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NEW METHODS AND REAGENTS IN ORGANIC SYNTHESIS. 68.[1]
REACTION OF THIOKETONES WITH LITHIUM TRIMETHYLSILYLDIAZOMETHANE

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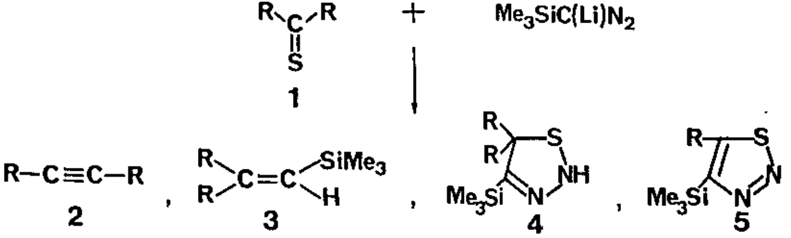
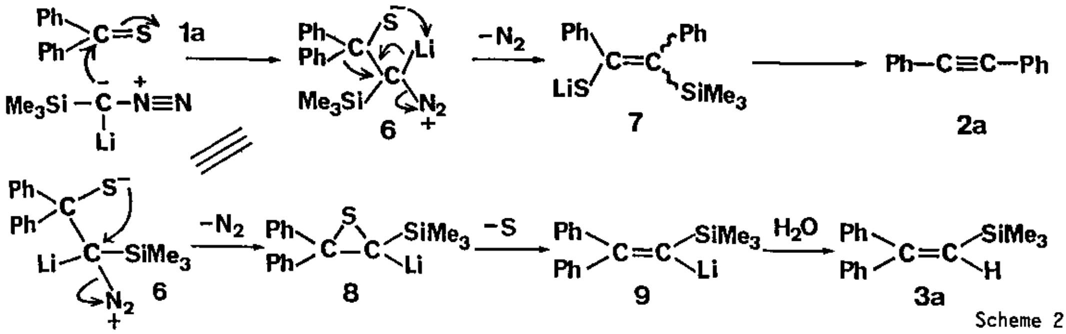
Abstract——Reaction of thioketones with lithium trimethylsilyldiazomethane affords alkynes, vinylsilanes, 1,2,3-thiadiazolines, or 1,2,3-thiadiazoles depending upon substrates and reaction solvents.

We have already demonstrated that the lithium salt of trimethylsilyldiazomethane (TMSC(Li)N_2), a useful [C-N-N] azole synthon,[2] smoothly reacts with thiocarbonyl compounds such as thionoesters, dithioesters, and carbon disulfide to give 5-substituted 1,2,3-thiadiazoles.[3] We now report the reaction of thioketones 1 with TMSC(Li)N_2, which gives various products **2**-**5** depending upon substrates and reaction solvents (Scheme 1).



Scheme 1.

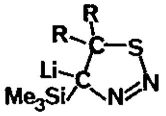
Diversity of the reaction will be apparent from the Table. Thiobenzophenone (**1a**) reacted with TMSC(Li)N_2 in tetrahydrofuran to give diphenylethyne (**2a**). This reaction has precedent in the reaction of benzophenone with TMSC(Li)N_2.[4] However, replacement of the reaction solvent from tetrahydrofuran 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)N_2 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]



Scheme 2.

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**.



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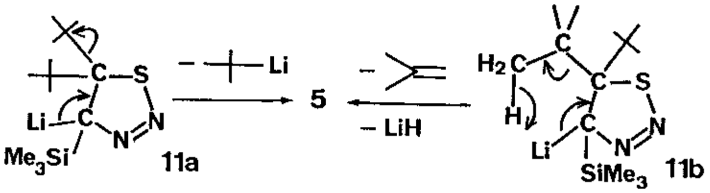
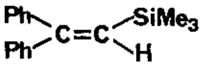
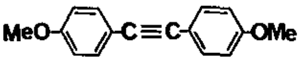
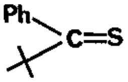
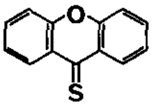
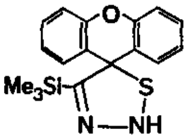
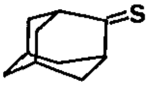
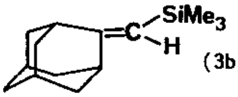
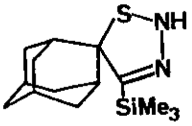
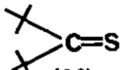
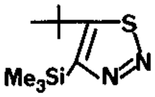
In contrast to the above results, the reaction of di-tert-butylthioketone (**1f**) gave rise to removal of the tert-butyl group and furnished 5-tert-butyl-4-trimethylsilyl-1,2,3-thiadiazole (**5**)[7] in good yield. A possible intermediate in this reaction would be **11a**, from which tert-butyllithium 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.



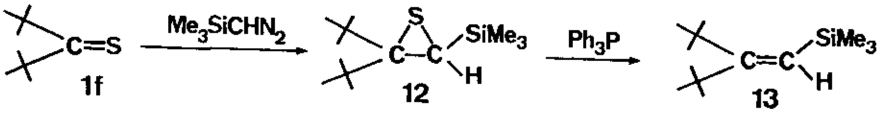
Scheme 3.

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 Solvent	Temp. & Time	Product[b]		Isolated Yield (%)	mp°C or bp°C/mmHg[c]
$Ph_2C{=}S$ (1a)	Et_2O	-70°C, 1h; 0°C, 1h		(3a)	41	140-150/17 [115/0.25][d]
	THF	-70°C, 1h; 0°C, 1h	Ph—C≡C—Ph	(2a)	46	59-60 [60-61][e]
$[p\text{-}MeOC_6H_4]_2C{=}S$ (1b)	Et_2O^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_2O	-70°C, 0.5h; 0°C, 2h		(2c)	57	70-80/17 [84/15][i]
	THF	-70°C, 0.5h; 0°C, 2h	2c		60	
 (1d)	Et_2O^j	-70°C, 0.5h; 0°C, 1h		(4a)	74	120-128 (dec)
 (1e)	Et_2O	-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_2O^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 $TMSC(Li)N_2$ in Et_2O (12ml) was added **1b** in Et_2O (1ml)-benzene (3ml). g) M. S. Newman and D. E. Reid, J. Org. Chem., **23**, 665 (1958). h) To $TMSC(Li)N_2$ in THF (10ml) was added **1b** in THF (3ml)-benzene (1ml). i) H. Bock and H. Alt, Chem. Ber., **103**, 1784 (1970). j) To $TMSC(Li)N_2$ in Et_2O (11ml) was added **1d** in Et_2O (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.



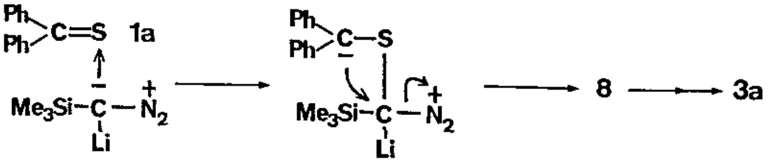
Scheme 4.

Diversity of the products and dramatic solvent effects observed in the reaction of thioketones with TMSC(Li)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 TMSC(Li)N_2, the reaction of thiobenzophenone (**1a**) with TMSC(Li)N_2 in tetrahydrofuran was carried out as follows: To a solution of trimethylsilyldiazomethane[8] (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

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



6. The alternative structure **14** of the product which was derived by thiophilic attack of TMSC(Li)N_2 will be excluded since the ^{1}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.

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7. Desilylation of **5** smoothly proceeded to give 5-tert-butyl-1,2,3-thiadiazole, bp 70-80°C/27mmHg(Kugelrohr), by the action of either the fluoride ion (KF·$2H_2O$, $\mathrm{Bu^n}_4$NCl, acetonitrile; r.t., 0.5h; 90%) or the hydroxide ion (LiOH·H_2O, H_2O-MeOH (1:5); reflux, 1h; 76%).
8. S. Mori, I. Sakai, T. Aoyama, and T. Shioiri, Chem. Pharm. Bull., **30**, 3380 (1982).

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