

NEW METHODS AND REAGENTS IN ORGANIC SYNTHESIS. 68.¹
 REACTION OF THIOKETONES WITH LITHIUM TRIMETHYLSILYLDIAZOMETHANE

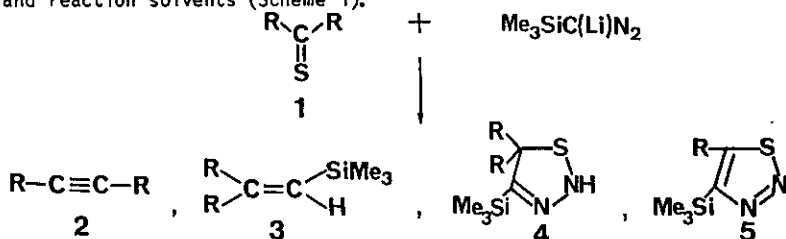
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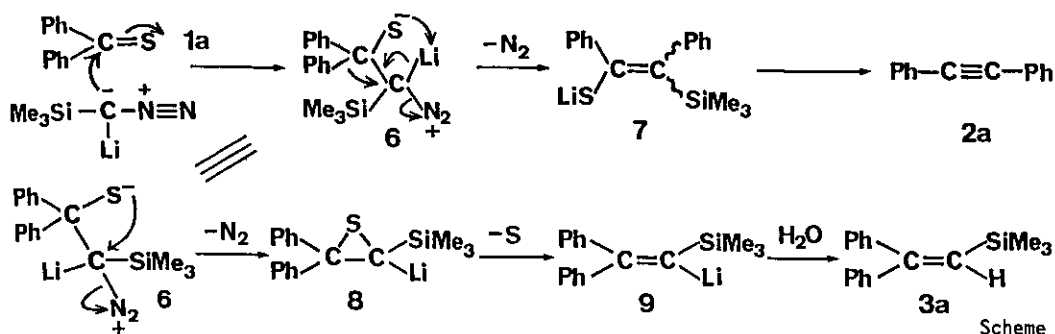
Abstract—Reaction of thioketones with lithium trimethylsilyldiazomethane affords alkynes, vinylsilanes, 1,2,3-thiadiazolines, or 1,2,3-thiadiazoles depending upon substrates and reaction solvents.

We have already demonstrated that the lithium salt of trimethylsilyldiazomethane (TMSC(Li)N₂), a useful [C–N–N] azole synthon,² smoothly reacts with thiocarbonyl compounds such as thioesters, dithioesters, and carbon disulfide to give 5-substituted 1,2,3-thiadiazoles.³ We now report the reaction of thioketones **1** with TMSC(Li)N₂, which gives various products **2–5** depending upon substrates and reaction solvents (Scheme 1).



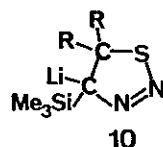
Scheme 1.

Diversity of the reaction will be apparent from the Table. Thiobenzophenone (**1a**) reacted with TMSC(Li)N₂ in tetrahydrofuran to give diphenylethyne (**2a**). This reaction has precedent in the reaction of benzophenone with TMSC(Li)N₂.⁴ However, replacement of the reaction solvent from tetrahydrofuran to diethyl ether took another reaction course, giving the vinylsilane **3a**. A possible mechanism for the formation of **2a** and **3a** would be as shown in Scheme 2: Nucleophilic attack of TMSC(Li)N₂ on the thiocarbonyl carbon of **1a** would give the betaine **6**. The Wolff rearrangement with expulsion of nitrogen would produce the stilbene derivative **7**, from which elimination of the sulfur and trimethylsilyl moieties would give **2a**. The formation of the vinylsilane **3a** would involve the intermediacy of the episulfide **8**, which would release the sulfur atom to give **9**. Aqueous work-up would give **3a**.⁵

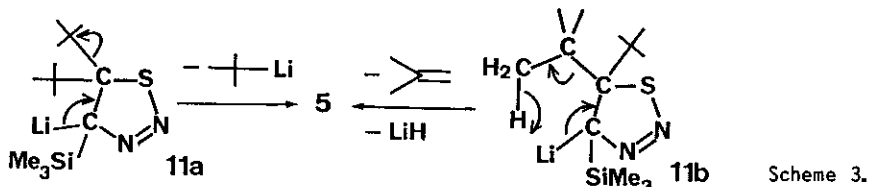


Interestingly, no solvent effect was observed in the reactions of (di-*p*-methoxy)thiobenzophenone (1b) and thiopivalophenone (1c) with TMSC(Li)N_2 , giving the homologous alkynes 2b and 2c, respectively, in both diethyl ether and tetrahydrofuran.

Reaction of xanthione (1d) with TMSC(Li)N_2 in diethyl ether afforded the 1,2,3-thiadiazoline 4a,⁶ while the use of tetrahydrofuran showed many spots on a thin layer chromatogram. Adamantanethione (1e), another cyclic thioketone, gave the vinylsilane 3b as a sole identified product in diethyl ether. Changing the reaction solvent to tetrahydrofuran produced the 1,2,3-thiadiazoline 4b, but 3b could not be found. An obvious intermediate in the formation of 4 would be 10 produced by nucleophilic attack of TMSC(Li)N_2 on the thiocarbonyl carbon of the cyclic thioketone 1d or 1e, followed by cyclization. Aqueous work-up of 10 would give 4.

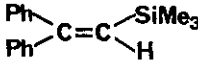
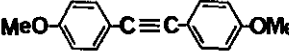
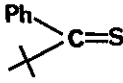
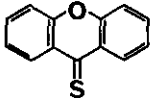
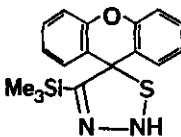

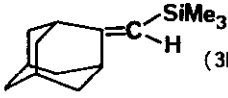
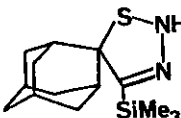
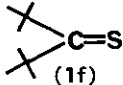
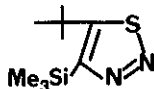


In contrast to the above results, the reaction of di-*tert*-butylthioketone (1f) gave rise to removal of the *tert*-butyl group and furnished 5-*tert*-butyl-4-trimethylsilyl-1,2,3-thiadiazole (5)⁷ in good yield. A possible intermediate in this reaction would be 11a, from which *tert*-butyllithium would be eliminated to give 5. Alternatively, expulsion of isobutylene and lithium hydride as depicted in 11b would afford 5 (Scheme 3). It is not decided which mechanism is actually involved, but we favor the former though all attempts to trap either *tert*-butyllithium or isobutylene failed.

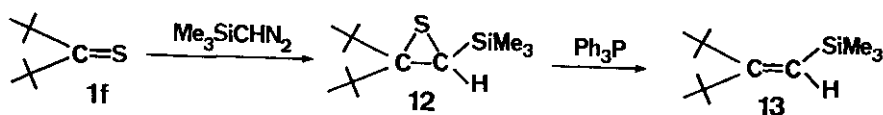


Incidentally, we found that di-*tert*-butylthioketone (1f) smoothly reacted with trimethylsilyldiazomethane in diethyl ether (0°C, 2h; r.t., 1h). After concentration in vacuo, the residue was heated at 80–90°C (26mmHg) for 1h to give the episulfide 12, bp 110–120°C/26mmHg(Kugelrohr), in 89% yield. Treatment of 12 with triphenylphosphine (80°C, 17h) afforded the vinylsilane 13, bp 85–95°C/30mmHg(Kugelrohr), (65%yield) and triphenylphosphine sulfide (95%yield) (Scheme 4).

Table. ^a Reaction of Thioketones (1) with Lithium Trimethylsilyldiazomethane

Thioketone	Reaction		Product ^b	Isolated Yield (%)	mp ^{°C} or bp ^{°C} /mmHg ^c
	Solvent	Temp. & Time			
$\text{Ph}_2\text{C}=\text{S}$ (1a)	Et ₂ O	-70°C, 1h; 0°C, 1h	 (3a)	41	140-150/17 [115/0.25] ^d
	THF	-70°C, 1h; 0°C, 1h	$\text{Ph}-\text{C}\equiv\text{C}-\text{Ph}$ (2a)	46	59-60 [60-61] ^e
$[\text{p-MeOC}_6\text{H}_4]_2\text{C}=\text{S}$ (1b)	Et ₂ O ^f	-70°C, 1h; 0°C, 1h; r.t., 6h	 (2b)	34	145-147 [145-147] ^g
	THF ^h	-70°C, 1h; 0°C, 1h	2b	33	
 (1c)	Et ₂ O	-70°C, 0.5h; 0°C, 2h	$\text{Ph}-\text{C}\equiv\text{C}-\text{X}$ (2c)	57	70-80/17 [84/15] ⁱ
	THF	-70°C, 0.5h; 0°C, 2h	2c	60	
 (1d)	Et ₂ O ^j	-70°C, 0.5h; 0°C, 1h	 (4a)	74	120-128 (dec)
 (1e)	Et ₂ O	-70°C, 1h; 0°C, 0.5h	 (3b)	8	100-110/17
	THF	-70°C, 1h; 0°C, 1h	 (4b)	31	124-127 (dec)
 (1f)	Et ₂ O ^k	0°C, 1h	 (5)	82	45-55/0.08

a) Unless otherwise stated, the reaction was carried out as a typical procedure. b) All of the products gave satisfactory IR and ¹H-NMR spectra. New compounds were further identified by elemental analysis. c) Distillation was carried out by a Kugelrohr apparatus. d) B.-Th. Gröbel and D. Seebach, *Chem. Ber.*, **110**, 852 (1977). e) Reference 4. f) To TMSC(Li)N₂ in Et₂O (12ml) was added 1b in Et₂O (1ml)-benzene (3ml). g) M. S. Newman and D. E. Reid, *J. Org. Chem.*, **23**, 665 (1958). h) To TMSC(Li)N₂ in THF (10ml) was added 1b in THF (3ml)-benzene (1ml). i) H. Bock and H. Alt, *Chem. Ber.*, **103**, 1784 (1970). j) To TMSC(Li)N₂ in Et₂O (11ml) was added 1d in Et₂O (2ml)-benzene (6ml). k) When THF was used, the formation of many products was observed on a thin layer chromatoplate, but 5 could not be found.



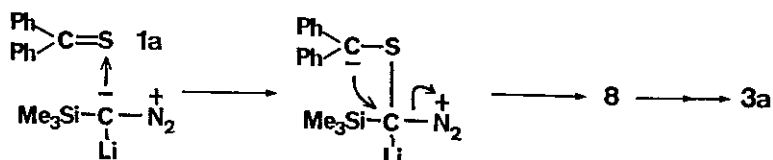
Scheme 4.

Diversity of the products and dramatic solvent effects observed in the reaction of thioketones with $\text{TMSC}(\text{Li})\text{N}_2$ may provide a clue to a new insight into the mechanism of organic reactions.

As a typical experimental procedure for the reaction of thioketones with $\text{TMSC}(\text{Li})\text{N}_2$, the reaction of thiobenzophenone (**1a**) with $\text{TMSC}(\text{Li})\text{N}_2$ in tetrahydrofuran was carried out as follows: To a solution of trimethylsilyldiazomethane⁸ (2.2M hexane solution, 0.55ml, 1.2mmol) in tetrahydrofuran (10ml) was added dropwise *n*-butyllithium (15% hexane solution, 0.76ml, 1.2mmol) at -70°C under argon, and the mixture was stirred at -70°C for 20min. A solution of thiobenzophenone (**1a**, 198mg, 1mmol) in tetrahydrofuran (3ml) was then added at -70°C . The mixture was stirred at -70°C for 1h, and then at 0°C for 1h. The mixture was treated with ice-water and extracted with diethyl ether. The ethereal extracts were washed with water, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (BW-820MH, Fuji Davison) with hexane to give diphenylethyne (**2a**, 81mg, 46%).

REFERENCES AND NOTES

- For Part 67, see Y. Hamada, M. Shibata, T. Sugiura, S. Kato, and T. Shioiri, *J. Org. Chem.*, in press.
- For a review, see T. Shioiri and T. Aoyama, *J. Synth. Org. Chem. Japan*, **44**, 149 (1986).
- T. Aoyama, Y. Iwamoto, and T. Shioiri, *Heterocycles*, **24**, 589 (1986).
- E. W. Colvin and B. J. Hamill, *J. Chem. Soc. Perkin I*, 869 (1977).
- The alternative mechanism through thiophilic attack followed by episulfide formation accompanied with expulsion of nitrogen can not be completely excluded.



- The alternative structure **14** of the product which was derived by thiophilic attack of $\text{TMSC}(\text{Li})\text{N}_2$ will be excluded since the $^1\text{H-NMR}$ spectrum of the product revealed that protons of the trimethylsilyl group were strongly deshielded (δ -0.17, 9H, s) by the benzene nucleus.



- Desilylation of **5** smoothly proceeded to give 5-*tert*-butyl-1,2,3-thiadiazole, bp $70-80^\circ\text{C}/27\text{mmHg}$ (Kugelrohr), by the action of either the fluoride ion ($\text{KF}\cdot 2\text{H}_2\text{O}$, Bu^n_4NCl , acetonitrile; r.t., 0.5h; 90%) or the hydroxide ion ($\text{LiOH}\cdot\text{H}_2\text{O}$, $\text{H}_2\text{O}-\text{MeOH}$ (1:5); reflux, 1h; 76%).
- S. Mori, I. Sakai, T. Aoyama, and T. Shioiri, *Chem. Pharm. Bull.*, **30**, 3380 (1982).

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