Functionalisation of 1,2,3-Triazole *via* Lithiation of 1-[2-(Trimethylsilyl)ethoxy]methyl-1*H*-1,2,3-triazole

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The preparation of a number of 5-substituted 1-[2-(trimethylsilyl)ethoxy]methyl-1*H*-1,2,3-triazoles *via* reaction of 1-[2-(trimethylsilyl)ethoxy]methyl-1*H*-1,2,3-triazole with *n*-butyllithium followed by addition of various electrophiles is reported. Removal of the protecting group by action of diluted aqueous hydrochloric acid or by tetrabutylammonium fluoride in tetrahydrofuran leads to the appropriate 4-substituted 1*H*-1,2,3-triazoles.

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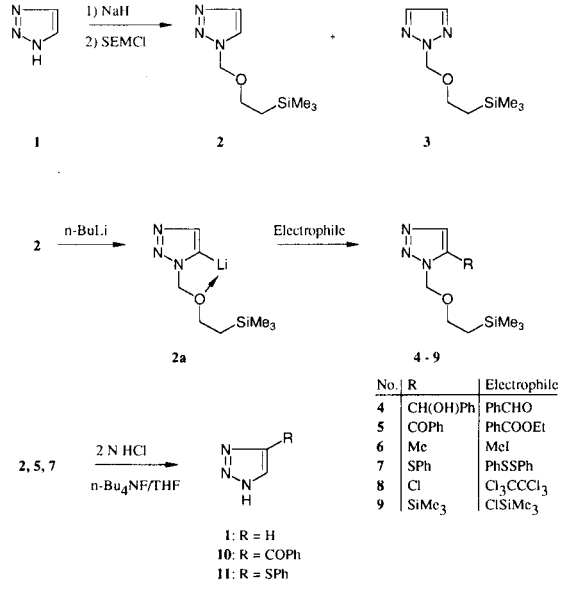
Introduction.

α-Lithiation followed by treatment with appropriate electrophiles represents an established strategy for the attachment of various functional groups onto an azole nucleus. However, this approach usually requires blocking the azole N-1 nitrogen by a suitable protecting group. Simple alkyl groups do not fulfill the requirements of such a group as deprotection is only possible under drastic conditions (*e.g.* for 1-methylpyrazoles:pyridine hydrochloride/200° [2]), for 1-benzylpyrazoles:sodium/ammonia [3]), which many other possible functionalities attached to the azole ring may not survive. Moreover, competetive lithiation at the *N*-methyl or *N*-methylene part can occur [4-6]. Thus, a number of other potential azole-*N*-protecting groups have been evaluated, each having their own advantages as well as disadvantages; particularly for the imidazole case some review articles have been published in this regard [7-10]. Some of the most suitable protecting groups incorporate the azole N-1 into an *N,N*-acetal or *N,O*-acetal moiety. The SEM [SEM = 2-(trimethylsilyl)ethoxymethyl] protecting group, which leads to the latter type of N-1 protected azoles, has been sucessfully applied in the course of lithiation reactions with pyrroles [11-14], indoles [14,15], imidazoles [16-18], pyrazoles [19] and 1,2,4-triazoles [19]. It can be easily attached to the azole-*N* and it is assumed to stabilize an intermediate azolyllithium species by intramolecular coordination [11,14,15]. Moreover, convenient deprotection by heating with diluted hydrochloric acid or - under very mild conditions - by treatment with tetrabutylammoniumfluoride in THF has been reported [11-19]. Together with the fact, that comparably little is known on metallations with 1,2,3-triazoles [20], these findings prompted us to evaluate the suitability of the SEM function as azole N-1 protecting group also for 1,2,3-triazoles.

Results and Discussion.

The protecting group was attached to the 1,2,3-triazole nucleus by reacting 1,2,3-triazole (**1**) with sodium hydride in dry tetrahydrofuran (THF) followed by reaction with one equivalent of SEM chloride. The nmr analysis of the crude reaction mixture revealed both possible *N*-SEM-1,2,3-triazoles **2**, **3** to be present (ratio ~3:1). Separation of these two regioisomers could be achieved by Kugelrohr-distillation. As considerable isomerisation of **2** to **3** was found to occur at elevated temperatures (>100°) it became advantageous to distill quickly and at low temperature.

SCHEME 1



Lithiation of 1-SEM-1,2,3-triazole (**2**) was accomplished by treatment of a THF-solution of **2** with a slight excess of *n*-butyllithium at −70° and allowing the mixture to reach −20° before adding the electrophile to the re-cooled solution of the thus formed lithio-intermediate **2a** (electrophiles and substitution products are given in Scheme 1). Treatment of **2a** with benzaldehyde afforded the expected alcohol **4** in 45% yield, whereas addition of ethyl benzoate led to the corresponding ketone **5**. Introduction of a methyl group into the 5-position of the azole ring was accomplished by employing iodomethane as the electrophile. The similar chromatographic behaviour of the thus obtained 5-methyl product **6** and educt **2** resulted in de-

creased yields of analytically pure **6** obtained upon mplc-separation of the reaction mixture. Problems were encountered when reacting **2a** with tosyl cyanide as the desired 1-SEM-1,2,3-triazole-5-carbonitrile could be detected in only small amounts (~5%) in the reaction mixture by glc/ms analysis [m/z (%): 181 (M^+-Me, 34), 151 (M^+-$SiMe_3$, 32), 73 ($SiMe_3$, 100)], whereas the greater predominating component was educt **2**. Dimethylformamide gave no reaction with the lithio species **2a**. In contrast, diphenyl disulfide turned out to be an excellent quenching agent since the corresponding 5-phenylthio-1-SEM-1,2,3-triazole **7** could be isolated in good yield (80%) from the reaction mixture. Attachment of chlorine to the triazole system (leading to compound **8**) proceeded smoothly using hexachloroethane as the electrophile. Finally, reaction of **2a** with chlorotrimethylsilane resulted in the formation of the 5-silylated 1-SEM-1,2,3-triazole **9**. Successive treatment of a THF solution of 2-SEM-1,2,3-triazole (**3**) with butyllithium and ethyl benzoate, applying the same reaction conditions as used in the preparation of ketone **5** from **2** and ethyl benzoate, did not lead to the formation of the corresponding phenyl 2-SEM-1,2,3-2*H*-triazol-4-yl ketone. Instead, mainly unchanged educt **3** was isolated from the reaction mixture. The lack of intramolecular coordinative stabilization in 4-lithio-1-SEM-2*H*-1,2,3-triazole possibly contributes to the decreased reactivity of **3** compared to that of its 1-SEM congener **2**.

In accordance with reported procedures removal of the protecting group could be achieved either by refluxing the 1-SEM-triazole with 2 *N* hydrochloric acid or by heating with an excess of an 1 *M* solution of tetra-*n*-butylammonium fluoride in THF. These methods were tested with 1-SEM-1,2,3-triazoles **2**, **5** and **7**, leading to the desired NH-triazoles **1**, **10**, and **11**.

The structure of all novel 1-SEM-1,2,3-triazoles was confirmed by elemental analysis, ir, ms and nmr spectra. The mass spectra of all *N*-SEM-1,2,3-triazoles are characterized by fragmentation of the C-$SiMe_3$ bond of the SEM moiety. Thus, all SEM protected compounds exhibit base peaks of m/z = 73 ($SiMe_3$), other peaks of high relative intensity are M^+-73 and M^+-42 (M^+-SiMe). *N*-SEM-triazoles **2** and **3** can be easily discriminated on basis of their ^{1}H-nmr spectra (in deuteriodimethyl sulfoxide) as compound **3** is a symmetrical molecule giving rise to only one type of heteroaromatic protons (relative intensity 2). The 1,5-disubstitution pattern of compounds **4-9** definitely follows from the ^{13}C-nmr data, particularly the fully ^{1}H-coupled spectra provide an unequivocal proof. Whereas the triazole C-4 signals are doublets due to coupling with the directly bonded proton H-4 [^{1}J(C4,H4) = 190.0-200.5 Hz], the corresponding triazole C-5 signals are split due to small couplings to triazole H-4 [doublet, ^{2}J(C5,H4) = 10.9-14.8 Hz] and NCH_2 [triplet, ^{3}J(C5,NCH_2) ~3.0 Hz] (and couplings to protons of the 5-substituent, if present). In addition, the 1,5-disubstitution pattern of compounds **6** and **7** was confirmed by NOE difference experiments [21]: irradiation of the triazole-CH_3 singlet in compound **6** leads to a remarkable NOE on the corresponding NCH_2O signal indicating spatial closeness of these two spins and thus 1,5-disubstitution (reversely, irradiation of NCH_2O enhances the *C*-methyl signal). Similarly, perturbation of the NCH_2O transition of compound **7** gives the phenyl-H signal a distinct enhancement, again confirming the assignments based on the ^{13}C-nmr data. NOE difference spectroscopy also permits a convenient discrimination between the heteroaromatic protons in compound **2** (in deuteriodimethyl sulfoxide): irradiation of the NCH_2O singlet leads to a strong NOE on the low-field proton (δ 8.26 ppm), whereas the high-field azole-H (δ 7.78 ppm) is not affected, thus assigning the former proton to be due to H-5 and the latter due to H-4 (Figure 1).

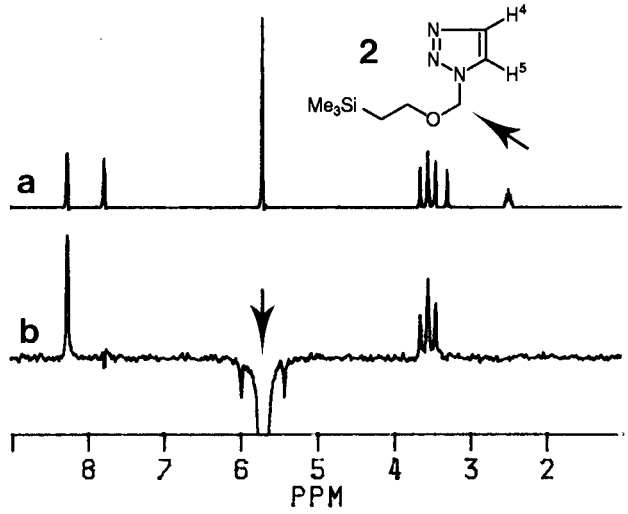


Figure 1. a) ^{1}H-nmr spectrum of **2** (deuteriodimethyl sulfoxide, 1.0-9.0 ppm), b) NOE difference spectrum of **2** resulting from irradiation of the NCH_2O resonance.

In summary, the SEM moiety has proven to be a possible protecting group in lithiation/electrophilic addition reactions with 1,2,3-triazole. The *N*-1-SEM-protected 1,2,3-triazole (**2**) can be readily metallated with *n*-butyllithium, the resulting 5-lithio species **2a** was shown to react with various electrophiles. Finally, the SEM moiety can be conveniently removed under mild conditions. Although the overall yields are only moderate, employment of the SEM group can be recommended if highly selective deprotection conditions (Bu_4NF/THF) are required. Moreover, as the SEM function is stable over a wide *p*H-range, it is assumed to be also advantageous if protection should continue for further reaction steps.

EXPERIMENTAL

Melting points were determined on a Reichert-Kofler hot-stage microscope and are uncorrected. The ir spectra were recorded on a Jasco IRA-1 spectrophotometer. The glc/ms analyses were performed on a Hewlett-Packard 5890A/5970B-GC/MSD instrument (70 eV). The nmr spectra were recorded on a Bruker AC-80 spectrometer (spectrometer frequency for ^{1}H: 80.13 MHz, for ^{13}C: 20.15 MHz; δ values in ppm) equipped with an Aspect 3000 computer and standard software. For the acquisition parameters of the NOE difference spectra see ref [21]. CHN-analyses were carried out by Mikroanalytisches Laboratorium, Institute of Physical Chemistry, University of Vienna. Column chromatography was carried out using Merck Kieselgel 60 (70-230 mesh) as the stationary phase. For thin layer chromatography (tlc), Merck aluminium sheets (Kieselgel 60 F_{254}) were used, the detection of some *N*-SEM-1,2,3-triazoles was achieved by spraying the chromatograms with a 5% aqueous solution of iron(III) chloride. Preparative thin layer chromatography was performed on Merck PLC plates (Kieselgel 60 F_{254}S, layer thickness 2 mm). Tetrahydrofuran was dried by passage through a column of aluminia (activity I, basic). All reactions with organolithium reagents were carried out under dry argon.

SEM-Protection of 1*H*-1,2,3-Triazole.

Under argon, 900 mg of sodium hydride (80% suspension in mineral oil, 30 mmoles) were suspended in 20 ml of dry THF. Then 30 mmoles of 1*H*-1,2,3-triazole (2.072 g) in 10 ml of dry THF was added and the mixture was stirred for 1 hour. After cooling to 0°, a solution of 5.002 g (30 mmoles) of [2-(trimethylsilyl)ethoxy]methyl chloride in 5 ml of dry THF was added slowly *via* a syringe. Then the cooling bath was removed and the mixture was stirred at room temperature for 1.5 hours. After addition of water (40 ml), the organic layer was separated, the water phase was exhaustively extracted with ethyl acetate and the combined organic layers were dried over anhydrous sodium sulfate. The solvents were evaporated *in vacuo* and the remaining residue was subjected to Kugelrohr-distillation.

1-[2-(Trimethylsilyl)ethoxy]methyl-1*H*-1,2,3-triazole (**2**).

Compound **2** came over at 80°/0.03 mbar as a colorless oil, which solidified on standing, mp 28-30°, yield, 2.33 g (39%); ^{1}H-nmr (deuteriochloroform): δ 7.74 (m, 2 H, triazole H-4,H-5), 5.70 (s, 2 H, NCH_2O), 3.57 (m, 2 H, OCH_2C), 0.89 (m, 2 H, CH_2Si), −0.04 (s, 9 H, $SiCH_3$); ^{1}H-nmr (deuteriodimethyl sulfoxide): δ 8.26 (d, J = 0.8 Hz, 1 H, triazole H-5), 7.78 (d, J = 0.8 Hz, 1 H, triazole H-4), 5.70 (s, 2 H, NCH_2O), 3.55 (m, 2 H, OCH_2C), 0.83 (m, 2 H, CH_2Si), −0.06 (s, 9 H, $SiCH_3$); ^{13}C-nmr (deuteriochloroform): δ 133.9 (triazole C-4, ^{1}J = 194.5 Hz, ^{2}J = 10.9 Hz), 123.2 (triazole C-5, ^{1}J = 194.4 Hz, ^{2}J = 15.6 Hz, ^{3}J = 2.6 Hz), 77.8 (NCH_2O, ^{1}J = 160.1 Hz), 66.9 (OCH_2C, ^{1}J = 142.7 Hz), 17.3 (CH_2Si, ^{1}J = 118.7 Hz), −1.9 ($SiCH_3$, ^{1}J = 118.8 Hz); ms: m/z (%) 184 (M^+-CH_3, 2), 170 (15), 156 (28), 142 (18), 126 (30), 98 (45), 83 (32), 75 (12), 73 (100), 70 (13), 54 (13).

Anal. Calcd. for $C_8H_{17}N_3OSi$: C, 48.21; H, 8.60; N, 21.08. Found: C, 48.30; H, 8.34; N, 21.21.

2-[2-(Trimethylsilyl)ethoxy]methyl-2*H*-1,2,3-triazole (**3**).

Compound **3** came over as a colorless oil at 50°/0.03 mbar, yield: 1.73 g (29%); ^{1}H-nmr (deuteriochloroform): δ 7.68 (s, 2 H, triazole H-4,5), 5.69 (s, 2 H, NCH_2O), 3.62 (m, 2 H, OCH_2C), 0.90 (m, 2 H, CH_2Si), −0.04 (s, 9 H, $SiCH_3$); ^{1}H-nmr (deuteriodimethyl sulfoxide): δ 7.86 (s, 2 H, triazole H-4,5), 5.65 (s, 2 H, NCH_2O), 3.57 (m, 2 H, OCH_2C), 0.80 (m, 2 H, CH_2Si), −0.08 (s, 9 H, $SiCH_3$); ^{13}C-nmr (deuteriochloroform): δ 134.9 (triazole C-4,C-5, ^{1}J = 192.7 Hz, ^{2}J = 12.9 Hz), 81.7 (NCH_2O, ^{1}J = 160.1 Hz), 67.2 (OCH_2C, ^{1}J = 142.7 Hz), 17.4 (CH_2Si, ^{1}J = 118.7 Hz), −1.7 ($SiCH_3$, ^{1}J = 118.7 Hz); ms: m/z (%) 184 (M^+-CH_3, 3), 157 (12), 156 (95), 126 (51), 99 (18), 98 (82), 83 (19), 82 (25), 73 (100), 70 (20), 59 (14), 58 (13), 55 (12).

Anal. Calcd. for $C_8H_{17}N_3OSi$: C, 48.21; H, 8.60; N, 21.08. Found: C, 48.41; H, 8.50; N, 21.35.

General Procedure for Lithiation/Electrophilic Addition of 1-[2-(Trimethylsilyl)ethoxy]methyl-1*H*-1,2,3-triazole.

At −70°, 2.1 ml of *n*-butyllithium (1.6 *M* solution in *n*-hexane, 3.3 mmoles) were added dropwise to a stirred solution of **2** (598 mg, 3 mmoles) in 8 ml of dry THF under argon. Stirring was continued for 30 minutes at this temperature, then the cooling bath was removed and the mixture was allowed to reach −20° within 1 hour before it was recooled to −70°. Then 3 mmoles of the appropriate electrophile (see Scheme 1) in 4 ml of dry THF was added *via* syringe and the mixture was allowed to reach ambient temperature within 3-4 hours, where stirring was continued for additional 12 hours. Then saturated ammonium chloride solution (15 ml) was added and the mixture was successively extracted with ether and ethyl acetate. The combined organic layers were dried and evaporated *in vacuo*. The residue was purified by column chromatography or mplc. Yields were not optimized and refer to analytically pure products obtained after chromatographic purification.

α-Phenyl-1-[2-(trimethylsilyl)ethoxy]methyl-1*H*-1,2,3-triazole-5-methanol (**4**).

Column chromatography (eluent: dichloromethane-ethyl acetate, 10:1) afforded 411 mg (45%) of **4** as yellowish oil; ^{1}H-nmr (deuteriodimethyl sulfoxide): δ 7.41 (s, 1 H, triazole H-4), 7.35 (s, 5 H, Ph-H), 6.30 (A-part of an AB-system, J = 5.0 Hz, exchangeable with deuterium oxide, 1 H, OH), 5.95 (B-part of an AB-system, J = 5.0 Hz, s after addition of D_2O, 1 H, C*H*OH), 5.75 and 5.57 (AB-system, J = 11.0 Hz, 2 H, NCH_2O), 3.42 (m, 2 H, OCH_2C), 0.73 (m, 2 H, CH_2Si), −0.08 (s, 9 H, $SiCH_3$); ^{13}C-nmr (deuteriochloroform): δ 139.9 (Ph C-1 and triazole C-5), 133.5 (triazole C-4, ^{1}J = 195.0 Hz), 128.5 (Ph C-3,5), 128.3 (Ph C-4), 126.4 (Ph C-2,6), 76.9 (NCH_2O, ^{1}J = 161.0 Hz), 67.1 (OCH_2C, ^{1}J = 143.0 Hz), 66.3 (CHOH), 17.5 (CH_2Si, ^{1}J = 118.9 Hz), −1.6 ($SiCH_3$, ^{1}J = 118.9 Hz); ms: m/z (%) 262 (M^+-$SiCH_3$, 21), 189 (22), 175 (13), 158 (12), 140 (14), 115 (14), 112 (20), 107 (22), 103 (13), 79 (29), 77 (28), 75 (42), 73 (100).

Anal. Calcd. for $C_{15}H_{23}N_3O_2Si$: C, 58.98; H, 7.59; N, 13.76. Found: C, 59.19; H, 7.35; N, 13.49.

Phenyl 1-[2-(Trimethylsilyl)ethoxy]methyl-1*H*-1,2,3-triazol-5-yl Ketone (**5**).

Column chromatography (eluent: dichloromethane-ethyl acetate, 15:1) afforded 191 mg (21%) of **5** as colorless crystals, mp 40-44°; ir (dichloromethane): 1660 cm^{-1} (C=O); ^{1}H-nmr (deuteriochloroform): δ 8.02 (s, 1 H, triazole H-4), 7.97-7.85 (m, 2 H, Ph H-2,6), 7.69-7.52 (m, 3 H, Ph H-3,4,5), 6.09 (s, 2 H, NCH_2O), 3.65 (m, 2 H, OCH_2C), 0.88 (m, 2 H, CH_2Si), −0.07 (s, 9 H, $SiCH_3$); ^{13}C-nmr (deuteriochloroform): δ 183.7 (C=O), 138.6 (triazole C-4, ^{1}J = 196.3 Hz), 136.9 (Ph C-1), 133.8 (Ph C-4), 132.9

(triazole C-5), 129.2 (Ph C-2,6), 128.7 (Ph C-3,5), 77.9 (NCH_2O, ^1J = 162.4 Hz), 67.4 (OCH_2C, ^1J = 142.8 Hz), 17.5 (CH_2Si, ^1J = 118.7 Hz), −1.7 ($SiCH_3$, ^1J = 118.7 Hz); ms: m/z (%) 303 (M^+, 1), 274 (20), 260 (23), 246 (13), 230 (28), 202 (21), 159 (13), 105 (25), 77 (22), 75 (11), 73 (100).

Anal. Calcd. for $C_{15}H_{21}N_3O_2Si$: C, 59.37; H, 6.98; N, 13.85. Found: C, 59.50; H, 6.92; N, 13.87.

5-Methyl-1-[2-(trimethylsilyl)ethoxy]methyl-1*H*-1,2,3-triazole (**6**).

Medium pressure liquid chromatography (eluent: dichloromethane-ethyl acetate, 13:1) afforded 189 mg (30%) of **6** as a colorless oil; ^{1}H-nmr (deuteriochloroform): δ 7.47 (s, 1 H, triazole H-4), 5.62 (s, 2 H, NCH_2O), 3.58 (m, 2H, OCH_2C), 2.38 (s, 3 H, triazole-CH_3), 0.89 (m, 2 H, CH_2Si), −0.03 (s, 9 H, $SiCH_3$); ^{13}C-nmr (deuteriochloroform): δ 133.0 (triazole C-4, ^1J = 191.7 Hz, ^3J = 3.6 Hz), 132.9 [triazole C-5, ^2J(C5,H4) = 14.7 Hz, ^2J(C5,CH_3) = 6.8 Hz, ^3J = 2.7 Hz], 75.8 (NCH_2O, ^1J = 159.3 Hz), 66.4 (OCH_2C, ^1J = 142.7 Hz), 17.2 (CH_2Si, ^1J = 118.6 Hz), 7.6 (triazole-CH_3, ^1J = 129.8 Hz), −1.9 ($SiCH_3$, ^1J = 118.8 Hz); ms: m/z (%) 184 (3), 170 (M^+-$SiCH_3$, 32), 140 (19), 112 (16), 97 (43), 84 (40), 73 (100), 59 (20).

Anal. Calcd. for $C_9H_{19}N_3OSi$: C, 50.67; H, 8.98; N, 19.69. Found: C, 50.77; H, 8.69; N, 19.64.

5-Phenylthio-1-[2-(trimethylsilyl)ethoxy]methyl-1*H*-1,2,3-triazole (**7**).

Column chromatography (eluent: dichloromethane-ethyl acetate, 15:1) afforded 739 mg (80%) of **7** as a yellowish oil; ^{1}H-nmr (deuteriochloroform): δ 7.77 (s, 1 H, triazole H-4), 7.25 (s, 5 H, Ph-H), 5.68 (s, 2 H, NCH_2O), 3.55 (m, 2 H, OCH_2C), 0.79 (m, 2 H, CH_2Si), −0.05 (s, 9 H, $SiCH_3$); ^{13}C-nmr (deuteriochloroform): δ 139.1 (triazole C-4, ^1J = 197.3 Hz), 132.9 (Ph C-1), 129.2 (Ph C-3,5), 128.9 (triazole C-5, ^2J = 14.0 Hz, ^3J = 3.1 Hz), 128.9 (Ph C-2,6), 127.4 (Ph C-4), 76.1 (NCH_2O, ^1J = 160.6 Hz), 67.0 (OCH_2C, ^1J = 142.7 Hz), 17.3 (CH_2Si, ^1J = 118.8 Hz), −1.7 ($SiCH_3$, ^1J = 118.8 Hz); ms: m/z (%) 308 (M^+, 1), 264 (10), 262 (10), 191 (14), 134 (11), 122 (14), 112 (11), 73 (100).

Anal. Calcd. for $C_{14}H_{21}N_3OSSi$: C, 54.69; H, 6.88; N, 13.67. Found: C, 54.91; H, 6.68; N, 13.64.

5-Chloro-1-[2-(trimethylsilyl)ethoxy]methyl-1*H*-1,2,3-triazole (**8**).

Column chromatography (eluent: dichloromethane-ethyl acetate, 15:1) afforded 353 mg (50%) of **8** as a colorless oil; ^{1}H-nmr (deuteriochloroform): δ 7.63 (s, 1 H, triazole H-4), 5.67 (s, 2 H, NCH_2O), 3.65 (m, 2 H, OCH_2C), 0.91 (m, 2 H, CH_2Si), −0.02 (s, 9 H, $SiCH_3$); ^{13}C-nmr (deuteriochloroform): δ 131.6 (triazole C-4, ^1J = 200.5 Hz), 125.8 (triazole C-5, ^2J = 12.7 Hz, ^3J = 2.8 Hz), 75.8 (NCH_2O, ^1J = 161.2 Hz), 67.3 (OCH_2C, ^1J = 142.9 Hz), 17.4 (CH_2Si, ^1J = 118.7 Hz), −1.7 ($SiCH_3$, ^1J = 118.7 Hz); ms: m/z (%) 218 (M^+-CH_3, 1), 190/192 (21/7), 132 (26), 117 (14), 103 (13), 93 (28), 75 (11), 74 (12), 73 (100), 61 (12), 59 (13), 52 (25).

Anal. Calcd. for $C_8H_{16}ClN_3OSi$: C, 41.10; H, 6.90; N, 17.97. Found: C, 41.38; H, 6.71; N, 18.24.

5-Trimethylsilyl-1-[2-(trimethylsilyl)ethoxy]methyl-1*H*-1,2,3-triazole (**9**).

Column chromatography (eluent: dichloromethane-ethyl acetate, 15:1) afforded 301 mg (37%) of colorless crystals, mp 37-40°; ^{1}H-nmr (deuteriochloroform): δ 7.70 (s, 1 H, triazole H-4), 5.72 (s, 2 H, NCH_2O), 3.50 (m, 2 H, OCH_2C), 0.89 (m, 2 H, CH_2Si), 0.37 (s, 9 H, triazole-$SiCH_3$), −0.03 (s, 9 H, $SiCH_3$ of SEM); ^{13}C-nmr (deuteriochloroform): δ 141.9 (triazole C-4, ^1J = 190.9 Hz), 124.5 (triazole C-5, ^2J = 14.8 Hz, ^3J = 3.0 Hz), 78.1 (NCH_2O, ^1J = 159.2 Hz), 66.6 (OCH_2C, ^1J = 142.5 Hz), 17.6 (CH_2Si, ^1J = 118.7 Hz), −1.2 (triazole-$SiCH_3$, ^1J = 120.2 Hz), −1.6 ($SiCH_3$ of SEM, ^1J = 118.8 Hz); ms: m/z (%) 228 (M^+-$SiCH_3$, 16), 171 (15), 170 (40), 155 (24), 73 (100).

Anal. Calcd. for $C_{11}H_{25}N_3OSi_2$: C, 48.66; H, 9.28; N, 15.48. Found: C, 48.65; H, 9.30; N, 15.53.

Deprotection of 1-[2-(Trimethylsilyl)ethoxy]methyl-1*H*-1,2,3-triazoles.

Method a).

To the SEM-protected substrate (1 mmole) in ethanol (1.5 ml) 2 *N* aqueous hydrochloric acid (4 ml) was added and the mixture was refluxed for 2 hours. After evaporation of ethanol, the cooled reaction mixture was neutralized with saturated potassium carbonate solution and was then exhaustively extracted with dichloromethane followed by ethyl acetate. After drying, the solvents were evaporated and the residue was purified by chromatography.

Method b).

The SEM-protected azole (1 mmole) was treated with 5 ml of an 1 *M* solution of tetrabutylammonium fluoride in THF and the mixture was refluxed for 4 hours. The residue obtained after evaporation of the solvent was subjected to preparative tlc or column chromatography to give the corresponding NH-azoles. Thus were obtained:

1*H*-1,2,3-Triazole (**1**).

Starting from **2**, after column chromatography (eluent: ethyl acetate) compound **1** was obtained in 71% yield (method a).

Phenyl 1*H*-1,2,3-Triazol-4-yl Ketone (**10**).

Starting from **5**, compound **10** was obtained as colorless crystals with mp 122° (lit [22] mp 122-123°) after preparative tlc (eluent: dichloromethane-ethyl acetate, 4:1); *via* method a) 75% yield was obtained, application of method b) gave a 78% yield; ^{1}H-nmr (deuteriochloroform): δ 16.00-10.00 (very broad s, 1 H, exchangeable with deuterium oxide, NH), 8.39 (s, 1 H, triazole-H), 8.36-8.23 (m, 2 H, Ph H-2,6), 7.66-7.51 (m, 3 H, Ph H-3,4,5); ms: m/z (%) 173 (M^+, 53), 145 (14), 118 (15), 117 (40), 105 (79), 96 (31), 90 (16), 77 (100), 51 (55), 50 (24).

4-Phenylthio-1*H*-1,2,3-triazole (**11**).

Starting from **7**, compound **11** was obtained as colorless crystals with mp 80-82° after column chromatography (eluent: dichloromethane-ethyl acetate, 4:1); *via* method a) 89% yield was obtained, application of method b) resulted in a 70% yield; ^{1}H-nmr (deuteriochloroform): δ 15.00-10.00 (very broad s, 1 H, exchangeable with deuterium oxide, NH), 7.69 (s, 1 H, triazole-H), 7.30 (m, 5 H, Ph-H); ms: m/z (%) 177 (M^+, 2), 149 (54), 109 (100), 69 (14), 51 (12).

Anal. Calcd. for $C_8H_7N_3S$: C, 54.22; H, 3.98; N, 23.71. Found: C, 54.20; H, 3.83; N, 23.46.

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