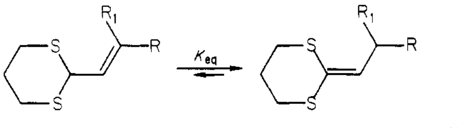
Communications

Dithiane Chemistry. 5.[1] Silyl and Lithio Derivatives of a Propynal Dithioacetal

Summary: 2-Ethynyl-1,3-dithiane and its various silyl and lithio derivatives are reported together with data on the regiochemistry of alkylation and proton abstraction. The α-lithio γ-silyl derivative **4b** is a particularly useful carbon nucleophile giving clean α-alkylation without complications due to allene formation.

Sir: Several years ago we prepared a variety of 2-alkynyl-1,3-dithiane derivatives as part of studies of the acidifying effects of 2-substituents on this ring system.[2] Recent applications[3] of ethynyldithianes in total synthesis prompt us to report these studies.

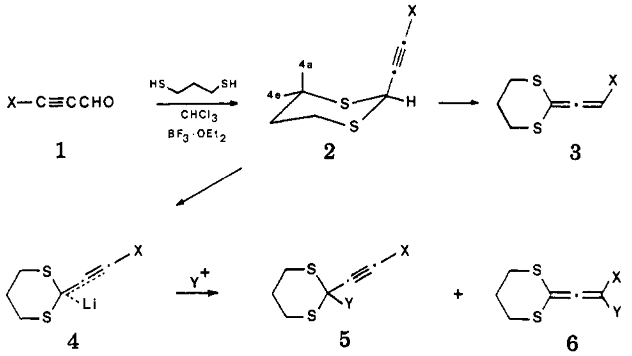
Our initial attempts to prepare the parent 2-ethynyl-1,3-dithiane (**2a**; Scheme I) from propynal, using Lewis ($BF_3 \cdot Et_2O$, $TiCl_4$, $SnCl_4$) or protic (TsOH) acid catalyzed dithioacetalization procedures,[4] were uniformily unsuccessful, the highest yield achieved being 7%. Dithiane **2a** can be prepared (35% yield) by the addition of ethynylmagnesium bromide[5] to in situ generated 2-chloro-1,3-dithiane.[6] Dithiane **2a** is a stable, readily sublimed solid [mp 71-72 °C; NMR (CCl_4) δ 2.0 (2 H, m, H-5), 2.60 (1 H, d, ^4J = 2.4 Hz), 2.70 (2 H, H-4,6 equatorial, ^3J = 3.4, 4.8 Hz), 3.28 (2 H, H-4,6 axial, ^2J = 14, $\sum {}^3J$ = 13.1 Hz), 4.43 (H-2, ^4J = 2.4 Hz)], which is isomerized, however, by basic catalysts or upon chromatography (Woelm Basic Al_2O_3, activity I) to the unstable allene **3a** [IR ν 1980 cm^{-1}; NMR δ 2.01 (2 H, m), 2.78 (4 H, m), 4.85 (2 H, m)]. This isomerization is yet another example of the exocyclic preference of olefinic bonds of this ring system, which has been noted previously (eq 1). Although allene formation is a concern for applications of dithiane **2a**, we have made its three distinct lithio species [**2e**, **4e**, and **5** (X = H, Y = Li)] and explored their reactions with electrophiles.



(1)

K_{eq} (R, R_1): 1.0-2.0 (C_6H_5, H),[2,7a] $\geqslant$99 (CN, H),[7b] 3.1 (CN, Et),[7b] $\geqslant$100 (H, H)[2]

Scheme I[a]



[a] The designations a-e apply uniformly for **1** → **6**: a, X = H; b, X = $SiMe_3$; c, X = Me; d, X = D; and e, X = Li.

Table I

molar proportions	products, % yield
0.29 **2a**, 1.8 MeI, then 1.0 $(Me_3Si)_2NLi$	**5c** (Y = Me), 90^+
0.29 **2a**, 21 MeI, then 1.0 $(Me_3Si)_2NLi$	**5c** (Y = Me), 53 **2c**, 40 **5a** (Y = Me), <2
0.60 **2a**, 18 MeI, then 0.85 $(Me_3Si)_2NLi$	**2c**, 70 **5c** (Y = Me), 12

In THF, dithiane **2a** is a dibasic carbon acid toward BuLi and many lithio amides (including *i*-Pr_2NLi, Et_2NLi, $C_6H_{11}NHLi$, $(CH_2)_4NLi$, and $C_6H_5CH_2NHLi$). With limiting quantities of BuLi the ethynyl H is abstracted. The solution resulting from treating **2a** with 1.1 molar equiv of BuLi affords only γ products upon quenching: D_3O^+ gives a 1:1 ratio of **2d** and **3d**, MeI also give a 1:1 ratio of alkyne (**2c**) and allene (**3c**), and Me_3SiCl provides a 5:1 ratio (**2b**/**3b**). The γ abstraction apparently corresponds to the thermodynamic preference. Equilibration (1 h at -70 °C) of the dideuterio derivative (**5**, X = Y = D), vide infra, with lithio-*n*-butylanilide and *n*-butylaniline gives exclusively the γ-protio species (**5a**, X = H, Y = D) upon quenching in acid-buffered H_2O; a D_2O quench returns nearly pure dideuterio compound. On this basis we estimate the first ionization constant as $pK_a \leq 23.1$.[8] The second ionization pK_a, **2e** → **4e**, is estimated at 26 from equilibration data with C_6H_5NHLi and $(Me_3Si)_2NLi$.

The dilithio species (**4e**) derived from alkyne **2a** or **2d** is a practical reagent. For synthetic applications, it is generated from **2a** by addition of 2.5 equiv of BuLi/THF-hexane (0.5 h at -70 °C). Quenching with excess electrophile (H_2O, D_2O, MeI, Me_3SiCl) affords in each case ethynyl product **5** (X = Y) to the virtual exclusion of allene **6**. The disilyl derivative **5b** (Y = $SiMe_3$) undergoes selective α-desilylation (→ **2b**) upon chromatography (basic Al_2O_3, activity I) or treatment with *n*-Bu_4NF/THF.

When **5b** is treated with 0.10 equiv of dry *n*-Bu_4NF/THF in the presence of piperonal, two products are formed in a ratio of 3:1. The major product by NMR is the allene **6** (X = Me_3Si, Y = CHOTMSAr); the minor product is the α-alkylated material **5**. When **5b** is treated with 0.10 equiv

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[1] For part 4 and references to earlier studies in this series, see D. B. Grotjahn and N. H. Andersen, *Chem. Commun.*, 306 (1981).

[2] A. D. Denniston, Ph.D. Thesis, University of Washington, 1979; *Diss. Abstr. Int. B*, **40**, 749 (1979). Reported in part as "A Basicity Scale for Lithium Amides in THF and THF-Hexamethylphosphoric Triamide", N. H. Andersen, A. D. Denniston, Second Chemical Congress of North America, Las Vegas, NV, Aug 25-29, 1980, ORGN-33.

[3] The α-lithio derivative (**4b**) of 2-[(trimethylsilyl)ethynyl]-1,3-dithiane has been used in the construction of acyclic polyene precursors for the olefin-carbocation route to corticosteroids; W. S. Johnson, Pauling Award Symposium, April 1980, Bellevue, WA; see W. S. Johnson, B. Frei, and A. S. Gopalan, *J. Org. Chem.* **46**, 1512 (1981).

[4] D. Seebach and E. J. Corey, *J. Org. Chem.*, **40**, 231 (1975).

[5] The use of lithium acetylide results in carbene formation from 2-chloro-1,3-dithiane rather than addition. Other Grignards have been reported[6] to be alkylated in an analogous manner.

[6] K. Arai and M. Oki, *Bull. Soc. Chem. Jpn.*, **49**, 553 (1976).

[7] (a) D. F. Coffen, T. E. McEntee, Jr., and D. R. Williams, *Chem. Commun.*, 913 (1970); (b) A. I. Meyers and R. C. Strickland, *J. Org. Chem.*, **37**, 2579 (1972).

[8] This "pK_a scale" for the formation of alkyllithiums in THF solution is based on a value of 30.6[10] for Ph_3CH → Ph_3CLi. The "pK_a values" for other 2-substitued-1,3-dithianes, for comparison, are as follows: 2-Me (~35), 2-phenyl (27.5), 2-cyano (19.7).[2]

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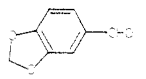
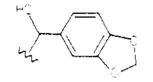
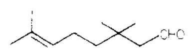
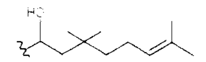
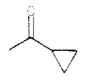
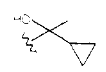
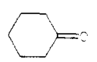
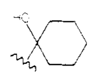
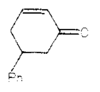
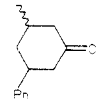
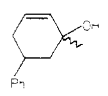
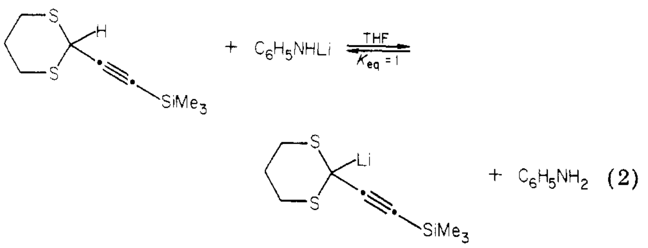
Table II. Reaction of 2-Lithio-2-[(trimethylsilyl)ethynyl]-1,3-dithiane with Electrophiles (Y^+)

Y^+	product 5b; Y	% yield
H_2O	H	>90
D_2O	D	>90
CH_3I	CH_3	>90
Me_3SiCl	$SiMe_3$	98
		67
		72
		78
		92
	 -  cis/trans 1:1 cis/trans 1:1	53

of dry n-Bu_4NF/THF in C_6D_6 with no electrophile, the isomerization to **6** (X = Y = Me_3Si) can be observed by NMR (ratio of **5b**/**6** ≤ 1:9). Unfortunately the lability of the allenes (**6**) has precluded their isolation and complete characterization to date.

The reactivity sequence of species **4e** was probed by partial alkylation. It would appear that initial reaction of this "dianion" occurs at the α-carbon: treatment with 1 equiv of MeI followed by a water quench affords **5a** (Y = Me) in >85% yield (GC). γ selective reaction without allene formation can be achieved through the stoichiometric γ-lithio derivative or by kinetic control, as illustrated by the product distributions given in Table I. In each case a THF solution of $(Me_3Si)_2NLi$ containing a 2-fold excess of $(Me_3Si)_2NH$ was added to a stirred mixture of dithiane **2a** and excess MeI in THF at −20 °C. After 30 min the product ratios were determined (by GC and/or NMR) after an aqueous quench.

Although the use of dianion **4e** alleviates the difficulties with allene formation inherent with anion **2e**, we have found γ-silyl derivative **2b** the most effective synthetically and the most readily available. Conversion of 3-(trimethylsilyl)propynal (**1b**)[9] to the corresponding dithiane (**2b**), mp 46–48 °C, occurs in acceptable yield (70–80%) under typical thioacetalization procedures.[4] Dithiane **2b** undergoes rapid and stoichiometric transmetalation in the presence of n-BuLi, i-Pr_2NLi, $(Me_3Si)_2NLi$, or $C_6H_5CH_2NHLi$ in THF solution. The acidity of **2b** is comparable to aniline in THF solution when lithium is the counterion (eq 2). This observation places dithiane **2b** at ca. 23 on our "pK_a" scale.[8]



(2)

The lithio species **4b** reacts with a variety of electrophiles (H_2O, D_2O, Me_3SiCl, MeI, allyl chlorides,[3] R_2CO, and RCHO; see Table II) to produce ethynyl (**5b**) rather than allenyl (**6b**) products in fair to excellent isolated yields. Aromatic and aliphatic aldehydes and aliphatic ketones are equally acceptable as electrophiles. It is interesting to note (Table I) the complete lack of regio- and stereoselectivity in reaction with 5-phenyl-2-cyclohexenone. Amide-catalyzed desilylation is not a drawback in synthetic applications; e.g., **2b** shows no detectable desilylation in the presence of $C_6H_5CH_2NLi/C_6H_5CH_2NH_2$/THF after 43 h at −20 °C—and thus lithium or potassium amide solutions can be used to generate anion **4b** for synthetic applications.

Although preliminary studies indicate that selective α-alkylation can be expected when dianion **4e** is reacted with limited quantities of electrophiles, at present the γ-silyl derivative appears the superior reagent for this sequence (**2b** → **4b** → **5b**). Ethynyldithiane derivatives should prove useful in the synthesis of olefinic and allenic natural products; such studies are in progress.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for a PRF grant used in partial support of this work, and the National Institues of Health for grant support (GM-20848, HL-23103).

Registry No. **1b**, 6224-91-5; **2a**, 80593-70-0; **2b**, 76649-03-1; **2c**, 22094-10-6; **2d**, 80593-71-1; **3a**, 80593-72-2; **3b**, 80593-73-3; **3c**, 80593-74-4; **3d**, 80593-75-5; **4b**, 76665-49-1; **5a** (Y = D), 80593-76-6; **5a** (Y = CH_3), 80593-77-7; **5b** (Y = H), 76649-03-1; **5b** (Y = D), 80593-78-8; **5b** (Y = CH_3), 80593-79-9; **5b** (Y = $SiMe_3$), 80593-80-2; **5b** (Y = CH(OH)-1,3-benzodioxol-5-yl), 80593-81-3; **5b** (Y = $CH(OH)CH_2C(Me_2)(CH_2)_2CH{=}CMe_2$), 80593-82-4; **5b** (Y = $C(CH_3)(OH)$c-Pr), 80593-83-5; **5b** (Y = 1-hydroxycyclohex-1-yl), 80593-84-6; **5b** (Y = *cis*-3-oxo-5-phenylcyclohex-1-yl), 80593-85-7; **5b** (Y = *trans*-3-oxo-5-phenylcyclohex-1-yl), 80593-86-8; **5b** (Y = *cis*-1-hydroxy-5-phenyl-2-cyclohexen-1-yl), 80612-08-4; **5b** (Y = *trans*-1-hydroxy-5-phenyl-2-cyclohexen-1-yl), 80593-87-9; **5c** (Y = CH_3), 80593-88-0; **5d** (Y = D), 80593-89-1; **6b** (Y = $CH(OSiMe_3)$-1,3-benzodioxol-5-yl), 80593-90-4; **6b** (Y = $SiMe_3$), 80593-91-5; ethynyl bromide, 593-61-3; 2-chloro-1,3-dithiane, 57529-04-1; 3-(trimethylsilyl)prop-2-yn-1-ol, 5272-36-6; piperonal, 120-57-0; 3,3,7-trimethyl-6-octenal, 17920-90-0; cyclopropyl methyl ketone, 765-43-5; cyclohexanone, 108-94-1; 5-phenyl-2-cyclohexenone, 35376-41-1.

Supplementary Material Available: Full spectroscopic data for compounds **2a–d**, **3a**, and representative examples of **5a**,**b**; illustrative experimental procedures (3 pages). Ordering information is given on any current masthead page.

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[9] Prepared by oxidation of 3-(trimethylsilyl)propyn-1-ol[11] in 50–60% yield. See also: A. N. V. Komarov, O. G. Yarosh, and L. N. Astaf'eva, *Zh. Obsch. Khim.*, **36**, 907 (1966), from lithium (trimethylsilyl)acetylide and DMF; V. Jaeger, *Methoden Org. Chim.* (*Houben-Weyl*), 329 (1977).

[10] W. S. Matthews et al., *J. Am. Chem. Soc.*, **97**, 7006 (1975).

[11] E. J. Corey, G. W. J. Fleet, and M. Kato, *Tetrahedron Lett.* 3963 (1973).

$\Delta^{4,4'}$-4-Telluropyranyl-4*H*-telluropyrans. 1. Tellurosulfides and Tellurium-Sulfur Exchange

Summary: $\Delta^{4,4'}$-2,2′,6,6′-Tetraphenyl-4-telluropyranyl-4*H*-telluropyran and $\Delta^{4,4'}$-7,7′-dimethoxy-2,2′-diphenyl-4-(benzo[*b*]telluropyranyl)-4*H*-benzo[*b*]telluropyran were prepared from the corresponding 4*H*-telluropyran-4-thiones and copper powder in refluxing toluene and re-