Stereoselective Synthesis of Steroids and Related Compounds, IV^[1]

Addition of Cerium Reagents Derived from (Trimethylsilyl)propargyl Bromide to Aldehydes

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The addition of (trimethylsilyl)propargylmagnesium bromide (**9**) to aldehydes afforded predominantly the allenylic alcohols *rac*-**10**. The regioselectivity of this addition changes dramatically when organocerium reagents were used for the addition. In this case nearly exclusive formation of the homo-

propargylic alcohols *rac*-**8** was observed. Highest selectivity for this process was obtained when cerium(III) isopropoxide (**13**) was used as a precursor for the formation of the organocerium reagent.

The elements of the rare earth series having f orbitals exhibit unique electronic and stereochemical properties. Therefore, they provide intriguing potential as organometallic reagents and catalysts^[2]. Presently, one of the most important applications of lanthanide reagents in synthetic organic chemistry is the addition of organocerium reagents to carbonyl compounds. Imamoto and co-workers were the first to recognize that the attenuated basicity and high oxophilicity of organocerium reagents could be utilized for selective synthetic organic transformations^[3].

As a consequence of our continuing interest in the asymmetric synthesis of 7α-steroids, we undertook the synthesis

of protected 1-(trimethylsilyl)octa-1,7-diyn-4-ols (*rac*-**4**). According to our retrosynthetic analysis these diynes should serve as precursors of the A ring of the steroid nucleus. The alkylation of these diynes with electrophiles such as the halides **5** should yield the corresponding enediynes **3**, which upon intramolecular cobalt-mediated [2 + 2 + 2]-cycloaddition^[4] should afford the desired 7α-steroids **2** diastereoselectively.

Our initial efforts towards the synthesis of the diynes *rac*-**4** concentrated on the monosilylation of 4-hydroxy-1,7-octadiyne (*rac*-**7**). This diyne was obtained by addition of propargylmagnesium bromide to 4-pentynal (**6c**). Deprotonation with one equivalent of sodium hydride and 1.1 equivalents of *n*-butyllithium afforded after subsequent silylation with trimethylsilyl chloride (2.2 equivalents) and aqueous workup a 1:1 mixture of *rac*-**8c** and its regioisomeric monotrimethylsilyloctadiyne derivative (21%) together with the corresponding bisilylated derivative (24%) and starting material *rac*-**7** (28%). The low yield and the lack of selectivity of this reaction prompted us to investigate the course of the addition of (trimethylsilyl)propargylmag-

nesium bromide (**9**) to aldehydes, so that the trimethylsilyl group at C-1 would be introduced prior to the addition step.

6,8,10 R	Reagent	8 : 10	Yield of 8 + 10 (%)
a C ₆ H ₅	9	6 : 94	90
a C ₆ H ₅	9 /ZnCl ₂ (1.2 eq)	78 : 22	91
a C ₆ H ₅	9 /ZnCl ₂ (2.5 eq)	90 : 10	54
a C ₆ H ₅	9 /CeCl ₃	91 : 9	95
a C ₆ H ₅	9 /Ce(O- <i>i</i> -Pr) ₃	96 : 4	98
a C ₆ H ₅	9 /CeCl ₃ · 3 <i>i</i> -PrOH/ <i>n</i> -BuMgBr	85 : 15	41
b CH ₂ =CH	9	5 : 95	83
b CH ₂ =CH	9 /CeCl ₃	94 : 6	98
c HC≡C-(CH ₂) ₂	9	6 : 94	87
c HC≡C-(CH ₂) ₂	9 /CeCl ₃	89 : 11	98
d HC≡C-(CH ₂) ₃	9	4 : 96	75
d HC≡C-(CH ₂) ₃	9 /CeCl ₃	91 : 9	94

Thus, (trimethylsilyl)propargylmagnesium bromide (**9**) was prepared from (trimethylsilyl)propargyl bromide and magnesium in the presence of mercury(I) chloride and allowed to react with 4-pentynal (**6c**). After aqueous workup a 6:94 mixture of the desired monotrimethylsilyloctadiyne **rac-8c** and its corresponding allenylic derivative **rac-10c** was obtained in an overall yield of 87%. Similarly, benzaldehyde (**6a**), acrolein (**6b**) and 5-hexynal (**6d**) react with (trimethylsilyl)propargylmagnesium bromide (**9**) to afford predominantly the allenylic alcohols **rac-10a**, **b** and **d** in 72 to 86% yield.

Previously, the regioselective addition of organozinc reagents derived from (trimethylsilyl)propargyl bromide to aldehydes and ketones has been reported to afford predominantly homopropargylic alcohols^[5]. Consequently, (trimethylsilyl)propargylmagnesium bromide (**9**) was transmetalated with 1.2 equivalents of zinc chloride to form the corresponding organozinc reagent. Upon treatment of this species with benzaldehyde (**6a**) a 78:22 mixture of **rac-8a** and **rac-10a** was obtained in 91% yield. This result is in full agreement with those reported by Paquette et al. They isolated **rac-8a** in 66% yield after addition of a Reformatsky type reagent derived from (trimethylsilyl)propargyl bromide and granular zinc to benzaldehyde (**6a**)^[5b]. By using 2.4 equivalents of zinc chloride for the transmetalation of **9** the selectivity increased to 90:10 but the overall yield dropped down to 54%.

At this point, we decided to evaluate the utility of organocerium species derived from (trimethylsilyl)propargylmagnesium bromide (**9**). We assumed, that changing the character of the carbanionic species might result in the desired regioselectivity of the addition step^[6]. In our first studies, anhydrous cerium(III) chloride was allowed to react with (trimethylsilyl)propargylmagnesium bromide (**9**) to form an organocerium species of a hitherto unknown structure. This species furnished upon treatment with aldehydes **6** predominantly the homopropargylic alcohols **rac-8** in 85 to 92% yield. As byproducts the allenylic alcohols **rac-10** were isolated in 5 to 11% yield, which could be easily removed by silica gel chromatography from the main products **rac-8**.

Encouraged by these results a number of organocerium species were prepared and allowed to react with aldehydes. Cerium(III) isopropoxide (**13**)^[7] was found to be the reagent of choice and was prepared by an improved procedure according to the protocol given for the preparation of the analogous gadolinium(III) isopropoxide^[8]. CeCl₃ · 7 H₂O (**11**) was dehydrated with thionyl chloride to give anhydrous CeCl₃, which was then dissolved in hot 2-propanol to afford CeCl₃ · 3 *i*-PrOH (**12**) in 96% yield as colorless crystals. An X-ray crystallographical analysis showed that this compound crystallizes as a dimer, in which the two cerium atoms are bridged via two chlorine atoms^[9].

The deprotonation of CeCl₃ · 3 *i*-PrOH (**12**) was achieved with potassium isopropoxide in a refluxing mixture of benzene and 2-propanol to afford cerium(III) isopropoxide (**13**) as a pale brown air-sensitive solid in 50% yield. Instead of potassium isopropoxide sodium isopropoxide can be used for the deprotonation of **12**, but potassium isopropoxide proved to be superior, as the "in situ" formed potassium chloride is completely insoluble in 2-propanol. Furthermore, due to the larger size of its crystals, potassium chloride can be removed much easier than sodium chloride by filtration^[10]. Addition of the cerium reagent derived from (trimethylsilyl)propargylmagnesium bromide (**9**) and cerium(III) isopropoxide (**13**) to benzaldehyde (**6a**) furnished a 96:4 mixture of the homopropargylic alcohol **rac-8a** and the allenylic alcohol **rac-10a** almost quantitatively.

In order to avoid the isolation of the air- and moisture-sensitive cerium(III) isopropoxide (**13**) the "in situ" formation of this species was investigated. Therefore, CeCl₃ · 3 *i*-PrOH (**12**) was deprotonated with 3.1 equivalents of *n*-butylmagnesium bromide in diethyl ether to afford cerium(III) isopropoxide (**13**) which was allowed to react with (trimethylsilyl)propargylmagnesium bromide (**9**). Subsequent addition of benzaldehyde (**6a**) afforded a 85:15 mixture of the alcohols **rac-8a** and **rac-10a** in 41% yield.

The low yield might be a consequence of incomplete deprotonation of **12**.

It was demonstrated that a remarkable shift in the regioselectivity of the addition of (trimethylsilyl)propargylmagnesium bromide to aldehydes occurs when organometallic species derived from cerium(III) compounds were used. Cerium(III) isopropoxide proved to be the reagent of choice in these addition reactions and superior to the use of organozinc reagents.

The evaluation of cerium(III) isopropoxide (**13**) and its chiral modifications in C–C bond forming reactions is under current investigation.

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Experimental

Infrared (IR) Spectra: Perkin-Elmer 298 spectrometer. **NMR Spectra:** Varian XL 200 or VXR 200 spectrometer for ^1H and ^{13}C NMR. Chemical shifts are given in δ values by using tetramethylsilane as an internal standard. **Mass spectra:** Varian MAT 731 or 311 A spectrometers. **TLC Analyses:** Polygram Sil G/UV₂₅₄ silica gel plates. Silica gel (30–60 μm) from Macherey and Nagel was used for flash chromatography. **Combustion analyses:** Microanalytical laboratory of the University of Göttingen. All reactions were carried out under argon. All reagents were purified and dried if necessary before use. THF was freshly distilled from LiAlH_4 prior to use. Et_2O was distilled from sodium. (Trimethylsilyl)propargyl bromide was prepared from propargyl bromide according to ref.^[11]. $\text{CeCl}_3 \cdot 7 \text{H}_2\text{O}$ (**11**) was purchased from Fluka Chemie AG, CH-9470 Buchs, and dried at 150°C for 2 h prior to use.

Cerium(III) Chloride $\cdot$ 3 *i*-PrOH (12**):** $\text{CeCl}_3 \cdot 7 \text{H}_2\text{O}$ (**11**) (11.18 g, 30 mmol) was suspended in thionyl chloride (150 ml) and the suspension heated under reflux for 18 h. Subsequently, the thionyl chloride was removed by distillation, and the resulting white powder was dried in vacuo (120°C , 0.005 Torr) for 24 h. Upon addition of 2-propanol (130 ml), the still hot cerium(III) chloride completely dissolved to form a clear solution. Upon cooling to room temp. $\text{CeCl}_3 \cdot 3 \text{i-PrOH}$ (**12**) started to crystallize. After 12 h supernatant solvent was removed via syringe and the remaining wet crystals were dried in vacuo (20°C , 0.1 Torr) to afford 11.19 g (96%) of $\text{CeCl}_3 \cdot 3 \text{i-PrOH}$ (**12**).

Cerium(III) Isopropoxide (13**):** Potassium (1.20 g, 30 mmol) was suspended in benzene (30 ml) and 2-propanol (25 ml) was added within 30 min. The resulting suspension was added to a solution of $\text{CeCl}_3 \cdot 3 \text{i-PrOH}$ (**12**) (4.27 g, 10 mmol) in refluxing 2-propanol (100 ml). Upon this addition a white solid precipitated immediately. The mixture was heated under reflux for two additional hours and then slowly cooled to room temp. within 16 h. The solution was separated from the precipitated potassium chloride by filtration through a G4 sintered glass funnel, and the solvent was removed in vacuo (20°C , 0.005 Torr) to afford 1.60 g (50%) of cerium(III) isopropoxide (**13**) as a pale brown solid.

Addition of (Trimethylsilyl)propargylmagnesium Bromide **9 to the Aldehydes **6**.** – **General Procedure:** Magnesium (1.22 g, 50 mmol) and mercury(I) chloride (5 mg) were suspended in diethyl ether (20

ml) at room temp. and 1,2-dibromoethane (0.08 ml) was added. The mixture was stirred for 30 min and then cooled to 10°C . Within 1 h (trimethylsilyl)propargyl bromide (2.00 g, 10.5 mmol) was added while the temp. was maintained between 10 to 15°C . After one additional hour the Grignard reagent was added to THF (100 ml) and cooled to -78°C . Subsequently, a solution of the aldehyde **6** (4 mmol) in THF (2 ml) was added via a syringe. Within 12 h the reaction mixture was allowed to warm up to room temp. The solvent was evaporated (20°C , 12 Torr), the residue dissolved in diethyl ether (150 ml) and the resulting solution cooled to 0°C . After addition of 1 N HCl (15 ml) the layers were separated, and the aqueous layer was extracted twice with diethyl ether (50 ml each). The combined organic layers were reextracted with a saturated aqueous NaHCO_3 solution and a saturated aqueous NaCl solution (20 ml each), dried with MgSO_4 , and the solvent was removed in vacuo (20°C , 12 Torr). The crude products *rac*-**10** were purified by flash chromatography on silica gel.

1-Phenyl-2-trimethylsilyl-2,3-butadiene-1-ol (*rac*-10a**):** According to the general procedure magnesium (1.22 g, 50 mmol), (trimethylsilyl)propargyl bromide (2.00 g, 10.5 mmol) and benzaldehyde (**6a**) (0.42 g, 4 mmol) were used to afford 0.75 g (86%) of the 2,3-alkadiene *rac*-**10a** as a colorless liquid after chromatography with diethyl ether/petroleum ether (1:5) on silica gel (60 g); $R_f = 0.34$. (In addition, 0.07 g (9%) of the alkyne *rac*-**8a** was isolated as a colorless liquid; $R_f = 0.21$.) – IR (neat): $\tilde{\nu} = 3410$ (OH), 3070, 3045 and 3010 (aromat. CH), 1920 ($\text{C}=\text{C}=\text{C}$), 1595 (aromat. $\text{C}=\text{C}$), 1240 (Si–C), 755 and 695 cm^{-1} (δ_{CH} monosubst. aromat.). – ^1H NMR (200 MHz, CDCl_3): $\delta = -0.08$ [s; 9H, $\text{Si}(\text{CH}_3)_3$], 2.25 (m; 1H, OH), 4.58 and 4.64 (AB part of ABX, $J_{\text{AB}} = 11.2 \text{ Hz}$, $J_{\text{AX}} = 3.0 \text{ Hz}$, $J_{\text{BX}} = 2.9 \text{ Hz}$; 2H, $\text{C}=\text{CH}_2$), 5.18 (m; 1H, CHOH), 7.18–7.35 (m; 5H, C_6H_5). – ^{13}C NMR (50 MHz, CDCl_3): $\delta = -1.15$ [$\text{Si}(\text{CH}_3)_3$], 72.67 ($\text{C}=\text{CH}_2$), 72.86 (CHOH), 101.24 [$\text{C}-\text{Si}(\text{CH}_3)_3$], 126.85 (aromat. C-2/6), 127.65 (aromat. C-4), 128.15 (aromat. C-3/5), 142.97 (aromat. C-1), 207.01 ($\text{C}=\text{C}=\text{CH}_2$). – MS (70 eV): m/z (%) = 218 (1) [M^+], 179 (70) [$\text{M}^+ - \text{C}_3\text{H}_3$], 107 (100) [$\text{C}_7\text{H}_7\text{O}^+$], 73 (90) [$\text{Si}(\text{CH}_3)_3^+$]. – $\text{C}_{13}\text{H}_{18}\text{OSi}$ (218.4): calcd. C 71.50, H 8.31; found C 71.38, H 8.48.

4-Trimethylsilyl-1,4,5-hexatriene-3-ol (*rac*-10b**):** According to the general procedure magnesium (1.22 g, 50 mmol), (trimethylsilyl)propargyl bromide (2.00 g, 10.5 mmol) and acrolein (**6b**) (0.22 g, 4 mmol) were used to afford 0.53 g (79%) of the 1,4,5-alkatriene *rac*-**10b** as a colorless liquid after chromatography with diethyl ether/petroleum ether (1:4) on silica gel (60 g); $R_f = 0.37$. (In addition, 0.03 g (4%) of the alkyne *rac*-**8b** was isolated as a colorless liquid; $R_f = 0.21$.) – IR (neat): $\tilde{\nu} = 3380$ (OH), 3060 ($\text{C}=\text{CH}$), 1920 ($\text{C}=\text{C}=\text{C}$), 1635 ($\text{C}=\text{C}$), 1240 (Si–C), 835 cm^{-1} (Si– CH_3). – ^1H NMR (200 MHz, CDCl_3): $\delta = 0.15$ [s; 9H, $\text{Si}(\text{CH}_3)_3$], 1.89 (br. s; 1H, OH), 4.59 (dd, $J_1 = 3.2 \text{ Hz}$, $J_2 = 1.2 \text{ Hz}$; 2H, $\text{C}=\text{CH}_2$), 4.58–4.70 (m; 1H, CHOH), 5.14 (ddd, $J_{\text{cis}} = 10.0 \text{ Hz}$, $J_2 = 1.5 \text{ Hz}$, $J_3 = 1.2 \text{ Hz}$; 1H, $\text{CH}=\text{CH}_2$), 5.26 (ddd, $J_{\text{trans}} = 17.0 \text{ Hz}$, $J_2 = 1.7 \text{ Hz}$, $J_3 = 1.2 \text{ Hz}$; 1H, $\text{CH}=\text{CH}_2$), 5.91 (ddd, $J_{\text{trans}} = 17.0 \text{ Hz}$, $J_{\text{cis}} = 10.0 \text{ Hz}$, $J_3 = 6.5 \text{ Hz}$; 1H, $\text{CH}=\text{CH}_2$). – ^{13}C NMR (50 MHz, CDCl_3): $\delta = -0.93$ [$\text{Si}(\text{CH}_3)_3$], 71.83 (CHOH), 72.19 ($\text{C}=\text{C}=\text{CH}_2$), 99.68 [$\text{C}-\text{Si}(\text{CH}_3)_3$], 114.79 ($\text{CH}=\text{CH}_2$), 139.90 ($\text{CH}=\text{CH}_2$), 207.01 ($\text{C}=\text{C}=\text{CH}_2$). – MS (70 eV): m/z (%) = 168 (1) [M^+], 153 (8) [$\text{M}^+ - \text{CH}_3$], 135 (15) [$\text{M}^+ - \text{CH}_3 - \text{H}_2\text{O}$], 75 (58) [$\text{C}_2\text{H}_7\text{OSi}^+$], 73 (100) [$\text{Si}(\text{CH}_3)_3^+$]. – $\text{C}_9\text{H}_{16}\text{OSi}$ (168.3): calcd. C 64.23, H 9.58; found C 64.09, H 9.26.

3-Trimethylsilyl-1,2-octadiene-7-yn-4-ol (*rac*-10c**):** According to the general procedure magnesium (1.53 g, 63 mmol), (trimethylsilyl)propargyl bromide (2.41 g, 12.6 mmol) and 4-pentynal^[12] (**6c**) (0.52 g, 6.3 mmol) were used to afford 0.88 g (72%) of the 1,2-

alkadiene **rac-10c** as a colorless liquid after chromatography with diethyl ether/petroleum ether (1:4) on silica gel (60 g); $R_f = 0.37$. (In addition, 0.04 g (3%) of the alkyne **rac-8c** was isolated as a colorless liquid; $R_f = 0.21$.) – IR (neat): $\tilde{\nu} = 3420$ (OH), 3300 (C≡C–H), 2100 (C≡C), 1920 (C=C=C), 1240 (Si–C), 835 cm^{-1} (Si–CH₃). – ¹H NMR (200 MHz, CDCl₃): $\delta = 0.16$ [s; 9H, Si(CH₃)₃], 1.61–1.93 (m; 3H, CH₂CHOH), 1.96 (t, $J = 2.7$ Hz; 1H, C≡CH), 2.34 (dt, $J = 7.3$ Hz, $J = 2.7$ Hz; 2H, CH₂C≡CH), 4.20–4.36 (m; 1H, CHOH), 4.53 and 4.59 (AB part of ABX, $J_{AB} = 11.2$ Hz, $J_{AX} = 2.4$ Hz, $J_{BX} = 2.2$ Hz; 2H, C=CH₂). – ¹³C NMR (50 MHz, CDCl₃): $\delta = -0.98$ [Si(CH₃)₃], 14.89 (CH₂C≡CH), 36.29 (CHOHCH₂CH₂), 68.64 (C≡CH), 69.08 (CHOH), 72.00 (C=CH₂), 83.95 (C≡CH), 100.13 [C–Si(CH₃)₃], 207.11 (C=CH₂). – MS (70 eV): m/z (%) = 194 (1) [M⁺], 155 (22) [M⁺ – C₃H₃], 103 (82) [M⁺ – Si(CH₃)₃ – H₂O], 75 (81) [C₂H₇OSi⁺], 73 (100) [Si(CH₃)₃⁺]. – C₁₁H₁₈OSi (194.4): calcd. C 67.98, H 9.34; found C 67.74, H 9.44.

3-Trimethylsilyl-1,2-nonadien-8-yn-4-ol (rac-10d): According to the general procedure magnesium (1.22 g, 50 mmol), (trimethylsilyl)propargyl bromide (2.00 g, 10.5 mmol) and 5-hexynal^[13] (**6d**) (0.44 g, 4.3 mmol) were used to afford 0.73 g (82%) of the 1,2-alkadiene **rac-10d** as a colorless liquid after chromatography with diethyl ether/petroleum ether (1:3) on silica gel (60 g); $R_f = 0.38$. (In addition, 0.05 g (5%) of the alkyne **rac-8d** was isolated as a colorless liquid; $R_f = 0.20$.) – IR (neat): $\tilde{\nu} = 3400$ (OH), 3290 (C≡C–H), 2100 (C≡C), 1920 (C=C=C), 1240 (Si–C), 835 cm^{-1} (Si–CH₃). – ¹H NMR (200 MHz, CDCl₃): $\delta = 0.15$ [s; 9H, Si(CH₃)₃], 1.52–1.88 (m; 5H, CH₂ and OH), 1.95 (t, $J = 2.6$ Hz; 1H, C≡CH), 2.23 (dt, $J = 6.6$ Hz, $J = 2.6$ Hz; 2H, CH₂C≡CH), 4.10–4.25 (m; 1H, CHOH), 4.52 and 4.58 (AB part of ABX, $J_{AB} = 11.2$ Hz, $J_{AX} = 2.6$ Hz, $J_{BX} = 2.5$ Hz; 2H, C=CH₂). – ¹³C NMR (50 MHz, CDCl₃): $\delta = -0.94$ [Si(CH₃)₃], 18.10 (CH₂C≡CH), 24.47 (CH₂CH₂CH₂), 36.63 (CHOHCH₂), 68.50 (C≡CH), 69.98 (CHOH), 71.93 (C=CH₂), 84.24 (C≡CH), 100.52 [C–Si(CH₃)₃], 207.05 (C=CH₂). – MS (70 eV): m/z (%) = 208 (0.5) [M⁺], 207 (2) [M⁺ – H], 169 (22) [M⁺ – C₃H₃], 117 (85) [M⁺ – Si(CH₃)₃ – H₂O], 73 (100) [Si(CH₃)₃⁺]. – C₁₂H₂₀OSi (208.4): calcd. C 69.17, H 9.67; found C 68.94, H 9.74.

Addition of the (Trimethylsilyl)propargylcerium Reagent Derived from 9 and 11 to the Aldehydes 6. – **General Procedure:** Magnesium (1.22 g, 50 mmol) and mercury(I) chloride (5 mg) were suspended in diethyl ether (20 ml), and 1,2-dibromoethane (0.08 ml) was added. The mixture was stirred for 30 min and then cooled to 10°C. Within 1 h (trimethylsilyl)propargyl bromide (2.00 g, 10.5 mmol) was added maintaining the temp. between 10 to 15°C, and stirring was continued for one additional hour to afford the Grignard reagent **9**.

CeCl₃ [obtained from 3.72 g (10 mmol) of CeCl₃ · 7 H₂O (**11**)] was suspended in THF (100 ml) with stirring at room temp. and stirring was continued for 1 h. The suspension was cooled to 0°C, the solution of the Grignard reagent **9** in diethyl ether was added within 20 min and stirring was continued at 0°C for two additional hours. Subsequently the reaction mixture was cooled to –78°C, and a solution of the aldehyde **6** (4 mmol) in THF (2 ml) was added via a syringe. Within 12 h the reaction mixture was allowed to warm up to room temp. The solvent was evaporated (20°C, 12 Torr), the residue dissolved in diethyl ether (150 ml) and the reaction mixture cooled to 0°C. After addition of 1 N HCl (15 ml) the layers were separated, and the aqueous layer was extracted twice with diethyl ether (50 ml each). The combined organic layers were reextracted with a saturated aqueous NaHCO₃ solution and a saturated aqueous NaCl solution (20 ml each), dried with MgSO₄, and

the solvent was removed in vacuo (20°C, 12 Torr). The crude products **rac-8** were purified by flash chromatographed on silica gel.

1-Phenyl-4-trimethylsilyl-3-butyn-1-ol (rac-8a): According to the general procedure magnesium (1.22 g, 50 mmol), (trimethylsilyl)propargyl bromide (2.00 g, 10.5 mmol), CeCl₃ · 7 H₂O (**11**) (3.72 g, 10 mmol) and benzaldehyde (**6a**) (0.42 g, 4 mmol) were used to afford 0.74 g (85%) of the alkyne **rac-8a** as a colorless solid after chromatography with diethyl ether/petroleum ether (1:3) on silica gel (60 g); $R_f = 0.31$. (In addition, 0.04 g (5%) of the 2,3-alkadiene **rac-10a** was isolated as a colorless liquid; $R_f = 0.45$.) – M.p. 38°C. – IR (neat): $\tilde{\nu} = 3370$ (OH), 3075, 3055 and 3020 (aromat. CH), 2165 (C≡C–Si), 1597 (aromat. C=C), 1245 (Si–C), 755 and 695 cm^{-1} (δ_{CH} monosubst. aromat.). – ¹H NMR (200 MHz, CDCl₃): $\delta = 0.11$ [s; 9H, Si(CH₃)₃], 2.45 (d, $J = 2.8$ Hz; 1H, OH), 2.61 (d, $J = 6.4$ Hz; 2H, CH₂), 4.80 (dt, $J_1 = 6.4$ Hz, $J_2 = 2.8$ Hz; 1H, CHOH), 7.20–7.37 (m; 5H, C₆H₅). – ¹³C NMR (50 MHz, CDCl₃): $\delta = -0.04$ [Si(CH₃)₃], 31.11 (CH₂), 72.23 (CHOH), 87.85 (C≡C–Si), 102.92 (C≡C–Si), 125.71 (aromat. C-2/6), 127.80 (aromat. C-4), 128.31 (aromat. C-3/5), 142.47 (aromat. C-1). – MS (70 eV): m/z (%) = 218 (1) [M⁺], 179 (80) [M⁺ – C₃H₃], 107 (100) [C₇H₇O⁺], 73 (40) [Si(CH₃)₃⁺]. – C₁₃H₁₈OSi (218.4): calcd. C 71.50, H 8.31; found C 71.69, H 8.18.

6-Trimethylsilyl-1-hexen-5-yn-3-ol (rac-8b): According to the general procedure magnesium (1.22 g, 50 mmol), (trimethylsilyl)propargyl bromide (2.00 g, 10.5 mmol), CeCl₃ · 7 H₂O (**11**) (3.72 g, 10 mmol) and acrolein (**6b**) (0.22 g, 4 mmol) were used to afford 0.62 g (92%) of the alkyne **rac-8b** as a colorless liquid after chromatography with diethyl ether/petroleum ether (1:2) on silica gel (70 g); $R_f = 0.36$. (In addition, 0.04 g (6%) of the 1,4,5-alkatriene **rac-10b** was isolated as a colorless liquid; $R_f = 0.53$.) – IR (neat): $\tilde{\nu} = 3300$ (OH), 3060 (C=CH), 2160 (C≡C–Si), 1640 (C=C), 1240 (Si–C), 835 cm^{-1} (Si–CH₃). – ¹H NMR (200 MHz, CDCl₃): $\delta = 0.16$ [s; 9H, Si(CH₃)₃], 2.13 (d, $J = 4.8$ Hz; 1H, OH), 2.44 and 2.53 (AB part of ABX, $J_{AB} = 16.6$ Hz, $J_{AX} = 6.3$ Hz, $J_{BX} = 5.6$ Hz; 2H, CH₂C≡C–Si), 4.18–4.33 (m; 1H, CHOH), 5.18 (ddd, $J_{\text{cis}} = 10.5$ Hz, $J_2 = 1.5$ Hz, $J_3 = 1.2$ Hz; 1H, CH=CH₂), 5.31 (ddd, $J_{\text{trans}} = 17.1$ Hz, $J_2 = 1.5$ Hz, $J_3 = 1.3$ Hz; 1H, CH=CH₂), 5.92 (ddd, $J_{\text{trans}} = 17.1$ Hz, $J_{\text{cis}} = 10.5$ Hz, $J_3 = 5.6$ Hz; 1H, CH=CH₂). – ¹³C NMR (50 MHz, CDCl₃): $\delta = -0.01$ [Si(CH₃)₃], 28.82 (CH₂), 70.73 (CHOH), 87.61 [C–Si(CH₃)₃], 102.48 (C≡C–Si), 115.51 (CH=CH₂), 138.85 (CH=CH₂). – MS (70 eV): m/z (%) = 168 (0.2) [M⁺], 129 (20) [M⁺ – C₃H₃], 75 (34) [C₂H₇OSi⁺], 73 (100) [Si(CH₃)₃⁺]. – C₉H₁₆OSi (168.3): calcd. C 64.23, H 9.58; found C 63.85, H 9.64.

1-Trimethylsilyl-1,7-octadiyn-4-ol (rac-8c): According to the general procedure magnesium (1.22 g, 50 mmol), (trimethylsilyl)propargyl bromide (2.00 g, 10.5 mmol), CeCl₃ · 7 H₂O (**11**) (3.72 g, 10 mmol) and 4-pentynal^[12] (**6c**) (0.20 g, 2.4 mmol) were used to afford 0.40 g (85%) of the alkyne **rac-8c** as a colorless liquid after chromatography with diethyl ether/petroleum ether (1:2) on silica gel (60 g); $R_f = 0.36$. (In addition, 0.04 g (9%) of the 1,2-alkadiene **rac-10c** was isolated as a colorless liquid; $R_f = 0.53$.) – IR (neat): $\tilde{\nu} = 3300$ (OH), 3290 (C≡C–H), 2160 (C≡C–Si), 2100 (C≡C), 1240 (Si–C), 840 cm^{-1} (Si–CH₃). – ¹H NMR (200 MHz, CDCl₃): $\delta = 0.16$ [s; 9H, Si(CH₃)₃], 1.65–1.80 (m; 2H, CH₂CH₂C≡CH), 1.98 (t, $J = 2.7$ Hz; 1H, C≡CH), 2.14 (d, $J = 5.1$ Hz; 1H, OH), 2.36 (dt, $J_1 = 7.1$ Hz, $J_2 = 2.7$ Hz; 2H, CH₂C≡CH), 2.38 and 2.50 (AB part of ABX, $J_{AB} = 16.9$ Hz, $J_{AX} = 6.6$ Hz, $J_{BX} = 5.1$ Hz; 2H, CH₂C≡C–Si), 3.82–3.97 (m; 1H, CHOH). – ¹³C NMR (50 MHz, CDCl₃): $\delta = -0.06$ [Si(CH₃)₃], 14.78 (CH₂C≡CH), 28.62 (CH₂CH₂C≡CH), 34.51 (CHOHCH₂CH₂), 68.45 (CHOH), 68.80 (C≡CH), 83.69 (C≡CH), 87.51 [C–Si(CH₃)₃], 102.72 (C≡C–Si).

– MS (70 eV): m/z (%) = 194 (1) [M^+], 155 (30) [$M^+ - C_3H_3$], 75 (45) [$C_2H_7OSi^+$], 73 (100) [$Si(CH_3)_3^+$]. – $C_{11}H_{18}OSi$ (194.4): calcd. C 67.98, H 9.34; found C 67.74, H 9.44.

1-Trimethylsilyl-1,8-nonadiyn-4-ol (rac-8d): According to the general procedure magnesium (1.22 g, 50 mmol), (trimethylsilyl) propargyl bromide (2.00 g, 10.5 mmol), $CeCl_3 \cdot 7 H_2O$ (**11**) (3.72 g, 10 mmol) and 5-hexynal^[13] (**6d**) (0.41 g, 4 mmol) were used to afford 0.73 g (87%) of the alkyne **rac-8d** as a colorless liquid after chromatography with diethyl ether/petroleum ether (1:1.5) on silica gel (60 g); R_f = 0.39. (In addition, 0.09 g (11%) of the 1,2-alkadiene **rac-10d** was isolated as a colorless liquid; R_f = 0.46.) – B.p. 50°C/0.01 Torr. – IR (neat): $\tilde{\nu}$ = 3300 (OH), 3290 ($C\equiv C-H$), 2160 ($C\equiv C-Si$), 2100 ($C\equiv C$), 1240 ($Si-O$), 835 cm^{-1} ($Si-CH_3$). – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.16 [s; 9H, $Si(CH_3)_3$], 1.51–1.85 (m; 4H, CH_2), 1.95 (t, J = 2.6 Hz; 1H, $C\equiv CH$), 2.02 (d, J = 5.0 Hz; 1H, OH), 2.24 (dt, J_1 = 6.4 Hz, J_2 = 2.6 Hz; 2H, $CH_2C\equiv CH$), 2.35 and 2.48 (AB part of ABX, J_{AB} = 16.7 Hz, J_{AX} = 6.7 Hz, J_{BX} = 5.0 Hz; 2H, $CH_2C\equiv C-Si$), 3.67–3.85 (m; 1H, $CHOH$). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 0.02 [$Si(CH_3)_3$], 18.23 ($CH_2C\equiv CH$), 24.49 ($CH_2CH_2C\equiv CH$), 28.95 ($CH_2C\equiv C-Si$), 35.05 ($CHOHCH_2CH_2$), 68.60 ($C\equiv CH$), 69.34 ($CHOH$), 84.07 ($C\equiv CH$), 87.68 [$C-Si(CH_3)_3$], 102.94 ($C\equiv C-Si$). – MS (70 eV): m/z (%) = 208 (1) [M^+], 169 (75) [$M^+ - C_3H_3$], 75 (85) [$C_2H_7OSi^+$], 73 (100) [$Si(CH_3)_3^+$]. – $C_{12}H_{20}OSi$ (208.4): calcd. C 69.17, H 9.67; found C 68.98, H 9.62.

Addition of the (Trimethylsilyl)propargylcerium Reagent Derived from 9 and 12 to Benzaldehyde (6a): $CeCl_3 \cdot 3 i\text{-}PrOH$ (**12**) (2.56 g, 6 mmol) was dissolved in THF (100 ml) and *n*-butylmagnesium bromide (29.5 ml of a 0.623 M solution in diethyl ether, 18.4 mmol) was added at room temp. The mixture was stirred at 60°C for 2 h and then cooled to 0°C. A solution of (trimethylsilyl)propargylmagnesium bromide (**9**) in diethyl ether (10 ml, 6 mmol), prepared according to the general procedure described above, was added at 0°C, and stirring was continued for two hours. The reaction mixture was cooled to –78°C, a solution of benzaldehyde (**6a**) (0.27 g, 2.5 mmol) in THF (1 ml) was added, and the solution was allowed to warm up to room temp. within 10 h. The solvent was evaporated (20°C, 12 Torr), the residue dissolved in diethyl ether (150 ml) and the obtained solution cooled to 0°C. After addition of 1 N HCl (15 ml) the layers were separated, and the aqueous layer was extracted twice with diethyl ether (50 ml each). The combined organic layers were reextracted with a saturated aqueous $NaHCO_3$ solution and a saturated aqueous NaCl solution (20 ml each), dried with $MgSO_4$, and the solvent was removed in vacuo (20°C, 12 Torr). The crude product was purified by flash chromatography on silica gel (60 g) with diethyl ether/petroleum ether (1:3) to afford 0.19 g (35%) of the alkyne **rac-8a** as a colorless solid; R_f = 0.31. In addition, 0.03 g (6%) of the 2,3-alkadiene **rac-10a** was isolated as a colorless liquid; R_f = 0.45. – Spectroscopical data see above.

Addition of the (Trimethylsilyl)propargylcerium Reagent Derived from 9 and 13 to Benzaldehyde (6a): Cerium(III) isopropoxide (**13**) (1.50 g, 4.7 mmol) was dissolved in THF (100 ml), then a solution of (trimethylsilyl)propargylmagnesium bromide (**9**) (7.9 ml, 4.7 mmol) in diethyl ether, prepared according to the general procedure given above, was added at 0°C and stirring was continued for 2 h. The reaction mixture was cooled to –78°C, then a solution of benzaldehyde (**6a**) (0.32 g, 3 mmol) in THF (1 ml) was added, and the solution was allowed to warm up to room temp. within 10 h. The solvent was evaporated (20°C, 12 Torr), the residue dissolved in diethyl ether (150 ml) and the obtained solution cooled to 0°C. After addition of 1 N HCl (15 ml) the layers were separated, and the aqueous layer was extracted twice with diethyl ether (50 ml each). The combined organic layers were reextracted with a satu-

rated aqueous $NaHCO_3$ solution and a saturated aqueous NaCl solution (20 ml each), dried with $MgSO_4$, and the solvent was removed in vacuo (20°C, 12 Torr). The crude product was purified by flash chromatography on silica gel (60 g) with diethyl ether/petroleum ether (1:3) to afford 0.62 g (94%) of the alkyne **rac-8a** as a colorless solid; R_f = 0.31. In addition, 0.04 g (5%) of the 2,3-alkadiene **rac-10a** was isolated as a colorless liquid; R_f = 0.45. – Spectroscopical data see above.

Addition of the (Trimethylsilyl)propargylzinc Reagent Derived from 9 and Zinc Chloride to Benzaldehyde (6a): A solution of (trimethylsilyl)propargylmagnesium bromide (**9**) in diethyl ether, prepared according to the general procedure from magnesium (1.22 g, 50 mmol), (trimethylsilyl)propargyl bromide (2.00 g, 10.5 mmol) as described above, was diluted with THF (70 ml), then a solution of zinc chloride (1.76 g, 12.9 mmol) in THF (30 ml) was added at –5°C, and the solution was allowed to warm up to 15°C within 8 h. The reaction mixture was cooled to –78°C, then a solution of benzaldehyde (**6a**) (0.53 g, 5 mmol) in THF (5 ml) was added, and the solution was allowed to warm up to room temp. within 12 h. The solvent was evaporated (20°C, 12 Torr), the residue dissolved in diethyl ether (150 ml) and the obtained solution cooled to 0°C. After addition of 1 N HCl (15 ml) the layers were separated, and the aqueous layer was extracted twice with diethyl ether (50 ml each). The combined organic layers were reextracted with a saturated aqueous $NaHCO_3$ solution and a saturated aqueous NaCl solution (20 ml each), dried with $MgSO_4$, and the solvent was removed in vacuo (20°C, 12 Torr). The crude product was purified by flash chromatography on silica gel (60 g) with diethyl ether/petroleum ether (1:3) to afford 0.77 g (71%) of the alkyne **rac-8a** as colorless solid; R_f = 0.31. In addition, 0.22 g (20%) of the 2,3-alkadiene **rac-10a** was isolated as a colorless liquid; R_f = 0.45. – Spectroscopical data see above.

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