New Synthetic Applications of the Dithioacetal Functionality[†]

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Functional-group transformations leading to carbon–carbon bond formation are linchpins of synthetic endeavors. With the aid of transition-metal catalysts or reagents, the increasing numbers of new methodologies make the area highly fertile for synthetic surprise. A powerful addition to this arsenal includes the involvement of organosulfur compounds, the conversion of the carbon–sulfur bond(s) into carbon–carbon bond(s) being exceedingly useful.[1,2] The dithioacetal has two carbon–sulfur bonds attached to the same carbon atom. As such, the sequential displacement of these two bonds can be very versatile in synthesis. This functional group was first described in 1885.[3] However, most frequently this functionality is confined to serve as a latent carbonyl or methylene group.[4,5] Although the widespread use of 2-lithio-1,3-dithiane as a carbonyl anion synthon is fascinating,[6] the dithiane chemistry is still quite limited.
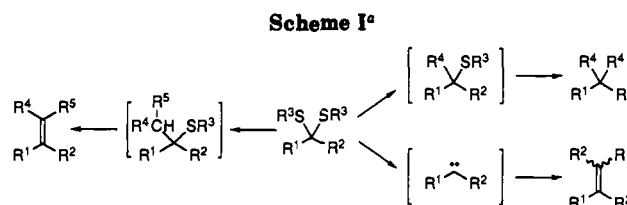
This Account reviews recent developments of synthetic applications of dithioacetals with respect to carbon–carbon bond formation. Three types of reactions are outlined in Scheme I. In the first instance, one of the carbon–sulfur bonds is replaced by a carbon–carbon bond, and subsequently the second carbon–sulfur bond is eliminated to produce an olefin. The second process involves replacement of both carbon–sulfur bonds by carbon–carbon bonds, which results in geminal dialkylation. The third possibility concerns desulfurization leading to a possible carbene-like intermediate, which may dimerize to give an olefin. Other carbon–carbon bond forming reactions, such as alkylative desulfurization, and related chemistry will also be briefly covered.

Nickel-Catalyzed Olefination Reactions

Nickel-catalyzed cross-coupling reactions of aryl, allyl, and vinyl organosulfur compounds with Grignard reagents (eq 1) are very effective in carbon–carbon bond formation.[1,2,7] Simple aliphatic substrates, however,

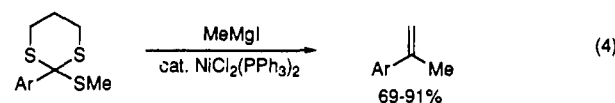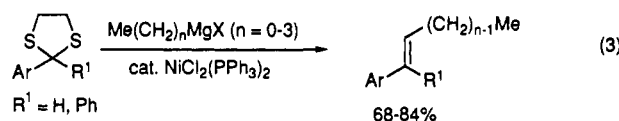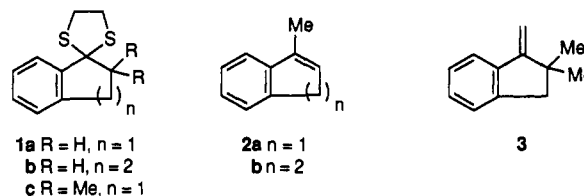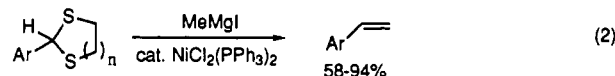$$R^1\text{-}S\text{-}R^2 + R^3MgX \xrightarrow{\text{cat. Ni(II)}} R^1\text{-}R^3 \quad (1)$$
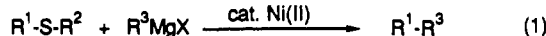
are inert, and benzylic thioethers and mercaptans give poor yields of the coupling products.[7] Our endeavor to expand the scope of the reaction resulted in the development of nickel-catalyzed olefinations of dithioacetals.[8] Thus, styrenes have been obtained in 58–94% yield (eq 2). This finding is a prototype of an olefination reaction from a dithioacetal functionality. Whereas cyclic ketone derivatives 1 give exclusively endocyclic

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Scheme I[a]

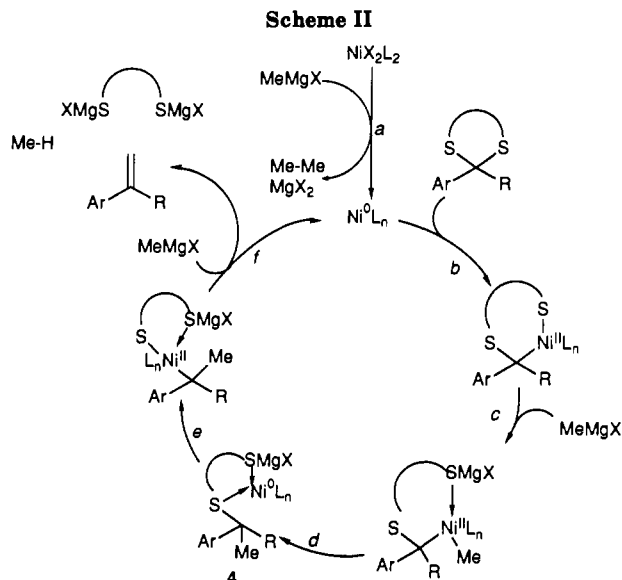[a]R^1 = aryl or vinyl; R^2 = H, alkyl, or aryl.

olefins 2, the highly sterically hindered dithioacetal 1c produces 3 in 78% yield. Homologous straight-chain Grignard reagents in the presence of a nickel catalyst react with aryl aldehyde and diaryl ketone derivatives similarly (eq 3).[8b] Further extension of this reaction to orthothioesters provides a new route for the alkylative olefination of an ester equivalent (eq 4).[9] Functional groups such as RO, F, Me_3Si, and Me_3Sn on the aromatic ring in dithioacetals remain intact under the reaction conditions. The benzylic trifluoromethyl group, on the other hand, is transformed into an isopropene moiety.[10]


$$(2)$$

58-94%

1a R = H, n = 1
 b R = H, n = 2
 c R = Me, n = 1

2a n = 1
 b n = 2

3

$$(3)$$

R^1 = H, Ph

68-84%

$$(4)$$

69-91%

[†] Dedicated to Professor Yau-Tang Lin on the occasion of his 80th birthday, from whom the author first learned organic chemistry.

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(2) (a) Naso, F. *Pure Appl. Chem.* 1988, 60, 79. (b) Fiandanese, V. *Pure Appl. Chem.* 1990, 62, 1987.

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(5) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*; 3rd ed.; Plenum: New York, 1990; Part B, p 266.

(6) For a recent review, see: Page, P. C. B.; van Niel, M. B.; Prodger, J. C. *Tetrahedron* 1989, 45, 7643 and references therein.

(7) (a) Okamura, H.; Miura, M.; Takei, H. *Tetrahedron Lett.* 1979, 43. (b) Wenkert, E.; Ferreira, T. W.; Michelotti, E. L. *J. Chem. Soc., Chem. Commun.* 1979, 637.

(8) (a) Ni, Z.-J.; Luh, T.-Y. *J. Chem. Soc., Chem. Commun.* 1987, 1515. (b) Ni, Z.-J.; Mei, N.-W.; Shi, X.; Wang, M. C.; Tzeng, Y.-L.; Luh, T.-Y. *J. Org. Chem.* 1991, 56, 4035.

(9) (a) Tzeng, Y.-L.; Luh, T.-Y.; Fang, J.-M. *J. Chem. Soc., Chem. Commun.* 1990, 399. (b) Weng, W.-W., unpublished results.

Scheme II

Aryl halides are expected to react under similar conditions (Kumada–Corriu reaction).[11] Palladium is an active catalyst for the cross coupling of Grignard reagents with aryl halides, but not with dithioacetals.[8b] Accordingly, selective transformations have been achieved (eq 5).[8b]
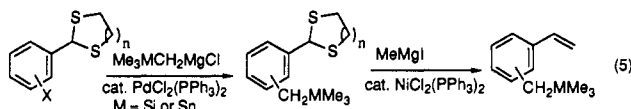
Mechanism. A plausible catalytic cycle for the nickel-catalyzed olefination of the dithioacetal with the Grignard reagent is presented in Scheme II.[8] Several points about this catalytic cycle are worthy of comment. First, the active Ni(0) catalyst is generated in situ by the reduction of $NiCl_2(PPh_3)_2$ with the Grignard reagent (step a).[8] Oxidative addition of this Ni(0) species with the dithioacetal (step b) and association of the Grignard reagent (step c) followed by reductive elimination (step d) afford intermediate 4. Further oxidative addition (step e) and β-elimination (step f) lead to the olefination product.

Secondly, the formation of the carbon–carbon bond precedes the elimination step, as clearly shown by the previous examples (eqs 2–5). In addition, treatment of 5 with Me_3SiCH_2MgCl gives the same product distribution (8 and 9) as that from the reaction of 6 with MeMgI (eq 6).[12a,13b] A common intermediate 7 must therefore be involved in both reactions.
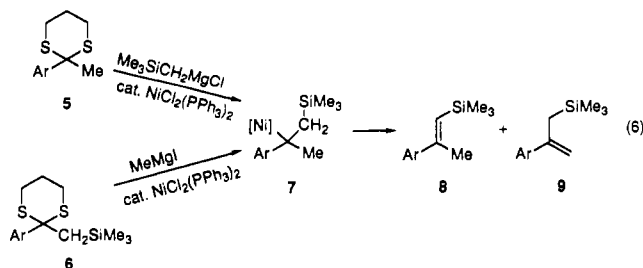
(10) Yu, C.-C., unpublished results.
(11) Kumada, M. *Pure Appl. Chem.* **1980**, *52*, 669.
(12) (a) Ni, Z.-J. Dissertation, The Chinese University of Hong Kong, 1989. (b) Wang, M. C., unpublished results.
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Table I
Product Distribution of the Nickel-Catalyzed Reactions of Dithioacetals with Me_3SiCH_2MgCl

Ar	% yield (9/8) from substrate 11a	% yield (9/8) from substrate 11b
2-fluorenyl	72 (90/10)	91 (32/68)
4-MeOC$_6$H$_4$	85 (73/27)	78 (14/86)
4-MeC$_6$H$_4$	77 (86/14)	73 (22/78)
4-PhC$_6$H$_4$	81 (89/11)	73 (34/66)
3-MeOC$_6$H$_4$	64 (86/14)	71 (40/60)
4-FC$_6$H$_4$	85 (80/20)	78 (32/68)

Thirdly, a benzylic thioether intermediate 4 may be involved. Benzylic thioethers are generally quite unreactive toward Grignard reagents even at elevated temperatures.[7,12] A possible scenario is that the cleavage of the remaining carbon–sulfur bond is facilitated by ligation of both sulfur atoms to nickel. The close proximity of the two sulfur atoms to each other apparently plays a part in the facile cleavage of both carbon–sulfur bonds during these nickel-catalyzed reactions. This phenomenon can be considered as a "sulfur tandem ancillary effect". To test the validity of this conjecture, the reactions of 10 (n = 2–4) with MeMgI at room temperature in the presence of the $NiCl_2(PPh_3)_2$ catalyst give the corresponding styrene in 60–70% yield (eq 7).[12b] On the other hand, when n = 6, 10 is relatively unreactive, presumably due to the unfavorable formation of a nine-membered chelate.[12b] These observations indicate that the terminal mercapto group may participate in the reaction, and a similar process (i.e., nickel insertion of the C–S bond, followed by β-elimination) is implied in the conversion of intermediate 4 into the product.
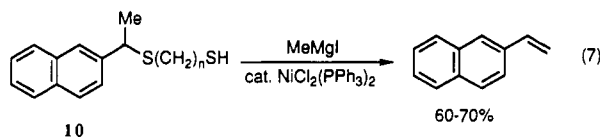
Fourthly, the reactions shown in eq 6 indicate that β-elimination of the organonickel intermediate 7 can occur in two different directions to give 8 and/or 9.[13] Interestingly, the ring size of the sulfur heterocycle in 11 affects the product distribution of the reactions (Table I), with five-membered dithiolanes 11a giving 9 predominantly, while six-membered dithianes 11b favor 8. This discrepancy disappears with the nickel catalyst contains a bidentate ligand such as dppe. Examination of the possible intermediate 12 reveals that both sulfur atoms of a dithioacetal may coordinate to the nickel throughout the catalytic cycle such that the stereoelectronic requirement of the metallacycle in 12 may determine the orientation of β-elimination.[13b]
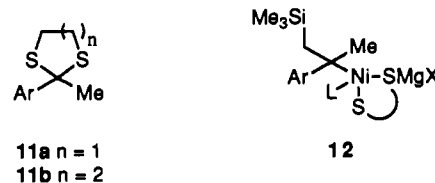
The fifth point concerning the catalytic cycle is the requirement of a second equivalent of the Grignard reagent for the elimination step (step f). The cross coupling of 13 with *i*-PrMgBr under the usual conditions gives, in addition to the desired olefin 14, the reduction product 15.[8] Cyclopentyl Grignard reagents

react similarly.[14] Intermediate **16** may undergo β-elimination competitively to give **17** and **18**. The latter may undergo reductive elimination producing **15** (eq 8).
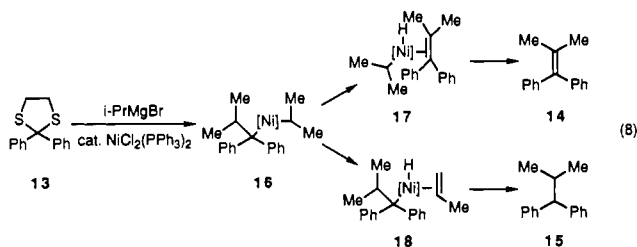
Syntheses of Dienes. Cyclopropylcarbinyl organometallic compounds readily undergo ring opening to give homoallylmetal species,[15] which may then be followed by a β-elimination leading to butadienes[16] (eq 9). On the basis of the mechanism shown in Scheme II, when a cyclopropyl Grignard reagent is employed, intermediate **19** is expected. Thus, the rearrangement of **19** according to eq 9 represents a facile stereoselective synthesis of substituted butadienes **20**.[17]

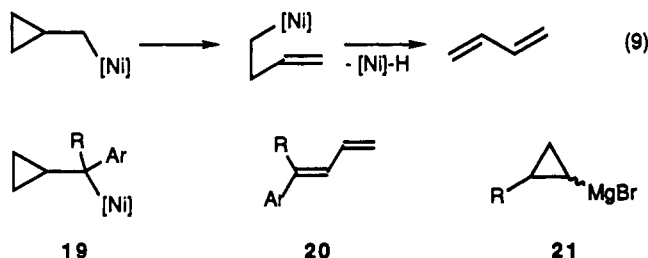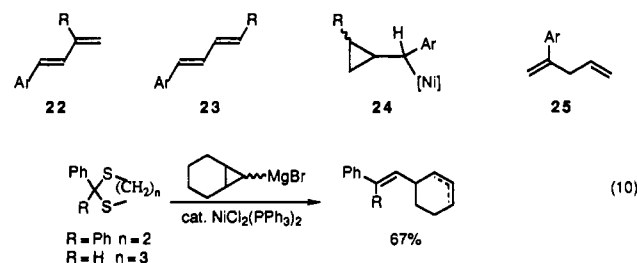The reaction of dithioacetals with 2-substituted cyclopropyl Grignard reagents **21** depends on the nature of the substituent. When R in **21** is an alkyl group, the reaction of **13** with **21** under the usual conditions yields a mixture of substituted butadienes **22** and **23**. The migration of the nickel atom and cleavage of the three-membered ring of intermediate **24** is nonselective. On the other hand, when R in **21** is an aryl group, regioselective rearrangement occurs and butadienes **23** are formed exclusively.[10,14] The reaction products from the norcarene Grignard reagent are mixtures of 1,4- and 1,5-dienes (eq 10).[17] The cyclobutyl analogue gives the normal cross-coupling product without ring opening.[17,18]

The coupling reactions involving cyclopropyl Grignard reagents illustrate the first example using cyclopropyl anion as an allyl anion synthon from which substituted butadienes can be conveniently synthesized. Mechanistically, the isolation of butadienes further validates the proposed catalytic cycle as shown in Scheme II, namely, the carbon–carbon bond formation preceding the elimination process.
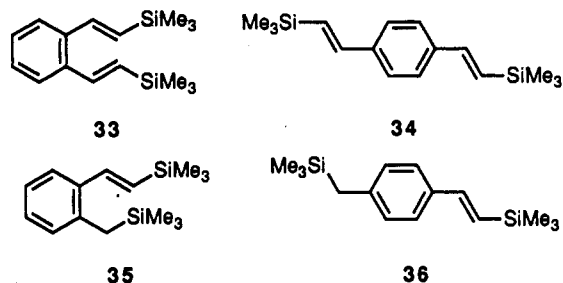
Reactions of dithioacetals **11** with allylmagnesium halides under the usual conditions provide a useful reference point to the reactions described above. Interestingly, 1,4-pentadienes **25** are the predominant, if not exclusive, products, and the conjugated diene **20** (R = Me) is a side product only when sterically hindered **11** (e.g., Ar = 1-naphthyl or 2-tolyl) is employed.[8b]

Syntheses of Vinylsilanes and Silylated Butadienes. Vinylsilanes and silylated butadienes have demonstrated an enormous variety of fascinating applications in organic synthesis.[19] Although synthetic methodologies for these building blocks are numerous, the nickel-catalyzed coupling reactions have provided a unified stereoselective synthesis of different kinds of vinylsilanes **26–28** (56–91% yield) and silylated butadienes **29–32** (65–97% yield).[20] In each olefin, the

	via dithioacetal	via Grignard reagent		R^1	R^2	R^3	R^4
			26	Ar-	Me₃Si	H	H
			27	Ar-	H	Me₃Si	H
			28	Ar-	Me₃Si	H	Me₃Si
			29	Ar-	Me₃Si	H₂C=CH-	H
			30	ArCH=CH-	Me₃Si	H	H
			31	RCH=CH-	H	Me₃Si	H
			32	RCH=CH-	Me₃Si	H	Me₃Si

left-hand-side moiety is derivable from a dithioacetal whereas the Grignard reagent provides the right-hand-side alkylidene moiety. The reaction is stereospecific, and only the *E* isomer, whenever applicable, is obtained.

Bis(vinylsilanes) **33** and **34** are obtained in 80 and 69% yields, respectively, from the corresponding bis-(dithioacetals).[20] As mentioned earlier, aryl halides also react under the reaction conditions.[11] Consequently, this reaction has been exploited for the one-step synthesis of **35** and **36**, each of which has both a vinylic and a benzylic silyl group.[20] Compounds like **35** would be very useful in annulation reactions.[21]

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(18) Ring opening has been found in cyclobutylcarbinyl organometallic systems. Cf.: (a) Lehmkuhl, H.; Rufinska, A.; Benn, R.; Schroth, G.; Mynott, R. *Liebigs Ann. Chem.* **1981**, 317. (b) Larock, R. C.; Varaprath, S. *J. Org. Chem.* **1984**, *49*, 3435 and references therein.

(19) For a recent review, see: Patai, S., Rappoport, Z., Eds. *The Chemistry of Organic Silicon Compounds*; Wiley: Chichester, 1989; Parts 1 and 2.

(20) (a) Ni, Z.-J.; Luh, T.-Y. *J. Org. Chem.* **1988**, *53*, 2129. (b) Ni, Z.-J.; Yang, P.-F.; Ng, D. K. P.; Tzeng, Y.-L.; Luh, T.-Y. *J. Am. Chem. Soc.* **1990**, *112*, 9356.

(21) (a) Sano, H.; Ohtsuka, H.; Migita, T. *J. Am. Chem. Soc.* **1988**, *110*, 2014. (b) Ito, Y.; Nakatsuka, M.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 863. (c) Ito, Y.; Miyata, S.; Nakatsuka, M.; Saegusa, T. *J. Org. Chem.* **1981**, *46*, 1043. (d) Djuric, S.; Sarkar, T.; Magnus, P. *J. Am. Chem. Soc.* **1980**, *102*, 6885.

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The reaction of an orthothioester with Me_3SiCH_2MgCl provides a facile synthesis of 37 which possesses both allyl- and vinylsilane functionalities (eq 11).[9] The product 37 may serve as a 1,3-dianion synthon (38) or a 1,1-dianion synthon (39).[9b]

$$37 \quad E/Z = 25\text{-}50/75\text{-}50$$
$$(48\text{-}79\%)$$
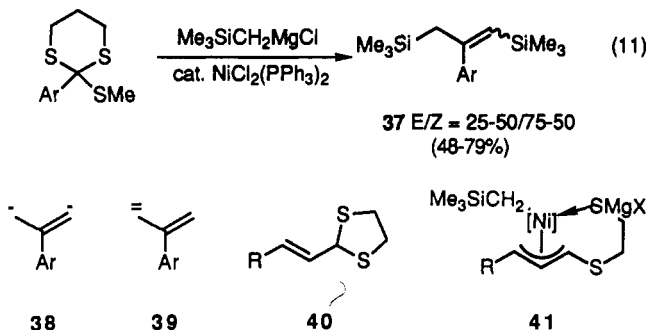
Allylic dithioacetal 40 has two possible sites (α vs γ positions) for coupling. While cross-coupling reactions of allylic geminal diacetates are generally nonselective,[22] the sulfur moiety in the proposed intermediate 41 may have a directive effect such that the regiochemistry of the reaction could be controlled. Thus, the synthesis of 1-(trimethylsilyl)butadienes 31 (R = alkyl or aryl) has been accomplished regio- and stereoselectively in 65–93% yield.[20b,23] 1-(Trimethylsilyl)hexatriene 42 has been prepared from the corresponding dienyldithiolane similarly.[20b,23a] A vinylsilane can be converted to an α,β-unsaturated aldehyde,[24] which can in turn serve as the precursor of a higher homologue of the vinylsilane. Consequently, by employing these two methodologies, homologation of enals can be achieved. The reaction of orthothioester 43 with an excess amount of Me_3SiCH_2MgCl under the usual conditions afforded 44.[20b]

The internal silyl dienes 30 can be prepared from the corresponding silylated dithioacetals 45 by reaction with MeMgI in the presence of a catalytic amount of $NiCl_2(PPh_3)_2$.[20b] As will be discussed later, simple allylic dithioacetals yield under similar conditions the corresponding geminal dimethyl derivatives as the major product, and the more sterically hindered dithioacetals give predominantly butadienes.[25] The exclusive formation of 30 must be due to the presence of the bulky Me_3Si group in 45. Similarly, the reactions of 45 (R = aryl) with Me_3SiCH_2MgCl give 32 in good yields stereospecifically.[20b] The reaction of the crotonaldehyde derivative 45 (R = Me) is worth noting, as none of the desired 32 (R = Me) is obtained. Instead, 46 is isolated as the sole product. It may be a consequence of steric control in the hydride elimination step that occurs preferably at the methyl carbon to give the more stable 46.
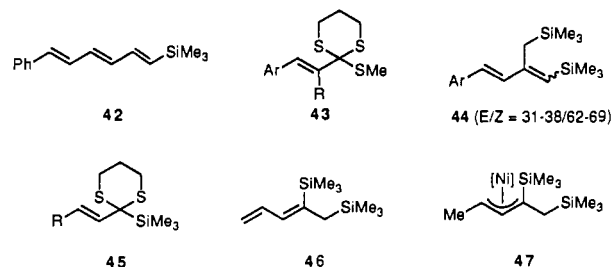
An approach to 1-aryl-1-(trimethylsilyl)butadienes 29 is based on the nickel-catalyzed coupling reaction of the

cyclopropyl Grignard reagent with trimethylsilyl-substituted dithioacetals (cf. eq 9). The reactions are stereospecific, and the yields are good.[20b]

A Possible β-Me_3Sn Elimination. Interestingly, the reactions of benzylic dithioacetals with Me_3SnCH_2MgI in the presence of a catalytic amount of $NiCl_2(PPh_3)_2$ afford styrenes in 62–84% yields (eq 12). No trace amount of vinylstannanes or allylstannanes has been detected.[26] It has been established that no transmetalation of vinylstannanes occurs under the reaction conditions. The active species for the dithioacetal cross-coupling reactions has been shown to be the "Me_3SnCH_2" moiety, and the reaction may proceed via a pathway similar to that shown in Scheme II. β-Elimination of the Me_3Sn group apparently occurs preferentially to give styrene. The actual mode of such an elimination step, however, is not clear. Either a concerted elimination mechanism or a stepwise radical process via the homolytic cleavage of the carbon–nickel bond from 48 followed by the elimination of a Me_3Sn radical would yield the same product.[27] An alternative possibility would be the elimination of a Me_3SnS moiety from a β-sulfurated organotin species 49.[26]
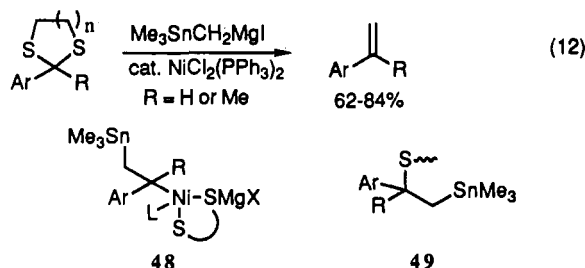
Tandem Reactions. As mentioned previously, simple aliphatic dithioacetals are inert toward Grignard reagents under similar conditions. A search for the activation of such a dithioacetal moiety has led to the development of the tandem coupling of bis(dithioacetals).[28] For example, the reaction of bis(dithioacetal) 50 with Me_3SiCH_2MgCl in the presence of a nickel catalyst produces dienes 51 in 50–70% yields with the Z isomers predominating ($Z/E \geq 6/1$). The success of this tandem reaction suggests the regioselective formation of the apparent intermediate 52.

Nickel-Catalyzed Geminal Dialkylation

Geminal Dimethylation of Allylic Dithioacetals.

Like many other transition-metal-catalyzed reactions,

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(23) (a) Ni, Z.-J.; Luh, T.-Y. *J. Org. Chem.* 1988, *53*, 5582. (b) Ni, Z.-J.; Luh, T.-Y. *Org. Synth.*, in press.
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(26) Shi, X.; Luh, T.-Y. *Organometallics* 1990, *9*, 3019.
(27) Curran, D. P.; van Elburg, P. A.; Giese, B.; Gilges, S. *Tetrahedron Lett.* 1990, *31*, 2861 and references therein.
(28) Wong, K.-T.; Luh, T.-Y., manuscript in preparation.

Dithioacetal Functionality
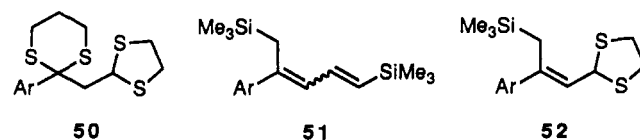
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the nickel-catalyzed coupling reaction of dithioacetals is very sensitive to the steric environment. When MeMgI is employed, the cross-coupling reactions of simple allylic dithioacetals **40** lead primarily to geminal dimethylation products **53** in addition to a small amount of butadienes **54**.[25] The formation of butadienes can be suppressed when bidentate ligands such as dppe or dppp are used in place of Ph₃P in the catalyst. The involvement of an 18-electron π-allyl intermediate **55** is likely to enhance the reductive elimination process, resulting in the facile formation of the second carbon–carbon bond.[29] The reactions are regiospecific, only geminal dimethylation products being obtained. This dimethylation reaction provides a unique procedure for the conversion of an α,β-unsaturated carbonyl equivalent into the corresponding geminal dimethyl group.

53 **54** **55**
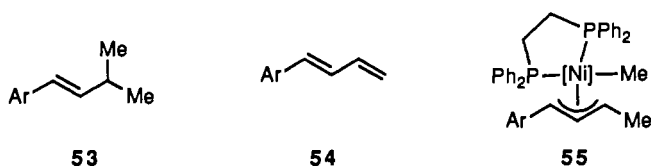
An extension of this reaction to allylic orthothioesters **43** (R = H) yields the trimethylated product **56**. To our surprise, the isolation of **57** indicates that the first methyl group is introduced at C-3. The presence of a substituent at C-2 in **43** (R = alkyl) would allow the coupling to be less selective; a mixture of **56** and **58** is generally obtained.[25b]

56 **57** **58**
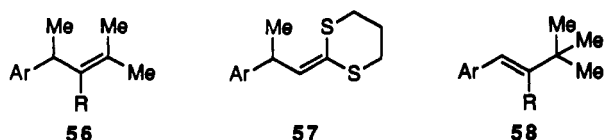
Geminal Dialkylation of Benzylic Dithioacetals. Other desulfurative geminal dialkylations of benzylic dithioacetals are also possible. Thus, the geminal diethyl products **59** have been isolated in 52–62% yields. Bisallylation of benzophenone and fluorenone dithioacetals gives **60**.[25b] Surprisingly, attempts to dimethylate benzylic substrates were unsuccessful; styrenes are always the major products. However, the presence of an ortho amino group (e.g., **61**) causes a dramatic change; e.g., 2-isopropylaniline **62** is obtainable in 60–70% yields.[25b] This neighboring amino moiety may enhance the rate of reductive elimination. An ortho hydroxyl group in the phenolic analogues, on the other hand, shows only a very weak neighboring effect; the corresponding styrenes were isolated as the predominant products.[25c]

59 **60** **61** **62**
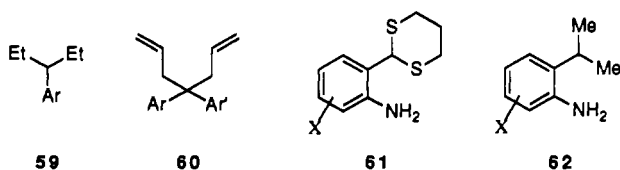
W(CO)₆-Mediated Desulfurdimerization of Dithioacetals

Thioketones react with a carbene precursor such as diazoalkane to give the corresponding 1,3-dithiolanes

(eq 13).[30] The reverse reaction considering a dithiolane as a carbene synthon would be useful in organic synthesis. Metal carbonyls are well documented to desulfurdimerize benzylic thioethers[31a] or thioketones.[31b,c] Our initial study has shown that the reaction of **63** with Mo(CO)₆ in refluxing THF gives a mixture of fluorene and bifluorenylidene **64** (eq 14).[32] The formation of **64** suggests that a carbene-like intermediate may be involved and can be considered as the reverse reaction shown in eq 13.

63 **64**
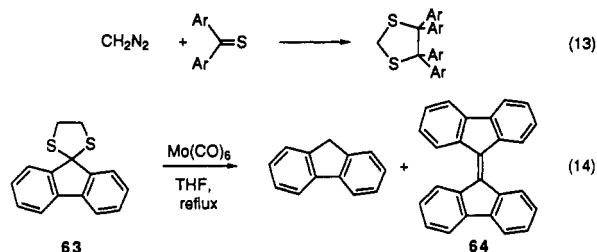
The group 6 metal carbonyl mediated C–S bond cleavage reaction has been established to occur via a free-radical mechanism.[31a,d] Therefore, the reduced product may arise from a hydrogen atom abstraction reaction from the solvent by a radical species. Halobenzenes have been shown to be an excellent solvent for the metal carbonyl promoted coupling of two in situ generated radical species.[33] Thus, upon treatment with W(CO)₆ in refluxing chlorobenzene, dithiolanes undergo desulfurdimerization reactions to give dimeric olefins in 45–97% yields (eq 15).[34,35] Dithiolanes derived from diaryl or alkyl aryl ketones work beautifully. Even adamantanone and diphenylketene dithioacetals desulfurdimerize to give biadamantylidene and tetraphenylbutatriene, respectively, in 71% yields. Functional groups such as ether, ester, nonbenzylic halide, acetal, and (aliphatic) thioether are stable under the reaction conditions. On the other hand, the presence of an acidic proton such as found in carboxylic acids or alcohols inhibits the dimerization reaction. The extension of this reaction to the synthesis of aryl-substituted poly(phenylenevinylenes) **65** has been performed (eq 16).[36]

65 X = H, Me, OMe (56-64%)

(29) (a) Kurosawa, H.; Ohnishi, H.; Emoto, M.; Kawasaki, Y.; Murai, S. *J. Am. Chem. Soc.* **1988**, *110*, 6272. (b) Kurosawa, H.; Ohnishi, H.; Emoto, M.; Chatani, N.; Kawasaki, Y.; Murai, S.; Ikeda, I. *Organometallics* **1990**, *9*, 3038.
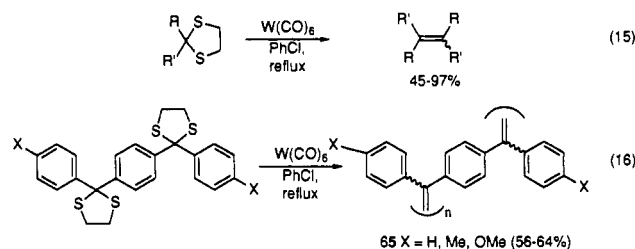
(30) (a) Schönberg, A.; König, B.; Einger, E. *Chem. Ber.* **1967**, *100*, 767. (b) Ohno, A.; Ohnishi, Y.; Fukuyama, M.; Tsuchihashi, G. *J. Am. Chem. Soc.* **1968**, *90*, 7038.

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The W(CO)$_6$-promoted intramolecular de-sulfurdimerization (eq 17) has been employed for the synthesis of bifluorenylidene-hinged crown ethers 66.[37] The first chiral bifluorenylidenes 67 were obtained by a similar reaction of two fluorene moieties linked with a chiral bridge.[37b,c] No dilution technique is required for this intramolecular reaction. Based on this procedure, (Z)-2,2'-disubstituted bifluorenylidenes 68 are conveniently prepared.[37]

$$X = \text{-O- or CO}_2\text{-}; \quad A = \text{-(CH}_2)_n\text{- (where } n = 2 \text{ to 11) or -(CH}_2\text{CH}_2\text{O)}_n\text{CH}_2\text{CH}_2\text{- (where } n = 0 \text{ to 4)}$$

67   68

Mechanism. The mechanism of the W(CO)$_6$-mediated desulfurdimerization reactions of dithiolanes 69 has been shown to proceed via a thioketone intermediate 71 (eq 18).[37c] The first carbon–sulfur bond is cleaved to generate a radical intermediate 70. Fragmentation of 70 gives 71 and ethylene as the organic products. Desulfurdimerization of thioketone promoted by metal carbonyls to give dimeric olefins has previously been established.[31b,c,37c]

The W(CO)$_6$-mediated reactions of 1,3-dithiane derivatives further support the involvement of a radical intermediate like 70. Treatment of the fluorenone dithiane with W(CO)$_6$ in refluxing chlorobenzene gives 64 and trimeric terfluorene 72 in 28% and 54% yields, respectively (eq 19).[38] The formation of 72 apparently involves a reduction process via an intramolecular 1,5-hydrogen atom transfer process.[39] Accordingly, 74 generated from 9-fluorenyl radical 73 may be the key intermediate leading to 72. The formation of 72 seems to be unique to substrates having the fluorenyl moiety. The benzophenone derivative, on the other hand, yields 75–77 (eq 20).[38] Generation of the reduced products 76 and 77 is also consistent with the proposed radical mechanism.

The extension of the desulfurdimerization to the coupling of a benzylic dithiolane moiety with a thio-amide group has been used as one of the key steps in a synthesis of functionalized benzazepines (eq 21).[40]

Miscellaneous Reactions

The open-chain dithioacetal functionality reacts with carbon nucleophiles in the presence of a thiophilic Lewis acid catalyst (eq 22).[41] High diastereoselectivity has been found in this coupling reaction (eq 23).[42] The reaction of allylstannane with dithioacetal is mediated by GaCl$_3$ to yield homoallyl sulfides (eq 24).[43] The Cu(I)-catalyzed intramolecular displacement of a γ-dithioacetal moiety with an enolate anion generated in situ constitutes a useful procedure for cyclo-propanation.[44] Ag(I)[45a] and TiCl$_4$[45b] have been employed to activate orthothioesters for the electrophilic substitution.

Other synthetic applications of the dithioacetal functionality have been sporadically investigated. Partial reduction of dithioacetals can be achieved by electrochemical methods[46] or by using a stoichiometric amount of n-Bu$_3$SnH[47] or (Me$_3$Si)$_3$SiH.[48] The tin hy-

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dride induced carbon–sulfur bond cleavage reaction has been used to generate a sulfur-stabilized radical that can add to a double bond, resulting in carbon–carbon bond formation.[49] Treatment of 1,3-dithiolanes with alkyllithium leads to mercaptans.[50] The carbon–sulfur bond in acyclic dithioacetals can be displaced by heteroatomic nucleophiles, which is a useful reaction in heterocycle syntheses.[51] The chemistry of ketene dithioacetals has been extensively studied.[52] Reductive metalation of ketene dithioacetals and subsequent reaction with carbon electrophiles provides a useful entry for carbon–carbon bond formation.[52c] The elimination of one of the carbon–sulfur bonds in acyclic dithioacetals has been used frequently in the preparation of vinyl sulfides.[53]

Conclusions

With the aid of various thiophilic reagents or catalysts, carbon–sulfur bonds in benzylic or allylic dithioacetals are readily replaced by carbon–carbon bond(s). The nickel chemistry and tungsten chemistry, together with other possibilities described in this Account, clearly demonstrate new types of useful synthetic reactions. The versatility of the dithioacetal functionality, at one time thought to be stable and not very useful, has now increased. Rather complicated reactions involving the carbonyl group (e.g., in vinylsilane synthesis) can now be simplified. The mechanistic insight of these reactions (e.g., the sulfur tandem ancillary effect) can pave the way to make predictions of other opportunities for new transformations, and room for new inventions emanating from the present research abounds. Because the chemistry of organosulfur compounds is so rich, such a prospect provides a major impetus for continuing the investigation of novel carbon–carbon bond formation methodologies starting from dithioacetals.

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