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NEW METHODS AND REAGENTS IN ORGANIC SYNTHESIS. 32.[1)]
LITHIUM TRIMETHYLSILYLDIAZOMETHANE:
A NEW SYNTHON FOR THE PREPARATION OF 1,2,3-TRIAZOLES

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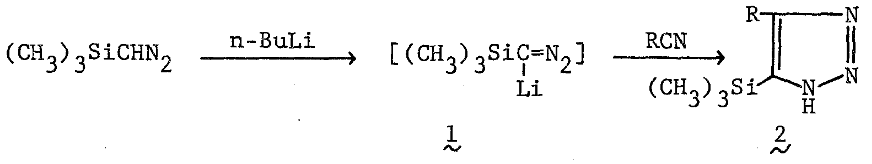
Lithium trimethylsilyldiazomethane, prepared from trimethylsilyldiazomethane and n-butyl lithium, reacts smoothly with various nitriles to give 4-substituted 5-trimethylsilyl-1,2,3-triazoles in excellent yields.

KEYWORDS —— trimethylsilyldiazomethane; lithiation; n-butyl lithium; 1,2,3-triazole; nitrile

Diazomethane is known to react with several activated nitriles, such as cyanogen, cyanogen halides, and cyanic acid esters, to give the corresponding 1,2,3-triazoles.[2)] However, with benzonitrile, the reaction requires Lewis acid catalysts and the products become a mixture of 1,2,3-triazole and its N-methyl derivatives.[2,3)] Furthermore, it has been reported that trimethylsilyldiazomethane (TMSCHN$_2$, $(CH_3)_3SiCHN_2$), as a stable and safe substitute for hazardous diazomethane, also reacts with cyanogen halides and trifluoroacetonitrile to afford 1,2,3-triazoles,[4)] but benzonitrile is completely unreactive toward TMSCHN$_2$.[5)] Apparently these reactions can not be used as general methods for the preparation of 1,2,3-triazoles since the nitriles used are limited to activated nitriles only.

In our preceding communication,[1)] we reported that the lithium salt of TMSCHN$_2$ reacts smoothly with various methyl esters of carboxylic acids to give 2-substituted 5-trimethylsilyltetrazoles in good yields. As an extension of this work, the present communication deals with a convenient and efficient preparation of 1,2,3-triazoles using the lithium salt of TMSCHN$_2$

We have found that lithium trimethylsilyldiazomethane (1), prepared from TMSCHN$_2$ and n-butyl lithium, reacts smoothly with nitriles at 0°C in diethyl ether to give 4-substituted 5-trimethylsilyl-1,2,3-triazoles (2) in excellent yields.



The utility of the procedure is well demonstrated in Table I. Various nitriles including aromatic, heteroaromatic, and aliphatic ones reacted efficiently with 1 to give 2. Lithium diisopropylamide (LDA) as well as n-butyl lithium could be used as

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the base. The double bond of neryl cyanide6) is completely intact to **1** (run 9). Nitrile functions adjacent to hetero atoms are also reactive to **1** to be transformed into 1,2,3-triazole functions. Thus, ethyl thiocyanate and phenyl cyanate afforded 4-ethylthio- and 4-phenoxy-5-trimethylsilyl-1,2,3-triazoles (runs 10 and 11). Diethyl phosphorocyanidate (DEPC) also reacted with **1** to give the 4-diethoxyphosphinyl derivative (run 12). Interestingly, however, cyanotrimethylsilane did not afford the corresponding 1,2,3-triazole, but gave bis(trimethylsilyl)diazomethane7) in 87% yield (run 13), which presumably resulted from the nucleophilic attack of **1** on the silicon atom of the nitrile. The trimethylsilyl group of **2** was easily removed with hydrochloric acid and potassium fluoride in ethanol to give 4-substituted 1,2,3-triazoles in high yields.8)

Table I9) Preparation of 4-Substituted 5-Trimethylsilyl-1,2,3-triazoles (**2**)

Run	R	Base	Reaction Time (h)	Yield (%)	mp(°C) or [bp(°C)/mmHg]
1	Phenyl	n-BuLi	3	93	89-90.5a,b)
2	Phenyl	LDA	3c)	93	
3	1-Naphthyl	n-BuLi	1.7	90	149.5-150a)
4	2-Pyridyl	n-BuLi	2.5	92	111.5-112.5a)
5	1-Isoquinolyl	n-BuLi	2	90	148.5-149.5a)
6	n-Propyl	n-BuLi	3	90	104.5-105a)
7	t-Butyl	n-BuLi	2	92	132.5-133.5a)
8	Benzyl	n-BuLi	2	96	143.5-144.5d)
9	Neryl	n-BuLi	2	75	[125/0.06]
10	Ethylthio	n-BuLi	2	90	55-57
11	Phenoxy	n-BuLi	2	44	91.5-93a)
12	Diethoxyphosphinyl	n-BuLi	5.3	63	73.5-74.5e)
13	Trimethylsilyl	n-BuLi	2.3	—f)	

a) Recrystallized from benzene-hexane. b) Lit.,10) mp 91°C.
c) Reaction was carried out at 0°C for 1.5 h, then at room temperature for 1.5 h. d) Recrystallized from benzene. e) Recrystallized from diethyl ether-hexane. f) Bis(trimethylsilyl)diazomethane was obtained in 87% yield, bp 90-100°C/13 mmHg (Lit.,7) bp 25°C/0.1 mmHg).

A typical experimental procedure for the preparation of **2** is as follows (run 1 in Table I): n-Butyl lithium (15% hexane solution, 0.76 ml, 1.2 mmol) was added dropwise to a solution of $TMSCHN_2$11) (0.55 ml, 1.2 mmol) in diethyl ether (10 ml) at 0°C under argon and the mixture was stirred for 20 min at 0°C. To the resulting solution was added dropwise a solution of benzonitrile (103 mg, 1 mmol) in diethyl ether (3 ml) at 0°C, then the mixture was stirred for 3 h at 0°C. The mixture was treated with saturated aqueous ammonium chloride and extracted with diethyl ether. The ethereal extracts were washed with water and dried over magnesium sulfate.

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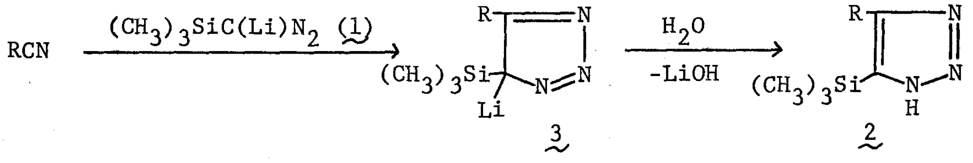
Concentration of the solvent gave the residue, which was purified by preparative layer chromatography (Merck silica gel 60 F_{254}, benzene: hexane: diethyl ether = 1:1:1) to give 4-phenyl-5-trimethylsilyl-1,2,3-triazole.[8)]

Müller and Ludsteck[12)] have reported that the reaction of lithium diazomethane with benzonitrile gives 3-phenyl-1,2,4-triazole in 42% yield. In contrast with the product using lithium diazomethane, the product was 1,2,3-triazole when lithium trimethylsilyldiazomethane (1) was used.

Mechanistically, this conversion of nitriles to 1,2,3-triazoles may be explained as follows: Either the nucleophilic attack of 1 on the nitrile carbon, followed by cyclization, or the 1,3-dipolar cycloaddition of the nitrile and 1 gives the intermediate 3. The resulting 3 is hydrolyzed with water to give 2.



1,2,3-Triazoles have been generally prepared by the cycloaddition of potentially explosive azides with acetylenes under forcing conditions.[2)] Our present method makes possible the conversion of nitriles to 1,2,3-triazoles, and will provide a mild and efficient methodology for the 1,2,3-triazole synthesis. Further works on the utility of lithium trimethylsilyldiazomethane as a synthon for the preparation of azoles are now under way in our laboratories.

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9) Satisfactory elemental analysis and spectral data were obtained for all the products.
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11) $TMSCHN_2$ used for the reaction was actually a solution of 2.2 mmol/ml in hexane, which was prepared by the diazo-transfer reaction of trimethylsilylmethylmagnesium chloride and diphenyl phosphorazidate (DPPA); see S. Mori, I. Sakai, T. Aoyama, and T. Shioiri, Chem. Pharm. Bull., 30, 3380 (1982).
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