Communications to the Editor

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NEW METHODS AND REAGENTS IN ORGANIC SYNTHESIS. 31.[1] LITHIUM TRIMETHYLSILYLDIAZOMETHANE: A NEW SYNTHON FOR THE PREPARATION OF TETRAZOLES

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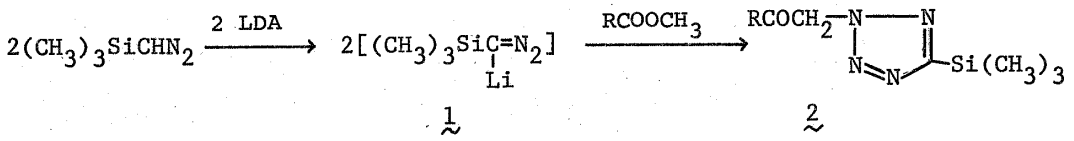
Lithium trimethylsilyldiazomethane, prepared from trimethylsilyldiazomethane and lithium diisopropylamide, reacts smoothly with methyl esters of carboxylic acids to give 2-substituted 5-trimethylsilyltetrazoles in good yields.

KEYWORDS —— trimethylsilyldiazomethane; lithiation; lithium diisopropylamide; methyl ester of carboxylic acid; tetrazole

Diazomethane is a well-known reagent for azole synthesis.[2] However, this reagent is highly toxic and potentially explosive and should be handled with great care. We have previously reported that trimethylsilyldiazomethane ($TMSCHN_2$, $(CH_3)_3SiCHN_2$), which is a stable and safe substitute for hazardous diazomethane, can be used for the Arndt-Eistert synthesis,[3] homologation of carbonyl compounds,[4] and methyl esterification of carboxylic acids.[5] As an extension of this work, we now wish to report that the lithium salt of $TMSCHN_2$ can be used as a synthon for the preparation of tetrazoles.

We have found that lithium trimethylsilyldiazomethane (1),[6] prepared from $TMSCHN_2$ and lithium diisopropylamide (LDA), reacts smoothly with the methyl esters of carboxylic acids at 0°C to give 2-substituted 5-trimethylsilyltetrazoles (2) in good yields.



1 2

The utility of the procedure is well demonstrated in Table I. Various methyl esters of aromatic carboxylic acids reacted efficiently with 1 to give 2. LDA seemed to be the base of choice, though n-butyl lithium could be used. Substituents on the benzene ring of the esters had no effect on the yields of 2. Methyl esters of heteroaromatic and aliphatic carboxylic acids also underwent the reaction with 1 to give 2. Removal of the trimethylsilyl group of 2 has been easily carried out with hydrochloric acid in methanol to give 2-substituted tetrazoles in high yields.[7]

A typical experimental procedure for the preparation of 2 is as follows (run 1

Table I[10] Preparation of 2-Substituted 5-Trimethylsilyltetrazoles (2)

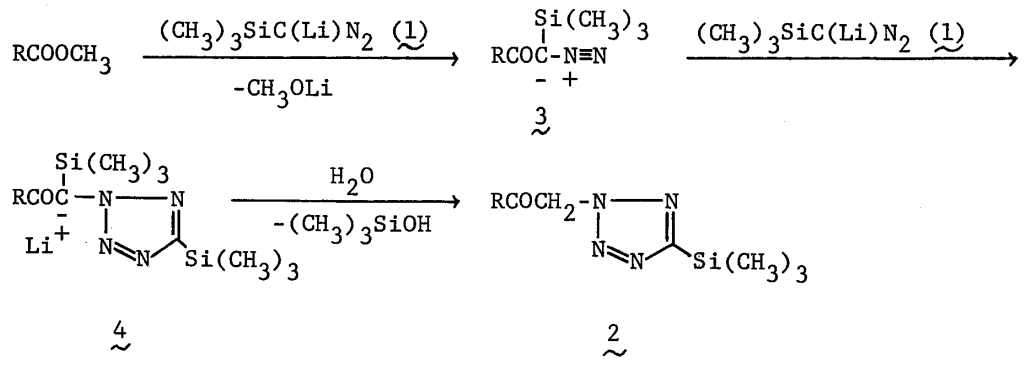
Run	$RCOOCH_3$ R=	Base	Yield(%)	2 Mp(°C)	NMR($CDCl_3$) δ ppm $Si(CH_3)_3$(s)	$COCH_2$(s)
1	Phenyl	LDA	90	oil	0.44	6.20
2	Phenyl	n-BuLi	70			
3	p-Tolyl	LDA	88	72-73.5[a]	0.44	6.12
4	p-Tolyl	n-BuLi	73			
5	p-Chlorophenyl	LDA	88	73-74[a]	0.44	6.12
6	p-Anisyl	LDA	81	101-102[a]	0.44	6.06
7	3-Pyridyl	LDA	60[b]	oil	0.43	6.10
8	Benzyl	LDA	49	100-101[a]	0.44	5.52
9	Ethyl	LDA	62	oil	0.41	5.42

a) Recrystallized from benzene-hexane. b) Reaction was carried out at -25~-20°C.

in Table I): A solution of LDA, prepared from diisopropylamine (243 mg, 2.4 mmole) and n-butyl lithium (15% hexane solution, 1.52 ml, 2.4 mmole) in diethyl ether (5 ml), was added dropwise to a solution of $TMSCHN_2$[8] (422 mg, 2.4 mmole) in diethyl ether (5 ml) at 0°C under argon atmosphere. The mixture was stirred at 0°C for 20 min. To the resulting solution was added dropwise a solution of methyl benzoate (136 mg, 1 mmole) in diethyl ether (3 ml) at 0°C, then the mixture was stirred for 3 h at 0°C. The mixture was treated with ice-water and extracted with diethyl ether. The ethereal extracts were washed with water and saturated aqueous sodium chloride, and dried over magnesium sulfate. Evaporation of the solvent gave a yellow oil, which was purified by preparative layer chromatography (Merck silica gel 60 F_{254}, benzene:hexane = 5:1) to give 2-phenacyl-5-trimethylsilyltetrazole.[7,9]

Müller and Ludsteck[11] have reported that the reaction of lithium diazomethane with ethyl benzoate gives 2-phenyl-1,3,4-oxadiazole in 20% yield. In contrast with the product using lithium diazomethane, the product was tetrazole when lithium trimethylsilyldiazomethane (1) was used.

Mechanistically, the interesting conversion of esters to tetrazoles may be explained as follows: Initial attack of 1 on the ester carbonyl carbon affords the α-silyldiazomethylketone 3. Either the nucleophilic attack at the terminal nitrogen of 3 with a second molecule of 1, followed by cyclization, or the 1,3-dipolar cycloaddition of 3 and 1 gives the intermediate 4, which is hydrolyzed with water to give 2.



Tetrazoles have been generally prepared by the cycloaddition of potentially explosive azides to nitriles.[12] Our present method makes possible the conversion of esters to tetrazoles, and provides a novel and convenient method for the tetrazole synthesis. Further work on the utility of lithium trimethylsilyldiazomethane (1) as a synthon for the preparation of azoles is now under way in our laboratories.[13,14]

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REFERENCES AND NOTES

1) For Part 30, see S. Toyama, T. Aoyama, and T. Shioiri, Chem. Pharm. Bull., 30, No.8, in press (1982).
2) J. S. Pizey, "Synthetic Reagents", Vol.II, Ellis Horwood Ltd., Chichester, 1974, Chapter 2.
3) a) T. Aoyama and T. Shioiri, Tetrahedron Lett., 21, 4461 (1980); b) T. Aoyama and T. Shioiri, Chem. Pharm. Bull., 29, 3249 (1981).
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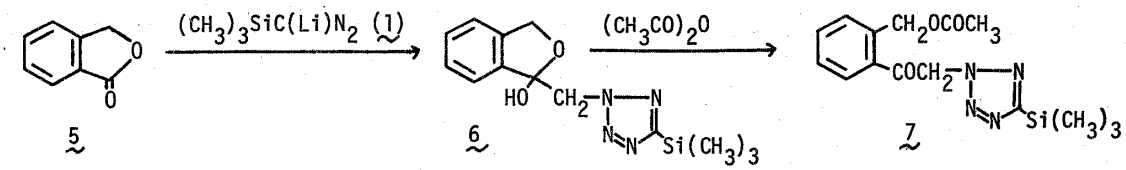
6) A few limited studies on the synthetic use of 1 have been reported: a) U. Schöllkopf and H.-U. Scholz, Synthesis, 1976, 271; b) E. W. Colvin and B.J. Hamill, J. Chem. Soc. Perkin I, 1977, 869.
7) For example, 2-phenacyl-5-trimethylsilyltetrazole (0.4 mmole) was refluxed with concentrated hydrochloric acid (two drops) in methanol (10 ml) for 1 h to give 2-phenacyltetrazole in 89% yield, mp 99-100°C, whose structure was unambiguously confirmed by comparing it with the authentic sample prepared from tetrazole and phenacyl bromide; see P. Yates, R. G. F. Giles, and D. G. Farnum, Can. J. Chem., 47, 3997 (1969).
8) $TMSCHN_2$ used for the reaction was a mixture of trimethylsilyldiazomethane (65 w/w%) and hexamethyldisiloxane (35 w/w%).[3b]
9) Benzoyl chloride and benzoyl cyanide also reacted with lithium trimethylsilyldiazomethane (1) to give 2-phenacyl-5-trimethylsilyltetrazole in 72 and 45% yields, respectively.
10) Satisfactory elemental analysis and spectral data were obtained for all the products.
11) E. Müller and D. Ludsteck, Chem. Ber., 88, 921 (1955).
12) a) F. R. Benson, "Heterocyclic Compounds", Vol.8, ed. by R. C. Elderfield, John Wiley and Sons, Inc., New York, 1967, Chapter 1. b) R. N. Butler, "Advances in Heterocyclic Chemistry", Vol.21, ed. by A. R. Katritzky and A. J. Boulton, Academic Press, New York, 1977, p. 323.
13) Phthalide (5) also reacted with 1 to give the tetrazole 6 in 42% yield, which on treatment with acetic anhydride in pyridine afforded the keto acetate 7.



5 6 7

14) A new preparation of 1,2,3-triazoles by the reaction of 1 with various nitriles will be the subject of our forthcoming publication.

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