

Chelation Assistance in the Activation of C_{sp}³–S Bonds in Nickel-Catalyzed Cross-Coupling Reactions†

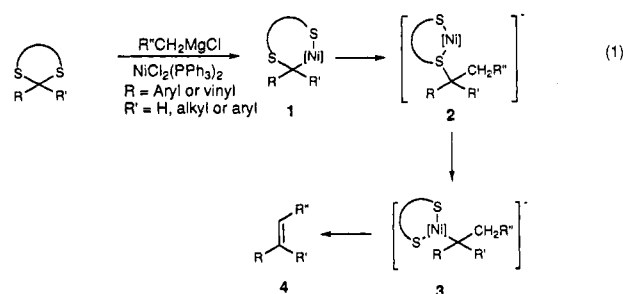
Ken-Tsung Wong,^{1a} Tien-Min Yuan,^{1b} Maw Cherng Wang, Hsiao-Hsian Tung, and Tien-Yau Luh*

Contribution from the Department of Chemistry, National Taiwan University, Taipei, Taiwan 106, Republic of China

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Abstract: An unprecedented chelation approach to activate C_{sp}³–S bonds in nickel-catalyzed cross-coupling reactions is described. Our theme was based on the formation of a chelation complex which results in the enhancement of the reactivity of aliphatic carbon–sulfur bonds. When two dithioacetal functionalities are located in close proximity, selective olefination of one of these two dithioacetal groups can thus be achieved conveniently. Depending on the relative positions of the newly formed double bond and the remaining dithioacetal group, tandem olefination occurs to give the corresponding 1,5-bis-silyl-substituted pentadienes. Various neighboring heteroatom substituents (OR, OH, NR₂, as well as SR groups) can facilitate the olefination of a dithioacetal group. Poly(thioether) linkage afforded the corresponding degradation products via a β-sulfur elimination process. 1,3-Dimercapto- and 1,3-dithiolatopropanes furnish the cyclopropane formation under nickel-catalyzed reaction conditions. The reaction of a dihydrothiopyran with MeMgI in the presence of the nickel catalyst proceeds via a sulfur-coordinated π-allyl complex, which can further activate the C–S bond to give vinylcyclopropane.

Transition-metal-catalyzed cross-coupling reactions leading to the formation of carbon–carbon bonds are important in organic synthesis.² Overwhelmingly, the C–X bond in the substrates should be allylic, aryl, benzylic, or vinylic. There have been very limited cases of alkyl iodides which undergo such coupling reactions.^{3,4} To illustrate, neopentyl iodides can react with aryl Grignard reagents in the presence of NiCl₂(dppf) catalyst to give the corresponding coupling products.^{3a} More recently, primary alkyl iodides have been found to couple with an organoboron reagent under Suzuki reaction conditions.^{3b} Other substrates, however, undergo various side reactions such as reduction or dimerization via a radical intermediate or β-hydride elimination leading to olefin formation.⁵ It is interesting to note that only the iodide leaving group so far is known to undergo such a coupling reaction.³ We recently reported that benzylic and allylic dithioacetals readily undergo olefination or geminal dimethylation reactions upon treatment with a Grignard reagent in the presence of the nickel catalyst (eq 1).^{2f,g,6,7} The high reactivity found in benzylic dithioacetals^{2f,6,7} versus the low activity observed for benzylic thiols or thioethers⁸ in cross-coupling reactions illustrates



that the overall reaction is a tandem cascade process. In other words, the first oxidative addition across the carbon–sulfur bond in the dithioacetal will lead to an α-sulfur-substituted organonickel species 1, which may facilitate carbon–carbon bond formation.⁹ The benzylic carbon–sulfur bond in intermediate thioether 2 is activated because of the chelation with the terminal thiolato moiety (eq 1).¹⁰ Further oxidative addition followed by β-hydride elimination gives the corresponding olefination product. Aliphatic dithioacetals, on the other hand, remain intact under these conditions.⁶ The major impetus apparently arises from the low reactivity of the C–S bond in the oxidative addition process. More recently, we found that more reactive tetrathioorthocarbonate yields the corresponding coupling products under nickel-catalyzed cross-coupling conditions (eq 2).⁴ This observation indicates that the displacements of the carbon–sulfur bonds in tetrathioorthocarbonate occur similarly via a cascade process. In other words, as soon as the first carbon–sulfur bond is activated, the following steps involving the reactions of the remaining carbon–sulfur bonds

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(1) (a) Recipient of Li-Ching Foundation Scholarship, 1992, and Yen's Chemistry Thesis Award, National Taiwan University, 1993. (b) Recipient of Li-Ching Foundation Scholarship, 1993, and Yen's Chemistry Thesis Award, 1994.

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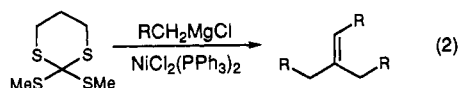
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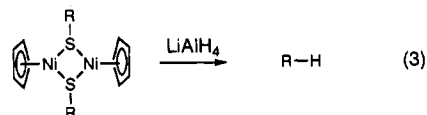
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(9) Organometallic alkyl complexes or intermediates having an α-alkoxy or thioalkoxy substituent are known to undergo CO insertion in pyranosyl or furanosyl manganese complexes (cf.: DeShong, P.; Slough, G. A.; Elango, V.; Trainor, G. L. *J. Am. Chem. Soc.* **1985**, *107*, 7788) or reductive elimination in Stille coupling reactions (cf.: Bhatt, R. K.; Shin, D.-S.; Falck, J. R.; Mioskowski, C. *Tetrahedron Lett.* **1992**, *33*, 4885), although β-hydride elimination has also been reported (cf. ref. 3c).

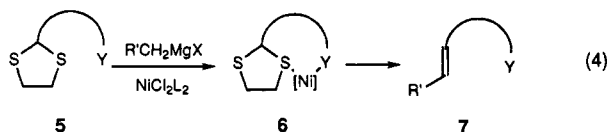
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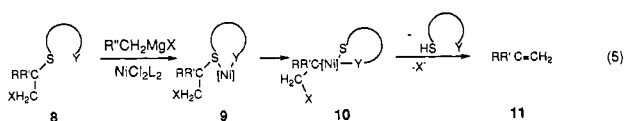
would occur facily. It is known that polythioethers form stable transition-metal complexes.¹¹ Indeed, the C–S bonds in certain complexes containing thiolato ligands are activated, and the reduction of these C–S bonds to give the corresponding hydrocarbons can readily be achieved (eq 3).¹² Our previous work also



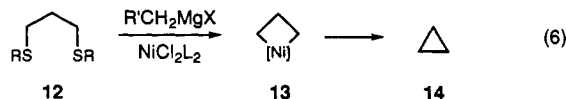
suggests that chelation will result in the enhancement of the reactivity of the benzylic carbon–sulfur bond.¹⁰ Accordingly, we felt that this kind of chelation formation may also assist the cleavage of the aliphatic C–S bond leading to the cross-coupling reactions. A specialized designed substrate is necessary to increase the reactivity of the C–S bond in the oxidative addition reaction and, in the meantime, to stabilize the organometallic intermediate. The strategy is outlined in eq 4. When a dithioacetal moiety **5**



having a heteroatom(s) Y at a close proximal position is treated with a Grignard reagent in the presence of a nickel catalyst, a chelation complex **6** would be expected. Nickel-catalyzed olefination of the dithioacetal moiety with the Grignard reagent^{2f,g,6} might then occur. Alternatively, when the corresponding thioether **8** is allowed to react under similar conditions, oxidative addition of the carbon–sulfur bond in **8** might also occur, because of chelation (cf. **9**), to give organonickel intermediate **10** (eq 5).



Without any α -stabilizing substituent in **10**, it might undergo rapid β -hydride or β -heteroatom¹³ elimination to generate a carbon–carbon double bond (cf. **11**). This route also represents the steps involved in the olefination of aliphatic dithioacetals (from **5** to **7**). The third possibility is oxidative addition across both carbon–sulfur bonds in **12** producing a metallacycle **13**, which may render reductive elimination to give the corresponding cyclopropanes **14**. In this paper, we report the scope of the nickel-catalyzed cross-coupling reactions of a variety of aliphatic organosulfur compounds with Grignard reagents based on the conjecture summarized in eqs 4–6.¹⁴



Results and Discussion

Reactions of Bis(dithioacetals) with Grignard Reagents. Our initial effort focused on the nickel-catalyzed cross-coupling

Table 1. $\text{NiCl}_2(\text{PPh}_3)_2$ -Catalyzed Reactions of Bis(dithioacetals) with Grignard Reagents

entry	substrate	RMgX	product	%yield
1		MeMgI		16a 80
2		$\text{Me}_3\text{SiCH}_2\text{MgCl}$		16b 83
	15		16a R = Me 16b R = Me_3SiCH_2	
3		MeMgI		78
4	17	PhMgBr		68 ^a
5		MeMgI		68
6 ^b	20			21a:21b = 1:1 68 21a:21b = 3:1
7		MeMgI		76
	22			23a:23b = 1:1
8 ^c		MeMgI		72
	24			25a:25b = 5:1
9		MeMgI		72
	26			27a:27b = 8:1
10		MeMgI		76
	28			
11		MeMgI		82
	30			31a:31b:31c = 1:1:4
12 ^d		MeMgI		33a 72
13	32	$\text{PhMe}_2\text{SiCH}_2\text{MgCl}$		33b 67 ^a
			33a R = Me 33b R = $\text{PhMe}_2\text{SiCH}_2$	
14		MeMgI		70
	34		35	

^a Starting material **17** was recovered in 23% yield. Yield was based on unrecovered **17**.

reactions of certain rigid bis(dithioacetals). To illustrate this, the two endo sulfur moieties in **15** are located in close proximity and therefore can readily form a chelation complex with the nickel catalyst. Treatment of **15** with excess MeMgI¹⁵ in the presence of 5 mol % of $\text{NiCl}_2(\text{PPh}_3)_2$ afforded olefin dithioacetal **16** in good yield (entry 1, Table 1). Representative examples are outlined in Table 1. Nickel catalysts having bidentate ligands such as dppe or the like behaved similarly (entries 6 and 8). It is noteworthy that no reaction between bis(dithioacetals) and

(15) Throughout this investigation an excess amount of the Grignard reagent was normally used to drive the reaction to completion. Starting material was recovered when only a stoichiometric amount of the Grignard reagent was employed.

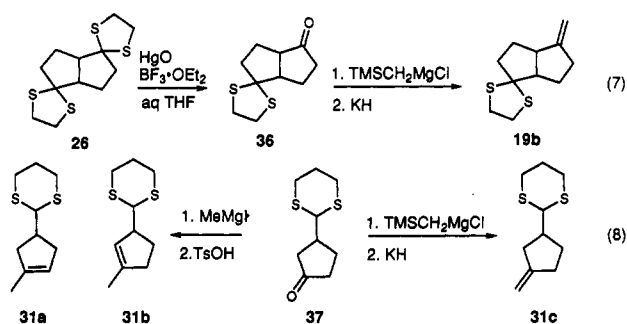
(11) For leading references, see: (a) Cooper, S. R. *Acc. Chem. Res.* **1988**, *21*, 141. (b) Cooper, S. R.; Rawle, S. C. *Structure Bonding* **1990**, *72*, 1.

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(14) Preliminary communication: Wong, K.-T.; Luh, T.-Y. *J. Am. Chem. Soc.* **1992**, *114*, 7308.

Grignard reagents occurred in the absence of a nickel catalyst. Bis(dithioacetals) derived from cyclic (entries 1–9) or acyclic (entries 12–14) diketones gave readily the corresponding monoolefination products. Methyl, silylmethyl, and aryl Grignard reagents reacted smoothly with bis(dithioacetals). The structures of certain isomeric mixtures were proved by independent synthesis (eqs 7 and 8). It is particularly interesting to note that *only one*



of the dithioacetal groups of these substrates underwent an olefination reaction under these conditions. Even in the presence of a large excess of the Grignard reagent, no further coupling reaction was observed at all. This reaction can thus be considered as a selective modification of one of the two carbonyl equivalents, while the remaining one is still protected.

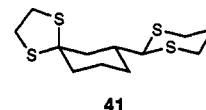
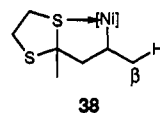
A plausible mechanism of this selective olefination may follow a pathway similar to those described for benzylic or allylic substrates (cf. eq 1).^{2,6,7} Our previous work on tetrathioortho-carbonate⁴ and benzylic and allylic dithioacetals and ortho-esters^{2f,8,6,7} and some of the present investigation (entries 3–9) clearly demonstrate that the formation of a carbon–carbon bond precedes the elimination step in these cross-coupling reactions. Oxidative addition of one of the carbon–sulfur bonds and association of the Grignard reagent with the nickel catalyst followed by a reductive elimination process form the basis for the carbon–carbon bond formation. Indeed, organometallic alkyl intermediates having an α -alkoxy or thioalkoxy substituent are known to undergo reductive elimination in the Stille coupling reaction.⁹ We have previously shown that the cleavage of the second carbon–sulfur bond in benzylic and allylic substrates would require a nickel catalyst.¹⁶ As will be described later, the nickel catalyst may also play an important role in the chelation-assisted cleavage of the carbon–sulfur bond of a thioether followed by β -sulfur elimination.

Regioselectivity of β -Hydride Elimination. When bis(dithioacetals) derived from 1,3-diketones were employed, homoallylic dithioacetals were obtained regioselectively (entries 8 and 12–14). The nickel center of intermediate **38** may form a chelation complex with the sulfur atom in the remaining dithioacetal moiety. Since the exocyclic C–H bond in **38** can readily exist in the preferred cis-coplanar conformation relative to the carbon–nickel bond, β -hydride elimination would lead preferentially to the formation of the corresponding homoallylic dithioacetals.

The selectivity for the formation of the double bond in bis(dithioacetals) derived from 1,4- or 1,5-diketones, on the other hand, depends on the nature of the substrates (entries 1–4, 7, and 9–11). The activation of one of the two dithioacetal groups will

(16) Evidence which supports this conjecture has been described. To illustrate, the nickel-catalyzed cross-coupling reaction of benzophenone dithioacetal with *i*-PrMgBr afforded, in addition to the normal olefination product, a significant amount of the corresponding reduced product and propene (ref 6). Allylic and certain benzylic dithioacetals readily undergo geminal dimethylation under similar conditions using $\text{NiCl}_2(\text{dppe})$ catalyst (ref 7). Furthermore, the orientation of the double bond formation has been shown to depend on the ring size of the sulfur heterocycles (cf. ref 17). These results are consistent with the proposal that the oxidative addition of the second carbon–sulfur bond by the nickel catalyst appeared to be essential for the overall nickel-catalyzed olefination reactions.

(17) Wong, K.-T.; Ni, Z.-J.; Luh, T.-Y. *J. Chem. Soc., Perkin Trans. 1* 1991, 3113.



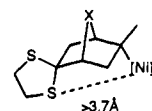
be expected because of the chelation of the proximal sulfur moieties with the nickel catalyst. However, unlike bis(dithioacetals) derived from 1,3-diketones, no intermediate like **38** would be expected from these reactions because the remaining sulfur atom would be too far away from the nickel center for coordination.¹⁸ Consequently, the orientation of β -hydride elimination would depend on the relative stability of the product or on the availability of the cis-coplanar β -hydrogen. When the relatively unstrained five-membered-ring substrates were employed, an endocyclic double bond was formed predominantly, if not exclusively (entries 1, 2, and 9). This is understandable because the cis-coplanar β -hydrogen was readily accessible in the intermediate for elimination. On the other hand, the exocyclic methylenenorbornane derivative **18** was isolated as the sole product from the reaction of the more strained substrate **17** (entry 3). Presumably, the relative strain of the exocyclic double bond versus the endocyclic double bond plays a key role in the selectivity.^{19,20}

Six-membered-ring substrates, however, were less selective. An isomeric mixture of endo- and exocyclic double bonds was usually obtained (entries 5–7). When $\text{NiCl}_2(\text{chiraphos})$ was employed, **20** gave 68% of a 3:1 mixture of racemic **21a** and **21b** (entry 6). Although the reaction gave no chiral selectivity, the regioselective formation of an exocyclic double bond was noted. Apparently, the steric environment around the nickel may determine the orientation of β -hydride elimination in these cross-coupling reactions of dithioacetals.¹⁷

The nature of the dithioacetal group also determines the regio- and chemoselectivity of the reaction. When one of the bis(dithiolane) moieties was derived from an aldehyde and the other from a ketone, the former, which is less sterically hindered, was converted into the olefinic group (entry 10). However, the ring size of the sulfur heterocycle appeared to be more important in determining the reactivity. In this respect, the dithiolane group was transformed into the olefinic product when the starting bis(dithioacetal) **30** contained both a dithiolane moiety and a dithiane group (entry 11). Since the first step of this catalytic process would involve oxidative addition across a carbon–sulfur bond,^{28,8} a five-membered dithiolane would give a six-membered metallacycle whereas a dithiane would lead to a seven-membered intermediate.

As shown in eq 4, the general criterion for the success of these transformations is the ability of the two sulfur moieties to coordinate simultaneously to the nickel catalyst. Poor chelation resulted in the recovery of a significant amount of the starting

(18) MM2 calculations indicated that the distances between two endo sulfur atoms in **17** and **22** were 3.85 and 3.77 Å, respectively. Accordingly, the corresponding organonickel intermediate formed by oxidative addition would be unable to form a chelation complex **A** with the remaining endo sulfur moiety (cf.: Murray, S. G.; Hartley, F. R. *Chem. Rev.* 1981, 81, 365).

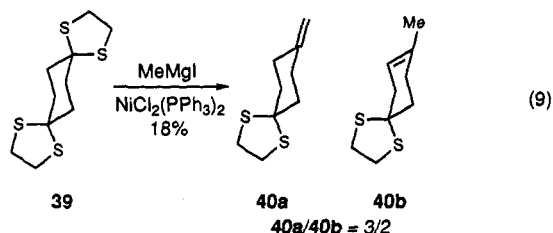


A (X = CH_2 or CH_2CH_2)

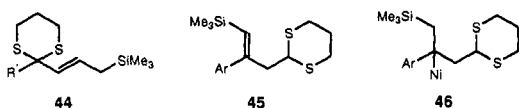
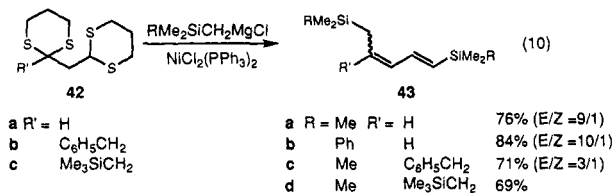
(19) 2-Methylenenorbornane is about 2 kcal/mol more stable than 2-methyl-2-norbornene (cf.: Kozina, M. P.; Timofeeva, L. P.; Skuratov, S. M.; Belikova, N. A.; Milvitskaya, E. M.; Platé, A. F. *J. Chem. Thermodyn.* 1971, 3, 563.)

(20) At this stage, we could not distinguish which of the dithiane groups in **42** would react first. As just described, since bis(dithioacetals) **32** and **34** afforded only the homoallylic dithioacetals **33** and **35**, respectively, upon treatment with the appropriate Grignard reagent under the nickel-catalyzed cross-coupling conditions (entries 12–14), it seems likely that the sulfur heterocycle derived from an aldehyde functional group in **42** might react first to afford intermediate **44**.

materials. Accordingly, the reaction of **39** afforded the corresponding coupling products **40a** and **40b** in 18% yield, starting **39** being recovered in 75% yield (eq 9). In a similar manner, the reaction of **41** with MeMgI under the same conditions resulted in the recovery of the starting material in 91% yield.

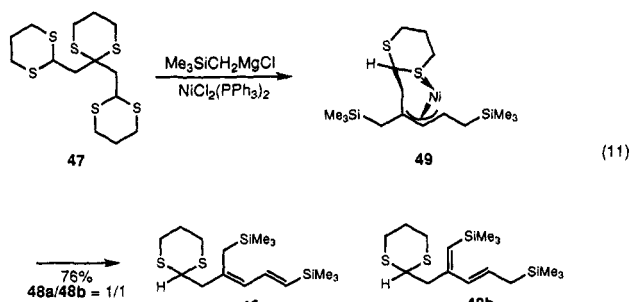


Tandem Cross-Coupling Reactions. The reactions with less rigid acyclic substrates were intriguing. As can be seen from Table 1, when both dithioacetal moieties were derived from ketone groups (entries 12–14), the reaction behaved just as with the cyclic substrates. On the other hand, when one of these two dithioacetal moieties was derived from an aldehyde group, the selectivity changed. To illustrate this, upon treatment with $\text{RMe}_2\text{SiCH}_2\text{MgCl}$ ($\text{R} = \text{Me}$ and Ph) under the similar conditions, 1,3-bis(dithianes) **42** afforded the corresponding silyl-substituted dienes **43** in good yields (eq 10). Presumably, an allylic



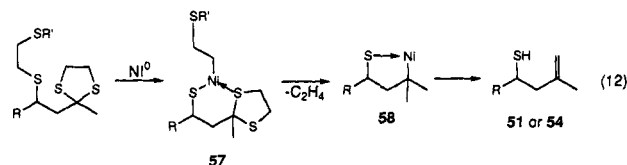
dithioacetal intermediate **44** was involved. Further coupling with the Grignard reagent,^{20,21} led to **43**. The regioselective formation of intermediate **44** is somewhat striking. It is interesting to note that the corresponding aryl-substituted bis(dithianes) (**42**, $\text{R}' = \text{Ar}$) gave, in addition to **43** ($\text{R}' = \text{Ar}$), a significant amount of **45**.^{21c} Although the discrepancy between this study and our earlier work is not clear, the benzylic organonickel intermediate **46** might be more stable and, hence, have a tendency to form a thermodynamically more stable vinylsilane **45**. Nevertheless, given the simplicity of such a tandem reaction and the easy accessibility of the starting materials, this procedure has provided a convenient stereoselective synthesis of bis(silyl)pentadienes that cannot easily be obtained by other means.²²

Tris(dithiane) **47** behaved interestingly under the reaction conditions. Only two sulfur heterocycles underwent a cross-coupling reaction to give **48a** and **48b**, and the third dithiane ring, which is homoallylic in nature, remained intact (eq 11). Presumably, chelation of the nickel catalyst with sulfur atoms arisen from two dithiane moieties may occur, resulting in tandem coupling with these sulfur heterocycles. The sulfur atom of the third dithiane ring may coordinate to the nickel such that π -allyl intermediate **49** would undergo regioselective β -hydride elimination giving **48**.



Reactions of Thioether Dithioacetals with Grignard Reagents. The extension of the cross-couplings to thioether dithioacetals has been executed. Homoallylic thiols were obtained as the sole products from these reactions. Table 2 summarizes some representative results.

The fate of the carbon fragments in the thioether linkage has been determined. The gaseous product from the reaction of **50** was trapped with bromine in carbon tetrachloride, 1,2-dibromoethane being obtained in 65% yield. One of the C–S bonds in the thioether linkage in **50** might be activated because of the chelate formation, intermediate **57** being formed. Rapid β -sulfur elimination¹³ would liberate ethylene and the other fragments which would lead to homoallylic mercaptan **51** or **54** (eq 12).



Three interesting features are worth mentioning. First, the dithioacetal group is transformed to an alkene moiety *regioselectively*. Because of the coordination of the sulfur moiety to the nickel (such as in intermediate **58**) and the requirement of cis-coplanarity for the β -hydride elimination, the regioselective formation of the double bond in these reactions can be rationalized. Second, the carbon–sulfur bond in the thioether moiety is cleaved to give a mercaptan. As can be seen in Table 2, the nature of the thioether linkage varied but the product type was the same. It is interesting to note that dithioacetal mercaptan **52** also underwent a similar coupling reaction to give **51** (entry 16). However, when the reactions of **50** or **55** or **56** were stopped before completion, no trace amount of the corresponding mercaptan dithioacetal like **52** was detected. If **52** or the like were the intermediate in these reactions, **52** would react much faster than the thioether analogs under the reaction conditions. This would be plausible because the chelation ability of a mercaptide ion is better than that of a thioether moiety; hence, better chelation would be expected in the reaction of **52** in comparison with those of other substrates listed in Table 2. Third, no reaction was observed when **50** was treated with the Grignard reagent in the absence of a nickel catalyst. This observation indicates that the cleavage of the C–S bond of thioethers in these reactions requires a nickel catalyst and supports our earlier suggestion that the reactions of both C–S bonds in the dithioacetal are assisted by a nickel catalyst.

Other Heteroatom-Assisted Olefinations of Dithioacetals. Other heteroatom substituents such as hydroxy, methoxy, and amino groups also assisted the alkenation of aliphatic dithioacetals; and homoallylic alcohols, ether, and amine, respectively, were obtained in reasonably good yields (Table 3). Similar to sulfur analogs, the double bond was also formed regioselectively, when the heteroatom substituent was located at the β -position. Presumably, an intermediate like **58** where S is replaced by a heteroatom moiety may be involved. This procedure provides an interesting route for the preparation of homoallylic alcohols,

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(22) (a) Yasuda, H.; Hishi, T.; Lee, K.; Nakamura, A. *Organometallics* **1983**, *2*, 21. (b) For a review on the silyl-substituted dienes, see: Luh, T.-Y.; Wong, K.-T. *Synthesis* **1993**, 349.

Table 2. $\text{NiCl}_2(\text{PPh}_3)_2$ -Catalyzed Reactions of Thioether Dithioacetals with Grignard Reagents

entry	substrate	product (% yield)	%yield
15			70
16			67
17			65
18			68
19 ^a			58

^a $\text{NiCl}_2(\text{dppe})$ was used as the catalyst. Surprisingly, when $\text{NiCl}_2(\text{PPh}_3)_2$ was employed as the catalyst, the yield of **54** dropped to 9%.

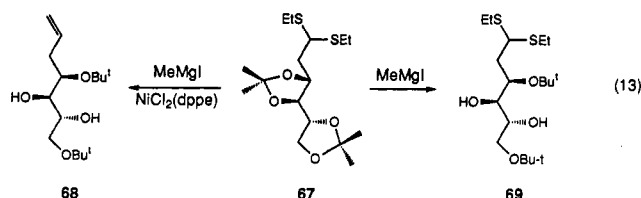
Table 3. $\text{NiCl}_2(\text{PPh}_3)_2$ -Catalyzed Reactions of Heteroatom Dithioacetals with Grignard Reagents

entry	substrate	product	%yield
20			75
21			77
22 ^a			71
23 ^a			73 66a:66b = 65:35

^a $\text{NiCl}_2(\text{dppe})$ was used as the catalyst.

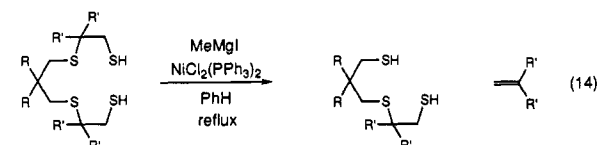
ethers, and thiols as well as amines. A substrate having a γ -hydroxyl substituent such as **65**, on the other hand, gave a mixture of **66a** and **66b** under the same conditions (entry 23). The structures of isomeric products **66a** and **66b** were proved by independent syntheses (see Experimental Section).

The use of the heteroatom-assisted olefination of dithioacetals has been extended to a sugar derivative, **67** (eq 13).²³ In the presence of the nickel catalyst, oxygen atom assisted olefination coupled with regioselective ring opening of both acetonide moieties occurred to give **68**. When the nickel catalyst was absent, **69** was



obtained and the carbon–sulfur bonds remained intact. This result implies that the base-promoted (Grignard reagent) elimination of RSH giving a carbon–carbon double bond would not occur under the reaction conditions and, therefore, again echoes the argument that the formal elimination of the second sulfur moiety leading to the double bond (from **2** to **4**) in eq 1 is nickel-catalyzed.

Reactions of Poly(thioethers) with Grignard Reagents. The results depicted in the previous section suggested that the behavior of the aliphatic thioether and mercaptans was very much different from that of the dithioacetal functionality under the conditions of the nickel-catalyzed reaction with Grignard reagents. The dithioacetal group underwent the normal olefination reaction, whereas no carbon–carbon bond formation was observed with the sulfide or mercaptan functionalities. Thus, it would be highly intriguing to investigate the reaction behavior of poly(thioethers) **70** under these conditions. Because of the chelate formation, the C–S bonds in **70** will be activated. Thus, treatment of poly(thioethers) **70** under conditions similar to those described above afforded 1, ω -dimercapto thioethers **71** in good yields (eq 14). In



70a R = Bn, R' = H

70b R = H, R' = Bn

70c R = R' = H

71a R = Bn, R' = H 72%

71b R = H, R' = Bn 78%

71c R = R' = H 71%

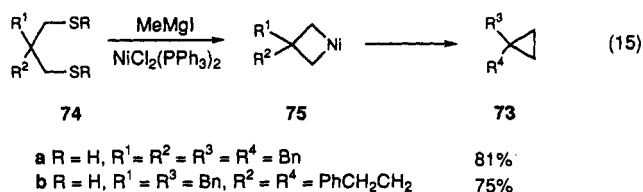
72a R' = H 58%

72b R' = Bn 82%

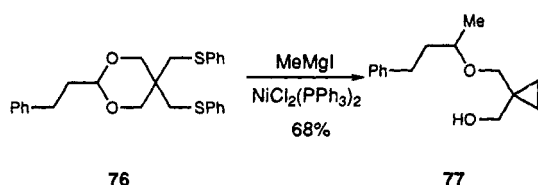
a similar manner, the reaction of thioether **70a** afforded in 58% yield ethylene which was trapped as 1,2-dibromoethane. The isolation of the olefinic products from these reactions established that a β -sulfur elimination process¹³ may be involved in these nickel-catalyzed reactions.

It is interesting to note that the reaction under these conditions was highly selective and only one of the mercapto thioether chains was cleaved. The products **71** could again form chelation complexes with the nickel catalyst; hence, further desulfurative processes could occur under more drastic conditions. When 1, ω -dimercapto thioether **71a** was allowed to react with excess Grignard reagent in the presence of 40 mol % of $\text{NiCl}_2(\text{PPh}_3)_2$ for 4 h and then worked up as usual, a mixture of **73a** (16%) and **74a** (10%) was obtained, and **71a** (60%) was recovered. Under similar conditions, treatment of mercapto thioether **71a** with MeMgI in refluxing benzene for 18 h afforded 1,1-dibenzylcyclopropane (**73a**) in 68% yield. Presumably, intermediate **74a** formed via a similar desulfurative elimination process (cf. eq 14) will react further to yield **73a**. Furthermore, treatment of **74a** under the same conditions gave **73a** in 81% yield (eq 15). Similarly, the reaction of **70a** with MeMgI in the presence of 40 mol % of $\text{NiCl}_2(\text{PPh}_3)_2$ in refluxing benzene for 13 h produced **73a** in 78% yield. The sulfur moiety was trapped as dibenzyl sulfide in 40% yield when the reaction mixture was quenched

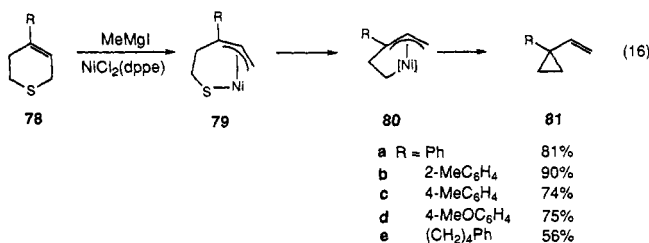
(23) (a) A referee questioned whether magnesium ion from the Grignard reagent may also form a chelation complex with the substrates leading to the activation of the carbon–sulfur bond. Our recent investigations on the reactions of acetones of monosaccharide derivatives revealed that magnesium does form a chelate with the oxygen moieties resulting in the regioselective alkylative cleavage of the carbon–oxygen bond rather than the carbon–sulfur bond (ref 23b). (b) For a preliminary communication, see: Cheng, W.-L.; Yeh, S.-M.; Luh, T.-Y. *J. Org. Chem.* 1993, 58, 5576.



with NaOH followed by treatment with benzyl bromide. Presumably, an S^{2-} moiety was formed from the reaction via the nickel-catalyzed cleavage of the carbon–sulfur bonds in **74a** or via a β -sulfide elimination process from the reactions of **70** or **71**. These results demonstrate an interesting example on a stepwise nickel-catalyzed cleavage of the carbon–sulfur bonds in 1, ω -dimercapto thioethers. Exhaustive reaction would lead to the formation of a nickelacyclobutane **75a** such that further reductive elimination would generate the corresponding cyclopropane **73a** (eq 15). In a similar manner, the reactions of **74b** and **76** also afforded **73b** and **77**, respectively. It is noteworthy that the acetal group in **76** also underwent ring-opening reactions with the Grignard reagent to give **77**. The procedure furnished the first example of the desulfurative coupling reaction of 1,3-bis-thio-substituted propanes leading to cyclopropanes under homogeneous conditions.²⁴



Desulfurative Coupling of Thiopyrans. In the previous sections, we have demonstrated that heteroatoms such as oxygen, nitrogen, and sulfur can play a unique role in the activation of carbon–sulfur bonds under nickel-catalyzed cross-coupling reaction conditions. It would be highly intriguing if a π -alkyl complex could also assist the cleavage of the chelated carbon–sulfur bond. 5,6-Dihydro-2H-thiopyran **78** may serve as a useful model because it has two different kinds of carbon–sulfur bonds, one being allylic and the other aliphatic. Oxidative addition with the nickel catalyst would occur readily at the allylic C–S bond to give possibly the sulfur-coordinated π -allyl intermediate **79**. The remaining C–S bond, which may be activated owing to chelation, would undergo further cleavage leading to an organonickel intermediate **80** (eq 16). Indeed, when **78a–e** were treated with MeMgI in the presence

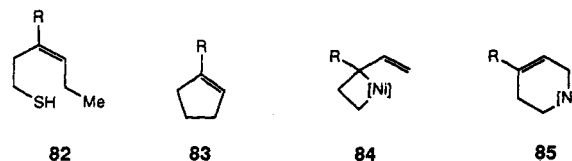


of 5 mol % of NiCl₂(dppe) in refluxing benzene, they gave the corresponding vinylcyclopropanes **81** in good to excellent yields. Strikingly, neither a cross-coupling product like **82** nor five-membered-ring analog **83** has been observed. Presumably, the activation of the carbon–sulfur bond in the chelation complex **79** is faster than the reaction of the π -allyl nickel species with the Grignard reagent. In addition, intermediate **80** may be prone to

(24) Desulfurative cyclopropane formation from thietanes under heterogeneous conditions on a molybdenum single-crystal surface (cf. ref 25a) or with Raney nickel (cf. ref 25b) has been described.

(25) (a) Roberts, J. T.; Friend, C. M. *J. Am. Chem. Soc.* **1987**, *109*, 3872. (b) Lawrence, A. H.; Liao, C. C.; de Mayo, P.; Ramamurthy, V. *J. Am. Chem. Soc.* **1976**, *98*, 2219.

behave like a vinyl-substituted metallacyclobutane **84** rather than a metallacyclohexene **85**. Consequently, reductive elimination gave **81** exclusively under the reaction conditions.



Conclusion

We have demonstrated an unprecedented approach to activate C_{sp^3} –S bonds in nickel-catalyzed cross-coupling reactions. Our theme was based on the formation of a chelation complex which results in the enhancement of the reactivity of aliphatic carbon–sulfur bonds. Selective olefination of one dithioacetal group of bis(dithioacetals) can thus be achieved conveniently. Various neighboring groups such as those with heteroatom substituents (OR, OH, NR₂, as well as SR groups) and those with π -allyl complex can activate C–S bonds under nickel-catalyzed cross-coupling conditions.

Poly(thioether) linkage afforded the corresponding degradation products via a β -sulfur elimination process, eventually leading to cyclopropane formation. Dihydrothiopyrans, on the other hand, yielded the corresponding vinylcyclopropanes. These reactions can be considered as an unprecedented desulfurative coupling reaction of a 1,3-bis-thio-substituted propane leading to cyclopropane.

Experimental Section

The experimental details for the preparation of organosulfur substrates used in this investigation are described in the supplementary material.

Reaction of Bis(dithioacetal) 15 with MeMgI. Under N₂, the Grignard reagent MeMgI (2.0 M, 2.0 mL, 4.0 mmol) in ether was evacuated to remove ether. A solution of **15** (318 mg, 1.0 mmol) and NiCl₂(PPh₃)₂ (33 mg, 0.05 mmol) in benzene (15 mL) was added, and the mixture was refluxed for 8 h. After being cooled to room temperature, the mixture was quenched with saturated NH₄Cl and extracted with ether. The organic solution was washed with NaOH (10%) and brine, dried (MgSO₄), and evaporated to give the residue, which was chromatographed on silica gel (EtOAc:hexane = 1:100) to afford **16a** (192 mg, 80%): IR (neat) ν 3025, 2960, 2918, 2910, 2866, 1663, 1439, 828 cm⁻¹; ¹H NMR (200 MHz) δ 1.00 (s, 3 H), 1.07 (s, 3 H), 1.64 (br s, 3 H), 2.14–2.31 (m, 4 H), 2.37–2.46 (m, 2 H), 3.14–3.26 (m, 4 H), 4.99 (br s, 1 H); ¹³C NMR (75 MHz) δ 16.6, 23.0, 25.0, 38.4, 40.4, 50.2, 53.7, 57.5, 58.4, 62.6, 67.8, 133.9, 137.7; MS (*m/z*, 70 eV) 240 (100), 225 (15), 212 (66), 179 (75), 154 (48), 106 (85); HRMS calcd for C₁₃H₂₀S₂ 240.1006, found 240.1011.

Reaction of Bis(dithioacetal) 15 with Me₃SiCH₂MgCl. According to the procedure described above, a mixture of **15** (318 mg, 1.0 mmol), Me₃SiCH₂MgCl (3.0 M, 2.0 mL, 6.0 mmol), and NiCl₂(PPh₃)₂ (33 mg, 0.05 mmol) in benzene was refluxed for 18 h to afford **16b** (259 mg, 83%): ¹H NMR (300 MHz) δ 0.00 (s, 9 H), 0.96 (s, 3 H), 1.05 (s, 3 H), 1.38 (d, *J* = 13.7 Hz, 1 H), 1.52 (d, *J* = 13.7 Hz, 1 H), 2.14–2.47 (m, 6 H), 3.17–3.27 (m, 4 H), 4.87 (br s, 1 H); ¹³C NMR (75 MHz) δ -1.1, 21.4, 23.2, 24.6, 38.8, 40.3, 50.4, 54.1, 57.9, 58.5, 62.2, 67.9, 132.0, 138.7; MS (*m/z*, 70 eV) 312 (8), 284 (5), 251 (9), 219 (8), 180 (48), 145 (11), 106 (18), 73 (100); HRMS calcd for C₁₆H₂₆S₂Si 312.1402, found 302.1410.

Reaction of Bis(dithioacetal) 17 with MeMgI. According to the procedure described above, a benzene solution of MeMgI (3.0 M, 2.0 mL, 6.0 mmol), **17** (276 mg, 1.0 mmol), and NiCl₂(PPh₃)₂ (33 mg, 0.05 mmol) was allowed to react for 8 h to afford **18** (154 mg, 78%): IR (neat) ν 3069, 2963, 2922, 1666, 974, 879 cm⁻¹; ¹H NMR (200 MHz) δ 1.60 (dm, *J* = 10.2 Hz, 1 H), 1.79 (dm, *J* = 10.2 Hz, 1 H), 2.02 (dd, *J* = 2.7, 13.7 Hz, 1 H), 2.19 (dm, *J* = 16.6 Hz, 1 H), 2.41 (dd, *J* = 4.1, 13.9 Hz, 2 H), 2.56 (dm, *J* = 16.9 Hz, 1 H), 2.69 (d, *J* = 3.9 Hz, 1 H), 3.12–3.35 (m, 4 H), 4.62 (br s, 1 H), 4.85 (br s, 1 H); ¹³C NMR (50 MHz) δ 35.6, 39.8, 40.0, 40.4, 46.0, 49.4, 52.5, 71.3, 103.0, 152.5; MS (*m/z*, 70 eV) 198 (66), 170 (100), 137 (21), 105 (25), 79 (25); HRMS calcd for C₁₀H₁₄S₂ 198.0537, found 198.0525.

Reaction of Bis(dithioacetal) 17 with PhMgBr. The ether solvent of PhMgBr prepared from bromobenzene (0.63 mL, 6.0 mmol) and magnesium turnings (194 mg, 8.0 mg-atom) in Et₂O (10 mL) was removed under vacuum. Benzene (15 mL), bis(dithioacetal) 17 (276 mg, 1.0 mmol), and NiCl₂(PPh₃)₂ (33 mg, 0.05 mmol) were then added, and the mixture was heated under reflux for 48 h followed by the same workup procedure as described above to afford 19 (138 mg, 53%, 68% based on unrecovered 17) and recovered 17 (64 mg, 23%): ¹H NMR (300 MHz) δ 1.78–1.89 (m, 2 H), 2.05 (dd, *J* = 2.8, 13.0 Hz, 1 H), 2.54 (dd, *J* = 3.7, 13.0 Hz, 1 H), 3.09–3.11 (m, 1 H), 3.20–3.40 (m, 5 H), 6.43 (d, *J* = 3.0 Hz, 1 H), 7.20–7.25 (m, 1 H), 7.29–7.34 (m, 2 H), 7.39–7.43 (m, 2 H); ¹³C NMR (75 MHz) δ 39.9, 40.5, 43.6, 46.7, 49.2, 58.1, 71.5, 125.1, 127.4, 128.4, 128.5, 134.7, 150.7; MS (*m/z*, 70 eV) 260 (17), 232 (2), 142 (100), 118 (33); HRMS calcd for C₁₅H₁₆S₂ 260.0693, found 260.0697.

Reaction of Bis(dithioacetal) 20 with MeMgI. According to the procedure described above, a mixture of MeMgI (2.0 M, 2.0 mL, 4.0 mmol), 20 (304 mg, 1.0 mmol), and NiCl₂(PPh₃)₂ (33 mg, 0.05 mmol) in benzene was allowed to react for 10 h to afford 21a and 21b (154 mg, 68%, 1:1). Isomers were separated by HPLC (EtOAc:hexane = 1:100). 21a: IR (neat) ν 3069, 2945, 2865, 1648, 879 cm⁻¹; ¹H NMR (300 MHz) δ 0.82 (s, 3 H), 1.30–1.37 (m, 2 H), 1.62–1.75 (m, 1 H), 2.08–2.17 (m, 5 H), 2.41 (t, *J* = 2.9 Hz, 1 H), 3.20–3.35 (m, 4 H), 4.76 (br s, 1 H), 4.87 (br s, 1 H); ¹³C NMR (75 MHz) δ 26.2, 26.9, 31.3, 32.2, 39.3, 39.5, 40.4, 49.7, 54.6, 68.6, 108.8, 148.4; MS (*m/z*, 70 eV) 226 (100), 211 (14), 198 (64), 171 (70), 142 (45), 106 (55), 93 (32); HRMS calcd for C₁₂H₁₈S₂ 226.0850, found 226.0856. 21b: IR (neat) ν 3021, 2597, 2865, 1651, 803 cm⁻¹; ¹H NMR (300 MHz) δ 1.04–1.11 (m, 4 H, a singlet δ 1.09 for the methyl group is embodied), 1.26–1.37 (m, 2 H), 1.86 (s, 3 H), 1.94–2.18 (m, 3 H), 2.47 (s, 1 H), 3.18–3.34 (m, 4 H), 5.59 (s, 1 H); ¹³C NMR (75 MHz) δ 21.8, 24.6, 24.8, 33.1, 35.7, 39.4, 39.7, 49.0, 54.0, 70.5, 131.5, 142.6; MS (*m/z*, 70 eV) 226 (36), 212 (11), 119 (66), 108 (100), 93 (78); HRMS calcd for C₁₂H₁₈S₂ 226.0850, found 226.0842.

Under the same conditions, a mixture of MeMgI (2.0 M, 2.0 mL, 4.0 mmol), bis(dithioacetal) 20 (304 mg, 1.0 mmol), and NiCl₂(chiraphos) (27 mg, 0.05 mmol) in benzene was allowed to react for 6 h to afford 21a and 21b (154 mg, 68%, 3:1). No optical selectivity was observed.

Reaction of Bis(dithioacetal) 22 with MeMgI. According to the procedure described above, a mixture of MeMgI (2.0 M, 2.0 mL, 4.0 mmol), 22 (290 mg, 1.0 mmol), and NiCl₂(PPh₃)₂ (33 mg, 0.05 mmol) in benzene was allowed to react for 8 h to give 23a and 23b (161 mg, 76%, 1:1). Isomers were separated by chromatography (EtOAc:hexane = 1:100). 23a: ¹H NMR (300 MHz) δ 1.60–1.68 (m, 3 H), 2.03–2.15 (m, 2 H), 2.29–2.42 (m, 4 H), 2.81 (br d, *J* = 17.4 Hz, 1 H), 3.20–3.34 (m, 4 H), 4.67 (br s, 1 H), 4.77 (br s, 1 H); ¹³C NMR (75 MHz) δ 24.6, 24.8, 34.5, 37.7, 39.2, 39.3, 40.8, 47.5, 69.4, 106.3, 149.3; MS (*m/z*, 70 eV) 212 (100), 184 (73), 151 (50), 119 (38), 108 (27), 91 (22); HRMS calcd for C₁₁H₁₆S₂ 212.0693, found 212.0699. 23b: ¹H NMR (200 MHz) δ 1.24–1.30 (m, 2 H), 1.48–1.57 (m, 1 H), 1.79 (br s, 3 H), 1.95–2.15 (m, 1 H), 2.20–2.23 (m, 2 H), 2.33–2.40 (m, 1 H), 2.65–2.70 (m, 1 H), 3.16–3.34 (m, 4 H), 5.96 (br d, *J* = 6.4 Hz, 1 H); ¹³C NMR (75 MHz) δ 20.2, 24.1, 24.5, 37.3, 39.4, 39.8, 44.8, 47.1, 70.9, 126.7, 143.6; MS (*m/z*, 70 eV) 212 (36), 184 (34), 151 (35), 119 (62), 108 (28), 91 (100); HRMS calcd for C₁₁H₁₆S₂ 212.0693, found 212.0699.

Reaction of Bis(dithioacetal) 24 with MeMgI. According to the procedure described above, a benzene solution of MeMgI (3.0 M, 2.0 mL, 6.0 mmol), 24 (292 mg, 1.0 mmol), and NiCl₂(dppf) (34 mg, 0.05 mmol) was allowed to react for 12 h, to give 25a and 25b (154 mg, 72%, 5:1). 25a was obtained by preparative GC (6 ft SE30). 25a: ¹H NMR (300 MHz) δ 0.99 (s, 6 H), 1.90 (s, 2 H), 2.08 (s, 2 H), 2.61 (s, 2 H), 3.26 (s, 4 H), 4.75 (br s, 1 H), 4.80 (br s, 1 H); ¹³C NMR (75 MHz) δ 29.6, 39.0, 47.7, 52.5, 53.3, 67.5, 111.6, 144.1; MS (*m/z*, 70 eV) 214 (17), 186 (15), 159 (100); HRMS calcd for C₁₁H₁₈S₂ 214.0850, found 214.0856. 25b was assigned from the mixture of 25a and 25b: ¹H NMR (300 MHz) δ 1.07 (s, 6 H), 1.64 (s, 3 H), 2.09 (s, 2 H), 2.47 (s, 2 H), 3.24–3.31 (m, 4 H), 5.16 (br s, 1 H).

Reaction of Bis(dithioacetal) 26 with MeMgI. According to the procedure described above, a benzene solution of MeMgI (2.0 M, 2.0 mL, 4.0 mmol), 26 (318 mg, 1.0 mmol), and NiCl₂(PPh₃)₂ (33 mg, 0.05 mmol) was allowed to react for 8 h to give 27a and 27b (153 mg, 72%, 8:1). Isomer 27a was obtained by preparative GC (6 ft SE30). 27a: ¹H NMR (300 MHz) δ 1.48–1.68 (m, 4 H, involved one singlet δ 1.68, 3 H), 1.82–2.15 (m, 3 H), 2.25–2.45 (m, 1 H), 2.49–2.57 (m, 1 H), 2.95–3.10 (m, 2 H), 3.20–3.28 (m, 4 H), 5.15 (br s, 1 H); ¹³C NMR (75 MHz) δ 14.9, 29.5, 38.2, 38.4, 39.3, 42.9, 52.4, 54.3, 123.2, 141.8; MS (*m/z*,

70 eV) 212 (46), 184 (100), 151 (46), 131 (67), 119 (71), 91 (43); HRMS calcd for C₁₁H₁₆S₂ 212.0693, found 212.0704. 27b was identified by comparing its spectroscopic properties with those of an authentic sample.

Preparation of 27b. Bis(dithioacetal) 26 (290 mg, 1.0 mmol) in THF (3.0 mL) was slowly added to a solution of red HgO (432 mg, 2.0 mmol) and BF₃·OEt₂ (0.25 mL, 2.0 mmol) in a 15% THF–water solution (5.0 mL). The mixture was stirred at room temperature for 20 h, diluted with Et₂O (15 mL), filtered, and dried (MgSO₄). The solvent was removed in vacuo, and the residue was chromatographed on silica gel (EtOAc:hexane = 5:100) to give monoketonedithioacetal 36 (77 mg, 36%) and recovered 26 (126 mg, 43%). 36: IR (neat) ν 2960, 2924, 1736, 1455, 1142 cm⁻¹; ¹H NMR (200 MHz) δ 1.52–1.92 (m, 2 H), 1.99–2.44 (m, 6 H), 2.66–2.78 (m, 1 H), 2.93–3.06 (m, 1 H), 3.21–3.31 (m, 4 H); ¹³C NMR (50 MHz) δ 25.8, 27.9, 38.6, 39.1, 39.3, 42.4, 50.5, 53.4, 75.4, 221.0; MS (*m/z*, 70 eV) 214 (100), 186 (53), 153 (17), 131 (68), 118 (23), 97 (30), 83 (25); HRMS calcd for C₁₀H₁₄OS₂ 214.0486, found 214.0490.

Treatment of 36 (55 mg, 0.25 mmol) with Me₃SiCH₂MgCl (1.0 M, 1 mL, 1.0 mmol) in THF (5.0 mL) at room temperature for 3 h was followed by quenching with NH₄Cl at 0 °C. The mixture was extracted with Et₂O, and the organic layer was washed with brine, dried (MgSO₄), and filtered. After removal of the solvent, the crude oily product was taken up into THF (5.0 mL) to which a trace amount of KH (ca. 10 mg) was added. The mixture was stirred at room temperature for 3 h and quenched with NH₄Cl at 0 °C. The organic layer was separated, and the aqueous layer was extracted twice with Et₂O (2 × 5.0 mL). The combined organic solution was washed with brine, dried (MgSO₄), and filtered. The solvent was removed in vacuo, and the residue was chromatographed on silica gel (EtOAc:hexane = 1:100) to afford 27b (33 mg, 62%): ¹H NMR (300 MHz) δ 1.36–1.49 (m, 1 H), 1.55–1.67 (m, 1 H), 1.92–2.40 (m, 6 H), 2.82 (q, *J* = 8.4 Hz, 1 H), 2.95–3.02 (m, 1 H), 3.20–3.34 (m, 4 H), 4.77 (br s, 1 H), 4.86 (br s, 1 H); ¹³C NMR (75 MHz) δ 31.4, 32.5, 34.9, 38.5, 39.0, 42.4, 46.8, 57.2, 104.8, 158.1; MS (*m/z*, 70 eV) 212 (71), 184 (80), 151 (37), 131 (100), 119 (32), 91 (42); HRMS calcd for C₁₁H₁₆S₂ 212.0693, found 212.0692.

Reaction of Bis(dithioacetal) 28 with MeMgI. According to the procedure described above, a mixture of MeMgI (3.0 M, 2.0 mL, 6.0 mmol), 28 (292 mg, 1.0 mmol), and NiCl₂(PPh₃)₂ (33 mg, 0.05 mmol) in benzene was allowed to react for 16 h to give 29 (163 mg, 76%), which was purified by HPLC (EtOAc:hexane = 1:100): IR (neat) δ 3024, 2926, 2854, 1727, 1445, 1276, 968 cm⁻¹; ¹H NMR (300 MHz) δ 1.24–1.45 (m, 3 H), 1.58–1.72 (m, 6 H involved one doublet δ 1.67, *J* = 6.0 Hz, 3 H), 1.85–1.94 (m, 1 H), 2.13–2.30 (m, 1 H), 2.30–2.38 (m, 1 H), 3.16–3.21 (m, 4 H), 5.50 (dq, *J* = 6.0, 15.4 Hz, 1 H), 5.61 (dd, *J* = 7.8, 15.4 Hz, 1 H); ¹³C NMR (75 MHz) δ 18.2, 24.3, 26.0, 32.8, 38.6, 39.3, 43.9, 52.2, 126.3, 132.8; MS (*m/z*, 70 eV) 214 (2), 186 (100), 153 (40), 131 (79); HRMS calcd for C₁₁H₁₈S₂ 214.0850, found 214.0851.

Reaction of Bis(dithioacetal) 30 with MeMgI. According to the procedure described above, a mixture of MeMgI (2.0 M, 2.0 mL, 4.0 mmol), 30 (278 mg, 1.0 mmol), and NiCl₂(PPh₃)₂ (33 mg, 0.05 mmol) in benzene was allowed to react for 20 h to give a mixture of 31a, 31b, and 31c (162 mg, 82%, 1:1:4). These products exhibited the same physical properties as those of the authentic samples.

Preparation of 31a and 31b. Ketone 37 (404 mg, 2.0 mmol) in ether (5.0 mL) was treated with MeMgI (2.0 M, 2.0 mL, 4.0 mmol) at room temperature for 1 h. The mixture was cooled to 0 °C and quenched with NH₄Cl. The organic layer was separated, and the aqueous solution was extracted twice with Et₂O (2 × 15 mL). The combined organic solution was washed with brine, dried (MgSO₄), and filtered. The solvent was removed in vacuo to give an oil, which was dissolved in benzene (20 mL). *p*-TsOH (10 mg) was added. The mixture was refluxed for 20 h using a Dean–Stark water separator to remove water. After the mixture was cooled to room temperature, the solvent was removed in vacuo and the residue was chromatographed on silica gel (EtOAc:hexane = 1:100) to afford a mixture of 31a and 31b (300 mg, 74%, 2:3). Isomers were separated by HPLC (EtOAc:hexane = 1:100). 31a: ¹H NMR (300 MHz) δ 1.71 (br s, 3 H), 1.74–1.95 (m, 2 H), 2.01–2.13 (m, 2 H), 2.18–2.29 (m, 2 H), 2.75–2.90 (m, 4 H), 2.96–3.05 (m, 1 H), 4.05 (d, *J* = 6.5 Hz, 1 H), 5.34 (br s, 1 H); ¹³C NMR (75 MHz) δ 16.6, 26.1, 28.2, 30.5, 30.6, 36.5, 50.7, 54.2, 124.5, 143.0; MS (*m/z*, 70 eV) 200 (4), 119 (100), 106 (4), 94 (37), 91 (9), 79 (27); HRMS calcd for C₁₀H₁₆S₂ 200.0693, found 200.0687. 31b: IR (neat) ν 3040, 2922, 1439, 1421, 1015, 910 cm⁻¹; ¹H NMR (300 MHz) δ 1.68 (br s, 3 H), 1.75–1.90 (m, 1 H), 2.03–2.13 (m, 1 H), 2.31–2.51 (m, 4 H), 2.55–2.65 (m, 1 H), 2.77–2.89 (m, 4 H), 4.06 (d, *J* = 7.3 Hz, 1 H), 5.20 (br s, 1 H); ¹³C NMR (75 MHz) δ 16.4, 26.1, 30.5, 36.7, 40.7, 43.0, 54.0, 123.1, 139.2; MS

(m/z , 70 eV) 200 (6), 119 (100), 106 (11), 93 (61), 77 (18); HRMS calcd for $C_{10}H_{16}S_2$ 200.0693, found 200.0693.

Preparation of 31c. Ketone **37** (404 mg, 2.0 mmol) in THF (10 mL) was treated with Me_3SiCH_2MgCl (1.5 M, 3.0 mL, 4.5 mmol) at 0 °C. The mixture was allowed to warm to room temperature and stirred for another 2 h. After the mixture was cooled to 0 °C and quenched with NH_4Cl (10 mL), the organic layer was separated and the aqueous solution was extracted twice with Et_2O (2×10 mL). The combined organic solution was washed with brine, dried ($MgSO_4$), and filtered. After removal of solvent in vacuo, the residue was taken up in THF (20 mL) and treated with KH (400 mg, 10.0 mmol). The mixture was stirred at room temperature for 4 h. After the mixture was cooled to 0 °C and quenched with NH_4Cl (10 mL), the organic layer was separated and the aqueous solution was extracted twice with Et_2O (2×10 mL). The combined organic solution was washed with brine, dried ($MgSO_4$), and filtered. The solvent was removed in vacuo, and the residue was chromatographed on silica gel ($EtOAc$:hexane = 1:100) to afford **31c** (260 mg, 65%): 1H NMR (300 MHz) δ 1.49–1.64 (m, 1 H), 1.77–1.93 (m, 1 H), 1.96–2.15 (m, 2 H), 2.19–2.32 (m, 2 H), 2.37–2.48 (m, 1 H), 2.57 (br q, J = 7.9 Hz, 1 H), 2.79–2.91 (m, 4 H), 3.99 (d, J = 7.9 Hz, 1 H), 4.81–4.83 (m, 2 H); ^{13}C NMR (75 MHz) δ 26.1, 30.4, 30.6, 32.3, 37.6, 44.7, 52.7, 105.8, 150.9; MS (m/z 70 eV) 200 (47), 119 (100), 106 (31); HRMS calcd for $C_{10}H_{16}S_2$ 200.0693, found 200.0693.

Reaction of 32 with MeMgI. Following the general procedure, the reaction of **32** (252 mg, 1.0 mmol), $MeMgI$ (2.5 mL of a 2.0 M solution in ether, 5.0 mmol), and $NiCl_2(dppe)$ (26 mg, 0.05 mmol) in THF gave **33a** (125 mg, 72%): IR 2964, 2921, 1642, 1442, 1373, 897 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 1.73 (s, 3 H), 1.85 (s, 3 H), 2.72 (s, 2 H), 3.32 (s, 4 H), 4.84 (s, 1 H), 4.90 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 32.3, 39.6, 52.9, 65.5, 115.7, 142.4; MS (m/z (relative intensity) 174 (M^+ , 4), 119 (100), 105 (6), 77 (7), 59 (26); HRMS calcd for $C_8H_{14}S_2$ 174.0536, found 174.0537.

Reaction of 32 with $PhMe_2SiCH_2MgCl$. Following the general procedure, the reaction of **32** (252 mg, 1.0 mmol), $PhMe_2SiCH_2MgCl$ (5.0 mL of a 1.0 M solution in benzene, 5.0 mmol), and $NiCl_2(PPh_3)_2$ (33 mg, 0.05 mmol) in benzene gave recovered **32** (55 mg, 22%) and **33b** (161 mg, 52%): IR 3069, 2957, 2921, 1628, 883, 836 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 0.31 (s, 6 H), 1.72 (s, 3 H), 1.99 (s, 2 H), 2.55 (s, 2 H), 3.19–3.34 (m, 4 H), 4.71 (s, 1 H), 4.77 (s, 1 H), 7.33–7.35 (m, 3 H), 7.50–7.52 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –3.0, 26.8, 32.0, 39.4, 52.7, 65.8, 113.3, 127.7, 129.0, 133.7, 138.9, 143.4; MS (m/z (relative intensity) 308 (M^+ , 9), 135 (100), 119 (79); HRMS calcd for $C_{16}H_{24}S_2Si$ 308.1089, found 308.1084.

Reaction of 34 with MeMgI. Following the general procedure, the reaction of **34** (280 mg, 1.0 mmol), $MeMgI$ (2.5 mL of a 2.0 M solution in ether, 5.0 mmol), and $NiCl_2(PPh_3)_2$ (33 mg, 0.05 mmol) in benzene gave **35** (132 mg, 70%): IR 3074, 2908, 1642, 897 cm^{-1} ; 1H NMR (200 MHz, $CDCl_3$) δ 1.66 (s, 3 H), 1.89 (s, 3 H), 1.89–1.98 (m, 2 H), 2.65 (s, 2 H), 2.83–2.89 (m, 4 H), 4.80 (s, 1 H), 4.94 (s, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.8, 25.2, 26.8, 28.0, 48.4, 49.4, 116.5, 141.1; MS (m/z (relative intensity) 188 (M^+ , 3), 133 (100), 113 (7), 99 (15), 85 (23), 83 (37), 59 (13); HRMS calcd for $C_9H_{16}S_2$ 188.0693, found 188.0698.

Reaction of Bis(dithioacetal) 39 with MeMgI. According to the procedure described above, a mixture of $MeMgI$ (2.0 M, 2.0 mL, 4.0 mmol), bis(dithioacetal) **39** (264 mg, 1.0 mmol), and $NiCl_2(PPh_3)_2$ (33 mg, 0.05 mmol) in benzene was allowed to react for 24 h to give **40a** and **40b** (33 mg, 18%, **40a**:**40b** = 3:2) and recovered **39** (198 mg, 75%). Isomers were separated by HPLC ($EtOAc$:hexane = 1:100). **40a**: 1H NMR (200 MHz) δ 2.05–2.11 (m, 4 H), 2.28–2.34 (m, 4 H), 3.29 (s, 4 H), 4.64 (br s, 2 H); ^{13}C NMR (50 MHz) δ 34.5, 38.4, 43.7, 68.1, 108.2, 146.7; MS (m/z , 70 eV) 186 (100), 158 (24), 125 (20), 118 (19), 93 (62); HRMS calcd for $C_9H_{14}S_2$ 186.0537, found 186.0522. **40b**: 1H NMR (300 MHz) δ 1.66 (br s, 3 H), 2.07–2.11 (m, 2 H), 2.14–2.18 (m, 2 H), 2.61 (br s, 2 H), 3.26–3.36 (m, 4 H), 5.34 (m, 1 H); ^{13}C NMR (75 MHz) δ 23.2, 30.4, 38.6, 38.8, 42.3, 65.5, 120.3, 134.0; MS (m/z , 70 eV) 186 (71), 158 (3), 118 (100), 93 (9); HRMS calcd for $C_9H_{14}S_2$ 186.0537, found 186.0530.

Reaction of Bis(dithioacetal) 41 with MeMgI. According to the procedure described above, a mixture of $MeMgI$ (2.0 M, 2.0 mL, 4.0 mmol), bis(dithioacetal) **41** (292 mg, 1.0 mmol), and $NiCl_2(PPh_3)_2$ (33 mg, 0.05 mmol) in benzene was allowed to react for 28 h to recover **41** (278 mg, 95%).

Reaction of Bis(dithioacetal) 42a with Me_3SiCH_2MgCl . Under N_2 , Me_3SiCH_2MgCl (1.5 M, 4.0 mL, 6.0 mmol) in ether was evacuated to remove ether. Bis(dithioacetal) **42a** (252 mg, 1.0 mmol) and $NiCl_2(PPh_3)_2$ (33 mg, 0.05 mmol) in benzene (15 mL) were added, and the

mixture was refluxed for 12 h. After being cooled to room temperature, the mixture was quenched with saturated NH_4Cl and extracted with ether. The organic solution was washed with $NaOH$ (10%) and brine. The combined organic layers were dried ($MgSO_4$) and evaporated to give the residue, which was purified by flash chromatography on silica gel (hexane) to afford **43a**²² (161 mg, 76%, $E:Z$ = 9:1). (*1E,3E*)-**43a** was obtained by HPLC (hexane): 1H NMR (300 MHz) δ –0.02 (s, 9 H), 0.06 (s, 9 H), 1.52 (d, J = 8.2 Hz, 2 H), 5.57 (d, J = 18.3 Hz, 1 H), 5.73 (dt, J = 8.2, 15.0 Hz, 1 H), 5.92 (dd, J = 9.7, 15.0 Hz, 1 H), 6.45 (dd, J = 9.7, 18.3 Hz, 1 H); ^{13}C NMR (50 MHz) δ –1.9, –1.1, 23.7, 128.6, 132.3, 132.7, 144.8; MS (m/z , 20 eV) 212 (25), 124 (47), 109 (44), 73 (100).

Reaction of Bis(dithioacetal) 42a with $PhMe_2SiCH_2MgCl$. According to the procedure described above, a solution of $PhMe_2SiCH_2MgCl$ (1.5 M, 4.0 mL, 6.0 mmol), bis(dithioacetal) **42a** (252 mg, 1.0 mmol), and $NiCl_2(PPh_3)_2$ (33 mg, 0.05 mmol) in benzene was refluxed for 16 h to give **43b** (282 mg, 84%, $E:Z$ = 10:1). (*1E,3E*)-**43b**: IR (neat) ν 3007, 2957, 1696, 1631, 1427, 1250, 1114, 999, 831 cm^{-1} ; 1H NMR (300 MHz) δ 0.26 (s, 6 H), 0.31 (s, 6 H), 1.78 (d, J = 8.3 Hz, 2 H), 5.66–5.78 (m, 2 H, involved one doublet δ 5.69, J = 18.5 Hz), 5.98 (dd, J = 10.3, 14.9 Hz, 1 H), 6.49 (dd, J = 10.3, 18.5 Hz, 1 H), 7.34–7.35 (m, 6 H), 7.47–7.50 (m, 4 H); ^{13}C NMR (75 MHz) δ –3.3, –2.5, 22.8, 126.4, 127.7, 127.8, 128.8, 129.1, 132.6, 132.9, 133.5, 133.8, 138.5, 139.2, 146.3; MS (m/z , 70 eV) 336 (8), 197 (15), 186 (27), 135 (100), 124 (38); HRMS calcd for $C_{21}H_{28}S_2$ 336.1730, found 336.1729. (*1E,3Z*)-**43b**: 1H NMR (300 MHz) δ 0.26 (s, 6 H), 0.31 (s, 6 H), 1.88 (d, J = 10.4 Hz, 2 H), 5.53 (q, J = 10.4 Hz, 1 H), 5.83 (d, J = 18.2 Hz, 1 H), 5.98 (t, J = 10.4 Hz, 1 H), 6.73 (dd, J = 10.4, 18.2 Hz, 1 H), 7.30–7.35 (m, 6 H), 7.45–7.51 (m, 4 H); ^{13}C NMR (75 MHz) δ –3.4, 0.0, 22.6, 112.9, 127.7, 127.8, 127.9, 129.1, 129.7, 130.5, 131.4, 133.0, 133.6, 133.9, 137.5.

Reaction of Bis(dithioacetal) 42b with Me_3SiCH_2MgCl . According to the procedure described above, a solution of Me_3SiCH_2MgCl (2.0 M, 3.0 mL, 6.0 mmol), bis(dithioacetal) **42b** (304 mg, 1.0 mmol), and $NiCl_2(PPh_3)_2$ (33 mg, 0.05 mmol) in benzene was refluxed for 36 h to give **43g** (206 mg, 69%, $E:Z$ = 3:1). (*1E,3E*)-**43g**: IR (neat) ν 3026, 2953, 1625, 1566, 983, 870, 837 cm^{-1} ; 1H NMR (300 MHz) δ 0.00 (s, 9 H), 0.06 (s, 9 H), 1.46 (s, 2 H), 3.49 (s, 2 H), 5.69 (d, J = 18.0 Hz, 1 H), 5.88 (d, J = 10.4 Hz, 1 H), 6.85 (dd, J = 10.4, 18.0 Hz, 1 H), 7.14–7.20 (m, 3 H), 7.24–7.29 (m, 2 H); ^{13}C NMR (75 MHz) δ –1.1, 27.7, 38.5, 126.1, 128.4, 128.7, 130.0, 139.9, 140.2, 140.5; MS (m/z , 70 eV) 302 (100), 229 (5), 199 (37), 185 (3), 155 (14), 135 (86), 123 (38), 91 (15); HRMS calcd for $C_{18}H_{30}S_2Si$ 302.1886, found 302.1891. (*1E,3Z*)-**43g**: IR (neat) ν 2953, 2896, 1627, 1570, 1171, 987, 879, 837 cm^{-1} ; 1H NMR (200 MHz) δ 0.05 (s, 9 H), 0.06 (s, 9 H), 1.67 (s, 2 H), 3.30 (s, 2 H), 5.66 (d, J = 18.2 Hz, 1 H), 5.78 (d, J = 10.6 Hz, 1 H), 6.63 (dd, J = 10.6, 18.2 Hz, 1 H), 7.13–7.32 (m, 5 H); ^{13}C NMR (50 MHz) δ –1.1, –0.6, 22.4, 46.2, 126.2, 127.0, 128.3, 129.2, 130.0, 139.7, 141.2, 141.6; MS (m/z , 70 eV) 302 (100), 199 (42), 155 (13), 135 (63), 123 (29), 91 (26); HRMS calcd for $C_{18}H_{30}S_2Si$ 302.1886, found 302.1885.

Reaction of Bis(dithioacetal) 42c with Me_3SiCH_2MgCl . According to the procedure described above, a solution of Me_3SiCH_2MgCl (2.0 M, 3.0 mL, 6.0 mmol), bis(dithioacetal) **42c** (304 mg, 1.0 mmol), and $NiCl_2(PPh_3)_2$ (33 mg, 0.05 mmol) in benzene was refluxed for 24 h to give **43d** (206 mg, 69%): IR (neat) ν 2948, 1611, 1245, 984, 884, 836 cm^{-1} ; 1H NMR (300 MHz) δ 0.01 (s, 9 H), 0.02 (s, 9 H), 0.05 (s, 9 H), 1.46 (s, 2 H), 1.66 (s, 2 H), 5.45 (d, J = 18.2 Hz, 1 H), 5.61 (d, J = 10.8 Hz, 1 H), 6.57 (dd, J = 10.8, 18.2 Hz, 1 H); ^{13}C NMR (75 MHz) δ –1.1, –0.9, –0.7, 25.1, 31.0, 123.6, 125.6, 141.3, 141.9; MS (m/z , 70 eV) 298 (15), 211 (5), 195 (4), 122 (15), 73 (100), 45 (22); HRMS calcd for $C_{15}H_{34}S_2Si$ 298.1968, found 298.1968.

Reaction of Substrate 47 with Me_3SiCH_2MgCl . According to the procedure described above, a solution of Me_3SiCH_2MgCl (1.5 M, 5.5 mL, 8.2 mmol), **47** (384 mg, 1.0 mmol), and $NiCl_2(PPh_3)_2$ (33 mg, 0.05 mmol) in benzene was refluxed for 14 h to give, after workup **48a** and **48b** (263 mg, 76%, 1:1). Isomers were separated by HPLC (hexane). **48a**: IR (neat) ν 3008, 2953, 2897, 1625, 1567, 1420, 1246, 1148, 984, 838 cm^{-1} ; 1H NMR (300 MHz) δ 0.01 (s, 9 H), 0.05 (s, 9 H), 1.62 (s, 2 H), 1.79–1.90 (m, 1 H), 2.06–2.13 (m, 1 H), 2.54 (d, J = 7.2 Hz, 2 H), 2.77–2.91 (m, 4 H), 4.15 (t, J = 7.2 Hz, 1 H), 5.66 (d, J = 18.1 Hz, 1 H), 5.84 (d, J = 10.5 Hz, 1 H), 6.71 (dd, J = 10.5, 18.1 Hz, 1 H); ^{13}C NMR (75 MHz) δ –1.2, –1.1, 25.7, 28.5, 30.8, 38.4, 46.9, 129.7, 130.7, 137.2, 139.8; MS (m/z , 70 eV) 344 (14), 149 (8), 119 (100), 73 (55); HRMS calcd for $C_{16}H_{32}S_2Si$ 344.1484, found 344.1480. **48b**: IR (neat) ν 3014, 2952, 2897, 1627, 1577, 1422, 1247, 1147, 967, 838 cm^{-1} ; 1H NMR (300 MHz) δ 0.02 (s, 9 H), 0.15 (s, 9 H), 1.54 (d, J = 7.6 Hz, 2 H), 1.73–1.88 (m, 1 H), 2.02–2.12 (m, 1 H), 2.66 (d, J = 7.5 Hz, 2

H), 2.74–2.86 (m, 4 H), 4.22 (t, $J = 7.5$ Hz, 1 H), 5.45 (s, 1 H), 5.77 (dt, $J = 7.6, 16.0$ Hz, 1 H), 5.90 (d, $J = 16.0$ Hz, 1 H); ^{13}C NMR (75 MHz) δ -1.7, 0.6, 23.7, 25.8, 31.2, 37.4, 47.3, 127.7, 130.4, 133.4, 149.4; MS (m/z , 70 eV) 344 (3), 147 (30), 119 (98), 91 (10), 73 (100); HRMS calcd for $\text{C}_{16}\text{H}_{32}\text{S}_2\text{Si}_2$ 344.1484, found 344.1483.

General Procedure for the Coupling Reaction of a Thioether Dithioacetal with a Grignard Reagent. To a benzene (15 mL) solution of dithioacetal (1.0 mmol) and $\text{NiCl}_2(\text{PPh}_3)_2$ (0.05 mmol) was added MeMgI (3.0 mL, 2 M in ether, 6 mmol). The mixture was refluxed for 16 h. Saturated NH_4Cl (15 mL) was added, and the mixture was extracted with ether (15 mL \times 2). The organic layer was washed with sodium hydroxide (10%, 15 mL \times 2) and brine and then dried (MgSO_4). The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel (2% ethyl acetate in hexane) to give the corresponding product.

Reaction of 50 with MeMgI. Following the general procedure, the reaction of **50** (322 mg, 1.0 mmol), MeMgI (3.0 mL of a 2 M solution in ether, 6 mmol), and $\text{NiCl}_2(\text{PPh}_3)_2$ (33 mg, 0.05 mmol) in benzene gave **51** (129 mg, 70%): IR 2926, 2853, 1647, 1448, 891 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.08–1.27 (m, 5 H), 1.37 (d, $J = 5.4$ Hz, 1 H), 1.46 (m, 1 H), 1.62–1.76 (m, 5 H), 1.69 (s, 3 H), 2.12 (dd, $J = 14.2, 9.9$ Hz, 1 H), 2.41 (dd, $J = 14.2, 4.9$ Hz, 1 H), 2.94 (m, 1 H), 4.75 (s, 1 H), 4.83 (s, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 21.7, 26.2, 26.4, 28.2, 30.8, 43.1, 44.1, 44.7, 113.2, 143.1; MS (m/z (relative intensity)) 184 (M^+ , 9), 129 (19), 128 (19), 101 (14), 95 (100), 55 (73), 41 (87); HRMS calcd for $\text{C}_{11}\text{H}_{20}\text{S}$ 184.1285, found 184.1286.

Reaction of 52 with MeMgI. Following the general procedure, the reaction of **52** (262 mg, 1.0 mmol), MeMgI (2.5 mL of a 2.0 M solution in ether, 5.0 mmol), and $\text{NiCl}_2(\text{PPh}_3)_2$ (33 mg, 0.05 mmol) in benzene gave **51** (123 mg, 67%).

Reaction of 53 with MeMgI. Following the general procedure, the reaction of **53** (235 mg, 0.5 mmol), MeMgI (3.0 mL of a 2 M solution in ether, 6 mmol), and $\text{NiCl}_2(\text{PPh}_3)_2$ (33 mg, 0.05 mmol) in benzene gave **54** (94 mg, 65%): IR 3074, 2930, 1647, 1461, 890 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 0.92 (d, $J = 6.8$ Hz, 3 H), 0.98 (d, $J = 6.8$ Hz, 3 H), 1.29 (d, $J = 5.6$ Hz, 1 H), 1.70 (s, 3 H), 1.84 (m, 1 H), 2.13 (dd, $J = 14.0, 9.7$ Hz, 1 H), 2.36 (dd, $J = 14.0, 5.3$ Hz, 1 H), 2.97 (m, 1 H), 4.75 (s, 1 H), 4.83 (s, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 17.2, 20.5, 21.6, 32.7, 44.9, 113.2, 143.0; MS (m/z (relative intensity)) 144 (M^+ , 4), 101 (34), 89 (36), 67 (17), 55 (100), 41 (46); HRMS calcd for $\text{C}_8\text{H}_{16}\text{S}$ 144.0946, found 144.0973.

Reaction of 55 with MeMgI. Following the general procedure, the reaction of **55** (250 mg, 1.0 mmol), MeMgI (2.5 mL of a 2 M solution in ether, 5 mmol), and $\text{NiCl}_2(\text{PPh}_3)_2$ (33 mg, 0.05 mmol) in benzene gave **54** (98 mg, 68%).

Reaction of 56 with MeMgI. Following the general procedure, the reaction of **56** (310 mg, 1.0 mmol), MeMgI (3.0 mL of a 2 M solution in ether, 6 mmol), and $\text{NiCl}_2(\text{dppe})$ (26 mg, 0.05 mmol) in benzene gave **54** (84 mg, 58%).

Reaction of 59 with MeMgI. Following the general procedure, the reaction of **59** (282 mg, 1.0 mmol), MeMgI (2.5 mL of a 2 M solution in ether, 5 mmol), and $\text{NiCl}_2(\text{PPh}_3)_2$ (33 mg, 0.05 mmol) in benzene gave **60** (153 mg, 75%): IR 3473, 3071, 3028, 1642, 1605, 891 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.27 (s, 3 H), 1.66 (s, 1 H), 1.80 (m, 2H), 1.87 (s, 3 H), 2.24 (d, $J = 13.4$ Hz, 1 H), 2.30 (d, $J = 13.4$ Hz, 1 H), 2.72 (m, 2 H), 4.80 (s, 1 H), 4.95 (s, 1 H), 7.18–7.30 (m, 5 H); ^{13}C NMR (50 MHz, CDCl_3) δ 25.0, 27.0, 30.4, 44.3, 49.5, 72.2, 115.0, 125.7, 128.3, 128.4, 142.5, 142.6; exact mass calcd for $\text{C}_{14}\text{H}_{20}\text{O}$ 204.1514, found 204.1516.

Reaction of 61 with MeMgI. Following the general procedure, the reaction of **61** (296 mg, 1.0 mmol), MeMgI (2.0 mL of a 2 M solution in ether, 4 mmol), and $\text{NiCl}_2(\text{PPh}_3)_2$ (33 mg, 0.05 mmol) in benzene gave **62** (168 mg, 77%): IR 3069, 3027, 1643, 1605, 890 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.20 (s, 3 H), 1.77 (m, 2 H), 1.83 (s, 3 H), 2.23 (d, $J = 14.0$ Hz, 1 H), 2.30 (d, $J = 14.0$ Hz, 1 H), 2.64 (m, 2 H), 3.24 (s, 3 H), 4.75 (s, 1 H), 4.87 (s, 1 H), 7.18–7.30 (m, 5 H); ^{13}C NMR (75 MHz, CDCl_3) δ 22.9, 24.2, 30.0, 40.0, 45.2, 48.9, 76.6, 114.4, 125.7, 128.3, 128.4, 142.8, 142.9; exact mass calcd for $\text{C}_{15}\text{H}_{22}\text{O}$ 218.1670, found 218.1666.

Reaction of 63 with MeMgI. Following the general procedure, the reaction of **63** (219 mg, 1.0 mmol), MeMgI (2.0 mL of a 2 M solution in ether, 4.0 mmol), and $\text{NiCl}_2(\text{dppe})$ (26 mg, 0.05 mmol) in toluene gave **64**²⁶ (100 mg, 71%): ^1H NMR (200 MHz, CDCl_3) δ 1.00 (t, $J = 7.2$ Hz, 6 H), 1.71 (s, 3 H), 2.09–2.17 (m, 2 H), 2.50–2.58 (m, 2 H), 2.52

(q, $J = 7.2$ Hz, 4 H), 4.66 (s, 1 H), 4.70 (s, 1 H); ^{13}C NMR (50 MHz, CDCl_3) δ 11.7, 22.7, 34.9, 46.8, 51.3, 110.6, 144.5.

Reaction of 65 with MeMgI. Following the general procedure, the reaction of **65** (296 mg, 1.0 mmol), MeMgI (2.5 mL of a 2 M solution in ether, 5 mmol), and $\text{NiCl}_2(\text{dppe})$ (26 mg, 0.05 mmol) in toluene gave **66a** and **66b** (159 mg, 73%, **66a**:**66b** = 65:35), which exhibited spectroscopic properties identical with those of the authentic samples obtained by independent syntheses.

3,6-Dimethyl-1-phenyl-6-hepten-3-ol (66a). To an ether solution (10 mL) of 5-methyl-5-hexen-2-one (112 mg, 1.0 mmol) was added $\text{PhCH}_2\text{-CH}_2\text{MgBr}$ (1.2 mL, 1 M in ether, 1.2 mmol). The mixture was stirred for 8 h. Saturated NH_4Cl (10 mL) was added, and the mixture was extracted with ether (10 mL \times 2). The organic layer was washed with brine and dried (MgSO_4). The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel (10% ethyl acetate in hexane) to give **66a** (201 mg, 92%): IR 3383, 3068, 3027, 1649, 1604, 886 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.27 (s, 3 H), 1.42 (s, 1 H), 1.65–1.70 (m, 2 H), 1.74–1.82 (m, 2 H), 1.76 (s, 3 H), 2.08–2.14 (m, 2 H), 2.66–2.72 (m, 2 H), 4.73 (s, 2 H), 7.16–7.32 (m, 5 H); ^{13}C NMR (75 MHz, CDCl_3) δ 22.6, 26.8, 30.3, 32.2, 39.9, 43.8, 72.6, 109.8, 125.7, 128.3, 128.4, 142.5, 146.1; MS (m/z (relative intensity)) 218 (M^+ , 2), 200 (9), 149 (44), 144 (79), 131 (33), 113 (62), 95 (75), 91 (100); HRMS calcd for $\text{C}_{15}\text{H}_{22}\text{O}$ 218.1671, found 218.1678.

3,6-Dimethyl-1-phenyl-5-hepten-3-ol (66b). To an ether (10 mL) solution of 5-methyl-4-hexen-2-one (112 mg, 1.0 mmol) was added $\text{PhCH}_2\text{CH}_2\text{MgBr}$ (1.2 mL, 1 M in ether, 1.2 mmol). The mixture was stirred for 8 h. Saturated NH_4Cl (10 mL) was added, and the mixture was extracted with ether (10 mL \times 2). The organic layer was washed with brine and dried (MgSO_4). The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel (10% ethyl acetate in hexane) to give **66b** (181 mg, 83%): IR 3417, 3062, 3027, 1673, 1604, 850 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.23 (s, 3 H), 1.51 (br s, 1 H), 1.66 (s, 3 H), 1.74–1.80 (m, 2 H), 1.76 (s, 3 H), 2.23 (d, 2 H, $J = 7.7$ Hz), 2.67–2.72 (m, 2 H), 5.24 (t, 1 H, $J = 7.7$ Hz), 7.15–7.30 (m, 5 H); ^{13}C NMR (75 MHz, CDCl_3) δ 18.0, 26.1, 26.7, 30.4, 40.5, 43.6, 73.0, 119.1, 125.7, 128.3, 128.4, 135.5, 142.7; HRMS calcd for $\text{C}_{15}\text{H}_{22}\text{O}$ 218.1671, found 218.1662.

General Procedure for the Nickel-Catalyzed Cross-Coupling Reactions of Poly(thioethers) with MeMgI. Under an N_2 atmosphere, to a benzene solution (10 mL) of thioether (0.5 mmol) and $\text{NiCl}_2(\text{PPh}_3)_2$ (0.025 mmol) was added MeMgI (5 equiv) in benzene (10 mL). The resulting mixture was refluxed for 18 h and quenched with NH_4Cl . The organic layer was separated, and the aqueous portion was extracted with ether. The combined organic layers were washed with NaOH (10%) and water, dried (MgSO_4), and filtered. After evaporation of the solvent, the residue was chromatographed on silica gel (EtOAc:hexanes = 3:97), to give the products.

Reaction of 70a with MeMgI. In a manner similar to that described in the general procedure, a mixture of **70a** (205 mg, 0.5 mmol), $\text{NiCl}_2(\text{PPh}_3)_2$ (16 mg, 0.025 mmol), and MeMgI (1.2 mL, 2.0 M, 2.4 mmol) in benzene (10 mL) was refluxed for 18 h to afford **71a** (125 mg, 72%): ^1H NMR (CDCl_3 , 200 MHz) δ 1.36 (t, $J = 8.1$ Hz, 1 H), 1.70 (t, $J = 7.6$ Hz, 1 H), 2.38–2.41 (m, 4 H), 2.66–2.77 (m, 4 H), 2.80 (s, 4 H), 7.19–7.32 (m, 10 H); ^{13}C NMR δ 24.7, 30.6, 37.8, 39.1, 40.4, 43.1, 126.5, 128.2, 130.6, 137.3; MS (m/z) 348 (M^+ , 12), 287 (46), 223 (13), 207 (10), 194 (11), 163 (12), 129 (100), 123 (47), 117 (59), 107 (23), 91 (86), 61 (25); HRMS calcd for $\text{C}_{19}\text{H}_{24}\text{S}_3$ 348.1040, found 348.1043.

Reaction of 70b with MeMgI. In a manner similar to that described in the general procedure, a mixture of **70b** (295 mg, 0.5 mmol), $\text{NiCl}_2(\text{PPh}_3)_2$ (16 mg, 0.025 mmol), and MeMgI (1.2 mL, 2.0 M, 2.4 mmol) in benzene (10 mL) was refluxed for 18 h to afford **71b** (136 mg, 78%) and **72b** (85 mg, 82%). **71b**: ^1H NMR (CDCl_3 , 200 MHz) δ 1.30 (t, $J = 8.0$ Hz, 1 H), 1.68–1.82 (m, 3 H), 2.25 (t, $J = 7.2$ Hz, 2 H), 2.50 (q, $J = 7.0$ Hz, 2 H), 2.62 (d, $J = 7.7$ Hz, 2 H), 2.92 (d, $J = 13.8$ Hz, 2 H), 3.07 (d, $J = 13.8$ Hz, 2 H), 7.22–7.32 (m, 10 H); ^{13}C NMR δ 23.8, 26.3, 31.4, 32.9, 43.3, 53.9, 126.8, 128.0, 130.9, 136.6; MS (m/z) 348 (M^+ , 12), 301 (8), 257 (53), 207 (6), 149 (24), 133 (23), 117 (58), 107 (100), 91 (50), 73 (13); HRMS calcd for $\text{C}_{19}\text{H}_{24}\text{S}_3$ 348.1040, found 348.1056. **72b**: ^1H NMR (CDCl_3 , 200 MHz) δ 3.27 (s, 4 H), 4.83 (s, 2 H), 7.13–7.33 (m, 10 H); ^{13}C NMR δ 42.1, 113.4, 126.1, 128.3, 129.1, 139.5, 148.3; MS (m/z) 208 (M^+ , 100), 193 (46), 179 (17), 167 (5), 154 (7), 129 (27), 117 (74), 104 (12), 91 (24); HRMS calcd for $\text{C}_{16}\text{H}_{16}$ 208.1252, found 208.1248.

Reaction of 70c with MeMgI. In a manner similar to that described in the general procedure, a mixture of **70c** (114 mg, 0.5 mmol), $NiCl_2 \cdot (PPh_3)_2$ (16 mg, 0.025 mmol), and MeMgI (1.2 mL, 2.0 M, 2.4 mmol) in benzene (10 mL) was refluxed for 18 h to afford **71c** (60 mg, 71%).

Reaction of 71a with MeMgI. In a manner similar to that described in the general procedure, a mixture of **71a** (100 mg, 0.29 mmol), $NiCl_2 \cdot (PPh_3)_2$ (37 mg, 0.058 mmol), and MeMgI (2 M, 0.9 mL, 1.8 mmol) in benzene (10 mL) was refluxed for 18 h to afford **73a** (44 mg, 68%); 1H NMR ($CDCl_3$, 300 MHz) δ 0.58 (s, 4 H), 2.62 (s, 4 H), 7.22–7.36 (m, 10 H); ^{13}C NMR δ 10.7, 20.8, 41.5, 125.9, 128.0, 129.5, 140.1; MS m/z 222 (M^+ , 74), 193 ($M - 29$, 29), 131 ($M - 91$, base peak), 91 ($M - 131$, 80).

A similar reaction was quenched with NH_4Cl after reacting for 4 h to give 2,2-dibenzyl 1,3-dithiol **74a** (8 mg, 10%), **73a** (10 mg, 16%), and recovered **71a** (60 mg, 60%). **74a**: 1H NMR ($CDCl_3$, 300 MHz) δ 1.40 (t, $J = 8.2$ Hz, 2 H), 2.46 (d, $J = 8.2$ Hz, 4 H), 2.86 (s, 4 H), 7.30–7.34 (m, 10 H); ^{13}C NMR δ 30.2, 39.7, 42.8, 126.5, 128.2, 130.5, 130.9; MS m/z 288 (M^+ , 100), 197 (18), 163 (32), 129 (70), 117 (42), 91 (54), 73 (18); HRMS calcd for $C_{17}H_{20}S_2$ 288.1006, found 288.0984.

Reaction of 74a with MeMgI. In a manner similar to that described in the general procedure, a mixture of **74a** (144 mg, 0.5 mmol), $NiCl_2 \cdot (PPh_3)_2$ (16 mg, 0.025 mmol), and MeMgI (1.2 mL, 2.0 M, 2.4 mmol) in benzene (10 mL) was refluxed for 18 h to afford **73a** (90 mg, 81%).

Reaction of 74b with MeMgI. In a manner similar to that described in the general procedure, a mixture of **74b** (151 mg, 0.5 mmol), $NiCl_2 \cdot (PPh_3)_2$ (16 mg, 0.025 mmol), and MeMgI (1.3 mL, 2.0 M in PhH , 2.6 mmol) in benzene (10 mL) was refluxed for 18 h to afford **73b** (89 mg, 75%); IR (neat) ν 3057, 2914, 2850, 1935, 1596, 1448, 1074, 904, 745, 698 cm^{-1} ; 1H NMR ($CDCl_3$, 300 MHz) δ 0.34–0.38 (m, 2 H), 0.46–0.49 (m, 2 H), 1.44–1.49 (m, 2 H), 2.67 (s, 2 H), 2.69–2.72 (m, 2 H), 7.08–7.32 (m, 10 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.7, 20.5, 33.1, 38.2, 41.7, 125.6, 126.0, 128.1, 128.2, 128.3, 129.3, 140.2, 142.7; MS m/z (relative intensity) 236 (M^+ , 60), 145 (100), 131 (23), 117 (18), 104 (52), 91 (84); HRMS calcd for $C_{18}H_{20}$ 236.1565, found 236.1575.

Reaction of 76 with MeMgI. In a manner similar to that described in the general procedure, a mixture of **76** (218 mg, 0.5 mmol), $NiCl_2 \cdot (PPh_3)_2$ (16 mg, 0.025 mmol), and MeMgI (1.8 mL, 2.0 M in $PhCH_3$, 3.6 mmol) in benzene (10 mL) was refluxed for 18 h to afford **77** (80 mg, 68%); IR (neat) ν 3479, 2921, 1490, 1449, 1371, 1134, 1028, 698 cm^{-1} ; 1H NMR ($CDCl_3$, 300 MHz) δ 0.45–0.49 (m, 2 H), 0.53–0.56 (m, 2 H), 1.15 (d, $J = 6.1$ Hz, 3 H), 1.71–1.87 (m, 2 H), 2.63–2.73 (m, 3 H), 3.32–3.47 (m, 3 H), 3.53–3.56 (m, 2 H), 7.14–7.28 (m, 5 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 8.9, 19.5, 22.7, 31.8, 38.2, 69.6, 75.1, 75.4, 125.8, 128.4, 142.1; MS m/z (relative intensity) 234 (M^+ , 1), 202 (2), 132 (100), 117 (30), 91 (38); HRMS calcd for $C_{15}H_{22}O_2$ 234.1620, found 234.1616.

1-Ethenyl-1-phenylcyclopropane (81a). Under N_2 , to a benzene solution (6 mL) of **78a** (704 mg, 4.0 mmol) and $NiCl_2(dppe)$ (106 mg, 0.2 mmol) was added MeMgI (6.0 mL, 1.5 M in benzene, 9.0 mmol). The resulting mixture was refluxed for 12 h and quenched with saturated NH_4Cl . The organic layer was separated, and the aqueous portion was extracted with ether. The combined organic layers were washed twice with brine, dried ($MgSO_4$), and filtered. The solvent was removed in vacuo, and the residue was subjected to flash chromatography (silica gel, hexane) to yield **81a**²⁹ (467 mg, 81%); 1H NMR (200 MHz, $CDCl_3$) δ 0.93–1.10 (m, 4 H), 4.58 (dd, $J = 1.4$, 17.1 Hz, 1 H), 4.88 (dd, $J = 1.4$, 10.3 Hz, 1 H), 5.71 (dd, $J = 10.3$, 17.1 Hz, 1 H), 7.23–7.29 (m, 5 H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 14.7, 28.7, 112.1, 126.3, 129.7, 143.0, 145.2; MS m/z (relative intensity) 144 (M^+ , 46), 129 (100), 115 (56), 102 (11), 91 (16).

1-Ethenyl-1-(2-tolyl)cyclopropane (81b). In a manner similar to that described above, a mixture of **78b** (760 mg, 4.0 mmol), $NiCl_2(dppe)$ (106 mg, 0.2 mmol), and MeMgI (6.0 mL, 1.5 M in benzene, 9.0 mmol) in benzene (6 mL) was refluxed for 36 h to give **81b** (569 mg, 90%); 1H NMR (300 MHz, $CDCl_3$) δ 0.98–1.11 (m, 4 H), 2.34 (s, 3 H), 4.54 (dd, $J = 1.4$, 17.1 Hz, 1 H), 4.85 (dd, $J = 1.4$, 10.3 Hz, 1 H), 5.50 (dd, 10.3, 17.1 Hz, 1 H), 7.14–7.27 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3, 19.4, 27.9, 111.6, 125.7, 126.7, 130.1, 130.8, 139.0, 140.4, 144.5; MS m/z (relative intensity) 158 (M^+ , 33), 143 (100), 128 (96), 115 (51); HRMS calcd for $C_{12}H_{14}$ 158.1096, found 158.1091.

1-Ethenyl-1-(4-tolyl)cyclopropane (81c). In a manner similar to that described above, a mixture of **78c** (760 mg, 4.0 mmol), $NiCl_2(dppe)$ (106 mg, 0.2 mmol), and MeMgI (6.0 mL, 1.5 M in benzene, 9.0 mmol) in benzene (6 mL) was refluxed for 10 h to give **81c** (468 mg, 74%); 1H NMR (200 MHz, $CDCl_3$) δ 1.00–1.13 (m, 4 H), 2.36 (s, 3 H), 4.58 (dd, $J = 1.4$, 17.1 Hz, 1 H), 4.87 (dd, $J = 1.4$, 10.3 Hz, 1 H), 5.50 (dd, 10.3, 17.1 Hz, 1 H), 7.14–7.27 (m, 4 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.7, 21.0, 30.9, 111.9, 128.7, 128.9, 129.7, 135.9, 145.5; MS m/z (relative intensity) 158 (M^+ , 31), 143 (100), 128 (74), 115 (35), 105 (5), 91 (9); HRMS calcd for $C_{12}H_{14}$ 158.1096, found 158.1091.

1-Ethenyl-1-(4-methoxyphenyl)cyclopropane (81d). In a manner similar to that described above, a mixture of **78d** (824 mg, 4.0 mmol), $NiCl_2(dppe)$ (106 mg, 0.2 mmol), and MeMgI (6 mL, 1.5 M in benzene, 9.0 mmol) in benzene (6 mL) was refluxed for 18 h to give **81d** (522 mg, 75%); 1H NMR (300 MHz, $CDCl_3$) δ 0.93–1.09 (m, 4 H), 3.80 (s, 3 H), 4.60 (dd, $J = 1.5$, 17.0 Hz, 1 H), 4.90 (dd, $J = 1.5$, 10.4 Hz, 1 H), 5.69 (dd, 10.4, 17.0 Hz, 1 H), 6.86 (dd, $J = 2.1$, 6.6 Hz, 2 H), 7.24 (dd, $J = 2.1$, 6.6 Hz, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.7, 28.0, 55.1, 111.8, 113.5, 130.9, 135.0, 145.7, 158.1; MS m/z (relative intensity) 174 (M^+ , 100), 159 (37), 143 (32), 128 (9), 122 (13), 91 (6); HRMS calcd for $C_{12}H_{14}O$ 174.1045, found 174.1050.

1-Ethenyl-1-(4-phenylbutyl)cyclopropane (81e). In a manner similar to that described above, a mixture of **78e** (928 mg, 4.0 mmol), $NiCl_2(dppe)$ (106 mg, 0.2 mmol), and MeMgI (6 mL, 1.5 M in benzene, 9.0 mmol) in benzene (6 mL) was refluxed for 24 h to give **81e** (448 mg, 56%); 1H NMR (200 MHz, $CDCl_3$) δ 0.51–0.56 (m, 4 H), 1.25–1.66 (m, 6 H), 2.59 (t, $J = 7.8$ Hz, 2 H), 4.54 (dd, $J = 1.4$, 17.1 Hz, 1 H), 4.84 (dd, $J = 1.4$, 10.4 Hz, 1 H), 4.91 (dd, $J = 10.4$, 17.1 Hz, 1 H), 7.12–7.31 (m, 5 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.0, 22.5, 26.8, 29.3, 31.8, 36.0, 110.5, 125.6, 128.2, 128.4, 142.8, 143.9; MS m/z (relative intensity) 200 (M^+ , 3), 185 (1), 171 (23), 143 (5), 129 (9), 117 (60), 104 (25), 91 (100), 79 (21); HRMS calcd for $C_{15}H_{20}$ 200.1565, found 200.1560.

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Supplementary Material Available: General procedures for the preparation of bis(dithioacetals) (**15**, **17**, **20**, **22**, **24**, **26**, **28**, **30**, **39**, **41**, **42b**, and **47**), thioether dithioacetals (**50**, **52**, **53**, **55**, **56**, **59**, **61**, **63**, **65**), poly(thioethers) (**70a–c**), and dihydrothiopyrans (**78b–e**) and their spectroscopic properties (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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