Selective Formation of Alkyl Azides Using Trimethylsilyl Azide and Carbonyl Compounds

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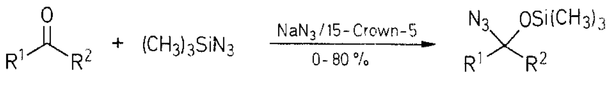
Whereas tin(II) chloride, or zinc chloride, catalyzed reaction of trimethylsilyl azide (TMSA) with carbonyl compounds gave *gem*-diazides **3**, a catalytic amount of sodium azide/15-crown-5 promoted an addition reaction of TMSA toward these compounds to give α-siloxy azides **2** exclusively. A stereoelectronic effect was found to be important for these reactions.

There have been some reports on the reactivity of silyl azides toward carbonyl compounds. The first example reported was a catalytic addition of trimethylsilyl azide (TMSA) to aliphatic aldehydes.[1] A similar addition reaction of TMSA to 2-methylpropanal and hexanal was studied as a part of carbonyl insertion reactions of silicon pseudohalides, but its application to unsaturated aldehydes and ketones proved to be unsuccessful.[2] The reaction of chlorotrimethylsilane, sodium azide, and cyclohexanone gave 1-azido-1-trimethylsiloxycyclohexane (**2o**).[3] However, this reacton did not involve prior *in situ* formation of TMSA.[4] Recently, we found metal halide-induced reactions, leading to *gem*-diazides **3** from both ketones[4] and aldehydes.[5] Thus, an isolation of α-siloxy azides **2** from the reactions of ketones, and aromatic and conjugated aldehydes with TMSA has never been hitherto achieved by either method reported so far.[1-5] In this paper, we describe selective and systematic formations of various alkyl azides, including α-siloxy azides **2** and *gem*-diazides **3**, using TMSA and carbonyl compounds induced by sodium azide/15-crown-5 or metal halide [zinc chloride or tin (II) chloride]. The former catalytic system converted these compounds into **2** and the latter into **3**. Furthermore, the importance of a stereoelectronic effect was observed for these reactions.

As described in our previous reports,[5] a reaction of 2-methylpropanal (**1b**) and TMSA (2.3 equiv) in the presence of a catalytic amount of zinc chloride gave 1,1-diazido-2-methylpropane (**3b**) in 69% yield. Even when the reaction was carried out by using 1.3 equivalent of TMSA, the sole product was analogously *gem*-diazide **3b** although in a low yield. In contrast to these results, 1-azido-2-methyl-1-trimethylsiloxypropane (**2b**) was exclusively obtained in 62% yield from a reaction of **1b** and TMSA catalyzed by sodium azide/15-crown-5 without solvent at room temperature. When solvent was used, the yield of **2b** was decreased to less than 10%. Other aldehydes were treated in a similar manner and the results are listed in Table 1. For the sake of comparison, the yields of **3** obtained from the zinc chloride-catalyzed reactions[5] are also shown in Table 1.



1 **2**

Table 1. Reaction of Carbonyl Compounds with TMSA Catalyzed by NaN_3/15-Crown-5 (Method A) and by Metal Halide (Method B)

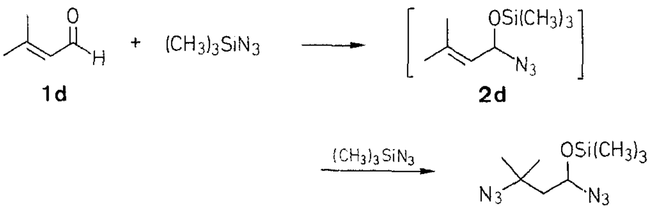
Carbonyl Compound	R^1	R^2	Product Yield (%) 2^a	3^b	3^c
1a	n-C_3H_7	H	52 (63)	78	–
1b	i-C_3H_7	H	62 (84)	69	–
1c	i-C_4H_9	H	58 (95)	62	–
1e	C_6H_5	H	27 (77)	87	–
1f	4-$CH_3C_6H_4$	H	8 (64)	88	–
1g	4-ClC_6H_4	H	45 (47)	93	–
1h	4-$NO_2C_6H_4$	H	52 (63)	58	–
1i	CH_3	C_2H_5	17 (32)	–	52
1j	CH_3	n-C_3H_7	8	–	47
1k	CH_3	i-C_3H_7	4	–	40
1l	CH_3	C_6H_5	0	–	27
1m	C_2H_5	C_2H_5	4	–	39
1n	$-(CH_2)_4-$		10	–	13[d]
1o	$-(CH_2)_5-$		80	–	48
1p	$-(CH_2)_4CH(CH_3)-$		36	–	–
1q	$-(CH_2)_6-$		trace	–	6[d]

[a] By Method A (Carbonyl compound: TMSA = 1 : 2). Spectroscopic yield is shown in parenthesis.
[b] From Ref. 5.
[c] By Method B (ketone: TMSA = 1 : 3). $SnCl_2 \cdot 2H_2O$ for **1i–m** and $ZnCl_2$ for **1n**, **1o** and **1q** were used as a catalyst.
[d] Tetrazole derivatives were included in 3% from **1n** and 13% from **1q**, respectively.

Table 2. Physical and Spectral Data of Compounds 2 Prepared

Compound	bp (°C)/mbar	Molecular Formula or Lit. bp (°C)/mbar	IR (Neat) ν(cm⁻¹) N_3	SiOC	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)
2a	45/8	65/21[1]	2100	1090	0.30 [s, 9H, $Si(CH_3)_3$]; 1.20 (t, 3H, J = 6.4, CH_3); 1.60–2.70 (m, 4H, CH_2CH_2); 4.95 (t, 1H, J = 5.4, CHN_3)
2b			2100	1090	0.21 [s, 9H, $Si(CH_3)_3$]; 0.95 (d, 6H, J = 6.2, CH_3); 4.49 (d, 1H, J = 5.5, CHN_3)
2c	43–45/7	$C_8H_{19}N_3OSi$ (201.4)	2100	1090	0.25 [s, 9H, $Si(CH_3)_3$]; 0.95 (d, 6H, J = 5.4, CH_3); 1.20–1.80 (m, 3H, CH_2CH_2); 4.78 (t, 1H, J = 7.0, CHN_3)
2e	51–53/0.33	$C_{10}H_{15}N_3OSi$ (221.3)	2080	1090	0.27 [s, 9H, $Si(CH_3)_3$]; 5.77 (s, 1H, CHN_3); 7.40 (m, 5H, C_6H_5)
2f		$C_{11}H_{17}N_3OSi$ (235.4)	2100	1080	0.25 [s, 9H, $Si(CH_3)_3$]; 2.38 (s, 3H, Ar–CH_3); 5.74 (s, 1H, CHN_3); 7.18, 7.35 (AB quartet, 4H_{arom}, J = 8.5)
2g		$C_{10}H_{14}ClN_3OSi$ (255.8)	2080	1080	0.23 [s, 9H, $Si(CH_3)_3$]; 5.70 (s, 1H, CHN_3); 7.33 (s, 4H_{arom})
2h		$C_{10}H_{14}N_4O_3Si$ (266.4)	2100	1080	0.27 [s, 9H, $Si(CH_3)_3$]; 5.80 (s, 1H, CHN_3); 7.60, 8.25 (AB quartet, 4H_{arom}, J = 8.7)
2i	40–42/9	$C_7H_{17}N_3OSi$ (187.3)	2100	1060	0.22 [s, 9H, $Si(CH_3)_3$]; 0.97 (t, 3H, J = 7.0, CH_2CH_3); 1.44 (s, 3H, CH_3); 1.67 (q, 2H, J = 7.0, CH_2CH_3)
2j	48/9	$C_8H_{19}N_3OSi$ (201.4)	2100	1120	0.20 [s, 9H, $Si(CH_3)_3$]; 0.96 (t, 3H, J = 6.2, CH_2CH_3); 1.43 (s, 3H, CH_3); 1.20–1.70 (m, 4H, CH_2CH_2)
2k		$C_8H_{19}N_3OSi$ (201.4)	2100	1080	0.20 [s, 9H, $Si(CH_3)_3$]; 0.95 [d, 6H, J = 6.4, $CH(CH_3)_2$]; 1.38 (s, 3H, CH_3); 1.7–2.1 (m, 1H, CH)
2m		$C_8H_{19}N_3OSi$ (201.4)	2090	1070	0.21 [s, 9H, $Si(CH_3)_3$]; 0.93 (t, 6H, J = 7.0, 2 × CH_2CH_3); 1.73 (q, 4H, J = 7.0, 2 × CH_2CH_3)
2n		$C_8H_{17}N_3OSi$ (199.3)	2100	1130	0.20 [s, 9H, $Si(CH_3)_3$]; 1.70–1.90 [m, 8H, $(CH_2)_4$]
2o		$C_9H_{19}N_3OSi$ (213.4)	2100	1110	0.20 [s, 9H, $Si(CH_3)_3$]; 1.30–1.80 [m, 10H, $(CH_2)_5$]
2p		$C_{10}H_{21}N_3OSi$ (227.4)	2090	1100	0.25 [s, 9H, $Si(CH_3)_3$]; 0.97 (d, 3H, J = 6.4, CH_3); 1.30–1.80 [m, 9H, $CH(CH_2)_4$]

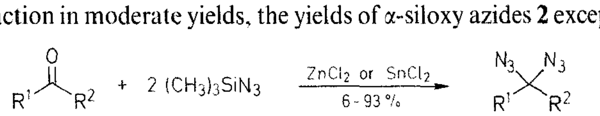
With aliphatic aldehydes **1a–1c**, isolated yields of α-siloxy azides **2a–c** were comparable with those of the zinc chloride-catalyzed reaction.[1] Although compounds of type **2** were never obtained from α,β-unsaturated and aromatic aldehydes,[2,5] the azide-crown ether catalytic system also converted these compounds into the corresponding adducts **2** or related compounds. For example, 3-methyl-2-butenal (**1d**) was converted into 1,3-diazido-3-methyl-1-trimethylsiloxybutane (**2d'**), which seems to be a further reaction product of the corresponding α-siloxy azide **2d**, in 55% yield (isolated by column chromatography on silica gel in 26% yield).



1d **2d** **2d'**

By spectroscopic analysis of adducts **2** obtained from aromatic carbonyl compounds no remarkable substituent effect was observed. However, there was a profound difference between spectroscopic yield and isolated yield for **2** when electron-withdrawing substituents are absent on the benzene ring. Generally, such trends seem to be attributable to the stability or the reactivity of the product itself. Therefore, in this case, the adducts are supposed to be reactive species toward moisture or another TMSA, or these would give the starting aldehydes and TMSA under the conditions because the addition process was definitely reversible.[5] Also, it may be concerned with the fact that the nitriles were obtained from these compounds in good yields by the zinc chloride-catalyzed reaction.[5]

Similarly, effective carbonyl insertion of TMSA employing ketones was attempted. The results concerning the reactions catalyzed by the azide-crown ether (Method A) and by metal halides (Method B) are also compiled in Table 1. Although the *gem*-diazides **3** were obtained from the metal halide-catalyzed reaction in moderate yields, the yields of α-siloxy azides **2** except



1 **3**

for 1-azido-1-trimethylsiloxycyclohexanes **2o** and **2p** were significantly lower than those from aldehydes. In both methods, the yields were drastically decresed when solvent was used. Cyclohexanone (**1o**) was converted into **2o** in 80% yield with the azide-crown ether catalyst. On the other hand, either **2o** (61%) or **3o** (48%) was obtained from the zinc chloride-catalzyed

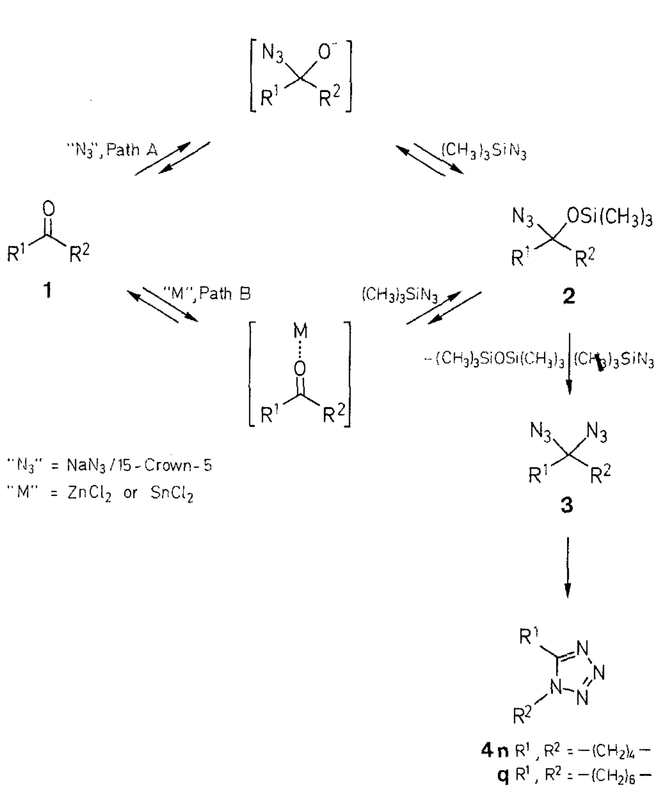
Table 3. Diazides 3 Prepared

Compound	Molecular Formula	IR (Neat) ν_{N_3} (cm⁻¹)	^{1}H-NMR ($CDCl_3$/TMS)	MS (30 eV) m/z
3j	$C_5H_{10}N_6$ (154.2)	2100	0.98 (t, 3H, J = 8.1, CH_2CH_3); 1.50 (s, 3H, CH_3); 1.30–1.70 (m, 4H, CH_2CH_2)	111 (M^+-C_3H_7)
3k	$C_5H_{10}N_6$ (154.2)	2100	0.91 [d, 6H, J = 7.2, $CH(CH_3)_2$]; 1.43 (s, 3H, CH_3); 1.80–2.00 (m, 1H, CH)	111 (M^+-C_3H_7)
3l	$C_8H_8N_6$ (188.2)	2100	1.80 (s, 3H, CH_3); 7.40 (m, 5H, C_6H_5)	146 (M^+-N_3)
3m	$C_5H_{10}N_6$ (154.2)	2100	0.90 (t, 6H, J = 8.5, 2 × CH_2CH_3); 1.70 (q, 4H, J = 8.5, 2 × CH_2CH_3)	125 (M^+-C_2H_5)
3n	$C_5H_8N_6$ (152.2)	2100	1.70–2.10 (m, CH_2)	82 (M^+-N_5)
3o	$C_6H_{10}N_6$ (166.2)	2100	1.30–2.10 (m, CH_2)	167 (M^+ + H)
3q	$C_7H_{12}N_6$ (180.2)	2100	1.40–1.70 (m, CH_2)	110 (M^+ – N_5)

reactions, depending upon the quantity of TMSA used. Conversions of cyclopentanone (**1n**) and cycloheptanone (**1q**) into the adducts **2n** (10%) and **2q** (trace) was low as were those of acyclic ketones **1i–1m**. Also, the isolated yields of **3n** and **3q** were relatively decreased when the metal halide-induced reaction of **1n** and **1q** was carried out.

Among several experiments, the best yields of **2** and **3** obtained are shown in Table 1. Such tendency has been investigated in the study on the relative reactivity of hydroboration toward carbonyl compounds,[6] i.e., cyclohexanone was reduced by sodium borohydride 23 times faster than cyclopentanone. The relative ease of conversion of carbon atoms from sp^3 to sp^2 or *vice versa* is accounted in terms of stereoelectronic effect. The reactions of carbonyl compounds with TMSA described herein would be also controlled by the effect.

From the controlled experiments, it was proven that compounds **2** and **3** were produced stepwise and the first step (addition process of TMSA to carbonyl group) induced by either procedure was reversible. Tetrazoles were obtained directly from carbonyl compounds and TMSA.[4,5] The reaction course is postulated to take place as shown. If the catalytic reaction suggested in path A is correct, it appears that azide ion is capable of affording azido alkoxide. α-Siloxy azide **2** was obtained from ketone in the small equilibrium concentration. The azide-crown ether catalyst did not promote the second step (condensation process of **2** with TMSA) under the conditions used. Thus, selective formations of **2** and **3** were easily achieved by varying the catalytic system.



IR spectra were taken on a Hitachi 260-10 spectrometer. ^{1}H- and ^{13}C-NMR spectra were recorded on a Hitachi R-600 and a Varian XL-300 spectrometers. Mass spectra were recorded on a JEOL DX-300 spectrometer. Aldehydes and ketones used are commercial products and purified by distillation if necessary.

Stability and Handling: All azides prepared including TMSA[8] are thermally stable in usual handling. Most of them can be distilled at reduced pressure. The stability of these azides to shock are not ascertained exactly.

Trimethylsilyl Azide:[7]

In a 1 L three-necked flask fitted with a reflux condenser and a mechanical stirrer is placed Me_3SiCl (134 g, 1.24 mol) and NaN_3 (97 g, 1.49 mol) without catalyst[8] in di-*n*-butyl ether (600 mL). The mixture is heated to 100 °C with continous stirring. After 48 h, the mixture is directly distilled from the reaction vessel through a Vigreux column and a fraction boiling at a range of 90–105 °C is collected. Redistillation of the crude TMSA containing di-*n*-butyl ether is carried out using an Widmer column to give a colorless liquid; yield: 114 g (80%); bp 95–96 °C.

IR (Neat): $\nu = 2100\ cm^{-1}$ (N_3).

^{1}H-NMR ($CDCl_3$/TMS): $\delta = 0.29$ [s, $Si(CH_3)_3$].

Formation of α-Siloxy Azides 2 (Method A):

As typical procedure the reaction of 2-methylpropanal (**1b**) and TMSA is shown. A mixture of 2-methylpropanal (**1b**; 3.0 g, 42 mmol), TMSA (9.6 g, 83 mmol), NaN_3 (0.27 g, 4 mmol), and 15-crown-5 (0.46 g, 2 mmol) is stirred in the absence of solvent at room temperature for 24 h. After careful evaporation of the unreacted TMSA *in vacuo*, aqueous $NaHCO_3$ (20 mL) is added to the mixture, the organic product is extracted with CH_2Cl_2 (3 × 50 mL) and the combined CH_2Cl_2 layer is dried ($MgSO_4$). The residue left on evaporation of the solvent is chromatographed on silica gel or neutral alumina. Elution with hexane gives a colorless oil; yield: 4.8 g (62%). The spectral data are given in Table 2.

1,3-Diazido-3-methyl-1-trimethylsiloxybutane (2d′):

A mixture of **1d** (1.73 g, 20.6 mmol), TMSA (4.75 g, 41.2 mmol), NaN_3 (0.135 g, 2.06 mmol) and 15-crown-5 (0.23 g, 1.03 mmol) is stirred for 39 h at room temperature. After similar work-up as given above, the mixture is chromatographed in silica gel. Elution with hexane gives a colorless liquid characterized as **2d**; yield: 1.22 g (26%).

IR (neat): $\nu = 2100$ (N_3), and $1100\ cm^{-1}$ (SiOC).

^{1}H-NMR ($CDCl_3$/TMS): $\delta = 0.22$ [s, 9H, $Si(CH_3)_3$]; 1.33 (s, 3H, CH_3); 1.34 (s, 3H, CH_3); 1.90 (d, 2H, $J = 5.6$ Hz, CH_2); 4.86 (t, 1H, $J = 5.6$ Hz, CH).

^{13}C-NMR ($CDCl_3$/TMS): $\delta = -0.21$ (q, SiC); 26.44 (q, CH_3); 26.82 (q, CH_3); 47.73 (t, CH_2); 59.54 (s, CN_3); 83.38 (d, CHOSi).

MS (30 eV): $m/z = 144$ [$CH(N_3)OTMS^+$].

Formation of *gem*-Diazides 3 (Method B):

As typical procedure the reaction of 2-butanone (**1i**) and TMSA is representative. To a mixture of 2-butanone (**1i**; 3.1 g, 43 mmol) and $SnCl_2 \cdot 2H_2O$ (0.3 g, 1.3 mmol) is added dropwise TMSA (15 g, 130 mmol) at 0 °C during the course of 1 h with stirring, which is kept for additional 20 h at room temperature. The reaction is quenched by the addition of aqueous $NaHCO_3$ (20 mL) and extracted with ether (3 × 50 mL). The combined ether extract is dried ($MgSO_4$) and the solvent evaporated to give a colorless liquid; yield: 3.1 g (52%); bp 52–53 / 39 mbar (stable at this temperature).

IR (Neat): $\nu = 2100\ cm^{-1}$ (N_3).

^{1}H-NMR ($CDCl_3$/TMS): $\delta = 0.93$ (t, 3H, $J = 9.6$ Hz, CH_3); 1.40 (s, 3H, CH_3); 1.71 (q, 2H, $J = 9.6$ Hz, CH_2).

MS (30 eV): $m/e = 111$ ($M^+ - Et$).

The spectral data of other diazides are given in Table 3.

Received: 11 May 1987; revised: 24 August 1987

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