Thioether-Directed Platinum-Catalyzed Hydrosilylation of Olefins

Joe B. Perales and David L. Van Vranken*

Department of Chemistry, University of California, Irvine, California 92697

dlvanvra@uci.edu

Received February 27, 2001

Homoallylic thioethers facilitate the platinum-catalyzed hydrosilylation of olefins with phenyldimethylsilane. As a control, thioether substrates are shown to hydrosilylate at room temperature under conditions where no hydrosilylation is observed for isosteric substrates that lacked thioether groups. Modest diastereoselection is observed, between 2 and 5 to 1. Hydrogenation is a competing reaction that becomes prominent for internal olefins. The internal diene **6a** undergoes regioselective 1,2-hydrogenation of the double bond proximal to the homoallyl thioether moiety.

I. Introduction

Thioethers are powerful ligands for transition metals, and a variety of sulfur-containing ligands have been used in transition metal-catalyzed reactions.[1] Many transition metal-mediated processes tolerate the presence of divalent sulfur in the substrate,[2a,b] but more often, the presence of thioethers augurs poorly for reactivity.[3a−c] The affinity of thioether groups for transition metals has been used to direct the outcome of stoichiometric reactions mediated by transition metals. For example, early work by Holton and co-workers on carbopalladation revealed that allylic and homoallylic thioethers could effect complete control over the regiochemistry of the reaction.[4a−c] More recently Krafft and co-workers have shown that the Pauson−Khand reaction gives excellent regiocontrol with thioether substrates.[5a,b] The most dramatic advance in this area has been the demonstration that sulfur can exert its influence in palladium-catalyzed allylic alkylations, reversing the normal preference for attack at the less-substituted terminus of the allyl group.[6] This important work shows that palladium not only binds to the thioether, but it also lets go.

Hydrosilylation is an important reaction for introduction of silicon into organic substrates.[7a−d] One of the disadvantages of hydrosilylation is that rates of hydrosilylation are dramatically influenced by steric hindrance in the substrate and electronic effects within the silane. Thus, terminal olefins hydrosilylate readily with $PhMe_2SiH$ using platinum catalysts.[8a,b] However, disubstituted olefins are sluggish and generally require silanes with electron-withdrawing groups such as Cl_3SiH.[9] A disadvantage of these reactive silanes is that the hydrosilylation products are sensitive to water.

II. Results and Discussion

Platinum is the most active metal for hydrosilylations although important mechanistic details await resolution.[10a−c] Thia-calixarene ligands have been used for platinum-catalyzed hydrosilylation of terminal olefins.[11] However, if the substrate possesses a thioether moiety, then the rates of thioether ligand exchange must be relatively fast in order to achieve catalytic turnover. Voronkov has hydrosilylated vinyl sulfides, allyl sulfides, and hex-5-enyl sulfides with chloroplatinic acid under standard conditions: 150 °C, 24 h, neat.[7d] Murai has shown that eneamides are readily hydrosilylated by $Rh_2(OAc)_4$, but vinyl sulfides were poor substrates for this catalyst.[7c]

To test the potential for directing effects, we compared the platinum-catalyzed hydrosilylation of two thioether substrates: an allylic thioether and a homoallylic thioether (Scheme 1). The reactions were carried out at room temperature using 5 mol % of the readily available hexahydrate of chloroplatinic acid. An excess of phenyldimethylsilane was used to offset the loss of silane due

---

* To whom correspondence should be addressed. Fax 949-824-8571.

[1] (a) Allen, J. V.; Coote, S. J.; Dawson, G. J.; Frost, C. G.; Martin, C. J.; Williams, J. M. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2065−72. (b) Evans, D. A.; Campos, K. R.; Tedrow, J. S.; Michael, F. E.; Gagne, M. R. *J. Org. Chem.* **1999**, *64*, 2994−2995. (c) Orejon, A.; Masdeu-Bulto, A. M.; Echarri, R.; Dieguez, M.; Fornies-Camer, J.; Claver, C.; Cardin, C. J. *J. Organomet. Chem.* **1998**, *559*, 23−29.

[2] (a) Birch, A. J.; Walker, K. A. M. *Tetrahedron Lett.* **1967**, 1935−6. (b) Ishibashi, H.; Ohnishi, M.; Senda, T.; Ikeda, M. *Synth. Commun.* **1989**, *19*, 857−64.

[3] (a) Shon, Y.-S.; Lee, T. R. *Tetrahedron Lett.* **1997**, *38*, 1283−1286. (b) Wender, P. A.; Howbert, J. J. *Tetrahedron Lett.* **1982**, *23*, 3983−6. (c) Faller, J. W.; Parr, J. *J. Am. Chem. Soc.* **1993**, *115*, 804−5.

[4] (a) Holton, R. A.; Kjonaas, R. A. *J. Am. Chem. Soc.* **1977**, *99*, 4177−9. (b) Holton, R. A.; Kjonaas, R. A. *J. Organomet. Chem.* **1977**, *142*, C15−C18. (c) Holton, R. A.; Zoeller, J. R. *J. Am. Chem. Soc.* **1985**, *107*, 2124−31. (d) Zhang, Y.; Shi, X.; Dai, L. *Huaxue Xuebao* **1992**, *50*, 726−8. (e) Albeniz, A. C.; Espinet, P.; Lin, Y.-S. *Organometallics* **1996**, *15*, 5010−5017.

[5] (a) Krafft, M. E.; Juliano, C. A.; Scott, I. L.; Wright, C.; McEachin, M. D. *J. Am. Chem. Soc.* **1991**, *113*, 1693−703. (b) Krafft, M. E.; Scott, I. L.; Romero, R. H.; Feibelmann, S.; Van Pelt, C. E. *J. Am. Chem. Soc.* **1993**, *115*, 7199−207.

[6] (a) Krafft, M. E.; Wilson, A. M.; Fu, Z.; Procter, M. J.; Dasse, O. A. *J. Org. Chem.* **1998**, *63*, 1748−1749.

[7] (a) Ojima, I.; Nihonyanagi, M.; Nagai, Y. *J. Chem. Soc., Chem. Commun.* **1972**, 938. (b) Tamao, K.; Nakagawa, Y.; Arai, H.; Higuchi, N.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 3712−14. (c) Murai, T.; Kimura, F.; Tsutsui, K.; Hasegawa, K.; Kato, S. *Organometallics* **1998**, *17*, 926−932. (d) Voronkov, M. G.; Vlasova, N. N.; Volshakova, S. A.; Kirpichenko, S. V. *J. Organomet. Chem.* **1980**, *190*, 335−41.

[8] (a) Rumin, R. *J. Organomet. Chem.* **1983**, *247*, 351−6. (b) Caseri, W.; Pregosin, P. S. *Organometallics* **1988**, *7*, 1373−80.

[9] Fink, W. *Helv. Chim. Acta* **1971**, *54*, 1304−10.

[10] (a) Speier, J. L. *Adv. Organomet. Chem.* **1979**, *17*, 407−47. (b) Sakaki, S.; Mizoe, N.; Sugimoto, M. *Organometallics* **1998**, *17*, 2510−2523. (c) Sakaki, S.; Mizoe, N.; Sugimoto, M.; Musashi, Y. *Coord. Chem. Rev.* **1999**, *190−192*, 933−960. (d) Hemmer, R.; Unsin, J. *Methoden der Organischen Chemie*; Thieme: Stuttgart, 1986; Vol. E18. (e) Hiyama, T.; Kusumoto, T. In *Comprehensive Organic Synthesis: Selectivity, Strategy & Efficiency in Modern Organic Chemistry*, 1st ed.; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3, Chapter 12.

10.1021/jo010214e CCC: $20.00

to siloxane formation and to favor hydrosilylation over hydrogenation, an important side reaction. The hydrosilylation worked, but the distance between the sulfur atom and the double bond was important. The allylic sulfide **1a** reacted sluggishly, giving about 10% of the hydrosilylated product **1b** (not isolated) after 10 days. In contrast, the homoallylic sulfide was completely consumed in 1.5 h, giving hydrosilylated product **2b** in 68% yield along with 26% of the hydrogenated product **2c**. Presumably, the hydrogenated material arose from the reaction of water (from the catalyst) with the silane, but addition of 5 equiv water or 4 Å molecular sieves did not dramatically change the ratio of hydrosilylated product **2b** to hydrogenated product **2c** (Table 1). However, by reducing the concentration of the hexahydrate catalyst from 5 mol % to 0.7 mol % the yield of hydrosilylated product increased to 94%. As expected, with less catalyst, the reaction took longer to reach completion.

Scheme 1

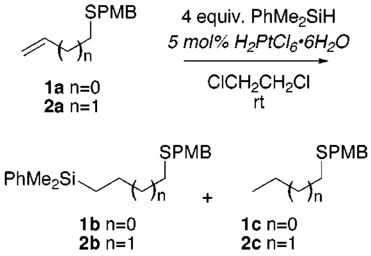


Table 1. The Effect of Catalyst on the Ratio of Hydrosilylation to Hydrogenation of 2a

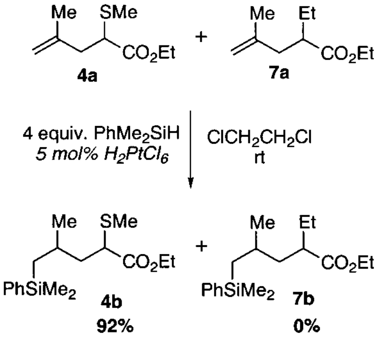
mol % calalyst	additive	**2b**	**2c**
5 mol %	5 equiv of H_2O	66%	33%
5 mol %	none	68%	26%
5 mol %	4 Å MS	56%	33%
0.7 mol %	none	94%	–

The importance of the thioether moiety was demonstrated in a competition experiment. When homoallyl sulfide **2a** was mixed with octene and subjected to hydrosilylation at room temperature, only the thioether substrate underwent hydrosilylation. Likewise, hydrosilylation of octene fails under these conditions, demonstrating that the homoallylic thioether was accelerating an otherwise sluggish reaction. Armed with confidence in the guiding effect of the thioether moiety, we next evaluated a variety of substrates for their ability to participate in hydrosilylation reactions (Table 2). The substrates **3a**–**6a** were prepared by alkylation of the lithium enolate of ethyl (methylthio)acetate with the corresponding allyl bromide.

The yields range from modest to excellent, depending on the pattern of substitution. Hydrogenation becomes increasingly problematic as the level of subsitution on the olefin increases. Unfortunately, with sluggish substrates it was impractical to reduce the catalyst loading as a strategy for reducing the amount of competitive hydrogenation. Karstedt's catalyst ([(H_2C=CHSiMe_2)$_2$O]-Pt), which is sometimes superior to chloroplatinic acid in hydrosilylation reactions, gave poorer results in the hydrosilylation of **5a**.

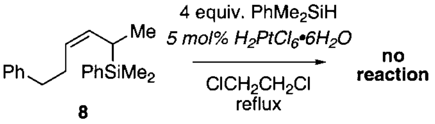
As before, the importance of these results were best revealed in a competition experiment. When substrate **4a** and the α-ethyl analogue **7a**[12] were mixed in an equimolar ratio, only the sulfide substrate underwent hydrosilylation; 97% of alkene **7a** was recovered, whereas the thioether substrate **4a** gave hydrosilylated product **4b** in 92% yield (Scheme 2). In a similar competition experiment between substrate **5a** and its α-ethyl analogue, the thioether substrate again prevailed. The diastereoselection in these reactions was modest, only 5:1 for the geminally substituted olefin **4a** and even lower (2.6:1) for the vicinally substituted olefin **5a**. Unfortunately, the diastereoselection in the absence of sulfur could not be determined since the α-ethyl substrate **7a** did not hydrosilylate. The stereochemistry of the major and minor diastereomers has not yet been assigned.

Scheme 2



Hydrogenation was a major competing reaction with conjugated substrates **5a** and **6a**. The hydrosilylation of styrene **5a** proceeded with complete control of regiochemistry, but the hydrogenation predominates over hydrosilylation by a 2.6:1 ratio. Hydrogenation was even more problematic with the diene **6a** which underwent hydrogenation of both double bonds; no hydrosilylated product was isolated under these conditions. Hydrogenated product **6b** might form by protodesilylation of the desired allylsilane followed by hydrogenation. However, a control experiment showed that a related allylsilane **8**[13] is completely stable to the reaction conditions (Scheme 3).

Scheme 3



Alkoxysilanes and chlorosilanes are more reactive reagents for hydrosilylation,[14a,b,c] but the products are more difficult to purify because of the lability of the Si–X bonds. Attempted hydrosilylation of diene **6a** with triethoxysilane gave extensive hydrogenation; however, substantial amounts of mono-hydrogenated product were observed. Switching from chloroplatinic acid to platinum chloride led to exclusive mono-hydrogenation of the double bond proximal to the thioether group, giving alkene **6c** in 85% yield (Scheme 4). These are exceptionally mild conditions considering that hydrogenation of

---

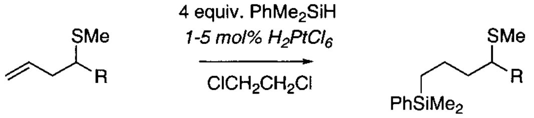
(11) Bayon, J. C.; Claver, C.; Masdeu-Bulto, A. M. *Coord. Chem. Rev.* **1999**, *193–195*, 73–145.

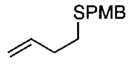
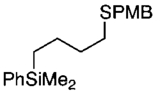
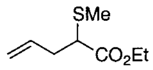
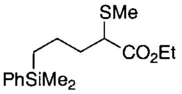
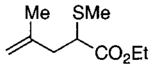
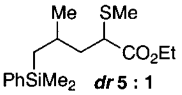
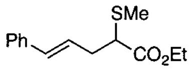
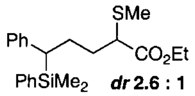
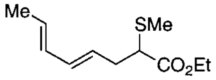
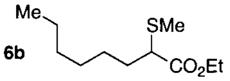
(12) Kirmse, W.; Feyen, P.; Gruber, W.; Kapmeyer, W. *Chem. Ber.* **1975**, *108*, 1839–54.

(13) Tsukamoto, M.; Iio, H.; Tokoroyama, T. *Tetrahedron Lett.* **1987**, *28*, 4561–4.

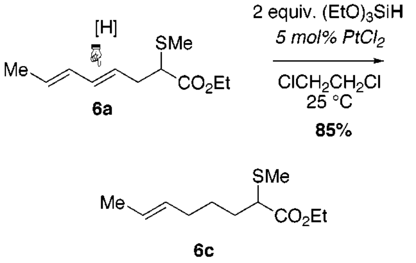
(14) (a) Benkeser, R. A.; Muench, W. C. *J. Organomet. Chem.* **1980**, *184*, C3–C9. (b) Kopylov, V. M.; Kovyazina, T. G.; Buslaeva, T. M.; Sinitsyn, N. M.; Kireev, V. V.; Gorshkov, A. V. *Zh. Obshch. Khim.* **1987**, *57*, 1117–27. (c) Capka, M.; Svoboda, P.; Bazant, V.; Chvalovsky, V. *Collect. Czech. Chem. Commun.* **1971**, *36*, 2785–94.

Table 2.



Starting Material		Mol% cat.	Conditions	Product		Yield
2a		5% 1%	23 °C, 8 h 23 °C, 1.5 h	**2b**		**68%** **94%**
3a		5% 1%	23 °C, 16 h 23 °C, 13 h	**3b**		**92%** **94%**
4a		5%	23 °C, 13 h	**4b**	 *dr* **5 : 1**	**95%**
5a		5% 1%	23 °C, 23 h 83 °C, 36 h	**5b**	 *dr* **2.6 : 1**	**23%** **25%**
6a		5%	23 °C, 21 h	**6b**		**90%**

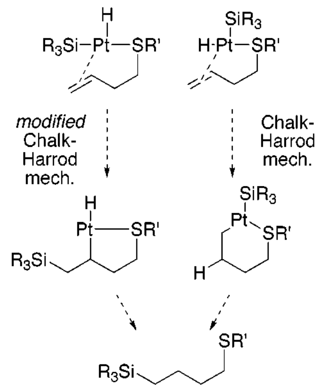
Scheme 4



double bonds with soluble platinum catalysts is typically carried out at elevated temperature under 30−50 atm H_2.[15a−c] However Bertani and co-workers have shown that the highly coordinatively unsaturated complex [(t-Bu)$_3$P]-Pt•propene selectively hydrogenates butadiene and 2,3-dimethylbutadiene at low temperature under 1 atm H_2 with 1,2-selectivity.[16]

The formation of colloidal platinum is an essential step in the hydrosilylation of olefins with COD_2Pt and $CODPtCl_2$ in dichloromethane,[17] but in the presence of strong ligands, such as thiocalixarenes, platinum colloids have been discounted as intermediates.[18a,b] The mechanism of these directed reactions is uncertain, but the preferential reactivity of homoallylic thioethers conjures up five-membered ring platinum chelates as potential intermediates. The widely accepted Chalk−Harrod mechanism for platinum-catalyzed hydrosilylation involves an initial insertion of the olefin into the Pt−H bond followed by reductive elimination, forming the new C−Si bond.[19] If homoallylic sulfides direct platinum-catalyzed hydrosilylation via the Chalk−Harrod mechanism, then olefin insertion would generate a six-membered ring platinacycle. Platinum is known to form analogous six-membered ring complexes with methionine and its derivatives.[20] The alternative *modified* Chalk−Harrod mechanism, implicated in some rhodium-catalyzed hydrosilylations, would involve initial insertion of the olefin into the C−Si bond followed by reductive elimination to form a new C−H bond (Scheme 5). The modified Chalk−Harrod mechanism would involve a rather satisfying five-membered ring platinacycle. Unfortunately, MP2 calculations predict the insertion of olefins into Pt−Si bonds to be energetically prohibitive, and there is currently no evidence for the modified Chalk−Harrod mechanism in platinum-catalyzed hydrosilylation reactions.[19]

Scheme 5



---

[15] (a) Adams, R. W.; Batley, G. E.; Bailar, J. C., Jr. *Inorg. Nucl. Chem. Lett.* **1968**, *4*, 455−8. (b) Kopylov, V. M.; Kovyazina, T. G.; Buslaeva, T. M.; Sinitsyn, N. M.; Kireev, V. V.; Gorshkov, A. V. *Zh. Obshch. Khim.* **1987**, *57*, 1117−27. (c) Paganelli, S.; Matteoli, U.; Scrivanti, A.; Botteghi, C. *J. Organomet. Chem.* **1990**, *397*, 375−81.

[16] Bertani, R.; Carturan, G.; Scrivanti, A. *Angew. Chem.* **1983**, *95*, 241−2.

[17] Lewis, L. N.; Lewis, N. *J. Am. Chem. Soc.* **1986**, *108*, 7228−31.

[18] (a) Chen, Y. Y.; Zhou, Y. S.; Tong, X. H.; Liu, Q.; Zhong, Z. L. *Chem. Res. Chin. Univ.* **1998**, *14*, 101−103. (b) Chen, Y. Y.; Zhong, Z. L.; Zhou, Y. S.; Zhang, B. L.; Lu, X. R. *Chin. Chem. Lett.* **1997**, *8*, 213-214.

[19] Sakaki, S.; Mizoe, N.; Sugimoto, M.; Musashi, Y. *Coord. Chem. Rev.* **1999**, *190−192*, 933−60.

[20] Freeman, H. C.; Golumb, M. L. *J. Chem. Soc. D* **1970**, *22*, 1523.

III. Conclusions

These results clearly strengthen the notion that thioethers can direct platinum-catalyzed reactions in a useful manner. These reactions work because the rates of thioether ligand exchange are fast enough to allow catalytic turnover. Homoallylic thioethers are shown to direct the platinum-catalyzed hydrosilylation of terminal olefins, with excellent regiocontrol and modest diastereocontrol. Internal olefins give primarily hydrogenation. In the case of conjugated dienes, homoallylic thioethers lead to selective 1,2-hydrogenation of the double bond proximal to the sulfur atom.

IV. Experimental Section

1-Allylsulfanylmethyl-4-methoxybenzene 1a. To a solution of KOH (5.4 mmol) in aqueous methanol (41.4 mL 6.7:1 MeOH:H_2O) was added (4-methoxyphenyl)methanethiol (0.50 mL, 3.6 mmol). After 5 min, allyl bromide (0.31 mL, 3.6 mmol) was added. The reaction was quenched after 1 h with saturated aqueous NaCl (100 mL). The aqueous layer was extracted with ether (3 × 25 mL), dried over $MgSO_4$, and concentrated in vacuo to give a pale yellow oil. The oil was purified by silica gel flash chromatography (1:24 EtOAc/hexanes) to yield thioether **1a** (648 mg, 93%) as a colorless oil: R_f = 0.28 (1:24 EtOAc/hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, J = 6.6 Hz, 2H), 6.87 (d, J = 6.6 Hz, 2H), 5.83 (ddt, J = 17.0, 10.0, 7.1 Hz, 1H), 5.14 (ddd, J = 10.0, 1.6, 0.8 Hz, 1H), 5.12 (ddd, J = 17.0, 2.9, 1.6 Hz, 1H), 3.82 (s, 3H), 3.66 (s, 2H), 3.06 (ddd, J = 7.1, 2.9, 0.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.6, 134.3, 130.2, 130.0, 117.1, 113.9, 55.2, 34.3, 34.0; IR (thin film) 2833, 1600, 1510, 1245, 1033, 824 cm^{-1}; GCMS (EI) *m/z* 194, 152; HRMS (EI) *m/z* calcd for $C_{11}H_{14}OS$ 194.0765, found 194.0761. Anal. Calcd for $C_{11}H_{14}OS$: C, 68.00; H, 7.26. Found C, 68.05; H, 7.28.

1-But-3-enylsulfanylmethyl-4-methoxybenzene 2a. To a solution of KOH (5.4 mmol) in aqueous methanol (41.4 mL 6.7:1 MeOH:H_2O) was added (4-methoxyphenyl)methanethiol (0.50 mL, 3.6 mmol). After 5 min, allyl bromide (0.36 mL, 3.6 mmol) was added. The reaction was quenched after 1 h with saturated aqueous NaCl (100 mL). The aqueous layer was extracted with ether (3 × 25 mL), dried over $MgSO_4$, and concentrated in vacuo to give a pale yellow oil. The oil was purified by silica gel flash chromatography (1:24 EtOAc/hexanes) to yield thioether **2a** (530 mg, 71%) as a colorless oil: R_f = 0.25 (1:24 EtOAc/hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 5.80 (ddt, J = 17.1, 10.2, 6.6 Hz, 1H), 5.05 (ddd, J = 17.1, 3.2, 1.6 Hz, 1H), 5.01 (dd, J = 10.2, 1.6 Hz, 1H), 3.80 (s, 3H), 3.65 (s, 2H), 2.48 (t, J = 7.7, 2H), 2.30 (ddt, J = 7.7, 6.6, 3.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.6, 136.8, 130.4, 129.8, 115.8, 113.9, 55.2, 35.7, 33.5, 30.6; IR (thin film) 2833, 1612, 1510, 1245, 1033, 914, 824 cm^{-1}; GCMS (EI) 208, 121; HRMS (EI) *m/z* calcd for $C_{12}H_{16}OS$ 208.0922, found 208.0921. Anal. Calcd for $C_{12}H_{16}OS$: C, 69.19; H, 7.74. Found C, 69.26; H, 7.88.

[4-(4-Methoxybenzylsulfanyl)butyl]dimethylphenylsilane 2b. To a solution of **2a** (220 mg, 1.06 mmol) and chloroplatinic acid (3 mg 7 $\times 10^{-3}$ mmol) in 1,2-dichloroethane (11 mL) was added phenyldimethylsilane (0.65 mL, 4.2 mmol). After 12 h, the solution was filtered through a plug of silica gel (1:9 EtOAc/hexanes), concentrated in vacuo, and purified by silica gel flash chromatography (1:24 EtOAc/hexanes) to yield alkyl silane **2b** (343 mg, 94%): R_f = 0.13 (1:49 EtOAc/hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.51−7.49 (m, 2H), 7.41−7.36 (m, 3H), 7.20 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 3.80 (s, 3H), 3.57 (s, 2H), 2.38 (t, J = 7.4 Hz, 2H), 1.57 (tt, J = 7.4, 7.4 Hz, 2H), 1.38 (tt, J = 7.4, 3.2 Hz, 2H), 0.71 (t, J = 3.2 Hz, 2H), 0.25 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 139.4, 133.5, 130.6, 129.8, 128.8, 127.7, 113.8, 55.3, 35.7, 33.0, 30.9, 23.2, 15.4; IR (thin film) 1605, 1510, 1243, 1171, 1105, 829, 729, 700 cm^{-1}; GCMS (EI) *m/z* 344, 266, 135, 121; HRMS (EI) *m/z* calcd for $C_{20}H_{28}OSSi$ 344.1630, found 344.1627.

Ethyl 5-Dimethylphenylsilyl-2-thiomethylpentenoate 3b. To a solution of chloroplatinic acid (1 mg, 2 × 10^{-3} mmol) in 1,2-dichloroethane (2.3 mL) was added ethyl-2-thiomethyl-4-pentenoate **3a** (42 mg, 0.24 mmol). The reaction was monitored by GCMS. After 13 h the mixture was filtered through a plug of silica gel (1:9 EtOAc/hexanes) and concentrated in vacuo to give a yellow oil. The oil was purified by reverse phase preparative HPLC (3:1 acetonitrile/water) to yield alkyl silane **3b** (0.0729 g, 92%) as a colorless oil: R_f = 0.20 (1:19 EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.50−7.48 (m, 2H), 7.36−7.33 (m, 3H), 4.18 (q, J = 7.1 Hz, 2H), 3.17 (dd, J = 9.2, 6.4 Hz, 1H), 2.11 (s, 3H), 1.92−1.86 (m, 1H), 1.71−1.66 (m, 1H), 1.48−1.37 (m, 2H), 1.25 (t, J = 7.1 Hz, 3H), 0.76 (dd, J = 8.9, 8.0, 2H), 0.27 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.7, 133.5, 133.0, 128.8, 127.7, 60.9, 45.2, 41.3, 27.6, 24.4, 14.4, 13.6, −2.2; IR (thin film) 1730, 1420, 1249, 1155, 832, 722 cm^{-1}; GCMS (CI NH_4^+) *m/z* 328, 280, 152; HRMS (EI) *m/z* calcd for $C_{16}H_{22}O_2SSi$ 310.1423, found 310.1424.

Ethyl 4-Methyl-2-thiomethyl-4-pentenoate 4a. To a cooled solution (−78 °C) of diisopropylamine (2.7 mL, 19 mmol) in THF (90 mL) was added a solution of *n*-BuLi (7.8 mL, 2.4 M, 19 mmol) in hexane. The solution was warmed to 0 °C over 25 min and then cooled to −78 °C. A solution of ethylthiomethyl acetate (2.3 mL, 18 mmol) in THF (10 mL) was added by cannula to the LDA solution. After 40 min, the enolate solution was added to a solution of methallyl bromide (2.00 mL, 19.8 mmol) in DMSO. The solution was quenched after 1.3 h with saturated aqueous NH_4Cl (50 mL) and diluted with ether (100 mL). The ether layer was washed with saturated aqueous $NaHCO_3$ (20 mL), and the combined aqueous layers were extracted with ether (3 × 50 mL). The ether layer was washed with saturated aqueous NaCl (50 mL), dried over $MgSO_4$, and concentrated in vacuo to give a yellow oil. The oil was chromatographed on silica gel (1:19 EtOAc/hexanes) to yield homoallyl sulfide **4a** (2.29 g, 68%) as colorless oil: R_f = 0.20 (1:19 EtOAc/hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 4.82 (s, 1H), 4.76 (s, 1H), 4.20 (q, J = 7.2 Hz, 2H), 3.40 (dd, J = 9.5, 6.2 Hz, 1H), 2.63 (dd, J = 14.7, 9.5 Hz, 1H), 2.37 (dd, J = 14.7, 6.2 Hz, 1H), 2.17 (s, 3H), 1.76 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 141.6, 112.6, 60.9, 45.3, 38.7, 22.2, 14.1, 13.7; IR (thin film) 1727, 1649, 1220, 894 cm^{-1}; MS (CI isobutane) *m/z* 188, 141, 133; HRMS (CI isobutane) *m/z* calcd for $C_9H_{16}O_2S$ 188.0871, found 188.0878.

Ethyl 5-Dimethylphenylsilyl-4-methyl-2-thiomethylpentanoate 4b. To a solution of chloroplatinic acid (0.020 g, 0.048 mmol) and dimethylphenylsilane (0.59 mL, 3.8 mmol) in 1,2-dichloroethane (10 mL) was added ethyl 4-methyl-2-thiomethyl-4-pentenoate **4a** (0.18 g, 0.96 mmol). The reaction was monitored by GCMS. After 3 h, the reaction contents were filtered through a plug of silica gel (1:9 EtOAc/hexane), concentrated in vacuo, and purified by reverse phase preparative HPLC (1:9 acetonitrile/water) to yield alkyl silane **4b** (0.295 g, 95%, 5:1 mixture of diastereomers) as a colorless oil. The diastereomeric ratio was determined from the relative ratio of the thiomethyl groups in the ^1H NMR. The NMR solvent that gave the best resolution of these diastereotopic methyl groups was 17% C_6D_6 in $CDCl_3$: R_f = 0.21 (1:19 EtOAc/hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.52−7.49 (m, 2H), 7.35−7.33 (m, 3H), 4.15 (q, J = 7.2 Hz, 2H), 3.21 (dd, J = 9.5, 6.1 Hz, 1H), 2.08 (s, 3H), 1.89 (ddd, J = 13.7, 9.5, 5.7 Hz, 1H), 1.70 (qdddd, J = 8.5, 8.1, 6.6, 5.7, 5.3 Hz, 1H), 1.46 (ddd, J = 13.7, 8.1, 6.1 Hz, 1H), 1.26 (t, J = 7.2 Hz, 3H), 0.89 (d, J = 6.6 Hz, 3H), 0.86 (dd, J = 14.7, 5.3 Hz, 1H), 0.68 (dd, J = 14.7, 8.5 Hz, 1H), 0.31 (s, 3H), 0.30 (s, 3H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 172.4, 139.7, 133.5, 128.8, 127.7, 60.9, 45.3, 41.2, 29.7, 27.6, 24.4, 23.9, 22.6, 14.2, 13.6, −2.1, −2.2; IR (thin film) 1727, 1424, 1318, 1155, 1110, 824 cm^{-1}; GCMS (CI NH_4+) *m/z* 342, 296, 247; HRMS (EI) *m/z* calcd for $C_{16}H_{25}O_2SSi$ (M-Me) 309.1345, found 309.1344.

Ethyl *trans*-4-Phenyl-2-thiomethyl-4-penteneoate 5a. To a cooled solution (−78 °C) of diisopropylamine (1.10 mL, 7.8 mmol) in THF (50 mL) was added a solution of *n*-BuLi (3.2 mL, 2.4 M, 7.8 mmol) in hexane. The solution was warmed to 0 °C for 25 min and then cooled to −78 °C. A solution of ethylthiomethyl acetate (1.00 mL, 7.80 mmol) in THF (10 mL) was added by cannula to the LDA solution. After 40 min, a solution of cinnamyl bromide (1.53 g, 7.80 mmol) in THF (15 mL) was added to the enolate solution. The solution was warmed to room temperature and quenched after 10 h with saturated aqueous NH$_4$Cl (50 mL). The solution was diluted with ether (100 mL) and successively washed with saturated aqueous NaHCO$_3$ (20 mL) and saturated aqueous NaCl (50 mL). The solution was dried over MgSO$_4$ and concentrated in vacuo to give a yellow oil. The oil was purified by silica gel flash chromatography (1:19 EtOAc/hexanes) to yield homoallyl sulfide **5a** (1.33 g, 69%) as colorless oil: $R_f = 0.18$ (1:24 EtOAc/hexanes); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.34−7.29 (m, 4H), 7.23−7.20 (m, 1H), 6.48 (d, $J = 15.5$ Hz, 1H), 6.18 (dt, $J = 15.5, 7.1$ Hz, 1H), 4.21 (q, $J = 7.0$ Hz, 2H), 3.31 (dd, $J = 7.1, 6.9$ Hz, 1H), 2.79 (dt, $J = 14.5, 7.1$ Hz, 1H), 2.59 (ddd, $J = 14.5, 7.1, 6.9$ Hz, 1H), 2.18 (s, 3H), 1.28 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.7, 137.1, 132.8, 128.5, 127.4, 126.2, 125.7, 61.1, 47.3, 34.3, 14.2, 13.9; IR (thin film) 3024, 2986, 2919, 1729, 1490, 1433, 1367, 1267, 1171, 1024, 962, 748, 695 cm^{-1}; GCMS (EI) m/z 250, 202, 177, 157, 129, 117; HRMS (EI) m/z calcd for C$_{14}$H$_{18}$O$_2$S 250.1027, found 250.1021.

Ethyl 5-Phenyl-5-dimethylphenylsilyl-2-thiomethylpentanoate 5b. To a solution of **5a** (0.17 g, 0.68 mmol) and chloroplatinic acid (14 mg, 3.4×10^{-2} mmol) in 1,2-dichloroethane (7.0 mL) was added phenyldimethylsilane (0.41 mL, 2.7 mmol). The solution was heated to reflux and monitored by GCMS. After 24 h, the reaction contents were filtered through a plug of silica gel (1:9 EtOAc/hexanes) and concentrated in vacuo to give an oil. The oil was purified by reverse phase preparative HPLC (4:6 acetonitrile/water) to yield alkyl silane **5b** (60 mg, 23%): $R_f = 0.18$ (1:24 EtOAc/hexanes); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.54−7.50 (m, 2 H), 739−7.33 (m, 3 H), 7.25−7.21 (m, 2H), 7.17−7.10 (m, 3 H), 4.06 (q, $J = 8.9$ Hz, 2 H), 2.84−2.79 (m, 1H), 2.79−2.74 (m, 1H), 2.50−2.41 (m, 1H), 2.08−2.01 (m, 1H), 1.80 (s, 2.2 H), 1.75 (s, 0.8 H), 1.61−1.54 (m, 1H), 1.37−1.32 (m, 1H), 1.22 (t, $J = 8.9$ Hz, 3 H), 0.29 (s, 2.2 H), 0.29 (s, 2.2 H), 0.28 (s, 0.8 H), 0.24 (s, 0.8 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 172.0, 142.2, 137.7, 134.0, 133.9, 129.1, 128.8, 128.3, 127.8, 125.9, 60.8, 46.8, 46.5, 36.8, 31.2, 30.6, 25.5, 24.2, 14.2, 14.1, 13.3, 13.1, −4.0, −4.3, −4.4, −4.6; IR (thin film) 1724, 1490, 1424, 1252, 1148, 1110, 733, 700 cm^{-1}; GCMS (EI) m/z 386, 371, 309; HRMS (EI) m/z calcd for C$_{22}$H$_{30}$O$_2$SSi 386.1736, found 386.1739.

Ethyl 2-Thiomethyl-*trans,trans*-4,6-octadienoate 6a. To a cooled solution (−78 °C) of diisopropylamine (0.72 mL, 5.2 mmol) in THF (52 mL) was added a solution of *n*-BuLi (2.1 mL, 2.4 M, 5.2 mmol) in hexane. The solution was warmed to 0 °C for 25 min and then cooled to −78 °C. A solution of ethylthiomethyl acetate (0.66 mL, 5.2 mmol) in THF (10 mL) was added by cannula to the LDA solution. To a cooled (0 °C) solution of *trans*,*trans*-2,4-hexadien-1-ol (0.50 mL, 4.4 mmol) in CH$_2$Cl$_2$ (49 mL) were added carbon tetrabromide (1.6 g, 4.9 mmol) and diphenylphosphinoethane (2.0 g, 4.9 mmol). After 30 min, the diene solution was filtered through a plug of silica gel (1:9 EtOAc/hexanes), concentrated in vacuo, and diluted with THF (45 mL). The enolate solution was then added to the diene solution and quenched after 8 h with saturated aqueous NH$_4$Cl (25 mL). The organic layer was washed with saturated aqueous NaHCO$_3$ (50 mL), and the combined aqueous layers were extracted with ether (3 × 20 mL). The ether solution was washed with saturated aqueous NaCl (50 mL), dried over MgSO$_4$, and concentrated in vacuo to give a pale yellow oil. The oil was chromatographed over silica gel (1:24 EtOAc/hexanes) to yield homoallyl sulfide **6a** (417 mg, 44%): $R_f = 0.25$ (1:24 EtOAc/hexanes); ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.08 (dd, $J = 14.9, 10.4$ Hz, 1H), 6.00 (dd, $J = 16.2, 10.4$ Hz, 1H), 5.62 (m, 1H), 5.50 (m, 1H), 4.19 (q, $J = 7.0$ Hz, 2H), 3.21 (dd, $J = 8.6, 7.1$ Hz, 1H), 2.62 (m, 1H), 2.43 (m, 1H), 2.21 (s, 3H), 1.73 (d, $J = 7.0$ Hz, 3H), 1.27 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.8, 133.3, 131.1, 128.7, 126.3, 61.0, 47.4, 33.9, 18.0, 14.2, 13.9; IR (thin film) 3014, 2967, 2919, 1729, 986 cm^{-1}; GCMS (EI) m/z 214, 166, 133; HRMS (EI) m/z calcd for C$_{11}$H$_{18}$O$_2$S 214.1027, found 214.1025.

Ethyl 2-Methylsulfanyloct-6-enoate 6c. To a solution of **6a** (91 mg, 0.42 mmol) and PtCl$_2$ (6 mg, 2×10^{-2} mmol) in 1,2-dichloroethane (4.2 mL) was added triethoxysilane (0.16 mL, 0.85 mmol). The solution was heated to reflux for 10 h, filtered through a plug of silica gel (1:9 EtOAc/hexanes), and concentrated in vacuo to give a pale yellow oil. The oil was purified by silica gel flash chromatography (1:49 EtOAc/hexanes) to yield mono alkene **6c** (78 mg, 85%): $R_f = 0.15$ (1:49 EtOAc/hexanes); ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.45−5.30 (m, 2H), 4.19 (q, $J = 7.1$ Hz, 2H), 3.15 (dd, $J = 8.3,6.9$ Hz, 1H), 2.13 (s, 3H), 1.98 (dt, $J = 7.1,4.2$ Hz, 2H), 1.91−1.83 (m, 1H), 1.70−1.62 (m, 1H), 1.64 (d, $J = 5.5$ Hz, 3H), 1.50−1.38 (m, 2H), 1.29 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 172.4, 130.5, 125.5, 60.9, 47.3, 32.0, 30.1, 27.2, 17.9, 14.2, 13.7; IR (thin film) 2919, 1729, 1257, 962 cm^{-1}; GCMS m/z (EI) 216, 201, 169; HRMS (EI) m/z calcd for C$_{11}$H$_{20}$OS 216.1184, found 216.1187.

Acknowledgment. The authors wish to thank the National Science Foundation (CHE 9623903). Additional support was provided by Eli Lilly and the Dupont Aid to Education Program. D.L.V.V. is a fellow of the Alfred P. Sloan Foundation. J.B.P. is a recipient of a 2001 Glaxo-Wellcome Research Fellowship.

Supporting Information Available: General experimental procedures and ^{1}H NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO010214E