NEW METHODS AND REAGENTS IN ORGANIC SYNTHESIS. 52.†,[1] LITHIUM TRIMETHYLSILYLDIAZOMETHANE: A NEW SYNTHON FOR THE PREPARATION OF 1-SUBSTITUTED 5-HYDROXY-1,2,3-TRIAZOLES FROM ISOCYANATES[2]

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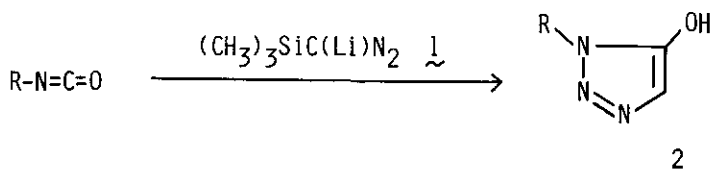
Abstract ——Lithium trimethylsilyldiazomethane reacts smoothly with isocyanates to give 1-substituted 5-hydroxy-1,2,3-triazoles in good yields.

Diazomethane is known to react with phenyl isocyanate with the elimination of nitrogen to give 1-phenyl-2-azetidinone.[3] Furthermore, it has been reported that trimethylsilyldiazomethane ($TMSCHN_2$, $(CH_3)_3SiCHN_2$) also reacts with phenyl isocyanate with loss of nitrogen to afford a red oil from which no heterocycle is isolated.[4] Unfortunately, the expected 1,3-dipolar cycloadducts, such as 1,2,3-triazoles, can not be obtained by these reactions.

We have already reported that the lithium salt of $TMSCHN_2$ is quite useful as a [C-N-N] synthon for the preparation of azoles.[5] As an extension of these works, the present communication deals with *a new and convenient preparation of 5-hydroxy-1,2,3-triazoles from isocyanates using the lithium* salt of $TMSCHN_2$.

We have found that lithium trimethylsilyldiazomethane (1), easily prepared from $TMSCHN_2$ and n-butyllithium, reacts smoothly with isocyanates to give 1-substituted 5-hydroxy-1,2,3-triazoles (2).



2

† Dedicated to Professor Shun-ichi Yamada on the occasion of his 70th birthday.

A typical experimental procedure for the preparation of 2 is as follows: To a solution of $TMSCHN_2$[6] (2M hexane solution, 0.6 ml, 1.2 mmol) in diethyl ether (10 ml) was added dropwise n-butyllithium (15% hexane solution, 0.76 ml, 1.2 mmol) at 0°C under argon and the mixture was stirred for 20 min at 0°C. A solution of 4-chlorophenyl isocyanate (154 mg, 1 mmol) in diethyl ether (3 ml) was then added dropwise at 0°C. After 2 h at 0°C, ice-water was added and the aqueous layer was separated. The organic layer was extracted with water and the combined aqueous layer was acidified with 2N hydrochloric acid. The resulting white precipitates were collected by filtration, dried in vacuo, and purified by silica gel column chromatography (Mallinckrodt, Silic AR CC-7 special, chloroform : ethanol= 10 : 1) to give 1-(4-chlorophenyl)-5-hydroxy-1,2,3-triazole (2b, 162 mg, 83%). In the preparation of 2a, 2d, and 2e, the white precipitates obtained after acidification were extracted with chloroform, washed with saturated aqueous sodium chloride, and dried over anhydrous magnesium sulfate. Concentration of the solvent gave the residue, which was purified as described above.

Table[a] Preparation of 1-Substituted 5-Hydroxy-1,2,3-triazoles (2)

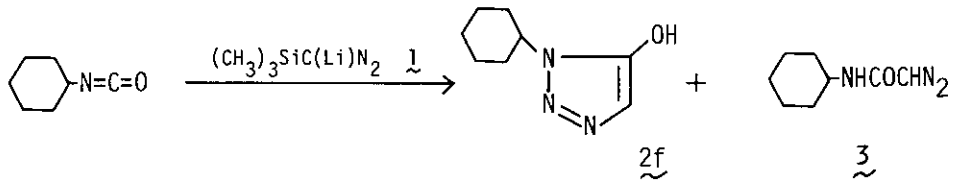
Product No.	R	Reaction Conditions	Yield (%)	mp (°C)	Recry. Solvent
2a	Phenyl	0°C, 2 h	79	113-115[b] (decomp.)	
2b	4-Chlorophenyl	0°C, 2 h	83	110.5 (decomp.)	Et_2O-Benzene
2c	1-Naphthyl	0°C, 1 h	83	125 (decomp.)	EtOH-Benzene
2d	n-Butyl	-78°C, 1.5 h r.t., 3.5 h	63	132-133	$CHCl_3$-Hexane
2e	t-Butyl	0°C, 1 h reflux, 6 h	53	125.5-130.5 (decomp.)	Benzene-Hexane
2f	Cyclohexyl	0°C, 1 h r.t., 1.7 h	71	147.5	

a) Unless otherwise stated, the reaction was carried out as a typical procedure. All products gave satisfactory elemental analysis and spectral data. b) Lit.,[7] mp 115°C.

The results are summarized in Table. Diethyl ether seems to be the solvent of choice. Aromatic isocyanates smoothly undergo the reaction with 1 at 0°C to give 2 in good yields. With aliphatic isocyanates, however, higher reaction temperature is required for the completion of the reaction, since the reaction proceeds slowly at 0°C. 1-Aryl-5-hydroxy-1,2,3-triazoles (2) obtained are

rather labile to heat in solution: for example, when 1-(1-naphthyl)-5-hydroxy-1,2,3-triazole (2c) was warmed at 50°C for 30 min in ethyl acetate, N-(1-naphthyl)-α-diazoacetamide was formed quantitatively.

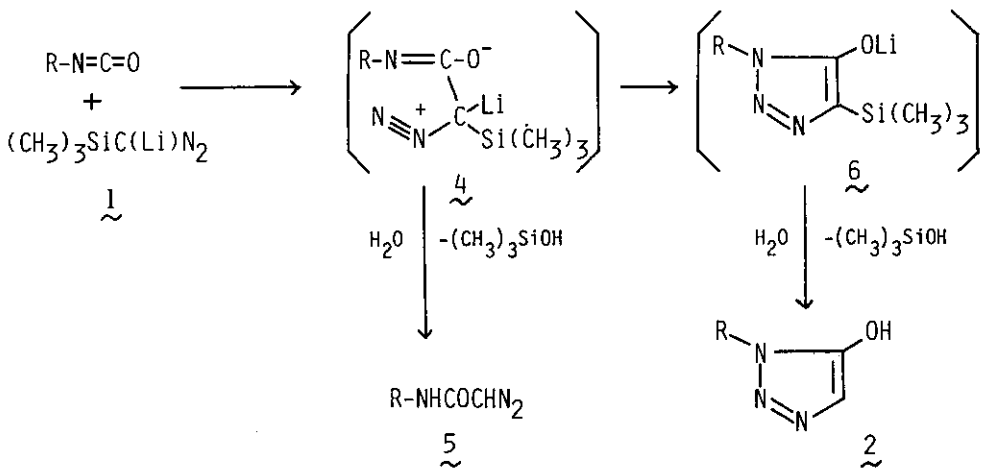
Treatment of cyclohexyl isocyanate with 1 at 0°C for 1 h, followed by quenching with water at 0°C afforded 1-cyclohexyl-5-hydroxy-1,2,3-triazole (2f) as a minor product (24%), and the major product (46%) was N-cyclohexyl-α-diazoacetamide (3).



2f 3

As shown in Table, however, only the desired 1,2,3-triazole 2f was obtained in 71% yield when the reaction temperature was raised to room temperature after the reaction at 0°C.

These experiments clearly demonstrate that the conversion of isocyanates to 5-hydroxy-1,2,3-triazoles 2 proceeds by a stepwise process, not by a concerted 1,3-dipolar cycloaddition process. Nucleophilic attack of 1 on the carbon atom of the isocyanate group will first produce the intermediate 4. Quenching with water at this stage will give the N-substituted α-diazoacetamide 5 with expulsion of the trimethylsilyl function. Prolonging the reaction time and/or raising the reaction temperature will promote the cyclization of 4 to furnish the 1,2,3-triazole intermediate 6, which is hydrolyzed with water during work-up to yield 2.



5-Hydroxy-1,2,3-triazoles have been generally prepared by the condensation of activated methylene compounds with highly explosive azides in the presence of base.[7,8] However, this method is applicable to only 5-hydroxy-1,2,3-triazoles bearing aryl or carbonyl containing groups in the 4-

position, except for 1-phenyl-5-hydroxy-1,2,3-triazole. The method described here has generality for the conversion of isocyanates to 1-substituted 5-hydroxy-1,2,3-triazoles under mild conditions, and will provide a new and convenient method for the preparation of 5-hydroxy-1,2,3-triazoles. As an extension of this work, a new preparation of 2-amino-1,3,4-thiadiazoles by the reaction of 1 with isothiocyanates will be reported in the following communication.[9]

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