Regiocontrol in Pd(0)-Mediated Couplings of a Bis(enol triflate) with Alkynes – Stereoselective Syntheses of Monocyclic Dienediynes Related to the Neocarzinostatin Chromophore

Stefan W. Scheuplein[a], Klaus Harms[b][*], Reinhard Brückner*[a], and Jean Suffert*[c]

Institut für Organische Chemie der Julius-Maximilians-Universität[a],
Am Hubland, W-8700 Würzburg, F.R.G.

Fachbereich Chemie der Philipps-Universität[b],
Hans-Meerwein-Straße, W-3550 Marburg, F.R.G.

Laboratoire de Pharmacochimie Moléculaire, Centre de Neurochimie du CNRS UPR 421[c],
5, rue Blaise Pascal, F-67084 Strasbourg Cedex, France

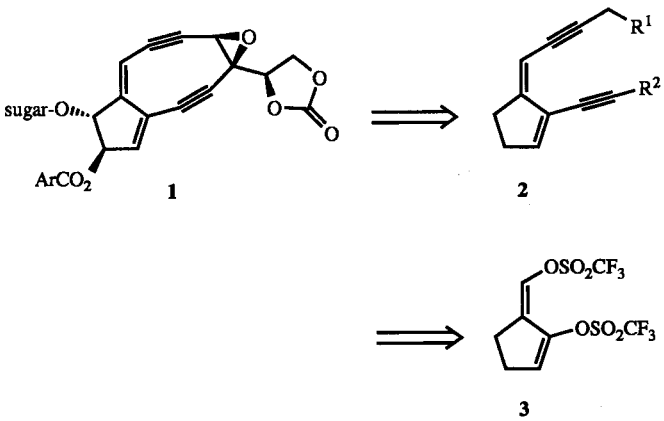
Received September 16, 1991

Key Words: C–C coupling / Dienediynes / Enol triflates / Neocarzinostatin / Palladium catalysis

The stereoselective synthesis of (Z)-dienediynes **2** related to the neocarzinostatin chromophore **1** is described. (Z)-Bis(enol triflate) **3**, accessible stereoselectively from 2-formylcyclopentanone in 2 steps, serves as the key intermediate. It is subjected to consecutive Pd(0)-catalyzed couplings with two different alkynes and furnishes **2** via monocoupling products **8**.

Neocarzinostatin is a highly potent antitumor chromoprotein from *Streptomyces*[1]. Its biological activity stems from its chromophore **1**[2] which is readily transformed into a highly reactive diradical ready to attack – and thereby cleave – single- and double-strand DNA[3]. Various synthetic approaches to **1** or simplified models thereof have been described during the past three years[4].

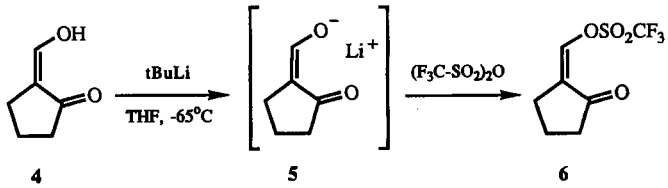
Our own approach[5] assumes that bicyclic dienediynes like **1** (or its analogs) would be accessible if monocyclic dienediynes **2** were at hand. In the synthesis of **2** endowing the semicyclic C=C bond with the proper (Z) configuration would be required. This seemed feasible if the correct stereochemistry was already established earlier, i.e. in the bis(enol triflate) **3**. From **3**, we wanted to proceed to the dienediynes **2** by palladium(0)-mediated coupling reactions with alkynes. The application of these conditions should leave the geometry of the crucial double bond unchanged.



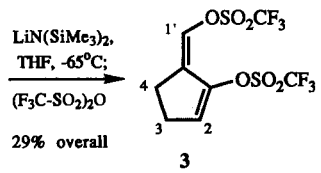
1 **2** **3**

[*] To whom inquiries concerning the X-ray structural analysis should be addressed.

Recently, we have shown how this method was utilized in the synthesis of (Z)-dienediynes **7** derived from *one* kind of alkyne[5]. At the same time we reported on an analogous synthesis of the corresponding (E)-dienediynes which was stereoselective, too[6]. A later publication by Terashima et al.[7] revealed closely related results.



4 **5** **6**



3

Bistriflate **3** was obtained from formylcyclopentanone **4**[4h,8] by reaction of its lithium enolate **5** with triflic anhydride. Sulfonylation occurred selectively at the former formyl oxygen atom. The resulting monotriflate **6**, due to its instability, was converted *without purification* into bistriflate **3**. To this end, **6** was deprotonated with lithium hexamethyldisilazide at –65°C and sulfonylated once more. Using triflic anhydride for this purpose, we obtained bistriflate **3** in 29% yield in the two steps. *N,N*-bis(trifluoromethanesulfonyl)aniline[9], which we had employed previously, had secured 36% overall yield[5] but at distinctly higher costs.

The (Z) configuration of **3** did not emerge from NOE experiments: Irradiation of the endocyclic olefinic proton

  0009–2940/92/0101–0271 $ 3.50+.25/0

[δ = 6.23 (m_c); distinguishable from 1'-H due to a 3.0-Hz coupling with two sp^3-bound protons (cf. Experimental)] *enhanced* absorption by the neighboring 3-H_2 as expected [δ = 2.61 – 2.65 (m)]. However, irradiation of the semicyclic olefinic proton [δ = 6.54 (m_c)] had *no* effect on the integral of 4-H_2. This observation seemed to be in contradiction to the suggested (Z) configuration. On the other hand, we had prepared the bistriflate *stereoisomer* of **3** which *also* showed no NOE under similar conditions[6]. Recourse had therefore to be taken to low-temperature X-ray crystallography. As depicted in Figure 1, crystalline **3** possesses the desired (Z) double bond.

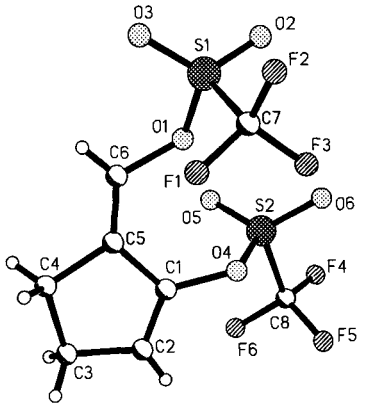
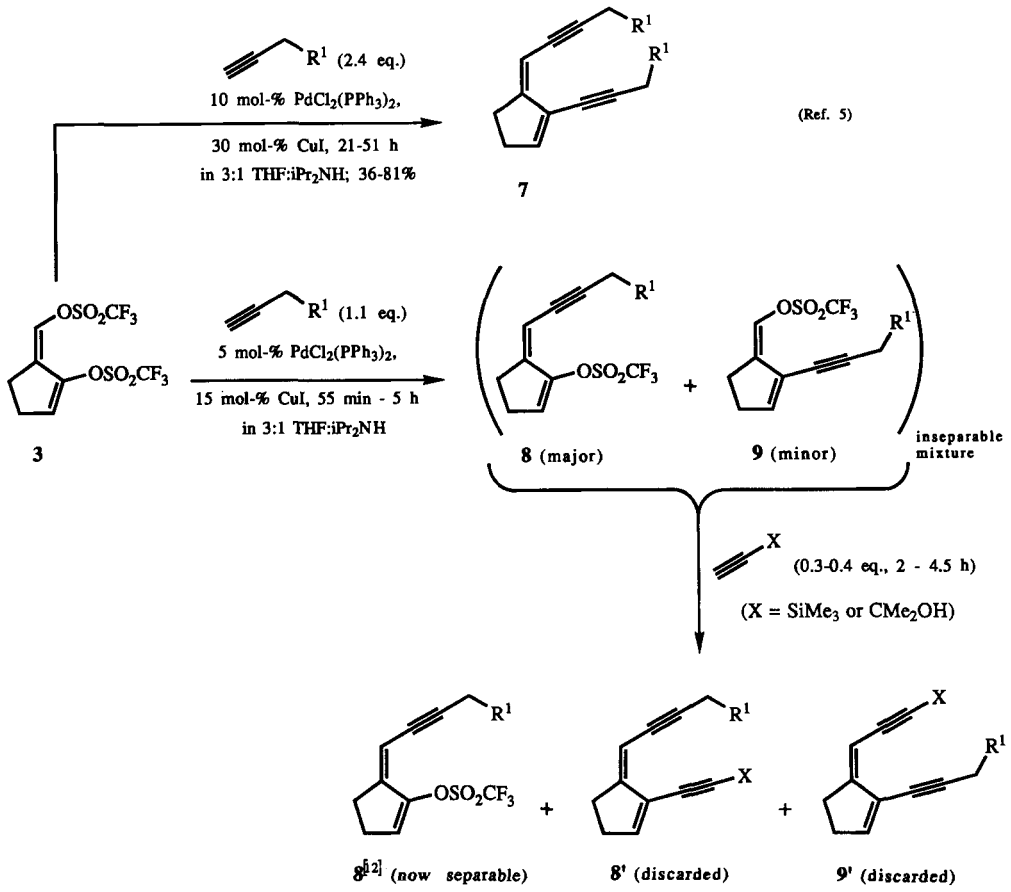


Figure 1. SCHAKAL plot of the solid-state structure of bistriflate **3**[10]

We have previously coupled **3** in the presence of catalytic $PdCl_2(PPh_3)_2$ and CuI with ⩾2 equiv. of *one* alkyne. In THF/iPr_2NH rather than in Cacchi's Et_2NH/DMF[11] we obtained dienediynes **7** with two *identical* alkyne moieties[5].

In the present study we treated bistriflate **3** under otherwise similar conditions with a *stoichiometric* amount of the alkyne (in fact, 1.1 equiv. of alkyne was used but 0.1 equiv. was consumed by reduction of the added 0.05 equiv. of Pd^{II}). As a result, we obtained a mixture consisting only of the isomeric monocoupling products **8** (ca. 80–90%) and **9**. This finding implies firstly that the *bis*triflate **3** undergoes coupling faster than any of the newly formed *mono*triflates. Secondly, it shows that the exocyclic triflate moiety of **3** couples more readily with alkynes than its endocyclic counterpart; this order would have been expected on steric grounds.

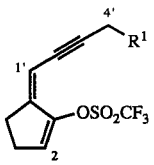


8	a	b	c	d	e	f
R^1	OTHP	$OSiPh_2Me$	CH_2OH	CH_2CH_2OH	$SiMe_3$	[a]
Yield (from 3)	47%	35%[b]	36%	37%	37%	52%

[a] CH_2-R^1 = $SiMe_3$.- [b] Over 2 steps (cf. *Experimental*)

Unfortunately, we were unable to separate **8** from **9** by flash chromatography[13]. Instead, the mixture of **8** and **9** was resolved kinetically by the addition of *another* alkyne in substoichiometric amounts (0.3–0.4 equiv.). *This* alkyne reacted preferentially with the minor compound **9** by converting it into the biscoupling product **9′**. Much less coupling occurred with the major compound **8** leading to the formation of **8′**. Consequently, the desired monocoupling products **8** emerged essentially unaltered from this operation and were now easily separable. Their yields ranged from 36 to 52% based on the starting bistriflate **3**; they would be 52–74% if referred to the initially used alkyne and if complete incorporation of the second alkyne into the scavenging products **8′** or **9′** was assumed.

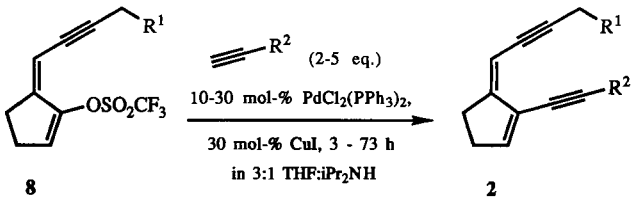
Table 1. Selected ^{1}H- and ^{13}C-NMR data of the monocoupling products **8**



8	δ(¹H) 2-H	1'-H	4'-H$_2$	$^5J_{1',4'}$ [Hz]	δ(¹³C) C-2	C-1'
a	6.19	5.49	4.38;4.46	2.3;2.2	129.15	97.04 or 98.98
b	6.15	5.41	4.55	2.1	129.07	98.92
c	6.16	5.46	2.64	2.7	128.57	99.58
d	6.12	5.42	2.47	2.5	128.39	99.80
e	6.07	5.45	1.67	2.9	127.16	100.90
f	6.23	5.49	-	-	128.63	99.53

The semicyclic C=C bond of all monocoupling products **8** must be (*Z*)-configurated. This follows from their role as (major) intermediates on the way to the previously described biscoupling products **7** which displayed (*Z*)-configuration according to NOE experiments[5]. The positional selectivity of the coupling reaction – attachment of the alkyne to the *semicyclic* sp^2-carbon atom of **8** – is inferred from the ^{1}H-NMR spectra (Table 1). In **8a–e**, the propargyl protons experience a long-range coupling J = 2.2–2.9 Hz across the C≡C bond. It is caused by the olefinic 1′-H as explicitly shown for **8a** or **b** by selective decoupling. If **8** carried the alkynyl chain at the site of the former *endocyclic* triflate, no such coupling would be observed. The monocoupling product **8f** is devoid of propargyl protons. Therefore, its regiochemistry could not be determined by the long-range coupling criterion. Nonetheless, it should be analogous to the regiochemistry encountered before because of the similarity of all ^{1}H- and ^{13}C-NMR data in the series (selected values: Table 1).

With monocoupling products **8** at hand, the stage was set for coupling with the second alkyne. This reaction again proceeded under Cacchi-like Pd(0) catalysis conditions. It afforded, with complete control of regioselectivity and retention of (*Z*) stereochemistry (vide infra), the biscoupling



8 2

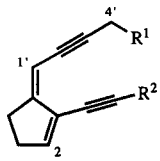
2	R^1	R^2	Yield
a	OTHP	$SiMe_3$	77%
b	OTHP	CH_2SiMe_3	52%
c	OTHP	nC_4H_9	29%
d	$OSiPh_2Me$	CH_2SiMe_3	55%
e	CH_2OH	$SiMe_3$	73%
f	CH_2OH	CH_2SiMe_3	65%
g	CH_2CH_2OH	$SiMe_3$	72%
h	$SiMe_3$	CH_2CH_2OH	60%
i	[a]	CH_2CH_2OH	60%
j	[a]	$CH_2CH_2CH_2OH$	57%

[a] CH_2-R^1 = $SiMe_3$.

products **2** containing *differentiated* alkynyl groups. Yields were 29–77% and might be higher if we were able to purify these exceedingly labile compounds without losses caused by decomposition.

We assigned the (*Z*) configuration to the biscoupling products **2** since the similarly prepared biscoupling products **7** were *proven* to possess (*Z*) geometry[5]. In addition, direct support for this assignment was obtained for **2b**. Thus, irradiation of the semicyclic sp^2-H (δ = 5.41) enhanced absorption of 4-H$_2$ (δ = 2.56–2.68) by 4% due to a nuclear Overhauser effect. This proves the proximity of these entities and consequently the (*Z*) geometry.

Table 2. Selected ^{1}H- and ^{13}C-NMR data of the biscoupling products **2**



2	δ(¹H) 2-H	1'-H	4'-H$_2$	$^5J_{1',4'}$ [Hz]	δ(¹³C) C-2	C-1'
a	6.65	5.48	4.35;4.42	2.5;2.5	151.78	98.47
b	6.38	5.41	4.37;4.44	2.4;2.3	147.54	97.23
c	6.49	5.45	4.38;4.45	2.5;2.3	148.35	97.71
d	6.40	5.38	4.54	2.3	146.95	97.62
e	6.66	5.44	superimposed	inaccessible	152.08	98.77
f	6.42	5.38	superimposed	inaccessible	147.98	97.86
g	6.63	5.42	superimposed	inaccessible	151.53	99.10
h	6.46	5.45	1.68	2.9	147.92	99.66
i	6.55	5.50	-	-	149.92	98.47
j	6.51	5.48	-	-	149.38	98.35
1[2a]	6.79	5.82	4.14	not resolved	139.4	106.5

The ^{1}H- and ^{13}C-NMR spectra of **2a–j** are consistent with the suggested structures (for representative data see Table 2). In compounds **2a–d** and **h**, the location of the different alkyne residues are revealed by couplings across *one* of the C≡C bonds ($^5J_{H,H}$ = 2.3–2.9 Hz). These couplings invariably concern the alkyne introduced *first* into the bistriflate **3**. This underlines the earlier observation that coupling occurs preferentially at the least hindered position. The regiochemistry of biscoupling products **2e–g** could not be determined similarly since here the propargyl signals were obscured by other resonances, and no splitting due to $^5J_{H,H}$ could be observed. Also, **2i** and **j** do not lend themselves to this kind of structural proof due to the *absence* of propargyl protons in the first reactant, trimethylsilylacetylene. Nonetheless, these compounds' precursors of established structures **8c,d** and **f** leave no doubt as to the suggested regiochemistry of the derived biscoupling products. The same applies to the consistency of all ^{1}H- and ^{13}C-NMR shifts within the series (Table 2).

In summary, dienediynes **2** with two different alkyne substituents have been prepared stereoselectively from formylcyclopentanone in 4 steps. The only previous synthesis of a compound of type **2** with (*Z*) configuration was achieved by Terashima et al.[4g]; it involved 9 steps starting from oxocyclopentanecarboxylic ester and the introduction of the stereogenic double bond with 37:63 selectivity.

We are indebted to Prof. *S. Berger* for his help in recording and assigning the NMR spectra, and to Dr. *G. Lange* and *F. Dadrich* for measuring the high-resolution mass spectra. To Dr. *D. Scheutzow, E. Ruckdeschel,* and *A. Mbonimana,* we express our gratitude for additional NMR- and to *F. Schmock* and *S. Schneider* for IR-spectroscopic assistance. Financial support from the *Fonds der Chemischen Industrie* and donations of triflic anhydride from *Merck-Schuchardt,* $PdCl_2$ from *Degussa,* and *n*- and *t*BuLi from *Chemetall GmbH* are gratefully acknowledged. S. W. S. thanks the *Graduiertenkolleg Marburg* for a fellowship.

Experimental

^{1}H NMR (tetramethylsilane as internal standard in $CDCl_3$) and ^{13}C NMR ($CDCl_3$ as internal standard and solvent): Bruker AC 300, AC 200, WM 400, or WH 400; coupling constants in Hz. – MS: MAT90, 8200, FINNIGAN MAT. – IR ($CDCl_3$ solution): Bruker IFF88. – All reactions were performed in oven-dried (100°C) glassware under dry nitrogen. Coupling reactions were carried out in Schlenk tubes. – THF was freshly distilled from K/Na, $HN(iPr)_2$ from CaH_2. – All products were purified by flash chromatography[13] on silica gel 60 (Merck; particle size 0.040–0.063 mm, 230–400 mesh ASTM); for each separation the column diameter, the fraction size, the eluent, and the product-containing fractions are given in parentheses [i.e.: 2 cm, 15 ml, diethyl ether/petroleum ether (1:10), F 2–3]. – Unless stated otherwise, the new compounds are colorless to yellow oils solidifying only in the freezer (< –30°C) if at all. They are highly labile and start to decompose at room temperature already within minutes (unless kept in solution). Therefore, the removal of the eluent from **2** and **8** had to be performed at 0°C/0.03 Torr and could not always be brought to completion prior to loss of product through decomposition. Accordingly, the yields of **2** and **8** are corrected for up to 21 mol-% of residual eluent. As another consequence, correct combustion analyses of **2** and **8** could not be obtained.

Alkynes: Trimethylsilylacetylene, Trimethylpropargylsilane, 3-Butyn-1-ol, 4-Pentyn-1-ol, 1-Hexyne, 2-Methyl-3-butyn-2-ol, and *Propargyl Alcohol* are commercially available.

2-(Propargyloxy)tetrahydropyran was prepared following the general procedure of ref.[14].

(Z)-5-[(Trifluoromethanesulfonyloxy)methylene]-1-cyclopentenyl Trifluoromethanesulfonate (**3**) *via (Z)-(2-Oxocyclopentylidene)methyl Trifluoromethanesulfonate* (**6**): At –65°C *t*BuLi (8.75 ml of a 1.28 M solution in hexanes, 11.2 mmol, 1.0 equiv.) was added very slowly to 2-formylcyclopentanone (**4**; 1.27 g, 11.2 mmol)[4h,8] in THF (70 ml) with vigorous stirring. After 15 min, $(CF_3SO_2)_2O$ (1.84 ml, 11.2 mmol, 1.0 equiv.) was added. After a few minutes, the cold reaction mixture was poured into satd. aq. $NaHCO_3$/brine (1:2). Extraction with diethyl ether and flash chromatography [3.5 cm, 60 ml, *t*BuOMe/petroleum ether (1:5 → 1:1), F 5–12] gave **6** (1.16 g, ca. 4.73 mmol) as a brown oil which, because of its instability, was immediately dissolved in THF (10 ml) and added dropwise at –65°C to a stirred solution of $LiN(SiMe_3)_2$ [prepared at –65°C from a THF solution (40 ml) of $HN(SiMe_3)_2$ (1.18 ml, 5.66 mmol, ≥1.2 equiv.) and *n*BuLi (2.36 ml of a 2.20 M solution in hexanes, 5.19 mmol, ≥1.1 equiv.)]. After 5 min, $(CF_3SO_2)_2O$ (0.78 ml, 4.74 mmol, ≥1.0 equiv.) was added. The resulting mixture was poured cold into satd. aq. $NaHCO_3$/brine (1:2) and this mixture extracted with diethyl ether. Flash chromatography [3.5 cm, 60 ml, *t*BuOMe/petroleum ether (1:10), F 6–14] gave **3** (1.20 g, 29% based on **1**] as a brown oil. Repeated recrystallization of this oil from pentane at –35°C yielded colorless crystals (m.p. ca. –5–0°C) for the X-ray analysis.

3: ^{1}H NMR (400 MHz): δ = 2.61–2.65 (m, 3-H_2), 2.73–2.76 (m, 4-H_2), 6.23 (m_c, 2-H), 6.54 (m_c, 1′-H). – NOE experiments: Irradiation at δ = 6.54 resulted in no (!) signal enhancement, whereas irradiation at δ = 6.23 enhanced the absorption at δ = 2.61–2.65 by 2.5%. – H,H-decoupling experiments: Irradiation at δ = 6.54 converted the m_c at δ = 6.23 into a triplet (J = 3.0), and irradiation at δ = 6.23 caused a narrowing of the m_c at δ = 6.54. – ^{13}C NMR (gated decoupling, 101 MHz): δ = 24.43 (t with further unresolved splitting, $^1J_{C,H}$ = 134.4, C-3 or C-4), 26.56 (t with further unresolved splitting, $^1J_{C,H}$ = 136.1, C-3 or C-4), 118.46 (q, $^1J_{C,F}$ = 320.6, CF_3), 118.52 (q, $^1J_{C,F}$ = 321.0, CF_3), 126.24 (d, $^1J_{C,H}$ = 205.0, C-1′), 126.98 (m_c, C-5), 129.99 (dt, $^1J_{C,H}$ = 172.5, $^2J_{C,H}$ = 6.4, C-2), 144.98 (m_c, C-1). – Heterodecoupling experiment: Irradiation at δ(^{1}H) = 6.23 decoupled and enhanced the signal at δ(^{13}C) = 129.99. – IR: $\tilde{\nu}$ = 3110 cm^{-1}, 2920, 1675, 1620, 1430, 1220, 1140, 1080, 1020.

$C_8H_6F_6O_6S_2$ Calcd. 375.9510 Found 375.9517 (EI HRMS)

6: ^{1}H NMR (300 MHz): δ = 2.03 (tt, $J_{4',3'} = J_{4',5'}$ = 7.4, 4′-H_2), 2.41 (t, $J_{3',4'}$ = 7.8, 3′-H_2), 2.71 (td, $J_{5',4'}$ = 7.2, $J_{5',1}$ = 2.3, 5′-H_2), 6.62 (t, $J_{1,5'}$ = 2.4, 1-H). – ^{13}C NMR (50 MHz): δ = 20.35, 27.05, 39.44 (C-3′, C-4′, C-5′), 118.41 (q, $^1J_{C,F}$ = 321, CF_3), 126.27 (C-1′), 133.52 (C-1), 200.66 (C-2′). – IR: $\tilde{\nu}$ = 2950 cm^{-1}, 1735, 1650, 1430, 1225, 1215, 1140, 1030.

Monocoupling Products **8**

(Z)-5-[4-(2-Tetrahydropyranyloxy)-2-butynylidene]-1-cyclopentenyl Trifluoromethanesulfonate (**8a**): $Pd(PPh_3)_2Cl_2$ (79.4 mg, 0.113 mmol, 0.05 equiv.), CuI (64.7 mg, 0.340 mmol, 0.15 equiv.), and $HN(iPr)_2$ (3.5 ml) were successively added at room temperature to **3** (852 mg, 2.26 mmol) and THP-protected propargyl alcohol (349 mg, 2.49 mmol, 1.1 equiv.) in THF (14 ml). After stirring for 55 min, trimethylsilylacetylene (96.0 µl, 0.679 mmol, 0.3 equiv.) was added. After 2 h, the mixture was poured into satd. NaCl. The product was extracted with diethyl ether. Drying of the extract with Na_2SO_4 and charcoal, filtration through a pad of Celite, and flash

chromatography [2 cm, 20 ml, pentane → diethyl ether/pentane (1:3), F 18–27] furnished **8a** (409 mg, 47%). – ^{1}H NMR (200 MHz): δ = 1.40–1.97 (m, 3″-H_2, 4″-H_2, 5″-H_2), 2.47–2.60 and 2.67–2.81 (2 m, 3-H_2, 4-H_2), 3.45–3.60 and 3.76–3.94 (2 m, 6″-H_2), AB signal (δ_A = 4.38, δ_B = 4.46, $J_{A,B}$ = 15.9, in addition split by $J_{A,1'}$ = 2.3, $J_{B,1'}$ = 2.2, 4′-H_2), 4.81 (dd, $J_{2'',3''(A)} = J_{2'',3''(B)}$ = 3.2, 2″-H), 5.49 (m_c, 1′-H), 6.19 (m_c, 2-H). – Homodecoupling experiments for the assignments of 2-H and 1′-H: Splitting by $J_{4',1'}$ at δ(4′-H_2) vanished during irradiation at δ = 5.49 but remained unchanged during irradiation at δ = 6.19. – ^{13}C NMR (50 MHz): δ = 19.12, 22.45, 25.42, 26.24, 28.73, 30.31 (C-3, C-4, C-3″, C-4″, C-5″), 55.11, 61.96 (C-4′, C-6″), 80.18, 91.76 (sp C), 97.04, 98.98 (C-1′, C-2″), 118.50 (q, $^1J_{C,F}$ = 318.9, CF_3), 129.15 (C-2), 146.50, 148.99 (C-1, C-5); impurity signal at δ = 124.85. – IR: ṽ = 2930 cm^{-1}, 1745, 1430, 1240, 1215, 1185, 1140, 1120, 1070, 1055, 1040, 1025, 870, 855, 770, 600.

$C_{15}H_{17}F_3O_5S$ Calcd. 366.0749 Found 366.0762 (EI HRMS)

(Z)-5-[4-(Methyldiphenylsilyloxy)-2-butynylidene]-1-cyclopentenyl Trifluoromethanesulfonate (**8b**): $Pd(PPh_3)_2Cl_2$ (84.0 mg, 0.120 mmol, 0.1 equiv.) and CuI (68.3 mg, 0.359 mmol, 0.3 equiv.) were added at room temperature to **3** (450 mg, 1.20 mmol) and propargyl alcohol (0.21 ml, 3.60 mmol, 3.0 equiv.) in THF (5 ml) followed by the addition of HN(*i*Pr)$_2$ (1.5 ml). After 50 min, the reaction mixture was worked up as described for the synthesis of **8a**. Flash chromatography [2 cm, 20 ml, diethyl ether/pentane (1:1), F 6–11] yielded a severely contaminated monocoupling product (207 mg). It was dissolved in CH_2Cl_2 (4 ml) and the solution added at room temperature to imidazole (149 mg, 2.20 mmol, ≥3.1 equiv.) and chloro(methyl)diphenylsilane (0.23 ml, 1.10 mmol, ≥1.5 equiv.) in CH_2Cl_2 (4 ml). After 3.5 h, more imidazole (99.6 mg, 1.46 mmol, ≥2.0 equiv.) and chloro(methyl)diphenylsilane (0.15 ml, 0.73 mmol, ≥1.0 equiv.) were added. After 2 h, the mixture was extracted with diethyl ether/H_2O and purified by flash chromatography [2 cm, 20 ml, pentane → diethyl ether/pentane (1:10), F 20–24] to give **8b** (206 mg, 35% from **3**). – ^{1}H NMR (200 MHz): δ = 0.71 [s, $Si(CH_3)Ph_2$], 2.43–2.55 and 2.63–2.76 (2 m, 3-H_2, 4-H_2), 4.55 (d, $J_{4',1'}$ = 2.1, 4′-H_2), 5.41 (m_c, 1′-H), 6.15 (m_c, 2-H), 7.29–7.46 and 7.56–7.69 (2 m, 6 and 4H, respectively; 2 Ph). – Homodecoupling experiments for the assignments of 2-H and 1′-H: Splitting by $J_{4',1'}$ at δ(4′-H_2) vanished during irradiation at δ = 5.41 but remained unchanged during irradiation at δ = 6.15. – ^{13}C NMR (50 MHz): δ = –2.99 ($SiCH_3Ph_2$), 26.11, 28.61 (C-3, C-4), 52.65 (C-4′), 80.86, 93.71 (sp C), 98.92 (C-1′), 118.53 (q, $^1J_{C,F}$ = 321.1, CF_3), 127.76, 129.79, 134.39, 135.49 (Ph), 129.07 (half as intense as 129.79, C-2), 146.23, 149.01 (C-1, C-5). – MS [CI (NH_3)]: *m/z* (%) = 496 (89) [$M^+ + NH_4^+$], 479 (70) [$M^+ + H^+$]; HRMS by CI was impossible for technical reasons and also by EI due to rapid decomposition of the sample at the required temperature.

(Z)-5-(5-Hydroxy-2-pentynylidene)-1-cyclopentenyl Trifluoromethanesulfonate (**8c**) was prepared from **3** (400 mg, 1.06 mmol), $Pd(PPh_3)_2Cl_2$ (37.3 mg, 0.053 mmol, 0.05 equiv.), CuI (30.3 mg, 0.159 mmol, 0.15 equiv.), and 3-butyn-1-ol (88.4 µl, 1.17 mmol, 1.10 equiv.; coupling time 4 h) as described for the preparation of **8a** except for the use of 0.40 equiv. rather than 0.30 equiv. of trimethylsilylacetylene (60.0 µl, 0.425 mmol; coupling time 4.5 h). Flash chromatography [2 cm, 20 ml, diethyl ether/pentane (1:1), F 10–16] gave the product (150 mg, 36%). – ^{1}H NMR (200 MHz): δ = 1.83 (t, $J_{OH,5'}$ = 6.5, OH), 2.48–2.59 and 2.69–2.79 (2 m, 3-H_2, 4-H_2), 2.64 (td, $J_{4',5'}$ = 6.1, $J_{4',1'}$ = 2.6, 4′-H_2), 3.75 (dt, $J_{5',OH} = J_{5',4'}$ = 6.2, 5′-H_2), 5.46 (m_c, 1′-H), 6.16 (m_c, 2-H). – ^{13}C NMR (50 MHz): δ = 24.30, 26.14, 28.69 (C-3, C-4, C-4′), 60.93 (C-5′), 78.00, 93.41 (sp C), 99.58 (C-1′), 118.72 (q, $^1J_{C,F}$ = 327.6, CF_3), 128.57 (C-2), 145.41, 149.32 (C-1, C-5). – IR: ṽ = 3620 cm^{-1}, 3020, 2930, 2340, 1605, 1425, 1240, 1220, 1180, 1140, 1070, 1050, 870, 855, 775, 620, 600.

$C_{11}H_{11}F_3O_4S$ Calcd. 296.0330 Found 296.0319 (EI HRMS)

(Z)-5-(6-Hydroxy-2-hexynylidene)-1-cyclopentenyl Trifluoromethanesulfonate (**8d**) was prepared from **3** (229 mg, 0.609 mmol), $Pd(PPh_3)_2Cl_2$ (21.4 mg, 0.030 mmol, 0.05 equiv.), CuI (17.4 mg, 0.091 mmol, 0.15 equiv.), 4-pentyn-1-ol (62.0 µl, 0.670 mmol, 1.1 equiv.; coupling time 4 h), and trimethylsilylacetylene (34.4 µl, 0.244 mmol, 0.4 equiv.; coupling time 2 h) as described for the preparation of **8a**. Flash chromatography [2 cm, 20 ml, diethyl ether/pentane (1:1 → 2:1), F 9–11] furnished the product (87.2 mg, 37%). – ^{1}H NMR (200 MHz): δ = 1.77 [tt, $J_{5',6'} = J_{5',4'}$ = 6.5, 5′-H_2, superimposing signal at δ = 1.80 (s, OH)], 2.41–2.56 and 2.66–2.77 [2 m, 3-H_2, 4-H_2, superimposed in part by signal at δ = 2.47 (td, $J_{4',5'} \approx 7.0$, $J_{4',1'} \approx 2.5$, 4′-H_2)], 3.73 (t, $J_{6',5'}$ = 6.1, 6′-H_2), 5.42 (m_c, 1′-H), 6.12 (m_c, 2-H). – ^{13}C NMR (50 MHz): δ = 16.27, 26.09, 28.61, 31.09 (C-3, C-4, C-4′, C-5′), 61.69 (C-6′), 76.76, 96.35 (sp C), 99.80 (C-1′), 128.39 (C-2), 144.95 (C-5 *and* C-1 because of extra intensity); the signals of the CF_3 group did not emerge from the spectral noise. – IR: ṽ = 3625 cm^{-1}, 2930, 2340, 2250, 1605, 1425, 1265, 1240, 1220, 1180, 1140, 1070, 1005, 870, 855, 820, 620, 600.

$C_{12}H_{13}F_3O_4S$ Calcd. 310.0487 Found 310.0483 (EI HRMS)

(Z)-5-[4-(Trimethylsilyl)-2-butynylidene]-1-cyclopentenyl Trifluoromethanesulfonate (**8e**) was prepared from **3** (121 mg, 0.321 mmol), $Pd(PPh_3)_2Cl_2$ (11.3 mg, 0.016 mmol, 0.05 equiv.), CuI (9.2 mg, 0.048 mmol, 0.15 equiv.), and propargyltrimethylsilane (52.6 µl, 0.353 mmol, 1.1 equiv.; coupling time 3.5 h) according to the procedure described for the preparation of **8a** with the following exception: The addition of trimethylsilylacetylene was replaced by the addition of 2-methyl-3-butyn-2-ol (10.0 µl, 0.096 mmol, 0.3 equiv.; coupling time 2.5 h). Flash chromatography [2 cm, 20 ml, pentane → diethyl ether/pentane (1:20), F 12–13] yielded the product [46.6 mg, slightly contaminated with unknown compound(s), 37%]. – ^{1}H NMR (200 MHz): δ = 0.10 [s, $Si(CH_3)_3$], 1.67 (d, $J_{4',1'}$ = 2.9, 4′-H_2), 2.44–2.56 and 2.65–2.76 (2 m, 3-H_2, 4-H_2), 5.45 (m_c, 1′-H), 6.07 (m_c, 2-H). – ^{13}C NMR (50 MHz): δ = –2.00 [$Si(CH_3)_3$], 8.56 (C-4′), 26.05, 28.57 (C-3, C-4), 75.36, 96.04 (sp C), 100.90 (C-1′), 118.78 (q, $^1J_{C,F}$ = 323.6, CF_3), 127.16 (C-2), 142.93, 149.60 (C-1, C-5). – IR: ṽ = 2960 cm^{-1}, 2930, 2855, 2245, 2200, 2150, 1605, 1425, 1250, 1215, 1170, 1140, 1090, 1070, 850, 770, 620, 600.

$C_{13}H_{17}F_3O_3SSi$ Calcd. 338.0620 Found 338.0619 (EI HRMS)

(Z)-5-[3-(Trimethylsilyl)-2-propynylidene]-1-cyclopentenyl Trifluoromethanesulfonate (**8f**) was prepared from **3** (95.1 mg, 0.253 mmol), $Pd(PPh_3)_2Cl_2$ (8.9 mg, 0.013 mmol, 0.05 equiv.), CuI (7.2 mg, 0.038 mmol, 0.15 equiv.), trimethylsilylacetylene (39.3 µl, 0.278 mmol, 1.1 equiv.; coupling time 1.5 h), and 2-methyl-3-butyn-2-ol (7.3 µl, 0.076 mmol, 0.3 equiv.; coupling time 3 h) as described for the preparation of **8e**. Flash chromatography [2 cm, 20 ml, pentane → diethyl ether/pentane (1:10), F 10–11] yielded the product (42.4 mg, 52%). – ^{1}H NMR (200 MHz): δ = 0.18 [s, $Si(CH_3)_3$], 2.48–2.59 and 2.67–2.79 (2 m, 3-H_2, 4-H_2), 5.49 (m_c, 1′-H), 6.23 (m_c, 2-H). – ^{13}C NMR (50 MHz): δ = –0.32 [$Si(CH_3)_3$], 26.30, 28.82 (C-3, C-4), 99.53 (C-1′), 100.19 (1 sp C), 118.68 (q, $^1J_{C,F}$ = 322.0, CF_3), 128.63 (C-2), 146.86, 149.22 (C-1, C-5); the signal of the second sp C was obscured by the spectral noise. – IR: ṽ = 2960 cm^{-1}, 2925, 1425, 1250, 1240, 1215, 1175, 1140, 1090, 1060, 1035, 850, 765, 600.

$C_{12}H_{15}F_3O_3SSi$ Calcd. 324.0463 Found 324.0463 (EI HRMS)

Biscoupling Products **2**[15]

(Z)-5-[4-(2-Tetrahydropyranyloxy)-2-butynylidene]-1-[2-(trimethylsilyl)-1-ethynyl]-1-cyclopentene (**2a**): $Pd(PPh_3)_2Cl_2$ (36.2 mg,

0.052 mmol, 0.2 equiv.), CuI (14.7 mg, 0.077 mmol, 0.3 equiv.), and $HN(iPr)_2$ (1 ml) were successively added at room temperature to **8a** (94.5 mg, 0.258 mmol) and trimethylsilylacetylene (72.9 µl, 0.516 mmol, 2.0 equiv.) in THF (3 ml). After 5.5 h, the reaction mixture was extracted with brine/diethyl ether. Flash chromatography [2 cm, 20 ml, diethyl ether/pentane (1:10 → 1:5), F 5–7] yielded the product (62.6 mg, 77%). – ^{1}H NMR (200 MHz): δ = 0.20 [s, $Si(CH_3)_3$], 1.40–1.95 (m, 3″-H_2, 4″-H_2, 5″-H_2), 2.42–2.54 and 2.57–2.70 (2 m, 3-H_2, 4-H_2), 3.43–3.58 and 3.76–3.92 (2 m, 6″-H_2), AB signal (δ_A = 4.35, δ_B = 4.42, $J_{A,B}$ = 15.6, in addition split by $J_{A,1'}$ = $J_{B,1'}$ = 2.5, 4′-H_2), 4.81 (dd, $J_{2'',3''(A)} \approx J_{2'',3''(B)} \approx$ 3.2, 2″-H), 5.48 (m_c, 1′-H), 6.65 (m_c, 2-H). – ^{13}C NMR (50 MHz): δ = −0.09 [$Si(CH_3)_3$], 19.14, 25.39, 30.30, 30.69, 31.45 (C-3, C-4, C-3″, C-4″, C-5″), 55.23 (C-4′), 61.93 (C-6″), 82.76, 89.07, 98.77, 99.14 (sp C), 96.83 (C-2″*), 98.47 (C-1′*), 126.73 (C-1), 151.78 (C-2), 154.09 (C-5); * assigned in analogy to **2b**. – IR: ṽ = 2945 cm^{-1}, 2875, 2855, 2245, 2150, 1435, 1345, 1250, 1200, 1120, 1075, 1055, 1040, 1025, 840, 815, 520.

$C_{19}H_{26}O_2Si$ Calcd. 314.1702 Found 314.1698 (EI HRMS)

(Z)-5-[4-(2-Tetrahydropyranyloxy)-2-butynylidene]-1-[3-(trimethylsilyl)-1-propynyl]-1-cyclopentene (**2b**) was prepared from **8a** (222 mg, 0.605 mmol), propargyltrimethylsilane (0.18 ml, 1.20 mmol, 2.0 equiv.), $Pd(PPh_3)_2Cl_2$ (42.5 mg, 0.061 mmol, 0.1 equiv.), and CuI (34.6 mg, 0.182 mmol, 0.3 equiv.) as described for the preparation of **2a**. The total reaction time was 7 h, but after 3 h more $Pd(PPh_3)_2Cl_2$ (21.2 mg, 0.030 mmol, 0.05 equiv.) was added. Flash chromatography [2 cm, 20 ml, diethyl ether/pentane (1:10 → 1:4), F 8–10] yielded the product (103 mg, 52%). – ^{1}H NMR (200 MHz): δ = 0.12 [s, $Si(CH_3)_3$], 1.44–1.90 [m, 3″-H_2, 4″-H_2, 5″-H_2, superimposing signal at δ = 1.69 (s, 3‴-H_2)], 2.39–2.51 (m, 3-H_2), 2.56–2.68 (m, 4-H_2), 3.43–3.58 and 3.75–3.91 (2 m, 6″-H_2), AB signal (δ_A = 4.37, δ_B = 4.44, $J_{A,B}$ = 15.6, in addition split by $J_{A,1'}$ = 2.4, $J_{B,1'}$ = 2.3, 4′-H_2), 4.84 (dd, $J_{2'',3''(A)} \approx J_{2'',3''(B)} \approx$ 3.1, 2″-H), 5.41 (m_c, 1′-H), 6.38 (m_c, 2-H). – Homodecoupling experiments for the assignments of 2-H and 1′-H: Splitting by $J_{4',1'}$ at δ(4′-H_2) vanished during irradiation at δ = 5.41 but remained unchanged during irradiation at δ = 6.38. NOE experiments for the assignment of 3-H_2 vs. 4-H_2 and for assignment of the (Z) configuration: Irradiation at δ = 5.41 enhanced absorption at δ = 2.56–2.68 by 4%; irradiation at δ = 6.38 enhanced absorption at δ = 2.39–2.51 by the same amount. – ^{13}C NMR (101 MHz, gated decoupling): δ = −1.99 [q, $^1J_{C,H}$ = 119.3, $Si(CH_3)_3$], 7.96 (t, $^1J_{C,H}$ = 125.1, 3‴-C), 18.98 (t, $^1J_{C,H}$ = 128.5) and 25.24 (t, $^1J_{C,H}$ = 125.9) and 28.5–32.5 (m, C-3, C-4, C-3″, C-4″, C-5″), 55.10 (t with further unresolved splittings, $^1J_{C,H}$ = 148.0, C-4′), 61.85 (t with further unresolved splittings, $^1J_{C,H}$ = 143.1, C-6″), 73.39, 82.98 (2 s, C-2′, C-1‴), 89.23 [m_c (perhaps unresolved dt), C-3′], 93.20 (t, $^2J_{C-2'',3''-H}$ = 11.1, C-2‴), 96.48 (d, $^1J_{C,H}$ = 165.6, C-2″), 97.23 (d, $^1J_{C,H}$ = 161.7, C-1′), 127.25 (s, C-1), 147.54 (d, $^1J_{C,H}$ = 166.3, C-2), 156.15 (s, C-5). – Heterodecoupling experiments for the assignment of individual δ(^{13}C): Irradiation at δ(^{1}H) = 4.37/4.44 decoupled and enhanced signal at δ(^{13}C) = 55.10 and simplified signal at δ(^{13}C) = 89.23 to a very closely spaced doublet (tentatively assigned); irradiation at δ(^{1}H) = 5.41 decoupled and enhanced signal at δ(^{13}C) = 97.23; irradiation at δ(^{1}H) = 6.38 decoupled and enhanced signal at δ(^{13}C) = 147.54. – IR: ṽ = 2945 cm^{-1}, 2875, 2855, 2245, 2205, 1345, 1250, 1200, 1120, 1075, 1055, 1025, 845, 815.

$C_{20}H_{28}O_2Si$ Calcd. 328.1858 Found 328.1861 (EI HRMS)

(Z)-1-(1-Hexynyl)-5-[4-(2-tetrahydropyranyloxy)-2-butynylidene]-1-cyclopentene (**2c**) was prepared from **8a** (171 mg, 0.466 mmol), 1-hexyne (80.2 µl, 0.699 mmol, 1.5 equiv.), $Pd(PPh_3)_2Cl_2$ (32.7 mg, 0.047 mmol, 0.1 equiv.), and CuI (26.6 mg, 0.140 mmol, 0.3 equiv.) as described for the preparation of **2a**. The total reaction time was 73 h. Flash chromatography [2 cm, 20 ml, diethyl ether/pentane (1:10 → 1:5), F 11–14] furnished the product (40.7 mg, 29%). – ^{1}H NMR (200 MHz): δ = 0.92 (t, $J_{6''',5'''}$ = 7.1, 6‴-H_3), 1.33–1.90 (m, 3″-H_2, 4″-H_2, 5″-H_2, 4‴-H_2, 5‴-H_2), 2.39 (t, $J_{3''',4'''}$ = 7.0, 3‴-H_2), 2.43–2.53 and 2.60–2.70 (2 m, 3-H_2, 4-H_2), 3.45–3.59 and 3.78–3.92 (2 m, 6″-H_2), AB signal (δ_A = 4.38, δ_B = 4.45, $J_{A,B}$ = 15.6, in addition split by $J_{A,1'}$ = 2.5, $J_{B,1'}$ = 2.3, 4′-H_2), 4.85 (dd, $J_{2'',3''(A)} \approx J_{2'',3''(B)} \approx$ 3.2, 2″-H), 5.45 (m_c, 1′-H), 6.49 (m_c, 2-H); impurity signal at δ = 1.25 (s). – ^{13}C NMR (50 MHz): δ = 13.63 (C-6‴), 19.15, 19.33, 22.15, 25.39, 30.34, 30.49, 30.76, 31.28 (C-3, C-4, C-3″, C-4″, C-5″, C-3‴, C-4‴, C-5‴), 55.17 (C-4′), 61.93 (C-6″), 74.57, 83.00, 89.58, 95.10 (sp C), 96.68 (C-2″*), 97.71 (C-1′*), 127.10 (C-1), 148.35 (C-2), 155.59 (C-5); * assigned in analogy to **2b**. – IR: ṽ = 2935 cm^{-1}, 2875, 2245, 1710, 1610, 1445, 1355, 1345, 1265, 1200, 1185, 1120, 1075, 1055, 1035, 1020, 815.

$C_{20}H_{26}O_2$ Calcd. 298.1933 Found 298.1927 (EI HRMS)

(Z)-5-[4-(Methyldiphenylsilyloxy)-2-butynylidene]-1-[3-(trimethylsilyl)-1-propynyl]-1-cyclopentene (**2d**) was prepared from **8b** (181 mg, 0.376 mmol), 1-trimethylsilyl-2-propyne (0.11 ml, 0.75 mmol, 2.0 equiv.), $Pd(PPh_3)_2Cl_2$ (52.8 mg, 0.075 mmol, 0.2 equiv.), and CuI (21.5 mg, 0.113 mmol, 0.3 equiv.) as described for the preparation of **2a**. The total reaction time was 5.5 h, but already after 70 min $Pd(PPh_3)_2Cl_2$ (26.4 mg, 0.038 mmol, 0.1 equiv.) was added. Flash chromatography [2 cm, 20 ml, pentane → diethyl ether/pentane (1:10), F 12–14] yielded the product [95.6 mg, slightly contaminated with unknown compound(s), 55%]. – ^{1}H NMR (200 MHz): δ = 0.07 [s, $Si(CH_3)Ph_2$], 0.13 [s, $Si(CH_3)_3$], 1.57 (s, 3″-H_2), 2.41–2.53 and 2.58–2.70 (2 m, 3-H_2, 4-H_2), 4.54 (d, $J_{4',1'}$ = 2.3, 4′-H_2), 5.38 (m_c, 1′-H), 6.40 (m_c, 2-H), 7.30–7.47 and 7.58–7.68 (2 m, 6H and 4H, respectively, 2 Ph). – ^{13}C NMR (50 MHz): δ = −2.64 [$Si(CH_3)Ph_2$], −1.99 [$Si(CH_3)_3$], 7.89 (C-3″), 30.36, 31.28 (C-3, C-4), 52.89 (C-4′), 64.63, 74.43, 82.85, 91.72 or 93.08 (sp C), 97.62 (C-1′), 125.48 (C-1), 127.82, 129.85, 134.48, 135.56 [$Si(CH_3)Ph_2$], 146.95 (C-2), 155.53 (C-5). – HRMS: Neither EI (70 eV) nor CI (NH_3) nor CI (isobutane) gave an [M^+] peak.

(Z)-5-(5-Hydroxy-2-pentynylidene)-1-[2-(trimethylsilyl)-1-ethynyl]-1-cyclopentene (**2e**) was prepared in 3.5 h from **8c** (64.2 mg, 0.216 mmol), trimethylsilylacetylene (0.15 ml, 1.1 mmol, 5.0 equiv.), $Pd(PPh_3)_2Cl_2$ (30.4 mg, 0.043 mmol, 0.2 equiv.), and CuI (12.4 mg, 0.065 mmol, 0.3 equiv.) according to the procedure described for the preparation of **2a**. Flash chromatography [1.5 cm, 4 ml, diethyl ether/pentane (1:1), F 9–13] yielded the product (41.6 mg, 73%). – ^{1}H NMR (200 MHz): δ = 0.21 [s, $Si(CH_3)_3$], 1.96 (m_c, OH), 2.43–2.70 (m, 3-H_2, 4-H_2, 4′-H_2), 3.73 (br. t, $J_{5',4'} \approx$ 5.7, 5′-H_2), 5.44 (m_c, 1′-H), 6.66 (m_c, 2-H). – ^{13}C NMR (50 MHz): δ = 0.07 [$Si(CH_3)_3$], 24.39 (C-4′), 30.70, 31.43 (C-3, C-4), 61.11 (C-5′), 79.64, 91.10, 99.77 (3 sp C), 98.77 (C-1′), 126.55 (C-1), 152.08 (C-2), 153.08 (C-5); one sp-C signal was obscured by the spectral noise. Heterodecoupling experiments for the assignment of individual δ(^{13}C) values: Irradiation at δ(^{1}H) = 6.66 decoupled and enhanced signal at δ(^{13}C) = 152.08; irradiation at δ(^{1}H) = 5.44 decoupled and enhanced signal at δ(^{13}C) = 98.77. – IR: ṽ = 3625 cm^{-1}, 3580, 2960, 2845, 2245, 2145, 1445, 1425, 1385, 1250, 1110, 1080, 1050, 1005, 845, 815, 520.

$C_{15}H_{20}OSi$ Calcd. 244.1283 Found 244.1272 (EI HRMS)

(Z)-5-(5-Hydroxy-2-pentynylidene)-1-[3-(trimethylsilyl)-1-propynyl]-1-cyclopentene (**2f**) was prepared from **8c** (84.5 mg, 0.285 mmol), 1-trimethylsilyl-2-propyne (0.21 ml, 1.4 mmol, 5.0 equiv.), $Pd(PPh_3)_2Cl_2$ (40.0 mg, 0.057 mmol, 0.2 equiv.), and CuI (16.3 mg, 0.086 mmol, 0.3 equiv.) as described for the preparation of **2a**. The reaction time was 3.5 h. Flash chromatography [1.5 cm, 4 ml, di-

ethyl ether/pentane (1:2 → 1:1), F 14–18] gave 48.6 mg (65%). – ^{1}H NMR (200 MHz): δ = 0.13 [s, Si(CH$_3$)$_3$], 1.68 (s, 3″-H$_2$), 2.13 (br. s, OH), 2.40–2.52 (m, 3-H$_2$ or 4-H$_2$), 2.56–2.69 (m, 3-H$_2$ or 4-H$_2$, 4′-H$_2$), 3.71 (m$_c$, 5′-H$_2$), 5.38 (m$_c$, 1′-H), 6.42 (m$_c$, 2-H). – ^{13}C NMR (50 MHz): δ = –1.93 [Si(CH$_3$)$_3$], 8.32 (C-3″), 24.54, 30.37, 31.34 (C-3, C-4, C-4′), 61.14 (C-5′), 74.21, 80.00, 90.55, 92.68 (sp C), 97.86 (C-1′), 127.45 (C-1), 147.98 (C-2), 154.50 (C-5). – IR: ṽ = 3620 cm^{-1}, 3545, 2960, 2930, 2885, 2850, 2245, 2225, 1250, 1150, 1050, 850, 815.

$C_{16}H_{22}OSi$ Calcd. 258.1440 Found 258.1444 (EI HRMS)

(Z)-5-(6-Hydroxy-2-hexynylidene)-1-[2-(trimethylsilyl)-1-ethynyl]-1-cyclopentene (**2g**) was prepared from **8d** (84.4 mg, 0.272 mmol), trimethylsilylacetylene (0.19 ml, 1.4 mmol, 5.0 equiv.), $Pd(PPh_3)_2Cl_2$ (38.2 mg, 0.054 mmol, 0.2 equiv.), and CuI (15.5 mg, 0.082 mmol, 0.3 equiv.) as described for the preparation of **2a**. The reaction time was 4.5 h. Flash chromatography [1.5 cm, 4 ml, diethyl ether/pentane (1:2 → 2:1), F 16–20] provided 51.2 mg (72%). – ^{1}H NMR (200 MHz): δ = 0.21 [s, Si(CH$_3$)$_3$], 1.71 (br. s, OH), 1.79 (tt, $J_{5',4'} = J_{5',6'} = 6.5$, 5′-H$_2$), 2.38–2.53 (m, 3-H$_2$ or 4-H$_2$, 4′-H$_2$), 2.56–2.69 (m, 3-H$_2$ or 4-H$_2$), 3.75 (t, $J_{6',5'} = 6.1$, 6′-H$_2$), 5.42 (m$_c$, 1′-H), 6.63 (m$_c$, 2-H). – ^{13}C NMR (50 MHz): δ = 0.07 [Si(CH$_3$)$_3$], 16.63, 30.70 (half as intense as the following resonance), 31.37 (C-3, C-4, C-4′, C-5′), 61.96 (C-6′), 78.18, 94.13, 98.41, 99.62 (sp C), 99.10 (C-1′), 126.54 (C-1), 151.53 (C-2), 152.44 (C-5). – IR: ṽ = 3625 cm^{-1}, 2960, 2845, 2340, 2245, 2150, 1675, 1620, 1445, 1430, 1250, 1080, 1005, 845, 815, 520.

$C_{16}H_{22}OSi$ Calcd. 258.1440 Found 258.1428 (EI HRMS)

(Z)-1-(4-Hydroxy-1-butynyl)-5-[4-(trimethylsilyl)-2-butynylidene]-1-cyclopentene (**2h**) was prepared from **8e** (112 mg, 0.332 mmol), 3-butyn-1-ol (50.3 µl, 0.664 mmol, 2.0 equiv.), $Pd(PPh_3)_2Cl_2$ (23.3 mg, 0.033 mmol, 0.1 equiv.), and CuI (19.0 mg, 0.100 mmol, 0.3 equiv.) as described for the preparation of **2b**. During a total reaction time of 19.5 h, additional portions of $Pd(PPh_3)_2Cl_2$ (23.3 mg, 0.033 mmol, 0.1 equiv.) were added after 1.5 and 4 h. Flash chromatography [2 cm, 20 ml, diethyl ether/pentane (1:10 → 1:1), F 29–31] yielded 53.3 mg (60%). – ^{1}H NMR (200 MHz): δ = 0.12 [s, Si(CH$_3$)$_3$], 1.68 (d, $J_{4',1'} = 2.9$, 4′-H$_2$), 2.07 (t, $J_{OH,4''} = 6.7$, OH), 2.41–2.53 and 2.58–2.70 [2 m, 3-H$_2$, 4-H$_2$, superimposed in part by signal at δ = 2.66 (t, $J_{3'',4''} = 5.8$, 3″-H$_2$)], 3.76 (dt, $J_{4'',OH} = J_{4'',3''} = 6.2$, 4″-H$_2$), 5.45 (m$_c$, 1′-H), 6.46 (m$_c$, 2-H). – ^{13}C NMR (50 MHz): δ = –1.93 [Si(CH$_3$)$_3$], 8.69 (C-4′), 24.27, 30.46, 31.15 (C-3, C-4, C-3″), 60.93 (C-4″), 76.82, 90.31, 93.31 (3 sp C), 99.66 (C-1′), 126.51 (C-1), 147.92 (C-2), 151.32 (C-5); one sp-C signal was obscured by the spectral noise. – IR: ṽ = 3430 cm^{-1}, 2960, 2930, 2245, 2200, 1705, 1405, 1250, 1215, 1110, 1050, 850, 770.

$C_{16}H_{22}OSi$ Calcd. 258.1440 Found 258.1430 (EI HRMS)

(Z)-1-(4-Hydroxy-1-butynyl)-5-[3-(trimethylsilyl)-2-propynylidene]-1-cyclopentene (**2i**) was prepared from **8f** (94.7 mg, 0.292 mmol), 3-butyn-1-ol (44.2 µl, 0.584 mmol, 2.0 equiv.), $Pd(PPh_3)_2Cl_2$ (41.0 mg, 0.058 mmol, 0.2 equiv.), and CuI (16.7 mg, 0.088 mmol, 0.3 equiv.) as described for the preparation of **2b**. The total reaction time was 3 h, but already after 2 h more $Pd(PPh_3)_2Cl_2$ (20.5 mg, 0.029 mmol, 0.1 equiv.) was added. Flash chromatography [2 cm, 10 ml, diethyl ether/pentane (1:4 → 1:2), F 14–16] yielded 43.2 mg (60%). – ^{1}H NMR (200 MHz): δ = 0.18 [s, Si(CH$_3$)$_3$], 2.03 (br. s, OH), 2.42–2.53 (m, 3-H$_2$ or 4-H$_2$), 2.56–2.68 (m, 3-H$_2$ or 4-H$_2$, 3″-H$_2$), 3.77 (t, $J_{4'',3''} = 6.2$, 4″-H$_2$), 5.50 (m$_c$, 1′-H), 6.55 (m$_c$, 2-H). – ^{13}C NMR (50 MHz): δ = 0.20 [Si(CH$_3$)$_3$], 24.18 (C-3″), 30.52, 31.52 (C-3, C-4), 60.93 (C-4″), 90.86, 102.59 (2 sp C), 98.47 (C-1′), 126.63 (C-1), 149.92 (C-2), 155.26 (C-5); 2 sp-C signals were obscured by the spectral noise. – IR: ṽ = 3625 cm^{-1}, 2960, 2930, 2850, 2245, 2165, 2115, 1610, 1425, 1250, 1080, 1050, 845, 815.

$C_{15}H_{20}OSi$ Calcd. 244.1283 Found 244.1283 (EI HRMS)

(Z)-1-(5-Hydroxy-1-pentynyl)-5-[3-(trimethylsilyl)-2-propynylidene]-1-cyclopentene (**2j**) was prepared from **8f** (98.1 mg, 0.302 mmol), 4-pentyn-1-ol (56.0 µl, 0.605 mmol, 2.0 equiv.), $Pd(PPh_3)_2Cl_2$ (42.4 mg, 0.060 mmol, 0.2 equiv.), and CuI (17.3 mg, 0.091 mmol, 0.3 equiv.) as described for the preparation of **2b**. The total reaction time was 3 h, but already after 1.5 h more $Pd(PPh_3)_2Cl_2$ (21.2 mg, 0.030 mmol, 0.1 equiv.) was added. Flash chromatography [2 cm, 10 ml, diethyl ether/pentane (1:3 → 3:1), F 16–18] gave 47.6 mg (contaminated with small amounts of an aromatic compound; 57%). – ^{1}H NMR (200 MHz): δ = 0.13 [s, Si(CH$_3$)$_3$], 1.76 (br. s, OH), 1.82 (tt, $J_{4'',5''} \approx J_{4'',3''} \approx 6.4$, 4″-H$_2$), 2.40–2.52 (m, 3-H$_2$ or 4-H$_2$, 3″-H$_2$), 2.57–2.68 (m, 3-H$_2$ or 4-H$_2$), 3.77 (t, $J_{5'',4''} = 6.1$, 5″-H$_2$), 5.48 (m$_c$, 1′-H), 6.51 (m$_c$, 2-H). – ^{13}C NMR (50 MHz): δ = 0.23 [Si(CH$_3$)$_3$], 16.42, 30.49, 31.21, 31.52 (C-3, C-4, C-3″, C-4″), 61.84 (C-5″), 75.39, 93.83, 99.16, 102.56 (sp C), 98.35 (C-1′), 126.94 (C-1), 149.38 (C-2), 155.59 (C-5). – IR: ṽ = 3625 cm^{-1}, 3560, 2960, 2930, 2850, 2245, 2165, 2120, 1610, 1430, 1250, 1080, 845, 815.

$C_{16}H_{22}OSi$ Calcd. 258.1440 Found 258.1436 (EI HRMS)

Structure Determination of **3**[16]. – *Crystal Data:* $C_8H_6F_6O_6S_2$ (376.2); colorless crystal, size: 0.3 × 0.3 × 0.3 mm; monoclinic; $P2_1/c$; a = 9.612(2), b = 14.335(2), c = 9.814(2) Å; β = 97.530(10)°; V = 1340.6(4) Å^3; Z = 4; ϱ(calcd.) = 1.864 Mg/m^3; μ = 4.568 mm^{-1}; F(000) = 752. – *Data Collection:* Enraf-Nonius CAD4 diffractometer; Cu-K_α (λ = 1.54178 Å); T = 183 K; graphite monochromator; 6.2° ≤ 2Θ ≤ 110.0°; ω scan; prescan limit, σ-option: σ = 3.00 · I, 0.015; prescan speed parameter: 1; maximum scan time: 20.00 s; ω = (1.20 + 0.14 tgΘ)°; 3 orientation reflections measured every 250 reflections; 0 ≤ h ≤ 10, –15 ≤ k ≤ 3, –10 ≤ l ≤ 10; 2282 reflections collected; 1665 independent reflections (R_{int} = 5.39%); 1617 observed reflections [$F > 4.0\sigma(F)$]. – *Solution and Refinement:* Siemens SHELXTL PLUS (VMS); Direct Methods; full-matrix least squares; minimized quantity: $\Sigma w(F_o - F_c)^2$; extinction correction: χ = 0.0031(3), where $F^* = F[1 + 0.002\chi F^2/\sin(2\Theta)]^{-1/4}$; hydrogen atoms: refined, common isotropic U; weighting scheme: $w^{-1} = \sigma^2(F) + 0.0000 \cdot F^2$; 219 parameters refined; R = 5.16%, wR = 5.27% (observed data); R = 5.34%, wR = 5.86% (all data); goodness of fit: 6.93; largest, mean Δ/σ: 0.004, 0.001; data-to-parameter ratio: 7.4:1; largest difference peak:

Table 3. Coordinates and equivalent isotropic temperature factors U for **3** (U calculated as one third of the trace of the orthogonal U_{ij} tensor)

	x	y	z	U(eq)
S(1)	2623(1)	-967(1)	-2499(1)	30(1)
S(2)	6663(1)	-2315(1)	-1005(1)	25(1)
F(1)	3505(3)	-339(2)	-4707(3)	64(1)
F(2)	1661(4)	-1163(3)	-5049(4)	107(2)
F(3)	3629(4)	-1816(2)	-4475(3)	85(2)
F(4)	8396(3)	-3566(2)	62(3)	55(1)
F(5)	8795(3)	-3097(2)	-1905(3)	58(1)
F(6)	9343(3)	-2234(2)	-138(3)	64(1)
O(1)	4163(3)	-883(2)	-1810(3)	28(1)
O(2)	2125(3)	-1832(2)	-2110(3)	45(1)
O(3)	1890(3)	-135(2)	-2362(4)	52(1)
O(4)	6829(3)	-1620(2)	-2203(3)	26(1)
O(5)	6480(3)	-1843(2)	209(3)	37(1)
O(6)	5759(3)	-3027(2)	-1571(3)	39(1)
C(1)	7239(4)	-682(3)	-1892(4)	25(1)
C(2)	8522(5)	-377(3)	-1824(5)	37(2)
C(3)	8603(5)	647(3)	-1532(6)	45(2)
C(4)	7065(5)	943(3)	-1591(5)	33(2)
C(5)	6218(4)	41(2)	-1743(4)	24(1)
C(6)	4854(5)	5(3)	-1728(4)	29(2)
C(7)	2871(6)	-1080(3)	-4301(5)	47(2)
C(8)	8423(5)	-2840(3)	-734(5)	36(2)

0.44 eÅ^{-3}; largest difference hole: −0.35 eÅ^{-3}. – Coordinates and temperature factors see Table 3.

CAS Registry Numbers

2a: 137568-96-8 / **2b**: 137568-97-9 / **2c**: 137568-98-0 / **2d**: 137568-99-1 / **2e**: 137569-00-7 / **2f**: 137569-01-8 / **2g**: 137569-02-9 / **2h**: 137569-03-0 / **2i**: 137569-04-1 / **2j**: 137569-05-7 / **3**: 134329-52-5 / **4**: 1192-54-7 / **6**: 134251-47-1 / **8a**: 137568-91-3 / **8b**: 137568-92-4 / **8c**: 137568-93-5 / **8d**: 137568-94-6 / **8e**: 137568-95-7 / **8f**: 128878-88-6 / HC≡CCH$_2$OTHp: 6089-04-9 / HC≡CCH$_2$OH: 107-19-7 / HC≡CCH$_2$CH$_2$OH: 927-74-2 / HC≡CCH$_2$CH$_2$CH$_2$OH: 5390-04-5 / HC≡CCH$_2$TMS: 13361-64-3 / HC≡C−TMS: 1066-54-2

[1] N. Ishida, K. Miyazaki, K. M. Kumagai, M. Rikimura, *J. Antibiot.* **1965**, *18*, 68–76.
[2] Structure: [2a] K. Edo, M. Mizugaki, Y. Koide, H. Seto, K. Furihata, N. Otake, N. Ishida, *Tetrahedron Lett.* **1985**, *26*, 331–334. – [2b] A. G. Myers, P. J. Proteau, T. M. Handel, *J. Am. Chem. Soc.* **1988**, *110*, 7212–7214.
[3] The modes of action of Neocarzinostatin chromophore and related antibiotics were recently reviewed by I. H. Goldberg, *Acc. Chem. Res.* **1991**, *24*, 191–198, and by K. C. Nicolaou, W.-M. Dai, *Angew. Chem.* **1991**, *103*, 1453–1481; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1387–1416.
[4] [4a] P. A. Wender, M. Harmata, D. M. Jeffrey, C. Mukai, J. Suffert, *Tetrahedron Lett.* **1988**, *29*, 909–912. – [4b] M. Hirama, K. Fujiwara, K. Shigematsu, Y. Fukazawa, *J. Am. Chem. Soc.* **1989**, *111*, 4120–4122. – [4c] P. A. Wender, J. A. McKinney, C. Mukai, *J. Am. Chem. Soc.* **1990**, *112*, 5369–5370. – [4d] K. Fujiwara, A. Kurisaki, M. Hirama, *Tetrahedron Lett.* **1990**, *31*, 4329–4332. – [4e] T. Wehlage, A. Krebs, T. Link, *Tetrahedron Lett.* **1990**, *31*, 6625–6628. – [4f] J. Suffert, *Tetrahedron Lett.* **1990**, *31*, 7437–7440. – [4g] K. Nakatani, K. Arai, N. Hirayama, F. Matsuda, S. Terashima, *Tetrahedron Lett.* **1990**, *31*, 2323–2326. – [4h] A. G. Myers, P. M. Harrington, E. Y. Kuo, *J. Am. Chem. Soc.* **1991**, *113*, 694–695. – [4i] P. Magnus, T. Pitterna, *J. Chem. Soc., Chem. Commun.* **1991**, 541–543. – [4j] K. Fujiwara, H. Sakai, M. Hirama, *J. Org. Chem.* **1991**, *56*, 1688–1689. – [4k] T. Doi, T. Takahashi, *J. Org. Chem.* **1991**, *56*, 3465–3467. – [4l] M. Hirama, M. Tokuda, K. Fujiwara, *Synlett* **1991**, 651–653.
[5] R. Brückner, S. W. Scheuplein, J. Suffert, *Tetrahedron Lett.* **1991**, *32*, 1449–1452.
[6] J. Suffert, R. Brückner, *Tetrahedron Lett.* **1991**, *32*, 1453–1456.
[7] K. Nakatani, K. Arai, K. Yamada, S. Terashima, *Tetrahedron Lett.* **1991**, *32*, 3405–3406.
[8] P. E. Eaton, P. G. Jobe, *Synthesis* **1983**, 796–797.
[9] J. E. McMurry, W. J. Scott, *Tetrahedron Lett.* **1983**, *24*, 979–982.
[10] Further details of the crystal structure investigation are available on request from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-7514 Eggenstein-Leopoldshafen 2, on quoting the depository number CSD-320312, the names of the authors, and the journal citation.
[11] S. Cacchi, E. Morera, G. Ortar, *Synthesis* **1986**, 320–322.
[12] Monocoupling product **8b** was obtained in a slightly different manner, cf. Experimental.
[13] W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923–2925.
[14] T. W. Greene, *Protective Groups in Organic Synthesis*, John Wiley & Sons, New York, **1981**, p. 21.
[15] In the ^{13}C-NMR spectra of **2**, the assignment of C-1 (shielded) vs. C-5 (deshielded) was performed in analogy to Edo's values for **1** [2a] ($\delta_{C\text{-}1}$ = 129.8, $\delta_{C\text{-}5}$ = 160.2). In the ^{1}H-decoupled ^{13}C-NMR spectra of **2**, C-2 (tertiary) and C-5 (quaternary) were distinguished by the more intense resonance of the former.
[16] N. Walker, D. Stuart, *Acta Crystallogr., Sect. A: Found. Crystallogr.* **1983**, *A39*, 158–166; A. L. Spek, *PLATON 88, Program for Geometrical Analysis of Crystal Structures*, Utrecht, **1988**; E. Keller, *SCHAKAL-88B, A FORTRAN Program for the Graphic Representation of Molecular and Crystallographic Models*, Univ. of Freiburg, **1988**.

[351/91]