

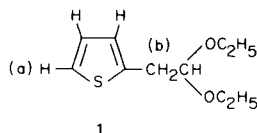
## The Reaction of (2-Thienyl)acetaldehyde Diethylacetal with Alkali Metal Bases

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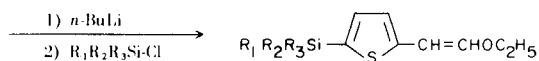
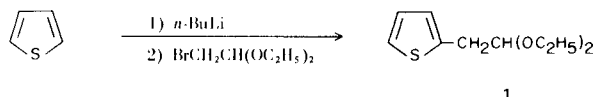
Received June 10, 1971

Our initial investigations employed the 1,3-dioxolane (2) and acetal (3) moieties as carbonyl blocking groups during *n*-butyllithium metalations of the heterocyclic nuclei of thiophene and furan. Subsequently we became interested in the production of multiple anions from a heterocyclic substrate containing a "blocked" carbonyl group. Consequently,  $\alpha$ -(2-thienyl)acetaldehyde diethylacetal (1) with active hydrogens at positions *a* and *b* was selected for reaction with *n*-butyllithium.



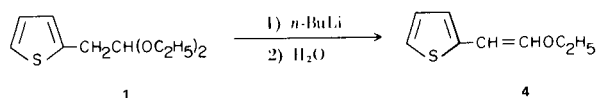
When treated with *n*-butyllithium 1 did not provide a stable dianion but instead was found to undergo a unique elimination-substitution reaction. Treatment of the generated anion with an appropriate electrophile, trimethylchlorosilane or phenyldimethylchlorosilane, resulted in the production of [5-(trimethylsilyl)-2-thienyl]- $\beta$ -vinylethyl ether (2) and [5-(phenyldimethylsilyl)-2-thienyl]- $\beta$ -vinylethyl ether (3) (Scheme I), respectively.

SCHEME I



- 2  $R_1 = R_2 = R_3 = -CH_3$   
3  $R_1 = R_2 = -CH_3$ ;  $R_3 = -C_6H_5$

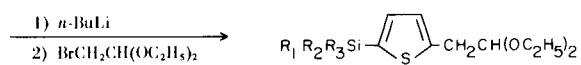
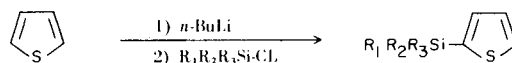
Decomposition of the intermediate anion with water provided 78% of 2-thienyl- $\beta$ -vinylethyl ether (4).



Thus it is apparent that metalation provides for dianion formation which gives rise concomitantly or otherwise, to both elimination and substitution products, where the elimination product is a result of the loss of ethoxide ion. Such was verified by the isolation of trimethylethoxysilane and phenyldimethylethoxysilane when an excess of the electrophilic reagents trimethylchlorosilane and phenyldimethylchlorosilane, respectively, were employed.

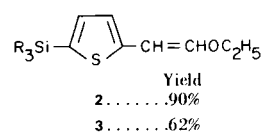
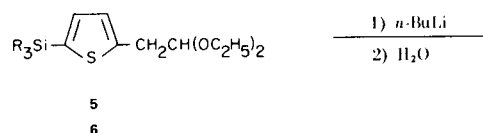
Although our previous experimental results (2,3) would indicate ring substitution in the 5-thienyl position, this was shown unequivocally to be the case by an unambiguous synthetic route (Scheme II and III).

SCHEME II



- 5  $R_1 = R_2 = R_3 = -CH_3$ -  
6  $R_1 = R_2 = -CH_3$ ;  $R_3 = -C_6H_5$ -

SCHEME III



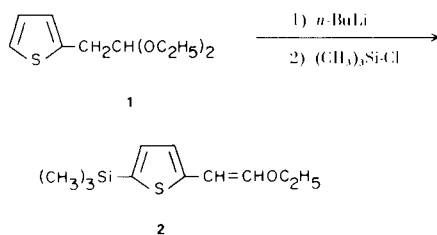
Yield  
2 . . . . . 90%  
3 . . . . . 62%

Treatment of **5** and **6** with one molecular equivalent of *n*-butyllithium afforded **2** and **3** respectively, in good yields (Scheme III).

Our initial experiments employing only one equivalent of *n*-butyllithium for the reaction with **1** resulted in rather poor yields of **2**. Such results would be expected if the production of each anion required the presence of an equivalent amount of *n*-butyllithium. This was confirmed when glpc showed none of **2** after treatment of **4** with an equivalent amount of lithium ethoxide followed by condensation with an excess of trimethylchlorosilane. We were able to isolate only recovered starting material, **4**; however, when **4** was treated with an equivalent amount of *n*-butyllithium followed by an excess of trimethylchlorosilane good yields of **2** were isolated.

In order to gain further insight into the reaction mechanism variations in reaction temperature and reactant concentrations were made (Table I).

TABLE I

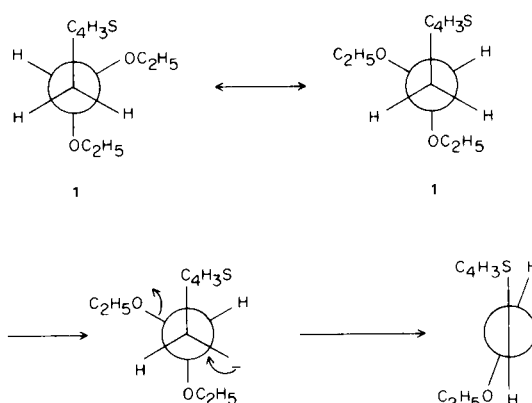


Equiv. of <b>1</b>	Equiv. of <i>n</i> -BuLi	Equiv. of (CH <sub>3</sub> ) <sub>3</sub> SiCl	Yield %	Reaction time and temp.	
1	1	1	34.5	3 hours	36°
1	2	2	62	2.5 hours	36°
1	1	1	27	5 min.	24°
1	2	2	87	5 min.	24°

The data suggests that lower reaction temperature, two equivalents of *n*-butyllithium per equivalent of **1**, and short reaction times are the preferred reaction conditions. It was noted that the reaction mixture becomes extensively discolored with increased reaction time, probably a result of decomposition of the intermediary anion.

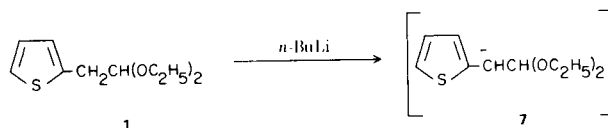
It is interesting to note that **2** and **3** possessed, in addition to the olefinic absorption at  $\sim 1645\text{ cm}^{-1}$ , a strong absorption at  $990\text{ cm}^{-1}$ , characteristic of the *trans* isomer. This evidence, combined with the fact that only a single absorption was observed in the vapor phase chromatogram led us to believe that the elimination takes place stereospecifically to provide the *trans* product in preference to the *cis* isomer. Examination of the Newman projection formulas for **1** verifies that, sterically, *trans* elimination is indeed more favorable.

SCHEME IV

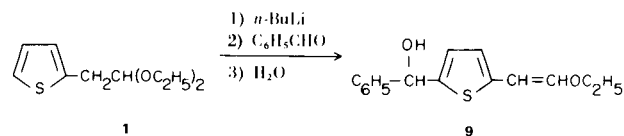


All attempts to trap the intermediate anion **7**, Scheme V, were futile. For instance, when the metalation was attempted at  $-70^\circ$  in the normal manner and the reaction mixture was treated with phenyldimethylchlorosilane, no product attributable to **7** was isolated but instead only starting material **1** and phenyldimethylbutylsilane. Reaction temperatures of  $0^\circ$  were unfavorable as only small quantities of **2** could be isolated with trimethylchlorosilane as the trapping reagent.

SCHEME V



The utility of such a reaction was indicated by the preparation of phenyl-2-thienyl-[5-( $\beta$ -ethoxyvinyl)]carbinol (**9**) in good yields (66%). The preparation of **9** was affected by the treatment of **1** with two equivalents of *n*-butyllithium followed by condensation of the intermediary anion with freshly distilled benzaldehyde.



In an effort to determine the influence of bases other than *n*-butyllithium, the metalation of **1** was attempted with sodamide in liquid ammonia. Treatment of **1** with two molecular equivalents of sodamide followed by condensation with phenyldimethylchlorosilane afforded **4** as the only isolable product. Apparently sodamide, while potent enough to affect elimination, is not sufficiently strong to provide metalation at the 5-thienyl position.

These results were substantiated when thiophene itself was subjected to identical reaction conditions in a futile effort to produce 2-(trimethylsilyl)thiophene.

### EXPERIMENTAL

#### $\alpha$ -(2-Thienyl)acetaldehyde Diethylacetal (**1**).

A solution of thiophene (0.47 mole, 40 g.) in anhydrous tetrahydrofuran under dry nitrogen was treated with *n*-butyllithium (0.47 mole, 1.6 *N*) for six hours. Bromoacetaldehyde diethylacetal (0.47 mole, 92.6 g.) was added to the solution and allowed to reflux for 72 hours. The solution was cooled and the salts removed by filtration. The solvent was removed *in vacuo* and the residue fractionated to afford 37.6 g. (40%) of **1** boiling at 128°/25 mm.;  $n_D^{24} = 1.4888$ .

*Anal.* Calcd. for  $C_{10}H_{16}O_2S$ : C, 59.96; H, 8.05. Found: C, 60.08; H, 8.10.

#### [5-(Trimethylsilyl)-2-thienyl]- $\beta$ -vinylethyl Ether (**2**).

An anhydrous ethereal solution of **1** (0.059 mole, 11.8 g.) under dry nitrogen was treated with *n*-butyllithium (0.118 mole, 1.6 *N*) at ambient temperature for five minutes. Trimethylchlorosilane (0.118 mole, 12.7 g.) was added to the reaction mixture and allowed to reflux overnight. The salts were filtered, the solvent removed *in vacuo* and the residue fractionated to afford 10.7 g. (87%) of **2** boiling at 72-74°/0.025 mm.

*Anal.* Calcd. for  $C_{11}H_{18}OSSi$ : C, 58.35; H, 8.01; S, 14.16; Si, 12.40. Found: C, 58.18; H, 8.15; S, 14.37; Si, 12.33.

#### [5-(Phenyldimethylsilyl)-2-thienyl]- $\beta$ -vinylethyl Ether (**3**).

In a manner similar to the preparation of **2**, **1** (0.05 mole, 10 g.) and phenyldimethylchlorosilane (0.1 mole, 17 g.) were reacted to yield 8.9 g. (62%) of **3** boiling at 156°/0.45 mm.;  $n_D^{26.5} = 1.5637$ .

*Anal.* Calcd. for  $C_{16}H_{20}OSSi$ : C, 66.62; H, 6.99. Found: C, 66.39; H, 7.02.

#### 2-Thienyl- $\beta$ -vinylethyl Ether (**4**).

An anhydrous ethereal solution of **1** (0.05 mole, 10 g.) under dry nitrogen was treated with *n*-butyllithium (0.05 mole, 1.6 *N*) for 30 minutes at ambient temperature. To this mixture was carefully added 20 ml. of water. The layers were separated, the aqueous layer extracted several times with ether, and the ethereal extracts combined and dried over anhydrous sodium sulfate. The solids were filtered, the solvent removed *in vacuo* and the residue fractionated to afford 6.0 g. (78%) of **4** boiling at 116-117°/25 mm.

*Anal.* Calcd. for  $C_8H_{10}SO$ : C, 62.30; H, 6.54. Found: C, 62.37; H, 7.19.

#### $\alpha$ -[2-(5-Trimethylsilyl)thienyl]acetaldehyde Diethylacetal (**5**).

To 2-trimethylsilylthiophene (0.067 mole, 10.5 g.), prepared by the method of Benkeser and Currie (4), in anhydrous tetrahydrofuran was added *n*-butyllithium (0.067 mole, 1.6 *N*) and the mixture refluxed for three hours. Bromoacetaldehyde diethylacetal (0.067 mole, 13.2 g.) was added to the reaction mixture and refluxed for 48 hours. The solvent was removed by distillation, the salt filtered and the residue distilled *in vacuo* to afford 5.48 g. (30%) of **5** boiling at 77°/0.02 mm.;  $n_D^{24} = 1.4775$ .

*Anal.* Calcd. for  $C_{13}H_{24}O_2SSi$ : C, 57.30; H, 8.88; Si, 10.31. Found: C, 57.19; H, 9.01; Si, 10.05.

#### $\alpha$ -[2-(5-Phenyldimethylsilyl)thienyl]acetaldehyde Diethylacetal (**6**).

2-Phenyldimethylsilylthiophene (0.25 mole, 54.8 g.), prepared according to the procedure of Thames, *et al.*, (5) *n*-butyllithium (0.25 mole, 1.6 *N*) and bromoacetaldehyde diethylacetal (0.25 mole, 49.5 g.) were allowed to react in the manner described for the preparation of **5** to yield 30 g. (36%) of **6** boiling at 132°/0.15 mm.;  $n_D^{24} = 1.5456$ .

*Anal.* Calcd. for  $C_{18}H_{26}O_2SSi$ : C, 64.62; H, 7.83. Found: C, 64.81; H, 7.88.

#### Treatment of **5** with *n*-Butyllithium.

An anhydrous ethereal solution of **5** (0.043 mole, 11.6 g.) was treated with *n*-butyllithium (0.043 mole, 1.6 *N*) at ambient temperature for five minutes. Water (30 ml.) was added to the reaction mixture. The layers were separated and the aqueous layer extracted several times with ether. The combined ethereal extracts were dried over anhydrous sodium sulfate. The salts were filtered, the solvent removed *in vacuo* and the residue fractionated to afford 8.3 g., (90%) of **2** as verified by the comparison of the boiling point and ir spectra with those of an actual sample.

#### Treatment of **6** with *n*-Butyllithium.

An ethereal solution of **6** (0.0298 mole, 10 g.), *n*-butyllithium (0.0298 mole, 1.6 *N*) and water (10 ml.) were allowed to react in the manner described above to afford 5.3 g. (62%) of **3** as verified by the comparison of the boiling point and ir spectra with that of an actual sample.

#### Treatment of **4** with *n*-Butyllithium.

An ethereal solution of **4** (6 g., 0.039 mole) was treated with *n*-butyllithium (0.040 mole, 1.6 *N*) for 12 hours under reflux. Trimethylchlorosilane (4.2 g., 0.040 mole) was added and the mixture allowed to stir at reflux for 12 hours. The salts were removed by filtration, the solvent removed *in vacuo* and the residue fractionated to afford 3.9 g. (43%) of **2** boiling at 89°/0.25 mm.

#### Treatment of **1** with One Molecular Equivalent of *n*-Butyllithium for Three Hours.

An anhydrous ethereal solution of **1** (0.05 mole, 10 g.) was treated with *n*-butyllithium (0.05 mole, 1.6 *N*) and allowed to reflux for three hours. The mixture was allowed to reflux overnight. The salts were filtered, the solvent removed *in vacuo* and the residue fractionated to yield 3.9 g. (35%) of **2** as verified by boiling points and ir data.

#### Treatment of **1** with Two Molecular Equivalents of *n*-Butyllithium for 2.5 Hours.

An ethereal solution of **1** (0.05 mole, 10 g.) under anhydrous conditions was treated with *n*-butyllithium (0.10 mole, 1.6 *N*) and allowed to reflux 2.5 hours. The reaction was cooled and trimethylchlorosilane (0.10 mole, 10.8 g.) was added. The salts were filtered, the solvent removed *in vacuo* and the residue fractionated to afford 7.0 g. (62%) of **2** as verified by boiling points and ir data.

#### Treatment of **1** with One Molecular Equivalent of *n*-Butyllithium for Five Minutes.

An anhydrous ethereal solution of **1** (0.085 mole, 17 g.) was treated with *n*-butyllithium (0.085 mole, 1.6 *N*) for five minutes at ambient temperature. Trimethylchlorosilane (0.085 mole, 8.4 g.) was added and allowed to reflux overnight. The salts were

filtered, the solvent removed *in vacuo* and the residue fractionated to afford 5.5 g. (27%) of **2** as verified by boiling point and ir data.

Phenyl-2-thienyl-[5-( $\beta$ -ethoxyvinyl)]carbinol (**9**).

An anhydrous ethereal solution of **1** (0.029 mole, 5.9 g.) was treated with *n*-butyllithium (0.058 mole, 1.6 *N*) at ambient temperature for approximately 10 minutes. Freshly distilled benzaldehyde (0.058 mole, 6.15 g.) was added and allowed to reflux three hours at which time the heat was removed and the stirring allowed to continue at ambient temperature for an additional 48 hours. Water (100 ml.) was added and allowed to stir for an additional 48 hours. The layers were separated and the aqueous layer extracted several times with ether. The combined ethereal extracts were dried over anhydrous sodium sulfate. The salts were filtered and the solvent removed *in vacuo*. Fractionation of the residue yielded 5 g. (66%) of **9** boiling at 214°/0.025 mm.;  $n_D^{27} = 1.5970$ .

*Anal.* Calcd. for  $C_{15}H_{16}O_2S$ : C, 69.20; H, 6.19; S, 12.32. Found: C, 68.84; H, 6.22; S, 12.48.

Treatment of **1** with Sodamide.

To a stirred solution of sodamide (0.1 mole, 3.95 g.) in 500 ml. of commercial, anhydrous liquid ammonia (The liquid ammonia was further dried by the addition of small pieces of sodium metal until the blue color persisted) was added **1** (0.05 mole, 10 g.) in 100 ml. of anhydrous ether. The ammonia was allowed to evaporate and phenyldimethylchlorosilane (0.1 mole, 17 g.) in

100 ml. of anhydrous ether was added. The mixture was allowed to stir at ambient temperature for twelve hours. The salts were filtered, the solvent removed *in vacuo* and the residue fractionated to afford 3.5 g. (45.5%) of **4**, as evidenced by the boiling point and ir data, and phenyldimethylethoxysilane (7.2 g., 80%) boiling at 75°/7 mm. Literature (6) gives 93°/25 mm.

Treatment of Thiophene with Sodamide.

Thiophene (0.25 mole, 21 g.), sodamide (0.25 mole, 9.75 g.) and trimethylchlorosilane (0.25 mole, 27 g.) were allowed to react in the manner described above. However, only the starting thiophene was isolated.

#### REFERENCES

- (1) To whom correspondence should be addressed.
- (2) S. F. Thames and J. E. McCleskey, *J. Heterocyclic Chem.*, **3**, 104 (1966).
- (3) S. F. Thames and J. E. McCleskey, *ibid.*, **4**, 146 (1967).
- (4) R. A. Benkeser and R. B. Currie, *J. Am. Chem. Soc.*, **70**, 1780 (1948).
- (5) S. F. Thames, J. E. McCleskey, and P. L. Kelly, *J. Heterocyclic Chem.*, **5**, 749 (1969).
- (6) H. Freiser, M. V. Eagle, and J. L. Speier, *J. Am. Chem. Soc.*, **75**, 2824 (1953).