Propargylic Dithioacetal as an Allene 1,3-Dication Synthon. Nickel-Catalyzed Cross-Coupling Reactions of Propargylic Dithioacetals with Grignard Reagents†

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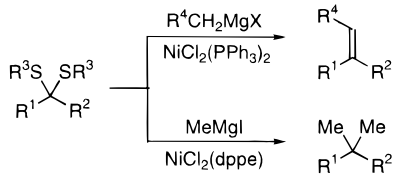
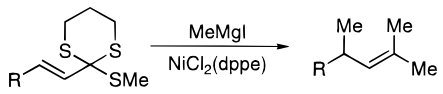
The synthesis of allenes from propargylic derivatives is well documented.[1,2] In general, a good leaving group is required to facilitate the S_N2' reaction leading to the formation of allenes. A series of the nickel-catalyzed cross-coupling reactions of dithioacetals with Grignard reagents was recently reported.[3−5] To illustrate, the reactions of allylic compound under these conditions give the corresponding geminal dimethylation[4] or the olefination products.[5]



The reaction can formally be considered as using the dithioacetal functionality as a geminal dication synthon. Interestingly, the $NiCl_2$(dppe)-catalyzed cross couplings of allylic trithioorthoesters with MeMgI afford the corresponding 1,1,3-trimethylation products, the first methyl group being introduced at the γ-position.[5a]



† Dedicated to Professor Y.-S. Cheng on the occasion of her 65th birthday.

(1) For reviews, see: (a) Tsuji, J.; Mandai, T. *J. Organomet. Chem.* **1993**, *451*, 15. (b) Tsuji, J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2589. (c) Tsuji, J.; Mandai, T. *Synthesis* **1996**, 1. (d) Landor, S. R., Ed. *The Chemistry of Allenes*; Academic Press: London, 1982.

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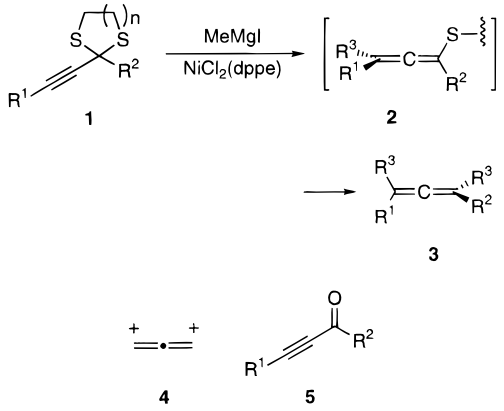
Table 1. $NiCl_2$(dppe)-Catalyzed Cross-Coupling Reactions of 1 with Grignard Reagents

reactant	*n*	R^1	R^2	R^3	product (% yield)
1a	2	Ph	H	Me	**3a** (88)[a]
1b	1	Ph	Me	Me	**3b** (90)
1c	1	Ph	Ph	Me	**3c** (79)
1d	1	Bu	Me	Me_3SiCH_2	**3d** (90)
1b	1	Ph	Me	Me_3SiCH_2	**3e** (92)
1e	1	Me_3Si	Me	Me_3SiCH_2	**3f** (95)[a]
1f	1	PhC≡C	Me	Me	**3g** (78)[a]
1b	1	Ph	Me	Ph	**3h** (56)
1c	1	Ph	Ph	Et	**3i** (55)[a,b]
1c	1	Ph	Ph	Bu	**3j** (57)[a,b]

[a] $NiCl_2$(dppf) was employed as the catalyst. [b] The reaction was carried out in benzene solvent at room temperature.

The analogous coupling reactions with propargylic dithioacetals (**1**) have not been investigated. Since the S_N2' reaction is so facile in the propargylic substrates, it was felt that the nickel-catalyzed cross-coupling reactions of **1** with the Grignard reagent R^3MgX would lead to an allenyl thioether **2** intermediate that can further couple with the Grignard reagent affording the substituted allenes **3**. Thus, the reaction can be viewed as employing the **1** as an allene 1,3-dication synthon **4**.

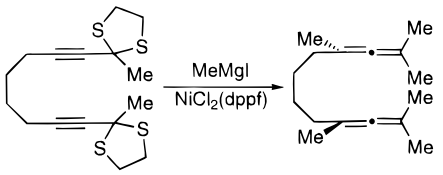


The propargylic dithioacetals **1** were obtained conveniently from the BF_3·OEt_2-catalyzed reactions of the corresponding ketones **5** with 1,2-ethanedithiol or 1,3-propanedithiol in methanol.[6] A benzene solution of **1** and 2.5 equiv of the Grignard reagent in the presence of 5 mol % of $NiCl_2$(dppe) or $NiCl_2$(dppf) was warmed at 65 °C for 4−12 h. After usual workup, the corresponding allenes **3** were obtained in good to excellent yield. No corresponding geminal dialkylation products were detected at all. Representative results are summarized in Table 1. The reaction proceeded extremely well when methyl or silylmethyl Grignard reagent was employed. Aryl or primary alkyl Grignard reagents gave the corresponding coupling products in moderate yields. However, secondary alkyl Grignard reagents afforded a mixture of products that were difficult to separate. No reaction was observed in the absence of the nickel catalyst.

Both tri- and tetrasubstituted allenes were efficiently synthesized by this procedure (Table 1). Silyl as well as alkynyl substituents are stable under these conditions. Allenylsilanes and silylmethyl-substituted allenes **3d**−**f** were prepared accordingly. Bisallene **7** was obtained in 81% yield from the reaction of bisdithioacetal **6** under the same conditions.

(6) Methanol solvent is essential for this transformation. (Cf. Williams, J. R.; Sarkisian, G. M. *Synthesis* **1974**, 32. Yuan, T.-M.; Luh, T.-Y. *Org. Synth.* **1996**, *74*, in press).

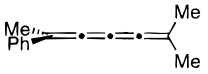
S0022-3263(96)01514-9 CCC: $12.00



6 **7**

The reaction may occur via a similar pathway for the cross-coupling reaction of allylic dithioacetals. However, the regioselective carbon−carbon bond formation at C_1 and C_3 appears to be different from the allylic counterpart. Presumably, the first coupling process may occur at the γ-position leading to an allenyl thioether intermediate **2** that undergoes further coupling with the Grignard reagent.

An attempt to synthesize cumulene **8** from **1f** by this procedure was unsuccessful. Rather, the corresponding alkynylallene **3g** was obtained. Again, a γ-attack may occur first followed by a similar displacement of the allenyl thioether intermediate to give **3g**.



8

Experimental Section

2- (Phenylethynyl)dithiane (1a). To a sodium-dried 2-propanol solution (30 mL) of 3-phenylpropynal (**5a**) (3.40 g, 39 mmol) and 1,3-propanedithiol (3.2 mL, 31 mmol) at 0 °C was added dropwise BF_3·OEt_2 (4.2 mL, 33 mmol). The mixture was stirred at 0 °C for 30 min, quenched with aqueous NaOH (10%), and extracted with ether (50 mL × 3). The organic layer was dried ($MgSO_4$) and the solvent was removed in vacuo to give a pale yellow oil, which was chromatographed on silica gel (1% EtOAc in hexane) to give **1a** as a white solid (4.21 g, 73%): mp 51−53 °C (lit.[7] 54−55.5 °C).

2- (Phenylethynyl)-2-methylditholane (1b). In a manner similar to that described for **1a**, a mixture of 4-phenylbutyn-2-one (**5b**) (5.61 g, 39 mmol), 1,2-ethanedithiol (3.9 mL, 47 mmol) and BF_3·OEt_2 (6.3 mL, 50 mmol) in methanol (125 mL) was converted to **1b** as a white solid (7.80 g, 91%): mp 43−45 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.11 (s, 3 H), 3.44−3.62 (m, 4 H), 7.25−7.28 (m, 3 H), 7.38−7.42 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.1, 40.5, 54.6, 82.6, 92.8, 122.6, 128.0, 128.1, 131.4; IR (KBr) 2220 cm^{-1}; HRMS calcd for $C_{12}H_{12}S_2$ 220.0380, found 220.0380.

2- (Phenylethynyl)-2-phenylditholane (1c). In a manner similar to that described for **1a**, phenyl phenylethynyl ketone (**5c**) (1.03 g, 5.0 mmol) was allowed to react with 1,2-ethanedithiol (0.5 mL, 6.0 mmol) in the presence of BF_3·OEt_2 (0.9 mL, 6.4 mmol) in methanol (25 mL) to yield **1c** as a white solid (0.71 g, 50%): mp 52−54 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.64−3.84 (m, 4 H), 7.28−7.41 (m, 6 H), 7.45−7.52 (m, 2 H), 7.96−8.03 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.3, 62.2, 86.8, 91.1, 122.7, 127.6, 128.2, 128.3, 128.4, 131.6, 138.7; IR (KBr) 2208 cm^{-1}; HRMS calcd for $C_{17}H_{14}S_2$ 282.0537, found 282.0532.

2- (Hex-1-yn-1-yl)-2-methylditholane (1d). In a manner similar to that described for **1a**, oct-3-yn-2-one (**5d**) (3.80 g, 30 mmol) was allowed to react with 1,2-ethanedithiol (3.0 mL, 36 mmol) in the presence of BF_3·OEt_2 (4.8 mL, 38 mmol) in methanol (40 mL) to yield **1d** as a colorless oil (2.39 g, 40%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.87 (t, J = 7.3 Hz, 3 H), 1.24−1.47 (m, 4 H), 1.98 (s, 3 H), 2.19 (t, J = 6.8 Hz, 2 H), 3.40−3.58 (m, 4 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.6, 18.6, 21.9, 30.6, 32.0, 40.5, 54.8, 83.7, 83.9; IR (neat) 2236 cm^{-1}; HRMS calcd for $C_{10}H_{16}S_2$ 200.0693, found 220.0703.

2-[(Trimethylsilyl)ethynyl]-2-methylditholane (1e). In a manner similar to that described for **1a**, 4- (trimethylsilyl)-butyn-2-one (**5e**) (6.56 g, 46 mmol) was allowed to react with 1,2-ethanedithiol (5.5 mL, 55 mmol) in the presence of BF_3·OEt_2 (9.6 mL, 59 mmol) in methanol (60 mL) to yield **1e** (5.85 g, 59%), bp 65−68 °C (0.9 mmHg), which solidified upon standing: mp 48−50 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.13 (s, 9 H), 1.98 (s, 3 H), 3.39−3.56 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −0.1, 31.0, 40.5, 54.3, 86.8, 108.7; IR (KBr) 2157 cm^{-1}; HRMS calcd for $C_9H_{16}S_2Si$ 216.0463, found 216.0467.

2-Ethynyl-2-methyldithiolane. Dithiolane **1e** (432 mg, 20.0 mmol) and K_2CO_3 (100 mg) in 20 mL methanol was stirred at room temperature for 3 h. Water (20 mL) was then added, and the mixture was extracted with ether (20 mL × 3). The organic layer was dried ($MgSO_4$), and the solvent was removed in vacuo to give a pale yellow oil that was distilled (275 mg, 96%), bp 40−42 °C (0.9 mmHg), and that solidified upon standing; mp 36−38 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.00 (s, 3 H), 2.65 (s, 1 H), 3.44−3.58 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.6, 40.6, 53.6, 70.9, 87.8; IR (KBr) 2108 cm^{-1}; HRMS calcd for $C_6H_8S_2$ 144.0067, found 144.0068.

2-(4-Phenylbutadiynyl)-2-methyldithiolane (1f). To a mixture of NH_2OH·HCl (0.5 g, 7.0 mmol), diethylamine (2 mL, 20 mmol), 2-ethynyl-2-methyldithiolane (710 mg, 5.00 mmol), and CuCl (75 mg, 0.75 mmol) in methanol/H_2O (14 mL, v/v = 5/9) was added at room temperature 1-bromo-2-phenylacetylene (1.09 g, 6.00 mmol) under a nitrogen atomsphere. The mixture was stirred for 30 min. A solution of KCN (0.25 g, 4.0 mmol) and NH_4Cl (1.0 g, 20 mmol) in water (15 mL) was then added with vigorous stirring. The mixture was extracted with ether. The organic layer was dried ($MgSO_4$), and the solvent was removed in vacuo to give a pale yellow solid, which was chromatographed on silica gel (1% EtOAc in hexane) to give **1f** as a white solid (1.10 g, 90%):; mp 65−67 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.05 (s, 3 H), 3.46−3.62 (m, 4 H), 7.28−7.34 (m, 3 H), 7.45 (dd, J = 1.5, 6.0 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.8, 40.7, 54.5, 67.6, 73.3, 80.9, 85.1, 121.6, 128.4, 129.2, 132.4; IR (KBr) 2172, 2231 cm^{-1}; HRMS calcd for $C_{14}H_{12}S_2$ 244.0380, found 244.0378.

Dodeca-3,9-diyne-2,11-dione Bis(ethylene dithioacetal) (6). To a sodium-dried methanol solution (40 mL) of dodeca-3,9-diyne-2,11-dione (1.90 g, 10.9 mmol) and 1,2-ethanedithiol (1.92 mL, 25.1 mmol) at 0 °C was added dropwise BF_3·OEt_2 (3.29 mL, 26.2 mmol). The mixture was stirred at 0 °C for 30 min, quenched with aqueous NaOH (10%), and extracted with ether. The organic layer was dried ($MgSO_4$), and the solvent was removed in vacuo to give a pale yellow solid, which was chromatographed on silica gel (5% EtOAc in hexane) to give **6** as a white solid (1.76 g, 47%): mp 54−56 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.54−1.59 (m, 2 H), 1.98 (s, 3 H), 2.20−2.24 (m, 2 H), 3.40−3.56 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.5, 27.6, 31.9, 40.5, 54.7, 83.2, 84.3; IR (KBr) 2213, 2233 cm$^{-1;}$ MS (20eV) m/z (rel intensity) 342 (M^+, 1), 316 (6), 280 (2), 242 (4), 209 (5), 171 (5), 131 (6), 119 (100).

2-Phenyl-2,3-pentadiene (3a). An ether solution of MeMgI (2.0 mL of 2 M solution, 4.0 mmol) was evacuated to remove the ether solvent. Under nitrogen atmosphere, a mixture of **1a** (220 mg, 1.00 mmol) and $NiCl_2$(dppf) (34 mg, 0.05 mmol) in benzene/THF (5mL, 19/1) was stirred at 65 °C for 12 h, quenched with saturated NH_4Cl (10 mL), and extracted with ether (10 mL × 3). The organic layer was dried ($MgSO_4$), and the solvent was removed in vacuo to give a pale yellow oil, which was chromatographed on silica gel (hexane) to give **3a** as a colorless oil (124 mg, 88%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.74 (d, J = 6.9 Hz, 3 H), 2.07 (d, J = 3.0 Hz, 3 H), 5.43 (qq, J = 3.0, 6.9 Hz, 1 H), 7.17 (t, J = 7.6 Hz, 1 H), 7.32 (dd, J = 7.6, 7.8 Hz, 2 H), 7.45 (d, J = 7.8 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 17.1, 87.5, 99.7, 125.6, 126.3, 128.2, 137.8, 204.9; IR (neat) 1955 cm^{-1}; HRMS calcd for $C_{11}H_{12}$ 144.0939, found 144.0935.

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Supporting Information Available: Experimental procedures for **3b-j** and **7** and ^{1}H NMR spectra for **3a**−**j** and **7** (14 pages). This material is contained in 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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