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Synthesis of *Bis*trimethylsilylated Hydroxy Alkynes

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Summary. The syntheses of several *bis*trimethylsilyl hydroxy alkynes and one *tris*trimethylsilyl hydroxy alkyne are described. Addition of lithium trimethylsilyl acetylide to mono- or *bis*trimethylsilylated aldehydes and ketones afforded compounds **4a–f** in good to moderate yields. The products are mixtures of diastereomers; the diastereoselectivity of the reactions amounts to 53 to 68%.

Keywords: Synthesis; *Bis*trimethylsilyl hydroxy alkynes.

Synthese *bis*trimethylsilylierter Hydroxyalkine

Zusammenfassung. Die Synthesen mehrerer *Bis*trimethylsilylhydroxyalkine und eines *Tris*trimethylsilylhydroxyalkins werden beschrieben. Addition von Lithiumtrimethylsilylacetylid an mono- oder *bis*trimethylsilylierte Aldehyde und Ketone ergab die Verbindungen **4a–f** in guten bis mäßigen Ausbeuten. Die Produkte sind Mischungen von Diastereomeren und entstehen mit Diastereoselektivitäten von 53 bis 68%.

Introduction

Alkynyl alcohols are an important class of compounds [1]. Alkynols comprising the terminal alkynyl carbon protected with a trimethylsilyl (*TMS*) group are conveniently and widely used organic synthons due to their reactivity and large variety of synthetic transformations. The alkynyl group is also a good handle for further transformations [2]. Many of these silylated alkynols are biologically important compounds, combining pharmacological activity with low toxicity. The development of synthetic reactions is an area of active study [3–5]. It is well known that silicon groups can be readily but discriminatively cleaved from carbon atoms. A terminal trimethylsilyl group can be removed selectively in *bis*trimethylsilylated alkynols for further transformation. The syntheses of silylated aldehydes and ketones were reported previously [6–10].

In this paper we wish to report a mild and efficient conversion of silylated aldehydes and ketones to *bis*trimethylsilylated alkynols comprising a terminal

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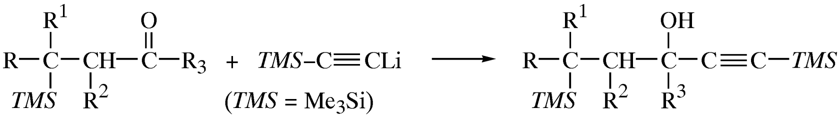
alkynyl carbon with a *TMS* group. Silylated aldehydes and ketones were prepared by different methods as racemic mixtures.

Results and Discussion

Treatment of a variety of silylated aldehydes or ketones with lithium trimethylsilyl acetylide at room temperature under an atmosphere of argon furnished the expected *bis*trimethylsilylated alkynols **4a**–**f** in good to moderate yields. Both sterically hindered and conjugated silylated aldehydes or ketones as well as

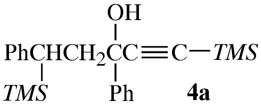
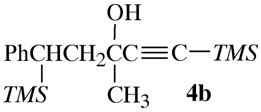
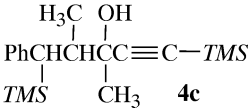
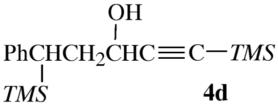
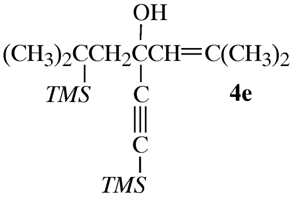
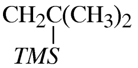
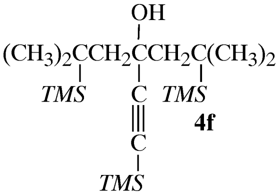
Table 1. Reaction of lithium trimethylsilyl acetylide with silylated aldehydes and ketones



$$\mathrm{R{-}}\underset{TMS}{\overset{\mathrm{R^1}}{\mathrm{C}}}\mathrm{{-}}\underset{\mathrm{R^2}}{\mathrm{CH}}\mathrm{{-}}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{{-}R_3} + TMS\text{-}\mathrm{C{\equiv}CLi} \longrightarrow \mathrm{R{-}}\underset{TMS}{\overset{\mathrm{R^1}}{\mathrm{C}}}\mathrm{{-}}\underset{\mathrm{R^2}}{\mathrm{CH}}\mathrm{{-}}\underset{\mathrm{R^3}}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{{-}C{\equiv}C{-}}TMS$$

(*TMS* = $\mathrm{Me_3Si}$)

1a–f **4a–f**

Starting material				Product	Yield (%)	Ratio of diastereomers
R	*R*^{1}	*R*^{2}	R^3			
Ph	H	H	Ph	 $\mathrm{Ph}\underset{TMS}{\mathrm{CH}}\mathrm{CH_2}\underset{\mathrm{Ph}}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{C{\equiv}C{-}}TMS$ **4a**	75	59:41
Ph	H	H	CH_3	 $\mathrm{Ph}\underset{TMS}{\mathrm{CH}}\mathrm{CH_2}\underset{\mathrm{CH_3}}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{C{\equiv}C{-}}TMS$ **4b**	70	68:32
Ph	H	CH_3	CH_3	 $\mathrm{Ph}\underset{TMS}{\mathrm{CH}}\overset{\mathrm{H_3C}}{\mathrm{CH}}\underset{\mathrm{CH_3}}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{C{\equiv}C{-}}TMS$ **4c**	65	53:47
Ph	H	H	H	 $\mathrm{Ph}\underset{TMS}{\mathrm{CH}}\mathrm{CH_2}\overset{\mathrm{OH}}{\mathrm{CH}}\mathrm{C{\equiv}C{-}}TMS$ **4d**	55	59:41
CH_3	CH_3	H	$CH{=}C(CH_3)_2$	 $\mathrm{(CH_3)_2}\underset{TMS}{\mathrm{C}}\mathrm{CH_2}\underset{\mathrm{C{\equiv}C{-}}TMS}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{CH{=}C(CH_3)_2}$ **4e**	66	
CH_3	CH_3	H	 $\mathrm{CH_2}\underset{TMS}{\mathrm{C}}\mathrm{(CH_3)_2}$	 $\mathrm{(CH_3)_2}\underset{TMS}{\mathrm{C}}\mathrm{CH_2}\underset{\mathrm{C{\equiv}C{-}}TMS}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{CH_2}\underset{TMS}{\mathrm{C}}\mathrm{(CH_3)_2}$ **4f**	62	

silylated dialkyl and arylalkyl ketones proved to be suitable substrates. In the case of alkynols **4a–d**, mixtures of two diastereomers were obtained with a diastereoselectivity of 53 to 68%. The facial selectivity was interpreted as a result of bulky substituted groups in α- or β-positions, respectively. The results are shown in Table 1.

Experimental

Diethyl ether was distilled from Na/benzophenone under Ar. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-80 NMR spectrometer in $CDCl_3$. IR spectra were recorded on a Perkin-Elmer spectrometer (Model 883). Mass spectra were obtained with a Fisons TRIO 1000 instrument.

General procedure for the preparation of bistrimethylsilyl alkynols

The silylated ketone or the corresponding aldehyde (2 mmol) was dissolved in 5 ml of anhydrous diethyl ether, and the mixture was placed in a three-necked flask equipped with a magnetic stirrer and a condenser. Then, 0.23 g (2.2 mmol) of a 56% solution of lithium trimethysilyl acetylide in *THF* was added during 30 min at room temperature under an argon atmosphere. After stirring for 2 h, 0.15 g (3 mmol) of powdered NH_4Cl was added, preferably followed by stirring overnight. Water was added, and the crude residue was extracted with CH_2Cl_2 (2×20 ml). The solvent was evaporated to obtain a crude material. All new products gave satisfactory C and H analyses. The spectroscopic data (^{13}C, ^{1}H NMR and IR) of the major diastereomer are shown below.

3,5-Diphenyl-1,5-bistrimethylsilyl-3-ol-1-pentyne (**4a**; $C_{23}H_{32}OSi_2$)

Yellow viscous liquid after distillation with a *Kugelrohr* apparatus (oven temperature: 100°C, 150 mm Hg); ^{1}H NMR (80 MHz, δ, $CDCl_3$): 0.00 (s, 9H), 0.24 (s, 9H), 2.16 (s, 1H), 2.84 (d of d, $J = 8.9$, 3.8, 1H), 3.38–3.55 (m, 2H), 6.70–7.88 (m, 10H) ppm; ^{13}C NMR (20 MHz, δ, $CDCl_3$): −2.84 (CH_3), 0.15 (CH_3), 32.50 (CH), 45.39 (CH_2), 74.62 (C), 90.67 (C), 108.44 (C), 125.91 (CH), 127.95 (CH), 128.16 (CH), 128.59 (CH), 129.63 (CH), 131.71 (CH), 143.96 (C), 144.56 (C) ppm; IR (film): $\nu = 3485$, 2164, 1250, 845 cm^{-1}; MS: $m/z = 380$ [M$^+$], 177, 73 (base peak).

3-Methyl-5-phenyl-1,5-bistrimethylsilyl-3-ol-1-pentyne (**4b**; $C_{18}H_{30}OSi_2$)

Colourless viscous liquid after distillation with a *Kugelrohr* apparatus (oven temperature: 100°C, 150 mm Hg); ^{1}H NMR (80 MHz, δ, $CDCl_3$): −0.04 (s, 9H), 0.14 (s, 9H), 1.22 (s, 3H), 2.18 (s, 1H), 2.25–2.75 (m, 3H), 6.90–7.40 (m, 5H) ppm; ^{13}C NMR (20 MHz, δ, $CDCl_3$): −3.12 (CH_3), −0.10 (CH_3), 29.86 (CH_3), 33.39 (CH), 43.28 (CH_2), 70.25 (C), 109.62 (C), 113.62 (C), 124.36 (CH), 127.69 (CH), 128.51 (CH), 143.51 (C) ppm; IR (film): $\nu = 3421$, 2165, 1249, 840 cm^{-1}; MS: $m/z = 318$ [M$^+$], 105, 73 (base peak).

2,4-Dimethyl-5-phenyl-1,5-bistrimethylsilyl-3-ol-1-pentyne (**4c**; $C_{19}H_{32}OSi_2$)

Pale yellow viscous liquid after distillation with a *Kugelrohr* apparatus (oven temperature: 100°C, 150 mm Hg); ^{1}H NMR (80 MHz, δ, $CDCl_3$): 0.08 (s, 9H), 0.22 (s, 9H), 0.99 (d, $J = 4.1$, 1H), 1.31 (d, $J = 7.1$, 3H), 1.58 (s, 3H), 2.13–2.38 (m, 1H), 2.04 (s, 1H), 7.22 (s, 5H) ppm; ^{13}C NMR (20 MHz, δ, $CDCl_3$): −1.17 (CH_3), −0.01 (CH_3), 14.06 (CH_3), 27.61 (CH_3), 38.70 (CH), 44.69 (CH), 72.99 (C), 103.11 (C), 107.70 (C), 124.95 (CH), 127.69 (CH), 130.73 (CH), 141.44 (C) ppm; IR (film): $\nu = 3441$, 2165, 1252, 847 cm^{-1}; MS, $m/z = 314$ [M$^+$-18], 73 (base peak).

5-Phenyl-1,5-bistrimethylsilyl-3-ol-1-pentyne (**4d**; $C_{17}H_{28}OSi_2$)

Brown liquid after distillation with a *Kugelrohr* apparatus (oven temperature: 100°C, 150 mm Hg); ^{1}H NMR (80 MHz, δ, $CDCl_3$): 0.00 (s, 9H), 0.22 (s, 9H), 1.82–2.0 (m, 1H), 2.13 (s, 1H), 3.72 (m, 2H), 4.02–4.37 (d of d, $J = 3.62$, 8.51, 1H), 7.15 (s, 5H) ppm; ^{13}C NMR (20 MHz, δ, $CDCl_3$): −2.97 (CH_3), −0.01 (CH_3), 33.57 (CH), 60.67 (CH_2), 78.62 (C), 106.98 (C), 107.86 (C), 124.46 (CH), 127.58 (CH), 128.29 (CH), 142.53 (C) ppm; IR (film): $\nu = 3397$, 2169, 1250, 840 cm^{-1}; MS: *m*/*z* = 286 [M$^+$-18], 199, 141, 73 (base peak).

6-Methyl-3-(2-methyl-2-trimethylsilylpropyl)-4-hexene-1-yn-3-ol (**4e**; $C_{17}H_{34}OSi_2$)

Orange viscous liquid after distillation with a *Kugelrohr* apparatus (oven temperature: 100°C, 150 mm Hg); ^{1}H NMR (80 MHz, δ, $CDCl_3$): −0.00 (s, 9H), 0.18 (s, 9H), 0.94 (s, 6H), 1.52 (s, 1H), 1.74 (d, $J = 1.37$, 3H), 1.86 (s, 2H), 1.92 (d, $J = 1.19$, 3H), 5.39 (m, 1H) ppm; ^{13}C NMR (20 MHz, δ, $CDCl_3$): −4.46 (CH_3), −0.45 (CH_3), 18.72 (CH_3), 22.88 (CH_3), 26.78 (CH_3), 49.14 (CH_2), 69.79 (C), 73.62 (C), 103.50 (C), 110.33 (C), 131.14 (CH), 134.49 (C) ppm; IR (film): $\nu = 3429$, 2163, 1250, 840 cm^{-1}.

5-Methyl-5-trimethylsilyl-3-(2-methyl-2-trimethylsilylpropyl)-3-ol-hexyne (**4f**; $C_{20}H_{44}OSi_3$)

Dark yellow viscous liquid after distillation with a *Kugelrohr* apparatus (oven temperature: 100°C, 150 mm Hg). ^{1}H NMR (80 MHz, δ, $CDCl_3$): 0.00 (s, 18H), 0.16 (s, 9H), 1.02 (s, 12H), 2.17 (s, 4H), 2.28 (s, 1H) ppm; ^{13}C NMR (20 MHz, δ, $CDCl_3$): −4.16 (CH_3), −0.48 (CH_3), 23.46 (CH_3), 30.67 (C), 49.99 (CH_2), 73.06 (C), 103.52 (C), 110.34 (C) ppm; IR (film): $\nu = 3440$, 2060, 1250, 839 cm^{-1}.

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References

[1] Niwa S, Soai K (1990) J Chem Soc Perkin Trans 1, 937
[2] Wang KK, Liu B, Lu Y (1995) J Org Chem **60**: 1885
[3] Bridges AJ, Fedij V, Turowski EC (1983) J Chem Soc Chem Commun 1093; Kuroda S, Katsuki T, Yamaguchi M (1987) Tertahedron Lett **28**: 803
[4] Pornet J, Damour D, Randrianoelina B, Miginiac L (1986) Tetrahedron **42**: 2501; Lautens M, Huboux AH (1990) Tetrahedron Lett **31**: 3105; Soai K, Chem Abstr 113: 171485t, JP02 142 742; Lutjens H, Nowotny S, Knochel P (1995) Tetrahedron Asymmetry **6**: 2675
[5] Sinkula AA, Yalkowsky SH (1975) J Pharm Sci **64**: 181
[6] Calas R, Dounogues J, Bolourtchian M (1971) J Organometallic Chem **26**: 195
[7] Dounogues J, Calas R, Bolourtchian M, Biran C, Duffaut N (1973) J Organometallic Chem **57**: 55
[8] Dounogues J, Bolourtchian M, Calas R, Duffaut N, Picard J (1972) J Organometallic Chem **43**: 157
[9] Bolourtchian M, Saednya A (1990) J Science IR Iran **1**: 277
[10] Bolourtchian M, Saednya A (1978) Bull Soc Chem Fr **11**: 170

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