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Synthesis of original polycycles containing five-, six- and seven-membered rings through cyclocarbopalladations/C–H activation cascade reactions

Synthèse de polycycles originaux contenant des cycles à 5, 6 et 7 atomes par réactions en cascade de cyclocarbopalladations/activation CH

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ABSTRACT

Different types of starting materials have been designed and their ability to undergo cascade reactions has been investigated. New polycycles containing five-, six-, and seven-membered rings are described via original cascade reactions. The process works via a twofold cyclocarbopalladation followed by C(sp^2)-H or C(sp^3)-H activation. During these cascades, the palladium is moving several times along the carbon structure forming three new C–C bonds and three new cycles.

Mots clés:
Réactions en cascade
Cyclocarbopalladations
Activation CH
Palladium
cycle à 7 atomes
cycle à 5 atomes
dérivé naphthalène

RÉSUMÉ

Différents types de substrats de départ ont été conçus et leur capacité à subir des réactions en cascade a été étudiée. De nouveaux polycyles contenant des cycles à 5, 6 ou 7 atomes ont été synthétisés par des réactions en cascade originales. Le processus fonctionne via une double cyclocarbopalladation suivie d'une activation C(sp^2)-H ou C(sp^3)-H. Au cours de cette cascade, le palladium se déplace plusieurs fois sur la structure en formant trois nouvelles liaisons C–C et trois nouveaux cycles.

1. Introduction

The development of new cyclization reactions has been greatly advanced by the use metal-catalyzed processes called cascade or domino reaction [1]. These processes

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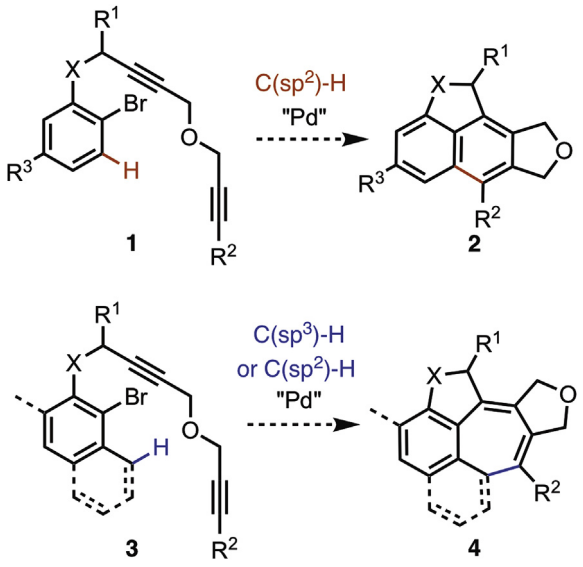
allow a succession of events that are triggered by well-placed functionalities in the structure of the starting material. In this direction, a useful transformation that has been extensively used is the intramolecular carbopalladation of alkynes [2] ended, for example, by a cross-coupling reaction such as Stille [3], Heck–Mizoroki [4], Suzuki–Miyaura [5], or Sonogashira reaction [5], a pericyclic reaction such as electrocyclization [6], or a CO insertion [7]. C–H activation has been also used after cyclocarbopalladations to end cascade reactions, C(sp^2)-H activation was the most common one [8], C(sp^3)-H activation is lightly described in the literature [9]. In this context, to develop novel cyclocarbopalladation/C–H activation cascade reactions, we have designed starting materials of types **1** and **3** (Scheme 1). Depending on the starting material, C(sp^2)-H or C(sp^3)-H activation should finish the cascade process leading to naphthalene derivatives (type **2**) and to original polycycles containing seven-membered rings (type **4**).

2. Carbopalladations/C(sp^2)-H activation cascade reactions

We started our investigations with the diyne **1a** to yield naphthalene derivatives. First, we decided to start our investigations with conditions that are classically used in our laboratory for such type of cascades, $Pd(PPh_3)_4/K_2CO_3$/PhH, at 100 °C under microwave irradiations (Table 1, entry 1). We were pleased to observe the formation of compound **5**, which represents the desilylated derivative of the desired product, in 33% yield. The protodesilylation is probably because of the proton source coming from the in situ formation of protonated base during the cascade process [10]. It is important to note that even if the desilylated compound **5** is obtained, the silyl group on the starting material is necessary to avoid degradation of the reaction mixture



Scheme 1. Synthesis of polycycles containing five- and seven-membered rings.

Table 1
Optimization of the cascade reaction.

Entry	Catalyst (mol %)	Base (equiv)	Time	**1a** (%)	**2a** (%)	**5** (%)
1	$Pd(PPh_3)_4$ (20)	K_2CO_3 (5)	2 h	34	–	33
2	$Pd(PPh_3)_4$ (20)	Et_3N (5)	30 min	–	24	65
3	$Pd(PPh_3)_4$ (20)	$^iPr_2NH$ (5)	30 min	–	25	64
4	$Pd(PPh_3)_4$ (20)	$^iPr_2NH$ (1)	30 min	–	15	80
5	$Pd(PPh_3)_4$ (5)	$^iPr_2NH$ (1)	30 min	–	19	72
6	$Pd(OAc)_2$ (5)/ PPh_3 (10)	$^iPr_2NH$ (1)	30 min	66	8	20

[11]. With an organic base, such as Et_3N and $^iPr_2NH$, the reaction was complete and a separable mixture of **2a** and **5** was obtained (entries 2 and 3). Yields were around 25% and 65% for **2a** and **5**, respectively. By decreasing the amount of base (1 equiv instead of 5), the yield of **5** was improved (80%, entry 4). Finally, the use of less amount of catalyst (5 mol % instead of 20 mol %), gave similar result in terms of yield and ratio between **2a** and **5** (entry 5). When the palladium diacetate/triphenylphosphine system was used, the quantity of compound **5** formed decreased and a large quantity of the starting material was recovered (entry 6). Eventually, the use of $Pd(PPh_3)_4$ (5 mol %) and diisopropylamine in benzene under microwave irradiation proved to be the conditions of choice to obtain **5** in good yield (72%, entry 5, Table 1).

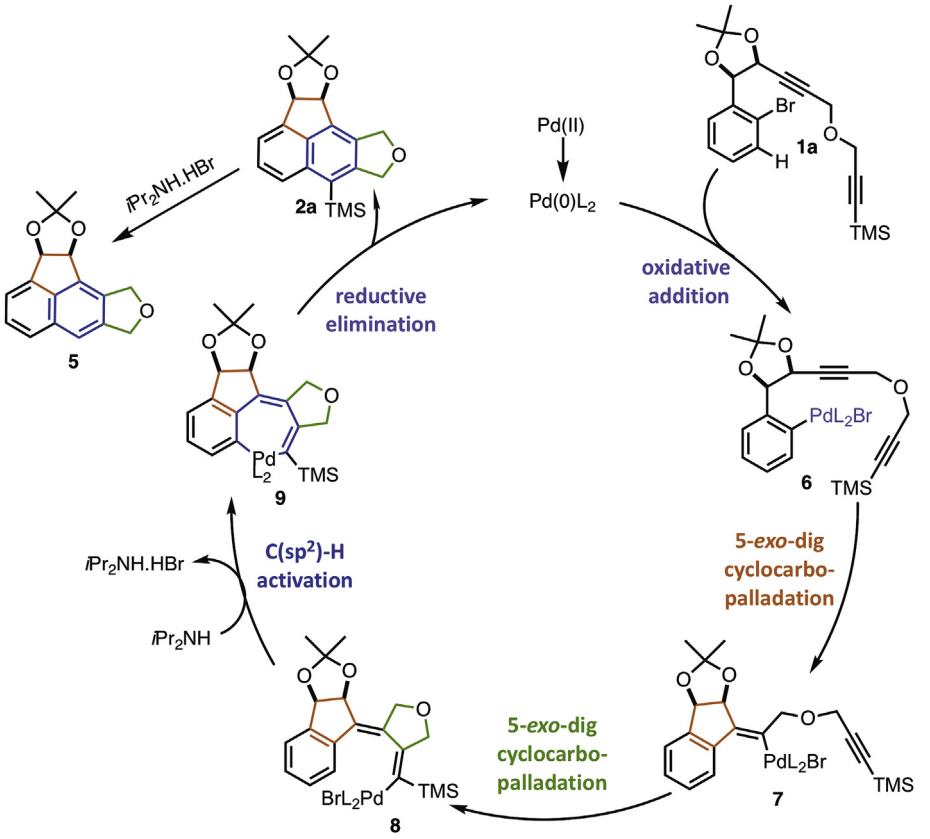
Concerning the formation of compound **5**, we propose the following mechanism (Scheme 2): after oxidative addition of the active palladium species into the C–Br bond of **1a**, a 5-*exo*-dig cyclocarbopalladation gives rise to intermediate **7** which undergoes a 5-*exo*-dig cyclocarbopalladation giving **8**. A C(sp^2)-H activation takes place to provide **9** followed by a reductive elimination leading to silylated compound **2a**. Finally, compound **5** was obtained by protodesilylation of **2a**.

A structural confirmation was obtained by an X-ray crystallographic analysis of compounds **2a** and **5** (Fig. 1).

The scope and limitations of this reaction were next investigated. As summarized in Scheme 3, substrates **1a**–**f** were treated under the optimized conditions to provide the naphthalene derivatives **2a**–**f** and **5** in 6–72% yields. With starting material **1b**, bearing a triethylsilyl group, the optimized conditions also induce a desilylation of the final product leading to a separable mixture of **2b** and **5** in, respectively, 12% and 54% yield. The use of propargyl alcohol derivative **1c** gave the naphthalene derivative **2c** in only poor yield. Almost the same result was observed with the ethyl or the phenyl starting materials **1d**–**f**.

The optimized conditions were applied on phenol derivative **10**, which was synthesized in three steps from the 2-bromophenol (Scheme 4). Only degradation of the starting material was observed. With the system $Pd(OAc)_2/P(OPh)_3/Cs_2CO_3$ in 1,4-dioxane, compound **10** underwent the desired cascade reaction ended by a protodesilylation to afford compound **11** in 65% yield.

To have an access to more challenging polycycles containing seven-membered rings, a similar starting material **3a** was designed in three steps in 69% yield starting from 1-bromonaphthalen-2-ol. Of note, because of the naphthalene moiety, the last step of the cascade reaction should as well be a C(sp^2)-H activation leading to the formation of a



Scheme 2. Proposed catalytic cycle for the formation of **2a** and **5**.

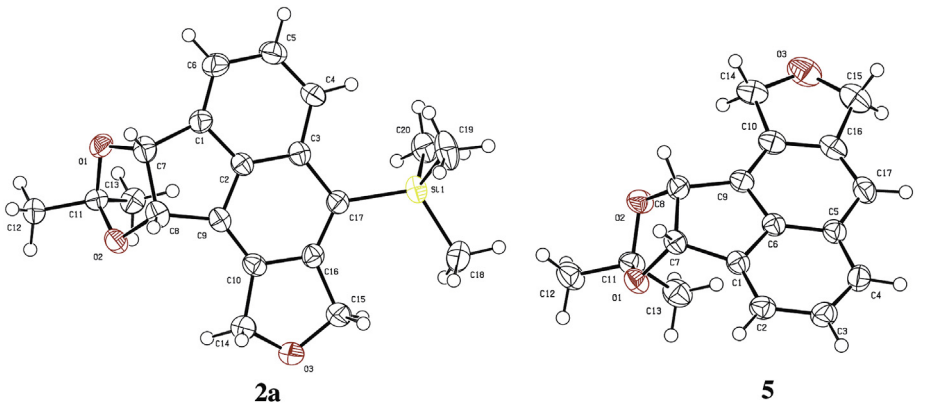
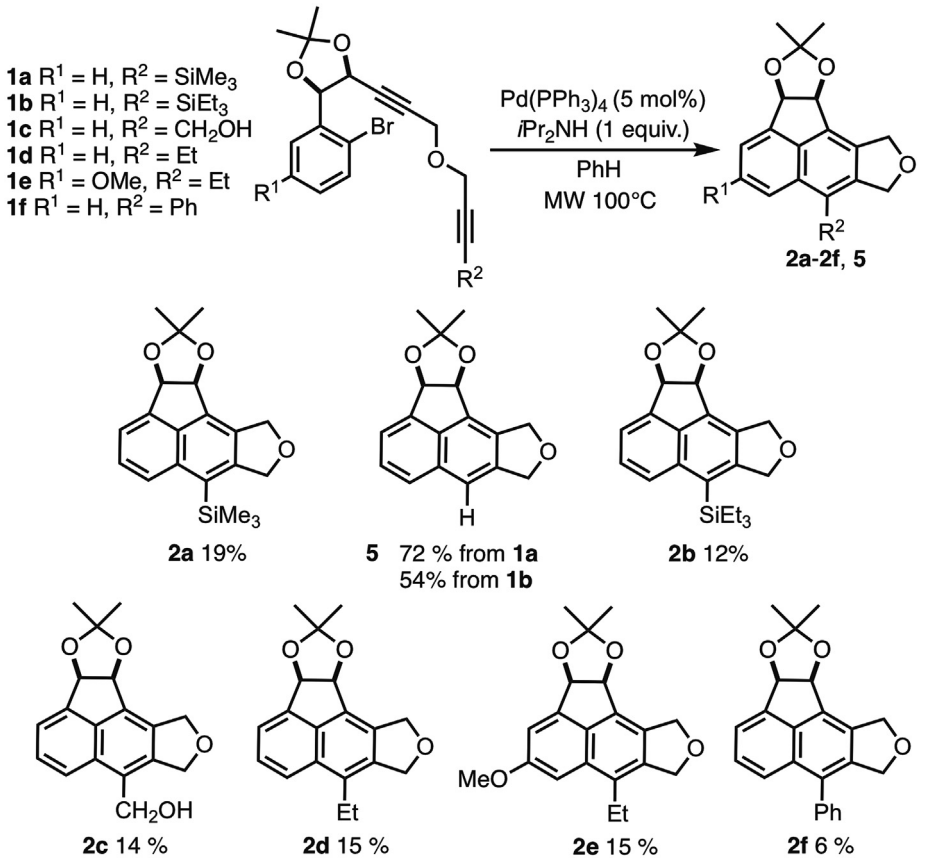


Fig. 1. X-ray crystal analysis of the compounds **2a** and **5**.

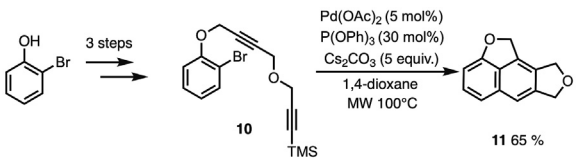
seven-membered ring. Degradation occurred with the use of $Pd(PPh_3)_4$ in PhH/$^iPr_2NH$ (Table 2, entry 1). The catalytic system $Pd(OAc)_2/P(OPh)_3/Cs_2CO_3$ in 1,4-dioxane was the best catalytic system to obtain compound **12** (entries 2–5). Yields were quite similar in toluene or 1,4-dioxane and under microwave irradiation or with an oil bath (15–25%). In one case, it was possible to isolate the desilylated compound **13** (entry 4, 10% yield). The proposed mechanism is similar: a twofold 5-*exo*-dig cyclocarbopalladation ended by a C(sp^2)-H activation. Yields are modest but during this process three carbon–carbon bonds are formed in a single step, and the resulting compounds are original pentacycles containing seven-membered rings.

3. Carbopalladations/C(sp^3)-H activation cascade reactions

Following these investigations, we were interested in an access to other polycycles containing a seven-membered rings. To this purpose, we have designed other compounds



Scheme 3. Scope and limitations.



Scheme 4. Synthesis of naphthalene derivative **11**.

of type **3** (Scheme 1) bearing a methyl group in the *ortho* position to the bromine. One key point of this method is the final C(sp^3)-H activation. Because of structural similitudes between **3b** and the nonmethylated analogue **1a**, the previously reported "optimal" conditions (Table 1) have been used first: $Pd(PPh_3)_4$ (5 mol %) and diisopropylamine in benzene under microwave irradiation (Table 3). No conversion was observed after 3 h (entry 1). With the same conditions in an oil bath instead of microwave irradiation and after 18 h, we observed the formation of compound **14** in 25% yield (entry 2). It seems that during the process the desired compound **4b** undergoes a protodesilylation leading to compound **14**. With $^iPr_2NH$ as solvent, a separable mixture of **4b** and **14** was observed in, respectively, 12% and 19% yield (entry 3).

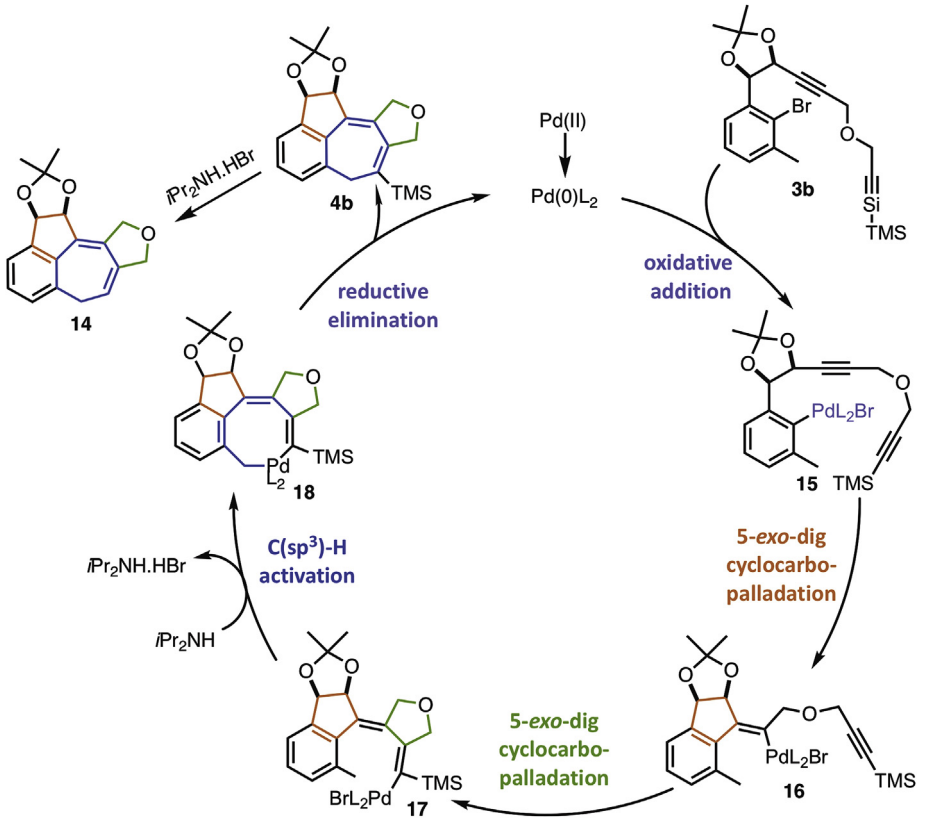
Table 3
Optimization of the cascade reaction from **3b**.

Entry	Solvent	Heating	Time	**3b** (%)	**4b** (%)	**14** (%)
1	PhH	MW	3 h	100	–	–
2	PhH	Δ	18 h	20	Traces	25
3	$^iPr_2NH$	Δ	22 h	–	12	19

Table 2
Optimization of the cascade reaction from **3a**.

Entry	Catalyst	Base/additive	Solvent	Heating	Time	**3a** (%)	**12** (%)	**13** (%)
1	$Pd(PPh_3)_4$ (5)	$^iPr_2NH$[a]	PhH	MW	1.5 h[b]	–	9	–
2	$Pd(OAc)_2$ (15)/$P(OPh)_3$ (30)	Cs_2CO_3 (5)	1,4-Dioxane	MW	30 min	24	15	–
3	$Pd(OAc)_2$ (15)/$P(OPh)_3$ (30)	Cs_2CO_3 (5)	1,4-Dioxane	Δ	30 min	12	25	–
4	$Pd(OAc)_2$ (15)/$P(OPh)_3$ (30)	Cs_2CO_3 (5)	Toluene	Δ	30 min	9	19	10
5	$Pd(OAc)_2$ (15)/$P(OPh)_3$ (30)	Cs_2CO_3 (5)	Toluene	MW	30 min	5	22	–

[a] As cosolvent.
[b] Then 12 h at 100 °C, Δ



Scheme 5. Proposed catalytic cycle for the formation of **4b** and **14**.

Concerning the formation of these two compounds, we propose the following mechanism (Scheme 5): after oxidative addition of the active palladium species into the C—Br bond of **3b**, a 5-*exo*-dig cyclocarbopalladation gives rise to intermediate **16**, which undergoes a 5-*exo*-dig cyclocarbopalladation giving **17**. A C(sp^3)-H activation takes place to provide **18** followed by a reductive elimination leading to silylated compound **4b**. Compound **14** is obtained by protodesilylation.

To the best of our knowledge, this represents the first example of a cascade reaction using carbopalladations/C(sp^3)-H activation allowing the formation of seven-membered rings in a polycyclic scaffold. However, because of modest yields in the seven-membered formation, we decided to design other substrates.

Compound **3c** was synthesized in five steps and 14% yield starting from the commercially available 2,5-dimethylphenol. With compound **3c** in hand, we tried diverse reaction conditions (Table 4). With $Pd(PPh_3)_4$ in PhH/$^iPr_2NH$, mainly degradation occurred, no desired compound **4c** was observed but only 7% of compound **19** (entry 1). After the twofold 5-*exo*-dig cyclocarbopalladation and the C(sp^3)-H activation, the desired compound **4c** undergoes a 1,5-prototropy giving compound **19**. This compound shows a similar skeleton to the natural product malibatol A, which exhibits cytotoxic and human immunodeficiency virus (HIV)-inhibitory activity [12].

Compound **19** was obtained in better yield with $Pd(OAc)_2$/$P(OPh)_3$/Cs_2CO_3 in 1,4-dioxane (40% yield, entry 2). By decreasing the amount of base (entry 3) in toluene instead of 1,4-dioxane (entry 4), with nBu$_4$NCl as additive (entry 5) or with PPh_3 instead of $P(OPh)_3$ (entry 6), the reaction gave compound **19** in lower yield.

A new starting material **3d** was synthesized from 2-bromo-3-methylbenzoic acid in six steps and in 45% yield. This compound could undergo a new cascade

Table 4
Optimization of the cascade reaction from **3c**.

Entry	Catalyst	Base/additive	Solvent	Time	**3c** (%)	**19** (%)
1	$Pd(PPh_3)_4$ (5)	$^iPr_2NH$[a]	PhH	30 min[b]	19	7
2	$Pd(OAc)_2$ (10)/$P(OPh)_3$ (20)	Cs_2CO_3 (5)	1,4-Dioxane	1.5 h	–	40
3	$Pd(OAc)_2$ (10)/$P(OPh)_3$ (20)	Cs_2CO_3 (1, 3)	1,4-Dioxane	1.5 h	14	30
4	$Pd(OAc)_2$ (10)/$P(OPh)_3$ (20)	Cs_2CO_3 (5)	Toluene	1.5 h	–	36
5	$Pd(OAc)_2$ (10)/$P(OPh)_3$ (20)	Cs_2CO_3 (5)/nBu$_4$NCl(1)	Toluene	1.5 h	–	11
6	$Pd(OAc)_2$ (10)/PPh_3 (20)	Cs_2CO_3 (5)	Toluene	30 min	11	28

[a] As cosolvent.
[b] Then 1.5 h at 130 °C.

reaction: a 6-*exo*-dig carbopalladation, followed by a 5-*exo*-dig cyclocarbopalladation and ended by a C(sp^3)-H activation. After a long optimization of the reaction conditions, with the screening of the different ligands (XPhos, dppp, PPh_3, and $P(OPh)_3$), palladium ($Pd(OAc)_2$, PdI_2, Herrmann–Beller catalyst, and $Pd(PPh_3)_4$), solvent (1,4-dioxane, toluene, DMF, DCM, and CH_3CN), base (Cs_2CO_3, K_2CO_3, CsOPiv, and Hünig base), and temperature (85, 100, 130 °C, oil bath, or under microwave irradiation), the best found condition was $Pd(PPh_3)_4$, Cs_2CO_3 in 1,4-dioxane. However, only 10% of the desired compound **21** was formed (Scheme 6). During this optimization, either degradation or starting material is often observed. In some case the intermediate **20** was formed, this later arises from the 6-*exo*-dig cyclocarbopalladation followed by a demetalation. It seems that this substrate is not suitable to undergo the cascade reaction completely.

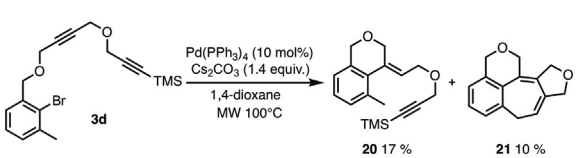
4. Conclusions

In summary, different types of polycyclic molecules were synthesized by the palladium-catalyzed cascade reaction. The cascade cyclocarbopalladations followed by a C(sp^2)-H activation allowed the synthesis of eight fused naphthalenes in 6–72% yield. With cyclocarbopalladations ended by a C(sp^2 or sp^3)-H, we were able to synthesize six polycycles containing one seven-membered ring in 10–40% yield, leading to original scaffolds by using an elegant pathways to get them. During these cascades, the palladium is moving several times along the carbon structure forming three new C–C bonds and three new cycles. Work is currently in progress to increase yields and to design new starting materials that should lead to original scaffolds containing seven-membered ring.

5. Experimental section

5.1. General information

All reagents, chemicals, and dry solvents were purchased from commercial sources and used without purification. Reactions were monitored by thin-layer silica gel chromatography (TLC) using Merck silica gel 60 F254 on aluminum sheets. TLC plates were visualized under UV light and revealed with acidic *p*-anisaldehyde or $KMnO_4$ stain. Crude products were purified by flash column chromatography on Merck silica gel Si 60 (40–63 μm). All NMR spectra were recorded in $CDCl_3$, C_6D_6, or CD_2Cl_2 on a Bruker Avance III 400 MHz $BBFO^+$ probe spectrometer for ^1H NMR and 100 MHz for ^{13}C NMR, and a Bruker Avance 300 MHz dual probe spectrometer for ^1H NMR. Proton chemical shifts are reported in parts per million (ppm) (δ), relatively to residual solvent. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublet (dd), triplet (t), quartet (q), broad singlet (br s), multiplet (m). Coupling constant (J) values are given in hertz (Hz). Carbon chemical shifts are reported in ppm with the respective solvent resonance as the internal standard. ^1H NMR and ^{13}C NMR signals were assigned mostly on the basis of distortionless enhanced polarization transfer (DEPT) and 2D-NMR (correlation spectroscopy [COSY], heteronuclear multiple-bond correlation spectroscopy [HMBC], and heteronuclear multiple-quantum correlation [HMQC]) experiments. High resolution mass spectrometry (HRMS) was performed using an Agilent 1200 rapid resolution liquide chromatographie (RRLC) high performance liquid chromatography (HPLC) chain and an Agilent 6520 accurate mass quadrupole time-of-flight (QToF). Microwave irradiation was carried out with a microwave reactor from Biotage using pressurized vials. Infrared spectra (IR) were recorded on a FT IR Thermo Nicollet ATR 380, diamond spectrometer. Microwave irradiations have been performed using a Biotage Smith Creator apparatus.



Scheme 6. Synthesis of seven-membered ring starting from **3d**.

5.2. Experimental procedures

5.2.1. General procedure A: protection of diols in acetonide

A solution of diol (1 equiv), 2,2-dimethoxypropane (5 equiv) and *p*-TsOH (0.1 equiv) in acetone (0.19 M) was stirred at room temperature for 1 h. The mixture was quenched by addition of brine and extracted with Et_2O. Combined organic layers were washed with water, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was purified by flash column chromatography over silica gel to afford the corresponding acetonide.

5.2.2. General procedure B: deprotection of alkyne

A solution of silylated alkyne (1 equiv) and K_2CO_3 (1 equiv) in MeOH (0.2 M) was stirred at room temperature for 1 h. The mixture was quenched by addition of a saturated solution of NH_4Cl and extracted with EtOAc. Combined organic layers were washed with water, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was purified by flash column chromatography over silica gel to afford the corresponding terminal alkyne.

5.2.3. General procedure C: preparation of propargyl alcohol

A solution of terminal alkyne (1 equiv) and EtMgBr (1 M in THF, 2.5 equiv) in anhydrous THF (0.09 M) was heated at 50 °C and stirred for 30 min. Paraformaldehyde (2.5 equiv) was added and the suspension was stirred at 50 °C for 3.5 h. The mixture was quenched by addition of a saturated solution of NH_4Cl and extracted with Et_2O. Combined organic layers were washed with water, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was purified by flash column chromatography over silica gel to afford the corresponding propargyl alcohol.

5.2.4. General procedure D: biphasic Williamson ether synthesis

To a solution of propargyl alcohol (1 equiv) in CH_2Cl_2 (0.18 M) were added propargyl bromide (80% in toluene,

3.5 equiv), n-Bu_4NHSO_4 (0.1 equiv), and NaOH (0.5 M, 50% aq). The reaction mixture was stirred at room temperature for 2 h and extracted with CH_2Cl_2. Combined organic layers were washed with water, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was purified by flash column chromatography over silica gel to afford the corresponding propargyl ether.

5.2.5. General procedure E: silylation of alkyne

A solution of propargyl ether (1 equiv) and EtMgBr (1 M in THF, 2.5 equiv) in anhydrous THF (0.1 M) was heated at 50 °C and stirred for 1 h. Trimethylsilyl chloride (freshly distilled, 2.5 equiv) was added and the suspension was stirred at 50 °C. The mixture was quenched by addition of a saturated solution of $NaHCO_3$ and extracted with Et_2O. Combined organic layers were washed with water, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was purified by flash column chromatography over silica gel to afford the corresponding silylated compound.

5.2.6. General procedure F: palladocatalyzed cascade reactions 5-exo-dig/C–H activation

A solution of cascade reactions' substrate (1 equiv) and diisopropylamine (1.3 equiv) in benzene (0.1 M) was degassed with argon. $Pd(PPh_3)_4$ (0.05 equiv) was added. The reaction mixture was degassed again and heated at 100 °C under microwave irradiation. The mixture was concentrated in vacuo and purified by flash column chromatography over silica gel to afford the corresponding polycyclic compound.

5.2.6.1. (((4S,5R*)-5-(2-Bromophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethynyl)trimethylsilane (**23**).* Compound **23** (white solid) was prepared following the general procedure A starting from diol **22** [13] (1.995 g, 6.37 mmol).

R_f = 0.74 (Heptane/EtOAc 8:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.66 (dd, ^3J = 7.6 Hz, ^4J = 0.8 Hz, 1H, H-6), 7.51 (dd, ^3J = 7.6 Hz, ^4J = 1.2 Hz, 1H, H-3), 7.34 (br t, ^3J = 7.6 Hz, 1H, H-5), 7.17 (td, ^3J = 7.6 Hz, ^4J = 0.8 Hz, 1H, H-4), 5.49 (d, ^3J = 6 Hz, 1H, H-7), 5.27 (d, ^3J = 6 Hz, 1H, H-8), 1.71 (s, 3H, H-12 or 12′), 1.49 (s, 3H, H-12 or 12′), −0.08 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 136.8 (C-1), 132.1 (C-3), 129.3 (C-4), 128.8 (C-6), 127.1 (C-5), 122.1 (C-2), 110.6 (C-11), 101.4 (C-9), 93.6 (C-10), 79.8 (C-7), 69.7 (C-8), 27.5 (C-12 or 12′), 26.2 (C-12 or 12′), −0.5 (TMS). IR ($CDCl_3$) ν (cm^{-1}) = 2989, 2957, 1246, 1208, 1164, 1061, 1044, 1025, 841, 758. HRMS (ESI, 120 eV) calculated for $C_{16}H_{21}BrO_2Si$ [M] 352.04942, found 352.04991 (Diff.: −1.39 ppm). Mp = 65 °C.

5.2.6.2. (4R,5S*)-4-(2-Bromophenyl)-5-ethynyl-2,2-dimethyl-1,3-dioxolane (**24**).* Terminal alkyne **24** (colorless oil) was prepared following the general procedure B starting from silylated alkyne **23** (1 g, 2.83 mmol).

R_f = 0.46 (Heptane/EtOAc 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.70 (dd, ^3J = 8 Hz, ^4J = 1.6 Hz, 1H, H-6), 7.53 (dd, ^3J = 8 Hz, ^4J = 0.8 Hz, 1H, H-3), 7.36 (td, ^3J = 8 Hz, ^4J = 0.8 Hz, 1H, H-5), 7.19 (td, ^3J = 8 Hz, ^4J = 1.6 Hz, 1H, H-4), 5.48 (d, ^3J = 6 Hz, 1H, H-7), 5.33 (dd, ^3J = 6 Hz, ^4J = 2 Hz, 1H, H-8), 2.20 (d, ^4J = 2 Hz, 1H, H-10), 1.71 (s, 3H, H-12 or 12′), 1.50 (s, 3H, H-12 or 12′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 136.2 (C-1), 132.2 (C-3), 129.5 (C-4), 128.7 (C-6), 127.3 (C-5), 121.9 (C-2), 110.6 (C-11), 79.8 (C-9), 79.6 (C-7), 76.4 (C-10), 69.1 (C-8), 27.6 (C-12 or 12′), 26.3 (C-12 or 12′). IR ($CDCl_3$) ν (cm^{-1}) = 3246, 2993, 2936, 2877, 2117, 1567, 1231, 1161, 1073, 1056, 1046, 1025, 863, 747. HRMS (GC EI, 70 eV) calculated for $C_{13}H_{13}BrO_2$ [$M^{+\cdot}$] 280.00989, found 280.00933 (Diff.: −2 ppm).

5.2.6.3. 3-((4S,5R*)-5-(2-Bromophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-yn-1-ol (**25**).* Propargyl alcohol **25** (colorless oil) was prepared following the general procedure C starting from terminal alkyne **24** (1.5 g, 5.49 mmol).

R_f = 0.17 (Heptane/EtOAc 7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.68 (dd, ^3J = 8 Hz, ^4J = 1.6 Hz, 1H, H-6), 7.54 (dd, ^3J = 8 Hz, ^4J = 0.8 Hz, 1H, H-3), 7.36 (td, ^3J = 7.6 Hz, ^4J = 0.8 Hz, H-5), 7.19 (td, ^3J = 8 Hz, ^4J = 1.6 Hz, 1H, H-4), 5.51 (d, ^3J = 6 Hz, 1H, H-7), 5.35 (dt, ^3J = 6.4 Hz, ^5J = 1.6 Hz, 1H, H-8), 4.02–3.91 (m, 2H, H-13), 1.70 (s, 3H, H-12 or 12′), 1.50 (s, 3H, H-12 or 12′), 0.96 (t, ^3J = 6 Hz, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 136.7 (C-1), 132.3 (C-3), 129.5 (C-4), 128.7 (C-6), 127.1 (C-5), 122.1 (C-2), 110.6 (C-11), 86.6 (C-10), 82.2 (C-9), 79.7 (C-7), 69.3 (C-8), 50.9 (C-13), 27.7 (C-12 or 12′), 26.1 (C-12 or 12′). IR ($CDCl_3$) ν (cm^{-1}) = 3423, 3061, 2886, 2935, 2861, 1569, 1381, 1232, 1067, 1025, 865, 755. HRMS (GC EI, 70 eV) calculated for $C_{14}H_{15}BrO_3$ [$M^{+\cdot}$] 310.02046, found 310.01924 (Diff.: −3.93 ppm).

5.2.6.4. (4R,5S*)-4-(2-Bromophenyl)-2,2-dimethyl-5-(3-(prop-2-yn-1-yloxy)prop-1-yn-1-yl)-1,3-dioxolane (**26**).* Compound **26** (colorless oil) was prepared following the general procedure D starting from propargyl alcohol **25** (449 mg, 1.44 mmol).

R_f = 0.55 (Heptane/Et_2O 7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.69 (dd, ^3J = 8 Hz, ^4J = 1.6 Hz, 1H, H-6), 7.54 (dd, ^3J = 8 Hz, ^4J = 1.2 Hz, 1H, H-3), 7.37 (td, ^3J = 7.6 Hz, ^4J = 1.2 Hz, H-5), 7.18 (td, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1H, H-4), 5.49 (d, ^3J = 6 Hz, 1H, H-7), 5.38 (dt, ^3J = 6 Hz, ^5J = 2 Hz, 1H, H-8), 4.03 (d, ^5J = 2 Hz, 2H, H-13), 3.74 (d, ^4J = 2.4 Hz, 2H, H-14), 2.37 (t, ^4J = 2.4 Hz, 1H, H-16), 1.70 (s, 3H, H-12 or 12′), 1.50 (s, 3H, H-12 or 12′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 136.6 (C-1), 132.3 (C-3), 129.6 (C-4), 128.5 (C-6), 127.3 (C-5), 121.9 (C-2), 110.5 (C-11), 83.3 (C-9 or 10), 83.2 (C-9 or 10), 79.7 (C-7), 79.0 (C-15), 74.8 (C-16), 69.3 (C-8), 56.4 (C-13), 55.9 (C-14), 27.7 (C-12 or 12′), 26.1 (C-12 or 12′). IR ($CDCl_3$) ν (cm^{-1}) = 3293, 3074, 2987, 2936, 2892, 2855, 2196, 2119, 1569, 1471, 1441, 1381, 1338, 1233, 1166, 1123, 1070, 1048, 1027, 866, 756, 669. HRMS (ESI, 120 eV) calculated for $C_{17}H_{17}BrO_3$ [M] 348.03611, found 348.03506 (Diff.: 2.8 ppm).

5.2.6.5. (3-((3-((4S,5R*)-5-(2-Bromophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-yn-1-yl)oxy)prop-1-yn-1-yl)trimethylsilane (**1a**).* Compound **1a** (pale yellow oil) was prepared following the general procedure E starting from compound **26** (313 mg, 0.9 mmol).

R_f = 0.39 (Heptane/Et_2O 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.68 (dd, ^3J = 7.6 Hz, ^4J = 0.8 Hz, 1H, H-6), 7.53 (dd, ^3J = 8 Hz, ^4J = 0.8 Hz, 1H, H-3), 7.36 (br t, ^3J = 7.6 Hz, 1H, H-5), 7.18 (td, ^3J = 8 Hz, ^4J = 1.6 Hz, 1H, H-4), 5.49 (d, ^3J = 6 Hz, 1H, H-7), 5.37 (dt, ^3J = 6 Hz, ^5J = 2 Hz, 1H, H-8), 4.01 (d, ^5J = 2 Hz,

2H, H-13), 3.74 (s, 2H, H-14), 1.70 (s, 3H, H-12 or 12′), 1.50 (s, 3H, H-12 or 12′), 0.18 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 136.6 (C-1), 132.3 (C-3), 129.6 (C-4), 128.6 (C-6), 127.3 (C-5), 121.9 (C-2), 110.5 (C-11), 100.8 (C-15), 91.9 (C-16), 83.5 (C-10), 83.1 (C-9), 79.7 (C-7), 69.3 (C-8), 56.8 (C-14), 56.4 (C-13), 27.7 (C-12 or 12′), 26.2 (C-12 or 12′), −0.04 (TMS). IR ($CDCl_3$) ν (cm^{-1}) = 3066, 2985, 2958, 2892, 2848, 2174, 1570, 1440, 1338, 1233, 1070, 920, 844, 756, 700. HRMS (ESI, 120 eV) calculated for $C_{20}H_{25}BrO_3Si$ [M] 420.07563, found 420.07475 (Diff.: 2.1 ppm).

5.2.6.6. (3-((3-((4S,5R*)-5-(2-Bromophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-yn-1-yl)oxy)prop-1-yn-1-yl)triethylsilane (**1b**).* Compound **1b** (pale yellow oil) was prepared following the general procedure E starting from compound **26** (313 mg, 0.9 mmol).

R_f = 0.34 (Heptane/Et_2O 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.68 (dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1H, H-6), 7.53 (dd, ^3J = 8 Hz, ^4J = 0.8 Hz, 1H, H-3), 7.36 (br t, ^3J = 7.6 Hz, 1H, H-5), 7.17 (td, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1H, H-4), 5.49 (d, ^3J = 6 Hz, 1H, H-7), 5.38 (dt, ^3J = 6 Hz, ^5J = 1.6 Hz, 1H, H-8), 4.03 (d, ^5J = 1.6 Hz, 2H, H-13), 3.75 (s, 2H, H-14), 1.70 (s, 3H, H-12 or 12′), 1.50 (s, 3H, H-12 or 12′), 0.99 (t, ^3J = 8 Hz, 9H, CH_3-TES), 0.60 (q, ^3J = 8 Hz, 6H, CH_2-TES). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 136.6 (C-1), 132.3 (C-3), 129.5 (C-4), 128.6 (C-6), 127.3 (C-5), 121.9 (C-2), 110.5 (C-11), 101.8 (C-15), 89.3 (C-16), 83.6 (C-10), 83.0 (C-9), 79.7 (C-7), 69.4 (C-8), 56.7 (C-13), 56.2 (C-14), 27.7 (C-12 or 12′), 26.2 (C-12 or 12′), 7.6 (CH_3-TES), 4.4 (CH_2-TES). IR ($CDCl_3$) ν (cm^{-1}) = 2985, 2954, 2874, 2848, 1458, 1440, 1372, 1337, 1232, 1165, 1123, 1069, 999, 865, 725. HRMS (GC FI, 10,000 V) calculated for $C_{23}H_{31}BrO_3Si$ [$M^{+\cdot}$] 462.12258, found 462.12162 (Diff.: −2.09 ppm).

5.2.6.7. 4-((3-((4S,5R*)-5-(2-Bromophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-yn-1-yl)oxy)but-2-yn-1-ol (**1c**).* A solution of compound **26** (150 mg, 0.43 mmol, 1 equiv) and EtMgBr (1 M in THF, 1 mL, 1 mmol, 2.5 equiv) in anhydrous THF (5 mL) was heated at 55 °C and stirred for 1 h. Paraformaldehyde (32 mg, 1.1 mmol, 2.5 mmol, 2.5 equiv) was added and the suspension was stirred at 55 °C for 2 h. TLC showed that the reaction was not completed. Paraformaldehyde (10 mg, 0.33 mmol) was added again and the reaction mixture was stirred at room temperature overnight. The mixture was quenched by addition of a saturated solution of NH_4Cl (10 mL) and extracted with Et_2O (3 × 10 mL). Combined organic layers were washed with water, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was purified by flash column chromatography over silica gel (heptane/EtOAc 7:3) to afford the corresponding propargyl alcohol **1c** as a yellow oil.

R_f = 0.26 (Heptane/EtOAc 7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.68 (dd, ^3J = 8 Hz, ^4J = 1.6 Hz, 1H, H-6), 7.53 (dd, ^3J = 8 Hz, ^4J = 1.2 Hz, 1H, H-3), 7.37 (td, ^3J = 7.6 Hz, ^4J = 0.8 Hz, 1H, H-5), 7.19 (td, ^3J = 8 Hz, ^4J = 2 Hz, 1H, H-4), 5.49 (d, ^3J = 6 Hz, 1H, H-7), 5.38 (dt, ^3J = 6 Hz, ^5J = 2 Hz, 1H, H-8), 4.29 (t, ^5J = 1.6 Hz, 2H, H-14), 4.01 (d, ^5J = 1.6 Hz, 2H, H-13), 3.85–3.74 (m, 2H, H-17), 1.70 (s, 3H, H-12 or 12′), 1.56 (br s, 1H, OH), 1.50 (s, 3H, H-12 or 12′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 136.6 (C-1), 132.3 (C-3), 129.5 (C-4), 128.6 (C-6), 127.3 (C-5), 121.9 (C-2), 110.5 (C-11), 85.0 (C-15 or 16), 83.4 (C-10), 83.2 (C-9), 81.3 (C-15 or 16), 79.7 (C-7), 69.4 (C-8), 56.6 (C-13), 56.3 (C-17), 51.3 (C-14), 27.7 (C-12 or 12′), 26.1 (C-12 or 12′). IR ($CDCl_3$) ν (cm^{-1}) = 3422, 3066, 2987, 2933, 2854, 1439, 1373, 1231, 1121, 1067, 1018, 865, 755. HRMS (ESI, 120 eV) calculated for $C_{18}H_{19}BrO_4$ [M] 378.04667, found 378.04712 (Diff.: −1.18 ppm).

5.2.6.8. (4R,5S*)-4-(2-Bromophenyl)-2,2-dimethyl-5-(3-(pent-2-yn-1-yloxy)prop-1-yn-1-yl)-1,3-dioxolane (**1d**).* To a solution of propargyl alcohol **25** (257 mg, 0.82 mmol, 1 equiv) in CH_2Cl_2 (4.6 mL) were added 1-bromopent-2-yne (0.3 mL, 2.9 mmol, 3.6 equiv), n-Bu_4NHSO_4 (28 mg, 0.08 mmol, 0.1 equiv), and NaOH (1.5 mL, 50% aq). The reaction mixture was stirred at room temperature for 2 h and extracted with CH_2Cl_2 (3 × 10 mL). Combined organic layers were washed with water, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was purified by flash column chromatography over silica gel (heptane/Et_2O 96:4) to afford compound **1d** (87%) as a pale yellow oil.

R_f = 0.63 (Heptane/EtOAc 8:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.68 (dd, ^3J = 8 Hz, ^4J = 1.6 Hz, 1H, H-6), 7.53 (dd, ^3J = 8 Hz, ^4J = 1.2 Hz, 1H, H-3), 7.36 (td, ^3J = 7.6 Hz, ^4J = 1.2 Hz, 1H, H-5), 7.18 (td, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1H, H-4), 5.49 (d, ^3J = 6 Hz, 1H, H-7), 5.37 (dt, ^3J = 6 Hz, ^5J = 1.6 Hz, 1H, H-8), 4.00 (d, ^5J = 2 Hz, 2H, H-13), 3.74 (t, ^3J = 2.4 Hz, 2H, H-14), 2.21 (qt, ^3J = 7.6 Hz, ^5J = 2 Hz, 2H, H-17), 1.70 (s, 3H, H-12 or 12′), 1.50 (s, 3H, H-12 or 12′), 1.14 (t, ^3J = 7.2 Hz, 3H, H-18). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 136.6 (C-1), 132.3 (C-3), 129.5 (C-4), 128.6 (C-6), 127.3 (C-5), 121.9 (C-2), 110.5 (C-11), 88.8 (C-16), 83.8 (C-10), 82.8 (C-9), 79.7 (C-7), 74.6 (C-15), 69.4 (C-8), 56.6 (C-14), 56.2 (C-13), 27.7 (C-12 or 12′), 26.2 (C-12 or 12′), 13.9 (C-18), 12.6 (C-17). IR ($CDCl_3$) ν (cm^{-1}) = 2983, 2937, 2853, 2364, 2181, 1971, 1440, 1381, 1233, 1123, 1071, 1027, 866, 754. HRMS (ESI, 120 eV) calculated for $C_{19}H_{21}BrO_3$ [M] 376.06741, found 376.06679 (Diff.: 1.64 ppm).

5.2.6.9. (((4S,5R*)-5-(2-Bromo-5-methoxyphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethynyl)trimethylsilane (**28**).* Acetonide **28** (pale yellow oil) was prepared following the general procedure A starting from diol **27** [13] (1.967 g, 5.73 mmol).

R_f = 0.42 (Heptane/EtOAc 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.39 (d, ^3J = 8.4 Hz, 1H, H-3), 7.23 (d, ^4J = 3.2 Hz, 1H, H-6), 6.73 (dd, ^3J = 8.4 Hz, ^4J = 3.2 Hz, 1H, H-4), 5.44 (d, ^3J = 6 Hz, 1H, H-7), 5.26 (d, ^3J = 6 Hz, 1H, H-8), 3.81 (s, 3H, H-13), 1.70 (s, 3H, H-12 or 12′), 1.49 (s, 3H, H-12 or 12′), −0.07 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 158.9 (C-5), 137.8 (C-1), 132.7 (C-3), 115.1 (C-4), 114.5 (C-6), 112.3 (C-2), 110.7 (C-11), 101.4 (C-9), 93.5 (C-10), 79.8 (C-7), 69.7 (C-8), 55.5 (C-13), 27.6 (C-12 or 12′), 26.3 (C-12 or 12′), −0.49 (TMS). IR ($CDCl_3$) ν (cm^{-1}) = 2988, 2958, 2900, 2179, 1472, 1231, 1066, 844. HRMS (GC EI, 70 eV) calculated for $C_{17}H_{23}BrO_3Si$ [$M^{+\cdot}$] 382.05998, found 382.05961 (Diff.: −0.99 ppm).

5.2.6.10. (4R,5S*)-4-(2-Bromo-5-methoxyphenyl)-5-ethynyl-2,2-dimethyl-1,3-dioxolane (**29**).* Terminal alkyne **29** (white solid) was prepared following the general procedure B starting from silylated alkyne **28** (1.068 g, 2.79 mmol).

R_f = 0.31 (Heptane/EtOAc 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.40 (d, ^3J = 8.8 Hz, 1H, H-3), 7.25 (d, ^4J = 2.8 Hz, 1H, H-6), 6.74 (dd, ^3J = 8.4 Hz, ^4J = 3.2 Hz, 1H, H-4), 5.42 (d, ^3J = 6 Hz, 1H, H-7), 5.31 (dd, ^3J = 6 Hz, ^4J = 2 Hz, 1H, H-8), 3.82 (s, 3H, H-13), 2.23 (d, ^4J = 2.4 Hz, 1H, H-10), 1.70 (s, 3H, H-12 or 12′), 1.49 (s, 3H, H-12 or 12′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 159 (C-5), 137.2 (C-1), 132.8 (C-3), 115.3 (C-4), 114.4 (C-6), 112.1 (C-2), 110.6 (C-11), 79.8 (C-9), 79.6 (C-7), 76.3 (C-10), 69.0 (C-8), 55.6 (C-13), 27.6 (C-12 or 12′), 26.3 (C-12 or 12′). IR ($CDCl_3$) ν (cm^{-1}) = 3292, 2987, 2937, 2837, 1575, 1472, 1228, 1161, 1068, 863. HRMS (GC EI, 70 eV) calculated for $C_{14}H_{15}BrO_3$ [$M^{+\cdot}$] 310.02046, found 310.01832 (Diff.: −6.89 ppm). Mp = 58 °C.

5.2.6.11. 3-((4S,5R*)-5-(2-Bromo-5-methoxyphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-yn-1-ol (**30**).* Propargyl alcohol **30** (pale yellow oil) was prepared following the general procedure C starting from terminal alkyne **29** (760 mg, 2.44 mmol).

R_f = 0.09 (Heptane/EtOAc 7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.41 (d, ^3J = 8.8 Hz, 1H, H-3), 7.25 (d, ^4J = 3.2 Hz, 1H, H-6), 6.75 (dd, ^3J = 8.8 Hz, ^4J = 3.2 Hz, 1H, H-4), 5.46 (d, ^3J = 6 Hz, 1H, H-7), 5.32 (dt, ^3J = 6 Hz, ^5J = 1.6 Hz, 1H, H-8), 4.00 (dd, ^3J = 6 Hz, ^5J = 1.6 Hz, 2H, H-14), 3.82 (s, 3H, H-13), 1.70 (s, 3H, H-12 or 12′), 1.49 (s, 3H, H-12 or 12′), 1.08 (t, ^3J = 6 Hz, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 158.9 (C-5), 137.7 (C-1), 132.8 (C-3), 115.2 (C-4), 114.5 (C-6), 112.4 (C-2), 110.6 (C-11), 86.6 (C-10), 79.7 (C-9), 79.6 (C-7), 69.3 (C-8), 55.7 (C-13), 51.0 (C-14), 27.7 (C-12 or 12′), 26.1 (C-12 or 12′). IR ($CDCl_3$) ν (cm^{-1}) = 3422, 2986, 2937, 2837, 2361, 2337, 1575, 1473, 1297, 1230, 1165, 1068, 864. HRMS (GC EI, 70 eV) calculated for $C_{15}H_{17}BrO_4$ [$M^{+\cdot}$] 340.03102, found 340.03032 (Diff.: −2.05 ppm).

5.2.6.12. (4R,5S*)-4-(2-Bromo-5-methoxyphenyl)-2,2-dimethyl-5-(3-(pent-2-yn-1-yloxy)prop-1-yn-1-yl)-1,3-dioxolane (**1e**).* To a solution of propargyl alcohol **30** (100 mg, 0.29 mmol, 1 equiv) in CH_2Cl_2 (1.6 mL) were added 1-bromopent-2-yne (0.1 mL, 0.98 mmol, 3.3 equiv), *n*-Bu_4NHSO_4 (10 mg, 0.03 mmol, 0.1 equiv), and NaOH (0.5 mL, 50% aq). The reaction mixture was stirred at room temperature for 4 h and extracted with CH_2Cl_2 (3 × 10 mL). Combined organic layers were washed with water, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was purified by flash column chromatography over silica gel (heptane/Et_2O 96:4) to afford compound **1e** (76%) as a pale yellow oil.

R_f = 0.65 (Heptane/EtOAc 8:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.40 (d, ^3J = 8.8 Hz, 1H, H-3), 7.24 (d, ^4J = 2.8 Hz, 1H, H-6), 6.74 (dd, ^3J = 8.8 Hz, ^4J = 3.2 Hz, 1H, H-4), 5.43 (d, ^3J = 6 Hz, 1H, H-7), 5.36 (dt, ^3J = 6 Hz, ^5J = 1.6 Hz, 1H, H-8), 4.03 (d, ^5J = 1.6 Hz, 2H, H-14), 3.82 (s, 3H, H-13), 3.79–3.76 (m, 2H, H-15), 2.20 (qt, ^3J = 7.2 Hz, ^5J = 2.4 Hz, 2H, H-18), 1.70 (s, 3H, H-12 or 12′), 1.50 (s, 3H, H-12 or 12′), 1.13 (t, ^3J = 7.6 Hz, 3H, H-19). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 159.1 (C-5), 137.6 (C-1), 132.9 (C-3), 115.4 (C-4), 114.1 (C-6), 112.2 (C-2), 110.5 (C-11), 88.8 (C-17), 83.7 (C-10), 82.8 (C-9), 79.6 (C-7), 74.6 (C-16), 69.4 (C-8), 56.6 (C-15), 56.3 (C-14), 55.6 (C-13), 27.7 (C-12 or 12′), 26.2 (C-12 or 12′), 13.9 (C-19), 12.6 (C-18). IR ($CDCl_3$) ν (cm^{-1}) = 2987, 2937, 2851, 1575, 1473, 1373, 1297, 1230, 1165, 1124, 1070, 1026, 864. HRMS (ESI, 120 eV) calculated for $C_{20}H_{23}BrO_4$ [M] 406.07797, found 406.07766 (Diff.: 0.77 ppm).

5.2.6.13. (4R,5S*)-4-(2-Bromophenyl)-2,2-dimethyl-5-(3-((3-phenylprop-2-yn-1-yl)oxy)prop-1-yn-1-yl)-1,3-dioxolane (**1f**).* To a solution of propargyl alcohol **25** (157 mg, 0.50 mmol, 1 equiv) in CH_2Cl_2 (2.8 mL) were added (3-chloroprop-1-yn-1-yl)benzene (0.24 mL, 1.7 mmol, 3.5 equiv), *n*-Bu_4NHSO_4 (18 mg, 0.05 mmol, 0.1 equiv), and NaOH (0.9 mL, 50% aq). The reaction mixture was stirred at room temperature for 2 h and extracted with CH_2Cl_2 (3 × 10 mL). Combined organic layers were washed with water, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was purified by flash column chromatography over silica gel (heptane/Et_2O 96:4) to afford compound **1f** (87%) as a yellow oil.

R_f = 0.56 (Heptane/EtOAc 8:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.71 (dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1H, H-6), 7.54 (dd, ^3J = 8 Hz, ^4J = 1.2 Hz, 1H, H-3), 7.45–7.40 (m, 2H, H-18 & 18), 7.37 (td, ^3J = 7.2 Hz, ^4J = 0.8 Hz, 1H, H-5), 7.34–7.30 (m, 3H, H-19 & 19′ & 20), 7.17 (td, ^3J = 8 Hz, ^4J = 2 Hz, 1H, H-4), 5.51 (d, ^3J = 6.4 Hz, 1H, H-7), 5.40 (dt, ^3J = 6.4 Hz, ^5J = 1.6 Hz, 1H, H-8), 4.09 (d, ^5J = 1.6 Hz, 2H, H-13), 3.97 (s, 2H, H-14), 1.71 (s, 3H, H-12 or 12′), 1.51 (s, 3H, H-12 or 12′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 136.7 (C-1), 132.3 (C-3), 131.9 (C-18 & 18′), 129.6 (C-4), 128.7 (C-6), 128.6 (C-20), 128.5 (C-19 & 19′), 127.4 (C-5), 122.7 (C-17), 121.9 (C-2), 110.5 (C-11), 86.7 (C-16), 84.4 (C-15), 83.5 (C-10), 83.2 (C-9), 79.7 (C-7), 69.4 (C-8), 56.7 (C-14), 56.4 (C-13), 27.7 (C-12 or 12′), 26.2 (C-12 or 12′). IR ($CDCl_3$) ν (cm^{-1}) = 2988, 2930, 2851, 1490, 1441, 1380, 1338, 1232, 1165, 1123, 1070, 1027, 866, 755, 691. HRMS (ESI, 120 eV) calculated for $C_{23}H_{21}BrO_3$ [M] 424.06741, found 424.06761 (Diff.: −0.48 ppm).

5.2.6.14. ((3aR,10cS*)-2,2-Dimethyl-3a,8,10,10c-tetrahydrofuro[3′,4′:3,4]acenaphtho[1,2-d][1,3]dioxol-7-yl)trimethylsilane (**2a**) and (3aR*,10cS*)-2,2-dimethyl-3a,8,10,10c-tetrahydrofuro[3′,4′:3,4]acenaphtho[1,2-d][1,3]dioxole (**5**).* Compounds **2a** and **5** were obtained in a separable mixture (91%, ratio **2a/5** 21:79) and were prepared following the general procedure F starting from substrate **1a** (51 mg, 0.11 mmol).

Compound **2a** (white solid): R_f = 0.17 (heptane/Et_2O 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.98 (dd, ^3J = 7.6 Hz, ^4J = 1.2 Hz, 1H, H-4), 7.48 (m, 2H, H-5 & 6), 5.87 (d, ^3J = 6 Hz, 1H, H-7), 5.79 (d, ^3J = 6 Hz, 1H, H-8), 5.35–5.24 (m, 4H, H-13 & 14), 1.47 (s, 3H, H-12 or 12′), 1.09 (s, 3H, H-12 or 12′), 0.42 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 148.0 (C-15), 141.3 (C-1), 136.6 (C-2), 135.4 (C-3), 134.1 (C-9), 133.3 (C-10), 128.2 (C-16), 127.7 (C-5 or 6), 126.6 (C-4), 121.3 (C-5 or 6), 112.9 (C-11), 82.5 (C-7), 81.1 (C-8), 74.4 (C-13 or 14), 70.7 (C-13 or 14), 27.4 (C-12 or 12′), 25.9 (C-12 or 12′), 1.9 (TMS). IR ($CDCl_3$) ν (cm^{-1}) = 3065, 2976, 2937, 2851, 1459, 1371, 1251, 1204, 1079, 1020, 923, 839, 770. HRMS (GC EI, 70 eV) calculated for $C_{20}H_{24}O_3Si$ [$M^{+\cdot}$] 340.14947, found 340.14955 (Diff.: 0.24 ppm). Mp = 163 °C. CCDC 1509122 contains the supplementary crystallographic data. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/.

Compound **5** (white solid): $R_f = 0.11$ (heptane/Et_2O 9:1). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.76 (dd, $^3J = 7.6$ Hz, $^4J = 1.2$ Hz, 1H, H-4), 7.62 (br s, 1H, H-16), 7.58–7.52 (m, 2H, H-5 & 6), 5.97 (d, $^3J = 6$ Hz, 1H, H-7), 5.89 (d, $^3J = 6$ Hz, 1H, H-8), 5.33 (AB system, $J_{AB} = 13.2$ Hz, $\Delta\sqrt{} = 25.6$ Hz, 2H, H-13), 5.25 (s, 2H, H-14), 1.54 (s, 3H, H-12 or 12′), 1.15 (s, 3H, H-12 or 12′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 141.6 (C-15), 140.6 (C-1), 137.3 (C-2), 134.1 (C-10), 132.8 (C-9), 131.2 (C-3), 128.3 (C-5 or 6), 125.6 (C-4), 121.5 (C-5 or 6), 117.0 (C-16), 112.9 (C-11), 82.8 (C-7), 81.4 (C-8), 72.9 (C-14), 71.3 (C-13), 27.4 (C-12 or 12′), 25.9 (C-12 or 12′). IR ($CDCl_3$) ν (cm^{-1}) = 3057, 2897, 2857, 1469, 1377, 1253, 1202, 1063, 1010, 863, 767. HRMS (GC EI, 70 eV) calculated for $C_{17}H_{16}BrO_3$ [$M^{+\cdot}$] 268.10994, found 268.10897 (Diff.: −3.65 ppm). Mp = 152 °C. CCDC 1509123 contains the supplementary crystallographic data. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/.

5.2.6.15. ((3aR,10cS*)-2,2-dimethyl-3a,8,10,10c-tetrahydrofuro[3′,4′:3,4]acenaphtho[1,2-d][1,3]dioxol-7-yl)triethylsilane (**2b**).* Compounds **2b** and **5** were obtained in a separable mixture (66%, ratio **2a/5** 18:82) and were prepared following the general procedure F starting from substrate **1b** (51 mg, 0.11 mmol).

Compound **2b** (colorless oil): R_f = 0.14 (heptane/Et_2O 9:1). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 8.08 (d, $^3J = 8.1$ Hz, 1H, H-4), 7.57–7.51 (m, 2H, H-6 & 5), 5.94 (d, $^3J = 5.9$ Hz, 1H, H-7), 5.87 (d, $^3J = 5.7$ Hz, 1H, H-8), 5.35–5.25 (m, 4H, H-13 & 14), 1.54 (s, 3H, H-12 or 12′), 1.17 (s, 3H, H-12 or 12′), 1.06–1.00 (m, 6H, CH_2-TES), 0.97–0.92 (m, 9H, CH_3-TES). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 149.4 (C-15), 141.3 (C-1), 136.6 (C-2), 136.0 (C-3), 134.0 (C-9), 133.3 (C-10), 127.7 (C-5), 126.5 (C-4), 126.2 (C-16), 121.3 (C-6), 112.9 (C-11), 82.5 (C-7), 81.1 (C-8), 74.6 (C-14), 70.7 (C-13), 27.4 (C-12 or 12′), 25.9 (C-12 or 12′), 7.8 (TES-CH_3), 5.3 (TES-CH_2). IR ($CDCl_3$) ν (cm^{-1}) = 3070, 2954, 2935, 2909, 2874, 1459, 1380, 1371, 1250, 1205, 1078, 1020, 1001, 924, 766, 729, 697. HRMS (GC FI, 10,000 V) calculated for $C_{23}H_{30}O_3Si$ [$M^{+\cdot}$] 382.19642, found 382.19662 (Diff.: 0.52 ppm).

5.2.6.16. ((3aR,10cS*)-2,2-Dimethyl-3a,8,10,10c-tetrahydrofuro[3′,4′:3,4]acenaphtho[1,2-d][1,3]dioxol-7-yl)methanol (**2c**).* Compound **2c** (white solid) was prepared following the general procedure F starting from substrate **1c** (44 mg, 0.11 mmol).

R_f = 0.39 (Heptane/EtOAc 5:5). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 8.04–8.00 (m, 1H, H-4), 7.61–7.58 (m, 2H, H-5 & 6), 5.96 (d, ^3J = 6 Hz, 1H, H-7), 5.85 (d, $^3J = 5.6$ Hz, 1H, H-8), 5.39–5.26 (m, 4H, H-13 & 14), 5.06 (s, 1H, H-17), 1.53 (s, 3H, H-12 or 12′), 1.13 (s, 3H, H-12 or 12′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 141.1 (C-1), 140.5 (C-15), 137.8 (C-2), 134.2 (C-10), 133.0 (C-9), 129.6 (C-3), 128.6 (C-6), 127.7 (C-16), 122.4 (C-4), 121.7 (C-5), 113.0 (C-11), 82.8 (C-7), 81.0 (C-8), 72.4 (C-14), 71.5 (C-13), 59.9 (C-17), 27.4 (C-12 or 12′), 26.0 (C-12 or 12′). IR ($CDCl_3$) ν (cm^{-1}) = 3421, 2985, 2934, 2852, 1726, 1468, 1373, 1254, 1204, 1038, 914, 732. HRMS (GC FI, 10,000 V) calculated for $C_{18}H_{18}O_4$ [$M^{+\cdot}$] 298.12051, found 298.12069 (Diff.: 0.18 ppm).

5.2.6.17. (3aR,10cS*)-7-Ethyl-2,2-dimethyl-3a,8,10,10c-tetrahydrofuro[3′,4′:3,4]acenaphtho[1,2-d][1,3]dioxole (**2d**).* Compound **2d** (white solid) was prepared following the general procedure F starting from substrate **1d** (50 mg, 0.13 mmol).

R_f = 0.21 (Heptane/Et_2O 8:2). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.92–7.87 (m, 1H, H-4), 7.59–7.54 (m, 2H, H-5 & 6), 5.96 (d, ^3J = 6 Hz, 1H, H-7), 5.86 (d, ^3J = 6 Hz, 1H, H-8), 5.35 (AB system, J_{AB} = 13.2 Hz, $\Delta\sqrt{}$ = 26.9 Hz, 2H, H-13), 5.25 (s, 2H, H-14), 3.02–2.88 (m, 2H, H-17), 1.54 (s, 3H, H-12 or 12′), 1.28 (t, ^3J = 7.6 Hz, 3H, H-18), 1.16 (s, 3H, H-12 or 12′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 141.1 (C-1), 138.6 (C-15), 137.9 (C-2), 133.8 (C-10), 132.2 (C-16), 130.5 (C-9), 129.7 (C-3), 127.8 (C-6), 122.2 (C-4), 121.3 (C-5), 112.7 (C-11), 82.8 (C-7), 81.1 (C-8), 72.4 (C-14), 72.0 (C-13), 27.4 (C-12 or 12′), 25.9 (C-12 or 12′), 22.8 (C-17), 14.6 (C-18). IR ($CDCl_3$) ν (cm^{-1}) = 3061, 2967, 2933, 2873, 2848, 1463, 1372, 1252, 1204, 1059, 766. HRMS (ESI, 120 eV) calculated for $C_{19}H_{20}O_3$ [M] 296.14124, found 296.14135 (Diff.: −0.35 ppm).

5.2.6.18. (3aR,10cS*)-7-Ethyl-5-methoxy-2,2-dimethyl-3a,8,10,10c-tetrahydrofuro[3′,4′:3,4]acenaphtho[1,2-d][1,3]dioxole (**2e**).* Compound **2e** (orange solid) was prepared following the general procedure F starting from substrate **1e** (45 mg, 0.11 mmol).

R_f = 0.20 (Heptane/Et_2O 8:2). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.25 (d, $^4J = 2$ Hz, 1H, H-arom), 7.17 (d, $^3J = 2$ Hz, 1H, H-arom), 5.87 (d, $^3J = 6$ Hz, 1H, H-7), 5.84 (d, $^3J = 6$ Hz, 1H, H-8), 5.32 (AB system, J_{AB} = 13.2 Hz, $\Delta\sqrt{}$ = 26.5 Hz, 2H, H-13), 5.23 (s, 2H, H-14), 3.95 (s, 3H, H-19), 2.97–2.83 (m, 2H, H-17), 1.53 (s, 3H, H-12 or 12′), 1.28 (t, ^3J = 7.6 Hz, 3H, H-18), 1.15 (s, 3H, H-12 or 12′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 160.5 (C-5), 142.7 (C-9), 139.4 (C-15), 133.5 (C-2), 131.4 (C-10), 130.9 (C-16), 130.4 (C-3 & 1), 113.5 (C-6), 112.9 (C-11), 102.1 (C-4), 82.5 (C-7), 81.4 (C-8), 72.4 (C-14), 72.0 (C-13), 55.9 (C-19), 27.5 (C-12 or 12′), 26.0 (C-12 or 12′), 22.9 (C-17), 14.2 (C-18). IR ($CDCl_3$) ν (cm^{-1}) = 2965, 2934, 2872, 1760, 1625, 1603, 1458, 1412, 1236, 1202, 1157, 1059, 1040. HRMS (ESI, 120 eV) calculated for $C_{20}H_{22}O_4$ [M] 326.15181, found 326.15304 (Diff.: −3.78 ppm).

5.2.6.19. (3aR,10cS*)-2,2-Dimethyl-7-phenyl-3a,8,10,10c-tetrahydrofuro[3′,4′:3,4]acenaphtho[1,2-d][1,3]dioxole (**2f**).* Compound **2f** was prepared following the general procedure F starting from substrate **1f** (52.3 mg, 0.12 mmol).

R_f = 0.22 (Heptane/Et_2O 8:2). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.74–7.67 (m, 1 ou 2H, H-arom), 7.64 (d, ^3J = 8 Hz, 1H, H-arom), 7.59 (d, ^3J = 8 Hz, 1H, H-arom), 7.55–7.31 (m, 4 ou 5H, H-arom), 6.01 (d, ^3J = 6 Hz, 1H, H-7), 5.93 (d, ^3J = 6 Hz, 1H, H-8), 5.40 (AB system, J_{AB} = 13.2 Hz, $\Delta\sqrt{}$ = 26.0 Hz, 2H, H-13), 5.09 (m, 2H, H-14), 1.57 (s, 3H, H-12 or 12′), 1.22 (s, 3H, H-12 or 12′).

*5.2.6.20. 4-(2-Bromophenoxy)but-2-yn-1-ol (**31**).* To a suspension of K_2CO_3 (2 g, 14.5 mmol, 5 equiv) in acetone (18 mL) was added 2-bromophenol (524 mg, 3.0 mmol, 1.04 equiv) and 4-chlorobut-2-yn-1-ol (0.25 mL, 2.9 mmol, 1 equiv) under argon atmosphere at room temperature. The reaction mixture was refluxed and stirred for 24 h and then quenched

with water (10 mL) and extracted with EtOAc (3 × 10 mL). The organic layers were washed with a saturated aqueous solution of $NaHCO_3$ (2 × 10 mL) and brine (10 mL). The organic layers were then dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (pentane/EtOAc 80:20) to afford compound **31** as an orange oil.

R_f = 0.22 (Pentane/EtOAc 8:2). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.56 (dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1H, H-3), 7.30–7.25 (m, 2H, H-5 & 4), 7.04 (dd, ^3J = 8.4 Hz, ^4J = 1.6 Hz, 1H, H-6), 4.82 (t, ^5J = 2 Hz, 2H, H-7), 4.31 (dt, ^3J = 6.4 Hz, ^5J = 1.6 Hz, 2H, H-10), 1.55 (t, ^3J = 6 Hz, 1H, OH). Spectral data were in accordance with literature data [14].

*5.2.6.21. 1-Bromo-2-((4-(prop-2-yn-1-yloxy)but-2-yn-1-yl) oxy)benzene (**32**).* Compound **32** (yellow oil) was prepared following the general procedure D starting from propargyl alcohol **31** (180 mg, 0.75 mmol).

R_f = 0.21 (Heptane/EtOAc 96:4). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.55 (dd, ^3J = 8 Hz, ^4J = 1.6 Hz, 1H, H-3), 7.30–7.25 (m, 1H, H-5), 7.05 (dd, ^3J = 8 Hz, ^4J = 1.2 Hz, 1H, H-6), 6.89 (td, ^3J = 7.6 Hz, ^4J = 1.2 Hz, 1H, H-4), 4.83 (t, ^5J = 1.6 Hz, 2H, H-7), 4.30 (t, ^5J = 1.6 Hz, 2H, H-10), 4.21 (d, ^4J = 2.4 Hz, 2H, H-11), 2.44 (t, ^4J = 2.4 Hz, 1H, H-13). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 154.2 (C-1), 133.7 (C-3), 128.4 (C-5), 123.0 (C-4), 114.5 (C-6), 112.7 (C-2), 83.3 (C-9), 81.5 (C-8), 78.9 (C-12), 75.3 (C-13), 57.3 (C-7), 56.9 (C-10), 56.7 (C-11). IR ($CDCl_3$) ν (cm^{-1}) = 2959, 2852, 2367, 1478, 1250, 844. HRMS (ESI, 120 eV) calculated for $C_{13}H_{11}BrO_2$ [M] 277.99424, found 277.99404 (Diff.: 0.74 ppm).

*5.2.6.22. (3-((4-(2-Bromophenoxy)but-2-yn-1-yl)oxy)prop-1-yn-1-yl)trimethylsilane (**10**).* Compound **10** (yellow oil) was prepared following the general procedure E starting from propargyl ether **32** (167.5 mg, 0.6 mmol).

R_f = 0.47 (Heptane/EtOAc 9:1). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.55 (dd, ^3J = 8 Hz, ^4J = 1.6 Hz, 1H, H-3), 7.30–7.25 (m, 1H, H-5), 7.05 (dd, ^3J = 8 Hz, ^4J = 1.2 Hz, 1H, H-6), 6.89 (td, ^3J = 7.6 Hz, ^4J = 1.2 Hz, 1H, H-4), 4.83 (t, ^5J = 1.6 Hz, 2H, H-7), 4.28 (t, ^5J = 1.6 Hz, 2H, H-10), 4.20 (s, 2H, H-11), 0.18 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 154.2 (C-1), 133.7 (C-3), 128.5 (C-5), 123.0 (C-4), 114.5 (C-6), 112.7 (C-2), 100.5 (C-12), 92.4 (C-13), 83.5 (C-9), 81.3 (C-8), 57.6 (C-7), 57.3 (C-10), 56.8 (C-11), −0.06 (TMS). IR ($CDCl_3$) ν (cm^{-1}) = 2959, 2852, 2367, 1478, 1250, 844. HRMS (ESI, 120 eV) calculated for $C_{16}H_{19}BrO_2Si$ [M] 350.03377, found 350.03295 (Diff.: 2.33 ppm).

*5.2.6.23. 7,9-Dihydro-1H-naphtho[1,8-bc:6,7-c′]difuran (**11**).* A solution of compound **10** (43 mg, 0.12 mmol, 1 equiv) and Cs_2CO_3 (197 mg, 0.60 mmol, 5 equiv) in 1,4-dioxane (1 mL) was degassed with argon. A solution of $Pd(OAc)_2$ (5 mg, 22 μmol, 0.18 equiv) and $P(OPh)_3$ (9 μL, 36 μmol, 0.30 equiv) in dioxane (1 mL) was then added. The reaction mixture was degassed again and heated for 30 min at 100 °C under microwave irradiation. The mixture was passed through a short Celite pad, concentrated in vacuo, and purified by flash column chromatography over silica gel (pentane/EtOAc 96:4) to afford compound **11** (65%), as a white solid.

Naphthalene 53: R_f = 0.41 (heptane/EtOAc 9:1). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.46 (br s, 1H, H-13), 7.36 (t, ^3J = 8 Hz, 1H, H-5), 7.25–7.19 (m, 1H, H-4), 6.70 (d, ^3J = 7.2 Hz, 1H, H-6), 5.69 (s, 2H, H-7), 5.22 (s, 2H, H-11), 5.1 (s, 2H, H-10). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 161.8 (C_{quat}), 141.9 (C_{quat}), 131.8 (C_{quat}), 130.7 (C_{quat}), 129.8 (C_{quat}), 129.6 (C-5), 128.9 (C_{quat}), 127.8 (C_{quat}), 115.6 (C-4), 115.4 (C_{quat}), 114.7 (C-13), 100.7 (C-6), 76.0 (C-7), 73.0 (C-11), 71.3 (C-10). HRMS (GC EI, 70 eV) calculated for $C_{13}H_{10}O_2$ [$M^{+\cdot}$] 198.06808, found 198.06980 (Diff.: 1.73 mmu).

*5.2.6.24. 4-((1-Bromonaphthalen-2-yl)oxy)but-2-yn-1-ol (**33**).* To a suspension of K_2CO_3 (15 g, 108 mmol, 4.8 equiv) in acetone (144 mL) was added 1-bromo-2-naphthol (5 g, 22 mmol, 1 equiv) and 4-chlorobut-2-yn-1-ol (2.1 mL, 24 mmol, 1.09 equiv) under argon atmosphere at room temperature. The reaction mixture was refluxed and stirred under argon atmosphere for 24 h. The reaction was quenched with water (150 mL) and extracted with EtOAc (3 × 100 mL). The combined organic layer was washed with a saturated solution of $NaHCO_3$ and brine. Then it was dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (heptane/EtOAc 8:2) to afford compound **33** as a white solid.

R_f = 0.21 (Pentane/EtOAc 8:2). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 8.24 (dd, ^3J = 8.4 Hz, ^4J = 0.8 Hz, 1H, H-4), 7.83–7.79 (m, 2H, H-9 & 7), 7.60–7.56 (m, 1H, H-5), 7.45 –7.41 (m, 1H, H-6), 7.37 (d, ^3J = 9.2 Hz, 1H, H-10), 4.94 (t, ^5J = 1.6 Hz, 2H, H-11), 4.30 (dt, ^3J = 6 Hz, ^5J = 1.6 Hz, 2H, H-14), 1.63 (t, ^3J = 6 Hz, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 152.3 (C-1), 133.3 (C-3), 130.7 (C-8), 128.9 (C-9), 128.2 (C-7), 127.9 (C-5), 126.5 (C-4), 125.0 (C-6), 115.9 (C-10), 110.5 (C-2), 86.4 (C-12), 80.6 (C-13), 58.2 (C-11), 51.2 (C-14). IR ($CDCl_3$) ν (cm^{-1}) = 3332, 3063, 2924, 2865, 1624, 1594, 1503, 1464, 1351, 1333, 1267, 1224, 1132, 1049, 1019, 801, 764, 747. HRMS (GC FI, 10,000 V) calculated for $C_{14}H_{11}BrO_2$ [$M^{+\cdot}$] 289.99424, found 289.99327 (Diff.: −3.36 ppm). Mp = 76 °C.

*5.2.6.25. 1-Bromo-2-((4-(prop-2-yn-1-yloxy)but-2-yn-1-yl) oxy)naphthalene (**34**).* Compound **34** (yellow solid) was prepared following the general procedure D starting from propargyl alcohol **33** (543 mg, 1.9 mmol).

R_f = 0.29 (Heptane/EtOAc 9:1). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 8.24 (br dd, ^3J = 8.8 Hz, ^4J = 1.2 Hz, 1H, H-4), 7.83–7.79 (m, 2H, H-9 & 7), 7.60–7.56 (m, 1H, H-5), 7.45 –7.41 (m, 1H, H-6), 7.39 (d, ^3J = 8.8 Hz, 1H, H-10), 4.95 (t, ^5J = 2 Hz, 2H, H-11), 4.30 (t, ^5J = 2 Hz, 2H, H-14), 4.19 (d, ^4J = 2.4 Hz, 2H, H-15), 2.42 (t, ^4J = 2.4 Hz, 1H, H-17). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 152.3 (C-1), 133.3 (C-3), 130.6 (C-8), 128.9 (C-9), 128.2 (C-7), 127.9 (C-5), 126.6 (C-4), 125.0 (C-6), 116.1 (C-10), 110.7 (C-2), 83.4 (C-12 or 13), 81.8 (C-12 or 13), 78.8 (C-16), 75.2 (C-17), 58.3 (C-11), 56.9 (C-14), 56.7 (C-15). IR ($CDCl_3$) ν (cm^{-1}) = 3290, 3064, 2949, 2918, 2898, 2853, 1624, 1594, 1502, 1464, 1348, 1332, 1266, 1223, 1149, 1127, 1079, 1048, 1020, 801, 765, 747, 642, 520, 413. HRMS (ESI, 120 eV) calculated for $C_{17}H_{13}BrO_2$ [M] 328.00989, found 328.01071 (Diff.: −2.49 ppm). Mp = 57 °C.

*5.2.6.26. (3-((4-((1-Bromonaphthalen-2-yl)oxy)but-2-yn-1-yl) oxy)prop-1-yn-1-yl)trimethylsilane (**3a**).* Compound **3a** (colorless oil) was prepared following the general procedure E starting from compound **34** (200 mg, 0.61 mmol).

R_f = 0.46 (Heptane/EtOAc 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 8.24 (br d, ^3J = 8.8 Hz, 1H, H-4), 7.81 (br t, ^3J = 8.8 Hz, 2H, H-9 & 7), 7.60–7.56 (m, 1H, H-5), 7.45–7.41 (m, 1H, H-6), 7.39 (d, ^3J = 8.8 Hz, 1H, H-10), 4.95 (t, ^5J = 2 Hz, 2H, H-11), 4.28 (t, ^5J = 2 Hz, 2H, H-14), 4.19 (s, 2H, H-15), 0.17 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 152.3 (C-1), 133.3 (C-3), 130.6 (C-8), 128.9 (C-9), 128.2 (C-7), 127.9 (C-5), 126.6 (C-4), 124.9 (C-6), 116.1 (C-10), 110.6 (C-2), 100.5 (C-16), 92.4 (C-17), 83.4 (C-12 or 13), 81.8 (C-12 or 13), 58.3 (C-11), 57.6 (C-15), 56.9 (C-14), −0.06 (TMS). IR ($CDCl_3$) ν (cm^{-1}) = 3066, 2958, 2896, 2851, 2225, 2173, 1624, 1595, 1502, 1464, 1349, 1250, 1224, 1126, 1080, 1048, 1020, 1000, 842, 80, 762, 644, 528. HRMS (ESI, 120 eV) calculated for $C_{20}H_{21}BrO_2Si$ [M] 400.04942, found 400.05059 (Diff.: −2.94 ppm).

*5.2.6.27. 3,6-Dihydro-5*H*-1,4-dioxacyclopenta[*h*]naphtho [2,1,8-*cde*]azulen-6-yl(trimethyl)silane (**12**).* A solution of substrate **3a** (49.4 mg, 0.12 mmol, 1 equiv) in 1,4-dioxane (1.5 mL) was degassed. Then $Pd(OAc)_2$ (4.4 mg, 20 μmol, 0.16 equiv), $P(OPh)_3$ (10 μL, 38 μmol, 0.31 equiv), and Cs_2CO_3 (200 mg, 0.61 mmol, 5 equiv) were added. The reaction mixture was degassed again and heated in a sealed tube at 100 °C for 30 min. The mixture was passed through a short Celite pad, concentrated in vacuo, and purified by preparative TLC (UV254) on silica gel (toluene/CH_2Cl_2 9:1) to afford compound **12** as an orange/pink oil.

R_f = 0.44 (Heptane/EtOAc 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.73 (dd, ^3J = 6.8 Hz, ^4J = 0.8 Hz, 1H, H-7), 7.64 (AB system, J_{AB} = 7.2 Hz, $\Delta\sqrt{}$ = 50.7 Hz, 2H, H-9 & 10), 7.44 (s, 1H, H-11), 7.37 (dd, ^3J = 6.8 Hz, ^3J = 6 Hz, 1H, H-6), 5.60 (br d, 1H, H-5), 5.14–5.10 (m, 1H, H-14 or 14′), 4.88 −4.84 (m, 1H, H-14 or 14′), 4.78–4.76 (m, 2H, H-15), 3.40 (s, 1H, H-17), −0.21 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 152.9 (C-1), 138.3 (C-11), 134.6 (C-16), 133.1 (C-4), 131.6 (C-8), 127.5 (C-3), 126.8 (C-7 or 9), 126.7 (C-7 or 9), 125.1 (C-6), 120.8 (C-13 or 2), 120.7 (C-13 or 2), 117.7 (C-12), 112.4 (C-10), 79.8 (C-15), 76.6 (C-14), 39.9 (C-17), −1.77 (TMS). MS (GC EI, 70 eV) 320.04 ([$M^{+\cdot}$], 27%), 72.94 (100%).

*5.2.6.28. 3,6-Dihydro-5*H*-1,4-dioxacyclopenta[*h*]naphtho [2,1,8-*cde*]azulene (**13**).* A solution of substrate **3a** (39 mg, 0.1 mmol, 1 equiv) in toluene (1.25 mL) was degassed. Then $Pd(OAc)_2$ (3.5 mg, 16 μmol, 0.16 equiv), $P(OPh)_3$ (8 μL, 29 μmol, 0.3 equiv), and Cs_2CO_3 (157 mg, 0.48 mmol, 5 equiv) were added. The reaction mixture was degassed again and heated in a sealed tube at 110 °C for 30 min. The mixture was passed through a short Celite pad, concentrated in vacuo, and purified by prep. The crude product was directly purified by flash column chromatography on silica gel (heptane/EtOAc 95:5) to afford compound **13** as an orange oil.

R_f = 0.31 (Heptane/EtOAc 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.85 (d, ^3J = 8 Hz, 1H, H-7), 7.71 (AB system, J_{AB} = 8.8 Hz, $\Delta\sqrt{}$ = 50.4 Hz, 2H, H-9 & 10), 7.52 (s, 1H, H-11), 7.44 (br t, ^3J = 7.6 Hz, 1H, H-6), 7.35 (br dd, ^3J = 7.2 Hz, ^4J = 0.8 Hz, 1H, H-5), 5.05–5.02 (m, 2H, H-14), 4.84–4.82 (m, 2H, H-15), 4.10 (s, 2H, H-17). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 153.2 (C-1), 138.8 (C-11), 132.2 (C-13 & 16), 131.7 (C-8), 131.1 (C-3), 128.1 (C-5), 127.9 (C-7), 126.8 (C-9), 125.2 (C-6), 123.5 (C-4), 119.8 (C-2), 116.8 (C-12), 112.5 (C-10), 79.6 (C-15), 76.6 (C-14), 33.7 (C-17). IR ($CDCl_3$) ν (cm^{-1}) = 2953, 2925, 2849, 1248, 1106, 841. HRMS (GC EI, 70 eV) calculated for $C_{17}H_{12}O_2$ [$M^{+\cdot}$] 248.08373, found 248.08617 (Diff.: 9.82 ppm).

*5.2.6.29. (2-Bromo-3-methylphenyl)methanol (**35**).* A solution of 2-bromo-3-methylbenzoic acid (3.7 g, 17.2 mmol, 1 equiv), 2,2-dimethoxypropane (9 g, 86.3 mmol, 5 equiv), and hydrochloric acid (12 M, 2.9 mL, 34.4 mmol, 2 equiv) in methanol (44 mL) was refluxed overnight. After cooling, the solvent was removed in vacuo. The residue was dissolved in Et_2O and washed with water. Organic extract was dried over Na_2SO_4, filtered, and concentrated in vacuo. Crude product was purified by flash column chromatography over silica gel (heptane/Et_2O 97:3) to give the methyl 2-bromo-3-methylbenzoate (3.3 g, 96%) as a colorless oil.

R_f = 0.37 (Pentane/Et_2O 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.47–7.45 (m, 1H, H-6), 7.34 (ddd, ^3J = 7.6 Hz, ^4J = 2 Hz, ^5J = 0.8 Hz, 1H, H-4), 7.24 (br t, ^3J = 7.6 Hz, 1H, H-5), 3.93 (s, 3H, H-9), 2.46 (s, 3H, H-7). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 167.9 (C-8), 139.9 (C-3), 134.2 (C-1), 133.2 (C-4), 128.0 (C-6), 127.0 (C-5), 123.2 (C-2), 52.6 (C-9), 24.0 (C-7). IR ($CDCl_3$) ν (cm^{-1}) = 2951, 1729, 1433, 1293, 1193, 1142, 1029, 973, 874, 789, 752, 701, 573. MS (GC EI, 70 eV) 227.79 ([$M^{+\cdot}$], 38%), 196.79 (100%), 168.81 (23%), 88.92 (43%).

To a suspension of $LiBH_4$ (10 mg, 0.48 mmol, 1.1 equiv) in THF (0.4 mL) was added the methyl 2-bromo-3-methylbenzoate (100 mg, 0.44 mmol, equiv) in Et_2O (1.3 mL) at 0 °C. The reaction mixture was then stirred at room temperature overnight, quenched with 0.5 M HCl to pH 6–7, and extracted with Et_2O. Combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was purified by flash column chromatography over silica gel (pentane/Et_2O 8:2) to give the (2-bromo-3-methylphenyl) methanol **35** (75 mg, 85%) as a white powder.

R_f = 0.16 (Pentane/Et_2O 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.31–7.29 (m, 1H, H-6), 7.23 (br t, ^3J = 7.6 Hz, 1H, H-5), 7.19 (dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1H, H-4), 4.76 (d, ^3J = 6 Hz, 1H, H-8), 2.43 (s, 3H, H-7), 2.09 (t, ^3J = 6.4 Hz, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 140.2 (C-1), 138.6 (C-3), 130.2 (C-4), 127.3 (C-5), 126.5 (C-6), 125.3 (C-2), 65.9 (C-8), 23.5 (C-7). IR ($CDCl_3$) ν (cm^{-1}) = 3311, 2973, 2918, 2857, 1576, 1452, 1408, 1372, 1349, 1240, 1103, 1056, 1025, 989, 769, 618. HRMS (GC FI, 10,000 V) calculated for C_8H_9BrO [$M^{+\cdot}$] 199.98368, found 199.98480 (Diff.: −5.63 ppm). Mp = 75 °C.

*5.2.6.30. 2-Bromo-3-methylbenzaldehyde (**36**).* A solution of the (2-bromo-3-methylphenyl)methanol **35** (100 mg, 0.49 mmol, 1 equiv), PCC (161 mg, 0.75 mmol, 1.5 equiv), and Celite (0.48 mg) in anhydrous CH_2Cl_2 (4.5 mL) was stirred at room temperature overnight. The mixture was quenched by addition of brine and extracted with Et_2O. Combined organic layers were washed with water, brine,

dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was passed through a silica/Celite plug and concentrated to give **36** (94 mg, 95%) as a white solid.

R_f = 0.57 (Pentane/Et_2O 95:5). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 10.45 (d, ^4J = 0.8 Hz, 1H, H-8), 7.75–7.73 (m, 1H, H-6), 7.48 (ddd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, ^5J = 0.8 Hz, 1H, H-4), 7.32 (br t, ^3J = 7.6 Hz, 1H, H-5), 2.48 (s, 3H, H-7). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) = 192.8 (C-8), 139.7 (C-3), 136.4 (C-4), 134.1 (C-1), 129.7 (C-2), 127.52 (C-5 or 6), 127.45 (C-5 or 6), 23.0 (C-7). IR ($CDCl_3$) ν (cm^{-1}) = 3339, 2982, 2920, 2866, 1889, 1695, 1674, 1573, 1448, 1373, 1237, 1031, 912, 779, 690, 536. HRMS (GC FI, 10,000 V) calculated for C_8H_7BrO [$M^{+\cdot}$] 197.96803, found 197.96767 (Diff.: −1.80 ppm). Mp = 50 °C.

5.2.6.31. (((4S,5R*)-5-(2-Bromo-3-methylphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethynyl)triethylsilane (**38**).* A solution of *n*-butyllithium (1.75 M in hexanes, 1.2 equiv) was added dropwise to a dried round-bottom flask containing the triethyl(3-((2-methoxypropan-2-yl)oxy)prop-1-yn-1-yl)silane (1.2 equiv) in anhydrous THF (1.40 M) at −78 °C. The reaction was stirred for 30 min at −78 °C. A solution of 2-bromo-3-methylbenzaldehyde **36** (2.2 g, 11.05 mmol, 1 equiv.) in anhydrous THF (0.61 M) was then added at −78 °C. The mixture was stirred for 2 h at −78 °C and then quenched by addition of saturated aqueous $NaHCO_3$ solution and water. After extraction with Et_2O, combined organic layers were washed with water, brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure.

Resulting oil was dissolved in methanol (0.35 M) containing PPTS (0.1 equiv). The solution was stirred for 1 h at room temperature and quenched by the addition of brine. The mixture was extracted with Et_2O and combined extract was washed with water, brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The *anti* and *syn* diols **37** compounds were not characterized because of inseparable impurities. Acetonide **38** (pale yellow oil) was prepared following the general procedure A starting from diol **37** (*anti* diol) (51 mg, 0.14 mmol).

R_f = 0.84 (Heptane/EtOAc 8:2). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.50 (dd, ^3J = 7.8 Hz, ^3J = 1.7 Hz, 1H, H-6), 7.22 (br t, ^3J = 7.6 Hz, 1H, H-5), 7.17 (dd, ^3J = 7.6 Hz, ^3J = 2 Hz, 1H, H-4), 5.52 (d, ^3J = 6.2 Hz, 1H, H-8), 5.38 (d, ^3J = 6.1 Hz, 1H, H-9), 2.40 (s, 3H, H-7), 1.71 (s, 3H, H-13 or 13′), 1.50 (s, 3H, H-13 or 13′), 0.76 (br t, ^3J = 8 Hz, 9H, H-15), 0.37–0.31 (m, 6H, H-14). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 137.8 (C-3), 137.3 (C-1), 130.2 (C-4), 126.9 (C-5), 126.2 (C-6), 124.4 (C-2), 110.4 (C-12), 102.6 (C-10), 90.6 (C-11), 80.3 (C-8), 69.8 (C-9), 27.6 (C-13 or 13′), 26.4 (C-13 or 13′), 23.5 (C-7), 7.3 (C-15), 4.1 (C-14). IR ($CDCl_3$) ν (cm^{-1}) = 2986, 2954, 2911, 2875, 1456, 1380, 1233, 1162, 1077, 1023, 864, 768, 726. HRMS (GC FI, 10,000 V) calculated for $C_{20}H_{29}BrO_2Si$ [$M^{+\cdot}$] 408.11202, found 408.10995 (Diff.: −5.08 ppm).

5.2.6.32. (4R,5S*)-4-(2-Bromo-3-methylphenyl)-5-ethynyl-2,2-dimethyl-1,3-dioxolane (**39**).* TBAF (1 M in THF, 5.6 mL, 5.6 mmol, 2.2 equiv) was added dropwise to a cooled solution of compound **38** (1.05 g, 2.57 mmol, 1 equiv) in anhydrous THF (25 mL) at 0 °C. The reaction mixture was stirred 10 min at 0 °C. The mixture was quenched by addition of a saturated aqueous solution of NH_4Cl (30 mL). After extraction with EtOAc (3 × 30 mL), the combined organic layers were washed with water, brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (pentane/Et_2O 99:1) to give compound **39** (88%) as a colorless oil.

R_f = 0.35 (Heptane/EtOAc 97:3). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.54 (dd, ^3J = 7.6 Hz, ^4J = 2 Hz, 1H, H-6), 7.26 (br t, ^3J = 7.2 Hz, 1H, H-5), 7.21 (dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1H, H-4), 5.52 (d, ^3J = 5.9 Hz, 1H, H-8), 5.36 (dd, ^3J = 6 Hz, ^4J = 2.4 Hz, 1H, H-9), 2.43 (s, 3H, H-7), 2.20 (d, ^4J = 2.4 Hz, 1H, H-11), 1.71 (s, 3H, H-13 or 13′), 1.50 (s, 3H, H-13 or 13′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 137.9 (C-3), 136.5 (C-1), 130.5 (C-4), 126.9 (C-5), 126.2 (C-6), 124.4 (C-2), 110.5 (C-12), 80.0 (C-8), 76.2 (C-11), 69.0 (C-9), 27.7 (C-13 or 13′), 26.3 (C-13 or 13′), 23.6 (C-7). IR ($CDCl_3$) ν (cm^{-1}) = 3294, 2986, 2935, 1577, 1454, 1372, 1231, 1160, 1078, 1025, 863, 753, 657. HRMS (GC FI, 10,000 V) calculated for $C_{14}H_{15}BrO_2$ [$M^{+\cdot}$] 294.02554, found 294.02699 (Diff.: 4.92 ppm).

5.2.6.33. 3-((4S,5R*)-5-(2-Bromo-3-methylphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-yn-1-ol (**40**).* Propargyl alcohol **40** (colorless oil) was prepared following the general procedure C starting from terminal alkyne **39** (660 mg, 2.24 mmol).

R_f = 0.38 (Pentane/Et_2O 7:3). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.51 (dd, ^3J = 7.2 Hz, ^4J = 1.6 Hz, 1H, H-6), 7.25 (br t, ^3J = 7.6 Hz, 1H, H-5), 7.20 (dd, ^3J = 7.2 Hz, ^4J = 1.6 Hz, 1H, H-4), 5.56 (d, ^3J = 6 Hz, 1H, H-8), 5.36 (td, ^3J = 6 Hz, ^5J = 2 Hz, 1H, H-9), 4.00–3.91 (m, 2H, H-14), 2.43 (s, 3H, H-7), 1.70 (s, 3H, H-13 or 13′), 1.50 (s, 3H, H-13 or 13′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 138.0 (C-3), 137.0 (C-1), 130.5 (C-4), 126.7 (C-5), 126.1 (C-6), 124.6 (C-2), 110.4 (C-12), 86.5 (C-11), 82.4 (C-10), 80.2 (C-8), 69.2 (C-9), 50.9 (C-14), 29.8 (C-13 or 13′), 27.7 (C-13 or 13′), 23.6 (C-7). IR ($CDCl_3$) ν (cm^{-1}) = 3422, 2985, 2930, 2856, 1453, 1373, 1230, 1128, 1107, 1024, 865, 778. HRMS (GC FI, 10,000 V) calculated for $C_{15}H_{17}BrO_3$ [$M^{+\cdot}$] 324.03611, found 324.03674 (Diff.: 1.96 ppm).

5.2.6.34. (4R,5S*)-4-(2-Bromo-3-methylphenyl)-2,2-dimethyl-5-(3-(prop-2-yn-1-yloxy)prop-1-yn-1-yl)-1,3-dioxolane (**41**).* Compound **41** (colorless oil) was prepared following the general procedure D starting from propargyl alcohol **40** (630 mg, 1.94 mmol).

R_f = 0.24 (Pentane/Et_2O 95:5). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.51 (dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1H, H-6), 7.26 (br t, ^3J = 7.6 Hz, 1H, H-5), 7.20 (dd, ^3J = 7.2 Hz, ^4J = 1.2 Hz, 1H, H-4), 5.54 (d, ^3J = 6 Hz, 1H, H-8), 5.41 (dt, ^3J = 6 Hz, ^5J = 1.6 Hz, 1H, H-9), 4.07–3.98 (m, 2H, H-14), 3.70 (doublet of AB system, J_{AB} = 16 Hz, ^5J = 2.4 Hz, $\Delta\sqrt{}$ = 9 Hz, 2H, H-15), 2.43 (s, 3H, H-7), 2.36 (t, ^4J = 2.4 Hz, 1H, H-17), 1.69 (s, 3H, H-13 or 13′), 1.50 (s, 3H, H-13 or 13′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 138.1 (C-3), 137.0 (C-1), 130.5 (C-4), 127.0 (C-5), 126.0 (C-6), 124.4 (C-2), 110.4 (C-12), 83.4 (C-10), 83.0 (C-11), 80.1 (C-8), 79.1 (C-16), 74.7 (C-17), 69.3 (C-9), 56.4 (C-14), 55.8 (C-15), 27.7 (C-13 or 13′), 26.2 (C-13 or 13′), 23.6 (C-7). IR ($CDCl_3$) ν (cm^{-1}) = 3929, 2986, 2936, 2896, 2848, 1453, 1372, 1335, 1229, 1075, 1025, 861, 778, 653. HRMS (GC

FI, 10,000 V) calculated for $C_{18}H_{19}BrO_3$ [$M^{+\cdot}$] 362.05176, found 362.04955 (Diff.: −6.11 ppm).

5.2.6.35. (3-((3-((4S,5R*)-5-(2-Bromo-3-methylphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-yn-1-yl)oxy)prop-1-yn-1-yl)trimethylsilane (**3b**).* Compound **3b** (colorless oil) was prepared following the general procedure E starting from compound **41** (590 mg, 1.62 mmol).

R_f = 0.13 (Pentane/Et_2O 97:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.51 (br d, ^3J = 7.6 Hz, 1H, H-6), 7.26 (t, ^3J = 7.6 Hz, 1H, H-5), 7.20 (br d, ^3J = 7.6 Hz, 1H, H-4), 5.54 (d, ^3J = 6 Hz, 1H, H-8), 5.40 (dt, ^3J = 6 Hz, ^5J = 2 Hz, 1H, H-9), 4.05−3.96 (m, 2H, H-14), 3.69 (AB system, J_{AB} = 15.6 Hz, $\Delta\sqrt{}$ = 8.1 Hz, 2H, H-15), 2.43 (s, 3H, H-7), 1.69 (s, 3H, H-13 or 13′), 1.50 (s, 3H, H-13 or 13′), 0.18 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 138.1 (C-3), 137.0 (C-1), 130.5 (C-4), 127.0 (C-5), 126.0 (C-6), 124.4 (C-2), 110.4 (C-12), 100.8 (C-16), 91.8 (C-17), 83.3 (C-10 or 11), 83.2 (C-10 or 11), 80.1 (C-8), 69.4 (C-9), 56.7 (C-14), 56.5 (C-15), 27.7 (C-13 or 13′), 26.2 (C-13 or 13′), 23.6 (C-7), −0.03 (TMS). IR ($CDCl_3$) ν (cm^{-1}) = 2958, 1453, 1372, 1336, 1249, 1231, 1166, 1125, 1077, 1026, 999, 840, 776, 759, 652. HRMS (ESI, 120 eV) calculated for $C_{21}H_{27}BrO_3Si$ [M] 434.09128, found 434.09222 (Diff.: −2.16 ppm).

5.2.6.36. ((8bR,11aS*)-10,10-Dimethyl-3,5,8b,11a-tetrahydro-1H-benzo[3,4]furo[3′,4′:7,8]azuleno[1,2-d][1,3]dioxol-4-yl)trimethylsilane (**4b**).* A solution of substrate **3b** (50 mg, 0.12 mmol, 1 equiv) in diisopropylamine (1 mL) was degassed with argon. $Pd(PPh_3)_4$ (6.7 mg, 6 μmol, 0.05 equiv) was added. The reaction mixture was degassed again and heated at 100 °C for 22 h (no microwave irradiation). The mixture was filtered through Celite and concentrated in vacuo. Further purification by flash column chromatography over silica gel (pentane/Et_2O 9:1) afforded a separable mixture of compounds **4b** (12%, pale yellow oil) and **14** (19%, colorless oil).

R_f = 0.18 (Pentane/Et_2O 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.43 (t, ^3J = 7.2 Hz, 1H, H-5), 7.37 (d, ^3J = 7.2 Hz, 1H, H-6), 7.11 (d, ^3J = 7.6 Hz, 1H, H-4), 5.67 (d, ^3J = 6 Hz, 1H, H-8), 5.34 (d, ^3J = 5.6 Hz, 1H, H-9), 4.89 (AB system, J_{AB} = 13.6 Hz, $\Delta\sqrt{}$ = 70.3 Hz, 2H, H-14), 4.57−4.49 (m, 2H, H-15), 3.26 (AB system, J_{AB} = 13.6 Hz, $\Delta\sqrt{}$ = 56 Hz, 2H, H-7), 1.49 (s, 3H, H-13 or 13′), 1.26 (s, 3H, H-13 or 13′), 0.22 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 146.3 (C-16), 139.6 (C-1), 138.7 (C-2), 136.8 (C-11), 135.2 (C-10), 131.7 (C-5), 130.0 (C-3), 128.7 (C-17), 127.6 (C-4), 123.2 (C-6), 112.8 (C-12), 82.4 (C-8), 81.4 (C-9), 72.6 (C-15), 70.6 (C-14), 36.0 (C-7), 27.6 (C-13 or 13′), 26.4 (C-13 or 13′), −0.4 (TMS). IR ($CDCl_3$) ν (cm^{-1}) = 2987, 2949, 2933, 2853, 2835, 1455, 1379, 1371, 1249, 1206, 1159, 1144, 1063, 1036, 837, 764, 689. HRMS (GC FI, 10,000 V) calculated for $C_{21}H_{26}O_3Si$ [$M^{+\cdot}$] 354.16512, found 354.16623 (Diff.: 3.12 ppm).

5.2.6.37. (8bR,11aS*)-10,10-Dimethyl-3,5,8b,11a-tetrahydro-1H-benzo[3,4]furo[3′,4′:7,8]azuleno[1,2-d][1,3]dioxole (**14**).* Desilylated compound **14** was prepared following general procedure F starting from substrate **3b** (50 mg, 0.11 mmol).

R_f = 0.12 (Pentane/Et_2O 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.41−7.35 (m, 2H, H-5 & 6), 7.05 (br d, ^3J = 7.2 Hz, 1H, H-4), 5.61 (d, ^3J = 5.6 Hz, 1H, H-8), 5.53−5.50 (m, 1H, H-17), 5.28 (d, ^3J = 5.6 Hz, 1H, H-9), 4.88 (AB system, J_{AB} = 13.6 Hz, $\Delta\sqrt{}$ = 60.5 Hz, 2H, H-14), 4.52−4.44 (m, 2H, H-15), 3.50−3.36 (m, 2H, H-7), 1.48 (s, 3H, H-13 or 13′), 1.27 (s, 3H, H-13 or 13′). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 140.5 (C-1), 139.0 (C-16), 138.5 (C-2), 135.9 (C-11), 134.3 (C-10), 131.6 (C-5), 130.2 (C-3), 128.9 (C-4), 123.9 (C-6), 115 (C-17), 112.7 (C-12), 82.1 (C-8), 80.9 (C-9), 72.6 (C-15), 71.5 (C-14), 32.9 (C-7), 27.6 (C-13 or 13′), 26.4 (C-13 or 13′). IR ($CDCl_3$) ν (cm^{-1}) = 2984, 2930, 2852, 1456, 1371, 1248, 1206, 1158, 1061, 920, 868, 836, 769. HRMS (GC FI, 10,000 V) calculated for $C_{18}H_{18}O_3$ [$M^{+\cdot}$] 282.12559, found 282.12623 (Diff.: 2.25 ppm).

*5.2.6.38. 2-Bromo-3,6-dimethylphenol (**42**).* Compound **42** is already known and was synthesized following the literature method [15]. Compound **42** was not separated from 2,4-dibromo-3,6-dimethylphenol.

*5.2.6.39. 2-Bromo-1,4-dimethyl-3-(prop-2-yn-1-yloxy)benzene (**43**).* Potassium carbonate (241 mg, 1.74 mmol, 5 equiv) and propargyl bromide (80% in toluene, 45 μL, 1.2 equiv) were added to the mixture of **42** (68 mg, 0.34 mmol, 1 equiv) and 2,4-dibromo-3,6-dimethylphenol in acetone (1.75 mL). The resulting mixture was stirred and refluxed overnight. The reaction was quenched by filtration and the solvent was concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (heptane/EtOAc 99:1) to give a separable mixture of compounds **43** and 2,6-dibromo-1,4-dimethyl-3-(prop-2-yn-1-yloxy)benzene. Compound **43** was obtained in 79% yield as a white solid from **42**.

R_f = 0.20 (Heptane 100%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 6.98 (AB system, J_{AB} = 8 Hz, $\Delta\sqrt{}$ = 33 Hz, 2H, H-4 & 5), 4.65 (d, ^4J = 2.4 Hz, 2H, H-9), 2.52 (t, ^4J = 2.4 Hz, 1H, H-11), 2.38 (s, 3H, H-8), 2.36 (s, 3H, H-7). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 153.6 (C-1), 137.4 (C-3), 130.9 (C-6), 129.6 (C-5), 126.7 (C-4), 120.1 (C-2), 79.1 (C-10), 75.4 (C-11), 60.1 (C-9), 23.2 (C-8), 17.0 (C-7). IR ($CDCl_3$) ν (cm^{-1}) = 3296, 3061, 3021, 2950, 2924, 2863, 2123, 1478, 1455, 1359, 1271, 1169, 1134, 1042, 1009, 991, 807, 672, 635. HRMS (GC FI, 10,000 V) calculated for $C_{11}H_{11}BrO$ [$M^{+\cdot}$] 237.99933, found 237.99897 (Diff.: −1.51 ppm). Mp = 53 °C.

*5.2.6.40. 4-(2-Bromo-3,6-dimethylphenoxy)but-2-yn-1-ol (**44**).* Propargyl alcohol **44** (white solid) was prepared following the general procedure C starting from terminal alkyne **43** (423 mg, 1.77 mmol).

R_f = 0.25 (Heptane/EtOAc 8:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 6.97 (AB system, J_{AB} = 7.6 Hz, $\Delta\sqrt{}$ = 34.0 Hz, 2H, H-4 & 5), 4.66 (t, ^5J = 1.6 Hz, 2H, H-9), 4.33 (m, 2H, H-12), 2.37 (s, 3H, H-8), 2.35 (s, 3H, H-7). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 153.5 (C-1), 137.4 (C-3), 130.8 (C-6), 129.6 (C-5), 126.6 (C-4), 120.2 (C-2), 85.5 (C-10), 81.3 (C-11), 60.3 (C-9), 51.3 (C-12), 23.1 (C-8), 16.3 (C-7). IR ($CDCl_3$) ν (cm^{-1}) = 3335, 2922, 2862, 1478, 1453, 1358, 1261, 1169, 1133, 1038, 1006, 976, 805, 638, 520. HRMS (ESI,

120 eV) calculated for $C_{12}H_{13}BrO_2$ [M] 268.00989, found 268.01035 (Diff.: −1.71 ppm). Mp = 51 °C.

*5.2.6.41. 2-Bromo-1,4-dimethyl-3-((4-(prop-2-yn-1-yloxy)but-2-yn-1-yl)oxy)benzene (**45**).* Terminal alkyne **45** (pale yellow oil) was prepared following the general procedure D starting from propargyl alcohol **44** (352 mg, 1.21 mmol).

R_f = 0.65 (Heptane/EtOAc 8:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 6.97 (AB system, J_{AB} = 7.6 Hz, $\Delta\sqrt{}$ = 34.0 Hz, 2H, H-4 & 5), 4.70 (t, ^5J = 2 Hz, 2H, H-9), 4.31 (t, ^5J = 1.6 Hz, 2H, H-12), 4.21 (d, ^4J = 2.4 Hz, 2H, H-13), 2.45 (t, ^4J = 2.4 Hz, 1H, H-15), 2.37 (s, 3H, H-8), 2.35 (s, 3H, H-7). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 153.5 (C-1), 137.4 (C-3), 130.9 (C-6), 129.6 (C-5), 126.6 (C-4), 120.2 (C-2), 82.5 (C-10 & 11), 79.0 (C-14), 75.1 (C-15), 60.3 (C-9), 56.9 (C-12), 56.6 (C-13), 23.2 (C-8), 17.0 (C-7). IR ($CDCl_3$) ν (cm^{-1}) = 3292, 2923, 2856, 1478, 1455, 1357, 1262, 1134, 1080, 1040, 981, 932, 808, 638. HRMS (ESI, 120 eV) calculated for $C_{15}H_{15}BrO_2$ [M] 306.02554, found 306.02521 (Diff.: 1.1 ppm).

*5.2.6.42. (3-((4-(2-Bromo-3,6-dimethylphenoxy)but-2-yn-1-yl)oxy)prop-1-yn-1-yl)trimethylsilane (**3c**).* A solution of terminal alkyne **45** (750 mg, 2.44 mmol, 1 equiv) and EtMgBr (1 M in THF, 6.5 mL, 6.5 mmol, 2.7 equiv) in anhydrous THF (27 mL) was heated at 51 °C and stirred for 1 h. Trimethylsilyl chloride (freshly distilled, 0.4 mL, 3.13 mmol, 1.3 equiv) was added and the suspension was stirred at 53 °C for 2.5 h. The mixture was quenched by addition of a saturated aqueous solution of $NaHCO_3$ (30 mL) and extracted with Et_2O (3 × 30 mL). Combined organic layers were washed with water, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was purified by flash column chromatography over silica gel (heptane/EtOAc 98:2) to afford **3c** as a pale yellow oil.

R_f = 0.22 (Heptane/EtOAc 98:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 6.97 (AB system, J_{AB} = 8 Hz, $\Delta\sqrt{}$ = 33.9 Hz, 2H, H-4 & 5), 4.70 (t, ^5J = 2 Hz, 2H, H-9), 4.29 (t, ^5J = 2 Hz, 2H, H-12), 4.19 (s, 2H, H-13), 2.37 (s, 3H, H-8), 2.35 (s, 3H, H-7), 0.19 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 153.5 (C-1), 137.4 (C-3), 130.9 (C-6), 129.6 (C-5), 126.6 (C-4), 120.2 (C-2), 100.7 (C-14), 92.3 (C-15), 82.7 (C-10), 82.3 (C-11), 60.3 (C-9), 57.5 (C-13), 56.9 (C-12), 23.2 (C-8), 17.0 (C-7), −0.04 (TMS). IR ($CDCl_3$) ν (cm^{-1}) = 2958, 2924, 2896, 2851, 1478, 1455, 1346, 1250, 1134, 1082, 1040, 1001, 844, 761. HRMS (ESI, 120 eV) calculated for $C_{18}H_{23}BrO_2Si$ [M] 378.06507, found 378.06490 (Diff.: 0.46 ppm).

*5.2.6.43. Trimethyl(3-methyl-6,7,8,10-tetrahydrofuro[3′,4′:6,7]cyclohepta[1,2,3-cd][1]benzofuran-7-yl)silane (**19**).* A solution of $Pd(OAc)_2$ (4.4 mg, 20 μmol, 0.12 equiv) and $P(OPh)_3$ (10 μL, 0.038 mmol, 0.24 equiv) in anhydrous 1,4-dioxane (0.2 mL) was degassed. Then substrate **3c** (60 mg, 0.16 mmol, 1 equiv) in anhydrous 1,4-dioxane (1.7 mL) and Cs_2CO_3 (258 mg, 0.79 mmol, 5 equiv) were added. The reaction mixture was degassed again and heated at 100 °C for 1.5 h under microwave irradiation. The mixture was passed through a short Celite pad, concentrated in vacuo, and purified by flash column chromatography over silica gel (heptane/EtOAc 98:2) to afford compound **19** (40%) as a pale yellow lace.

R_f = 0.44 (Heptane/EtOAc 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.38 (s, 1H, H-9), 6.95 (AB system, J_{AB} = 7.6 Hz, $\Delta\sqrt{}$ = 45.6 Hz, 2H, H-4 & 5), 5.08–5.03 (m, 1H, H-12 or 12′), 4.96–4.92 (m, 1H, H-12 or 12′), 4.76–4.67 (m, 2H, H-13), 3.35 (br d, ^2J = 15.2 Hz, 1H, H-8 or 8′), 3.05 (dd, ^2J = 15.2 Hz, ^4J = 4 Hz, 1H, H-8 or 8′), 2.49 (s, 3H, H-7), 2.16 (br t, ^3J = 3.6 Hz, 1H, H-15), −0.24 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 154.1 (C-1), 138.9 (C-14), 138.3 (C-9), 133.2 (C-3), 125.7 (C-5), 125.2 (C-2), 122.9 (C-4), 120.9 (C-10 or 11), 119.6 (C-6), 116.5 (C-10 or 11), 80.2 (C-13), 76.5 (C-12), 33.3 (C-8), 29.9 (C-15), 14.9 (C-7), −1.58 (TMS). IR ($CDCl_3$) ν (cm^{-1}) = 2951, 2925, 2842, 1751, 1248, 1105, 1069, 838, 776. HRMS (GC EI, 70 eV) calculated for $C_{18}H_{22}O_2Si$ [$M^{+\cdot}$] 298.13891, found 298.14060 (Diff.: 5.68 ppm). Mp = 103 °C.

*5.2.6.44. 2-Bromo-1-methyl-3-((prop-2-yn-1-yloxy)methyl)benzene (**46**).* Compound **46** (pale yellow oil) was prepared following general procedure D starting from benzyl alcohol **35** (2.286 g, 11.37 mmol).

R_f = 0.58 (Heptane/EtOAc 9:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.31 (br d, ^3J = 7.5 Hz, 1H, H-6), 7.22 (br t, ^3J = 7 Hz, 1H, H-5), 7.18 (dd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1H, H-4), 4.70 (s, 2H, H-8), 4.27 (d, ^4J = 2.5 Hz, 2H, H-9), 2.49 (br t, ^4J = 2.5 Hz, 1H, H-11), 2.43 (s, 3H, H-7). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) = 138.6 (C-3), 137.3 (C-1), 130.2 (C-4), 127.1 (C-5), 126.8 (C-6), 125.6 (C-2), 79.7 (C-10), 74.9 (C-11), 71.8 (C-8), 58.0 (C-9), 23.6 (C-7). IR ($CDCl_3$) ν (cm^{-1}) = 3295, 3054, 2977, 2949, 2924, 2852, 1578, 1453, 1348, 1252, 1108, 1081, 1027, 773, 669, 633. HRMS (GC EI, 70 eV) calculated for $C_{11}H_{11}BrO$ [$M^{+\cdot}$] 237.99933, found 237.99883 (Diff.: −2.09 ppm).

*5.2.6.45. 4-((2-Bromo-3-methylbenzyl)oxy)but-2-yn-1-ol (**47**).* Propargyl alcohol **47** (pale yellow oil) was prepared following the general procedure C starting from benzyl propargyl ether **46** (2.583 g, 10.8 mmol).

R_f = 0.22 (Heptane/EtOAc 8:2). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.30 (dd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1H, H-6), 7.21 (t, ^3J = 7.5 Hz, 1H, H-5), 7.18 (dd, ^3J = 7.5 Hz, ^4J = 2 Hz, 1H, H-4), 4.68 (s, 2H, H-8), 4.34 (dt, ^3J = 6 Hz, ^5J = 2 Hz, 2H, H-12), 4.31 (t, ^5J = 1.5 Hz, 2H, H-9), 2.42 (s, 3H, H-7), 1.60 (t, ^3J = 6 Hz, 1H, OH). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) = 138.6 (C-3), 137.3 (C-1), 130.2 (C-4), 127.1 (C-5), 126.8 (C-6), 125.6 (C-2), 85.0 (C-11), 81.9 (C-10), 72.0 (C-8), 58.2 (C-9), 51.3 (C-12), 23.6 (C-7). IR ($CDCl_3$) ν (cm^{-1}) = 3364, 3047, 2920, 2856, 1578, 1452, 1380, 1347, 1252, 1124, 1100, 1077, 1024, 774. HRMS (GC EI, 70 eV) calculated for $C_{12}H_{13}BrO_2$ [$M^{+\cdot}$] 268.00989, found 268.00918 (Diff.: −2.66 ppm).

*5.2.6.46. 2-Bromo-1-methyl-3-(((4-(prop-2-yn-1-yloxy)but-2-yn-1-yl)oxy)methyl)benzene (**48**).* Propargyl ether **48** (pale yellow oil) was prepared following the general procedure D starting from propargyl alcohol **47** (2.16 g, 8.03 mmol).

R_f = 0.44 (Heptane/EtOAc 90:10). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.30 (dd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1H, H-6),

7.21 (t, ^3J = 7.5 Hz, 1H, H-5), 7.18 (dd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1H, H-4), 4.68 (s, 2H, H-8), 4.34 (t, ^5J = 1.5 Hz, 2H, H-12), 4.32 (t, ^5J = 1.5 Hz, 2H, H-9), 4.27 (d, ^4J = 2 Hz, 2H, H-13), 2.45 (t, ^4J = 2.5 Hz, 1H, H-15), 2.42 (s, 3H, H-7). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) = 138.6 (C-3), 137.3 (C-1), 130.2 (C-4), 127.1 (C-5), 126.8 (C-6), 125.6 (C-2), 83.0 (C-10 or 11), 81.9 (C-10 or 11), 79.0 (C-14), 75.2 (C-15), 72.0 (C-8), 58.2 (C-9), 57.0 (C-12), 56.7 (C-13), 23.6 (C-7). IR ($CDCl_3$) ν (cm^{-1}) = 3292, 3050, 2952, 2898, 2853, 1579, 1454, 1441, 1343, 1249, 1073, 1026, 932, 887, 774, 669, 635. HRMS (ESI, 120 eV) calculated for $C_{15}H_{15}BrO_2$ [M] 306.02554, found 306.02541 (Diff.: 0.43 ppm).

*5.2.6.47. (3-((4-((2-Bromo-3-methylbenzyl)oxy)but-2-yn-1-yl) oxy)prop-1-yn-1-yl)trimethylsilane (**3d**).* Silylated compound **3d** (colorless oil) was prepared following the general procedure E starting from terminal alkyne **48** (2.16 g, 8.03 mmol).

R_f = 0.38 (Heptane/EtOAc 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.30 (dd, ^3J = 7.2 Hz, ^4J = 2 Hz, 1H, H-6), 7.23–7.17 (m, 2H, H-5 & 4), 4.68 (s, 2H, H-8), 4.31 (s, 4H, H-9 & 12), 4.26 (s, 2H, H-13), 2.42 (s, 3H, H-7), 0.18 (s, 9H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 138.3 (C-3), 137.0 (C-1), 129.9 (C-4), 126.8 (C-5), 126.5 (C-6), 125.3 (C-2), 100.4 (C-14), 92.0 (C-15), 82.6 (C-10 or 11), 81.8 (C-10 or 11), 71.6 (C-8), 57.9 (C-9), 57.2 (C-13), 56.6 (C-12), 23.3 (C-7), −0.37 (TMS). IR ($CDCl_3$) ν (cm^{-1}) = 3048, 2957, 2850, 2173, 1579, 1343, 1249, 1074, 1026, 999, 840, 760. HRMS (GC EI, 70 eV) calculated for $C_{18}H_{23}BrO_2Si$ [$M^{+\cdot}$] 378.06507, found 378.06527 (Diff.: 0.53 ppm).

*5.2.6.48. (Z)-Trimethyl(3-(2-(5-methylisochroman-4-ylidene) ethoxy)prop-1-yn-1-yl)silane (**20**) and 3,7,9,11-tetrahydro-1H-furo[3′,4′:6,7]cyclohepta[1,2,3-de]isochromene (**21**)..* A solution of silylated substrate **3d** (51 mg, 0.13 mmol, 1 equiv) in 1,4-dioxane (1.6 mL) was degassed thoroughly. Then $Pd(PPh_3)_4$ (15 mg, 13 μmol, 0.1 equiv) and Cs_2CO_3 (58 mg, 0.18 mmol, 1.3 equiv) were added. The reaction mixture was degassed again and the mixture was heated at 100 °C for 2 × 30 min under microwaves irradiation. The mixture was then filtered through Celite and the solvent was evaporated under reduced pressure. Further purification by flash column chromatography on silica gel (heptane/EtOAc 9:1) gave three compounds, which seemed to be compounds **20** and **21**.

Compound **21** (colorless oil): R_f = 0.24 (heptane/EtOAc 90:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.32 (t, ^3J = 7.2 Hz, 1H, H-5), 7.10 (d, ^3J = 7.6 Hz, 1H, H-4), 7.02 (d, ^3J = 7.6 Hz, 1H, H-6), 5.67 (t, ^3J = 6.4 Hz, 1H, H-15), 4.69 (s, 2H, H-8), 4.68 (s, 2H, H-12), 4.59 (s, 2H, H-9), 4.46 (d, ^4J = 1.6 Hz, 2H, H-13), 3.12 (d, ^3J = 6.4 Hz, 2H, H-7). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 138.6 (C-14), 134.8 (C-1), 133.6 (C-3), 133.1 (C-11), 130.6 (C-2), 128.9 (C-5), 128.1 (C-10), 127.5 (C-4), 122.4 (C-6), 117.6 (C-15), 71.5 (C-13), 70.4 (C-12), 69.0 (C-8), 68.6 (C-9), 34.5 (C-7). MS (GC–MS) (CI^+, NH_3): $[M + H]^+$ = 227, $[M + NH_4]^+$ = 244.

Compound **20** (yellow oil): R_f = 0.35 (heptane/EtOAc 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.19 (t, ^3J = 7.6 Hz, 1H, H-5), 7.11 (d, ^3J = 7.6 Hz, 1H, H-4), 7.04 (d, ^3J = 7.6 Hz, 1H, H-6), 5.50 (t, ^3J = 2.4 Hz, 1H, H-11), 4.64 (dd, ^2J = 13.2 Hz, ^3J = 2.0 Hz, 1H, H-12a or 12b), 4.56–4.51 (m, 4H, H-8a or 8b, 12a or 12b & 13), 4.44–4.36 (m, 2H, H-8a or 8b & 9a or 9b), 4.22 (d, ^3J = 12.8 Hz, 1H, H-9a or 9b), 2.26 (s, 3H, H-7), 0.02 (TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 150.6 (C_{quat}), 139.3 (C_{quat}), 134.8 (C_{quat}), 124.2 (C_{quat}), 129.5 (C-4), 127.4 (C-5), 122.7 (C-6), 122.5 (C-11), 81.9 (C-14), 80.7 (C-15), 73.1 (C-13), 71.1 (C-12), 68.1 (C-8), 67.7 (C-9), 20.2 (C-7), −0.55 (TMS). MS (GC–MS) (CI^+, NH_3): $[M + H]^+$ = 301, $[M + NH_4]^+$ = 318.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.crci.2017.01.005.

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