

Reaction of 1-Lithio-1-arylthio(or alkylthio)methyltrimethylsilane with Acid Derivatives. A Novel Synthesis of Functionalized Vinyl Sulfides

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Reactions of 1-lithio-1-phenylthiomethyl- (**1a**) and 1-lithio-1-methylthiomethyltrimethylsilane (**1b**) with amides, an ester, acid anhydrides, a urea, and a carbonate are described which provide useful routes to functionalized vinyl sulfides. The reaction of **1** with amides gave β -functionalized vinyl sulfides, 1-dialkylamino-2-phenylthio (or methylthio)ethylenes, in 40—95% yields and the reaction could be extended to the sulfonyl derivatives of **1** to afford 1-dialkylamino-2-phenylsulfonyl(or methylsulfonyl)ethylenes. Although ethyl benzoate and some acid anhydrides were not good substrates for this reaction, tetramethylurea and diethyl carbonate gave α -functionalized vinyl sulfides, 1-amidovinyl- and 1-(ethoxycarbonyl)vinyl sulfides, in moderate yields when treated with **1a** followed by addition of benzaldehyde.

Olefin-forming reaction of α -metallo-silanes is known as the Peterson reaction and plays an important role in organic synthesis. For example, 1-lithio-1-arylthio-(or alkylthio)methyltrimethylsilanes **1** react with ketones to give vinyl sulfide derivatives.¹⁾ However, only a few reports mention this type of reactions of the α -metallo-silanes **1** with acid derivatives,²⁾ since they are in general not good substrates for the Peterson olefination.

In our preliminary report we briefly described the reaction of the α -lithiosilanes **1** with several amides which provided a new synthetic method for 2-aminovinyl sulfides.³⁾ We further investigated the reaction using

acid derivatives and found that these reactions can be utilized for preparation of various functionalized vinyl sulfides.

Since vinyl sulfides are very versatile reagents as masked carbonyl compounds,⁴⁾ these functionalized vinyl sulfides are expected to have more potential in organic synthesis.⁵⁾

Results and Discussion

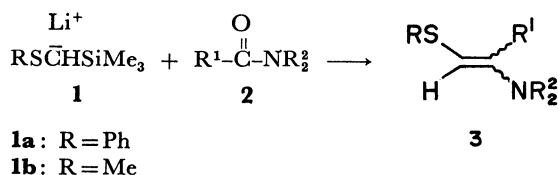
Reaction of the α -Lithiosilane **1** with Amides. 1-Lithio-1-phenylthiomethyltrimethylsilane (**1a**) gener-

TABLE 1. YIELDS, BOILING AND MELTING POINTS, AND SPECTRAL DATA OF **3** AND **8**

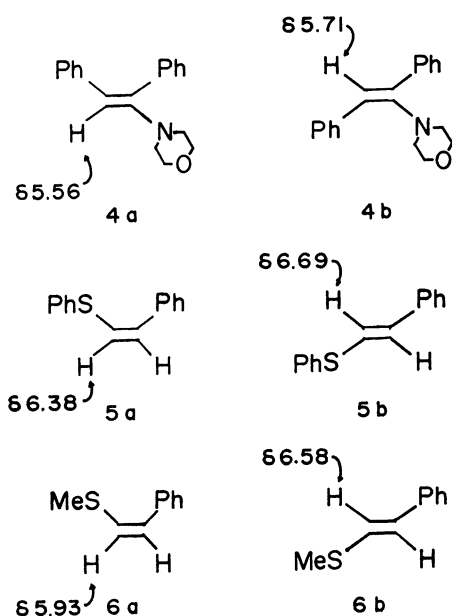
R	R ¹	R ₂ ²	Yield %	Isomer ratio ^{a)} E : Z	Bp $\theta_b/^\circ\text{C}$ (mmHg ^{b)}) [M _p $\theta_m/^\circ\text{C}$]	IR(ν/cm^{-1} , neat) C=C	¹ H NMR (δ , CDCl ₃)	MS(70 eV) m/e (M ⁺)
3a PhS	H	Me ₂	64	100 : 0	90 (0.01)	1630	2.80(6H,s), 4.56(1H,d, $J=13.0\text{Hz}$), 6.55 (1H,d, $J=13.0\text{Hz}$), 6.8—7.4(5H,m)	179
3b PhS	<i>t</i> -Bu	Me ₂	40	20 : 80	65—67 (2.0)	1580	1.13(7.2H,s, <i>Z</i> -Bu ^t), 1.19(1.8H,s, <i>E</i> -Bu ^t), 2.48(1.2H,s, <i>E</i> -Me), 2.75(4.8H,s, <i>Z</i> -Me), 5.63(0.2H,s, <i>E</i> -CH=), 5.99(0.8H,s, <i>Z</i> -CH=), 7.1—7.4(5H,m)	235
3c PhS	Ph	Me ₂	65	96 : 4	112—113 (0.03)	1580	2.70(5.76H,s, <i>E</i> -Me), 2.85(0.24H,s, <i>Z</i> -Me), 5.00($\approx$ 1H,s, <i>E</i> -CH=), 5.10($\approx$ 0H, <i>Z</i> -CH=), 6.8—7.4(10H,m)	255
3d PhS	Ph	-(CH ₂) ₂ -	87	80 : 20	145 (0.1)	1580	1.90(3.2H,s, <i>E</i> -CH ₂), 2.11(0.8H,s, <i>Z</i> -CH ₂), 5.73(0.8H,s, <i>E</i> -CH=), 5.91(0.2H,s, <i>Z</i> -CH=), 7.0—7.7(10H,m)	253
3e PhS	Ph	-(CH ₂) ₅ -	95	100 : 0	130 (0.02)	1580	1.2—1.8(6H,m), 2.6—3.2(4H,m), 5.21 (1H,s, CH=), 6.8—7.5(10H,m)	295
3f MeS	Ph	-(CH ₂) ₅ -	72 ^{a)}	87 : 13	120 (2.0)	1580	1.2—1.8(6H,m), 2.10(2.6H,s, <i>E</i> -Me), 2.27(0.4H,s, <i>Z</i> -Me), 2.6—3.2(4H,m), 5.03($\approx$ 0.9H,s, <i>E</i> -CH=), 5.12($\approx$ 0.1H,s, <i>Z</i> -CH=), 7.2—7.5(5H,m)	233
8a PhSO ₂	H	Me ₂	60	100 : 0	[131]	1610 ^{a)}	2.86(6H,s), 4.84(1H,d, $J=12.0\text{Hz}$, CH=), 7.1—8.0(6H,m, CH= and Ph)	211
8b PhSO ₂	H	-(CH ₂) ₅ -	81	100 : 0	150 (1.0) ^{d)}	1600	1.2—1.8(6H,m), 2.9—3.3(4H,m), 4.95 (1H,d, $J=13.0\text{Hz}$, CH=), 7.1—8.0(6H,m, CH= and Ph)	251
8c MeSO ₂	H	Me ₂	42	100 : 0	173 (1.0) ^{e)}	1600	2.90(9H,s), 4.90(1H,d, $J=12.0\text{Hz}$, CH=), 7.17(1H,d, $J=12.0\text{Hz}$, CH=)	149
8d MeSO ₂	H	-(CH ₂) ₅ -	24	100 : 0	150 (1.0) ^{d)}	1610	1.4—1.8(6H,m), 2.92(3H,s), 3.0—3.3 (4H,m), 4.98(1H,d, $J=12.8\text{Hz}$, CH=), 7.11(1H,d, $J=12.8\text{Hz}$, CH=)	189

a) Determined by NMR spectroscopy. b) 1 mmHg $\approx$ 133.322 Pa. c) In Nujol mull. d) Purified by pot distillation. e) Purified by Kugel Rohr.

ated by treating phenylthiomethyltrimethylsilane with butyllithium at 0 °C in THF was reacted with *N,N*-dimethylformamide at the same temperature and was allowed to stand overnight. Usual work-up of the reaction mixture gave 64% of (*E*)-1-dimethylamino-2-phenylthioethylene (**3a**). In this reaction only the (*E*)-isomer was obtained and the structure was determined by spectral data and elemental analysis. Similarly several 2-aminovinyl sulfides were obtained from the α -lithiosilanes **1** and amides **2** in good yields under very mild conditions and the results are summarized in Table 1.



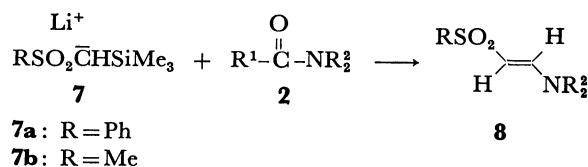
In most cases a mixture of (*E*)- and (*Z*)-isomers was obtained and the ratio was determined by NMR spectroscopy. Estimation of the coupling constant between the phenyl carbon and the vinyl proton ($^3J_{\text{CH}}$) by ^{13}C -NMR measurement under selective irradiation of the phenyl protons was tried. However, the values for the compounds **3c** (the major isomer only) and **3e** were ≈ 7 cps which was not decisive for determination of (*E*)- or (*Z*)-form of olefinic compounds. The assignment of (*E*)- and (*Z*)-isomers of the compounds **3c**–**f** was done by comparison of the chemical shifts of the vinyl protons with those of the known compounds **4**,⁶⁾ **5**,⁷⁾ and **6**.⁸⁾ Thus the isomer which



shows the vinyl proton signal in the higher field is determined to be the (*E*)-isomer of **3** (the vinyl proton is *trans* to the phenyl ring) and the other is the (*Z*)-isomer. For the vinyl sulfide **3b**, the methyl group which appears in the lower field is suggested to be that of the (*Z*)-isomer by comparing chemical shifts of the alkylamino groups of **3c** and **3d**. Hence the major product of the reaction was found to be an (*E*)-isomer except for the case of **3b**.

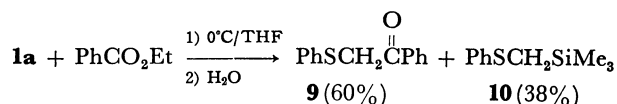
Although the sterically less favorable (*E*)-isomers were predominant, this result is consistent with the observation that **4a**, sterically less favorable, is thermodynamically more stable than **4b**, which is sterically less crowded.⁶⁾ This phenomenon was explained by the continuous overlap between the electron pair on the nitrogen atom and the phenyl group in its polar resonance form⁹⁾ and the same reason can be applied to the predominance of the (*E*)-isomers in this reaction. The only exception observed for **3b** may be ascribed to the large steric repulsion caused by the bulky *t*-butyl group which suppressed the formation of the (*E*)-isomer.

Extension of the reaction to sulfone derivatives was successful. The reaction of 1-lithio-1-phenylsulfonyl(or methylsulfonyl)methyltrimethylsilane **7** with amides **2** gave 2-aminovinyl sulfones **8** and the results are listed



in Table 1. Method of lithiation and reaction conditions are different from the preceding reactions (see Experimental). Contrary to the α -phenylthiosilane **1a**, the corresponding phenylsulfonylsilane **7a** gave very poor yields of vinyl sulfones when treated with less reactive amides such as *N,N*-dimethylbenzamide and *N*-benzoylpiperidine. Oxidation of the aminovinyl sulfides to sulfones were also examined, but it was difficult to isolate or to purify the oxidized products. Thus the present reaction is one of the better routes to 2-amino-vinyl sulfones.

Reaction with Ester and Acid Anhydride. Reaction of the α -lithiosilane **1a** with ethyl benzoate was carried out in a similar manner to the reaction with amides, and α -phenylthioacetophenone (**9**) was obtained in 60% yield with considerable amount of the starting phenylthiomethylsilane **10**. The anticipated product, 2-ethoxyvinyl sulfide, was not formed at all or the sulfide is quite sensitive to hydrolysis even under basic conditions, since no vinyl proton signals were detected in the NMR spectrum of the reaction mixture immediately after the quenching. Addition of benzaldehyde or



successive addition of lithium diisopropylamide and the aldehyde to the reaction mixture before the quenching was also carried out, but no vinyl sulfide derivatives were detected. Hence, it is not possible that the initial product of the reaction was an acylated phenylthiomethyltrimethylsilane which corresponds to **16** or **18** in Scheme shown later.

Similar reaction of the silane **1a** with benzoic anhydride gave only a small amount of α -phenylthioacetophenone (**9**) and the most part of **1a** was recovered as the starting phenylthiomethylsilane **10**. Some cyclic acid anhydrides such as phthalic anhydride and maleic anhydride were found to be quite unreactive with **1a**.

were prepared by silylation of methyl phenyl sulfide, dimethyl sulfide, methyl phenyl sulfone, and dimethyl sulfone with triemethylsilyl chloride, respectively, by the known method.¹⁰⁾

General Procedure for the Reactions of the Silanes 1 with Acid Derivatives. To a stirred solution of phenylthio(or methylthio)methyltrimethylsilane (**1**, 5.0 mmol) in THF (5 ml) was added butyllithium (3.8 ml of 15% hexane solution, 6.0 mmol) at 0–5 °C, and the solution was stirred for 2 h at room temperature. An acid derivative (5.0 mmol) in THF (5 ml) was added at 0–5 °C and the stirring was continued for 2 h at the same temperature. The mixture was stood overnight at room temperature, quenched with water after cooling, and extracted (ether). The organic layer was dried (Na₂SO₄) and evaporated to give a crude product, which was isolated and purified by distillation and/or chromatography on silica gel. 1-Dialkylamino-2-phenylthio(or methylthio)-ethylenes **3** could be purified only by distillation because of their ready hydrolysis. Hence, some of their elemental analyses were unsatisfactory.

1-Dimethylamino-2-phenylthioethylene (3a): Found: C, 66.88; H, 7.43; N, 7.53; S, 18.15%. Calcd for C₁₀H₁₃NS: C, 67.02; H, 7.31; N, 7.82; S, 17.86%.

α-Dimethylamino-β-phenylthiostyrene (3c): ¹³C NMR (CDCl₃) δ 40.7 (q), 86.8 (d, =CHS–), 158.2 (s, =CPh), and aromatic carbons at δ 123.9, 125.2, 127.6, 127.9, 128.2, 128.8, 136.6 and 141.2. Found: C, 75.17; H, 6.72; N, 5.54; S, 12.38%. Calcd for C₁₆H₁₇NS: C, 75.27; H, 6.71; N, 5.49; S, 12.53%.

β-Phenylthio-α-piperidinostyrene (3e): ¹³C NMR (CDCl₃) δ 24.5 (t), 25.8 (t), 50.2 (t), 91.2 (d, =CHS–), 158.2 (s, =CPh), and aromatic carbons at δ 124.4, 126.0, 127.8, 128.3, 128.5, 129.3, 137.1, and 140.7. Found: C, 76.81; H, 7.04; N, 4.54; S, 10.90%. Calcd for C₁₉H₂₁NS: C, 77.26; H, 7.12; N, 4.74; S, 10.83%.

α-Phenylthioacetophenone (9): Bp 120 °C/1.0 mmHg by pot distillation; IR (neat) 1680 cm^{–1} (C=O); ¹H NMR (CDCl₃) δ 4.30 (2H, s, CH₂), 7.1–7.5 (8H, m, PhS and a part of PhCO), 7.8–8.0 (2H, m, the rest of PhCO); MS, *m/e* 228 (M⁺).

N,N-Dimethyl-α-phenylthioacetamide (11): Bp 120 °C/3 mmHg, IR (neat) 1630 cm^{–1} (C=O); ¹H NMR (CDCl₃) δ 2.92 (3H, s), 2.98 (3H, s), 3.71 (2H, s), 7.0–7.6 (5H, m).

The Reactions of the Silanes 7 with Amides. To a stirred butyllithium (3.8 ml of 15% hexane solution) was added diisopropylamine (0.84 ml, 6.0 mmol) in THF (5 ml) at 0–5 °C. After stirring for 1 h at room temperature, the resulting lithium diisopropylamide (LDA) solution was cooled to –60–70 °C and phenylsulfonyl(or methylsulfonyl)trimethylsilane (5.0 mmol) was added to the solution. The stirring was continued for 1 h at room temperature followed by addition of an amide (6.0 mmol) in THF (5 ml). Then the mixture was warmed at 50–60 °C for 5 h with stirring. The reaction mixture was quenched with water after cooling, extracted (CH₂Cl₂), dried (Na₂SO₄), and concentrated to give a crude product, which was isolated and purified by crystallization or distillation. Elemental analyses of the products were not satisfactory because of their high sensitivity to hydrolysis.

1-Dimethylamino-2-phenylsulfonylthylene (8a): Found: C, 56.69; H, 6.18; N, 6.63; S, 15.10%. Calcd for C₁₀H₁₃NO₂S: C, 56.86; H, 6.20; N, 6.63; S, 15.15%.

Formation of the Cinnamamides 12 and the Cinnamate 13.

Benzaldehyde (5.0 mmol) in THF (5 ml) was added to a

reaction mixture obtained from phenylthiomethyltrimethylsilane (5.0 mmol), butyllithium (6.0 mmol), and tetramethylurea (5.0 mmol) according to the procedure shown above. The mixture was allowed to stand for 1 d at room temperature and was worked up similarly to the previous runs to give 0.58 g (41%) of *N,N*-dimethyl-α-phenylthiocinnamamide (**12a**) as a mixture (57 : 43) of two isomers: bp 130 °C/0.001 mmHg by pot distillation; IR (neat) 1630 cm^{–1} (C=O); ¹H NMR (CDCl₃) δ 2.63 (≈1.7H, s), 2.76 (≈1.7H, s), 2.89 (≈1.3H, s), 2.95 (≈1.3H, s), 6.60 (0.57H, s), 6.73 (0.43H, s), 7.1–7.7 (10H, m).

An analytical sample of the major isomer could be isolated by chromatography on silica gel; MS, *m/e* 283 (M⁺). Found: C, 71.84; H, 5.01; N, 6.11; S, 11.01%. Calcd for C₁₇H₁₇NOS: C, 72.06; H, 4.94; N, 6.05; S, 11.29%.

Similarly 0.30 g (27%) of *N,N*-dimethyl-α-methylthiocinnamamide (**12b**) was obtained from methylthiomethyltrimethylsilane (5.0 mmol), butyllithium (6.0 mmol), the urea (5.0 mmol), and the aldehyde (5.0 mmol) as a mixture (65 : 35) of two isomers: bp 150 °C/5 mmHg; IR (neat) 1620 cm^{–1} (C=O); ¹H NMR (CDCl₃) δ 2.24 (1.05H, s), 2.35 (1.95H, s), 2.81 (1.95H, s), 2.98 (≈2H, s), 3.04 (≈1H, s), 3.13 (≈1H, s), 6.48 (0.65H, s), 6.59 (0.35H, s), 7.1–7.6 (5H, m), MS, *m/e* 221 (M⁺).

In the case of the reaction starting with phenylthiomethyltrimethylsilane (5.0 mmol), butyllithium (6.0 mmol), and diethyl carbonate (5.0 mmol), THF solution of LDA (5.0 mmol) prepared by the method shown above was added to the reaction mixture at 0 °C. The mixture was stirred for 3 h at the same temperature and overnight at room temperature followed by addition of benzaldehyde (5.0 mmol) in THF (5 ml). The mixture was allowed to stand for 1 d at room temperature and worked up as the previous runs to afford 0.84 g (59%) of ethyl α-phenylthiocinnamate (**13**): bp 150 °C/1 mmHg by pot distillation; IR (neat) 1720 cm^{–1} (C=O); ¹H NMR δ 1.30 (3H, t), 4.07 (2H, q), 7.3–7.9 (10H, m), 8.30 (1H, s, =CH); MS, *m/e* 284 (M⁺).

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