallics with the carbonyl group is known to take place through an allylic rearrangement of the organometallics by a chelated transition state 9 (Fig. 1). Thus, the allyltitanium derivative of type 2 should react with aldehydes at α-position of trialkylsilyl group. On the other hand, the isomeric reagent 3 should give the product 5 in which the silyl group is located at δ-position to the hydroxyl function. Considering the steric factor between the ligands of titanium and geminal substituent, the titanium derivative 2 should be rather stable than the other isomer 3 because of the larger steric repulsion be-

Table 1. Synthesis of 1,4-disubstituted 1,3-diene.



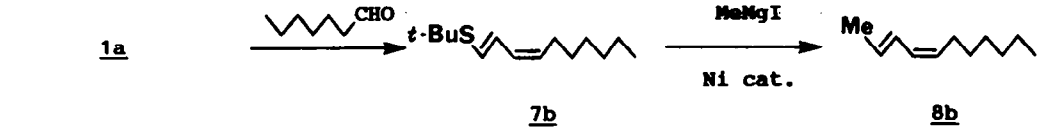

1 7a 8a

| Entry | 1[3] R¹ | R² | Base | Reagent R³ | 7a Yield[b] (%) | Cat.[a] | 8a Yield[b] (%) | 8a Ratio[c] (Z,E):(Z,Z):(E,E):(E,Z) |
|---|---|---|---|---|---|---|---|---|
| 1 | n-Pr | Ph | n-BuLi | i-Pr | (69)[d] | A | 85 | 62 : 24 : 9 : 5 |
| 2 | i-Pr | Ph | n-BuLi | i-Pr | (67)[d] | A | 53 | 74 : 17 : 6 : 5 |
| 3 | t-Bu | Ph | n-BuLi | i-Pr | 97 | B | 68 | 83 : 6 : 9 : 2 |
| 4 | t-Bu | Ph | n-BuLi | i-Bu | 90 | B | 71 | 90 : 8 : 2 : - |
| 5 | t-Bu | Ph | n-BuLi | t-Bu | 29 | B | 75 | 57 : 30 : 10 : - |
| 6 | t-Bu | Ph | n-BuLi | none | 23 | B | -- | 66 : 25 : 7 : 2 |
| 7 | t-Bu | Me | t-BuLi | i-Pr | 62 | B | 75 | 98 : 2 : - : - |
| 8 | t-Bu | Me | t-BuLi | i-Bu | 29 | B | -- | 97 : 3 : - : - |
| 9 | t-Bu | Me | t-BuLi | i-Pr | 55[e] | C | 75 | 94 : 2 : 4 : - |
| 10 | t-Bu | Me | t-BuLi | i-Pr | 54 | C | 93 | 96 : 2 : - : 3 |




8a'

| | | | | | | | | 8a' |
|---|---|---|---|---|---|---|---|---|
| 11 | t-Bu | Me | t-BuLi | i-Pr | 62 | C | 93 | >95 : <5 |



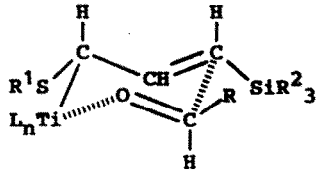

7b 8b

| | | | | | 7b | | | 8b |
|---|---|---|---|---|---|---|---|---|
| 12 | t-Bu | Me | t-BuLi | i-Pr | 55 | C | -- | 98 : 1 : 1 : - |

[a]A: $Ni(PPh_3)_2Cl_2$, B: $Ni(PPh_3)_2Cl_2$ + dppp, C: $Ni(dppp)Cl_2$. [b]Isolated yield. [c]All four possible isomers were independently synthesized using the Wittig reactions. [d]Over-all yields of two-step sequence. Thus, the intermediary hydroxyl silane 6 was isolated and treated with t-BuOK. [e]Using HMPA (1 equiv.) as a cosolvent.

tween the ligands of titanium and trialkylsilyl group. Notably, the high (E)-erythro selectivity of this reaction is also explained by considering the six-membered ring transition state 9 in which three bulky substituents such as alkylthio group and trialkylsilyl group of reagent 2 and alkyl group of aldehyde occupy the equatorial positions.

Fig. 1.

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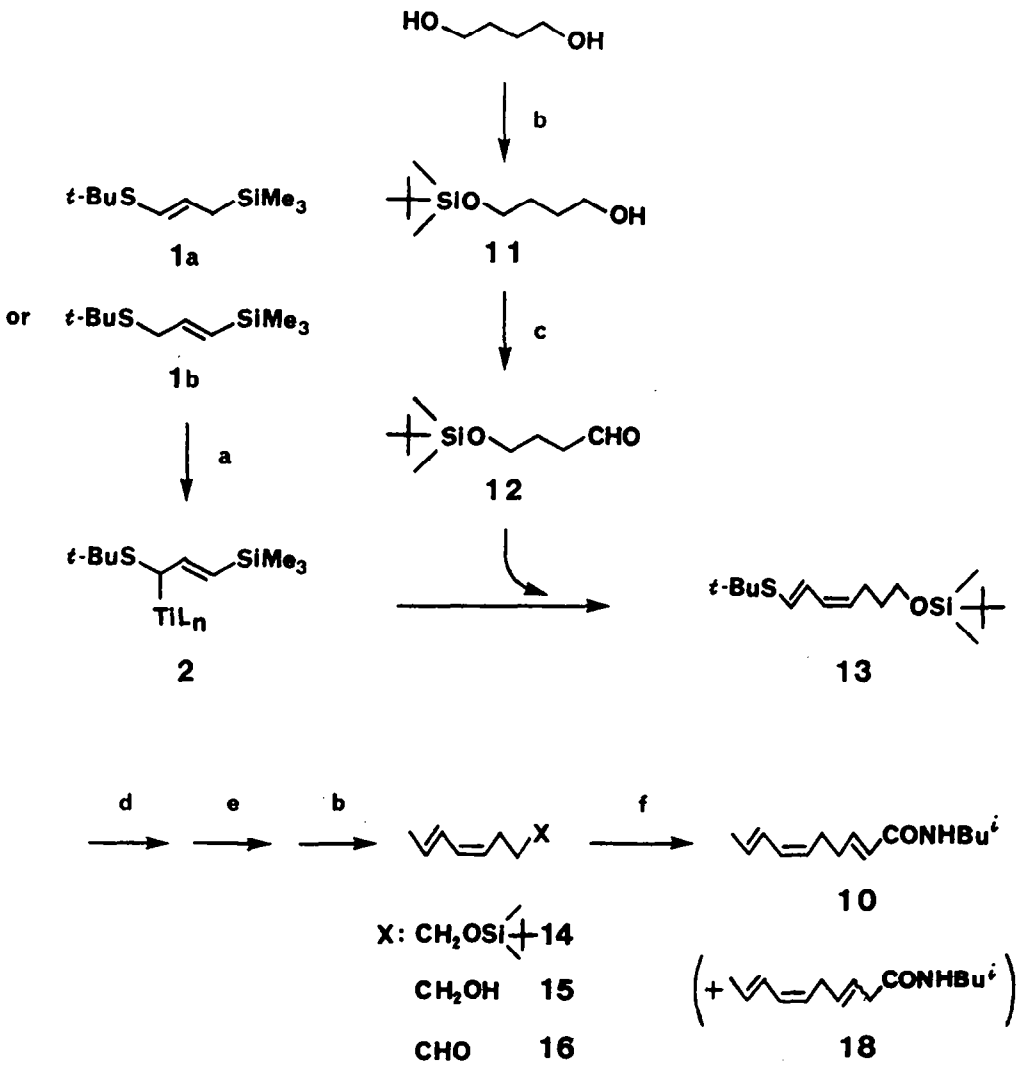
**Synthesis of Spilanthol (10)**: The pathway of the synthesis is as follows (Scheme 2). Oxidation of 4-(t-butyldimethylsilyloxy)-1-butanol (11), which was obtained from 1,4-butanediol with t-butylchlorodimethylsilane, pyridine and a catalytic amount of N,N-dimethyl-4-aminopyridine in dichloromethane in 88% yield, with oxalyl chloride-dimethyl sulfoxide (DMSO) and triethylamine in dichloromethane[15] afforded 4-(t-butyldimethylsilyloxy)butanal (12) in 90% yield. Reaction of 1-t-butylthio-3-trimethylsilyl-1-propene (1a)[1a] with an equivalent of t-butyllithium in THF-HMPA at -78°C for 10 min and at 0°C for 1 h followed by treatment with an equivalent of titanium tetraisopropoxide at -78°C for 40 min generated allylic titanium derivative of type 2 which upon reaction with 4-(t-butyldimethylsilyloxy)butanal (12) afforded 7-t-butyldimethylsilyloxy-1-t-butylthio-(E,Z)-1,3-heptadiene (13) in 53% yield. The t-butylthio group of 13 was cleanly replaced by methyl group with excess of methylmagnesium iodide in the presence of $Ni(dppp)Cl_2$ to give 1-t-butyldimethylsilyloxy-(Z,E)-4,6-octadiene (14) in 83% yield.[13] Gc analysis revealed the compound 14 was >97% isomerically pure; (Z,E)-isomer with minor isomer of 2.5%. The compound 14 exhibited fully consistent spectral data. Removal of t-butyldimethylsilyl protecting group could be effected cleanly by reaction with anhydrous tetrabutylammonium fluoride in THF for 30 min at room temperature to give (Z,E)-4,6-octadiene-1-ol (15) in quantitative yield.[16] Oxidation of the resulting alcohol with oxalyl chloride-DMSO and triethylamine in dichloromethane[15] afforded, after short path column chromatography on silica gel, (Z,E)-4,6-octadienal (16) in 54% yield. This unstable aldehyde 16 was transformed into spilanthol (10) by reaction with the Wittig reagent which was prepared *in situ* from N-isobutylaminocarbonylmethyl-triphenylphosphonium bromide (17) and LDA in THF at 0°C for 10 min.[17] **Spilanthol (10)** was obtained with 88% pure by gc analysis: spectroscopically identical with reported data,[10,18] in 61% yield from the aldehyde 16. The Δ3-isomer (18), which could be easily separated by column chromatography on silica gel, was also formed from the Wittig reaction in *ca.* 18% yield.

**Scheme 2.**




a, t-BuLi then $Ti(OPr^i)_4$; b, t-$BuMe_2SiCl$-pyridine; c, $(COCl)_2$-DMSO then $Et_3N$; d, MeMgI-cat. $Ni(dppp)Cl_2$-benzene reflux; e, Dried n-$Bu_4NF$ in THF f, $Ph_3{=}CHCONHBu^i$ from $Ph_3P{-}CH_2CONHBu^i$ Br (17) and LDA in THF.

## Experimental

**General.** The IR spectra were determined on a Hitachi 260-10 spectometer in a $CCl_4$ solution unless otherwise stated. The NMR spectra were recorded on a JNM-PMX 60 spectrometer, using tetramethylsilane as an internal standard. Splitting patterns are indicated as s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet, and br: broad peak. The isomeric ratio of the products was determined by gas chromatography (gc) on a 25-m PEG-HT capillary column using a Hitachi Model 163 and 164 instruments equipped with a flame ionization detector using nitrogen as carrier gas. The analyses were performed at the Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University. Tetrahydrofuran (THF) and ether were distilled from benzophenone ketyl. Benzene, hexane, and toluene were dried over sodium metal. Dichloromethane was dried over 4A molecular sieves. Hexamethylphosphoric triamide (HMPA) was distilled from $CaH_2$ under reduced pressure. All the experiments were carried out under an argon atmosphere. For thin layer chromatography (TLC) analyses throughout this work, Merck precoated TLC plates (silica gel 60 $GF_{254}$, 0.25 mm) were used. Purification of the product was carried out by column chromatography on silica gel Fuji BW-820.

**1-t-Butylthio-3-trimethylsilyl-1-propene (1a):** To a solution of allyl t-butyl sulfide (13 g, 100 mmol) in THF (200 ml) was added a solution of t-butyllithium in pentane (1.8 M, 67 ml, 120 mmol) at -78°C. The resulting solution was stirred at -78°C for 1 h. Chlorotrimethylsilane (15 ml, 120 mmol) was added to the above solution at -78°C. The reaction mixture was stirred at -78°C for 20 min and poured into ice-cold 2 N aqueous hydrochloric acid. The product was extracted three times with pentane. The organic layers were dried and concentrated *in vacuo*. The residual oil was purified by column chromatography on silica gel with hexane as elute to give **1a** (8.9 g, 44 mmol) as a colorless liquid in 44% yield: $R_f$= 0.28 (hexane); IR (neat) 2970, 1370, 1260, 1160, and 870 $cm^{-1}$; $^1H$ NMR($CDCl_3$) $\delta$= 0.16 (s, 9H), 1.41 (s, 9H), 1.62-1.82 (m, 2H), 5.93 (m, 2H); Anal. Found: C, 59.18; H, 11.10%. Calcd for $C_{10}H_{22}SSi$: C, 59.32; H, 10.96%.

**3-t-Butylthio-1-trimethylsilyl-1-propene (1b):** To a solution of 3-t-butylthio-1-trimethylsilyl-1-propyne **19** (11 g, 53 mmol) was added a solution of diisobutylaluminum hydride (11 ml, 58 mmol) in pentane (30 ml) dropwise at 0°C. The reaction mixture was stirred at 0°C for 1.5 h and at room temperature for 1.5 h. During this time, the solution turned to slurry. The reaction mixture was poured into ice-cold 6 N aqueous hydrochloric acid. The product was extracted twice with pentane, washed with 5 N aqueous sodium hydroxide and brine. The organic layers were dried and distilled to give a colorless liquid of the product (9.4 g, 46 mmol) in 88% yield: bp. 130°C (4 Torr) as a mixture of geometrical isomers (E/Z ratio= 4.2:1); (E)-isomer (**1b**) was separated by column chromatography and was used for the next reaction; $R_f$= 0.33 (hexane); IR (neat) 2950, 1600, 1450, 1360, 1245, 1160, 860, and 840 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$= 0.14 (s, 9H), 1.29 (s, 9H), 3.17 (d, J= 7Hz, 2H), 5.48 (d, 14Hz, 1H), 6.03-6.51 (m, 1H).

**Triphenylsilylated allylsulfides: 1-n-Propyl-3-triphenylsilyl-1-propene (1c); 1-Isopropyl-3-triphenylsilyl-1-propene (1d); 1-t-Butylthio-3-triphenylsilyl-1-propene (1e):** To a solution of allyl t-butyl sulfide (6.5 g, 50 mmol) in THF (100 ml) was added a solution of t-butyllithium in pentane (2.0 M, 25 ml, 50 mmol) at -78°C. The resulting solution was stirred at -78°C for 1 h. Chlorotriphenylsilane (14.7 g, 50 mmol) was added at -78°C. The reaction mixture was stirred at -78°C for 3 h, at room temperature overnight, and poured into ice-cold 2 N aqueous hydrochloric acid. The product was extracted twice with ether. The combined organic layers were dried and concentrated *in vacuo*. The residue was purified by recrystallization from hexane-ether to give **1e** (15.1 g, 39 mmol) as colorless crystals in 77% yield: mp. 74.3-75.8°C; $R_f$= 0.30 (60:1, hexane-ether); IR ($CCl_4$) 2975, 1435, and 1115 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$= 1.12 (s, 9H), 2.30-2.47 (m, 2H), 5.87 (m, 2H); Anal. Found: C, 77.37; H, 7.23%. Calcd for $C_{25}H_{28}SSi$: C, 77.26; H, 7.26%. **1-n-Propylthio-3-triphenylsilyl-1-propene (1c)** was similarly prepared in 60 % yield: $^1H$ NMR ($CCl_4$) $\delta$= 0.83-1.36 (6H), 2.20-3.10 (m, 3H), 5.63-5.87 (m, 2H), 7.00-7.60 (15H). **1-Isopropylthio-3-triphenylsilyl-1-propene (1d)** was similarly prepared in 78 % yield: $^1H$ NMR ($CCl_4$) $\delta$= 0.57-1.90 (5H), 2.17-2.83 (m, 4H), 5.57-5.96 (m, 2H), 7.07-7.87 (15H).

**Typical procedure of the synthesis of 1-alkylthio-(E,Z)-1,3-alkadienes:** To a solution of **1a** (0.30 g, 1.5 mmol) in THF (3 ml) was added a solution of t-butyllithium in pentane (1.8 M, 0.85 ml, 1.5 mmol) dropwise at -78°C, and the mixture was stirred at -78°C for 10 min, and then at 0°C for 1 h. Titanium tetraisopropoxide (0.45 ml, 1.5 mmol) was added dropwise at -78°C. The resulting mixture was stirred for 30 min. To a solution of allyltitanium reagent (**2**), thus

18 mmol) as a colorless oil in 90% yield:[15] IR (neat) 3550, 2950, 1740, 1260, and 1105 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$= 0.00 (s, 6H), 0.83 (s, 9H), 1.62-2.03 (m, 2H), 2.25-2.63 (m, 2H), 3.58 (t, J= 6H, 2H), 9.66 (s, 1H); Analitical data was not obtained by decomposition.

**7-t-Butyldimethylsilyloxy-1-t-butylthio-(E,Z)-1,3-heptadiene (13)**: To a solution of 1a (or 1b) (0.20 g, 1.0 mmol) in THF (3 ml) and HMPA (0.17 ml, 1.0 mmol) was added a solution of t-butyllithium in pentane (1.6 M, 0.63 ml, 1 mmol) dropwise at -78°C. The resulting solution was stirred at -78°C for 15 min and at 0°C for 1 h. After being cooled to -78°C, titanium tetraisopropoxide (0.33 ml, 1.1 mmol) was added, and the redish brown solution was stirred at -78°C for 40 min. 4-(t-Butyldimethylsilyloxy)butanal 12 was added dropwise at -78°C to the above solution of titanium reagent 2. The reaction mixture was stirred at -78°C for 1.5 h, at 0°C for 1 h, at room temperature for 21 h, and then poured into ice-cold 2 N aqueous hydrochloric acid. The product was extracted three times with hexane. The combined organic layers were dried and concentrated in vacuo. The residual oil was purified by column chromatography on silica gel to give 13 (0.17 g, 0.53 mmol) as a colorless oil in 53% yield: $R_f$= 0.09 (hexane); IR (neat) 2970, 2870, 1260, 1105, and 840 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$=0.08 (s, 6H), 0.83 (s, 9H), 1.28 (s, 9H), 1.37-2.43 (m, 4H), 3.55 (t, J= 6Hz, 2H), 5.33 (dt, J= 6 and 10Hz, 1H), 5.97 (t, J= 10Hz, 1H), 6.20 (d, J= 14Hz, 1H), 6.58 (dd, J= 10 and 14Hz, 1H); Anal. Found: C, 65.18; H, 10.61%. Calcd for $C_{17}H_{34}OSSi$: C, 64.90; H, 10.89%.

**1-t-butyldimethylsilyloxy-(Z,E)-4,6-octadiene (14)**: To a suspension of magnesium (0.37 g, 15 mmol) in ether (5 ml) was added iodomethane (0.63 ml, 10 mmol) at 0°C, the resulting mixture was stirred at 0°C for 30 min. To a solution of 13 (0.10 g, 0.32 mmol) and nickel(II) 1,3-bis(diphenylphosphino)propane chloride (17 mg, 0.032 mmol) in benzene (5 ml) was added an above solution of methylmagnesium iodide in ether at room temperature. The reaction mixture was heated at 80-90°C (bath temperature) for 15 min and poured into ice-cold 1 N aqueous hydrochloric acid after cooled down to room temperature. The product was extracted twice with ether. The combined organic layers were dried and concentrated in vacuo. The residual oil was purified by column chromatography on silica gel to give 14 (63 mg, 0.26 mmol) as a colorless oil in 83% yield: $R_f$= 0.38 (50:1, hexane-ether); IR (neat) 2970, 1480, 1440, 1260, 1110, 840, and 700 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$= 0.08 (s, 6H), 0.86 (s, 9H), 1.73 (d, J= 6Hz), 1.10-2.45 (m, 7H), 3.57 (t, J= 6Hz, 2H), 4.97-6.63 (m, 4H); 5.51 (d, J= 15Hz, 1H), 5.83 (dd, J= 10 and 10Hz, 1H), 6.24 (dd, J= 10 and 15Hz, 1H) on irradiation to the allylic methyl proton ($\delta$= 1.73); 5.20 (br d, J= 10Hz, 1H) on irradiation to the allylic methylene proton ($\delta$= 2.15); gc $t_R$ 8.5 min (Z,E)-isomer, 9.3 min unidentical minor isomer at 100°C; Anal. Found: C, 69.79; H, 11.88%. Calcd for $C_{14}H_{28}OSi$: C, 69.93; H, 11.74%.

**(Z,E)-4,6-Octadien-1-ol (15)**: To a solution of 14 (0.11 g, 0.47 mmol) in THF (1 ml) was added a solution of anhydrous tetrabutylammonium fluoride (TBAF : 1.0 ml) which was prepared from a solution of TBAF in THF (1 M, 15 ml) and molecular sieve 3A (2.5 g) at room temperature for 1 h. The reaction mixture was stirred at room temperature for 30 min and poured into brine. The product was extracted three times with ether. The combined organic layers were dried and concentrated in vacuo. The residual oil was purified by column chromatography on silica gel to give 15 (56 mg, 0.44 mmol) as a colorless oil in 94% yield: $R_f$= 0.16 (3:1, hexane-ether); IR ($CCl_4$) 3350, 2940, 2380, 1460, 1060, 985, and 950 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$= 0.66-2.50 (9H), 3.57 (t, J= 6Hz, 2H), 5.00-6.57 (m, 4H); Anal. Found: C, 75.85; H. 11.47%. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18%.

**(Z,E)-4,6-Octadienal (16)**: Oxidation of 15 (179 mg, 1.4 mmol) in dichloromethane (4.5 ml) with oxalyl chloride (0.28 ml, 3.2 mmol), dimethyl sulfoxide (0.49 ml, 6.9 mmol) and then triethylamine (1.0 ml, 7.1 mmol) afforded 16 (94 mg, 0.8 mmol) as an oil in 54% yield:[15] $R_f$= 0.42 (5:1, hexane-ether); IR ($CCl_4$) 3050, 2940, 1740, 1460, 995, and 960 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$= 1.80 (d, J= 6Hz, 3H), 2.40-2.63 (m, 4H), 5.13-6.60 (m, 4H).

**N-Isobutylaminocarbonylmethyltriphenylphosphonium bromide (17)**: N-Isobutyl 2-bromoacetamide[19] (1.0 g, 5.0 mmol) and triphenylphosphine (1.3 g, 5.0 mmol) in benzene was heated at reflux for 7 h. The solvent was removed in vacuo and the product was purified by recrystallization from benzene-hexane to give 17 (2.0 g, 4.3 mmol) as a colorless crystal in 86% yield: mp 191.5-192.3°C.

**N-Isobutyl-(E,Z,E)-2,6,8-decatrienoylamide (10; Spilanthol)**: To a solution of 17 (328 mg, 0.72 mmol) in THF (2 ml) was added dropwise a solution of LDA in THF which was prepared by treatment of diisopropylamine (66 mg, 0.65 mmol) in THF (2 ml) with a solution of n-butyllithium in hexane (1.6 M, 0.41 ml, 0.65 mmol) at 0°C. A solution of the aldehyde 16 (71 mg, 0.57 mmol) in THF (1 ml) was added dropwise to the above solution at 0°C. The reaction mixture was stirred at 0°C

prepared, cyclohexanecarbaldehyde (0.11 g, 1.0 mmol) was added at -78°C over a period of 5 min. The reaction mixture was stirred at -78°C for 2 h, at room temperature overnight, and poured into ice-cold 2 N aqueous hydrochloric acid. The product was extracted twice with hexane. The combined organic layers were dried and concentrated in vacuo. The residual oil was purified by column chromatography on silica gel to give **1-t-butylthio-4-cyclohexyl-(E,Z)-1,3-butadiene, 7a** (0.14 g, 0.62 mmol) as a colorless oil in 62% yield :[7] $R_f$= 0.22 (hexane); IR ($CCl_4$) 2930, 1450, 1370, 1250, 1160, and 840 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$= 0.96-2.00 (m, 19H), 2.00-2.79 (m, 1H), 5.10 (dd, J= 10Hz, 1H), 5.77 (dd, J= 10Hz, 1H), 6.13 (d, J= 14Hz, 1H), 6.57 (dd, J= 10 and 14Hz, 1H); 5.10 (br d, J= 10Hz) on irradiation to the methine proton ($\delta$= 2.34).

**Typical procedure of a nickel catalyzed cross coupling reaction of 1-alkylthio-(E,Z)-1,3-alkadiene (7) with Grignard reagent to 1,4-dialkyl-1,3-alkadiene (8)**: To a mixture of **7a** (0.28 g, 0.96 mmol), $Ni(PPh_3)_2Cl_2$ (65 mg, 0.1 mmol), and dppp (41 mg, 0.1 mmol) in benzene (10 ml) was added methylmagnesium iodide (9.6 mmol in 4 ml of ether) at room temperature. The reaction mixture was heated at reflux (80-90°C) for 25 min and poured into ice-cold 2 N aqueous hydrochloric acid after cooled down to room temperature. The product was extracted twice with pentane. The combined organic layers were dried and concentrated. The residual oil was purified by chromatography to give **1-cyclohexyl-(Z,E)-1,3-pentadiene (8a)** (0.10 g, 0.67 mmol) as a colorless oil in 71% yield: IR (neat) 2930, 1455, 985, 950, and 830 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$= 1.77 (d, J= 6Hz, methyl protons), 1.93-2.93 (m, methine proton), 0.63-2.93 (m, 14H), 5.11 (dd, J= 10 and 10Hz, 1H), 5.29-6.06 (m, 2H), 6.32 (dd, J= 10 and 16Hz, 1H); 5.11 (br d, J= 10Hz) on irradiation to the methine proton ($\delta$= 2.43), 5.59 (d, J= 16Hz, 1H), 5.79 (dd, J= 10 and 10Hz, 1H) on irradiation to the methyl proton ($\delta$= 1.77); gc $t_R$ 8.3 min (Z,E)($t_R$ of other isomers: Z,Z: 8.7; E,E: 9.2; E,Z: 9.5 min) at 80°C; Anal. Found: C, 87.84; H, 12.16%. Calcd for $C_{11}H_{18}$: C, 87.93; H, 12.07%.

**1-Cyclohexyl-(Z,E)-1.3-heptadiene (8a')** was synthesized in 93% yield (0.17 g, 0.9 mmol) by the same procedure as described above from **7a** (0.22 g, 1 mmol), propylmagnesium iodide (ca. 10 mmol in 10 ml of ether), and catalytic amount of $Ni(dppp)Cl_2$ (54 mg, 0.1 mmol) in benzene (10 ml): $R_f$= 0.61 (hexane); IR (neat) 2940, 1450, 985, and 950 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$= 0.70-2.78 (18H), 5.13 (dd, J= 10 and 10Hz, 1H), 5.34-5.95 (m, 2H), 6.32 (dd, J= 10 and 15Hz, 1H); 5.49 (d, J= 15Hz, 1H), 5.71 (dd, J= 10 and 10Hz, 1H) on irradiation to the allylic methylene proton ($\delta$= 2.10), 5.13 (d, J= 10Hz) on irradiation to the methine proton ($\delta$= 2.45); gc $t_R$ 12.5 min of the major isomer at 90°C; Anal. Found: C, 87.51; H, 12.49%. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44%.

**1-t-Butylthio-(E,Z)-1,3-decadiene (7b)** was prepared from **2** and heptanal (75 mg, 0.66 mmol) in 55% yield (83 mg, 0.36 mmol) by the method as described above: $R_f$= 0.31 (hexane); $^1H$ NMR ($CDCl_3$) $\delta$= 0.60-1.83 (20H involves singlet at $\delta$= 1.30 of t-butyl group), 1.83-2.40 (br m, 2H, allylic methylene), 5.00-5.53 (m, 1H), 5.91 (dd, J= 10 and 10Hz, 1H), 6.18 (d, 14Hz, 1H), 6.60 (dd, J= 10 and 14Hz, 1H); 5.28 (d, J= 10Hz, 1H) on irradiation to the allylic methylene proton ($\delta$= 2.12).

**(E,Z)-2,4-Undecadiene (8b)** was prepared from **7b** (81 mg, 0.36 mmol) in 77% yield (42 mg, 0.28 mmol) with methylmagnesium iodide (ca. 4 mmol in 2.8 ml of ether) in the presence of nickel catalyst (22 mg, 0.04 mmol) in benzene (5 ml) by the method as described above: $R_f$= 0.62 (hexane); $^1H$ NMR ($CDCl_3$) $\delta$= 0.56-1.60 (11H), 1.71 (d, 6Hz, 3H, allylic methyl), 1.83-2.40 (m, 2H, allylic methylene), 4.93-6.02 (m, 5H, olefinic protons), 6.31 (ddm, J= 1, 10 and 14Hz, 1H); 5.57 (d, J= 14Hz, 1H), 5.86 (dd, J= 10 and 10Hz, 1H) on irradiation to the allylic methyl proton ($\delta$= 1.71); 5.22 (d, J= 10Hz, 1H), 5.86 (dd, J= 10 and 10Hz), 6.31 (dd, J= 10 and 14Hz, 1H) on irradiation to the allylic methylene proton ($\delta$= 2.11); gc $t_R$ 9.5 min of the major isomer at 70°C.

**4-(t-Butyldimethylsilyloxy)-1-butanol (11)**: To a solution of 1,4-butanediol (18.0 g, 200 mmol), triethylamine (6.6 g, 65 mmol), and 4-N,N-dimethylaminopyridine (0.6 g, 5 mmol) in dichloromethane (180 ml) was added a solution of t-butylchlorodimethylsilane (7.5 g, 50 mmol) in dichloromethane (100 ml) over a period of 4 h at room temperature. The reaction mixture was stirred for an additional hour and poured into brine. The product was extracted three times with dichloromethane, washed with brine. The combined organic layers were dried and concentrated. The residual oil was purified by column chromatography on silica gel to give **11** (9.0 g, 44 mmol) as a colorless oil in 88% yield: $R_f$= 0.38 (3:1, hexane-AcOEt).

**4-(t-Butyldimethylsilyloxy)butanal (12)**: Oxidation of **11** (4.1 g, 20 mmol) with oxalyl chloride (1.9 ml, 22 mmol), dimethyl sulfoxide (3.1 ml, 44 mmol) and triethylamine (13.9 ml, 100 mmol) in dichloromethane (50 ml) afforded **12** (3.6 g,

for 10 min and poured into ice-cold 2 N aqueous hydrochloric acid. The product was extracted three times with ether, dried and concentrated in vacuo. The residual oil was purified by column chromatography on silica gel to give the desired product **10** (77 mg, 0.35 mmol) in 61% yield with 88% purity by gc analysis: $R_f$= 0.20 (1:1, hexane-ether); spectral data were identical with reported values:[10,19] IR (neat) 3280, 2950, 1670, 1630, 1550, 1450, 1370, 1350, 1240, 1165, 985, 950, and 825 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$= 0.91 (d, 6Hz, 6H, $-CH(CH_3)_2$), 1.10-1.30 (br, 2H), 1.75 (d, 6Hz, 3H, $CH_3C=C$), 2.24 (m, 3Hz, 4H, $=CCH_2CH_2C=$), 3.06 (t, 6Hz, 2H, $=NCH_2-$), 4.93-6.97 (m, 6H, olefinic protons); gc $t_R$ 13.4 min of the major peak at 180°C. N-Isobutyl-3,6,8-decatrienoylamide (**18**) was also produced (23 mg, 0.10 mmol) in 18% yield: $R_f$= 0.28 (1:1, hexane-ether); $^1H$ NMR $\delta$= 0.90 (d, 7Hz, 6H, $-CH(CH_3)_2$), 1.24 (br, 2H), 1.76 (d, 8Hz, 3H), 1.93-2.48 (dd, 6 and 7Hz, 2H), 2.65 (t, 6Hz, 2H), 3.02 (t, 6Hz, 2H, $=NCH_2-$), 4.83-6.56 (m, 6H, olefinic protons).

**t-Butyl Propargyl Sulfide (18)**: To a solution of sodium methoxide (28%, 50 ml, 0.26 mol) in methanol (50 ml) was added 2-methyl-2-propanethiol (27 g, 0.25 mol) at 0°C. To the above solution was added propargyl bromide (23 ml, 0.26 mol) at 0°C. The reaction mixture was heated at reflux for 1 h, and then poured into 5 N aqueous sodium hydroxide. The product was extracted twice with pentane. The combined organic layers were washed with 2 N aqueous hydrochloric acid and brine, dried and concentrated. The residual oil was distilled to give **18** (24 g, 0.19 mol) as a colorless liquid in 72% yield: bp. 150-154°C; $^1H$ NMR ($CCl_4$) $\delta$= 1.34 (s, 9H), 2.01 (t, J= 3Hz, 1H), 3.15 (d, J= 3Hz, 2H).

**3-t-Butylthio-1-trimethylsilyl-1-propyne (19)**: To a solution of **18** (19 g, 0.15 mol) in ether (200 ml) was added a solution of n-butyllithium in hexane (1.7 M, 90 ml, 0.15 mol) at 0°C. The resulting solution was stirred at 0°C for 30 min. Chlorotrimethylsilane (21 ml, 0.17 mol) was added dropwise to the above solution at 0°C. The reaction mixture was stirred at 0°C for 30 min, at room temparature for 1 h, and poured into ice-cold 5 N aqueous sodium hydroxide. The product was extracted three times with ether, washed with brine. The combined organic layers were dried over magnesium sulfate and filtered off. The product was purified by distillation to give **19** (19 g, 0.10 mol) as a colorless liquid in 64% yield: bp. 110-120°C (28 Torr); $R_f$= 0.18 (hexane); $^1H$ NMR ($CCl_4$) $\delta$= 0.13 (s, 9H), 1.34 (s, 9H), 3.00 (s, 2H).

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