

Efficient Synthesis of Tetrasubstituted Alkenes by Allylsilane-Terminated Domino-Heck Double Cyclisation

Lutz F. Tietze,* Klaus Kahle, and Thomas Raschke^[a]

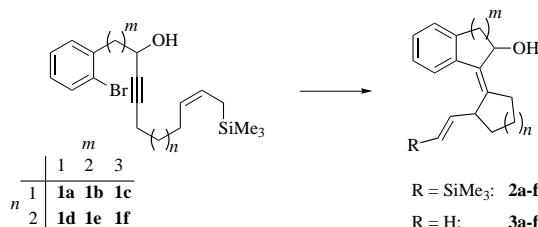
Dedicated to Professor Ernst Anders on the occasion of his 60th birthday

Abstract: The domino-Heck double cyclisation of the arylbromides **1**, which contain an allylsilane and an alkyne moiety and are easily accessible by an addition of the corresponding lithiated alkynes **5** to the aldehydes **4**, leads to the tetrasubstituted alkenes **2** and **3** in good yield. The reaction produces exclusively compounds with an *E* double bond and additionally proceeds with good to excellent induced diastereoselectivity in the case of **1e** and **1f**. Irradiation of **2e** leads to a steady state equilibrium of the *E* and *Z* compounds in a 1:1 ratio.

Keywords: alkenes • allylsilanes • domino reactions • Heck reaction • optical data storage

Introduction

Overcrowded tetrasubstituted alkenes can possess remarkable switching properties under UV light. They are thus of interest for the development of reversible optical data storage, which at the moment relies mainly on inorganic materials.^[1–3] Here, we report on an efficient synthesis of tetrasubstituted alkenes of type **2** and **3** (Scheme 1), in which the four substituents are



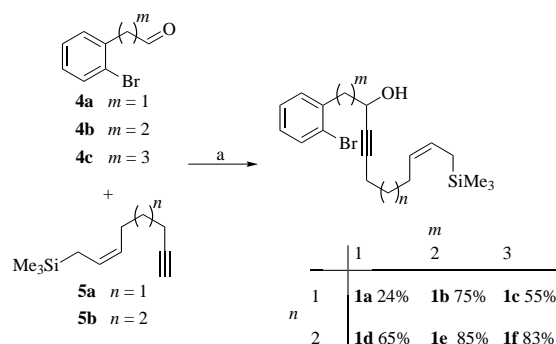
Scheme 1. Allylsilane-terminated domino-Heck double cyclisation.

part of two ring systems. The synthesis was performed as an allylsilane-terminated domino-Heck double cyclisation of the arylbromides **1a–f** containing an allylsilane and an alkyne moiety.^[4–9] We have recently shown that in ring forming Heck reactions the use of allylsilanes as terminating groups allows the formation of tertiary stereogenic centers.^[10–13] By using different tethers of different lengths between the aryl and the alkyne as well as the alkyne and the allylsilane moiety, we

were able to obtain variable ring sizes. Thus, we prepared the 5-5- (**2a**),^[14] 6-5- (**2b**), 7-5- (**2c**), 5-6- (**2d**), 6-6- (**2e**), and the 7-6-ring-system (**2f**).

Results and Discussion

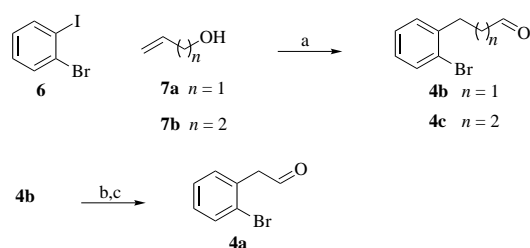
The substrates **1a–f** for the domino-Heck double cyclisations were synthesised in good yields by addition of the lithiated species of **5a–b** to the arylaldehydes **4a–c** at -78°C in THF in the presence of LiBr (Scheme 2).



Scheme 2. Synthesis of the substrates **1a–f** for the domino-Heck reaction: a) *n*BuLi, THF, LiBr, -78°C .

The necessary arylcarbaldehydes **4b** and **4c** were accessible from bromiodobenzene **6** and the alcohols **7a** and **7b**, respectively, under phase-transfer Heck conditions as described by Jeffery.^[15–17] The reaction conditions allowed a selective transformation of the iodine in the presence of the bromine atom (Scheme 3). In contrast, an analogous synthesis of the corresponding iodoarylcarbaldehydes (**4**, I instead of

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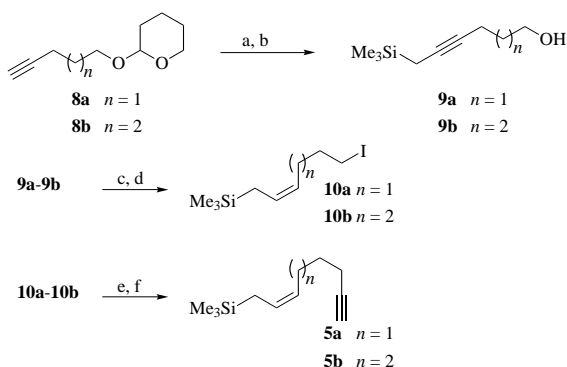


Scheme 3. Synthesis of the bromoarylaldehydes **4a–c**: a) $\text{Pd}(\text{OAc})_2$, NaHCO_3 , $n\text{Bu}_4\text{NCl}$, DMF, $50–60^\circ\text{C}$, 12–24 h, 83%; b) Ac_2O , NEt_3 , DMAP, $0^\circ\text{C} \rightarrow 20^\circ\text{C}$, 16 h, 66%; c) O_3 , CH_2Cl_2 , -78°C , 15 min, $(\text{CH}_3)_2\text{S}$, $-78^\circ\text{C} \rightarrow 20^\circ\text{C}$, 45%.

Br) using 1,2-diiodobenzene as starting material was less suitable because of its sluggish performance and the low selectivity towards monofunctionalisation.

The arylacetaldehyde **4a** was prepared from **4b** by formation of the enol acetate followed by ozonolysis. For the synthesis of the enynes **5a–b** the THP-protected commercially available alkynols **8a–b** were deprotected with $n\text{BuLi}$ and treated with $\text{Me}_3\text{SiCH}_2\text{I}$. Subsequent deprotection of the alcohol functionality yielded the propargylsilanes **9a–b**. Partial reduction of the triple bond in **9a–b** with H_2 and P-2 nickel,^[18] followed by transformation of the alcohol group into an iodide by the Appel procedure^[19] yielded the allylsilanes **10a–b**,^[10, 20] which were alkynylated with lithiated TMS-acetylene. Deprotection using $\text{MeOH}/\text{K}_2\text{CO}_3$ furnished the enynes **5a** and **5b** in good overall yield (Scheme 4).

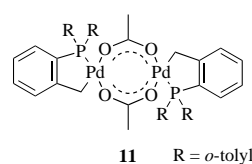
For the domino-Heck reaction of the substrates **1a–b** and **1d–e** the $\text{Pd}(\text{OAc})_2/\text{PPh}_3$ catalyst system at $80–100^\circ\text{C}$ was



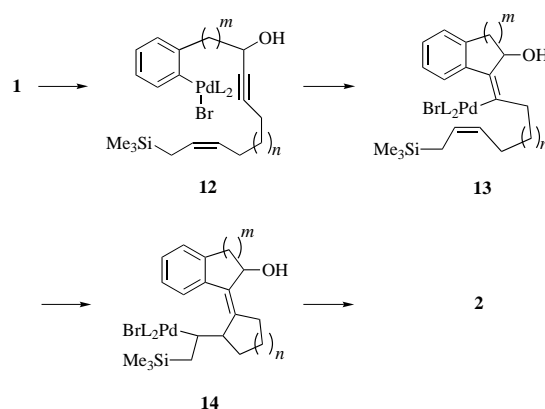
Scheme 4. Synthesis of the enynes **5a** and **5b**: a) $n\text{BuLi}$, $\text{Me}_3\text{SiCH}_2\text{I}$, THF, $-60^\circ\text{C} \rightarrow 60^\circ\text{C}$, 20 h; b) H_2SO_4 , MeOH , 20°C , 20 h, 62% **9a**, 63% **9b** (2 steps); c) P-2 Ni, H_2 , EtOH , 20°C , 4 h; d) PPh_3 , imidazole, I_2 , CH_3CN , $0^\circ\text{C} \rightarrow 20^\circ\text{C}$, 90 min., 69% **10a**, 77% **10b** (two steps); e) $\text{TMS-C}\equiv\text{C-Li}$, THF, $20^\circ\text{C} \rightarrow 50^\circ\text{C}$, 20 h; f) K_2CO_3 , MeOH , 20°C , 20 h, 81% **5a**, 87% **5b** (two steps).

most suitable, and led to the formation of the tetrasubstituted alkenes **2a,b,d,e** in 61–71% yield after 4–22 h. It was not necessary to protect the hydroxyl group in **1**, which is a general advantage of Heck reactions. However, the reaction of the corresponding silyl ethers gave similar results. In contrast, the corresponding ketones, easily accessible from **1** by oxidation, could only be cyclised in low yield.^[10]

The preparation of the alkenes **2c** and **2f** with a seven-membered system as ring B was more difficult since a reaction temperature of 130°C was necessary. $\text{Pd}(\text{OAc})_2$ in the presence of triphenylphosphane could thus not be used, since palladium black is formed, and this is not catalytically active under these conditions. However, the palladacycle **11** introduced by Herrmann and Beller^[21, 22] proved to be useful in these cases, and allowed the formation of **2c** and **2f** from **1c** and **1f** in 43% yield at 130°C .



In the transformations described, the vinylsilanes **2** with an *E* double bond connecting the two aliphatic ring systems were the major products. In addition, small amounts of the desilylated products **3** were formed. The selective formation of the *E* configuration in the tetrasubstituted alkenes **2** follows from the reaction mechanism. After the oxidative addition of **1** to Pd^0 to give **12** a *syn* addition took place, which led to the intermediate **13** (Scheme 5). Since isomerisation of



Scheme 5. Proposed mechanism for the allylsilane-terminated domino-Heck double cyclisation.

Table 1. Results of the allylsilane-terminated domino-Heck reactions of **1a–f**.

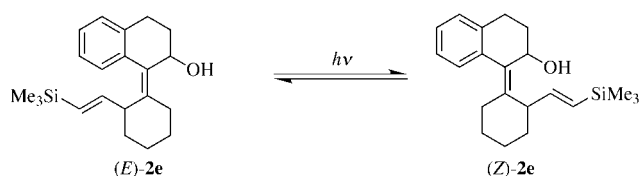
Entry	Substrate	<i>m/n</i>	Conditions	Product	Yield [%] 2 (3)	<i>dr</i> of 2 ^[a]
1	1a	1/1	$\text{Pd}(\text{OAc})_2/\text{PPh}_3/\text{KOAc}/\text{Pr}_4\text{NBr}/\text{DMF}/80^\circ\text{C}/4.5\text{ h}$	2a, 3a	71 (3)	1.2:1
2	1b	2/1	$\text{Pd}(\text{OAc})_2/\text{PPh}_3/\text{KOAc}/\text{Pr}_4\text{NBr}/\text{DMF}/95^\circ\text{C}/22\text{ h}$	2b, 3b	66 (5)	1.3:1
3	1c	3/1	$\text{HBC}^{[b]}/\text{KOAc}/\text{Pr}_4\text{NBr}/\text{DMF}/130^\circ\text{C}/21\text{ h}$	2c, 3c	43 (3)	2.6:1
4	1d	1/2	$\text{Pd}(\text{OAc})_2/\text{PPh}_3/\text{KOAc}/\text{Pr}_4\text{NBr}/\text{DMF}/80^\circ\text{C}/15\text{ h}$	2d, 3d	62 (8)	4.5:1
5	1e	2/2	$\text{Pd}(\text{OAc})_2/\text{PPh}_3/\text{KOAc}/\text{Pr}_4\text{NBr}/\text{DMF}/100^\circ\text{C}/17\text{ h}$	2e, 3e	61 (18)	9.4:1
6	1f	3/2	$\text{HBC}^{[b]}/\text{KOAc}/\text{Pr}_4\text{NBr}/\text{DMF}/130^\circ\text{C}/21\text{ h}$	2f, 3f	43 (7)	20:1

[a] Diastereomeric ratio (*cis:trans*) determined by NMR; [b] Herrmann–Beller catalyst **11**.^[21, 22]

the double bond does not take place under the reaction conditions, the final addition of the vinyl palladium species, again in a *syn* fashion, led to **2** via **14**. In this step an (*E*)-vinylsilane moiety and a new stereogenic center were formed. We assume that the trimethylsilyl group increases the CH acidity in its α position and thus facilitated the elimination of a HPdL₂X species from the intermediate **14**. By this means the regio- and stereoselectivity of the elimination were quantitative. The formation of the small amount of **3** bearing a vinyl group instead of the vinylsilane moiety may be due to a protodesilation, which is governed by the structure of the molecule. Thus in the series with a six-membered ring formed in the second cyclisation, the amount of **3** was noticeably higher than in the cases in which a five-membered ring was formed.

The stereoselectivity in the formation of the new stereogenic center in **2** varied from 1.2:1 to 20:1 depending on the structure of the products. It was lowest with *ds* 1.2:1 for the formation of the rather flexible and flat 5,5-ring system **2a** and increases to *ds* 20:1 for the more rigid 7,6-ring system **2f**. The high facial selectivity in the reaction of **1f** to give **2f** was surprising since it involves a 1,4-induction; however, we have recently shown that for an intermolecular hetero-Diels–Alder reaction excellent selectivity can be observed, even for a 1,6-induction.^[23]

In order to demonstrate the ability of the new tetrasubstituted alkenes to act as switches we investigated the behaviour of **2e** in solution at 0 °C upon irradiation with a high pressure mercury lamp. (*E*)-**2e** was isomerised to form a 1:1 mixture of (*E*)-**2e** and (*Z*)-**2e** in a steady state equilibrium after 60 min. No other products were found in the crude mixture. This indicates the reversible, light-induced isomerisation of the tetrasubstituted central double bond (Scheme 6).



Scheme 6. Photoisomerisation of (*E*)-**2e** and (*Z*)-**2e**.

The structures of the new compounds were primarily determined by NMR spectroscopy. In addition, an X-ray analysis of the major diastereomer of **2e** was obtained, which showed that the central and vinyl double bonds have an *E* configuration and a *rac*-(2*R*,2'*S*) orientation (*cis* orientation) at the stereogenic centers (Figure 1).^[24] Comparison of the NMR spectra of the diastereomers of **2e** and the other products **2a–d** and **2f** as well as of **3** allows a clear differentiation between the *cis* and the *trans* isomers: the protons of the trimethylsilyl group in the *trans* diastereomers consistently resonate at higher field ($\delta = -0.21$ – -0.03) than those of the *cis* diastereomers ($\delta = -0.02$ – -0.14).

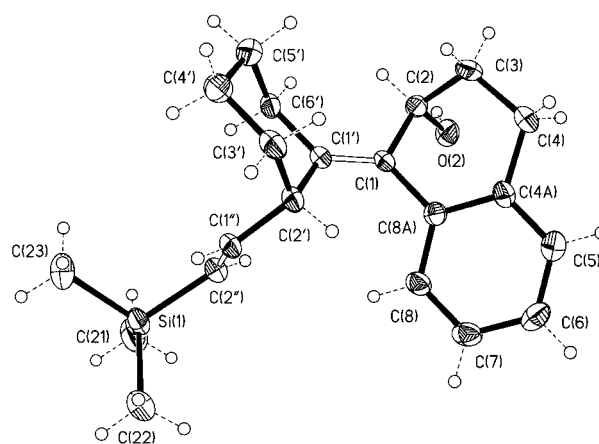


Figure 1. ORTEP plot of the major diastereomer of **2e**.

Conclusion

The allylsilane-terminated domino-Heck reaction of substrates of type **1** containing an alkyne and an allylsilane moiety allows for a highly efficient and also selective synthesis of the polycyclic structures **2a–f** with a tetrasubstituted double bond of defined configuration. The method also allows for variation of the size of rings B and C. Structures with such an overcrowded alkene moiety may be of interest for the development of optical switches for optical data storage.

Experimental Section

General: All reactions were performed under an inert atmosphere of argon or N₂ in predried glassware. Solvents were dried using standard procedures and were distilled. ¹H NMR and ¹³C NMR spectra were obtained on Varian XL 200, VXR-200, and Bruker AMX 300 spectrometers. UV/Vis spectra were obtained with a Perkin–Elmer Lambda 2 spectrophotometer. Elemental analyses were performed by the Analytical laboratory of the University of Göttingen. Column chromatography was performed using Machery & Nagel (0.04–0.063 mm), analytical TLC using Machery & Nagel (S G/UV₂₅₄) silica gels.

1,8-Bis-trimethylsilyloct-6-en-1-yne: *n*BuLi (46.8 mmol, 1.5 M solution in hexane) was added to a stirred solution of TMS-acetylene (4.60 g, 46.8 mmol) in THF (30 mL) at –78 °C, stirring was continued for 1 h before the mixture was warmed to room temperature and slowly added to a solution of **10a** (10.1 g, 36.0 mmol) in THF (100 mL). The mixture was stirred at 50 °C for 20 h, and after cooling to room temperature the mixture was washed with water and brine, the organic layer was dried (MgSO₄), and the solvent was removed in vacuo. Purification by flash chromatography yielded the title compound (7.61 g, 84%). *R*_f = 0.46 (petroleum ether); ¹H NMR (200 MHz, CDCl₃): δ = 5.51–5.36 (m, 1 H; 7-H), 5.30–5.16 (m, 1 H; 6-H), 2.23 (t, *J* = 7.1 Hz, 2 H; 3-H), 2.10 (dt, *J* = 7.2, 7.2 Hz, 2 H; 5-H), 1.55 (tt, *J* = 7.2, 7.2 Hz, 2 H; 4-H), 1.45 (d, *J* = 8.5 Hz, 2 H; 8-H), 0.15 (s, 9 H; SiMe₃), 0.00 (s, 9 H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): δ = 126.4, 126.3 (C-6, C-7), 107.5 (C-2), 84.45 (C-1), 28.63, 26.04 (C-3, C-4), 19.42, 18.48 (C-5, C-8), 0.19 (SiMe₃), –1.77 (SiMe₃).

8-Trimethylsilyl-oct-6-en-1-yne (5a): K₂CO₃ (1.03 g) was added to a solution of 1,8-bis-trimethylsilyloct-6-en-1-yne (7.50 g, 29.7 mmol) in methanol (250 mL), and the mixture was stirred at room temperature for 20 h. Water (100 mL) was added and the mixture was extracted with pentane. The organic layers were washed with brine and dried (MgSO₄). Careful removal of the solvent in vacuo yielded **5a** (5.12 g, 96%) in high purity. *R*_f = 0.39 (petroleum ether); ¹H NMR (200 MHz, CDCl₃): δ = 5.52–5.35 (m, 1 H; 7-H), 5.30–5.16 (m, 1 H; 6-H), 2.20 (dt, *J* = 2.7, 7.2 Hz, 2 H; 3-H),

2.11 (dt, $J = 7.5, 7.5$ Hz, 2H; 5-H), 1.94 (t, $J = 2.7$ Hz, 1H; 1-H), 1.58 (tt, $J = 7.2, 7.2$ Hz, 2H; 4-H), 1.48 (d, $J = 8.5$ Hz, 2H; 8-H), 0.00 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): $\delta = 126.5, 126.1$ (C-6, C-7), 84.55 (C-2), 68.22 (C-1), 28.56 (C-4), 26.06 (C-5), 18.50, 18.03 (C-3, C-8), -1.79 (SiMe₃).

1,9-Bis-trimethylsilyl-non-7-en-yne: The coupling of the iodide **10b** (35.61 g, 120.2 mmol) with TMS-acetylene (15.32 g, 156 mmol) was carried out as described for the synthesis of **5a**, and the crude 1,9-bis-trimethylsilyl-non-7-en-yne was used with no further purification. $R_f = 0.46$ (petroleum ether); ¹H NMR (200 MHz, CDCl₃): $\delta = 5.48-5.17$ (m, 2H, 7-H; 8-H), 2.22 (t, $J = 6.8$ Hz, 2H; 3-H), 1.99 (dt, $J = 6.7, 6.7$ Hz, 2H; 6-H), 1.60–1.42 (m, 4H; 4-H, 5-H), 1.46 (d, $J = 8.1$ Hz, 2H; 9-H), 0.14 (s, 9H; SiMe₃), 0.02 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): $\delta = 127.1, 125.6$ (C-7, C-8), 107.5 (C-2), 84.29 (C-1), 28.92 (C-H), 26.56 (C-4, C-5, C-6), 19.80 (C-3), 18.46 (C-9), 0.20 (SiMe₃), -1.74 (SiMe₃); IR (Film): $\tilde{\nu} = 3006, 2956, 2902, 2860$ (CH), 2176 (C≡C), 1646 cm⁻¹ (C=C); MS (70 eV, EI): m/z (%): 266 (10) [M]⁺, 193 (3) [$M - SiMe_3$]⁺, 178 (10) [$M - SiMe_3 - CH_3$]⁺, 163 (12), 73 (100) [$SiMe_3$]⁺; C₁₅H₃₀Si₂ (266.58).

9-Trimethylsilyl-non-7-en-1-yne (5b): Deprotection of 1,9-bis-trimethylsilyl-non-7-en-yne was carried out as described for the synthesis of **5a** using K₂CO₃ (4.2 g) in methanol (1000 mL). Distillation of the crude product afforded **5b** (20.40 g, 87% for last two steps) as a colourless liquid. B.p. 60–63 °C (2 mbar); $R_f = 0.47$ (petroleum ether); ¹H NMR (200 MHz, CDCl₃): $\delta = 5.48-5.17$ (m, 2H, 7-H; 8-H), 2.19 (dt, $J = 2.6, 6.9$ Hz, 2H; 4-H), 2.00 (dt, $J = 7.0, 7.0$ Hz, 2H; 6-H), 1.95 (t, $J = 2.6$ Hz, 1H; 1-H), 1.58–1.42 (m, 4H; 4-H, 5-H), 1.46 (d, $J = 8.1$ Hz, 2H; 9-H), 0.00 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): $\delta = 127.0, 125.7$ (C-7, C-8), 84.60 (C-2), 68.13 (C-1), 28.82 (C-6), 28.17 (C-5), 26.47 (C-4), 18.44, 18.31 (C-9, C-3), -1.77 (SiMe₃); IR (Film): $\tilde{\nu} = 3312$ (≡C–H), 3008, 2942, 2862 (CH), 2118 (≡C–H), 1646 cm⁻¹ (C=C); MS (70 eV, EI): m/z (%): 194 (2) [M]⁺, 179 (7) [$M - CH_3$]⁺, 151 (5), 120 (14) [$M - SiMe_3 - H$]⁺, 73 (100) [$SiMe_3$]⁺; elemental analysis calcd (%) for C₁₂H₂₂Si (194.39): C 74.15, H 11.41; found: C 73.85, H 11.25.

General procedure I

Addition of lithiated alkynes to aldehydes: A stirred solution of the alkyne (6.40 mmol) in THF (2 mL) at -78°C was lithiated with *n*BuLi (1.5 M in hexane, 4.27 mL, 6.40 mmol). LiBr (1.2 equiv, 7.68 mmol, 1.5 M in THF) was added at once followed by the dropwise addition of 1.2 equiv aldehyde (7.68 mmol, 1 M in THF). The temperature was kept at -78°C for a further 10 min and then was allowed to reach room temperature. Water (20 mL) was added, the organic layer separated off, and the aqueous phase extracted with Et₂O (4 × 25 mL). The combined extracts were washed with saturated NH₄Cl solution (20 mL) and brine (20 mL), dried (Na₂SO₄), and evaporated in vacuo. Column chromatography afforded the propargylic alcohol in high purity.

1-(2-Bromophenyl)-10-trimethylsilyl-dec-8-en-3-yn-2-ol (1a): Aldehyde **4a** (792 mg, 3.98 mmol) and enyne **5a** (600 mg, 3.25 mmol) were combined according to general procedure I. Column chromatography (petroleum ether/EtOAc 15:1 → 5:1) afforded pure **1a** (294 mg, 0.78 mmol, 24%). $R_f = 0.26$ (petroleum ether/EtOAc 10:1); ¹H NMR (200 MHz, CDCl₃): $\delta = 7.54$ (d, $J = 7.6$ Hz, 1H; 3'-H), 7.35–7.20 (m, 2H, 5'-H; 6'-H), 7.09 (ddd, $J = 8.0, 8.0, 2.0$ Hz, 1H; 4'-H), 5.49–5.30 (m, 1H; 8-H), 5.27, 5.14 (m, 1H; 9-H), 4.66 (brt, $J = 7.2$ Hz, 1H; 2-H), 3.14 (d, $J = 7.2$ Hz, 2H; 1-H), 2.20 (dt, $J = 7.4, 2.0$ Hz, 2H; 5-H), 2.03 (br dt, $J = 7.4, 7.2$ Hz, 2H; 7-H), 1.77 (brs, 1H; OH), 1.53 (tt, $J = 7.4, 7.4$ Hz, 2H; 6-H), 1.44 (d, 8.4 Hz, 2H; 10-H), -0.02 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): $\delta = 136.5$ (C-1'), 132.8 (C-9), 132.2 (C-3'), 128.5 (C-6'), 127.2, 126.44 (C-4', C-5'), 126.2 (C-10), 124.9 (C-2'), 86.50 (C-4), 80.42 (C-3), 62.01 (C-2), 44.59 (C-1), 28.59 (C-6), 26.15 (C-7), 18.52 (C-5), 18.32 (C-10), -1.74 (SiMe₃).

1-(2-Bromophenyl)-11-trimethylsilyl-undec-9-en-4-yn-3-ol (1b): Aldehyde **4b** (511 mg, 2.40 mmol) and enyne **5a** (361 mg, 2.00 mmol) were combined according to general procedure I. Column chromatography (petroleum ether/EtOAc 8:1) afforded pure **1b** (588 mg, 1.49 mmol, 75%). $R_f = 0.22$ (petroleum ether/EtOAc 10:1); ¹H NMR (200 MHz, CDCl₃): $\delta = 7.54$ (d, $J = 7.6$ Hz, 1H; 3'-H), 7.28–7.22 (m, 2H; 5'-H, 6'-H), 7.11–7.01 (m, 1H; 4'-H), 5.57–5.36 (m, 1H; 10-H), 5.32–5.17 (m, 1H; 9-H), 4.41 (dddd, $J = 6.6, 6.6, 1.8, 1.8$ Hz, 1H; 3-H), 2.97–2.87 (m, 2H; 1-H), 2.25 (dt, $J = 1.9, 7.1$ Hz, 2H; 6-H), 2.17–1.94 (m, 4H, 2-H; 8-H), 1.80 (brs, 1H; OH), 1.58 (tt, $J = 7.3, 7.3$ Hz, 2H; 7-H), 1.49 (d, $J = 8.7$ Hz, 2H; 11-H), 0.00 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): $\delta = 140.7$ (C-1'), 132.9, 130.4 (C-3', C-9), 127.1, 126.5, 126.2 (C-10, C-4', C-5'), 124.4 (C-2'), 85.98, 80.95 (C-4,

C-5), 62.04 (C-3), 37.97 (C-2), 31.93 (C-8), 28.72, 26.17 (C-1, C-7), 18.52, 18.32 (C-11, C-6), -1.77 (SiMe₃); IR (Film): $\tilde{\nu} = 3364$ (OH), 3006, 2950, 2864 (CH), 1646 cm⁻¹ (C=C); UV (CH₃CN): λ_{max} (log ϵ) = 195.5 (4.772); MS (70 eV, DCI): m/z (%): 804 (5) [$2M + NH_4$]⁺, 412 (100) [$M + NH_4$]⁺; elemental analysis calcd (%) for C₂₀H₂₉BrOSi (393.44): C 61.01, H 7.43; found: C 60.93, H 7.73.

1-(2-Bromophenyl)-12-trimethylsilyl-dodec-10-en-5-yn-4-ol (1c): Aldehyde **4c** (1.78 g, 7.80 mmol) and enyne **5a** (1.17 g, 6.50 mmol) were combined according to general procedure I. Column chromatography (petroleum ether/EtOAc 10:1) afforded pure **1c** (1.45 g, 3.56 mmol, 55%). $R_f = 0.38$ (petroleum ether/EtOAc 5:1); ¹H NMR (200 MHz, CDCl₃): $\delta = 7.52$ (d, $J = 7.8$ Hz, 1H; 3'-H), 7.27–7.20 (m, 2H; 5'-H, 6'-H), 7.05 (ddd, $J = 8.0, 8.0, 4.5$ Hz, 1H; 4'-H), 5.56–5.35 (m, 1H; 11-H), 5.30–5.15 (m, 1H; 10-H), 4.40 (brs, 1H; 4-H), 2.82–2.73 (m, 2H; 1-H), 2.22 (dt, $J = 2.0, 7.0$ Hz, 2H; 7-H), 1.55 (tt, $J = 7.3, 7.3$ Hz, 2H; 9-H), 1.47 (d, $J = 8.3$ Hz, 2H; 12-H), 0.00 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): $\delta = 141.3$ (C-1'), 132.7 (C-10), 130.2 (C-3'), 127.5, 127.3 (C-4', C-6'), 126.4, 126.2 (C-11, C-5'), 124.4 (C-2'), 85.59, 81.21 (C-5, C-6), 62.45 (C-4), 37.61 (C-3), 35.65 (C-1), 28.71 (C-8), 26.13, 25.44 (C-2, C-9), 18.48, 18.28 (C-7, C-12), -1.77 (SiMe₃); IR (film): $\tilde{\nu} = 3356$ (OH), 3006, 2948, 2864 (CH), 1644 cm⁻¹ (C=C); UV (CH₃CN): λ_{max} (log ϵ) = 195.0 (4.692); MS (70 eV, DCI): m/z (%): 441 (18) [$M + 2NH_4$]⁺, 424 (90) [$M + NH_4$]⁺; elemental analysis calcd (%) for C₂₁H₃₁BrOSi (407.47): C 61.90, H 7.67; found: C 62.13, H 7.80.

1-(2-Bromophenyl)-11-trimethylsilyl-undec-9-en-3-yn-2-ol (1d): Aldehyde **4a** (445 mg, 2.22 mmol) and enyne **5b** (362 mg, 1.86 mmol) were combined according to general procedure I. Column chromatography (petroleum ether/EtOAc 15:1 → 5:1) afforded pure **1d** (476 mg, 1.21 mmol, 65%). $R_f = 0.41$ (petroleum ether/EtOAc 5:1); ¹H NMR (200 MHz, CDCl₃): $\delta = 7.55$ (dd, $J = 8.0, 1.3$ Hz, 1H; 3'-H), 7.36–7.20 (m, 2H; 5'-H, 6'-H), 7.10 (ddd, $J = 7.6, 7.6, 2.0$ Hz, 1H; 4'-H), 5.49–5.30 (m, 1H; 10-H), 5.31–5.10 (m, 1H; 9-H), 4.67 (m, 1H; 2-H), 3.14 (dd, $J = 6.9, 1.7$ Hz, 2H; 1-H), 2.20 (dt, $J = 2.0, 7.0$ Hz, 2H; 5-H), 1.98 (dt, $J = 6.7, 6.7$ Hz, 2H; 8-H), 1.83 (d, $J = 5.0$ Hz, 1H; OH), 1.53–1.30 (m, 4H, 6-H; 7-H), 1.46 (d, $J = 7.8$ Hz, 2H; 11-H), 0.00 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): $\delta = 134.5$ (C-1'), 132.7, 132.2 (C-3', C-9), 128.4 (C-6'), 127.2, 127.0 (C-4', C-5'), 125.7 (C-10), 124.9 (C-2'), 86.49, 80.34 (C-3, C-4), 61.99 (C-2), 44.53 (C-1), 28.90, 28.21 (C-6, C-7), 26.48 (C-8), 18.63, 18.47 (C-5, C-11), -1.76 (SiMe₃); IR (Film): $\tilde{\nu} = 3350$ (OH), 3062, 2936, 2860 (CH), 1646 cm⁻¹ (C=C); UV (CH₃CN): λ_{max} (log ϵ) = 196.0 (4.730); MS (70 eV, DCI): m/z (%): 804 (4) [$2M + NH_4$]⁺, 411 (100) [$M + NH_4$]⁺; elemental analysis calcd (%) for C₂₀H₂₉BrOSi (393.44): C 61.06, H 7.43; found: C 61.36, H 7.40.

1-(2-Bromophenyl)-12-trimethylsilyl-dodec-10-en-4-yn-3-ol (1e): Aldehyde **4b** (1.30 g, 6.10 mmol) and enyne **5b** (988 mg, 5.08 mmol) were combined according to general procedure I. Column chromatography (petroleum ether/EtOAc 10:1) afforded pure **1e** (1.76 g, 4.32 mmol, 85%). $R_f = 0.36$ (petroleum ether/EtOAc 5:1); ¹H NMR (300 MHz, CDCl₃): $\delta = 7.51$ (d, $J = 7.9$ Hz, 1H; 3'-H), 7.26–7.18 (m, 2H; 5'-H, 6'-H), 7.04 (ddd, $J = 7.9, 6.4, 2.6$ Hz, 1H; 4'-H), 5.46–5.35 (m, 1H; 11-H), 5.30–5.21 (m, 1H; 10-H), 4.40 (m, 1H; 3-H), 2.92 (dd, $J = 9.1, 6.8$ Hz, 2H; 1-H), 2.24 (ddd, $J = 6.8, 6.8, 1.9$ Hz, 2H; 6-H), 2.05–1.95 (m, 4H; 2-H, 9-H), 1.77 (d, $J = 5.3$ Hz, 1H; OH), 1.60–1.43 (m, 4H; 7-H, 8-H), 1.46 (brd, $J = 8.6$ Hz, 2H; 12-H), 0.00 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): $\delta = 140.8$ (C-1'), 132.8 (C-10), 130.4, 127.6, 127.4, 127.0, 125.7 (C-11, C-3', C-4', C-5', C-6'), 124.4 (C-2'), 85.93, 80.87 (C-4, C-5), 61.98 (C-3), 37.92 (C-2), 31.89, 28.92, 28.32, 26.47 (C-1, C-2, C-8, C-9), 18.62, 18.43 (C-6, C-12), -1.78 (SiMe₃); MS (70 eV, EI): m/z (%): 406 (3) [M]⁺, 391 (6) [$M - CH_3$]⁺, 317 (41) [$M - SiMe_3 - H$]⁺, 147 (74), 73 (100) [$SiMe_3$]⁺; IR (Film): $\tilde{\nu} = 3344$ (OH), 3006, 2936, 2860 (CH), 2230 (C≡C), 1644 cm⁻¹ (C=C); UV (CH₃CN): λ_{max} (log ϵ) = 194.5 (4.799); elemental analysis calcd (%) for C₂₁H₃₁BrOSi (407.47): C 61.90, H 7.67; found: C 61.92, H 7.81.

1-(2-Bromophenyl)-13-trimethylsilyl-tridec-11-en-5-yn-4-ol (1f): Aldehyde **4c** (1.73 g, 7.62 mmol) and enyne **5b** (1.23 g, 6.35 mmol) were combined according to general procedure I. Column chromatography (petroleum ether/EtOAc 10:1) afforded pure **1f** (2.53 g, 6.00 mmol, 83%). $R_f = 0.27$ (petroleum ether/EtOAc 10:1); ¹H NMR (200 MHz, CDCl₃): $\delta = 7.52$ (d, $J = 7.8$ Hz, 1H; 3'-H), 7.27–7.20 (m, 2H; 5'-H, 6'-H), 7.11–6.90 (m, 1H; 4'-H), 5.48–5.10 (m, 2H; 11-H, 12-H), 4.40 (brs, 1H; 4-H), 2.83–2.70 (m, 2H; 1-H), 2.21 (dt, $J = 1.9, 6.9$ Hz, 2H; 7-H), 1.99 (dt, $J = 6.5, 6.5$ Hz, 2H; 10-H), 1.84–1.70 (m, 4H; 2-H, 3-H), 1.54–1.40 (m, 4H; 8-H, 9-H), 1.46 (d, $J = 8.1$ Hz, 2H; 13-H), 0.00 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): $\delta = 141.4$ (C-1'), 132.7 (C-11), 130.2 (C-3'), 127.5, 127.3, 127.0 (C-4',

C-5', C-6'), 125.7 (C-12), 124.4 (C-2'), 85.67, 81.11 (C-5, C-6), 62.51 (C-4), 37.62 (C-3), 35.68 (C-1), 28.95, 28.35 (C-8, C-9), 26.48, 25.45 (C-2, C-10), 18.62, 18.46 (C-7, C-17), -1.76 (SiMe₃); IR (film): $\bar{\nu}$ = 3354 (OH), 3006, 2938, 2860 (CH), 1644 cm⁻¹ (C=C); UV (CH₃CN): λ_{\max} (log ϵ) = 194.5 (4.789); MS (70 eV, DCI): m/z (%): 438 (100) [M+NH₄]⁺, 360 (40); elemental analysis calcd (%) for C₂₂H₃₃BrOSi (421.50): C 62.69, H 7.89; found: C 62.79, H 7.76.

General procedure II

Intramolecular Heck reaction: A flask was loaded with the Pd catalyst (usually 5 mol% palladium(II) acetate/10 mol% triphenylphosphane or 4 mol% of the palladacycle **11**), 1.0 equiv tetrapropylammoniumbromide, and 4.0 equiv potassium acetate. Then a solution of the cyclisation precursor (1 equiv, 0.05 M in DMF) was added. The stirred mixture was slowly heated and kept at the temperature indicated until the reaction was complete (TLC). Water was added (20 mL mmol⁻¹) and the mixture was extracted with Et₂O. The organic layers were washed with brine and dried (Na₂SO₄). After evaporation of the solvent the residue was purified by column chromatography.

Cyclisation of 1a: Reaction of of **1a** (40 mg) with Pd(OAc)₂/PPh₃ as catalyst according to general procedure II at 80 °C for 4.5 h yielded **2a** (71%) and 3% of one diastereomer of **3a**. The diastereomeric ratio of **2a** was determined to be 1.2:1 by crude NMR spectroscopy.

cis-2a: R_f = 0.29 (petroleum ether/EtOAc 10:1); ¹H NMR (300 MHz, CDCl₃): δ = 7.44–7.37 (m, 1H; 7-H), 7.26–7.20 (m, 1H; 5-H), 7.18–7.10 (m, 2H, 4-H; 6-H), 6.06 (dd, J = 18.5, 4.5 Hz, 1H; $-CH=$), 5.69 (dd, J = 18.5, 1.5 Hz, 1H; $=CH-SiMe_3$), 4.92 (brdd, J = 5.5, 5.5 Hz, 1H; 2-H), 3.66–3.59 (brm, 1H; 2'-H), 3.27 (dd, J = 17.0, 6.0 Hz, 1H; 3-H), 2.89 (d, J = 17.0 Hz, 1H; 3-H), 2.72 (ddd, J = 17.5, 8.5, 6.0 Hz, 1H; 5'-H), 2.56 (ddd, J = 17.5, 8.5, 8.0 Hz, 1H; 5'-H), 1.85–1.78 (m, 1H; 3'-H), 1.77–1.66 (m, 2H; 4'-H), 1.61 (d, J = 5.5 Hz, 1H; OH), -0.02 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): δ = 146.3 (CH=C), 143.8 (C-1'), 143.1 (C-3a), 139.0 (C-7a), 138.3 (C-1), 129.7 ($=CH-SiMe_3$), 127.1 (C-4), 126.6 (C-5), 125.3 (C-7), 124.5 (C-6), 73.84 (C-2), 48.27 (C-2'), 40.93 (C-3), 33.55 (C-3'), 31.30 (C-5'), 22.83 (C-4'), -1.15 (SiMe₃).

trans-2a: R_f = 0.20 (petroleum ether/EtOAc 10:1); ¹H NMR (300 MHz, CDCl₃): δ = 7.40–7.35 (m, 1H; 7-H), 7.23–7.17 (m, 1H; 5-H), 7.23–7.07 (m, 2H, 4-H; 6-H), 5.90 (dd, J = 18.5, 5.5 Hz, 1H; $-CH=$), 5.58 (dd, J = 18.5 Hz, 1.5 Hz, 1H; $=CH-SiMe_3$), 5.03 (brdd, J = 6.5, 6.0 Hz, 1H; 2-H), 3.80–3.73 (brm, 1H; 2'-H), 3.29 (dd, J = 17.0, 6.5 Hz, 1H; 3-H), 2.87 (d, J = 17.0 Hz, 1H; 3-H), 2.77 (ddd, J = 17.5, 8.5, 8.0 Hz, 1H; 5'-H), 2.63 (ddd, J = 17.5, 6.0, 6.0 Hz, 1H; 5'-H), 2.05–1.93 (m, 1H; 3'-H), 1.85–1.76 (m, 1H; 3'-H), 1.73–1.61 (m, 2H; 4'-H), 1.56 (d, J = 6.0 Hz, 1H; OH), -0.09 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): δ = 145.5 (CH=CH), 144.1 (C-1'), 143.4 (C-3a), 138.4 (C-7a), 137.6 (C-1), 129.6 ($=CH-SiMe_3$), 126.8 (C-4), 126.1 (C-5), 125.3 (C-7), 125.0 (C-6), 74.18 (C-2), 48.18 (C-2'), 41.08 (C-3), 34.54 (C-3'), 32.96 (C-5'), 23.38 (C-4'), -1.29 (SiMe₃); IR (film): $\bar{\nu}$ = 3332 (OH), 2952, 2910, 2868 (C-H), 1608 cm⁻¹ (C=C); UV (CH₃CN): λ_{\max} (log ϵ) = 262.0 (4.2361), 270.0 (4.1999), 292.5 (3.7725), 302.5 nm (3.6748); MS (70 eV, EI): m/z (%): 298 (48) [M]⁺, 208 (77) [M-SiMe₃-OH]⁺, 179 (60), 156 (60), 132 (96) [C₉H₉O]⁺, 73 (100) [SiMe₃]⁺; elemental analysis calcd (%) for C₁₉H₂₆Osi (298.50): C 76.45, H 8.78; found: C 76.74, H 8.69.

Cyclisation of 1b: Reaction of of **1b** (150 mg) with Pd(OAc)₂/PPh₃ as catalyst according to general procedure II at 95 °C for 22 h yielded **2b** (66%) and **3b** (4%). The diastereomeric ratio of **2b** was determined as 1.5:1 by crude NMR spectroscopy.

cis-2b: R_f = 0.35 (petroleum ether/EtOAc 5:1); ¹H NMR (300 MHz, CDCl₃): δ = 7.57–7.50 (m, 1H; 8-H), 7.14–7.10 (m, 3H; 5-H, 6-H, 7-H), 6.17 (dd, J = 18.8, 4.9 Hz, 1H; 1'-H), 5.71 (dd, J = 18.8, 1.8 Hz, 1H; 2'-H), 4.92 (dd, J = 6.0, 5.0 Hz, 1H; 2-H), 3.38 (dd, J = 5.2, 5.2 Hz, 1H; 2'-H), 2.87 (ddd, J = 13.6, 7.9, 5.4 Hz, 1H; 4-H), 2.69–2.40 (m, 3H; 4-H, 5'-H, 5'-H), 2.20 (dddd, J = 12.8, 8.0, 5.0, 5.0 Hz, 1H; 3-H), 1.85 (dddd, J = 12.8, 7.5, 6.4, 6.0 Hz, 1H; 3-H), 1.77–1.60 (m, 2H; 4'-H), 1.63–1.50 (m, 2H; 3'-H), 0.10 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): δ = 149.1 (C-1'), 144.2 (C-1'), 137.9 (C-4a), 135.1 (C-1), 132.0 (C-8a), 130.3 (C-2'), 128.7 (C-5), 127.5, 126.3, 125.4 (C-6, C-7, C-8), 68.96 (C-2), 49.81 (C-2'), 33.07, 31.50, 29.80 (C-3, C-4, C-3'), 25.97 (C-5'), 21.68 (C-4'), -1.13 (SiMe₃); IR (film): $\bar{\nu}$ = 3356 (OH), 3010, 2950, 2860 (C-H), 1604 cm⁻¹ (C=C); UV (CH₃CN): λ_{\max} (log ϵ) = 204.5 (sh, 4.339), 254.5 nm (4.156); MS (70 eV, EI): m/z (%): 312 (8) [M]⁺, 294 (48) [M-H₂O]⁺, 220 (100) [M-H₂O-SiMe₃-H]⁺, 73 (74)

[SiMe₃]⁺; elemental analysis calcd (%) for C₂₀H₂₈Osi (312.53): C 76.86, H 9.03; found: C 76.69, H 9.12.

trans-2b: R_f = 0.26 (petroleum ether/EtOAc 5:1); ¹H NMR (300 MHz, CDCl₃): δ = 7.40–7.30 (m, 1H; 8-H), 7.07–7.00 (m, 3H; 5-H, 6-H, 7-H), 5.53 (dd, J = 18.8, 6.7 Hz, 1H; 1'-H), 5.27 (dd, J = 18.8, 1.1 Hz, 1H; 2'-H), 4.93 (dd, J = 5.2, 5.2 Hz, 1H; 2-H), 3.80 (m, 1H; 2'-H), 2.83–2.70 (m, 2H; 4-H, 5'-H), 2.62–2.40 (m, 2H; 4-H, 5'-H), 2.24–2.10 (m, 1H; 3-H), 2.02–1.90 (m, 1H; 3-H), 1.84–1.50 (m, 4H; 3'-H, 4'-H), -0.21 (s, 9H; SiMe₃); ¹³C NMR (126 MHz, CDCl₃): δ = 147.3 (C-1'), 142.3 (C-1'), 138.4 (C-4a), 134.9 (C-1), 131.8 (C-8a), 129.5, 128.8 (C-5, C-2'), 127.1, 126.4, 125.3 (C-6, C-7, C-8), 69.16 (C-2), 48.84 (C-2'), 34.59 (C-3), 32.20, 31.95 (C-4, C-3'), 25.89, 24.03 (C-4', C-5'), -1.47 (SiMe₃); IR (film): $\bar{\nu}$ = 3364 (OH), 3018, 2952, 2866 (C-H), 1608 cm⁻¹ (C=C); UV (CH₃CN): λ_{\max} (log ϵ) = 194.0 (4.459), 252.0 nm (3.755); MS (70 eV, EI): m/z (%): 312 (10) [M]⁺, 294 (29) [M-H₂O]⁺, 220 (100) [M-H₂O-SiMe₃-H]⁺, 146 (56), 73 (96) [SiMe₃]⁺; HRMS: calcd for C₂₀H₂₈Osi: 312.53, found 312.1909 [M]⁺.

Cyclisation of 1c: Reaction of of **1c** (200 mg) with the palladacycle **11** as catalyst according to general procedure II at 130 °C for 21 h yielded 43% of **2c** and 3% of one diastereomer of **3c**. The diastereomeric ratio of **2c** was determined as 2.6:1 by crude NMR spectroscopy.

cis-2c: R_f = 0.29 (CH₂Cl₂/petroleum ether 2:1); ¹H NMR (300 MHz, CDCl₃): δ = 7.19–7.02 (m, 4H; 1-H, 2-H, 3-H, 4-H), 6.00 (dd, J = 18.7, 6.2 Hz, 1H; 1'-H), 5.48 (dd, J = 18.7, 1.5 Hz, 1H; 2'-H), 4.79–4.75 (m, 1H; 6-H), 2.71 (brs, 1H; 2'-H), 2.66–2.59 (m, 2H; 9-H), 2.58–2.40 (m, 1H; 5'-H), 2.37 (ddd, J = 17.0, 8.5, 8.5 Hz, 1H; 5'-H), 2.05–1.90 (m, 1H; 7-H), 1.87–1.60 (m, 5H; 8-H, 8-H, 4'-H, 4'-H, 7-H), 1.65–1.50 (m, 2H; 3'-H), 0.07 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): δ = 149.6 (C-1'), 141.0, 140.7, 138.0, 136.4 (C-4a, C-5, C-9a, C-1'), 131.4 (C-2'), 128.5, 128.2, 127.4, 125.3 (C-1, C-2, C-3, C-4), 69.20 (C-6), 49.95 (C-2'), 35.83, 35.50 (C-7, C-9), 33.18, 28.48, 22.54, 21.80 (C-8, C-3', C-4', C-5'), -1.21 (SiMe₃); IR (Film): $\bar{\nu}$ = 3404 (OH), 3016, 2950, 2867 (CH), 1666, 1608 cm⁻¹ (C=C); UV (CH₃CN): λ_{\max} (log ϵ) = 233.0 (sh, 3.851); MS (70 eV, EI): m/z (%): 326 (43) [M]⁺, 308 (14) [M-H₂O]⁺, 235 (42) [M-H₂O-SiMe₃]⁺, 234 (54) [M-H₂O-SiMe₃]⁺, 184 (62), 73 (100) [SiMe₃]⁺; elemental analysis calcd for C₂₁H₃₀Osi (326.56): C 77.24, H 9.26; found: C 77.11, H 9.03.

trans-2c: R_f = 0.16 (CH₂Cl₂/petroleum ether 2:1); ¹H NMR (300 MHz, CDCl₃): δ = 7.15–7.04 (m, 4H; 1-H, 2-H, 3-H, 4-H), 5.40 (dd, J = 18.4, 7.9 Hz, 1H; 1'-H), 4.76 (brs, 1H; 6-H), 4.73 (dd, J = 18.4, 1.2 Hz, 1H; 2'-H), 3.37–3.29 (m, 1H; 2'-H), 2.65–2.50 (m, 3H; 9-H, 9-H, 5'-H), 2.42–2.29 (m, 1H; 5'-H), 2.12–2.03 (m, 1H; 7-H), 1.85–1.67 (m, 5H; 8-H, 8-H, 4'-H, 4'-H, 7-H), 1.60–1.51 (m, 2H; 3'-H), -0.17 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): δ = 146.1 (C-1'), 141.4, 141.3, 138.2, 137.0 (C-4a, C-5, C-9a, C-1'), 130.4 (C-2'-H), 128.8, 127.3, 127.2, 126.1 (C-1, C-2, C-3, C-4), 69.19 (C-6), 49.06 (C-2'), 36.98, 35.91 (C-7, C-9), 32.91, 30.18, 24.66, 21.56 (C-8, C-3', C-4', C-5'), -1.21 (SiMe₃); IR (film): $\bar{\nu}$ = 3404 (OH), 3014, 2948, 2932, 2862 (CH), 1610 cm⁻¹ (C=C); UV (CH₃CN): λ_{\max} (log ϵ) = 234.0 (sh, 3.877); MS (70 eV, EI): m/z (%): 326 (56) [M]⁺, 308 (32) [M-H₂O]⁺, 254 (47) [M-C₃H₈Si]⁺, 236 (94) [M-C₃H₈Si-H₂O]⁺, 235 (62) [M-H₂O-SiMe₃]⁺, 234 (84) [M-H₂O-SiMe₃]⁺, 184 (54), 160 (97), 73 (100) [SiMe₃]⁺; HRMS: calcd for C₂₁H₃₀Osi: 326.2066, found 326.2065 [M]⁺.

Cyclisation of 1d: Reaction of of **1d** (50 mg) with Pd(OAc)₂/PPh₃ as catalyst according to general procedure II at 80 °C for 15 h yielded **2d** (62%) and one diastereomer of **3d** (8%). The diastereomeric ratio of **3d** was determined as 4.5:1 by crude NMR spectroscopy.

cis-2d: R_f = 0.31 (petroleum ether/CH₂Cl₂ 2:1); ¹H NMR (300 MHz, CDCl₃): δ = 7.48–7.44 (m, 1H; 7-H), 7.33–7.29 (m, 1H; 5-H), 7.20–7.16 (m, 2H; 4-H, 6-H), 6.21 (dd, J = 18.8, 3.8 Hz, 1H; 1'-H), 5.83 (dd, J = 18.8, 2.3 Hz, 1H; 2'-H), 5.12 (d, J = 5.6 Hz, 1H; 2-H), 3.96 (brs, 1H; 2'-H), 3.24 (dd, J = 16.6, 5.6 Hz, 1H; 3-H), 2.86 (d, J = 16.9 Hz, 1H; 3-H), 2.77 (brd, J = 14.7 Hz, 1H; 6'-H), 2.30 (ddd, J = 13.9, 13.9, 4.5 Hz, 1H; 6'-H), 1.96–1.81 (m, 2H; 3'-H, 5'-H), 1.70–1.54 (m, 3H; 3'-H, 4'-H, 4'-H), 1.48–1.35 (m, 1H; 5'-H), 0.10 (s, 9H; SiMe₃); ¹³C NMR (50.3 MHz, CDCl₃): δ = -1.03 (SiMe₃), 21.83, 27.57, 28.67 (C-4', C-5', C-6'), 32.71 (C-3'), 40.76 (C-3), 43.06 (C-2'), 72.81 (C-2), 124.7, 125.7, 126.4, 127.1 (C-4, C-5, C-6, C-7), 131.0 (C-2'), 138.6, 138.8 (C-1, C-7a), 140.6 (C-3a), 144.3 (C-1'), 147.8 (C-1'); IR (KBr): $\bar{\nu}$ = 3328 (OH), 3018, 2930, 2854 (CH), 1640, 1602 cm⁻¹ (C=C); UV (CH₃CN): λ_{\max} (log ϵ) = 204.5 (sh, 4.374), 259.5 (4.231), 290.0 (3.751); MS (70 eV, EI): m/z (%): 312 (40) [M]⁺, 294 (6) [M-H₂O]⁺, 221 (60) [M-H₂O-SiMe₃]⁺, 220 (64) [M-H₂O-SiMe₃]⁺, 179 (56), 73 (100) [SiMe₃]⁺;

elemental analysis calcd for $C_{20}H_{28}OSi$ (312.53): C 76.86, H 9.03; found: C 77.02, H 9.19.

trans-2d: $R_f = 0.25$ (petroleum ether/ CH_2Cl_2 2:1); 1H NMR (300 MHz, $CDCl_3$): $\delta = 7.64$ –7.58 (m, 1H; 7-H), 7.29–7.25 (m, 1H; 5-H), 7.19–7.15 (m, 2H; 4-H, 6-H), 6.09 (dd, $J = 18.8$, 4.2 Hz, 1H; 1'-H), 5.67 (dd, $J = 18.8$, 1.9 Hz, 1H; 2'-H), 5.11 (brd, $J = 6.6$ Hz, 1H; 2-H), 4.22 (brs, 1H; 2'-H), 3.27 (dd, $J = 17.3$, 6.6 Hz, 1H; 3-H), 2.90 (d, $J = 17.3$ Hz, 1H; 3-H), 2.78 (brd, $J = 13.4$ Hz, 1H; 6'-H), 2.22 (ddd, $J = 13.4$, 13.4, 4.2 Hz, 1H; 6'-H), 2.09–1.93 (m, 2H; 3'-H, 5'-H), 1.85–1.57 (m, 3H; 3'-H, 4'-H, 4'-H), 1.52–1.33 (m, 1H; 5'-H), 0.03 (s, 9H; $SiMe_3$); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 147.5$ (C-1'), 144.3, 142.5 (C-3a, C-1'), 139.0, 138.1 (C-1, C-7a), 130.7 (C-2'), 127.1, 126.6, 125.6, 124.7 (C-4, C-5, C-6, C-7), 72.96 (C-2), 42.77 (C-2'), 40.92 (C-3), 32.13 (C-3'), 29.01, 22.21, 21.69 (C-4', C-5', C-6'), –1.13 ($SiMe_3$); IR (KBr): $\tilde{\nu} = 3280$ (OH), 3022, 2930, 2854 (CH), 1642, 1604 cm^{-1} (C=C); UV (CH_3CN): λ_{max} (log ϵ) = 203.0 (sh, 4.410), 261.0 (4.213), 292.5 (3.782); MS (70 eV, EI): m/z (%): 312 (83) [M]⁺, 294 (11) [$M - H_2O$]⁺, 222 (100) [$M - OH - SiMe_3$]⁺, 221 (76) [$M - H_2O - SiMe_3$]⁺, 179 (88), 73 (92) [$SiMe_3$]⁺; HRMS: calcd for $C_{20}H_{28}OSi$: 312.1909, found 312.1909 [M]⁺.

Compound 3d, one diastereomer: $R_f = 0.20$ (CH_2Cl_2 /petroleum ether 2:1); 1H NMR (300 MHz, $CDCl_3$): $\delta = 7.53$ –7.49 (m, 1H; 7-H), 7.33–7.28 (m, 1H; 5-H), 7.21–7.16 (m, 2H; 4-H, 6-H), 6.04 (ddd, $J = 17.3$, 10.5, 4.2 Hz, 1H; 1'-H), 5.23 (ddd, $J = 10.5$, 1.9, 1.9 Hz, 1H; 2'-H), 5.17 (ddd, $J = 17.3$, 1.9, 1.9 Hz, 1H; 2'-H), 5.12 (brd, $J = 5.8$ Hz, 1H; 2-H), 3.96 (brs, 1H; 2'-H), 3.23 (dd, $J = 16.9$, 5.6 Hz, 1H; 3-H), 2.85 (d, $J = 16.9$ Hz, 1H; 3-H), 2.79 (brd, $J = 14.9$ Hz, 1H; 6'-H), 2.34 (ddd, $J = 13.9$, 13.9, 4.5 Hz, 1H; 6'-H), 1.91–1.81 (m, 2H; 3'-H, 5'-H), 1.68–1.53 (m, 3H; 3'-H, 4'-H, 4'-H), 1.49–1.34 (m, 1H; 5'-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 144.3$ (C-1'), 140.3 (C-3a), 140.1 (C-1'), 138.6, 138.5 (C-1, C-7a), 127.2, 126.5, 125.7, 124.8 (C-4, C-5, C-6, C-7), 115.8 (C-2'), 72.80 (C-2), 40.92 (C-2'), 40.70 (C-3), 32.73 (C-3'), 28.54, 27.51, 21.69 (C-4', C-5', C-6'); IR (film): $\tilde{\nu} = 3350$ (OH), 3036, 2926, 2854 (C-H), 1632, 1600 cm^{-1} (C=H); UV (CH_3CN): λ_{max} (log ϵ) = 258.0 (4.029), 289.5 (3.427); MS (70 eV, EI): m/z (%): 240 (58) [M]⁺, 222 (100) [$M - H_2O$]⁺, 207 (24) [$M - H_2O - CH_3$]⁺, 179 (55), 165 (38), 132 (50); HRMS: calcd for $C_{17}H_{20}O$: 240.1514, found 240.1514 [M]⁺.

Cyclisation of 1e: Reaction of **1e** (100 mg) with $Pd(OAc)_2/PPH_3$ as catalyst according to general procedure II at 100 °C for 17 h yielded **2e** (61 %) and one diastereomer of **3e** (18 %). The diastereomeric ratio of **2e** was determined as 9.4:1 by crude NMR spectroscopy.

cis-2e: $R_f = 0.25$ (CH_2Cl_2 /petroleum ether 2:1); 1H NMR (300 MHz, $CDCl_3$): $\delta = 7.31$ (d, $J = 7.5$ Hz, 1H; 8-H), 7.19–7.00 (m, 3H; 5-H, 6-H, 7-H), 6.26 (dd, $J = 19.0$, 4.0 Hz, 1H; 1'-H), 5.83 (dd, $J = 19.0$, 2.3 Hz, 1H; 2'-H), 5.16 (dd, $J = 5.8$, 5.8 Hz, 1H; 2-H), 3.60 (brs, 1H; 2'-H), 2.80 (brd, $J = 13.5$ Hz, 1H; 6'-H), 2.76 (ddd, $J = 15.4$, 5.8, 5.8 Hz, 1H; 4-H), 2.37 (ddd, $J = 15.4$, 9.0, 6.4 Hz, 1H; 4-H), 2.30 (ddd, $J = 15.4$, 6.1, 6.1 Hz, 1H; 3-H), 2.25 (ddd, $J = 13.5$, 13.5, 4.6 Hz, 1H; 6'-H), 1.91–1.80 (m, 1H; 5'-H), 1.82–1.70 (m, 2H; 3-H, 3'-H), 1.57–1.40 (m, 3H; 3-H, 4'-H, 4'-H), 1.35–1.20 (m, 1H; 5'-H), 0.14 (s, 9H; $SiMe_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 150.1$ (C-1'), 140.1, 139.5 (C-4a, C-1'), 134.8, 133.1 (C-1, C-8a), 131.3 (C-2'), 128.6, 127.2, 126.8, 125.3 (C-5, C-6, C-7, C-8), 66.61 (C-2), 45.29 (C-2'), 34.01, 32.67 (C-3, C-3'), 28.64, 26.87, 26.27, 22.31 (C-4, C-4', C-5', C-6'), –1.07 ($SiMe_3$); IR (film): $\tilde{\nu} = 3338$ (OH), 3012, 2926, 2854 (C-H), 1604 cm^{-1} (C=C); UV (CH_3CN): λ_{max} (log ϵ) = 207.0 (sh, 4.359), 252.5 nm (4.124); MS (70 eV, EI): m/z (%): 326 (42) [M]⁺, 308 (45) [$M - H_2O$]⁺, 235 (92) [$M - SiMe_3 - H_2O$]⁺, 234 (100) [$M - SiMe_3 - H_3O$]⁺, 193 (28), 180 (22), 73 (38) [$SiMe_3$]⁺; elemental analysis calcd for $C_{21}H_{30}OSi$ (326.56): C 77.24, H 9.26; found: C 77.13, H 9.17.

Compound 3e, one diastereomer: $R_f = 0.15$ (CH_2Cl_2 /petroleum ether 2:1); 1H NMR (300 MHz, $CDCl_3$): $\delta = 7.36$ (d, $J = 7.0$ Hz, 1H; 8-H), 7.19–7.10 (m, 3H; 5-H, 6-H, 7-H), 6.10 (ddd, $J = 17.7$, 10.5, 4.6 Hz, 1H; 1'-H), 5.28 (ddd, $J = 10.5$, 1.9, 1.9 Hz, 1H; 2'-H), 5.18 (ddd, $J = 17.7$, 1.9, 1.9 Hz, 1H; 2'-H), 5.15 (dd, $J = 5.6$, 5.6 Hz, 1H; 2-H), 3.60 (brs, 1H; 2'-H), 2.82 (brd, $J = 13.6$ Hz, 1H; 6'-H), 2.75 (ddd, $J = 15.4$, 5.8, 5.8 Hz, 1H; 4-H), 2.56 (ddd, $J = 15.1$, 9.1, 6.1 Hz, 1H; 4-H), 2.31 (ddd, $J = 13.6$, 6.1, 6.1 Hz, 1H; 3-H), 2.29 (ddd, $J = 13.6$, 13.6, 4.2 Hz, 1H; 6'-H), 1.92–1.80 (m, 1H; 5'-H), 1.78–1.60 (m, 2H; 3-H, 3'-H), 1.66–1.30 (m, 3H; 3-H, 4'-H, 4'-H), 1.35–1.20 (m, 1H; 5'-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 142.2$ (C-1'), 140.0, 139.6 (C-4a, C-1'), 134.8, 132.9 (C-1, C-8a), 128.7, 127.3, 126.9, 125.4 (C-5, C-6, C-7, C-8), 115.9 (C-2'), 66.64 (C-2), 43.16 (C-2'), 34.21, 32.69 (C-3, C-3'), 28.69, 26.74, 26.30, 22.15 (C-4, C-4', C-5', C-6'); IR (KBr): $\tilde{\nu} = 3278$, 3024, 2992, 2852 (CH), 1630, 1600 cm^{-1} (C=C); UV (CH_3CN): λ_{max} (log ϵ) = 194.0 (4.403),

246.0 nm (3.765); MS (70 eV, EI): m/z (%): 254 (28) [M]⁺, 236 (100) [$M - H_2O$]⁺, 221 (16) [$M - CH_3 - OH$]⁺, 208 (30), 193 (30), 141 (44); HRMS calcd for $C_{18}H_{22}O$: 254.1671, found 254.1670 [M]⁺.

Cyclisation of 1f: Reaction of **1f** (200 mg) with the palladacycle **11** as catalyst according to general procedure II at 130 °C for 21 h yielded **2f** (43 %) and one diastereomer of **3f** (7 %). The diastereomeric ratio of **2f** was determined as 20:1 by crude NMR spectroscopy.

cis-2f $R_f = 0.28$ (CH_2Cl_2 /petroleum ether 2:1); 1H NMR (300 MHz, $CDCl_3$): $\delta = 7.19$ –7.06 (m, 4H; 1-H, 2-H, 3-H, 4-H), 6.08 (dd, $J = 18.9$, 4.2 Hz, 1H; 1'-H), 5.29 (dd, $J = 18.9$, 1.9 Hz, 1H; 2'-H), 5.02 (brs, 1H; 6-H), 2.88 (brs, 1H; 2'-H), 2.81–2.71 (m, 1H; 9-H), 2.67–2.55 (m, 2H, 9H; 6'-H), 2.13 (ddd, $J = 13.5$, 13.5, 4.2 Hz, 1H; 6'-H), 2.08–2.02 (m, 1H; 7-H), 1.96–1.87 (m, 1H; 5'-H), 1.85–1.68 (m, 4H; 7-H, 8-H, 8-H, 3'-H), 1.58–1.48 (m, 2H; 4'-H), 1.42–1.29 (m, 2H; 3'-H, 5'-H), 0.08 (s, 9H; $SiMe_3$); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 149.1$ (C-1'), 141.2 (C-1'), 138.1, 137.0, 137.0 (C-4a, C-5, C-9a), 130.4, 129.8 (C-1, C-2'), 67.05 (C-6), 45.38 (C-2'), 37.66 (C-7), 35.33 (C-9), 33.19 (C-3'), 28.84 (C-6'), 25.82, 22.24, 21.76 (C-8, C-4', C-5'), –1.11 ($SiMe_3$); IR (Film): $\tilde{\nu} = 3432$ (OH), 3014, 2928, 2854 (CH), 1642, 1606 cm^{-1} (C=C); UV (CH_3CN): λ_{max} (log ϵ) = 231.0 (sh, 3.899); MS (70 eV, EI): m/z (%): 340 (27) [M]⁺, 322 (20) [$M - H_2O$]⁺, 307 (6) [$M - H_2O - CH_3$]⁺, 248 (64) [$M - SiMe_3 - H_3O$]⁺, 73 (100) [$SiMe_3$]⁺; elemental analysis calcd for $C_{22}H_{32}OSi$ (340.58): C 77.59, H 9.47; found: C 77.76, H 9.44.

Compound 3f, one diastereomer: $R_f = 0.15$ (CH_2Cl_2 /petroleum ether 2:1); 1H NMR (300 MHz, $CDCl_3$): $\delta = 7.19$ –7.10 (m, 4H; 1-H, 2-H, 3-H, 4-H), 5.92 (ddd, $J = 17.3$, 10.6, 5.0 Hz, 1H; 1'-H), 5.12 (ddd, $J = 10.6$, 1.0, 1.9 Hz, 1H; 2'-H), 5.04 (ddd, $J = 17.3$, 2.0, 2.0 Hz, 1H; 2'-H), 5.00 (brs, 1H; 6-H), 2.91 (brs, 1H; 2'-H), 2.82–2.71 (m, 1H; 9-H), 2.68–2.56 (m, 2H; 9-H, 6'-H), 2.18 (ddd, $J = 13.5$, 13.5, 4.1 Hz, 1H; 6'-H), 2.08–2.00 (m, 1H; 7-H), 1.99–1.90 (m, 1H; 5'-H), 1.84–1.63 (m, 4H; 7-H, 8-H, 8-H, 3'-H), 1.63–1.50 (m, 2H; 4'-H), 1.44–1.31 (m, 2H; 3'-H, 5'-H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 141.6$ (C-1'), 141.2 (C-1'), 138.1 (C-9a), 136.9, 136.9 (C-4a, C-5), 129.9 (C-1), 128.6 (C-2), 127.4 (C-4), 125.9 (C-3), 115.1 (C-1'), 67.02 (C-6), 43.25 (C-2'), 37.57 (C-7), 35.27 (C-9), 33.42 (C-3'), 28.88 (C-6'), 25.76, 22.06, 21.72 (C-8, C-4', C-5'); IR (Film): $\tilde{\nu} = 3414$ (OH), 3012, 2926, 2854 (CH), 1632, 1606 cm^{-1} (C=C); UV (CH_3CN): λ_{max} (log ϵ) = 231.0 (sh, 3.858); MS (70 eV, EI): m/z (%): 268 (38) [M]⁺, 250 (100) [$M - H_2O$]⁺, 207 (38), 186 (35), 91 (82) [C_7H_7]⁺; HRMS: calcd for $C_{19}H_{24}O$: 268.1827, found 268.1827 [M]⁺.

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- [24] Crystal data for compound **2e** ($C_{21}H_{30}OSi$, $M_r = 326.56$): crystal size $0.8 \times 0.8 \times 0.6 \text{ mm}^3$, triclinic, space group $P\bar{1}$, $a = 1126.5(2)$, $b = 1302.2(3)$, $c = 1381.5(3) \text{ pm}$, $\alpha = 79.65^\circ$, $\beta = 77.57^\circ$, $\gamma = 80.96^\circ$, $U = 1932.0(7) \text{ \AA}^3$, $\rho_{\text{calc}} = 1.123 \text{ g cm}^{-3}$, $F(000) = 712$, $\mu = 0.125 \text{ mm}^{-1}$, STOE AED2 diffractometer, $\lambda = 0.71073 \text{ \AA}$, $\theta_{\text{max}} = 25.08^\circ$, 6826 independent reflections and 6779 reflections used for refinement, 423 refined parameters, $R1 = 0.0672$ (observed reflections $[I \geq 2\sigma(I)]$), $wR2 = 0.1498$, residual electron density 0.461 and $-0.483 \text{ e \AA}^{-3}$, direct methods (SHELXL 97), hydrogen atoms calculated. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-168542. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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