[2+2+2]-Cycloaddition of 4-Hydroxy-Substituted Enediynes to 2-Hydroxy-Substituted Decahydrophenanthrenes[‡]

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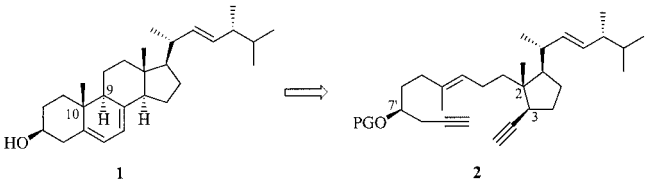
Enediynes *rac*-**4** were prepared in seven steps with an overall yield of 31% starting from 4-pentyn-1-ol (**5**). A cobalt mediated [2+2+2]-cycloaddition of these enediynes and subsequent removal of the metal fragment afforded the decahydrophenanthrenes *rac*-**3**/**13** in 37–56% yield.

Introduction

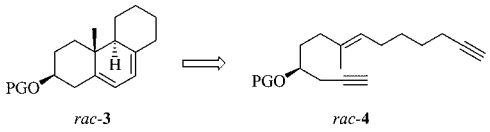
Aliphatic enediynes[2] with an internal double bond afford decahydrophenanthrene derivatives upon a cobalt mediated [2+2+2]-cycloaddition[3] and subsequent oxidative decomplexation. The configuration of the double bond is retained under these reaction conditions, e.g. enediynes with a *trans*-double bond undergo cyclization to decahydrophenanthrenes with a *trans*-configuration at C-4a−C-4b.[4]

In the course of our synthetic studies towards ergosterine derivatives, we were interested as to whether the stereogenic centers at C-7′ of enediyne **2** might have any influence on the formation of the new stereogenic centers at C-9 and C-10 in the ergosterine derivative **1** (Scheme 1). The formation of these stereogenic centers would otherwise be controlled by the substituents at C-2 and C-3 of the cyclopentane moiety of enediyne **2**. Consequently, the *O*-protected enediynes *rac*-**4** needed to be prepared and their [2+2+2] cycloadditions investigated to establish the diastereoselective outcome of this cyclization (Scheme 2).



1 **2**

Scheme 1



rac-**3** *rac*-**4**

Scheme 2

Results and Discussion

Enediynes *rac*-**4** were prepared as follows (Scheme 3). Cp_2ZrCl_2 catalyzed carbo-alumination of 4-pentyn-1-ol (**5**) gave the corresponding vinyl-alane which was treated with iodine to afford the (*E*)-vinyl iodide **6**.[5] The hydroxy group was protected with TBDMS-Cl/imidazole as its silyl ether **7**. The next step, a $[PPh_3]_4Pd$ catalyzed coupling[6] of **7** with the zinc organyl derived from 1-bromo-6-(trimethylsilyl)-5-hexyne (**8**)[7] which itself was prepared in two steps from 6-(trimethylsilyl)-5-hexyn-1-ol,[8] turned out to be cumbersome. The conversion of **8** into its magnesium derivative was always accompanied by an undesired ring closure reaction to the cyclopentylidene magnesium compound. Compound **8** was therefore treated with magnesium in the presence of zinc chloride to afford the corresponding zinc organyl without any side reactions. This organozinc compound was coupled with the vinyl iodide **7** in the presence of 5 mol % of $[PPh_3]_4Pd$ to afford the enyne **9** in 84% yield. Enyne **9** could be completely desilylated with nBu_4NF hydrate to alcohol **10** which was oxidized under Swern conditions[9] to aldehyde **11**. Addition of propargylmagnesium bromide gave the desired enediyne *rac*-**12** after aqueous workup. The hydroxy group at C-4 was protected as its silyl ether *rac*-**4a**[10] with TBDPS−Cl/imidazole, as its MEM-

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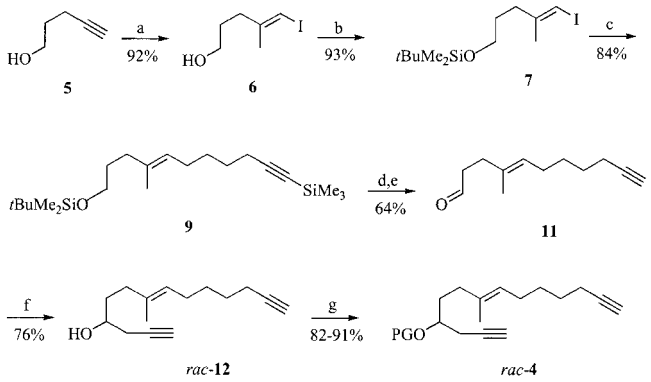
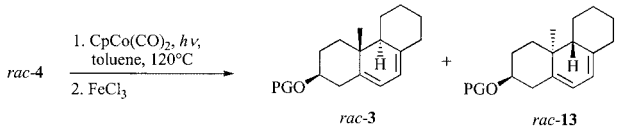


Scheme 3. Reagents and conditions: (a) (i) Cp_2ZrCl_2, $AlMe_3$, CH_2Cl_2, 0 °C, 15 min, then **5**, 45 °C, 76 h, (ii) I_2, 45 °C, 2 h, (b) TBDMS−Cl, imidazole, DMF, 0 °C to room temp., 5 h, (c) **8**, Mg, $ZnCl_2$, THF, 45 °C, 2 h, then $Pd(PPh_3)_4$, **7**, 25 °C, 24 h, (d) TBAF, THF, 25 °C, 4 h, (e) oxalyl chloride, DMSO, −65 °C, 20 min, then **10**, triethylamine, −65 °C to room temp., 30 min, (f) Mg, propargyl bromide, THF, 5 °C−15 °C, 1 h, then **11**, −15 °C to room temp., 1 h, (g) (i) for PG = tBuPh$_2$Si−: TBDPS−Cl, imidazole, DMF, 0 °C to room temp., 8 h, (89%), (ii) for PG = $CH_3OCH_2CH_2OCH_2$−: MEM−Cl, diisopropylamine, CH_2Cl_2, 0 °C to room temp., 18 h, (91%), (iii) for PG = CH_3−: KOH, MeI, DMSO, 25 °C, 30 min, (82%).

ether *rac*-**4b**[11] with MEM−Cl/Hünig base or as its methyl ether *rac*-**4c**[12] with methyl iodide/KOH.

The [2+2+2]-cycloadditions of the enediynes *rac*-**4** were carried out with 1.2 equivalents of $CpCo(CO)_2$ in toluene at reflux and with exposure to visible light (Scheme 4). According to analysis by TLC the cyclization was complete after between 90 min and 2 h. Oxidative decomplexation of the resultant cyclohexadiene cobalt complexes was investigated using iodine, copper(II)chloride or ferric(III) chloride as the oxidizing agent. The decomplexation of the cobalt complexes with iodine or copper(II)chloride led to complete decomposition of the ligands. Decomplexation with 1.5 equivalents of ferric(III) chloride hexahydrate in acetonitrile/pentane at −20 °C was more successful. The decahydrophenanthrenes *rac*-**3**/**13** were obtained in 37−56% yields as almost 1:1 mixtures of diastereomers. These compounds proved to be sensitive to air and light and could only be stored under argon at −30 °C in the dark. The best results were achieved by using the MEM substituent as a protecting group (PG) for the homoallylic hydroxy function (Table 1).



Scheme 4

Conclusion

It has been demonstrated that 4-hydroxysubstituted enediynes can be cyclized in a [2+2+2]-fashion to 2-hydroxy-substituted decahydrophenanthrene derivatives. A hydroxy group in the homoallylic position was able to tolerate the harsh reaction conditions. The stereogenic center at C-4 has no influence on the formation of the two stereogenic centers at C-4a and C-4b of the decahydrophenanthrene. Based on this result, a diastereoselective synthesis of ergosterole is under current investigation following the D → ABCD approach.

Table 1. [2+2+2]-Cycloaddition of enediynes **4**

PG (*rac*-**4**)	Yield of *rac*-**3**/*rac*-**13** (%)	Ratio *rac*-**3**:*rac*-**13**
a) TBDPS	37	1.7:1
b) MEM	56	1.9:1
c) Me	43	1.4:1

Experimental Section

Infrared spectra were recorded on Perkin−Elmer 298 and Perkin−Elmer FT IR 1600 spectrometers. ^{1}H and ^{13}C NMR spectra were acquired using a Varian XL 200, a Varian VXR 200, a Bruker AC 250 or a Jeol JNM−LA 400 spectrometer with chemical shifts (δ) given in parts per million relative to tetramethylsilane as an internal standard. Mass spectra were recorded using a Varian MAT 731 or 311 A or a Finnigan MAT 312 instrument. TLC analyses were performed using Polygram Sil G/UV_{254} silica gel plates. Silica gel (0.030−0.060 mm) from Baker was used for flash chromatography. Combustion analyses were carried out at the Microanalytical laboratory of the University of Konstanz. All reactions were carried out under argon except those involving aqueous workup procedures. All reagents were purified and dried if necessary before use. THF was freshly distilled from $LiAlH_4$ prior to use. The glassware used for the cobalt mediated cyclizations was rinsed with hexamethyldisilazane and dried in vacuo with a burner prior to use.

6-(Trimethylsilyl)-5-hexyn-1-ol: Sodium hydride (1.32 g, 55 mmol) was suspended in THF (70 mL). A solution of 5-hexyn-1-ol[13] (4.90 g, 50 mmol) in THF (10 mL) was added with stirring which was maintained until the evolution of hydrogen had ceased. A solution of *n*-butyllithium in hexane (1.6 M, 40 mL, 64 mmol) was then added at −30 °C with stirring. Stirring was continued for 30 min after which trimethylsilyl chloride (16.30 g, 150 mmol) was added at −70 °C. The reaction mixture was allowed to warm to room temperature and stirring was continued for 4 h. The solvent was removed in vacuo (40 °C/18 Torr) and diethyl ether (150 mL), a saturated aqueous NH_4Cl solution (50 mL) and 1 N HCl (150 mL) were added to the residue. The organic layer was separated and the solvent removed in vacuo (30 °C/18 Torr). The residue was dissolved in a solution of anhydrous HCl in methanol (1 M, 150 mL) with stirring which was continued at room temperature for 1 h. Most of the solvent was removed in vacuo (30 °C/18 Torr), H_2O (80 mL) was added to the residue and the resultant mixture was extracted three times with diethyl ether (50 mL each). The combined organic layers were dried with $MgSO_4$ and the solvent was removed in vacuo (25 °C/18 Torr). After distillation, 6-(trimethylsilyl)-5-hexyn-1-ol (7.92 g, 47 mmol, 93%) was obtained. B.p. 85 °C/0.01 Torr. IR (neat): $\tilde{\nu}$ = 3500−3150 (OH), 2170 [C≡C−Si$(CH_3)_3$] cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.15 [s, 9 H, Si$(CH_3)_3$], 1.50−1.85 (m, 5 H, CH_2CH_2 and OH), 2.14 (t, J = 7 Hz, 2 H, CH_2−C≡C−Si$(CH_3)_3$], 3.46 (t, J = 7 Hz, 2 H, CH_2-OH) ppm.

$C_9H_{18}OSi$ (170.3): calcd. C 63.47, H 10.65; found C 63.24, H 10.51.

1-Bromo-6-(trimethylsilyl)-5-hexyne (8): To a stirred solution of 6-(trimethylsilyl)-5-hexyn-1-ol (7.82 g, 46 mmol) in dichloromethane (80 mL) were added triethylamine (9.56 mL, 69 mmol) and methane sulfonyl chloride dropwise at −10 °C and stirring was continued for a further hour. The reaction mixture was poured into ice/1 N HCl and the organic layer was separated and washed with a saturated aqueous $NaHCO_3$ solution and H_2O (40 mL each). The organic layer was dried with $MgSO_4$ and the solvent removed in vacuo (15 °C/18 Torr) to afford 10.42 g (42 mmol, 91%) of the corresponding mesylate which was used for the next reaction step without any further purification.

To a stirred solution of this mesylate (10.42 g, 42 mmol) in acetone (100 mL) was added lithium bromide (17.4 g, 200 mol) and stirring was continued at 40 °C for 72 h. Most of the solvent was then removed in vacuo (0 °C/18 Torr) and diethyl ether (250 mL) and H_2O (40 mL) were added to the residue. The organic layer was washed with a saturated aqueous $NaHSO_3$ solution, a saturated aqueous $NaHCO_3$ solution and H_2O (40 mL each) and dried over $MgSO_4$. After removal of the solvent in vacuo (0 °C/18 Torr) distillation of the residue afforded 1-bromo-6-(trimethylsilyl)-5-hexyne (8.60 g, 37 mmol, 88%) as a clear colorless liquid. B.p. 110 °C/12 Torr. IR (neat): $\tilde{\nu}$ = 2175 [C≡C−Si$(CH_3)_3$] cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.19 [s, 9 H, Si$(CH_3)_3$], 1.35−2.10 (m, 4 H, CH_2CH_2), 2.17 [t, *J* = 7 Hz, 2 H, CH_2−C≡C−Si$(CH_3)_3$], 3.31 (t, *J* = 7 Hz, 2 H, CH_2Br) ppm. $C_9H_{17}BrSi$ (233.2): calcd. C 46.35, H 7.35, Br 34.26; found C 46.21, H 7.29, Br 34.08.

(*E*)-5-Iodo-4-methyl-4-penten-1-ol (6): To a stirred solution of Cp_2ZrCl_2 (5.0 g, 17 mmol) in dichloromethane (90 mL) was added a solution of trimethylaluminum in hexane (2.4 M, 62.5 mL, 150 mmol) at 0 °C. Stirring was continued for 15 min. 4-Pentyne-1-ol (**5**) (4.2 g, 50 mmol) was added and the reaction stirred at 45 °C for 76 h. Iodine (19.0 g, 75 mmol) was then added in small portions at room temperature and stirring was continued at this temperature for 2 h. A saturated aqueous $NaHCO_3$ solution (15 mL) was added carefully and the aluminum salts were dissolved by addition of 2 N HCl (70 mL). The organic layer was washed with H_2O until the aqueous layer was pH neutral, dried with $MgSO_4$ and the solvent was removed in vacuo (30 °C/18 Torr). Bulb to bulb distillation of the residue afforded the vinyl iodide **6** (10.4 g, 46 mmol, 92%) as a pale yellow liquid. B.p. 70−80 °C/0.01 Torr. IR (neat): $\tilde{\nu}$ = 3120−3580 (OH), 3050 (C=C−H), 1650 (C=C) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.50−1.80 (m, 2 H, HO−CH_2−CH_2), 1.78 [s, 3 H, C(CH_3)=CH], 2.07 (s, 1 H, OH), 2.23 (t, *J* = 7 Hz, 2 H, CH_2OH), 3.43 [t, *J* = 6 Hz, 2 H, CH_2(CH_3)=CH], 5.80 [s, 1 H, C(CH_3)=C*H*] ppm. $C_6H_{11}OI$ (226.0): calcd. C 31.86, H 4.91, I 56.15; found C 31.98, H 5.13, I 55.89.

(*E*)-5-(*tert*-Butyldimethylsilyloxy)-1-iodo-2-methyl-1-pentene (7): To a solution of the vinyl iodide **6** (4.52 g, 20 mmol) and *tert*-butyldimethylchlorosilane (3.62 g, 24 mmol) in DMF (35 mL) at 0 °C was added imidazole (3.40 g, 50 mmol) and the reaction mixture stirred at room temperature for 5 h. Petroleum ether (40 mL) and then a saturated aqueous NH_4Cl solution were added until the two layers had cleanly separated. The layers were separated, the aqueous layer was extracted three times with petroleum ether (25 mL each), the combined organic layers washed twice with H_2O (30 mL each) and then dried with $MgSO_4$. After the solvent had been removed in vacuo (25 °C/18 Torr) the residue was purified by bulb to bulb distillation to afford **7** (6.30 g, 18.52 mmol, 93%) as a pale yellow oil. B.p. 110−120 °C/0.1 Torr. IR (neat): $\tilde{\nu}$ = 3050 (C=C−H), 1620 (C=C), 1250 (C−Si) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.05 [s, 6 H, Si$(CH_3)_2$], 0.88 [s, 9 H, SiC$(CH_3)_3$], 1.82 [s, 3 H, C(CH_3)=CH], 1.22−1.95 (m, 3 H, *H*O−$CH_2$$CH_2$), 2.24 [t, *J* = 7 Hz, 2 H, CH_2C(CH_2)=CH], 3.40−3.76 (m, 2 H, HO−CH_2−CH_2), 5.85 (s, 1 H, C=CH) ppm. $C_{12}H_{25}OISi$ (340.2): calcd. C 42.33, H 7.41, I 37.30; found C 42.09, H 7.28, I 37.22.

(*E*)-1-(*tert*-Butyldimethylsilyloxy)-4-methyl-11-(trimethylsilyl)-undec-4-en-10-yne (9): Anhydrous zinc chloride (1.90 g, 14 mmol) was melted under a nitrogen atmosphere. At room temperature the molten zinc chloride was dissolved in THF (20 mL) and magnesium (0.63 g, 26 mmol), iodine (3 mg) and 1,2-dibromoethane (0.1 mL) were added with stirring. After the reaction mixture had become colorless and cloudy, a solution of 1-bromo-6-(trimethylsilyl)-5-hexyne (3.30 g, 14 mmol) in THF (15 mL) was added and stirring was continued at 45 °C for 2 h. At room temperature the solution was removed from the excess magnesium via syringe and added to a solution of $[PPh_3]_4Pd$ (0.58 g, 0.5 mmol) and vinyl iodide **7** (3.40 g, 10 mmol) in THF (10 mL). The reaction mixture was allowed to stir for 24 h at room temperature and the solvent was then removed in vacuo (25 °C/18 Torr). Diethyl ether (120 mL) and a saturated aqueous NH_4Cl solution (40 mL) were added to the residue, the organic layer was extracted with a saturated aqueous $NaHCO_3$ solution and H_2O (50 mL each), dried with $MgSO_4$ and the solvent was removed in vacuo (30 °C/18 Torr). After chromatographic purification with diethyl ether/petroleum ether (1:10) on silica gel (50 g) **9** (3.07 g, 8.40 mmol, 84%) was obtained as a colorless oil. R_f = 0.79. IR (neat): $\tilde{\nu}$ = 2175 (C≡C−Si$(CH_3)_3$], 1640 (C=C), 1250 (Si−C) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.03 [s, 6 H, Si$(CH_3)_2$], 0.13 (s, 9 H, C≡C−Si$(CH_3)_3$], 0.88 [s, 9 H, C$(CH_3)_3$], 1.24−1.78 [m, 8 H, $(CH_2)_3$C≡C and CH_2CH_2−OSi), 1.57 [[d, ^4J = 1 Hz, 3 H, C(CH_3)=CH], 1.92−2.09 [m, 2 H, C(CH_3)=CH−CH_2], 2.15 [t, *J* = 7 Hz, 2 H, CH_2C(CH_3)=CH], 3.56 (t, *J* = 7 Hz, 2 H, CH_2−OSi), 5.11 [tq, *J* = 7, ^4J = 1 Hz, 1 H, C(CH_3)=C*H*] ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = −5.27 [Si$(CH_3)_2$], 0.18 (C≡C−Si(CH_3)$_3$], 15.95 [C(CH_3)=CH), 19.76, 25.69, 27.34, 28.24, 28.97, 31.15 u. 35.81 [6 CH_2 and Si$C(CH_3)_3$], 25.81 [SiC(CH_3)$_3$], 62.83 (CH_2OSi), 84.24 (C≡*C*−Si$(CH_3)_3$], 107.53 [*C*≡C−Si$(CH_3)_3$], 124.29 [C(CH_3)=*C*H], 134.88 [*C*(CH_3)=CH] ppm. $C_{21}H_{42}OSi_2$ (366.5): calcd. C 68.76, H 11.55; found C 68.69, H 11.32.

(*E*)-4-Methylundec-4-en-10-yn-1-ol (10): To a stirred solution of tetra-*n*-butylammonium fluoride trihydrate (6.95 g, 22 mmol) in THF (50 mL) was added a solution of **9** (3.30 g, 9 mmol) in THF (15 mL) at room temperature and stirring was continued for an additional 4 h. The solvent was removed in vacuo (30 °C/18 Torr), the residue dissolved in diethyl ether (150 mL) and a saturated aqueous $NaHCO_3$ solution (50 mL) was added. The organic layer was washed with H_2O (50 mL), dried with $MgSO_4$ and the solvent was removed in vacuo (20 °C/18 Torr). After chromatographic purification of the residue with diethyl ether/petroleum ether (2:1) on silica gel (50 g) **10** (1.37 g, 7.60 mmol, 85%) was obtained as a colorless liquid. R_f = 0.40. IR (neat): $\tilde{\nu}$ = 3300 (OH), 3280 (C≡C−H), 2100 (C≡C) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.31−1.75 (m, 7 H, 3 CH_2 and OH), 1.59 [d, ^4J = 1 Hz, 3 H, C(CH_3)=CH], 1.92 (t, ^4J = 2.7 Hz, 1 H, C≡C−H), 1.93−2.07 (m, 4 H, CH_2−C(CH_3)=CH−CH_2), 2.17 (dt, *J* = 7, ^4J = 2.7 Hz, 2 H, CH_2−C≡CH), 3.61 (t, *J* = 6.5 Hz, 2 H, CH_2OH), 5.14 [tq, *J* = 7, ^4J = 1 Hz, 1 H, C(CH_3)=C*H*] ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.90 [C(CH_3)=CH], 18.32 (CH_2−C≡CH), 27.36, 28.09, 28.87, 30.78 and 35.86 (CH_2), 62.48 (CH_2OH), 68.27 (CH_2−C≡*C*−H), 84.60 (CH_2−*C*≡C−H), 124.53 [C(CH_3)=*C*H], 134.90 [*C*(CH_3)=CH] ppm. MS (70 eV): *(m/z)* (%) = 149 (2) [M^+

− CH_2OH], 85 (100) [$C_5H_9O^+$], 81 (16) [$(CH_2)_4-C\equiv CH^+$], 53 (10) [$(CH_2)_2-C\equiv CH^+$]. $C_{12}H_{20}O$ (180.2): calcd. C 79.93, H 11.19; found C 79.87, H 11.02.

(*E*)-4-Methylundec-4-en-10-yn-1-al (11): To a solution of oxalyl chloride (1.0 mL, 10.7 mmol) in dichloromethane (15 mL) at −65 °C was added a solution of DMSO (1.5 mL, 21.3 mmol) in dichloromethane (10 mL) with vigorous stirring over 10 min. Stirring was continued for an additional 10 min and a solution of the alcohol **10** (1.75 g, 9.7 mmol) in dichloromethane (8 mL) was then added. After 10 min. triethylamine (6.8 mL, 48.5 mmol) was added and the reaction mixture was allowed to warm to room temperature over 30 min. Diethyl ether (150 mL) and a dilute aqueous $NHCl_4$ solution (50 mL) were added, the layers were separated and the organic layer extracted with 1 N HCl, H_2O, a saturated aqueous $NaHCO_3$ solution and again with H_2O (50 mL each). After drying with $MgSO_4$ the solvent was removed in vacuo (25 °C/18 Torr) and the residue was purified by chromatography on silica gel (35 g) with diethyl ether/petroleum ether (1:4) to afford the aldehyde **11** (1.30 g, 7.30 mmol, 75%) as a colorless oil. R_f = 0.40. IR (neat): $\tilde{\nu}$ = 3280 (C≡C−H), 2100 (C≡C), 1715 cm^{-1} (C=O). ^1H NMR (200 MHz, $CDCl_3$): δ = 1.32−1.60 [m, 4 H, $(CH_2)_2-CH_2-C\equiv CH$], 1.61 [d, ^4J = 1 Hz, 3 H, $C(CH_3)=CH$], 1.94 (t, ^4J = 2 Hz, 1 H, C≡CH), 2.00 [dt, J = 7 Hz and 7 Hz, 2 H, $C(CH_3)=CH-CH_2$], 2.19 (dt, J = 7, ^4J = 2 Hz; $CH_2-C\equiv CH$), 2.32 [t, J = 8 Hz, 2 H, $CH_2-C(CH_3)=CH$], 2.53 (dt, J = 8 Hz and 1 Hz, 2 H, CH_2-CHO), 5.18 [tq, J = 7, ^4J = 1 Hz, 1 H, $C(CH_3)=CH$], 9.81 (t, J = 1 Hz, 1 H, CHO) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 16.09 [$C(CH_3)=CH$], 18.29 ($CH_2-C\equiv CH$), 27.34, 28.02, 28.71 and 31.82 (4 CH_2), 42.14 (CH_2-CHO), 68.21 (C≡*C*H), 84.50 (*C*≡CH), 125.26 [$C(CH_3)=CH$], 133.27 [$C(CH_3)=CH$], 202.33 (CHO) ppm. $C_{12}H_{18}O$ (178.2): calcd. C 80.85, H 10.18; found C 80.74, H 10.16.

(*E*)-7-Methyltetradec-7-ene-1,13-diyn-4-ol (*rac*-12): To a stirred suspension of magnesium (0.32 g, 13.2 mmol) in THF (20 mL) were added iodine (5 mg), $HgCl_2$ (5 mg) and 1,2-dibromoethane (0.05 mL). After the reaction mixture had become colorless and cloudy a solution of propargyl bromide (1.0 mL, 13.2 mmol) in THF (10 mL) was added at 5 °C with stirring which was maintained at 15 °C for 1 h. Titration of this solution with 0.1 N HCl indicated that this solution of propargyl magnesium bromide in THF was 0.34 N. A solution of the aldehyde **11** (0.98 g, 5.5 mmol) in THF (5 mL) was added at −15 °C to a solution of propargyl magnesium bromide in THF (0.34 N, 18 mL, 6.1 mmol) with stirring. The reaction mixture was allowed to warm to room temperature and stirring was continued for 1 h. Diethyl ether (20 mL) and a saturated aqueous $NHCl_4$ solution (10 mL) were added, the layers separated and the organic layer extracted with a saturated aqueous $NaHCO_3$ solution and a saturated aqueous NaCl solution (20 mL each). After drying with $MgSO_4$ the solvent was removed in vacuo (40 °C/18 Torr) and the residue purified by chromatography on silica gel (40 g) with diethyl ether/petroleum ether (2:1) to afford the enediyne *rac*-**12** (0.91 g, 4.17 mmol, 76%) as a colorless oil. R_f = 0.56. IR (neat): $\tilde{\nu}$ = 3350 (OH), 3270 (C≡C−H), 2100 (C≡C) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.27−1.80 (m, 6 H, 3 CH_2), 1.62 [d, ^4J = 1 Hz, 3 H, $C(CH_3)=CH$], 1.94 (t, ^4J = 2 Hz, 1 H, C≡CH), 1.97−2.13 [m, 5 H, $CH_2C(CH_3)=CH-CH_2$ and OH], 2.08 (t, ^4J = 2 Hz, 1 H, $CH-CH_2-C\equiv CH$), 2.19 (dt, 2 H, J = 6.5, ^4J = 2 Hz, $CH_2-CH_2-C\equiv CH$), 2.25−2.51 (m, 2 H, $CH-CH_2-C\equiv CH$), 3.75 (dddd, J = 5.8, 5.8, 5.8, and 5.8 Hz, 1 H, CHOH), 5.18 [tq, J = 7, J = 1 Hz; 1 H, $C(CH_3)=CH$] ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.93 [$C(CH_3)=CH$], 18.32 (C-12), 27.29, 27.36, 28.07 and 28.82 (C-3, C-6, C-10, C-11), 34.27 and 35.75 (C-5, C-9), 68.23, 69.67 and 70.79 (C-1, C-4, C-14), 80.90 and 84.60 (C-2, C-13), 124.84 (C-8), 134.76 (C-7) ppm. $C_{15}H_{22}O$ (218.2): calcd. C 82.51, H 10.16; found C 82.71, H 10.25.

(*E*)-4-(*tert*-Butyldiphenylsilyloxy)-7-methyltetradec-7-ene-1,13-diyne (*rac*-4a): To a solution of enediyne *rac*-**12** (0.26 g, 1.2 mmol) and *tert*-butyldiphenylchlorosilane (0.39 g, 1.4 mmol) in DMF (4 mL) at 0 °C was added imidazole (0.20 g, 2.9 mmol) and the reaction mixture was stirred at room temperature for 8 h. Petroleum ether (10 mL) and then a saturated aqueous $NHCl_4$ solution were added until the two layers had cleanly separated. The layers were separated, the aqueous layer extracted twice with petroleum ether (10 mL each), the combined organic layers washed twice with H_2O (10 mL each) and dried with $MgSO_4$. The solvent was removed in vacuo (25 °C/18 Torr) and the residue purified by chromatography on silica gel (20 g) with diethyl ether/petroleum ether (1:10) to afford the enediyne *rac*-**4a** (0.49 g, 1.07 mmol, 89%). R_f = 0.79. IR (neat): $\tilde{\nu}$ = 3300 (C≡C−H), 2100 cm^{-1} (C≡C). ^1H NMR (200 MHz, $CDCl_3$): δ = 1.07 [s, 9 H, $SiC(CH_3)_3$], 1.29−1.82 [m, 6 H, $CH_2-C(CH_3)=CH-(CH_2)_2$], 1.48 [d, ^4J = 1 Hz, 3 H, $C(CH_3)=CH$], 1.83−2.08 [m, 6 H, $CH_2-CH_2-C(CH_3)=CH-CH_2-CH_2$ and 2 C≡CH], 2.17 (dt, J = 7, ^4J = 2 Hz, 2 H, $CH_2-CH_2C\equiv CH$), 2.25−2.39 (m, 2 H, $CH-CH_2C\equiv CH$), 3.84 (dddd, J = 6, 6, 6 and 6 Hz; 1 H, CH−OSi), 5.01 [tq, J = 7, ^4J = 1 Hz, 1 H, $C(CH_3)=CH$], 7.31−7.45 (m, 6 H, *meta* and *para*-H), 7.60−7.74 (m, 4 H, ortho-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.73 [$C(CH_3)=CH$], 18.20, 19.23, 26.30, 27.19, 27.94, 28.71, 34.20 and 34.71 [C-3, C-5, C-6, C-9, C-10, C-11, C-12 and $SiC(CH_3)_3$], 26.88 [$SiC(CH_3)_3$], 68.06 and 69.94 (C-1 and C-14), 71.03 (C-4), 81.13 and 84.48 (C-2 and C-13), 124.06 (C-8), 127.40, 127.44, 129.51, 133.89, 134.02, 134.84 and 135.77 (aromat. CH, C and C-7) ppm. $C_{31}H_{40}OSi$ (456.6): calcd. C 81.52, H 8.83; found C 81.36, H 8.84.

(*E*)-4-(β-Methoxyethoxymethoxy)-7-methyltetradec-7-ene-1,13-diyne (*rac*-4b): To a solution of enediyne *rac*-**12** (0.22 g, 1.0 mmol) and diisopropylethylamine (0.2 mL, 1.6 mmol) in dichloromethane (5 mL) at 0 °C was added β-methoxyethoxymethyl chloride (0.3 mL, 1.6 mmol) and the reaction mixture stirred at room temperature for 18 h. Diethyl ether and a saturated aqueous $NHCl_4$ solution (10 mL each) were then added. The layers were separated, the aqueous layer extracted twice with diethyl ether (10 mL each) and the combined organic layers washed twice with H_2O (10 mL each) and dried with $MgSO_4$. The solvent was removed in vacuo (25 °C/18 Torr) and the residue purified by chromatography on silica gel (15 g) with diethyl ether/petroleum ether (1:4) to afford the enediyne *rac*-**4b** (0.28 g, 0.91 mmol, 92%). R_f = 0.14. IR (neat): $\tilde{\nu}$ = 3290 (C≡C−H), 2110 (C≡C), 1660 (C=C) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.30−2.32 (m, 14 H, CH_2 and C≡CH), 1.63 [d, ^4J = 1 Hz, 3 H, $C(CH_3)=CH$], 2.49 (dd, J = 7 and 3 Hz, 2 H, $CH-CH_2-C\equiv CH$), 3.39 (s, 3 H, OCH_3), 3.52−3.88 (m, 5 H, OCH_2CH_2O and CH−O), 4.70 and 4.87 (AB signal, J_{AB} = 8 Hz, 2 H, OCH_2O), 5.15 [tq, J = 6.5, ^4J = 1 Hz, 1 H, $C(CH_3)=CH$] ppm. $C_{19}H_{30}O_3$ (306.3): calcd. C 74.47, H 9.87; found C 74.52, H 9.82.

(*E*)-4-Methoxy-7-methyltetradec-7-ene-1,13-diyne (*rac*-4c): Powdered potassium hydroxide (0.62 g, 11 mmol) was suspended in DMSO (10 mL) with vigorous stirring. Enediyne *rac*-**12** (0.61 g, 2.8 mmol) and methyl iodide (0.35 mL, 5.7 mmol) were added and stirring was continued for 30 min. H_2O was then added to the reaction mixture until everything had completely dissolved. The reaction mixture was extracted three times with dichloromethane (10 mL each) and the combined organic layers were washed twice with H_2O (10 mL each) and dried with $MgSO_4$. The solvent was removed in vacuo (25 °C/18 Torr) and the residue purified by chro-

matography on silica gel (20 g) with diethyl ether/petroleum ether (1:20) to afford the enediyne *rac*-**4c** (0.53 g, 2.30 mmol, 82%). R_f = 0.23. IR (neat): $\tilde{\nu}$ = 3280 (C≡C−H), 2100 (C≡C) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.40−1.83 [m, 6 H, $(CH_2)_2CH_2$-C≡CH and OCH−CH_2CH_2], 1.65 [d, ^4J = 1 Hz, 3 H, C(CH_3)=CH], 1.98 [t, ^4J = 2 Hz, 1 H, $(CH_2)_2$C≡C*H*], 2.04 (t, ^4J = 2 Hz, 1 H, CH−CH_2−C≡C*H*), 2.00−2.17 [m, 4 H, CH_2C(CH_3)=CH−CH_2], 2.23 (dt, J = 7, ^4J = 2 Hz, 2 H, CH_2−CH_2−C≡CH), 2.40−2.51 (m, 2 H, CH−CH_2−C≡CH), 3.32 (dddd, J = 6, 6, 6 and 6 Hz, 1 H, C*H*−OCH_3), 3.42 (s, 3 H, OCH_3), 5.20 [tq, J = 7 Hz and ^4J = 1 Hz, 1 H, C(CH_3)=C*H*] ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.91 [C(CH_3)=CH], 18.32 (C-12), 23.04, 27.33, 27.36, 28.08, 31.87 and 35.32 (C-3, C-5, C-6, C-9, C-10, C-11), 56.98 (OCH_3), 68.21 and 69.91 (C-1 and C-14), 78.66 (C-4), 81.04 and 84.58 (C-2 and C-13), 124.58 (C-8), 134.76 (C-7) ppm. $C_{16}H_{24}O$ (232.3): calcd. C 82.70, H 10.41; found C 82.76, H 10.51.

Cobalt Mediated [2+2+2]-Cycloaddition of Enediynes *rac*-11 to Decahydrophenanthrenes *rac*-12/13. General Procedure: A solution of the enediyne *rac*-**4** (1 mmol) in toluene (30 mL) was cooled to −70 °C and the apparatus was evacuated for 3 min (0.5 Torr). The flask was allowed to warm to room temperature and argon was admitted to the apparatus. The solution of the enediyne in toluene was again cooled to −70 °C and the above procedure was repeated a further two times. $CpCo(CO)_2$ (1.2 mmol) was added and the reaction mixture was heated to reflux with concomitant irradiation with visible light until no more starting material could be detected by TLC analysis. The reaction mixture was cooled down to room temperature and volatile components were removed in vacuo (20 °C/0.1 Torr). The residue was dissolved in degassed diethyl ether/pentane (1:4, 5 mL) and filtered through celite under an argon atmosphere. Ferric chloride hexahydrate (0.49 g, 1.8 mmol) was dissolved in acetonitrile (20 mL), pentane (20 mL) was added and the mixture cooled to −20 °C. At this temperature the filtrate was added with stirring which was continued for 30 min. The reaction mixture was then cooled to −60 °C and the pentane layer was removed from the frozen acetonitrile layer. The acetonitrile layer was allowed to warm to −20 °C, pentane (15 mL) was added and the above procedure was repeated four times. The pentane layers were combined, the solvent was removed in vacuo (30 °C/18 Torr) and the residue purified by chromatography on silica gel.

***trans*-1,2,3,4,4a,4b,5,6,7,8-Decahydro-2-*tert*-butyldiphenylsilyloxy-4a-methylphenanthrene (*rac*-3a/13a):** According to the general procedure, enediyne *rac*-**4a** (0.18 g, 0.40 mmol) and $CpCo(CO)_2$ (0.11 g, 0.60 mmol) were used to prepare *rac*-**3a/13a** (68 mg, 0.15 mmol, 37%) as a colorless liquid after chromatography with diethyl ether/petroleum ether (1:50) on silica gel (15 g); R_f = 0.49. diastereomeric ratio 1.7:1. IR (neat): $\tilde{\nu}$ = 3050, 3020 (C=C−H), 1645 (C=C), 1580 (aromat. C=C), 1100 (C−O) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.85 (s, 3 H, CH_3 of **3a**), 0.88 (s, 3 H, CH_3 of **13a**), 1.08 [s, 9 H, $SiC(CH_3)_3$], 1.20−2.50 (m, 15 H, CH_2 and CH), 3.57−3.74 (m, 1 H, CH−OSi), 5.32−5.47 (m, 2 H, C=CH−CH=C), 7.10−7.50 (m, 6 H, *meta* and *para*-H),7.60−7.80 (m, 4 H, ortho-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.73 and 16.15 (CH_3), 19.15, 19.39, 23.93, 24.45, 25.08, 25.11, 27.00, 29.46, 32.15, 32.65, 32.71, 33.65, 36.77, 37.15, 38.07 and 38.30 (7 CH_2 and C-4a), 25.47 [Si−C(CH_3)$_3$], 41.06 [Si−*C*(CH_3)$_3$], 47.49 and 47.60 (C-4b), 67.74 and 72.07 (C-2), 117.52, 118.00, 118.98 and 119.79 (C-9 and C-10), 127.36, 127.46, 127.48, 129.44, 134.61, 134.71, 134.78, 135.74 and 135.93 (aromat. CH and C), 137.35, 138.07, 139.95 and 140.95 (C-8a and C-10a) ppm. MS (70 eV): *(m/z)* (%) = 456 (8) [M^+], 399 (10) [$M^+ - C_4H_9$], 239 (6) [$Si(C_6H_5)_2(C_4H_9)^+$], 199 (100), [$M^+ - Si(C_6H_5)_2(C_4H_9) - H_2O$]. $C_{31}H_{40}OSi$ (456.6): calcd. C 81.52, H 8.83; found C 81.24, H 8.71.

***trans*-1,2,3,4,4a,4b,5,6,7,8-Decahydro-2-(β-methoxyethoxymethoxy)-4a-methylphenanthrene (*rac*-3b/13b):** According to the general procedure, enediyne *rac*-**4b** (0.22 g, 0.72 mmol) and $CpCo(CO)_2$ (0.18 g, 1.0 mmol) were used to prepare *rac*-**3b/13b** (0.12 g, 0.40 mmol, 56%) as a colorless liquid after chromatography with diethyl ether/pentane (1:4) on silica gel (15 g); R_f = 0.15. diastereomeric ratio 1.9:1. IR (neat): $\tilde{\nu}$ = 3040 (C=C−H), 1625 (C=C) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.87, (s, 3 H, CH_3 of **3b**), 0.89 (s, 3 H, CH_3 of **13b**), 1.04−2.28 (m, 15 H, CH_2 and CH), 3.38 (s, 3 H, OCH_3), 3.44−3.82 (m, 5 H, OCH_2CH_2O and CH−O), 4.72 and 4.81 (AB signal, J_{AB} = 8 Hz, 2 H, OCH_2O), 5.48 (s, 2 H, C=CH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.92 and 16.02 (CH_3), 23.84, 24.39, 25.01, 25.06, 25.41, 26.33, 29.04, 32.64, 32.67, 33.79, 35.67, 37.02, 37.86, 38.06 (7 CH_2 and C-4a), 47.42 and 47.59 (C-4b), 58.97 (OCH_3), 66.62, 66.68, 69.41 and 70.89 (OCH_2CH_2O), 71.73 and 75.64 (C-2), 93.26 and 93.58 (OCH_2O), 117.48, 117.62, 119.39 and 119.76 (C-9 and C-10), 137.67, 138.96, 139.82 and 140.04 (C-8a and C-10a). $C_{19}H_{30}O_3$ (306.3): calcd. C 74.47, H 9.87; found C 74.13, H 9.64.

***trans*-1,2,3,4,4a,4b,5,6,7,8-Decahydro-2-methoxy-4a-methylphenanthrene (*rac*-3c/13c):** According to the general procedure, enediyne *rac*-**4c** (0.28 g, 1.20 mmol) and $CpCo(CO)_2$ (0.36 g, 2.0 mmol) were used to prepare *rac*-**3c/13c** (0.12 g, 5.17 mmol, 43%) as a colorless liquid after chromatography with diethyl ether/pentane (1:10) on silica gel (15 g); R_f = 0.34. Diastereomeric ratio 1.4:1. IR (neat): $\tilde{\nu}$ = 3015 (C=C−H), 1645 (C=C), 1195 (C−O) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.88 and 0.89 ppm(2s, 3 H, CH_3), 1.10−2.60 (m, 15 H, CH_2 and CH), 3.08−3.26 (m, 1 H, C*H*−OCH_3), 3.31 and 3.38 (2s, 3 H, OCH_3), 5.42−5.56 (m, 2 H, C=CH−CH=C) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.99 and 16.07 (CH_3), 24.02, 24.45, 25.10, 25.33, 25.47, 28.23, 32.68, 32.72, 33.55, 35.19, 37.09, 37.23, 37.33 and 38.00 (7 CH_2 and C-4a), 47.39 and 47.70 (C-4b), 55.55 and 55.64 (OCH_3), 74.93 and 79.13 (C-2), 117.60, 117.76, 119.47 and 119.77 (C-9 and C-10), 137.45, 138.20, 139.07 and 140.32 (C-8a and C-10a) ppm. MS (70 eV): *(m/z)* (%) = 232 (21) [M^+], 201 (35) [$M^+ - O CH_3$], 183 (100) [$M^+ - OCH_3 - H_2O$]. $C_{16}H_{24}O$ (232.3): calcd. C 82.70, H 10.41; found C 82.36, H 10.12.

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