A McMurry Route to the Dienediyne Portion of Models of the Neocarzinostatin Chromophore

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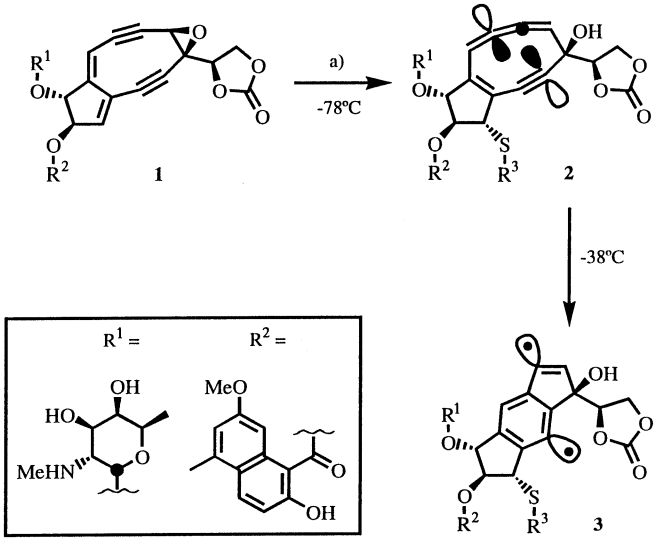
Received January 19, 1998

Keywords: C,C couplings / Cycloaromatization / Dienediynes / McMurry reaction / Neocarzinostatin

The 6-ring/10-ring dienediyne model **11** of the antitumor agent neocarzinostatin chromophore **1** and its 6-ring/11-ring homolog **12** have been obtained in 41 and 18% yields, respectively, by McMurry cyclizations of ketoaldehydes **8** and **9** using $TiCl_3 \cdot 2DME$ and Zn/Cu couple. Compounds **8** and **9** were obtained by multistep syntheses starting from the readily available acetylenic aldehydes $HC{\equiv}CC(CH_3)_2$-$(CH_2)_nCH{=}O$ (**18**, n = 1; **21**, n = 2). Dienediyne **11** was converted into the dienediyne ketone **33** which cycloaromatized at room temperature giving the octahydrophenanthrone **35** in 16% yield.

The chemical and biological novelty of a class of natural products termed "enediyne antibiotics" has evoked great interest.[1] Its members esperamicin,[2] calicheamicin,[3] dynemicin,[4] kedarcidin chromophore,[5] C-1027 chromophore,[6] and maduropeptine chromophore[7] are complex (!) derivatives of (*Z*)-3-hexene-1,5-diyne. The seventh "enediyne antibiotic" is neocarzinostatin,[8] a chromoprotein whose chromophore **1** contains no 3-hexene-1,5-diyne but a *branched di*enediyne (Scheme 1).[9]

Scheme 1. Ref.[10c]: a) Methyl thioglycolate (24 equiv.), 9:1 $[D_8]THF/CD_3OD$; 4 h → complete conversion of **1** into **2** for $R^3 = CH_2{-}CO_2Me$



The dienediyne motif of chromophore **1** in combination with the adjacent epoxide ring is essential for its propensity to form − after appropriate activation[10] − biradicals. The latters abstract H atoms from DNA and de-aminate or cleave it thereby.[11] This leads to the death of tumorous cells − the antitumor activity of neocarzinostatin − and benign cells as well − which is why neocarzinostatin is cytotocic. In the biologically most significant activation mode of the neocarzinostatin chromophore **1**, thiols ring-open the epoxide through an S_N2''' attack upon the terminus of the C=C−C=C−C≡C−C−O substructure (Scheme 1).[10a][10b][10c] Severely strained enyne[3]cumulenes **2** form thereby. Transannular overlap of their in-plane π orbitals initiates cycloaromatizations giving the styrene-α,*meta*-biradicals **3** which damage DNA as sketched above. Such cycloaromatizations **5** → **6** can be differentiated as "neocarzinostatin-type cycloaromatization" from the "Bergman cyclizations" of 3-hexene-1,5-diynes to benzene-1,4-biradicals,[12] the "Saito-Myers cyclizations" of enyneallenes to toluene-α,*meta*-biradicals[13] or their "Schmittel cyclizations" to pentafulvene-based biradicals,[14] the "Moore cyclizations" of enyneketenes to phenoxyl biradicals,[15] and Nicolaou's cyclization of diallenylsulfones to thiophene-*S*,*S*-dioxide based 1,4 biradicals.[16]

The protein-free neocarzinostatin chromophore **1** is exceedingly labile. Synthesizing analogues of **1** with a thiol-activable dienediyne core in a less fragile molecular environment has occupied many researchers.[17] From these investigations, conjugated dienediyne *ketones* emerged as a reliable source of biradicals: They are easily engaged in 1,6-additions of a thiol (e.g. **4** → **5**; Scheme 2)[18][19] or analogous 1,8-additions[18][20] giving enyneallenyl ketones **5** which cycloaromatize by the Saito-Myers mode.[18]

The present study aimed at synthesizing and cycloaromatizing (an)other type-**4** dienediyne(s) by ring-closing McMurry reactions **8** → **11** and **9** → **12** (Scheme 3). This approach complements our strategically different McMurry route to bicyclic *tri*enediynes[21] and follows conceptionally our synthesis of the tricyclic *di*enediyne **10** from ketoaldehyde **7**.[22]

The aldehyde moieties of the required ketoaldehydes **8** and **9** were derived from the ω-alkynals **18** and **21** (Scheme 4). Their syntheses followed mostly indications from the lit-

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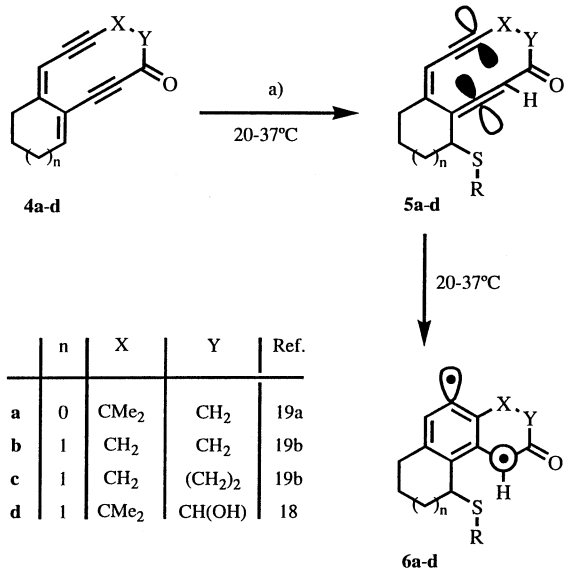
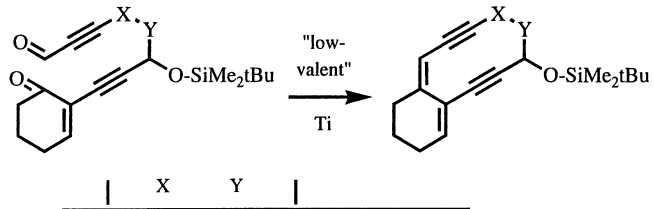
Scheme 2. a) Methyl thioglycolate (2.0−2.1 equiv.), 1,4-cyclohexadiene (0−30 equiv.), NEt_3 (1.0−ca. 4 equiv.), CH_2Cl_2 or C_6H_6.



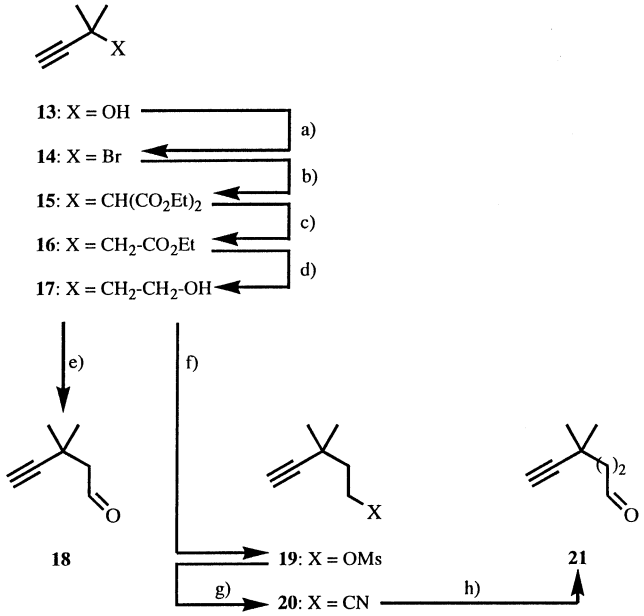
	n	X	Y	Ref.
a	0	CMe_2	CH_2	19a
b	1	CH_2	CH_2	19b
c	1	CH_2	$(CH_2)_2$	19b
d	1	CMe_2	CH(OH)	18

Scheme 3



	X	Y	
7			**10** (ref. [22])
8	CMe_2	CH_2	**11** (cf. Scheme 5)
9	CMe_2	$(CH_2)_2$	**12** (cf. Scheme 5)

Scheme 4. a) PBr_3 (0.4 equiv.), 15°C, 30 min; 60% (ref.[23] 50%). − b) Na (1.06 equiv.), diethyl malonate (1.06 equiv.), EtOH, 60°C, 4 h; 39% (lit[24]. 39%). − c) NaCl (1.0 equiv.), H_2O (1.5 equiv.), DMSO, 180°C, 19 h; 82% (ref.[24] 65%). − d) $LiAlH_4$ (0.8 equiv.), diethyl ether, reflux, 1 h, room temp., 10 h; 95% (ref.[24] 81%). − e) Oxalyl chloride (1.1 equiv.), DMSO (2.2 equiv.), NEt_3 (5.0 equiv.), CH_2Cl_2, −78°C, 30 min;[25] 73%. − f) MsCl (1.1 equiv.), NEt_3 (1.2 equiv.), CH_2Cl_2, 0°C, 30 min; 97% (ref.[24] 96%). − g) NaCN (2.0 equiv.), DMSO, 90°C, 30 min, 10 h, room temp.; 87% (ref.[24] 81%). − h) DIBAL (1.4 equiv.), toluene, −78°C, 2 h;[26] yield determined after conversion into alcohol **23** (Scheme 5)

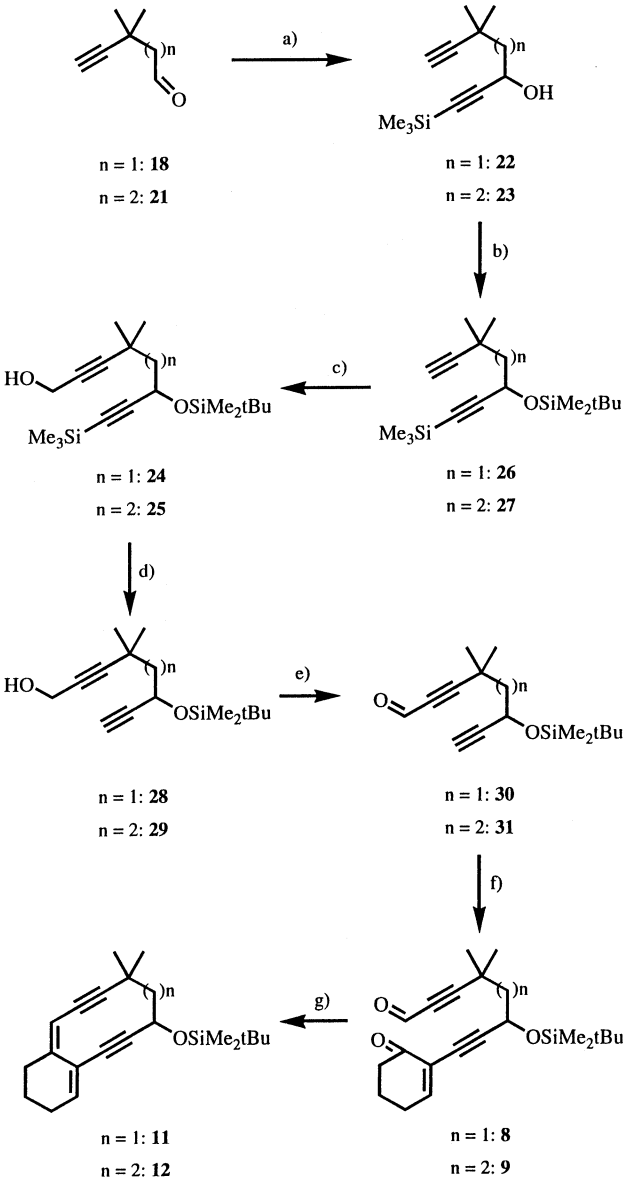


erature.[23][24] Thus, the dimethylated propargyl alcohol **13** was converted into the dimethylated propargyl bromide **14** (60%). It was combined with sodium diethyl malonate to the diester **15** in 39% yield. The latter was de-ethoxycarbonylated by heating with NaCl in wet DMSO. Monoester **16** was thereby obtained in 82% yield. Reduction with $LiAlH_4$ led to alcohol **17** (95%). Part of this material was oxidized to the ω-alkynal **18** under Swern's conditions[25] (73% yield). The residual alcohol **17** was C_1-elongated via the corresponding mesylate **19** (97%) to the unsaturated nitrile **20** (87%). A chemoselective reduction with DIBAL at −78°C[26] provided the second needed ω-alkynal, compound **21**.

Lithio-(trimethylsilyl)acetylene was added to the C=O bond of aldehydes **18** and **21** giving the trimethylsilylated diynols **22** (69%) and **23** (33% over 2 steps) (Scheme 5). Their respective OH group was silylated by treating with tBuMe$_2$SiCl and imidazole.[27] The resulting silyl ethers **26** (99%) and **27** (93%) were hydroxymethylated[28] via the derived lithium acetylides furnishing the diynols **24** (88%) and **25** (91%). Basic methanolysis of the $Me_3Si-C\equiv$ bond[29] in these compounds was possible leaving the tBuMe$_2$Si−O bond intact. Thus, we obtained the diynols **28** and **29** in better than 80% yield. The Dess-Martin periodinane[30] was the oxidant of choice for proceeding to the corresponding diynals **30** and **31** in yields of 99% and 92%, respectively. The Sonogashira/Tohda/Hagihara coupling between these diynals and 2-iodo-2-cyclohexenone[31] worked nicely after considerable fine-tuning of the reaction parameters.[32] The ketoaldehydes **8** (98%) and **9** (85%) became thereby conveniently available.

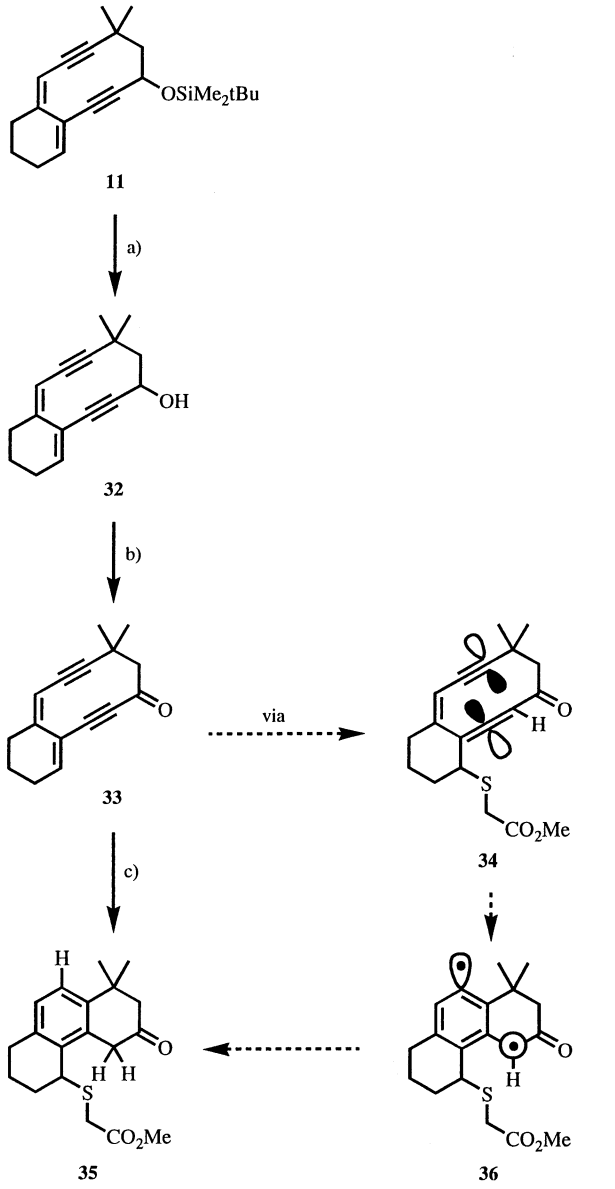
Unfortunately, the ensuing McMurry cyclizations[33] **8** → **11** and **9** → **12** were not nearly as efficient. The best variation which we tried consisted of (1) purifying $TiCl_3$ through crystallization of its DME complex, (2) reducing this complex with Zn/Cu couple,[34] and (3) pumping at room temp. during 14 h a DME solution of the substrate to the reducing mixture. TLC indicated the complete consumption of starting material under these conditions and the formation of a single *well*-defined new spot. It had a considerably higher R_F value than the ketoaldehyde precursors **8** and **9**, i. e. indicated a distinctly decreased polarity of the reaction products. They turned out to be, after isolation per flash chromatography on silica gel,[35] the desired dienediynes **11** (41%) and **12** (18%), respectively. The only other product detectable by TLC was "polymer". Conducting the McMurry reaction at 40°C lowered the yield of dienediyne **11** to 14%. Combining the reagents at 0°C gave no compound **11** at all but 27% recoverable starting ketoaldehyde

Scheme 5. a) *n*BuLi (1.15 equiv.), (trimethylsilyl)acetylene (1.2 equiv.), THF, −78°C, 1.5 h, 69% **22**, 33% (over 2 steps) **23**. − b) *t*-Butyldimethylsilyl chloride (1.5 equiv.), imidazole (3.0 equiv.), CH_2Cl_2, room temp., 16 h;[27] 99% **26**, 93% **27**. − c) *n*BuLi (1.2 equiv.), $(CH_2O)_n$ (3.0 equiv.), THF, −78°C, 3.5 h;[28] 88% **24**, 91% **25**. − d) K_2CO_3 (1.0 equiv.), MeOH, room temp., 14 h;[29] 84% **28**, 85% **29**. − e) Dess-Martin periodinane[30] (1.5 equiv.), CH_2Cl_2, 0°C, 30 min; 99% **30**, 92% **31**. − f) 2-Iodo-2-cyclohexen-1-one,[31] $Pd(PPh_3)_2Cl_2$ (0.05 equiv.), CuI (0.15 equiv.), benzene/NEt_3 (3:1), 0°C, 2 h;[32] 98% **8**, 85% **9**. − g) $TiCl_3$ (43 equiv./59 equiv.), Zn/Cu couple (160 equiv./219 equiv.), DME, room temp., 14 h;[34] 41% **11**, 18% **12**



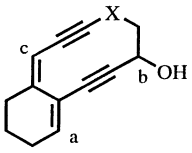
8. The ^{1}H-NMR spectrum of the crude product exhibited no new CH−O resonance from which we concluded that we had not generated cyclic pinacols as the alternatively imaginable[33] reductive coupling products. A pinacol had been obtained from the related ketoaldehyde **7** in 60% yield.[22] Clearly, the McMurry routes to the *di*enediynes **11** and **12** of Scheme 5 are not as efficient as our previous McMurry syntheses of *tri*enediynes.[21] This is true even if the ring sizes (10- or 11-membered) which these reactions establish are identical and the substituents at the involved carbonyl moieties closely related. Explaining this difference we are at a loss.

Scheme 6. a) HF/pyridine (6 equiv.), THF, 0°C, 3.5 h;[36] 76%. − b) Dess-Martin periodinane[30] (2.5 equiv.), $NaHCO_3$, molecular sieves 4 A, CH_2Cl_2, room temp., 1 h;[37] 72%. − c) Methyl thioglycolate (2.1 equiv.), NEt_3 (2.5 equiv.), 1,4-cyclohexadiene (23 equiv.), CH_2Cl_2, room temp., 14 h; 16%.

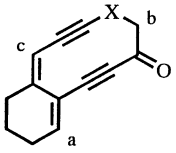


The 6-ring/10-ring dienediynyl *tert*-butyldimethylsilylether **11** was desilylated with the HF/pyridine complex (Scheme 6).[36] The dienediynol **32** resulted in 76% yield. Its ^{1}H-NMR spectrum in C_6D_6 resembles the ^{1}H-NMR spectrum of the des-dimethyl analog **37**[19b] in $CDCl_3$ considerably. Table 1 (top, left) illustrates this statement with the low-field signals C_{sp^2}-*H* (2 ×) and C*H*(OH). Oxidizing dienediynol **32** with a buffered[37] solution of the Dess-Martin periodinane[30] was the last step on the way to the target dienediyne ketone **33** (72%). The low-field ^{1}H-NMR signals of this compound in C_6D_6 resemble the corresponding res-

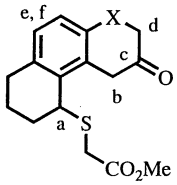
Table 1. Select 300 MHz ^{1}H NMR (**4a**[19b] in $CDCl_3$, **33** in C_6D_6, **37**[19b] and **38**[19b] in $CDCl_3$), 500 MHz ^{1}H NMR (**32**, **35** in C_6D_6), and 126 MHz ^{13}C-NMR data (**35** in C_6D_6, **38**[19b] in $CDCl_3$) of key compounds of the present and an earlier study



	X	$\delta_{a\text{-}H}$	$\delta_{b\text{-}H}$	$\delta_{c\text{-}H}$
32	CMe_2	6.12	4.54	5.26
37	CH_2	6.23	4.63	5.23



	X	$\delta_{a\text{-}H}$	$\delta_{b\text{-}H_2}$	$\delta_{c\text{-}H}$
33	CMe_2	6.05	2.42	5.21
4a	CH_2	6.57	2.67	5.31



	X	$\delta_{a\text{-}H}$	$\delta_{b\text{-}H_2}$	$\delta_{d\text{-}H_2}$	$\delta_{e,f\text{-}H}$	$\delta_{C\text{-}a}$	$\delta_{C\text{-}c}$	$\delta_{C\text{-}e,C\text{-}f}$
35	CMe_2	4.02	3.44 / 4.43	2.22	6.81 / 7.03	42.34	207.60	123.85 / 128.01
38	CH_2	4.18	3.50 / 4.00	2.56	6.95 / 7.05	41.80	210.75	127.08 / 127.81

onances of the des-dimethyl analog **4a**[19b] in $CDCl_3$ (Table 1; top, right) closely enough to underline the structural similarity.

Dienediyne ketone **33** was the wanted type-**4** ketone. As desired, it was amenable to a Saito-Myers cyclization (Scheme 6): When we treated it *at room temperature* in CH_2Cl_2 solution with methyl thioglycolate, 1,4-cyclohexadiene, and triethylamine it disappeared completely in the course of 14 h. We then isolated 16% of the octahydrophenanthrone **35** as inferred from the ^{1}H- and ^{13}C-NMR data. In particular they resemble closely the corresponding data of the analogous octahydrophenanthrone **38**[19b] (Table 1; bottom). The reaction cascade leading to product **35** entails a 1,6-addition of methyl thioglycolate to dienediyne ketone **33** leading to the enyneallenyl ketone **34** (Scheme 6). This species cycloaromatizes by the Saito-Myers mode to the toluene-α,*meta*-biradical **36**. The latter saturates the two valence electron septets by the uptake of one H atom at each of them. These H atoms could stem from excess methyl thioglycolate and/or from the 20 equivalents of 1,4-cyclohexadiene added to the reaction mixture from the beginning.

Our investigations demonstrate that a McMurry route to dienediyne models of the neocarzinostatin chromophore **1** is in principle possible. Importantly, the possibility of extending this route to the synthesis of *dienediynes whose 6-membered rings are similarly oxygenated as the 5-membered ring of* **1** is more obvious than a possibility of extending our bistriflate-based dienediyne strategy to the same targets.[18][19b][21][38] This possibility caused our interest in developing the chemistry of Schemes 4−6 and lets us pursue this strategy in ongoing work. With respect to the *step requirement*, however, our bistriflate strategy is superior; this is especially true in view of our findings of ref.[18].

We thank the *Fonds der Chemischen Industrie* for making this study possible through a doctoral fellowship for E. R. The *Sonderforschungsbereich 416* of the *Deutsche Forschungsgemeinschaft* supported part of this project and the *BASF AG* (Ludwigshafen) donated chemicals for which we are very grateful. We are indebted to *Dr. R. S. Matthews* (*Procter & Gamble*, Cincinnati; cf. ref.[24b]) and to *Dr. J. Suffert* (*CNRS*, Strasbourg; cf. ref.[32]) for providing unpublished experimental procedures.

Experimental Section

All reactions were performed in oven-dried (80°C) glassware under N_2. THF was freshly distilled from K, CH_2Cl_2 from CaH_2. Products were purified by flash chromatography[35] on Merck silica gel 60 (eluents given in brackets). Yields refer to analytically pure samples. − ^{1}H [$CHCl_3$ (7.26 ppm) as internal standard in $CDCl_3$ or C_6HD_5 (7.16 ppm) as internal standard in C_6D_6] and ^{13}C NMR [$CDCl_3$ (77.00 ppm) as internal standard in $CDCl_3$ or C_6D_6 (128.00 ppm) as internal standard in C_6D_6]: Varian VXR 200, Bruker AMX 300 and Varian VXR 500S; integrals in accord with assignments; coupling constants in Hz; APT ^{13}C NMR spectra: peak orientations in accord with assignments. The assignments of ^{1}H- and ^{13}C-NMR resonances refer to the IUPAC nomenclature; primed numbers belong to side-chain(s in the order of their appearance IUPAC in the name). Combustion analyses: F. Hambloch, Institute of Organic Chemistry, University of Göttingen. − MS: G. Remberg, Institute of Organic Chemistry, University of Göttingen. − IR spectra: Perkin-Elmer 1600 Series FTIR as $CDCl_3$ or C_6D_6 solution in a NaCl cuvette or as film.

2-[3-(tert-Butyldimethylsiloxy)-5,5-dimethyl-8-oxo-1,6-octadiynyl]-2-cyclohexen-1-one (**8**): A mixture of the alkyne **30** (350 mg, 1.26 mmol, 1.2 equiv.), 2-iodo-2-cyclohexen-1-one (215 mg, 0.967 mmol), $Pd(PPh_3)_2Cl_2$ (33.9 mg, 0.0484 mmol, 0.05 equiv.), and CuI (27.6 mg, 0.145 mmol, 0.15 equiv.) in benzene (10 ml) was cooled to 0°C. NEt_3 (3 ml) was added and the mixture was stirred for 3 h. It was diluted with *tert*-butyl methyl ether and hydrolyzed with H_2O (5 ml, each). The aqueous layer was extracted with *tert*-butyl methyl ether (2 × 10 ml). The combined organic layers were dried with Na_2SO_4. The solvent was removed in vacuo. Flash chromatography (petroleum ether/*tert*-butyl methyl ether, 5:1 → 1:4) of the residue afforded the title compound (462 mg, 98%) as a yellow oil. − ^{1}H NMR (300 MHz): δ = 0.16 and 0.19 [2 s, Si(*t*Bu)(CH_3)$_2$], 0.91 (s, *t*Bu), 1.35 and 1.37 [2 s, 5′-(CH_3)$_2$], 1.95−2.07 (m, 5-H_2, 4′-H_2), 2.41−2.51 (m, 4-H_2, 6-H_2), 4.81 (t, $J_{3',4'}$ = 6.3, 3′-H), 7.21

(t, $J_{3,4}$ = 4.4, 3-H), 9.19 (s, 8′-H). − APT ^{13}C NMR (50.3 MHz): δ = -4.85 and -4.21 [Si(*t*Bu)(*C*H$_3$)$_2$], 18.11, 22.34 and 26.37 [C-5, C-4′, *C*(CH$_3$)$_3$], 25.82 [C(*C*H$_3$)$_3$], 29.08 and 29.10 [5′-(CH$_3$)$_2$], 30.78, 38.04 and 49.84 (C-4, C-6, C-5′), 61.33 (C-3′), 79.56, 81.97, 93.64 and 104.69 (C-1′, C-2′, C-6′, C-7′), 124.84 (C-2), 154.01 (C-3), 177.16 (C-8′), ″-″195.37 (C-1). − IR (film): ṽ = 2955, 2930, 2855, 2255, 2205, 1685, 1665, 1470, 1385, 1360, 1350, 1255, 1095, 1060, 920, 885, 840, 755, 735, 710, 650 cm^{-1}. − $C_{22}H_{32}O_3Si$ [M$^+$]: calcd. 372.2121; exact molecular mass (±2 ppm; *R* = ca. 10000) checked by EI HRMS (70 eV).

2-[3-(tert-Butyldimethylsiloxy)-6,6-dimethyl-9-oxo-1,7-nonadiynyl]-2-cyclohexen-1-one (**9**) was prepared in a similar manner as **8** from **31** (230 mg, 0.786 mmol) and isolated as a yellow oil (199 mg, 85%). − ^{1}H NMR (300 MHz; triplet impurities at δ = 2.75 and 4.45): δ = 0.12 and 0.15 [2 s, Si(*t*Bu)(C*H*$_3$)$_2$], 0.90 (s, *t*Bu), 1.28 [s, 6′-(CH$_3$)$_2$], 1.55−1.77, 1.78−1.90 and 1.95−2.09 (3 m à 2 H, 5-H$_2$, 4′-H$_2$, 5′-H$_2$), 2.41−2.51 (m, 4-H$_2$, 6-H$_2$), 4.55 (t, $J_{3',4'}$ = 6.1, 3′-H), 7.23 (t, $J_{3,4}$ = 4.4, 3-H), 9.18 (s, 9′-H). − APT ^{13}C NMR (50.3 MHz; contains impuritie(s)]: δ = -5.04 and -4.41 [Si(*t*-Bu)(*C*H$_3$)$_2$], 18.24, 22.36 and 26.36 [C-5, C-5′, *C*(CH$_3$)$_3$], 25.81 [C(*C*H$_3$)$_3$], 28.13 and 28.24 [6′-(CH$_3$)$_2$], 31.39, 34.39, 37.73, 38.06 (C-4, C-6, C-4′, C-6′), 63.11 (C-3′), 78.95, 81.47, 93.25 and 105.25 (C-1′, C-2′, C-7′, C-8′), 124.89 (C-2), 153.98 (C-3), 177.36 (C-9′), ″-″195.44 (C-1). − IR (CDCl$_3$): ṽ = 2955, 2930, 2855, 2255, 1685, 1470, 1460, 1385, 1360, 1255, 1190, 1050, 1120, 1090, 1005, 975, 925, 900, 840 cm^{-1}. − $C_{19}H_{25}O_3Si$ [M$^+$-C(CH$_3$)$_3$]: calcd. 329.1573; exact fragment mass (±2 ppm; *R* = ca. 10000) checked by EI HRMS (70 eV).

4-(tert-Butyldimethylsiloxy)-6,6-dimethylbicyclo[8.4.0]tetradeca-1$^{(14)}$,9-diene-2,7-diyne (**11**): $Cl_3Ti(DME)_2$ was prepared by refluxing $TiCl_3$ (1.39 g, 9.01 mmol, 43 equiv.) in freshly distilled DME (30 ml) for 1.5 d. Zn/Cu couple (2.20 g, 33.8 mmol, 160 equiv.) was added and the resulting mixture was refluxed for 3 h. Ketoaldehyde **8** (78.6 mg, 0.211 mmol) in DME (24 ml) was added at room temp. by means of a syringe pump over a period of 14 h. After 1 h, the reaction mixture was diluted with diethyl ether (20 ml) and hydrolyzed by adding a saturated aqueous solution of $NaHCO_3$ (10 ml). The solid was filtered and the aqueous layer was extracted with diethyl ether (1 × 20 ml). The combined organic layers were washed with ice-water (10 × 30 ml) and dried with $MgSO_4$. The solvent was removed in vacuo. Flash chromatography (pentane) of the residue on deactivated silica gel (pretreated with 25% aq. NH_3) afforded the title compound (29.2 mg, 41%) as colorless oil. − ^{1}H NMR (300 MHz): δ = 0.13 and 0.15 [2 s, Si(*t*-Bu)(C*H*$_3$)$_2$], 0.90 (s, *t*Bu), 1.22 and 1.23 [2 s, 6-(CH$_3$)$_2$], AB signal (δ_A = 1.66, δ_B = 1.91, J_{AB} = 13.0, in addition split by $J_{A,4}$ = 3.8, $J_{B,4}$ = 10.6, 5-H$_2$), A part partly superimposed by 1.66−1.72 (m, 12-H$_2$), 2.21 (br. td, $J_{13,12}$ = $J_{13,14}$ = 5.6, 13-H$_2$), 2.32 (ddd, $J_{11,12\text{-}H(1)} \approx$ 7.5, $J_{11,12\text{-}H(2)} \approx$ 4.5, $^4J_{11,9}$ = 1.4, 11-H$_2$), 4.65 (dd, $J_{4,5\text{-}H(B)}$ = 10.4, $J_{4,5\text{-}H(A)}$ = 3.8, 4-H), 5.23 (poorly resolved d, $^5J_{9,14}$ = 0.9 , 9-H), 6.19 (td, $J_{14,13}$ = 4.5, $^5J_{14,9}$ = 1.1, 14-H). − ^{1}H NMR (300 MHz, C_6D_6; contains residual diethyl ether and pentane): δ = 0.22 and 0.31 [2 s, Si(*t*Bu)(C*H*$_3$)$_2$], 1.04 (s, *t*Bu), 1.14 and 1.17 [2 s, 6-(CH$_3$)$_2$], 1.20−1.28 (m, 12-H$_2$), 1.64−1.72 (m, 5-H^1, 13-H$_2$), 1.88−1.96 (m, 11-H$_2$), 2.09 (dd, J_{gem} = 12.8, $J_{5\text{-}H(2),4}$ = 10.1, 5-H^2, 4.83 (dd, $J_{4,5\text{-}H(2)}$ = 10.4, $J_{4,5\text{-}H(1)}$ = 4.0, 4-H), 5.27 (br. s, 9-H), 6.07 (m$_c$, presumable poorly resolved td, $J_{14,13}$ = 4.0, $^5J_{14,9}$ = 1.1, 14-H). − APT ^{13}C NMR: δ = −4.71 and -4.25 [Si(*t*-Bu)(*C*H$_3$)$_2$], 18.17, 22.04 and 26.24 [C-5, C-12, *C*(CH$_3$)$_3$], 25.83 [C(*C*H$_3$)$_3$], 27.57 and 30.82 [6-(CH$_3$)$_2$], 30.20, 33.08 and 48.77 (C-6, C-11, C-13), 61.20 (C-4), 81.39, 85.56, 92.02 and 102.32 (C-2, C-3, C-7 and C-8), 105.75 (C-9), 120.94 (C-1), 138.76 (C-14), 143.80 (C-10). − IR (film): ṽ = 3235, 2955, 2930, 2255, 2275, 2265, 2260, 1620, 1455, 1390, 1330, 1255, 1165, 1070, 835, 815, 800, 780 cm^{-1}. − $C_{22}H_{32}OSi$ [M$^+$]: calcd. 340.2222; exact molecular mass (±2 ppm; *R* = ca. 10000) checked by EI HRMS (70 eV).

4-(tert-Butyldimethylsiloxy)-7,7-dimethylbicyclo[9.4.0]pentadeca-1$^{(15)}$,9-diene-2,8-diyne (**12**) was prepared in a similar manner as **11** from **9** (75.6 mg, 0.196 mmol) and isolated as a colorless oil (12.7 mg, 18%). − ^{1}H NMR (300 MHz; impurity singlet at δ = 0.07*): δ = 0.11* and 0.14* [2 s, Si(*t*Bu)(C*H*$_3$)$_2$], 0.90 (s, *t*Bu), 1.16 and 1.19 [2 s, 7-(CH$_3$)$_2$], 1.68−1.73, 1.75−1.83 and 1.97−2.05 (3 m presumably à 3 H, 2 H, and 1 H, 5-H$_2$, 6-H$_2$, 13-H$_2$), 2.24 (td, $J_{14,13}$ = $J_{14,15}$ = 5.0, 14-H$_2$), 2.29 (ddd, $J_{12,13\text{-}H(1)} \approx$ 7.5, $J_{12,13\text{-}H(2)}$ = 4.2, $^4J_{12,10}$ = 1.5, 14-H$_2$), 4.51 (poorly resolved dd, $J_{4,5\text{-}H(1)}$ = 8.5, $J_{4,5\text{-}H(2)}$ = 1.6, 4-H), 5.33 (poorly resolved d, $^5J_{10,15}$ = 1.3 , 10-H), 6.26 (td, $J_{15,14}$ = 4.5, $^5J_{15,10}$ = 1.5, 15-H); *assignment interchangeable. − ^{1}H NMR (300 MHz, C_6D_6): δ = 0.22 and 0.30 [2 s, Si(*t*Bu)(C*H*$_3$)$_2$], 1.05 (s, *t*Bu), 1.145 and 1.153 [2 s, 7-(CH$_3$)$_2$], 1.20−1.31 (m, 13-H$_2$), 1.44−1.55 (m, 6-H$_2$), 1.73 (td, $J_{14,13}$ = $J_{14,15}$ = 5.6, 14-H$_2$), 1.81−1.95 (m, 12-H$_2$, 5-H^1), 2.05−2.18 (m, 5-H^2], 4.62 (poorly resolved dd, $J_{4,5\text{-}H(1)}$* = 8.3, $J_{4,5\text{-}H(2)}$* = 1.6, 4-H), 5.41 (poorly resolved d, $^5J_{10,15}$ = 0.8, 10-H), 6.19 (td, $J_{15,14}$ = 4.4, $^5J_{15,10}$ = 1.4, 15-H); *assignment interchangeable. − APT ^{13}C NMR (50.3 MHz): δ = −4.71 and −4.25 [Si(*t*-Bu)(*C*H$_3$)$_2$], 18.21, 22.23, 26.69, 29.66, 32.86, 32.94, 34.07 and 37.28 [C-5, C-6, C-7, C-12, C-13, C-14, *C*(CH$_3$)$_3$, and one impurity signal], 25.82 [C(*C*H$_3$)$_3$], 28.59 and 28.68 [7-(CH$_3$)$_2$], 64.20 (C-4), 77.93, 82.46, 91.77 and 103.88 (C-2, C-3, C-8 and C-9), 106.01 (C-10), 120.84 (C-1), 140.96 (C-15) and 142.74 (C-1). − IR (film): ṽ = 3235, 2930, 2860, 2390, 2370, 2350, 2285, 2275, 1620, 1455, 1390, 1330, 1260, 1165, 1100, 1015, 815, 805, 670 cm^{-1}. − $C_{23}H_{34}OSi$ [M$^+$]: calcd. 354.2379; exact molecular mass (±2 ppm; *R* = ca. 10000) checked by EI HRMS (70 eV).

3-Bromo-3-methyl-1-butyne (**14**): PBr_3 (5.70 ml, 16.3 g, 60.0 mmol, 0.4 equiv.) was added at 15°C to the alcohol **13** (14.5 ml, 12.6 g, 150 mmol). The solution was stirred for 0.5 h at room temp. Distillation of the reaction mixture (b.p. 30°C/80 mbar) afforded the title compound (13.2 g, 60%) as a colorless liquid.

2-(1,1-Dimethyl-2-propynyl)diethyl malonate (**15**): Diethyl malonate (39.3 ml, 41.4 g, 259 mmol, 1.06 equiv) was added to a solution of Na (5.95 g, 259 mmol, 1.06 equiv.) in EtOH (300 ml). After 30 min, bromide **14** (35.9 g, 244 mmol) was added. The reaction mixture was heated for 4 h at 60°C. The resulting suspension was poured into ice-water (300 ml). After extraction with *tert*-butyl methyl ether (4 × 100 ml) the combined organic layers were dried with Na_2SO_4. The solvent was removed in vacuo. Distillation (b.p. 120°C/12 mbar) of the residue afforded the title compound (21.4 g, 39%) as a colorless liquid. − ^{1}H NMR (300 MHz): δ = 1.28 (t, $J_{2'',1''}$ = 7.0, 2 × 2′′-H$_3$), 1.47 (s, 2 × 1′-CH$_3$), 2.20 (s, 3′-H), 3.45 (s, 1-H), 4.22 (q, $J_{1'',2''}$ = 7.0, 2 × 1′′-H$_2$). − IR (film): ṽ = 3285, 2980, 2940, 2905, 2875, 1755, 1735, 1465, 1445, 1390, 1340, 1320, 1235, 1200, 1180, 1150, 1120, 1095, 1040, 860 cm^{-1}. − $C_{12}H_{18}O_4$ (226.3): calcd. C 63.70, H 8.02; found C 63.62, H 8.05.

Ethyl 3,3-Dimethyl-4-pentynoate (**16**): NaCl (5.52 g, 94.5 mmol, 1.0 equiv.) and H_2O (2.55 ml, 2.55 g, 141 mmol, 1.5 equiv.) were added to the malonate **15** (21.4 g, 94.5 mmol) in DMSO (185 ml). The resulting suspension was heated at 180°C for 19 h and then poured into ice-water (300 ml). The aqueous layer was washed with pentane (4 × 100 ml). The combined organic layers were dried with Na_2SO_4 and the solvent was removed in vacuo. Distillation (b.p. 65°C/12 mbar) of the residue afforded the title compound (11.9 g, 82%) as a colorless liquid. − ^{1}H NMR (300 MHz): δ = 1.27 (t, $J_{2',1'}$ = 7.2, 2′-H$_3$), 1.36 [s, 3-(CH$_3$)$_2$], 2.16 (s, 5-H), 2.45 (s, 2-H$_2$), 4.16 (q, $J_{1',2'}$ = 7.1, 1′-H$_2$). − IR (film): ṽ = 3295, 2975, 2935,

2875, 1735, 1465, 1450, 1340, 1370, 1330, 1300, 1225, 1195, 1160, 1120, 1100, 1035 cm^{-1}. – $C_9H_{14}O_2$ (154.2): calcd. C 70.10, H 9.15; found C 70.30, H 9.26.

3,3-Dimethyl-4-pentyn-1-ol (**17**): Ester **16** (4.50 g, 29.2 mmol) was slowly added at 0°C to a suspension of $LiAlH_4$ (886 mg, 23.3 mmol, 0.8 equiv.) in diethyl ether (30 ml). The mixture was refluxed for 1 h and then stirred for 10 h at room temp. Ice-cold HCl (2 M, 50 ml) was added and the aqueous layer was extracted with *tert*-butyl methyl ether (3 × 30 ml). The combined organic layers were dried with Na_2SO_4. The solvent was removed in vacuo. Flash chromatography of the residue (petroleum ether/*tert*-butyl methyl ether, 4:1 → 1:2) afforded the title compound (3.11 g, 95%). – ^{1}H NMR (300 MHz): δ = 1.26 [s, 3-$(CH_3)_2$], 1.73 (t, $J_{2,1}$ = 6.8, 2-H_2), 1.78 (br. s., OH), 2.17 (s, 5-H), 3.87 (t, $J_{1,2}$ = 6.6, 1-H_2). – IR (film): $\tilde{\nu}$ = 3300, 2970, 2940, 2870, 2110, 1470, 1455, 1485, 1365, 1250, 1205, 1170, 1145, 1060, 1030, 990, 635 cm^{-1}. – $C_7H_{12}O$ (112.17): calcd. C 74.95, H 10.8; found C 75.32, H 11.0.

3,3-Dimethyl-4-pentyn-1-al (**18**): At −78°C DMSO (10.3 ml, 11.3 g, 145 mmol, 2.2 equiv.) was slowly added to oxalyl chloride (6.95 ml, 9.22 g, 72.6 mmol, 1.1 equiv.) in CH_2Cl_2 (300 ml). After 3 min, alcohol **17** (7.40 g, 66.0 mmol) was added and after 30 min, NEt_3 (46.0 ml, 33.4 g, 330 mmol, 5.0 equiv.), all at −78°C. After another 30 min, the reaction mixture was hydrolyzed with H_2O (300 ml). The aqueous layer was extracted with *tert*-butyl methyl ether (3 × 100 ml). The combined organic layers were washed with HCl (2 M), a saturated aqueous solution of Na_2CO_3, and H_2O (100 ml, each) and dried with Na_2SO_4. After removal of the solvent distillation of the residue (b.p. 32°C/12 mbar) afforded the title compound (5.31 g, 73%) as a colorless liquid. – ^{1}H NMR (300 MHz): δ = 1.34 [s, 3-$(CH_3)_2$], 2.26 (s, 5-H), 2.43 (d, $J_{2,1}$ = 3.0, 2-H_2), 9.91 (t, $J_{1,2}$ = 3.0, 1-H). – IR (film): $\tilde{\nu}$ = 3290, 2975, 2935, 2875, 2830, 2740, 1725, 1470, 1410, 1390, 1365, 1295, 1270, 1205, 1175, 1150, 1050, 645 cm^{-1}. – $C_7H_{10}O$ (110.2): calcd. C 76.33, H 9.15; found C 76.16, H 9.38.

(3,3-Dimethyl-4-pentynyl)methansulfonate (**19**): At 0°C MsCl (4.42 ml, 6.51 g, 56.9 mmol, 1.1 equiv.) and NEt_3 (8.65 ml, 6.28 g, 62.0 mmol, 1.2 equiv.) were added to alcohol **17** (5.80 g, 51.7 mmol) in CH_2Cl_2 (100 ml). After 30 min, the reaction mixture was hydrolyzed with HCl (2 M, 100 ml). The aqueous layer was extracted with *tert*-butyl methyl ether (2 × 50 ml). Drying of the organic layers with Na_2SO_4 and removal of the solvent gave the title compound (9.56 g, 97%) as a colorless liquid. – ^{1}H NMR (300 MHz): δ = 1.28 [s, 3′-$(CH_3)_2$], 1.89 (t, $J_{2',1'}$ = 7.4, 2′-H_2), 2.16 (s, 5′-H), 3.02 (s, SO_2Me), 4.44 (t, $J_{1',2'}$ = 7.4, 1′-H_2). – IR (film): $\tilde{\nu}$ = 3285, 3030, 2975, 2940, 2875, 1470, 1415, 1385, 1355, 1175, 1075, 1005, 960, 890, 840, 800, 650 cm^{-1}. – $C_8H_{14}O_3S$ (190.3): calcd. C 50.50, H 7.42; found C 49.70, H 7.38.

4,4-Dimethyl-5-hexyne-1-nitrile (**20**): NaCN (4.90 g, 101 mmol, 2.0 equiv.) was added to the sulfonate **19** (9.56 g. 50.2 mmol) in DMSO (100 ml). The reaction mixture was heated for 30 min at 90°C and then stirred for 12 h at room temp. It was diluted with *tert*-butyl methyl ether and hydrolyzed with H_2O (50 ml, each). The aqueous layer was extracted with *tert*-butyl methyl ether (3 × 30 ml). The combined organic layers were dried with Na_2SO_4. The solvent was removed in vacuo. Distillation (b.p. 68°C/12 mbar) of the residue afforded the title compound (5.30 g, 87%). – ^{1}H NMR (300 MHz): δ = 1.26 [s, 4-$(CH_3)_2$], 1.80 (m_c, 3-H_2), 2.52 (m_c, 2-H_2).

4,4-Dimethyl-5-hexyn-1-al (**21**): At -78°C DIBAL in toluene (1.05 M, 44.0 ml, 46.2 mmol, 1.4 equiv.) was added to the nitrile **20** (4.00 g, 33.0 mmol) in toluene (40 ml). After stirring for 2 h, no starting material could be detected by gas chromatography. The reaction mixture was hydrolyzed with HCl (2 M, 30 ml) and the solution stirred for 10 min at room temp. The aqueous layer was washed with *tert*-butyl methyl ether (3 × 25 ml). The combined organic layers were dried with Na_2SO_4 and concentrated in vacuo, but the title compound was not isolated.

5,5-Dimethyl-1-(trimethylsilyl)-1,6-heptadiyn-3-ol (**22**): At −78°C *n*-BuLi (2.35 M in hexane, 23.6 ml, 55.4 mmol 1.15 equiv.) was added dropwise to (trimethylsilyl)acetylene (8.00 ml, 5.68 g, 57.8 mmol, 1.2 equiv.). After stirring at −78°C for 30 min, aldehyde **18** (5.31 g, 48.2 mmol) in THF (80 ml) was added. After stirring 1.5 h at room temp., the reaction mixture was hydrolyzed with aqueous saturated solution of NH_4Cl (100 ml). The aquoues layer was extracted with *tert*-butyl methyl ether (3 × 30 ml). The combined organic layers were dried with Na_2SO_4 and the solvent was removed in vacuo. Distillation (b.p. 108°C/12 mbar) of the residue afforded the title compound (6.91 g, 69%) as a colorless liquid. – ^{1}H NMR (300 MHz): δ = 0.16 [s, $Si(CH_3)_3$], 1.29 and 1.30 [2 s, 5-$(CH_3)_2$], AB signal (δ_A = 1.83, δ_B = 1.93, J_{AB} = 14.2, in addition split by $J_{A,3}$ = 4.4, $J_{B,3}$ = 7.9, 4-H_2), 2.20 (s, 7-H), 2.39 (br. s, OH), 4.70 (dd, $J_{3,4\text{-H(B)}}$ = 8.1, $J_{3,4\text{-H(A)}}$ = 4.3, 3-H). – IR (film): $\tilde{\nu}$ = 3310, 2965, 2900, 2870, 2170, 1470, 1455, 1410, 1385, 1365, 1345, 1315, 1250, 1205, 1140, 1065, 1040, 1010, 990, 915, 845, 760, 700, 635 cm^{-1}. – $C_{12}H_{20}OSi$ (208.4): calcd. C 69.17, H 9.67; found C 69.11, H 9.63.

6,6-Dimethyl-1-(trimethylsilyl)-1,7-octadiyn-3-ol (**23**): At −78°C *n*-BuLi (1.18 M in hexane, 32.2 ml, 38.0 mmol 1.15 equiv. with respect to the nitrile **20** in the preparation of the aldehyde **21**) was added to (trimethylsilyl)acetylene (5.49 ml, 3.89 g, 39.6 mmol, 1.2 equiv. with respect to the nitrile **20** in the preparation of the aldehyde **21**) in THF (30 ml). After stirrring at −78°C for 30 min, the solution of the aldehyde **21** in toluene (ca. 80 ml) was added. After stirring 1.5 h at room temp., the reaction mixture was hydrolyzed with saturated aqueous solution of NH_4Cl (75 ml). The aqueous layer was washed with *tert*-butyl methyl ether (3 × 30 ml). The combined organic layers were dried with Na_2SO_4. The solvent was removed in vacuo. Flash chromatography (MTB/PE, 100:1 → 1:1) of the residue afforded the title compound (2.42 g, 33% over 2 steps) as a colorless liquid. – ^{1}H NMR (300 MHz): δ = 0.17 [s, $Si(CH_3)_3$], 1.23 [s, 6-$(CH_3)_2$], 1.49−1.66 (m, 5-H_2), 1.80−1.92 (m, 4-H_2, OH), 2.09 (s, 8-H), 4.37 (td, $J_{3,4}$ = $J_{3,OH}$ = 6.1, 3-H). – IR (film): $\tilde{\nu}$ = 3310, 2965, 2900, 2870, 2170, 1470, 1455, 1410, 1385, 1365, 1250, 1055, 1020, 845, 760, 700, 630 cm^{-1}. – $C_{13}H_{22}OSi$ (222.4): calcd. C 70.21, H 9.97; found C 70.01, H 9.86.

6-(tert-Butyldimethylsiloxy)-4,4-dimethyl-8-(trimethylsilyl)-2,7-octadiyn-1-ol (**24**) was prepared in a similar manner as **25** from **26** (7.32 g, 22.7 mmol) and isolated as a colorless oil (7.02 g, 88%). – ^{1}H NMR (300 MHz): δ = 0.14 and 0.17 [2 s, $Si(tBu)(CH_3)_2$], 0.15 [s, $Si(CH_3)_3$], 0.91 (s, *t*Bu), 1.25 and 1.27 [2 s, 4-$(CH_3)_2$], 1.56 (br. s*, presumably OH), 1.84 (d, $J_{5,6}$ = 6.0, 5-H_2), 4.25 (d, $J_{1,OH}$ = 6.1,1-H_2), 4.67 (t, $J_{6,5}$ = 6.3, 6-H); *since 1-H_2 is a dublet the OH resonance ought to be a triplet ($J_{OH,1}$ = 6.1) so that this assignment is not safe. – IR (film): $\tilde{\nu}$ = 3335, 2960, 2930, 2900, 2855, 2170, 1470, 1360, 1350, 1250, 1145, 1095, 1060, 1005, 840, 780, 760 cm^{-1}. – $C_{19}H_{36}O_2Si_2$ (352.7): calcd. C 64.71, H 10.29; found C 64.51, H 10.09.

7-(tert-Butyldimethylsiloxy)-4,4-dimethyl-9-(trimethylsilyl)-2,8-nonadiyn-1-ol (**25**): At −78°C *n*-BuLi (1.18 M in hexane, 6.58 ml, 7.77 mmol, 1.2 equiv.) was added to the alkyne **27** (2.18 g, 6.48 mmol) in THF (25). After stirring for 0.5 h at −78°C, paraformaldehyde (583 mg, 19.4 mmol. 3.0 equiv.) was added. After 3.5 h of stirring at room temp., the reaction mixture was diluted with *tert*-butyl methyl ether (10 ml) and hydrolyzed with saturated aqueous solution of NH_4Cl (25 ml). The aqueous layer was extracted with

tert-butyl methyl ether (2 × 15 ml). The combined organic layers were dried with Na_2SO_4. The solvent was removed in vacuo. Flash chromatography (petroleum ether → petroleum ether/*tert*-butyl methyl ether, 1:1) of the residue afforded the title compound (2.16 g, 91%) as a colorless liquid. − ^{1}H NMR (300 MHz): δ = 0.10 and 0.12 [2 s, Si(*t*Bu)(CH_3)$_2$], 0.15 [s, Si(CH_3)$_3$], 0.89 (s, *t*Bu), 1.18 [s, 4-(CH_3)$_2$], 1.36−1.61 and 1.68−1.83 (2 m à 2 and 3 H, 5-H$_2$, 6-H$_2$, OH), 4.23 (d, $J_{1,OH}$ = 5.7,1-H$_2$), 4.32 (t, $J_{7,6}$ = 6.2, 7-H). − IR (film): ṽ = 3355, 2960, 2930, 2855, 2170, 1470, 1465, 1410, 1385, 1360, 1340, 1250, 1205, 1145, 1095, 1005, 965, 940, 905, 840, 780, 760, 700, 650 cm^{-1}. − $C_{20}H_{38}O_2Si_2$ (366.7): calcd. C 65.51, H 10.45; found C 65.81, H 10.65.

3-(tert-Butyldimethylsiloxy)-5,5-dimethyl-1-(trimethylsilyl)-1,6-heptadiyne (**26**): Imidazole (6.70 g, 98.4 mmol, 3.0 equiv.) and *tert*-butyldimethylsilyl chloride (50% solution in toluene, 17.0 ml, 14.8 g of the solution, 7.4 g of the chloride, 49.2 mmol, 1.5 equiv.) were added to the alcohol **22** (6.83 g, 32.8 mmol) in CH_2Cl_2 (150 ml). After 16 h, the reaction mixture was hydrolyzed with H_2O (150 ml). The aqueous layer was extracted with *tert*-butyl methyl ether (2 × 50 ml). The combined organic layers were dried with Na_2SO_4. The solvent was removed in vacuo. Flash chromatography (petroleum ether → petroleum ether/*tert*-butyl methyl ether, 10:1 → 1:1) of the residue afforded the title compound (10.5 g, 99%) as a colorless oil. − ^{1}H NMR (300 MHz): δ = 0.14 and 0.17 [2 s, Si(*t*Bu)(CH_3)$_2$], 0.15 [s, Si(CH_3)$_3$], 0.91 (s, *t*Bu), 1.27 and 1.28 [2 s, 5-(CH_3)$_2$], 1.85 (d, $J_{4,3}$ = 6.4, 4-H$_2$), 2.13 (s, 7-H), 4.71 (t, $J_{3,4}$ = 6.2, 3-H). − IR (film): ṽ = 3310, 2960, 2930, 2900, 2860, 2170, 1470, 1360, 1345, 1250, 1150, 1095, 1050, 1020, 1005, 940, 840, 780, 760, 700, 635 cm^{-1}. − $C_{18}H_{34}OSi_2$ (322.6): calcd. C 67.01, H 10.62; found C 66.87, H 10.41.

3-(tert-Butyldimethylsiloxy)-6,6-dimethyl-1-(trimethylsilyl)-1,7-octadiyne (**27**) was prepared in a similar manner as **26** from **23** (2.30 g, 10.3 mmol) and isolated as a colorless oil (3.23 g, 93%). − ^{1}H NMR (300 MHz): δ = 0.11 and 0.13 [2 s, Si(*t*Bu)(CH_3)$_2$], 0.16 [s, Si(CH_3)$_3$], 0.90 (s, *t*Bu), 1.21 [s, 6-(CH_3)$_2$], 1.41−1.63 (m, 5-H$_2$), 1.73−1.88 (m, 4-H$_2$), 2.08 (s, 8-H), 4.34 (t, $J_{3,4}$ = 6.2, 3-H). − IR (film): ṽ = 3310, 2965, 2930, 2900, 2860, 2175, 2110, 1470, 1410, 1385, 1360, 1335, 1250, 1095, 1020, 965, 940, 895, 840, 780, 700, 630 cm^{-1}. − $C_{19}H_{36}OSi_2$ (336.7): calcd. C 67.78, H 10.78; found C 68.06, H 10.91.

6-(tert-Butyldimethylsiloxy)-4,4-dimethyl-2,7-octadiyn-1-ol (**28**) was prepared in a similar manner as **29** from **24** (11.1 g, 31.5 mmol) and isolated as a colorless liquid (7.42 g, 84%). − ^{1}H NMR (300 MHz): δ = 0.15 and 0.17 [2 s, Si(*t*Bu)(CH_3)$_2$], 0.91 (s, *t*Bu), 1.26 and 1.27 [2 s, 4-(CH_3)$_2$], 1.47 (t, $J_{OH,1}$ = 6.1, OH), extreme AB signal (δ_A = 1.85, δ_B = 1.88, J_{AB} = 13.9, in addition split by $J_{A,6}$ = 5.7, $J_{B,6}$ = 6.6, 5-H$_2$), 2.42 (d, $^4J_{8,6}$ = 2.2, 8-H), 4.25 (d, $J_{1,\ OH}$ = 6.1, 1-H$_2$), 4.67 (dd, $J_{6,5\text{-H(A)}} = J_{6,5\text{-H(B)}}$ 6.3, $^4J_{6,8}$ = 1.9, 6-H). − IR (film): ṽ = 3310, 2960, 2930, 2860, 1470, 1390, 1360, 1275, 1255, 1210, 1180, 1145, 1095, 1060, 1005, 920, 840, 780, 655, 630 cm^{-1}. − $C_{16}H_{28}O_2Si$ (280.5): calcd. C 68.52, H 10.06; found C 68.40, H 10.25.

7-(tert-Butyldimethylsiloxy)-4,4-dimethyl-2,8-nonadiyn-1-ol (**29**): K_2CO_3 (595 mg, 4.31 mmol. 1.0 equiv.) was added to the silyl alkyne **25** (1.58 g, 4.31 mmol) in MeOH (10 ml) and the resulting suspension stirred for 14 h. One hydrolyzed with H_2O (10 ml). The aqueous layer was extracted with *tert*-butyl methyl ether (2 × 10 ml). The combined organic layers were dried with Na_2SO_4. The solvent was removed in vacuo. Flash chromatography (petroleum ether/*tert*-butyl methyl ether, 100:1 → 1:1) of the residue afforded the title compound (1.08 g, 85%) als a colorless oil. − ^{1}H NMR (300 MHz): δ = 0.11 and 0.14 [2 s, Si(*t*Bu)(CH_3)$_2$], 0.90 (s, *t*Bu), 1.20 [s, 4-(CH_3)$_2$], 1.40−1.63 and 1.77−1.87 (2m à 3 H and 2 H, respectively, 6-H$_2$, 5-H$_2$, OH), 2.39 (d, $^4J_{9,7}$ = 1.9, 9-H), 4.24 (s, 1-H$_2$), 4.37 (td, $J_{7,6}$ = 6.3, $^4J_{6,8}$ = 2.0, 7-H). − IR (film): ṽ = 3310, 2950, 2930, 2855, 1470, 1385, 1360, 1310, 1250, 1095, 1005, 840, 780, 655, 630 cm^{-1}. − $C_{17}H_{30}O_2Si$ (294.5): calcd. C 69.33, H 10.27; found C 69.24, H 10.19.

6-(tert-Butyldimethylsiloxy)-4,4-dimethyl-2,7-octadiyn-1-al (**30**): At 0°C a solution of alcohol **28** (600 mg, 2.14 mmol) in CH_2Cl_2 (2 ml) was added to a stirred solution of the Dess-Martin periodinane (1.36 mg, 3.21 mmol, 1.5 equiv.) in CH_2Cl_2 (150 ml). After 1 h, the reaction mixture was diluted with *tert*-butyl methyl ether (2 ml) and filtered through celite. The solvent was removed in vacuo. Flash chromatography (petroleum ether/*tert*-butyl methyl ether, 3:1) afforded the title compound (590 mg, 99%) as a colorless oil. − ^{1}H NMR (300 MHz): δ = 0.15 and 0.18 [2 s, Si(*t*Bu)(CH_3)$_2$], 0.91 (s, *t*Bu), 1.35 and 1.37 [s, 4-(CH_3)$_2$], extreme AB signal (δ_A = 1.94, δ_B = 1.97, J_{AB} = 14.1, in addition split by $J_{A,6}$ = 5.7 and $J_{B,6}$ = 7.0, 5-H$_2$), 2.45 (d, $^4J_{8,6}$ = 1.9, 8-H), 4.63 (ddd, $J_{6,5\text{-H(B)}}$ = 6.8, $J_{6,5\text{-H(A)}}$ = 5.7, $^4J_{6,8}$ = 2.1, 6-H), 9.20 (s, 1-H). − IR ($CDCl_3$): ṽ = 3310, 2955, 2930, 2885, 2860, 2205, 1670, 1470, 1465, 1390, 1360, 1275, 1255, 1215, 1180, 1145, 1100, 1055, 1020, 1005, 940, 920, 840, 810, 780, 725, 660, 630 cm^{-1}. − $C_{16}H_{26}O_2Si$ (278.5): calcd. C 69.01, H 9.41; found C 69.23, H 9.47.

7-(tert-Butyldimethylsiloxy)-4,4-dimethyl-2,8-nonadiyn-1-al (**31**) was prepared in a similar manner as **30** from **29** (400 mg, 1.36 mmol) and isolated as a colorless oil (366 mg, 92%). − ^{1}H NMR (300 MHz): δ = 0.12 and 0.14 [2 s, Si(*t*Bu)(CH_3)$_2$], 0.90 (s, *t*Bu), 1.29 [s, 4-(CH_3)$_2$], 1.57−1.86 (m, 5-H$_2$, 6-H$_2$), 2.40 (d, $^4J_{9,7}$ = 2.3, 9-H), 4.39 (ddd, $J_{7,6\text{-H(1)}} = J_{7,6\text{-H(2)}}$ = 5.9, $^4J_{7,9}$ = 2.1, 7-H), 9.19 (s, 1-H). − IR ($CDCl_3$): ṽ = 3310, 2955, 2930, 2855, 2205, 1670, 1470, 1390, 1365, 1310, 1250, 1095, 1005, 940, 835, 780, 720 cm^{-1}. − $C_{17}H_{28}O_2Si$ (292.5): calcd. C 69.81, H 9.65; found C 70.06, H 9.73.

6,6-Dimethylbicyclo[8.4.0]tetradeca-1$^{(14)}$,9-diene-2,7-diyn-4-ol (**32**): At 0°C HF/pyridine complex (0.30 ml, 27 mg, 0.72 mmol, 6 equiv.) was added to the silyl ether **11** (37.2 mg, 0.109 mmol) in THF (5 ml) and the resulting solution stirred for 3.5 h. The reaction mixture was diluted with diethyl ether (5 ml) and hydrolyzed with H_2O (5 ml). The aqueous layer was extracted with diethyl ether (2 × 5 ml). The combined organic layers were dried with Na_2SO_4. The solvent was removed in vacuo. Flash chromatography (pentane/diethyl ether, 3:1q1:1) on deactivated silica gel (pretreated with 25% aq. NH_3) afforded the title compound (18.8 mg, 76%). − ^{1}H NMR (500 MHz, C_6D_6;): δ = 1.05 and 1.10 [2 s, 6-(CH_3)$_2$], 1.25 (m_c, transition of a tt to higher order signal, $J_{12,11} \approx J_{12,13} \approx$ 6.3, 12-H$_2$), ca. 1.54−1.64 (m, OH, 5-H^1), 1.72 (td, $J_{13,12} = J_{13,14}$ = 5.6, 13-H$_2$), 1.84 (dd, $J_{gem} = J_{5\text{-H(2),4}}$ = 11.8, 5-H^2), 1.93 (m_c, 11-H$_2$), 4.54 (br. d, $J_{4,5\text{-H(2)}}$ = 10.8, 4-H), 5.26 (poorly resolved d, $^5J_{9,14}$ = 1.4, 9-H), 6.12 (poorly resolved td, $J_{14,13}$ = 4.6, $^5J_{14,9}$ = 0.9, 14-H). − IR (film): ṽ = 3570, 3235, 2970, 2940, 2860, 2390, 2265, 1620, 1455, 1390, 1330, 1290, 1165, 1120, 1020, 965, 945, 810 cm^{-1}. − $C_{16}H_{18}O$ [M$^+$]: calcd. 226.1358; exact molecular mass (±2 ppm; *R* = ca. 10000) checked by EI HRMS (70 eV).

6,6-Dimethylbicyclo[8.4.0]tetradeca-1$^{(14)}$,9-diene-2,7-diyn-4-one (**33**): At 0°C alcohol **32** (18.8 mg, 0.0831 mmol) was added to a stirred mixture of the Dess-Martin periodinane (88.1 mg, 0.208 mmol, 2.5 equiv.), molecular sieves (4 Å), and $NaHCO_3$ (one spatular tip-full, each) in CH_2Cl_2 (3 ml). After 1 h, flash chromatography (pentane:diethyl ether, 5:1) on deactivated silica gel (pretreated with 25% aq. NH_3) of the reaction mixture afforded the title compound (13.4 mg, 72%) as a yellow solid. − ^{1}H NMR (300 MHz; C_6D_6; contains 1 weight-% diethyl ether and 7 weight-% pentane and a

small amount of non-solvent impurity): δ = 1.06 [s, 6-$(CH_3)_2$], adjoining to 1.07−1.17 (m, 12-H_2), 1.53 (td, $J_{13,12} = J_{13,14} = 5.7$, 13-$H_2$), 1.81 ($m_c$, 11-$H_2$), 2.42 (s, 5-$H_2$), 5.21 (br. s, 9-H), 6.05 (poorly resolved td, $J_{14,13} = 4.5$, $^5J_{14,9} = 1.5$, 14-H). − Because of the instability of this compound neither IR spectrum nor HRMS were measured.

Methyl [(8,8-Dimethyl-6-oxo-1,2,3,4,5,6,7,8-octahydrophenanthren-4-yl)thio]acetate (**35**): At room temp. NEt_3 (20.6 µl, 15.0 mg, 0.148 mmol, 2.5 equiv.), 1,4-cyclohexadiene (0.13 ml, 0.11 g, 1.4 mmol, 23 equiv.), and methyl thioglycolate (11.1 µl, 13.2 mg, 0.124 mmol, 2.1 equiv.) were added to a solution of the dienediynone **33** (13.4 mg, 0.0592 mmol) in CH_2Cl_2 (2 ml). After 14 h, flash chromatography (pentane/diethyl ether, 5:1) of the reaction mixture on deactivated silica gel (pretreated with 25% aq. NH_3) gave the impure title compound (7.3 mg). Preparative TLC (5 cm × 20 cm, pentane/diethyl ether, 5:1, $R_f = 0.39$) afforded the title compound (3.6 mg, 16%) as a colorless oil. − ^{1}H-NMR [500 MHz, C_6D_6; contains "polymer" (2 m at 1.87−1.98 and 1.25−1.46)]: δ = 1.00 and 1.01 [2 s, 8-$(CH_3)_2$], ca. 1.49−1.59 (m, 3-H^1, 2-H^1), 1.90−1.96 (m, 3-H^2)①, 2.22 (s, 7-H_2)②, 2.23−2.34 (m, 2-H^2)①, AB signal ($\delta_A = 2.50$, $\delta_B = 2.62$, $J_{AB} = 17.0$, in addition split by $J_{A,2\text{-}H(1)} = 12.1$*, $J_{A,2\text{-}H(2)} = 5.7$*, $J_{B,2\text{-}H(1)} = 6.1$**, 1-$H_2$)①, AB signal ($\delta_A = 2.73$, $\delta_B = 2.93$, $J_{AB} = 14.1$, 1′-H_2)③, AB signal ($\delta_A = 3.44$, $\delta_B = 4.43$, $J_{AB} = 21.7$, 5-H_2)②, 3.60 (s, CO_2CH_3), 4.02 (br. s, 4-H)①, 6.81 (d, $J_{9,10} = 8.3$, 9-H)***, 7.03 (d, $J_{10,9} = 8.0$, 10-H)***; *assignment interchangeable; **or $J_{B,2\text{-}H(2)} = 6.1$; ***assignment interchangeable① starting from $\delta_{4\text{-}H}$ (br. s at 4.02) crosspeaks in a 500 MHz H,H-correlation spectrum allowed to identify the chemical shifts of 3-H_2 (2 m at ca. 1.49−1.59 and 1.90−1.96) and, continuing from there, to recognize 2-H_2 (2 m at 1.49−1.59 and ca. 2.23−2.34) and ultimately 1-H_2 (AB signal, $\delta_A = 2.50$, $\delta_B = 2.62$);② 7-H_2 distinguished from 5-H_2 by means of a 300 MHz long-range C,H-correlation spectrum through a crosspeak $\delta_{C\text{-}8} = 36.88$ in the first case;③ identified through a crosspeak in a 300 MHz long-range C,H-correlation spectrums with $\delta_{CO2Me} = 170.14$. − Gated-decoupled ^{13}C NMR (125.7 MHz, C_6D_6; impure): δ = 17.88 (C-2)①, 27.34 (C-3)①, 29.30 (C-1)①, 29.93 and 30.17 [8-$(CH_3)_2$]②, 33.10 (C-1′)①, 36.99 (C-8)③, 40.33 (C-5)①, 42.34 (C-4)①, 52.14 (CO_2CH_3)①, 53.61 (C-7)①, 123.85 (C-9)*, ca. 128.01 (C-10)*, 132.75, 133.12, 135.89 and 142.81 (C-4a, C-4b, C-8a and C-10a), 170.14 (CO_2CH_3), 207.60 (C-6);① assigned because of the occurence of crosspeaks in a 500 MHz short-range C,H-correlation spectrum with the unambiguously assignable protons 1-H_2, 2-H_2, 3-H_2, 4-H, 5-H_2, 7-H_2, OCH_3, and 1′-H_2;② identified through the crosspeaks $\delta_H = 0.97$ and 1.01 in a 300 MHz short-range C,H-correlation spectrum;③ identified through the absence of a crosspeak in a 500 MHz short-range C,H-correlation spectrum; *assignment interchangeable, but identification of the chemical shift $\delta_C = 128.01$ (superimposed by the C_6D_6 signals) through extrapolation of a crosspeak with $\delta_H = 6.81$ in a 500 MHz short-range C,H-correlation spectrum. − IR (C_6D_6): $\tilde{\nu}$ = 3235, 3090, 3070, 3035, 2950, 2860, 2390, 2280, 1960, 1815, 1740, 1620, 1480, 1455, 1435, 1390, 1330, 1275, 1160, 1125, 1035, 1010, 815, 680 cm^{-1}. − $C_{19}H_{24}O_3S$ [M^+]: calcd. 332.1446; exact molecular mass (±2 ppm; R = ca. 10000) checked by EI HRMS (70 eV).

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