CHEMISTRY LETTERS, pp. 1477-1478, 1982.

REACTION OF TRIMETHYLSILYL AZIDE WITH ORGANIC HALIDES

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Trimethylsilyl azide reacted readily with benzyl, allyl, and aliphatic halides to give the corresponding azides in good to excellent yields.

Trimethylsilyl azide (TMSA) is known as a good reagent in organic synthesis. It has been reported that TMSA reacts with acetylenes,[1)] olefins,[2)] and nitriles[2a,3)] to give the corresponding 1,3-dipolar cycloadducts. The reactions of TMSA with aliphatic aldehydes[4)] and epoxides[5)] were also reported to give the corresponding trimethylsiloxy azides. As for azide synthesis, the use of sodium azide is well established, while little attention has been focused on the reaction of silyl azide with organic halides. In this communication, we wish to report the substitution reaction of organic halides, such as benzyl, allyl, and aliphatic halides, with TMSA under *homogeneous* and *neutral* conditions in *non-aqueous* solvent.

A solution of TMSA (1.35 g, 12 mmol) and benzyl chloride (0.63 g, 5 mmol) in hexamethylphosphoramide (3 ml) was heated at 60° for 24 hr. Benzyl azide was isolated in 65% yield along with recovered benzyl chloride by preparative thin layer chromatography on alumina; gas-chromatography showed the presence of trimethylchlorosilane (eq. 1). In the reaction with benzyl bromides, the corresponding benzyl azides, except for 1-phenylethyl azide, were obtained in the quantitative yields as shown in Table and no starting materials were detected by nmr or tlc. The reaction with p-cyanobenzyl bromide gave p-cyanobenzyl azide as the sole product, though the cyano group of benzonitrile was known to react with TMSA affording a 1,3-dipolar

$$\mathrm{ArCH_2X} \quad + \quad \mathrm{Me_3SiN_3} \quad \longrightarrow \quad \mathrm{ArCH_2N_3} \quad + \quad \mathrm{Me_3SiX} \qquad (1)$$

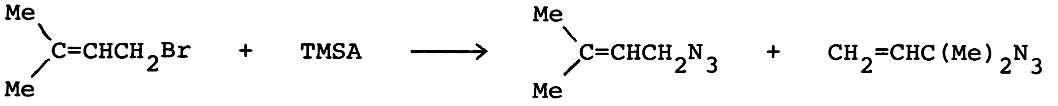
Table. Reaction of Benzyl Halides with Trimethylsilyl Azide

Starting Materials	Yield, %	
	isolated	nmr*
$PhCH_2Cl$	65	
$PhCH_2Br$	87	100
PhCH(Me)Br		46
p-$MeC_6H_4CH_2Br$	85	100
p-$MeOC_6H_4CH_2Br$		100
p-$NCC_6H_4CH_2Br$		100

*Determined by proton nmr and compared with authentic materials.

cycloadduct, 2-trimethylsilyl-5-phenyltetrazole.[3]

These results led us to try the reactions to allyl and aliphatic halides systems. Allyl azide, which had been obtained in only 30% yield from allyl halide and sodium azide,[6] was formed quantitatively in the reaction of allyl bromide with TMSA. Several mechanisms have been delineated for the reaction of allylic compounds with azide ion.[7] TMSA is expected to be a good reagent for mechanistic study of these reactions, because it would not involve free azide ion under the reaction conditions used. Work-up of a reaction mixture of TMSA and 3-methyl-2-butenyl bromide gave two isomeric azides, 3-methyl-2-butenyl azide (1, 85%) and 1-methyl-2-butenyl azide (2, 15%) (eq. 2). The structural assignments and the yields for 1 and 2 were made from their proton nmr spectra.



$$\mathrm{Me_2C{=}CHCH_2Br} + \mathrm{TMSA} \longrightarrow \underset{1}{\mathrm{Me_2C{=}CHCH_2N_3}} + \underset{2}{\mathrm{CH_2{=}CHC(Me)_2N_3}} \qquad (2)$$

It has been reported that the pure azides, separated by low temperature fractionation, isomerize very rapidly to an equilibrium mixture of the two isomers at moderate temperature.[8] In the reaction of TMSA and the bromide, the molar ratio of 1 to 2 was almost equal to that in Ref. 8. This finding indicates that 1 is formed in the substitution as a primary product, which isomerizes to 2 to give the equilibrium mixture. The reactions of chloroacetonitrile and ethyl chloroacetate with TMSA gave the azides in 65[9] and 60%[10] yields, respectively. In these cases, the cyano[3] and ethoxycarbonyl[11] groups did not react with TMSA under the reaction conditions as described above. These reactions are rationalized by strong affinity between silicon and halogen atoms.

These results indicate that TMSA may be a useful reagent, as well as sodium azide, for azide synthesis and that it may be used in synthesis of amino compounds under non-aqueous and neutral conditions because the azido group can be regarded as a precursor of amine. Work is in progress to extend the synthetic scope.

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(Received June 23, 1982)