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REACTION OF LITHIOTRIMETHYLSILYLDIAZOMETHANE WITH α-OXOKETENE DITHIOACETALS

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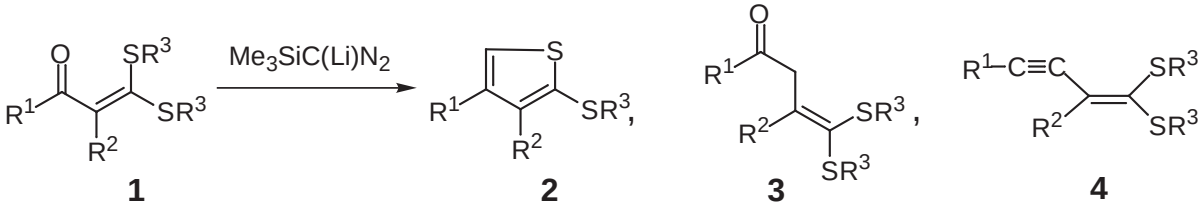
Abstract- Reaction of lithiotrimethylsilyldiazomethane with α-oxoketene dithioacetals affords thiophenes, homologous ketones , and homologous alkynes depending upon substrates used.

We have already reported that the reaction of lithiotrimethylsilyldiazomethane (TMSC(Li)N_2) with carbonyl compounds smoothly proceeds to generate alkylidenecarbenes which undergo various types of reactions to give homologous alkynes, aldehydes, and heterocycles.[1] For example, TMSC(Li)N_2 reacts with β-trimethylsiloxy ketones to give 5-trimethylsilyl-2,3-dihydrofurans *via* the oxonium ylide intermediates in good yields.[2] Furthermore, the reaction of TMSC(Li)N_2 with *N*,*N*-disubstituted β-amino ketones also gave 2-pyrrolines (Stevens rearrangement products) *via* the ammonium ylide intermediates although low yields.[3] As an extension of these works, we now report the reaction of TMSC(Li)N_2 with α-oxoketene dithioacetals (**1**) which gives various products (**2**-**4**) depending upon substrates used (Scheme 1).

Scheme 1

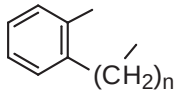


1 **2** **3** **4**

Diversity of the reaction will be apparent from the Table. α-Oxoketene dithioacetals (**1a**) derived from cyclohexanone reacted with TMSC(Li)N_2 to give the thiophene (**2a**). Similarly, **1b** and **1c** also gave the

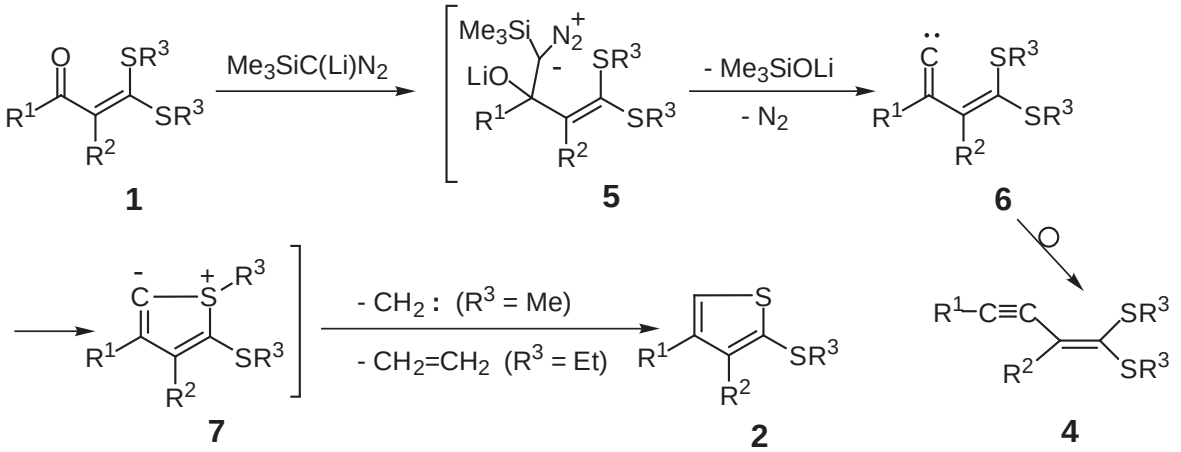
corresponding thiophenes (**2b** and **2c**), respectively. In this reaction, dimethoxyethane (DME) seemed to be the solvent of choice although tetrahydrofuran (THF) could also be used. Interestingly, no reaction occurred when diethyl ether was used as the reaction solvent.

Table. Reaction of Lithiotrimethylsilyldiazomethane with α-Oxoketene Dithioacetals (**1**)

Starting	Substrate						
1	R^1	R^2	R^3	Solvent	Reaction conditions	Product	Yield(%)
1a	$-(CH_2)_4-$		Me	DME	-78°C, 1 h; reflux, 2 h	**2a**	42
1b	$-(CH_2)_4-$		Et	DME	-78°C, 3 h; reflux, 2 h	**2b**	30
1c	$-(CH_2)_3-$		Me	DME	-78°C, 1 h; reflux, 2 h	**2c**	21
							
1d	n = 1			DME	-78°C, 2 h; reflux, 2 h	**3a**	10
1e	n = 2			DME	-78°C, 1 h; reflux, 2 h	**3b**	43
1f	Et	Me	Me	THF	-78°C, 2 h; reflux, 1 h	**4**	60

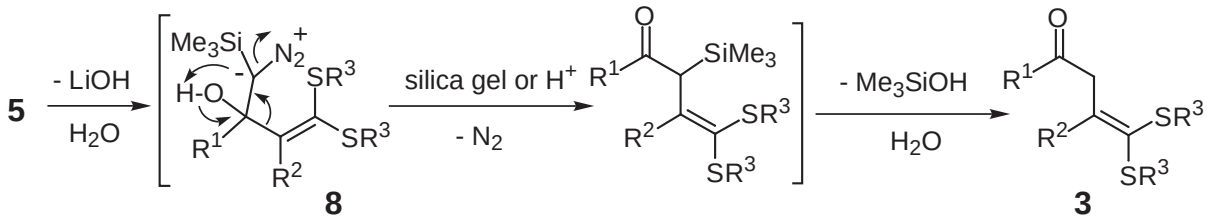
A possible mechanism for the formation of **2** may be explained as shown in Scheme 2 : the reaction of $TMSC(Li)N_2$ with **1** gives the alkylidenecarbene intermediate (**6**) *via* the diazo alkoxide (**5**). Subsequent cyclization of **6** affords the sulfonium ylide (**7**), from which elimination of methylene (for R^3 = Me) or ethylene (for R^3 = Et) gives **2**.

Scheme 2



In contrast to the above results, the α-oxoketene dithioacetals (**1d** and **e**) derived from 1-indanone and 1-tetralone gave the corresponding homologous β-dithiomethylene ketones (**3a** and **3b**) and no thiophenes could be detected. The formation of **3** would involve the decomposition of the first formed diazo alcohol (**8**) during the purification by the silica gel column chromatography (Scheme 3).

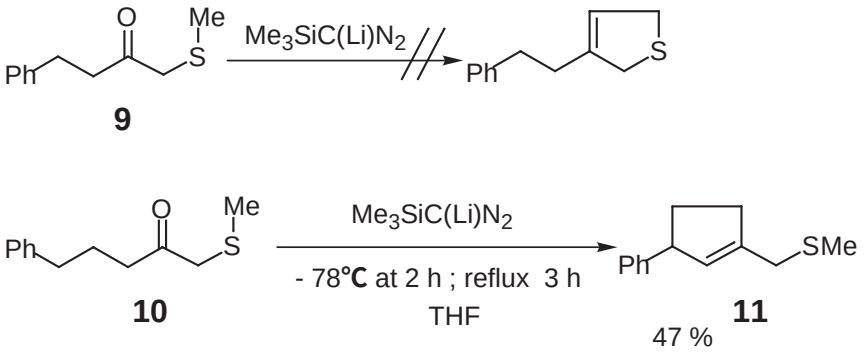
Scheme 3



Acyclic α-oxoketene dithioacetal (**1f**) also smoothly reacted with TMSC(Li)N_2, but the product was the ene-yne compound (**4**) resulting from the rearrangement of vinyl group (Scheme 2).[4]

In a previous paper, we reported that the reaction of TMSC(Li)N_2 with *N*,*N*-dialkyl-α-amino ketones gave 3-pyrrolines (C-H insertion products) in good yields.[5] We thought that dihydrothiophene could be obtained if α-methylthioketones were used as substrates. Unfortunately, the reaction of α-methylthioketone (**9**) with TMSC(Li)N_2 gave a complex mixture, while **10** bearing hydrogen at the γ-position smoothly reacted with TMSC(Li)N_2, but the product was the cyclopentene derivative (**11**)[6] and no dihydrothiophene could be detected (Scheme 4).

Scheme 4



ACKNOWLEDGEMENTS

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EXPERIMENTAL

Melting points were determined on a YANAGIMOTO micro melting point apparatus (hot plate). Distillation was carried out by a Kugelrohr apparatus. IR spectra were measured on a SHIMADZU FTIR-8100 spectrophotometer. ^{1}H-NMR spectra were measured at 270 MHz on a JEOL EX-270 spectrometer referred to TMS or $CHCl_3$ as an internal standard in $CDCl_3$. MS spectra were obtained on a JEOL JMS-SX 102A spectrometer. Column chromatography was performed on silica gel BW-200 MH (purchased from Fuji Davison Co.). Tetrahydrofuran was freshly distilled from benzophenone ketyl. Benzene, toluene, ethyl acetate, hexane, and acetonitrile were freshly distilled from calcium hydride. Dichloromethane and chloroform were dried by distillation from phosphorus pentoxide. Other solvents were distilled and stored over molecular sieves (4A).

General procedure : *n*-Butyllithium (1.5 M hexane solution, 0.40 mL, 0.6 mmol) was added dropwise to a solution of $TMSCHN_2$ (1.67 M hexane solution, 0.36 mL, 0.6 mmol) in DME (4 mL) at -78℃ under argon and the mixture was stirred at -78℃ for 15 min. A solution of the dithioacetal (**1**)[7] (0.5 mmol) in DME (1 mL) was then added dropwise at -78℃. The mixture was stirred at -78℃ for 1 h, and then refluxed for 2 h. After being quenched with cold water, the mixture was extracted with AcOEt (70 mL). The organic extracts were washed with saturated brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel to give the corresponding **2~4**.

1-Methylthio-4,5,6,7-tetrahydrobenzo[*c*]thiophene(2a)

Prepared from **1a** (101 mg, 0.5 mmol). The residue was purified by column chromatography on silica gel (AcOEt : hexane = 1:200) to give **2a** (39 mg, 42%) as a colorless oil. IR ν_{max} neat $_{cm}$-1: 1435, 1381, 1323, 1258, 1242. ^{1}H-NMR ($CDCl_3$) δ : 1.72-1.75 (m, 4H), 2.37 (s, 3H), 2.68 (m, 4H), 6.87 (s, 1H). HRMS (EI) Calcd for $C_9H_{12}S_2$: 184.0380. Found : 184.0379.

1-Ethylthio-4,5,6,7-tetrahydrobenzo[*c*]thiophene(2b)

Prepared from **1b** (115 mg, 0.5 mmol). The residue was purified by column chromatography on silica gel (AcOEt : hexane = 1 : 200) to give **2b** (30 mg, 30%) as a colorless oil. IR ν_{max} neat $_{cm}$-1 : 1447, 1435, 1381, 1258, 926. ^{1}H-NMR ($CDCl_3$) δ : 1.24 (t, 3H, J=7.4 Hz), 1.73-1.74 (m, 4H), 2.69-2.77 (m, 6H), 6.89 (s, 1H). HRMS (EI) Calcd for $C_{10}H_{14}S_2$: 198.0537. Found : 198.0507.

1-Methylthio-5,6-dihydro-4*H*-cyclopenta[*c*]thiophene(2c)

Prepared from **1c** (94 mg, 0.5 mmol). The residue was purified by column chromatography on silica gel (AcOEt : hexane = 1: 200) to give **2c** (18 mg, 21%) as a colorless oil. IR ν_{max}neat $_{cm}$-1 : 1435, 1372, 1312, 951. ^{1}H-NMR ($CDCl_3$) δ :2.09-2.13 (m, 5H) 2.35-2.40 (m, 4H) 6.47 (s, 1H). HRMS (EI) Calcd for $C_8H_{10}S_2$: 170.0224. Found : 170.0219.

3-[Bis(methylthio)methylene]-α-tetralone(3a)

Prepared from **1d** (118 mg, 0.5 mmol). The residue was purified by column chromatography on silica gel (AcOEt : hexane = 1 : 10) to give **3a** (13 mg, 10%) as a brown oil**.** IR ν_{max}neat $_{cm}$-1 : 1637, 1566, 1422, 1325, 1266. ^{1}H-NMR ($CDCl_3$) δ : 2.14 (s, 3H), 2.55 (s, 3H), 3.67 (s, 2H), 4.43 (s, 2H), 7.36 (dd, 1H, J=7.25, 7.42 Hz), 7.45 (d, 1H, J=7.42 Hz), 7.55 (dd, 1H, J=7.25, 7.42 Hz), 7.76 (d, 1H, J=7.58 Hz). HRMS (EI) Calcd for $C_{13}H_{14}OS_2$: 250.0480. Found : 250.0485.

3-[Bis(methylthio)methylene]-1-benzosuberone(3b)

Prepared from **1e** (125 mg, 0.5 mmol). The residue was purified by column chromatography on silica gel (AcOEt : hexane = 1 : 10) to give **3b** (57 mg, 43%) as a brown oil**.** IR ν_{max}neat $_{cm}$-1: 1682, 1599, 1455, 1433, 1306, 1223. ^{1}H-NMR ($CDCl_3$) δ : 2.19-2.25 (m, 1H), 2.29 (s, 3H), 2.31 (s, 3H), 2.47-2.54 (m, 1H), 3.03-3.13 (m, 2H), 3.93-3.99 (m, 1H), 6.02 (s, 1H), 7.23-7.34 (m, 2H), 7.45-7.50 (m, 1H), 8.08 (d, 1H, J=7.57 Hz). Anal. Calcd for $C_{14}H_{16}OS_2$: C, 63.63; H, 6.10. Found : C, 63.34; H, 6.08.

1-Bis(methylthio)-2-methyl-1-hexen-3-yne(4)

Prepared from **1f** (190 mg, 1 mmol). The residue was purified by column chromatography on silica gel (AcOEt : hexane = 1 : 80) to give **4** (113 mg, 60%) as a yellow oil. IR ν_{max}neat $_{cm}$-1 : 2215, 1433, 1318, 897. ^{1}H-NMR ($CDCl_3$) δ : 1.21 (t, 3H, J=7.4 Hz), 2.11 (s, 3H), 2.28 (s, 3H), 2.36 (s, 3H), 2.43 (q, 2H, J=7.4 Hz). HRMS (EI) Calcd for $C_9H_{14}S_2$: 186.0537. Found : 186.0537.

1-Methylthiomethyl-3-phenylcyclopentene(11)

Prepared from **10** (104 mg, 0.5 mmol). The residue was purified by column chromatography on silica gel (AcOEt : hexane = 1 : 150) to give **11** (48 mg, 47%) as a pale yellow oil. IR ν_{max}neat $_{cm}$-1 : 1601, 1491,

1453, 1250. ^{1}H-NMR ($CDCl_3$) δ : 1.75-1.90 (m, 1H), 2.06 (s, 3H), 2.43-2.56 (m, 3H), 3.26 (s, 2H), 3.85-3.93 (m, 1H) 5.59 (s, 1H), 7.18-7.28 (m, 5H). HRMS (EI) Calcd for $C_{13}H_{16}S$: 204.0973. Found : 204.0972.

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