Cyclocarbopalladation: serial Cyclization and C-H Activation/Stille Cross Coupling in the Pd-5-Exo Dig Reaction

Christophe Bour and Jean Suffert *

Laboratoire de Pharmacochimie de la Communication Cellulaire

(UMR 7081 CNRS / ULP), Faculté de Pharmacie, 64 route du Rhin 67401 ILLKIRCH Cedex, France

Supporting Information

General Method. Reactions were run under an atmosphere of argon in oven-dried glassware using a standard syringe, cannula, and septa apparatus. Et₂O and THF were distilled from sodium benzophenone. Benzene and DMF were distilled from CaH₂. CH₂Cl₂ was distilled from P₂O₅. EtN₃ and *i*-Pr₂NH were distilled from KOH. Crude products were purified by flash column chromatography on Merck 230-400 mesh silica gel. For some compounds, 5% EtN₃ treated silica gel was used to avoid decomposition. Analytical TLC, was carried out on Merck (Keisegel 60F-254) silica gelplates. ¹H spectra were recording at 200 or 300 MHz using the residual solvent signal as internal reference (CDCl₃, 7.27; C₆D₆, 7.16 ppm). Chemical shifts are quoted in ppm; coupling constants (*J*) are given in Hz. The following abbreviations are used to describe peak patterns when appropriate: s (singlet), d (doublet), t (triplet), q(quartet), quint (quintet), m (multiplet), ap (apparent), br (broad). ¹³C NMR spectra were recorded at 50 or 75 MHz at ambient temperature in CDCl₃ with δ (CDCl₃) at 77.0 as internal reference. Multiplicities were determined in some cases by Jmod pulse sequence and are given as follow. Melting points were determined with a glass capillary apparatus and are uncorrected. I.R were determined with a Perkin-Elmer 2000 apparatus. Mass spectra were obtained from the *Service de spectrométrie de Masse* of the Chemistry Institute of Strasbourg (France). High Resolution Mass Spectral Analysis (HRMS) were performed using a Mariner ESI-Tof instrument from Applied Bio-System Perking Elmer. *n*-BuLi was titrated using *N*-pivaloyl *o*-toluidine following the Suffert's procedure¹. X-ray Crystallographic Study was done by the X ray Central Service of the Chemistry Institute of Strasbourg: single crystals of compounds were respectively obtained by crystallisation in heptane by slow evaporation of the solvent and in a mixture of benzene/heptane. The crystal data were collected at 173 K for complex on a Kappa CCD diffractometer, using monochromated Mo Kα radiation (λ = 0.71073 Å). Details of data collection parameters and refinements results are listed in the following Tables; the structures were solved using direct methods after refinement of the non hydrogen atoms. Hydrogen atoms were introduced as fixed contributors at calculated positions (C-H = 0.95 Å, B(H) = 1.3 Beqv. All calculations were done using the Nonius OpenMoleN package ². Microwave irradiations has been performed using BIOTAGE Smith Creator.

Stannanes derivatives **6**, **13-16**, **33** are commercially available; and **7-12**, **34**, **38** were prepared by literature methods.^{3,4,5}

***Tert*-butyl(dimethyl){[5-(tributylstannyl)pent-4-ynyl]oxy}silane (**34**)**

To a cold (-78°C) solution of the protected 4-pentyn-1-ol (1 g, 4.71 mmol) in dry THF (10 mL) was added dropwise *n*-butyllithium (3.2 mL, 4.71 mmol, 1.45 M in hexane). The resulting solution was stirred for 30 min and Bu₃SnCl (1.5 mL, 6.05 mmol) was then added dropwise. The reaction mixture was warm to rt and stirred for 18 hours and then subjected to the normal work up. Bulb to bulb distillation (195°C, 0.1 mmHg) gave 2.2g (95%)

Bp: 135°C (0.1 mmHg)

¹H NMR (300 MHz, CDCl₃) δ 3.71 (t, 2H, *J* = 6.9 Hz); 2.33 (t, 2H, *J* = 6.9 Hz); 1.63 (q, 2H, *J* = 6.9 Hz); 1.60-1.50 (m, 6H); 1.41-1.27 (m, 12H); 0.98-0.91 (m, 18H); 0.06 (s, 6H). **¹³C NMR** (75 MHz, CDCl₃) δ 106.48; 81.08; 62.47; 31.18; 28.80; 25.93; 18.93; 13.60; 10.60; -5.14. **IR** (FTIR, film): ν = 3315; 2360; 2151; 1521; 1463; 1376; 1254; 1106; 1072; 836; 776; 667 cm⁻¹.

***Tert*-butyl(dimethyl){[4-(tributylstannyl)but-3-ynyl]oxy}silane (**35**)**

This compound (**31**) was prepared using the same experimental procedure than **30**, starting for 1g from protected 3-butyln-1-ol (1 g, 5.04 mmol), *n*-BuLi (3.5 mL, 5.04 mmol) and Bu₃SnCl (1.64 ml, 6.05 mmol) in 10 mL of anhydrous THF. Bulb to bulb distillation (175°C, 0.1 mmHg) gave 2.3g (96%).

Bp: 135°C (0.1 mmHg)

¹H NMR (300 MHz, CDCl₃) δ 3.73 (t, 2H, *J* = 6.9 Hz); 2.47 (t, 2H, *J* = 6.9 Hz); 1.60-1.54 (m, 6H); 1.37-1.30 (m, 7H); 0.98-0.91 (m, 18H); 0.07 (s, 6H). **¹³C NMR** (75 MHz, CDCl₃) δ 107.40; 80.89; 62.92; 28.80; 25.93; 18.93; 13.60; 10.60; -5.10.

Tributyl(pent-1-ynyl)stannane (36**)**

This compound (**32**) was prepared using the same experimental procedure than **30**, starting for 1g from pent-1-yne (1 g, 14.67 mmol), *n*-BuLi (10.3 mL, 14.67 mmol) and Bu₃SnCl (4.77ml, 17.61 mmol) in 10 mL of anhydrous THF. Bulb to bulb distillation (185°C, 0.1 mmHg) gave 4.05g (77%).

Bp: 185°C (0.1 mmHg)

¹H NMR (300 MHz, CDCl₃) δ 2.20 (t, 2H, *J* = 6.8 Hz); 1.57-1.47 (m, 9H); 1.35-1.28 (m, 8H); 0.99-0.86 (m, 22H). ¹³C NMR (75 MHz, CDCl₃) δ 107.44; 80.86; 28.85; 26.93; 21.95; 21.09; 13.60; 13.20; 10.80.

[3-(1-methoxy-1-methyl-ethoxy)-prop-1-ynyl]-trimethylsilyl

To a cold (-78°C) solution of the protected propargylic alcohol (20 g, 156 mmol) in dry THF (200 mL) was added dropwise *n*-butyllithium (110 mL, 171 mmol, 1.56 M in hexane). The resulting solution was stirred for 30 min and TMSCl (23.9 mL, *d* = 0.856, 187 mmol) was then added dropwise. The reaction mixture was kept at -78°C for 30 min and then allowed to warm up to rt for one hour before addition of the saturated NaHCO₃ (100 mL). The pH of the solution must be adjusted to 8 to avoid partial deprotection of the propargylic ether. The mixture was extracted with Et₂O and the combined organic layers were washed with water, saturated brine and dried over Na₂SO₄. After the solvent was removed in vacuo, the crude product was distilled under reduced pressure to give 27.30 g of the title compounds (136 mmol, 87%) as a colorless liquid.

Rf: 0.43 (ether/hexane 10:90). **Bp**: 70°C (0.1 mmHg)

¹H NMR (300 MHz, CDCl₃) δ 0.13 (s, 9H); 1.33 (s, 6H); 3.18 (s, 3H); 4.07 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 0.29; 24.25; 48.69; 49.62; 93.35; 100.70; 102.62. **IR** (FTIR, film): ν = 2990; 2960; 2176; 1380; 1221; 1213; 1149; 1049; 844; 760 cm⁻¹.

9-bromo-6,7-dihydro-5H-benzo[7]annulene-8-carbaldehyde

Dry DMF (12.6 mL, 132 mmol, 4.7 equiv) was dropwise added to a solution of phosphore tribromide (9.9 mL, 109 mmol, 3.9 equiv) in dry CH₂Cl₂ (30 mL) cooled at 0°C. After one hour stirring at 0°C, the mixture turns to white – green. Then a solution of α-benzosuberone (4.5 g, 28 mmol, 1 equiv) in dry CH₂Cl₂ (30 mL) was added dropwise at 0°C to the suspension and stirred 1h30 at reflux (T= 45°C). The solution was powered on ice while the pH is maintained at pH 7-8 by

regular addition of a NaHCO_3 solution and NaHCO_3 (solid). The mixture is extracted with ethylacetate (3 x 300 mL) and the combined organic phases were washed with distilled water and brine, dried over Na_2SO_4 and concentrated to oil. The crude bromo-aldehyde was purified by chromatography (elution with hexane/ether 20:80) on a silica gel column to give 4.49 g (63%) of yellow odorous oil. The product was stored at -20°C in etheral solution.

Rf: 0.31 ($\text{Et}_2\text{O}/\text{Hex}$, 20/80)

^1H NMR (300 MHz, CDCl_3) δ 10.21 (s, 1H, H-10); 7.69 (d, 1H, $J = 1.5$ Hz, H-1); 7.65-7.30 (m, 2H, H-2 and H-3); 7.22 (d, 1H, $J = 6.78$ Hz, H-4); 2.59 (t, 2H, $J = 7.17$ Hz, H-7); 2.22 (d, 2H, $J = 7.17$ Hz, H-5); 2.16-2.07 (m, 2H, H-6). **^{13}C NMR** (75 MHz, CDCl_3) δ 192.39 (C-10); 140.78 (C-9); 139.50 (C-8 and C-9a); 138.86 (C-4a); 130.88 (C_{arom}); 130.07 (C_{arom}); 129.26 (C_{arom}); 127.10 (C_{arom}); 34.24 (C-7 or C-5); 32.29 (C-7 or C-5); 24.05 (C-6). **IR** (FTIR, film): $\nu = 2937, 2859, 2353, 2340, 1672, 1601, 1580, 1564, 1254, 898, 767, 748\text{ cm}^{-1}$.

(1R*,2S*)-1-(9-bromo-6,7-dihydro-5H-benzo[7]annulen-8-yl)-4-trimethylsilanyl-but-3-yne-1,2-diol and (1R*,2R*)-1-(9-bromo-6,7-dihydro-5H-benzo[7]annulen-8-yl)-4-trimethylsilanyl-but-3-yne-1,2-diol (2)

A solution of *n*-butyllithium (4.17 mL, 1.5 equiv, 1.43 M in hexane) was added to a dried round-bottom flask containing 3-[(1-methoxy-1-methyl-ethoxy)-prop-1-ynyl]trimethylsilane (1.196 g, 5.97 mmol, 1.5 equiv) in freshly distilled THF (10 mL) at -78°C . The reaction was stirred 30 min at this temperature and was added *via cannula* at a solution of 9-bromo-6,7-dihydro-5H-benzo[7]annulene-8-carbaldehyde (1 g, 3.98 mmol, 1 equiv) in THF (15 mL). The mixture was stirred for 30 min at -78°C and then allowed to warm up to rt for one hour. Then the mixture was quenched by addition of saturated aqueous NaHCO_3 (20 mL). After extraction with Et_2O , the combined organic layers were washed with water, brine, dried over Na_2SO_4 and concentrated *in vacuo*. The alcohols were deprotected by dissolving this oil in methanol (15 mL) containing a catalytic quantity of PPTS. The solution was stirred over night (18 hours) at rt and quenched with the addition of water (5 mL). The mixture was extracted with Et_2O and the combined extracts were washed with water, brine and dried over Na_2SO_4 . The two diastereoisomers were separated by chromatography on silica gel ($\text{AcOEt}/\text{DCM}/\text{hex}$, 15:30:55) to afford compounds *anti* (*unlike*) (710 mg, 1.89 mmol) and *syn* (*like*) (320 mg, 0.84 mmol) as clear brown solid for a global yield of 84 % and a ratio of 7/3.

Compound *syn* (*like*)

Rf: 0.31 (AcOEt/DCM/Hex: 15:30:55)

1H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, 1H, $J = 7.8$ Hz, H-1); 7.32-7.15 (m, 3H, H-2, H-3 and H-4); 5.13 (d, 1H, $J = 8.4$ Hz, H-10); 4.42 (d, 1H, $J = 8.2$ Hz, H-11); 2.82-2.72 (q, 2H); 2.64-2.56 (m, 2H); 2.22-2.09 (m, 3H); 1.10-1.09 (m, 1H); 0.16 (s, 9H, H-14) **^{13}C NMR** (75 MHz, $CDCl_3$) δ 140.01; 139.9; 138.36; 129.44; 128.45; 128.23; 126.16; 120.81; 102.33 (C-12); 92.22 (C-13); 78.04 (C-11); 65.32 (C-10); 34.94 (CH_2); 31.28 (CH_2); 25.34 (CH_2); -0.27 (SiMe₃). **IR** (FTR, film): ν = (br) 3416, 2958, 2899, 2859, 2179, 1690, 1658, 1642, 1479, 1450, 1416, 1275, 1251, 1055, 898, 749 cm^{-1} . **HRMS** (ESI, positive ion 180 eV): calc'd for $(C_{18}H_{23}BrO_2SiNa)^+$ 401.0548, found 401.0556

Compound *anti* (unlike)

Rf: 0.39 (AcOEt/DCM/Hex: 15:30:55)

1H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, 1H, $J = 7.8$ Hz, H-1); 7.34-7.16 (m, 3H, H-2, H-3 and H-4); 5.10 (t, 1H, $J = 4.8$ Hz, H-10); 4.66 (t, 1H, $J = 4.6$ Hz, H-11); 2.78-2.63 (m, 4H), 2.31-1.98 (m, 4H); 0.16 (s, 9H, H-14). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 140.90; 140.31; 130.24; 129.44; 128.98; 128.85; 126.73; 119.54; 103.82 (C-13); 92.75 (C-12); 77.32 (C-11); 65.50 (C-10); 35.71 (CH_2); 32.55 (CH_2); 26.49 (CH_2); 0.37 (SiMe₃). **IR** (FTR, film): ν = 3731, (br) 3344, 3047, 2941, 2845, 1619, 1451, 1415, 1265, 1251, 1045, 892, 846, 746 cm^{-1} . **HRMS** (ESI, positive ion 180 eV): calc'd for $(C_{18}H_{23}BrO_2SiNa)^+$ 401.0548, found 401.0560

Determination of the relative stereochemistry of diol *anti* (unlike) and *syn* (like)

The relative stereoselective of compound *unlike* was established by NOESY experiments on the protected diol as a dioxolane. An unambiguous correlation is observed between the propargylic proton and the two β adjacent protons of the six membered cyclohexene ring system.

General Procedure: cyclocarbopalladation of the β -bromopropargylic diol

The reaction was carried out in an oven-dried 25 mL-bicol, equipped with a refluxed condenser, under argon atmosphere. To a solution of (1R*,2S*)-1-(5-bromo-8,9-dihydro-7H-

benzocycloheptene-6-yl)-4-trimethylsilanyl-but-3-yne-1,2-diol (**2**) (100 mg, 1 equiv) in dried benzene (10 mL), was added Pd(PPh₃)₄ (30 mg, 0.1 equiv) and followed stannylated reagent (1.3 equiv). The mixture was purged 20 min with argon and heated at 95°C under argon. The reaction was followed by TLC (Et₂O/Hex 50:50, anisaldehyde). After the time indicated in table, the mixture was cooled to room temperature, diluted in Et₂O, treated with active *charcoal*, filtrated over *celite*, and concentrated to dryness. The reaction mixture was purified by flash chromatography (two times if necessary).

(1Z,2R,3S)-10-ethenyl-1-[(trimethylsilyl)methylidene]-1,2,3,4,5,6-hexahydro-benzo[e]azulene-2,3-diol (17)

To a solution of (1R*,2S*)-1-(9-bromo-6,7-dihydro-5H-benzo[7]annulen-8-yl)-4-trimethylsilanyl-but-3-yne-1,2-diol (**2**) (100 mg, 1 equiv, 0.263 mmol) in dried benzene (10 mL), was added Pd(PPh₃)₄ (30 mg, 0.1 equiv) and tributylstannylethylene (100 mg, 1.3 equiv, 0.342 mmol). The mixture is purged 20 min with argon and heated at 95°C under argon during 8 hours. The reaction was followed by TLC (Et₂O/Hex 30:70, anisaldehyde). The mixture was cooled to room temperature, diluted in Et₂O, treated with active *charcoal*, filtrated over *celite*, and concentrated to dryness. The crude product was purified by flash chromatography on silica gel (elution with Et₂O/Hex 30:70) to afford 60 mg of two inseparable atropoisomer (70%). The two forms are in equilibrium.

(1Z,2R,3S)-10-ethenyl-1-[(trimethylsilyl)methylidene]-1,2,3,4,5,6-hexahydro-benzo[e]azulène-2,3-diol (17)

Time of heating: 8 hours

Eluent for chromatography: 30/70 (Et₂O/Hex)

R_f: 0.33 et 0.35 (Et₂O/Hex : 30/70) for the two atropoisomers

¹H NMR (300 MHz, CDCl₃) δ 7.55 (d, 1H, *J*_{ortho} = 7.53 Hz, H-9); 7.27 (t, 1H, *J*_{ortho} = 7.53 Hz, H_{arom}); 7.19 (d, 1H, *J*_{ortho} = 7.17 Hz, H_{arom}); 6.72 (dd, 1H, *J*_{H-11,H-12a} = 11 Hz, *J*_{H-11,H-12b} = 17 Hz, maj, H-11 of

one atropoisomer); 6.58 (dd, 1H, $J_{H-11,H-12a} = 11$ Hz, $J_{H-11,H-12b} = 17$ Hz, min, H-11 of the other atropoisomer); 5.64 (d, 1H, $J_{H-11,H-12b} = 17$ Hz, H-12b); 5.29 (s, 1H, min, H-1a of one atropoisomer); 5.20 (s, 1H, maj, H-1a of the other atropoisomer); 5.11 (d, 1H, $J_{H-11,H-12a} = 11$ Hz); 4.83-4.63 (m, 2H, H-2 and H-3); 2.78 (d, 1H, $J = 8.6$ Hz, CH₂); 2.58-1.98 (m, 7H including 2x OH); 0.17 (s, 9H, SiMe₃). **¹³C NMR** (75 MHz, CDCl₃) δ 158.89 (C_{quat}); 156.36 (C_{quat}); 150.41 (C_{quat}); 149.76 (C_{quat}); 141.77 (C_{quat}); 141.38 (C_{quat}); 141.23 (C_{quat}); 136.54 (C-11 of one atropoisomer); 136.35 (C-11 of the other atropoisomer); 132.48 (C_{quat}); 132.27 (C_{quat}); 128.37 (C_{arom}); 127.74 (C_{arom}); 123.44 (maj, C-9 of one atropoisomer); 123.05 (min, C-9 of the other atropoisomer); 113.52 (maj, C-1a of one atropoisomer); 113.13 (min, C-1a of one atropoisomer); 76.07 (min, C-2 of one atropoisomer); 74.74 (maj, C-2 of the other atropoisomer); 71.42 (min, C-3 of one atropoisomer); 71.20 (maj, C-3 of the other atropoisomer); 33.52 (CH₂); 33.15 (CH₂); 32.39 (CH₂); 32.21 (CH₂); 23.91 (CH₂); 22.15 (CH₂); 0.62 (SiMe₃). **HRMS** (ESI, positive ion 180 eV): calc'd for (C₂₀H₃₆O₂SiNa)⁺: 349.1600, found 349.1601. **X Ray** structure: see following tables.

Table 1: X-ray experimental data

Formula	C ₂₀ H ₂₆ O ₂ Si
Molecular weight	326.52
Crystal system	monoclinic
Space group	C 1 c 1
a(Å)	18.3268(6)
b(Å)	10.5670(3)
c(Å)	9.6519(4)
b(deg)	95.627(5)
V(Å ³)	1860.2(1)
Z	4
Color	colorless

Crystal dim(mm)	0.10*0.06*0.06
Dcalc(gcm ⁻³)	.17
F000	704
m(mm ⁻¹)	0.134
Temperature(K)	173
Wavelength(Å)	0.71073
Radiation	MoKa graphite monochromated
Diffractometer	KappaCCD
Scan mode	phi scans'
hkl limits	25,25/-13,14/-13,13
Theta limits(deg)	2.5/30.00
Number of data meas.	7220
Number of data with	2491
I > 3 s(I)	
Number of variables	206
R	0.045
Rw	0.054
GOF	1.058
Largest peak in final	0.234
difference (eÅ ⁻³)	

Table 2 of Positional Parameters and Their E.S.D.

Atom	x	y	z	Ueqv
C1	1.0754(1)	0.2592(3)	0.6191(3)	0.024(1)
C2	1.0886(2)	0.2966(3)	0.7513(3)	0.028(1)
C3	1.1668(2)	0.3378(3)	0.7844(3)	0.026(1)
O1	1.1712(1)	0.4634(2)	0.8392(2)	0.038(1)
C4	1.2004(2)	0.3276(3)	0.6448(3)	0.029(1)
O2	1.2143(2)	0.4506(2)	0.5975(2)	0.054(1)
C5	1.1431(1)	0.2558(3)	0.5488(3)	0.025(1)

C6	1.0025(1)	0.2097(3)	0.5609(3)	0.028(1)
C7	0.9693(2)	0.1163(3)	0.6380(3)	0.029(1)
C8	1.0109(2)	0.0622(3)	0.7670(4)	0.034(2)
C9	1.0177(2)	0.1508(3)	0.8944(3)	0.041(2)
C10	1.0339(2)	0.2886(3)	0.8570(3)	0.037(2)
C11	0.9002(2)	0.0720(3)	0.5893(4)	0.034(2)
C12	0.8639(2)	0.1204(3)	0.4688(4)	0.037(2)
C13	0.8960(2)	0.2124(3)	0.3949(3)	0.034(2)
C14	0.9655(1)	0.2597(3)	0.4370(3)	0.030(1)
C15	0.9984(2)	0.3595(3)	0.3583(3)	0.035(2)
C16	0.9833(2)	0.3840(4)	0.2240(4)	0.052(2)
C17	1.1539(2)	0.1946(3)	0.4309(3)	0.028(1)
SI	1.2355	0.16769(8)	0.3351	0.0313(4)
C18	1.2101(2)	0.2178(4)	0.1519(4)	0.060(2)

Anisotropically refined atoms are given in the form of the of the isotropic equivalent displacement parameter defined as one third of the ortogonalised Uij tensor. Starred atoms were refined isotropically. CCDC 240661 (17) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

(1Z,2R,3S)-10-[(E-2-(tributylstannyl)vinyl)]-1-[(trimethylsilyl)methylene]-1,2,3,4,5,6-hexahydro-benzo[e]azulene-2,3-diol (18)

$C_{32}H_{52}O_2SiSn$
Mol. Wt.: 615,55
brown oil
yield: 58%

Time of heating: 5 hours

Eluent for chromatography: 30/70 (Et₂O/Hex) on pretreated silica gel

R_f= 0.30 and 0.40 (70/30 Et₂O/Hex) for the two atropoisomers

¹H NMR (200 MHz, CDCl₃) δ 7.59 (d, 1H, J = 7.8 Hz, H-9); 7.28-7.20 (m, 3H_{arom}); 7.14 (d, J = 7.2 Hz); 6.84 (d, 1H, J = 8.4 Hz, $J_{H-117Sn} \approx J_{H-118Sn} = 47$ Hz); 6.76 (s, 1H); 5.31 (s, 1H, min H1a of one atropoisomer); 5.21 (s, 1H, maj, H1a of the other atropoisomer); 4.79-4.73 (br m, 2H, H-2 and H-3); 2.84 (br s, 1H, OH); 2.54-2.04 (m, 7H, including one OH and H-6, H-5, H-4); 1.61-0.79 (m, 29H, Bu₃Sn); 0.159 (s, 9H, SiMe₃). **¹³C NMR** (75 MHz, CDCl₃) δ 160.94 (C_{quat}); 159.69 (C_{quat}); 151.26 (C_{quat}); 149.99 (C_{quat}); 145.40; 142.01 (C_{quat} of one atropoisomer); 141.72 (C_{quat} of the other atropoisomer); 137.29; 129.73; 129.44; 128.45; 128.10; 123.49; 123.28; 122.44; 76.49 (C-2 of one atropoisomer); 75.11 (C-2 of the other atropoisomer); 72.06 (C-3 of one atropoisomer); 71.03 (C-3 of the other atropoisomer); 33.90 (CH₂); 33.00 (CH₂); 32.80 (CH₂); 29.52 (CH₂ of Bu₃Sn-); 27.71 (CH₂ of Bu₃Sn-); 24.31 (CH₂); 22.56; 14.34 (CH₂ of Bu₃Sn-); 9.96 (CH₂ of Bu₃Sn-); 0.76 (SiMe₃). **IR** (FTR, film): ν = 3383 (br), 3053, 2955, 2928, 2179, 1607, 1560, 1462, 1373, 1248, 1093, 984, 844, 763, 690 cm⁻¹. **HRMS** (ESI, positive ion 135 eV): calc'd for (C₃₂H₅₂O₂SiSnNa)⁺ 639.2656, found 639.2878.

(1Z,2R,3S)-1-[(trimethylsilyl)methylene]-10-[(E-2-(trimethylsilyl)vinyl)]-1,2,3,4,5,6-hexahydro-benzo[e]azulene-2,3-diol (19)

- Under the classical procedure

$C_{23}H_{34}O_2Si_2$
Mol. Wt.: 398,69
yellow solid
yield: 30%

Time of heating: 18 hours

Eluent for chromatography: 60/40 (Et₂O/Hex)

R_f=0.20 and 0.25 (60/40 Et₂O/Hex) for the two atropoisomers

¹H NMR (300 MHz, benzene-*d*₆) δ 7.61 (d, 1H, *J* = 7.6 Hz, H-9); 7.30-7.15 (m, 2H, H-8 and H-7); 6.91 (AB system of one atropoisomer, d, 1 H, *J*_{H-12,H-13} = 19.1 Hz, H-12); 6.76 (AB system of the other atropoisomer, d, 1H, *J*_{H-12,H-13} = 19.1 Hz, H-12); 6.40 (AB system of one atropoisomer, d, 1H, *J*_{H-13,H-12} = 19.1 Hz, H-13); 6.39 (AB system of the other atropoisomer, d, 1H, *J*_{H-13,H-12} = 19.1 Hz, H-13); 5.26 (d, 1H, *J* = 2Hz, H-1a of one atropoisomer); 5.18 (s, 1H, H-1a of the other atropoisomer); 4.82-4.67 (2 x br s, 2H, H-2 and H-3); 2.83 (d, 1H, *J* = 8.3 Hz, CH₂); 2.55-1.91 (m, 8H, including 2x OH); 0.16 (s, 9H, H-13); 0.10 (s, 9H, SiMe₃). **¹³C NMR** (75 MHz, CDCl₃) δ 160.94 (C_{quat}); 158.88 (C_{quat}); 151.05 (C_{quat}); 150.18 (C_{quat}); 144.01 (C-11); 142.56 (C_{quat}, of one atropoisomer); 142.41 (C_{quat}, of the other atropoisomer); 141.94; 137.73 (C_{quat}); 137.03 (C_{quat}); 133.63 (C_{quat}, maj); 133.53 (C_{quat}, min); 129.36 (C_{arom}); 129.29 (C_{arom}); 128.86 (C-12); 128.55 (C_{quat}); 124.19 (C-10); 122.95 (C-1a of one atropoisomer); 121.99 (C-1a of the other atropoisomer); 76.40 (C-2); 75.26 (C-2); 72.43 (C-3); 72.07 (C-3); 34.32 (CH₂); 33.18 (CH₂); 33.02 (CH₂); 32.80 (CH₂); 24.90 (CH₂); 22.85 (CH₂); 1.04 (SiMe₃); -0.61 (SiMe₃). **IR** (FTR, film): ν = 3412 (br), 3055, 2986, 2685, 2305, 1701, 1606, 1421, 1265, 1048, 896, 844, 749 cm⁻¹. **HRMS** (ESI, positive ion 135 eV): calc'd for (C₂₃H₃₄O₂Si₂Na)⁺ 401.1995, found 401.1925.

- Under Microwave irradiation

Reaction mixture prepared as described in the classical procedure was irradiated under microwave. Time of heating: 5 min at 100°C (100 W), then 5 min at 100°C (200 W) and finally 8 min at 120°C (220 W).

Yield: 75%

(1Z,2R,3S)-10-[(1E,3E)-5-hydroxy-3-methylpenta-1,3-dienyl-1-[(trimethylsilyl)methylene]-1,2,3,4,5,6-hexahydro-benzo[e]azulene-2,3-diol (20)

Time of heating: under microwave irradiation, 3 x 10 min at 130°C

Eluent for chromatography: (50/50 Et₂O/Hex)

R_f = 0.22 and 0.29 (10/30/60 EtOAc/DCM/Hex) for the two atropoisomers

¹H NMR (200 MHz, CDCl₃) δ 7.54 (d, 1H, *J* = 7.6 Hz, H-9); 7.30-7.15 (m, 3H); 6.36 (d, 1H, *J* = 6.4 Hz); 7.01 (d, 1 H, *J*_{H-12,H-11} = 14.8 Hz, H-11); 5.38 (d, 1H, *J*_{H-12,H-11} = 16.05 Hz, H-12); 5.78 (t, 1H, *J*_{H-14,H-15} = 6.7Hz, H-14); 5.29 (d, 1H, *J* = 1.6 Hz, H-1a of one atropoisomer); 5.18 (s, 1H, H-1a

of the other atropoisomer); 4.84-4.69 (m, 2H, H-2 and H-3); 4.34 (d, 2H, $J_{H-14,H-15} = 6.7\text{Hz}$, H-15); 2.41-1.91 (m, 8H, including OH); 1.83 (s, 3H, H-13 of one atropoisomer); 1.81 (s, 3H, H-13 of one atropoisomer); 0.14 (s, 9H, SiMe₃). ¹³C NMR (50 MHz, CDCl₃) δ 159.81 (C_{quat}); 141.61 (C_{quat}); 136.34 (C_{quat}); 135.24 (C_{quat}); 132.53 (C_{quat}); 132.35 (CH); 130.49 (CH); 128.34 (CH); 128.09 (CH); 127.87 (CH); 126.92 (CH); 125.55 (CH); 125.06 (CH); 123.51 (CH); 122.50 (CH); 117.14 (CH); 114.73 (CH); 76.22 (C-2); 74.92 (C-2); 71.67 (C-3); 71.48 (C-3); 59.24 (C-15); 33.72 (CH₂); 32.77 (CH₂); 32.54 (CH₂); 32.54 (CH₂); 32.31 (CH₂); 26.44 (CH₂); 24.84 (CH₂); 24.21 (CH₂); 23.45 (CH₂); 22.72 (CH₂); 22.21 (CH₂); 14.15 (C-13); 12.63 (C-13); 0.18 (SiMe₃).

(1Z,2R,3S)-10-[(E)-2-phenylvinyl]-1-[(trimethylsilyl)methylene]-1,2,3,4,5,6-hexahydrobenzo[e]azulene-2,3-diol (21)

- Under the classical procedure

Time of heating: 18 hours

Eluent for chromatography: 60/40 (Et₂O/Hex)

R_f = 0.20 and 0.25 (10/30/60 EtOAc/DCM/Hex) for the two atropoisomers

¹H NMR (200 MHz, CDCl₃) δ 7.66 (d, 1H, $J = 7.7\text{ Hz}$, H-9); 7.47-7.16 (m, 9H); 6.95 (AB system, d, 1 H, $J_{H-12,H-11} = 15.9\text{ Hz}$); 5.38 (d, 1H, $J = 1.7\text{ Hz}$, H-1a of one atropoisomer); 5.26 (s, 1H, H-1a of the other atropoisomer); 4.90-4.67 (m, 2H, H-2 and H-3); 2.86 (d, 1H, $J = 8.7\text{ Hz}$, CH₂); 2.59-2.01 (m, 8H, including OH); 0.05 (s, 9H, SiMe₃). ¹³C NMR (50 MHz, CDCl₃) δ 159.63 (C_{quat}); 157.25 (C_{quat}); 150.69 (C_{quat}); 150.32 (C_{quat}); 142.07 (C_{quat}); 141.68; 141.10 (C_{quat}); 137.74 (C_{quat}); 137.03 (C_{quat}); 128.59 (CH); 128.59 (CH); 128.21 (CH); 128.12 (CH); 127.87 (CH); 127.44 (CH); 126.44 (CH); 123.76 (CH); 123.45; 122.94 (CH); 76.23 (C-2); 74.99 (C-2); 72.39 (C-3); 71.70 (C-3); 33.66 (CH₂); 33.18 (CH₂); 32.77 (CH₂); 32.54 (CH₂); 32.32 (CH₂); 24.13 (CH₂); 22.23 (CH₂); 0.07 (SiMe₃). IR (FTR, film): $\nu = 3396$ (br), 3059, 2949, 2861, 1703, 1599, 1495, 1451, 1406, 1248, 1105, 967, 843, 777, 739, 694 cm. MS (ESI, positive ion 140 eV): calc'd for (C₂₆H₃₀O₂SiNa)⁺ 425.1913, found 425.1227.

- Under Microwave irradiation

Reaction mixture prepared as described in the classical procedure was irradiated under microwave.

Time of heating: 10 min at 130°C (300 W during 1min).

Yield: 75%

(1Z,2R,3S)-10-[(E)-2-[3-hydroxymethyl]phenyl]vinyl)-1-[(trimethylsilyl)methylene]-1,2,3,4,5,6-hexahydro-benzo[e]azulene-2,3-diol (22)

$C_{27}H_{32}O_3Si$
Mol. Wt.: 432,63
yellow oil
yield: 61%

Time of heating: 18 hours

Eluent for chromatography: 30/70 $\rightarrow$ 70/30 (Et_2O /Hex)

R_f = 0.28 and 0.35 (70/30 Et_2O /Hex) for the two atropoisomers

¹H NMR (200 MHz, $CDCl_3$) δ 7.75 (d, 1H, J = 7.7 Hz, H-9); 7.55 (d, 1H, J = 7 Hz); 7.43-7.24 (m, 7H, H_{arom} and H-12, H-13); 7.02 (AB system, d, 1 H, J = 16.1 Hz); 5.43 (d, 1H, J = 2Hz, min, H-1a of one atropoisomer); 5.33 (s, 1H, maj, H-1a of the other atropoisomer); 4.86-4.69 (m, 4H, H-2, H-3 and H-15); 2.63-2.04 (m, 8H, including OH); 0.14 (s, 9H, $SiMe_3$). **¹³C NMR** (50 MHz, $CDCl_3$) δ 156.75 (C_{quat}); 150.93 (C_{quat}); 150.36 (C_{quat}); 141.61 (C_{quat}); 141.09 (C_{quat}); 137.11 (C_{quat}); 136.57 (C_{quat}); 141.94; 136.52; 136.33 (C_{quat}); 135.34 (C_{quat}); 132.94 (C_{quat}); 131.42 (C_{arom}); 130.99 (C_{arom}); 130.49 (C_{arom}); 129.65 (C_{arom}); 128.55 (C_{arom}); 128.42 (C_{arom}); 128.074 (C_{arom}); 127.81 (C_{arom}); 127.81 (C_{arom}); 127.54 (C_{arom}); 127.32 (C_{arom}); 126.48 (C_{arom}); 125.90 (C_{arom}); 124.27 (C_{arom}); 123.58 (CH); 123.24 (CH); 122.49 (CH); 75.98 (min, C-2 of one atropoisomer); 74.67 (maj, C-2 of the other atropoisomer); 71.60 (min, C-3 of one atropoisomer); 71.05 (maj, C-3 of the other atropoisomer); 63.88 (maj, C-15 of one atropoisomer); 63.42 (min, C-15 of the other atropoisomer); 36.61 (CH_2); 33.59 (CH_2); 33.50 (CH_2); 32.28 (CH_2); 24.66 (CH_2); 24.10 (CH_2); 22.27 (CH_2); 0.11 ($SiMe_3$). **IR** (FTR, film): ν = 3357 (br), 3239, 3059, 2948, 2858, 2157, 1692, 1607, 1507, 1454, 1247, 1170, 1095, 864, 749, 691 cm^{-1} . **HRMS** (ESI, positive ion 135 eV): calc'd for $(C_{27}H_{32}O_3SiNa)^+$ 455.2018, found 455.1959.

***tert*-butyl(E)-2-[(1Z,2R,3S)-2,3-dihydroxy-1-[(trimethylsilyl)methylene]-1,2,3,4,5,6-hexahydrobenzo[e]azulene-10-yl]vinylcarbamate (23)**

Time of heating: 18 hours

Eluent for chromatography: 30/70 $\rightarrow$ 50/30 (Et_2O/Hex)

Rf = 0.35 and 0.38 (50/50 Et_2O/Hex) for the two atropoisomers

1H NMR (200 MHz, $CDCl_3$) δ 7.48-7.37 (m, 1H, H-9); 7.23-7.12 (m, 2H, H-8 and H-7); 6.57 (AB system, d, 1H, J = 15.9 Hz, maj, H-11 of one atropoisomer); 6.36 (AB system, d, 1H, J = 15.6 Hz, min, H-11 of the other atropoisomer); 6.10-5.92 (m, 2H, H-12, two atropoisomer) 5.23 (s, 1H, min, H-1a of one atropoisomer); 5.13 (s, 1H, maj, H-1a of the other atropoisomer); 4.85-4.64 (m, 3H, H-2 and H-3); 3.81 (br s, 2H, H-13); 2.72-1.94 (m, 10H, including OH); 1.43 (s, 9H, H-13); 0.15 (s, 9H, $SiMe_3$). **^{13}C NMR** (50 MHz, $CDCl_3$) δ 165.92 (C_{quat}); 159.31 (C_{quat}); 150.19 (C_{quat}); 141.47 (C_{12}); 131.41 (C_{arom}); 128.23 (C_{arom}); 128.07 (C_{arom}); 127.61 (C_{arom}); 125.99 (CH); 125.43 (CH); 125.15 (CH); 124.04 (CH); 123.72 (CH); 123.03 (CH); 122.20 (CH); 75.95 (min, C-2 of one atropoisomer); 74.67 (maj, C-2 of the other atropoisomer); 71.38 (min, C-3 of one atropoisomer); 71.07 (maj, C-3 of the other atropoisomer); 45.84 (CH_2); 42.50 (C-13); 33.45 (CH_2); 32.57 (CH_2); 32.34 (CH_2); 32.15 (CH_2); 28.32 (C-13); 23.90 (CH_2); 22.06 (CH_2); 0.19 ($SiMe_3$). **IR** (FTR, film): ν = 3391 (br), 2157, 1651, 1393, 1366, 1259, 1170, 749 cm^{-1} . **HRMS** (ESI, positive ion 150 eV): calc'd for $(C_{26}H_{37}O_4SiNa)^+$ 478.2390, found 478.2447.

With allyl-stannane derivatives:

(1Z,2R,3S)-10-allyl-1-[(trimethylsilyl)methylene]-1,2,3,4,5,6-hexahydrobenzo[e]azulene- 2,3-diol (24)

Time of heating: 20 hours

Eluent for chromatography: 30/70 (Et_2O/Hex)

Rf = 0.15 and 0.20 (40/60 Et_2O/Hex) for the two atropoisomers

1H NMR (300 MHz, $CDCl_3$) δ 7.28-7.13 (m, 3H, H_{arom}); 5.91-5.72 (m, 1H, H-12); 5.29 (d, 1H, J = 1.7 Hz, min, H-1a of one atropoisomer); 5.25 (s, 1H, maj, H-1a of the other atropoisomer); 5.64 (d,

1H, $J = 17\text{Hz}$), 5.03-4.95 (m, 2H, H-13a and H-13b), 4.78-4.63 (m, 2H, H-1 and H-2). 3.47-3.27 (m, 2H, H-11); 3.04 (d, 1H, $J = 8,2\text{ Hz}$, CH_2); 2,62-1,95 (m, 7H including 2x OH), 0,20 (s, 9H of one atropoisomer); 0.19 (s, 9H of the other atropoisomer). $^{13}\text{C NMR}$ (50 MHz, CDCl_3) δ 159.20 (C_{quat}); 156.30 (C_{quat}); 141.49 (C_{quat}); 138.67 (C_{quat}); 138.14 (C_{quat}); 138.01 (C_{quat}); 137.51 (C_{quat}); 137.18 (C_{quat}); 135.08 (C_{quat}); 132.83 (C_{quat}); 128.08 (C_{arom}); 127.89 (C_{arom}); 127.79 (C_{arom}); 127.75 (C_{arom}); 127.04 (C_{arom}); 126.85 (C_{arom}); 121.85; 121.56; 116.11; 115.39; 75.99 (C-2, min); 74.65 (C-2, min); 71.64 (C-3, min), 69.42; 65.83; 38.09; 37.12; 33.61; 32.77; 32.42; 23.67; 22.03; 15.23; 13.57; 0.22 (SiMe_3). **HRMS** (ESI, positive ion 180 eV): calc'd for $(\text{C}_{21}\text{H}_{28}\text{O}_2\text{SiNa})^+$: 363.1756, found 363.1570.

With heterocycles-stannane derivatives

(1Z,2R,3S)-10-pyridin-2-yl-1-[(trimethylsilyl)methylene]-1,2,3,4,5,6-hexahydrobenzo[e]azulène-2,3-diol (25)

The general procedure is the same, but we use [*trans*-dichlorobis(tri-*o*-tolylphosphine)]palladium^{II} as catalyst.

Time of heating: 20 hours

Eluent for chromatography: 50/50 ($\text{Et}_2\text{O}/\text{Hex}$)

Rf = 0.15 and 0.20 (50/50 $\text{Et}_2\text{O}/\text{Hex}$) for the two atropoisomers

$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 8.56 (d, 1H, $J_{\text{H-15,H-14}} = 4.9\text{Hz}$, H-15); 7.69-7.16 (m, 6H, H_{arom}); 7.00-6.85 (m, 2H, H-12 and H-11); 4.79-4.71 (br s, 1H, H-2); 4.77 (s, 1H, H-1a); 4.47 (br s, 1H, H-3); 3.25 (br s, 1H, OH); 2.65-2.07 (m, 7H, including 1x OH); -0.13 (s, 9H, SiMe_3). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 160.27 (C_{quat}); 154.99 (C_{quat}); 150.84 (C_{quat}); 149.02 (C-15); 142.23 (C_{quat}); 143.73 (C_{arom}); 142.23 (C_{quat}); 140.56 (C_{quat}); 139.33 (C_{quat}); 136.29 (maj, C-9); 135.46 (min, C-9); 129.60 (C_{quat}); 129.39 (C_{arom}); 128.60 (C_{arom}); 128.24 (C_{arom}); 127.85 (C_{arom}); 124.40 (C_{arom}); 123.50 (C_{arom}); 121.75 (C-14); 121.35 (C_{arom}); 120.60 (C-1a) (C_{arom}), 121.51 (C_{arom}); 76.30 (min, C-3); 75.57 (maj, C-3); 72.71 (maj, C-2); 71.99 (min, C-2); 32.99 (CH_2); 32.63 (CH_2); 26.79 (CH_2); 24.66 (CH_2); 22.33 (CH_2); 17.41 (CH_2); 0.06 (SiMe_3). **IR** (FTR, film): $\nu = 3419$ (br), 2924, 2843, 1715, 1630, 1585, 1501, 1382, 1249, 1104, 1069, 775, 666 cm^{-1} . **MS** (ESI, positive ion 120 eV): calc'd for $(\text{C}_{23}\text{H}_{27}\text{NO}_2\text{SiH})^+$ 378.1889, found 378.1557.

(1Z,2R,3S)-10-(2-furyl)-1-[(trimethylsilyl)methylene]-1,2,3,4,5,6-hexahydrobenzo[e]azulène-2,3-diol (26)

Time of heating: 5 hours

Eluent for chromatography: 30/70 (Et₂O/Hex) → 50/50 (Et₂O/Hex)

R_f = 0.25 and 0.30 (50/50 Et₂O/Hex) for the two atropoisomer

¹H NMR (200.13 MHz, CDCl₃) δ 7.41 (dd, 1H, *J* = 1.94 Hz, *J* = 0.72 Hz, H-13); 7.39-7.37 (m, 1H, H₉); 7.25-7.20 (m, 4H, H_{arom} and H_{1a}); 6.41 (dd, 1H, *J* = 3.18 Hz, *J* = 1.96 Hz, H-12); 6.41 (dd, 1H, *J* = 3.18 Hz, *J* = 0.72 Hz, H-11); 4.76-4.61 (m, 2H, H-1 and H-2); 2.80 (d, 1H, *J* = 8.2 Hz, CH₂); 2.65-2.39 (m, 4H including 2x OH); 2.30-2.05 (m, 4H); -0.31 (s, 9H). **¹³C NMR** (75 MHz, CDCl₃) δ 156.24 (C_{quat}); 154.28 (C_{quat}); 150.99 (C_{quat}); 141.23 (C_{quat}); 140.24 (C_{quat}); 140.14 (C_{quat}); 139.26; 133.56 (C_{quat}); 132.54 (C_{quat}); 131.19 (C_{quat}); 128.79 (C_{arom}); 128.67 (C_{arom}); 128.14 (C_{arom}); 127.67 (C_{arom}); 125.84 (C_{arom}); 125.64 (C_{arom}); 125.36 (C_{arom}); 125.17 (C_{arom}); 121.51 (C_{arom}); 75.66 (C-2); 71.32 (C-3); 33.39 (CH₂); 32.99 (CH₂); 32.64 (CH₂); 32.55 (CH₂); 25.13 (CH₂); -2.06 (SiMe₃). **IR** (FITR, film): ν = 3735, 3402 (br), 2950, 2858, 2685, 1653, 1558, 1541, 1457, 1325, 1247, 1107, 1088, 1016, 945, 889, 841, 764, 669 cm⁻¹. **HRMS** (ESI, positive ion 180eV): calc'd for (C₂₂H₂₆O₃SiNa)⁺: 389.1549, found 389.1552.

(1Z,2R,3S)-10-thien-2-yl-1-[(trimethylsilyl)methylene]-1,2,3,4,5,6-hexahydrobenzo[e]azulène-2,3-diol (27)

- Under the classical procedure

Time of heating: 24 hours

Eluent for chromatography: 50/50 (Et₂O/Hex)

R_f = 0.30 and 0.35 (50/50 Et₂O/Hex) for the two atropoisomers

¹H NMR (300 MHz, CDCl₃) δ 7.40-7.20 (m, 4H, H_{arom} and H-13); 7.00-6.85 (m, 2H, H-12 and H-11); 4.94 (s, 1H, H-1a); 4.73 (dd, 1H, *J*_{H-2,H-3} = 14.2 Hz, *J*_{H-2,OH} = 6 Hz, H-2); 4.56-4.53 (m, 1H, H-3); 3.25 (d, 1H, *J* = 9.4 Hz, CH₂); 2.60-2.20 (m, 7H, including 2x OH); -0.03 (s, 9H, SiMe₃ of one atropoisomer); -0.05 (s, 9H, SiMe₃ of other atropoisomer). **¹³C NMR** (75 MHz, CDCl₃) δ 157.24

(C_{quat}); 154.21 (C_{quat}); 151.89 (C_{quat}); 143.73 (C_{quat}); 142.24 (C_{quat}); 140.61 (C_{quat}); 140.26 ; 133.74 (C_{quat}); 132.54 (C_{quat}); 132.19 (C_{quat}); 128.79 (CH_{arom}); 128.70 (CH_{arom}); 128.48 (C_{arom}); 127.88 (C_{arom}); 126.84 (C_{arom}); 126.49 (C_{arom}); 125.64 (C_{arom}); 125.36 (C_{arom}); 125.17 (C_{arom}), 121.51 (C_{arom}); 75.33 (C-2); 71.66 (C-3); 34.32 (CH₂); 33.18 (CH₂); 32.64 (CH₂); 32.55 (CH₂); 22.13 (CH₂); 0.06 (SiMe₃).
IR (FTR, film): ν = 3398 (br), 3056, 2935, 1762, 1708, 1441, 1267, 1105, 898, 847, 744, 472 cm⁻¹.
MS (ESI, positive ion 120 eV): calc'd for (C₂₂H₂₆O₂SSiNa)⁺ 405.1320, found 405.1547.

- Under Microwave irradiation

Reaction mixture prepared as described in the classical procedure was irradiated under microwave.

Time of heating: 3 x 10 min at 120°C (220 W during 2min)

Yield: 53%

(1S*,2R*)-1(1-bromo-3,4-dihydronaphtalen-2-yl)-4-(trimethylsilyl)but-3-yne-1,2 diol and (1R*,2R*)-1(1-bromo-3,4-dihydronaphtalen-2-yl)-4-(trimethylsilyl)but-3-yne-1,2 diol (28)

A solution of *n*-butyllithium (3.25 mL, 1.5 equiv, 1.57 M in hexane) was added to a dried round-bottom flask containing 3-[(1-methoxy-1-methyl-ethoxy)-prop-1-ynyl]trimethylsilane (1.18 g, 5.90 mmol, 1.4 equiv) in freshly distilled THF (10 mL) at -78°C. The reaction was stirred 15 min at this temperature and was added *via cannula* at a solution of 1-bromo-3,4-sihydronaphtalene-2-carbaldehyde (1 g, 4.12 mmol, 1 equiv) in THF (15 mL). The mixture was stirred for 20 min at -78°C and then allowed to warm up to rt for one hour. Then the mixture was quenched by addition of saturated aqueous NaHCO₃ (20 mL). After extraction with Et₂O (3x 50 mL), the combined organic layers were washed with water, brine, dried over Na₂SO₄ and concentrated *in vacuo*. The alcohols were deprotected by dissolving this oil in methanol (25 mL) containing a catalytic quantity of PPTS. The solution was stirred over night (18 hours) at rt and quenched with the addition of water (5 mL). The mixture was extracted with Et₂O and the combined extracts were washed with water, brine and dried over Na₂SO₄. The two diastereoisomers were separated by chromatography on silica gel (AcOEt/DCM/Hex, 5:40:55) to afford compounds *anti (unlike)* (680 mg, 0.66 mmol) and *syn (like)* (388 mg, 0.28 mmol) as clear brown solid for a global yield of 73 % and a ratio of 5 / 3.

Compound *syn* (like)

C₁₇H₂₁BrO₂Si
Mol. Wt.: 365,34
yellow solid

R_f = 0.45 (Et₂O/Hex: 50/50)

¹H NMR (200 MHz, CDCl₃) δ 7.65 (d, 1, *J* = 7,1 Hz, H-8); 7.30-7.10 (m, 3H, H_{arom}); 5.09 (t ap, 1H, *J*_{H-10,H-9} = 3.4 Hz); 4.49 (t, 1H, *J*_{H-10,H-9} = 5.9 Hz); 2.96 (s, 1H); 2.89-2.78 (m, 3H); 2.68-2.34 (m, 4H including 2x OH); 0.12 (s, 9H, SiMe₃). **¹³C NMR** (50 MHz, CDCl₃) δ 137.23 (C-1); 136.74 (C-8a); 133.67 (C-4a); 128.20 (C_{arom}); 127.44 (C_{arom}); 126.83 (C_{arom}); 126.62 (C_{arom}); 121.51 (C-2); 102.24 (C-11); 92.12 (C-12); 77.51 (C-11); 65.08 (C-10); 27.88 (CH₂); 24.89; (CH₂); -0.35 (SiMe₃).

Compound *anti* (unlike)

C₁₇H₂₁BrO₂Si
Mol. Wt.: 365,34
yellow solid

R_f = 0.45 (Et₂O/Hex: 50/50)

¹H NMR (200 MHz, CDCl₃) δ 7.64 (d, 1, *J* = 7,5 Hz, H-8); 7.28-7.11 (m, 3H, H_{arom}); 5.09 (t ap, 1H, *J*_{H-10,H-9} = 4.5 Hz); 4.66 (t, 1H, *J*_{H-10,H-9} = 4.5 Hz); 2.96 (s, 1H); 2.83-2.71 (m, 3H); 2.53-2.44 (m, 3H including 2x OH); 0.19 (s, 9H, SiMe₃). **¹³C NMR** (50 MHz, CDCl₃) δ 137.59 (C-1); 136.79 (C-8a); 133.28 (C-4a); 128.27 (C_{arom}); 126.93 (C_{arom}); 126.83 (C_{arom}); 126.68 (C_{arom}); 119.82 (C-2); 102.76 (C-11); 92.16 (C-12); 76.34 (C-11); 64.53 (C-10); 27.97 (CH₂); 24.88; (CH₂); -0.28 (SiMe₃).

(1Z,2R,3S)-1-[1-(trimethylsilyl)prop-2-enylidene]-2,3,4,5-tetrahydro-1H-cyclopenta[*e*]naphthalene-2,3-diol (29)

C₁₉H₂₄O₂Si
Mol. Wt.: 312,48
brown oil

Reaction mixture prepared as described in the classical procedure was irradiated under microwave.

Time of heating: 30 min at 120°C, then 30 min at 130°C

Yield: 59%

Rf: 0.40 (Et₂O/Hex : 70/30)

¹H NMR (200 MHz, CDCl₃) δ 7.48 (d, 1H, J_{ortho} = 7.1 Hz, H-9); 7.27-7.08 (m, 3H, H_{arom}); 6.85 (dd, 1H, $J_{H-11,H-12}$ = 11 Hz, $J_{H-11,H-13}$ = 17 Hz, maj, H-11 of one atropoisomer); 6.42 (dd, 1H, $J_{H-11,H-12}$ = 11 Hz, $J_{H-11,H-13}$ = 17 Hz, min, H-11 of the other atropoisomer); 5.64 (dd, 1H, $J_{H-11,H-13}$ = 1 Hz, $J_{H-11,H-12}$ = 17 Hz, H-12); 5.11 (dd, 1H, $J_{H-13,H-12}$ = 1 Hz, $J_{H-11,H-12}$ = 11 Hz, H-13); 4.81-4.66 (m, 2H, H-2 and H-3); 2.80-2.39 (m, 6H including 2x OH); 0.32 (s, 9H, SiMe₃ of one atropoisomer); 0.19 (s, 9H, SiMe₃ of the other atropoisomer). **¹³C NMR** (75 MHz, CDCl₃) δ 159.25 (C_{quat}); 155.36 (C_{quat}); 150.75 (C_{quat}); 148.72 (C_{quat}); 141.72 (C_{quat}); 141.00 (C_{quat}); 139.95 (C_{quat}); 136.21 (C-11 of one atropoisomer); 136.18 (C-11 of the other atropoisomer); 132.48 (C_{quat}); 131.95 (C_{quat}); 128.25 (C_{arom}); 127.74 (C_{arom}); 126.95 (C_{arom}); 125.44 (C_{arom}); 123.05 (C_{arom}); 75.97 (min, C-2 of one atropoisomer); 74.65 (maj, C-2 of the other atropoisomer); 71.36 (min, C-3 of one atropoisomer); 71.16 (maj, C-3 of the other atropoisomer); 33.82 (CH₂); 32.49 (CH₂); 32.11 (CH₂); 23.89 (CH₂); 22.15 (CH₂); -0.22 (SiMe₃); -0.32 (SiMe₃). **MS** (ESI, positive ion 180 eV): calc'd for (C₁₉H₂₄O₂SiNa)⁺: 335.1443, found 335.2106

(1Z,3R*,4R*)-1-bromo-1-phenyl-6-(trimethylsilyl)hex-1-en-5-yne-3,4-diol and (1Z,3S*,4R*)-1-bromo-1-phenyl-6-(trimethylsilyl)hex-1-en-5-yne-3,4-diol (30)

solution of *n*-butyllithium (4 mL, 1.3 equiv, 1.45 M in hexane) was added to a dried round-bottom flask containing 3-[(1-methoxy-1-methyl-ethoxy)-prop-1-ynyl]trimethylsilane (1.2 g, 6.21 mmol, 1.2 equiv) in freshly distilled THF (10 mL) at -78°C. The reaction was stirred 15 min at this temperature and was added *via cannula* at a solution of (2Z)-3-bromo-3-phenylacrylaldehyde (1 g, 4.78 mmol, 1 equiv) in THF (10 mL). The mixture was stirred for 30 min at -78°C and then allowed to warm up to rt for 30 min. Then the mixture was quenched by addition of saturated aqueous NaHCO₃ (30 mL). After extraction with Et₂O, the combined organic layers were washed with water, brine, dried over Na₂SO₄ and concentrated *in vacuo*. The alcohols were deprotected by dissolving this oil in methanol (25 mL) containing a catalytic quantity of PPTS. The solution was stirred over night (18 hours) at rt and quenched with the addition of water (5 mL). The mixture was extracted with Et₂O and the combined extracts were washed with water, brine and dried over Na₂SO₄. The two diastereoisomers were separated by chromatography on silica gel (AcOEt/ Hex, 20/80) to

afford compounds *anti* (*unlike*) (237 mg) and *syn* (*like*) (109 mg) as clear brown solid for a global yield of 55 % and a ratio of 2 / 1.

Compound *syn* (*like*)

R_f = 0.25 (Et₂O/Hex: 5/5)

¹H NMR (200 MHz, CDCl₃) δ 7.44-7.28 (m, 5H, H_{arom}); 6.33 (d, 1H, J = 3.8 Hz, H-2); 4.77 (dd, 1H, J = 3.5 Hz ; J = 3.8 Hz, H-3); 4.44 (d, 1 H, J = 3.5 Hz, H-4); 2.03 (s br, 2x OH); 0.19 (s, 9H, SiMe₃). **¹³C NMR** (75 MHz, CDCl₃) δ 167.96 (C-1); 130.80 (C-7); 129.23 (C_{arom}); 128.61 (C_{arom}); 128.33 (C_{arom}); 128.00 (C_{arom}); 126.62 (C-2); 105.50 (C-5); 95.04 (C-6); 75.30 (C-3); 65.86 (C-2); - 0.22 (SiMe₃).

Compound *anti* (*unlike*)

R_f = 0.30 (Et₂O/Hex: 5/5)

¹H NMR (200 MHz, CDCl₃) δ 7.57-7.34 (m, 5H, H_{arom}); 6.38 (d, 1H, J = 3.9 Hz, H-2); 4.81 (dd, 1H, J = 4.8 Hz ; J = 3.6 Hz, H-3); 4.58 (d, 1 H, J = 3.5 Hz, H-4); 2.21 (s br, 2x OH); 0.20 (s, 9H, SiMe₃). **¹³C NMR** (75 MHz, CDCl₃) δ 168.21 (C-1); 130.63 (C-7); 129.23 (C_{arom}); 129.04 (C_{arom}); 128.83 (C_{arom}); 128.64 (C_{arom}); 128.35 (C_{arom}); 127.72 (C-2); 105.50 (C-5); 95.04 (C-6); 74.58 (C-3); 65.29 (C-2); -0.21 (SiMe₃).

(1R*,2S*,5Z)-5[(trimethylsilyl)methylene]-4-(2-vinylphenyl)cyclopent-3-ene-1,2-diol (31)

Reaction mixture prepared as described in the classical procedure was irradiated under microwave.

Time of heating: 40 min at 120°C

Yield: 43%

R_f = 0.30 (AcOEt/Hex: 3/7)

¹H NMR (300 MHz, CDCl₃) δ 7.63 (d, 1H, *J*_{ortho} = 7.14 Hz, H-11); 7.37-7.28 (m, 3H, H_{arom}); 7.17-7.11 (m, 1H, H_{arom}); 6.64 (dd, 1H, *J*_{H-12,H-13a} = 11 Hz, *J*_{H-11,H-13b} = 17 Hz, H-12); 6.10 (d, 1H, *J*_{H-13a,H-12} = 17 Hz, H-13b); 5.67 (d, 1H, *J*_{H-13b,H-12} = 17 Hz; H-13a); 5.34 (s, 1H, H-6); 5.19 (d, 1H, *J*_{H-3,H-2} = 11 Hz); 4.79 (d br, 2H, H-2 and H-3); 0.16 (s, 9H, SiMe₃). **¹³C NMR** (75 MHz, CDCl₃) δ 159.67 (C_{quat}); 138.55 (C_{quat}); 137.82 (C_{quat}); 136.62 (C_{quat}); 136.31 (C_{quat}); 135.00 (C_{quat}); 133.54 (C_{quat}); 129.65 (C_{arom}); 128.10 (C_{arom}); 127.91 (C_{arom}); 127.48 (C_{arom}); 127.26 (C_{arom}); 126.45 (CH); 125.08 (CH); 114.63 (C-6); 73.42 (C-1); 71.23 (C-2); -0.27 (SiMe₃). **HRMS** (ESI, positive ion 180 eV): calc'd for (C₂₀H₃₆O₂SiNa)⁺: 349.1600, found 349.1601

With alkynes-stannane derivatives

(1Z,2R,3S)-1-[3-phenyl-1-(trimethylsilyl)prop-2-ynylidene]-1,2,3,4,5,6-hexahydrobenzo[e]azulene-2,3-diol (**38**)

C₂₆H₂₈O₂Si
Mol. Wt.: 400,58
yellow solid
yield: 58%

Time of heating: 12 hours

Eluent for chromatography: 30/70 (Et₂O/Hex)

R_f = 0.30 and 0.35 (60/40 Et₂O/Hex) for the two atropoisomers

¹H NMR (200 MHz, CDCl₃) δ 7.45-7.08 (m, 8H); 6.66-6.61 (m, 1H, H-10); 4.86-4.72 (m, 2H, H-2 and H-3); 2.79 (d, 1H, *J* = 8.7 Hz, CH₂); 2.69-2.15 (m, 7H, including OH); 0.40 (s, 9H, maj, SiMe₃ of one atropoisomer); 0.12 (s, 9H, min, SiMe₃ of the other atropoisomer). **¹³C NMR** (50 MHz, CDCl₃) δ 157.99 (C_{quat}); 152.87 (C_{quat}); 141.72 (C_{quat}); 141.35 (C_{quat}); 140.90 (C_{quat}); 136.52 (C_{quat}); 134.76 (C_{quat}); 131.23 (C_{arom}); 131.13 (C_{arom}); 129.90 (C_{arom}); 129.06 (C_{arom}); 128.38 (C_{arom}); 128.24 (C_{arom}); 127.88 (C_{arom}); 127.79 (C_{arom}); 127.67 (C_{arom}); 127.29 (C_{arom}); 127.17 (C_{arom}); 126.04 (C_{arom}); 125.24 (C_{arom}); 124.14 (C_{arom}); 116.57 (C_{quat}); 102.76 (C-1c); 91.33 (C-1b); 76.37 (C-2); 73.54 (C-3); 33.12 (CH₂); 32.92 (CH₂); 32.30 (CH₂); 32.09 (CH₂); 28.18 (CH₂); 26.77 (CH₂); 23.73 (CH₂); 17.03 (CH₂); 0.39 (SiMe₃); 0.32 (SiMe₃). **IR** (FTR, film): ν = 3372 (br), 3064, 3014, 2948, 2845, 2168, 1591, 1549, 1489, 1446, 1398, 1247, 1158, 1109, 1085, 1015, 844, 756, 691 cm⁻¹. **HRMS** (ESI, positive ion 140 eV): calc'd for (C₂₆H₂₈O₂SiNa)⁺ 423.1756, found 423.1753.

(1Z,2R,3S)-1-[1,3-bis(trimethylsilyl)prop-2-ynylidene]-1,2,3,4,5,6-hexahydrobenzo[e]azulene-2,3-diol (39)

Time of heating: 5 hours

Eluent for chromatography: 30/70 (Et₂O/Hex)

R_f= 0.30 and 0.40 (60/40 Et₂O/Hex) for the two atropoisomer

¹H NMR (300 MHz, CDCl₃) δ 7.31-7.28 (m, 1H_{arom}); 7.20-7.12 (m, 3H_{arom}); 4.78-4.65 (m, 2H, H-2 and H-3); 2.67 (d, 1H, *J* = 8.7 Hz, CH₂); 2.60 (t, 2H, *J* = 6.4 Hz); 2.47-2.34 (m, 1H); 2.20-2.01 (m, 4H, including OH); 0.31 (s, 9H, H-11); 0.17 (s, 9H, SiMe₃). **¹³C NMR** (50 MHz, CDCl₃) δ 159.14 (C_{quat}); 152.62 (C_{quat}); 141.77 (C_{quat}); 140.67 (C_{quat}); 134.63 (C_{quat}); 130.13 (C_{arom}); 128.14 (C_{arom}); 127.19 (C_{arom}); 124.96 (C_{arom}); 117.02 (C_{quat}); 107.83 (C_{alkyne}); 105.51 (C_{alkyne}); 75.66 (C-2); 73.56 (C-3); 33.08 (CH₂); 32.15 (CH₂); 23.69 (CH₂); 0.11 (C-11); 0.05 (SiMe₃). **IR** (FTR, film): ν = 3309 (br), 2956, 2845, 2105, 1555, 1446, 1317, 1248, 1160, 1111, 934, 843, 760, 635 cm⁻¹. **MS** (ESI, positive ion 120 eV): calc'd for (C₂₃H₃₂O₂Si₂Na)⁺ 419.18, found 419.14.

(1Z,2R,3S)-1-[6-[[*tert*-butyl(dimethyl)silyl]oxy]-1-(trimethylsilyl)hex-2-ynylidene]-1,2,3,4,5,6-hexahydrobenzo[e]azulene-2,3-diol (40)

Time of heating: 8 hours

Eluent for chromatography: 30/70 (Et₂O/Hex) → 50/50 (Et₂O/Hex)

R_f= 0.20 and 0.25 (30/70 Et₂O/Hex) for the two atropoisomers

¹H NMR (300 MHz, CDCl₃) δ 7.30-7.14 (m, 4H, H_{arom}); 4.79-4.61 (m, 2H, H-2 and H-3); 3.75 (t, 2H, *J* = 6.3 Hz, H-13 of one atropoisomer); 3.35 (t, 2H, *J* = 7.3 Hz of the other atropoisomer); 3.08 (t, 2H, *J* = 8.4 Hz, H-13 of the other atropoisomer); 2.75-2.52 (m, 3H); 2.38-2.09 (m, 6H including OH and H-11); 1.90-1.63 (m, 2H, H-12 of the two forms); 0.87 (s, 9H, H-15); 0.30 (s, 6H, H-14); 0.01 (s, 9H, SiMe₃). **¹³C NMR** (50 MHz, CDCl₃) δ 150.95 (C_{quat}); 140.65 (C_{quat}); 134.64 (C_{quat}); 129.40 (C_{arom}); 128.08 (C_{arom}); 126.97 (C_{arom}); 125.61 (C_{arom}); 99.22 (C_{alkyne});

98.01 (C_{alkyne}); 75.72 (C-2); 73.46 (C-3); 61.68 (C-12); 33.01 (CH₂); 32.92 (CH₂); 32.30 (CH₂); 32.09 (CH₂); 25.96 (C-20); 24.05 (CH₂); 23.56 (CH₂); 0.23 (C-13); -5.31 (SiMe₃). **IR** (FTR, film): ν = 3402 (br), 3315, 2956, 2856, 2151, 1695, 1610, 1463, 1379, 1292, 1251, 1105, 1007, 959, 839, 758, 666 cm⁻¹. **HRMS** (ESI, positive ion 140 eV): calc'd for (C₂₉H₄₄O₃Si₂Na)⁺ 519.2727, found 519.2529.

(1Z,2R,3S)-1-[5-[[*tert*-butyl(dimethyl)silyl]oxy}-1-(trimethylsilyl)pent-2-ynylidene]-1,2,3,4,5,6-hexahydrobenzo[e]azulene-2,3-diol (41)

Time of heating: 8 hours

Eluent for chromatography: 30/70 (Et₂O/Hex) → 50/50 (Et₂O/Hex)

R_f = 0.17 and 0.24 (30/70 Et₂O/Hex) for the two atropoisomers

¹H NMR (200 MHz, CDCl₃) δ 7.31-7.16 (m, 4H, H_{arom}); 4.79-4.64 (m, 2H, H-2 and H-3); 3.08 (t, 2H, *J* = 7.4 Hz, H-12); 2.66-2.56 (m, 3H); 2.43-2.34 (m, 1H); 2.17-2.01 (m, 6H including 2x OH and H-11); 0.85 (s, 9H, H-15); 0.30 (s, 6H, H-14); 0.01 (s, 9H, SiMe₃). **¹³C NMR** (50 MHz, CDCl₃) δ 151.95 (C_{quat}); 140.65 (C_{quat}); 134.84 (C_{quat}); 129.80 (C_{arom}); 128.08 (C_{arom}); 126.97 (C_{arom}); 124.61 (C_{arom}); 100.22 (C_{alkyne}); 100.01 (C_{alkyne}); 75.72 (C-2); 73.46 (C-3); 61.68 (C-12); 33.01 (CH₂); 32.92 (CH₂); 32.30 (CH₂); 32.09 (CH₂); 25.96 (C-20), 24.05 (CH₂); 23.56 (CH₂); 0.23 (C-13); -5.31 (SiMe₃). **IR** (FTR, film): ν = 3402 (br), 3055, 2986, 2685, 2410, 2305, 1646, 1422, 1265, 1047, 895, 742 cm⁻¹. **HRMS** (ESI, positive ion 140 eV): calc'd for (C₂₈H₄₂O₃Si₂Na)⁺ 505.2570, found 505.2476.

(1Z,2R,3S)-1-[1-(trimethylsilyl)hex-2-ynylidene]-1,2,3,4,5,6-hexahydrobenzo[e]azulene-2,3-diol (42)

Time of heating: 18 hours

Eluent for chromatography: 30/70 (Et₂O/Hex)

R_f = 0.25 and 0.30 (50/50 Et₂O/Hex) for the two atropoisomers

¹H NMR (200 MHz, CDCl₃) δ 7.31-7.14 (m, 4H, H_{arom}); 5.07 (br, 1H, H-2 or H-3 of one atropoisomer); 4.75-4.70 (m, 2H, H-2 and H-3); 3.08 (t, 2H, *J* = 7.4 Hz, H-12); 3.02 (br m, 1 H, CH₂ of one atropoisomer); 2.84 (br m, 1H, CH₂ of the other atropoisomer); 2.66-2.56 (m, 3H); 2.62-2.05 (m, 7H including 2x OH); 1.77 (t, 2H, *J*_{H-11,H-12} = 6.9 Hz, min, H-11 of one atropoisomer); 1.62 (q ap, 2H, *J*_{H-11,H-12} = 7.2 Hz, maj, H-11 of the other atropoisomer); 1.45-1.26 (m, 2H, H-12); 1.04 (t, 3H, *J*_{H-12,H-13} = 7.1Hz, min, H-13 of one atropoisomer); 0.92 (t, 2H, *J*_{H-12,H-13} = 7.1 Hz, maj, H-13 of the other atropoisomer); 0.68 (t, 1H, *J* = 7.1 Hz); 0.30 (s, 9H, SiMe₃ of one atropoisomer); -0.22 (s, 9H, SiMe₃ of the other atropoisomer). **¹³C NMR** (50 MHz, CDCl₃) δ 156.75 (C_{quat}); 151.63 (C_{quat}); 141.49 (C_{quat}); 141.37 (C_{quat}); 140.61 (C_{quat}); 136.81 (C_{quat}); 134.86 (C_{quat}); 131.09 (C_{arom}); 130.02 (C_{arom}); 128.97 (C_{arom}); 128.15 (C_{arom}); 127.99 (C_{arom}); 127.60 (C_{arom}); 126.75 (C_{arom}); 125.94 (C_{arom}); 124.58 (C_{arom}); 117.79 (C_{quat}); 103.97 (C_{alkyne}); 91 (C_{alkyne}); 75.01 (C-2); 73.45 (C-3); 33.04 (C-6); 32.10 (C-6); 28.14 (min, C-5); 26.75 (maj, C-5); 23.53 (C-4); 22.55 (C-4); 21.81 (C-11); 21.72 (C-11); 17.31 (C-12); 13.65 (C-13); 13.55 (C-13); 0.25 (SiMe₃ of one atropoisomer); -0.46 (SiMe₃ of the other atropoisomer). **IR** (FTR, film): ν = 3412 (br), 2947, 2918, 1647, 1263, 1110, 965, 844, 762, 701 cm⁻¹. **HRMS** (ESI, positive ion 200eV): calc'd for (C₂₃H₃₀O₂SiNa)⁺ 389.1913, found 389.1904.

(1Z,2R,3S)-1-[(4E)-6-{*tert*-butyl(dimethyl)silyl}oxy]-4-methyl-1-(trimethylsilyl)hex-4-en-2-ynylidene]-1,2,3,4,5,6-hexahydrobenzo[e]azulene-2,3-diol (43)

Time of heating: under microwave irradiation, 3 x 10 min at 130°C

Eluent for chromatography: (50/50 Et₂O/Hex)

R_f = 0.22 and 0.29 (10/30/60 EtOAc/DCM/Hex) for the two atropoisomer

¹H NMR (200 MHz, CDCl₃) δ 7.29-7.16 (d, 4H, H_{arom}); 5.17(dt, 1H, *J*_{H-15,H-16} = 6.3 Hz, *J* = 1.4 Hz); 4.81-4.66 (m, 2H, H-2 and H-3); 4.29 (d, 2H, *J*_{H-15,H-16} = 9.7 Hz, min, H-16 of one atropoisomer); 4.08 (d, *J*_{H-15,H-16} = 9.7 Hz, maj, H-16 of the other atropoisomer); 2.67-2.47 (m, 3H); 2.44-2.03 (m, 5H, including 2x OH); 1.56 (s, 3H, H-14 of one atropoisomer); 1.44 (s, 3H, H-16 of the other atropoisomer); 0.87 (s, 9H, H-18); 0.33 (s, 9H, SiMe₃); 0.04 (s, 9H, H-17). **¹³C NMR** (75 MHz, CDCl₃) δ 158.9 (C_{quat}); 157.48 (C_{quat}); 152.38 (C_{quat}); 141.65 (C_{quat}); 140.76 (C_{quat}); 140.26 (C_{quat}); 135.50 (C_{quat}); 134.78 (C_{quat}); 129.77 (CH); 129.00 (CH); 119.55 (CH); 119.07 (CH); 116.86 (CH); 105.33 (C-1b); 88.88 (C-1c); 75.75 (C-2); 73.60 (C-3); 59.99 (C-16); 33.10 (CH₂); 32.74 (CH₂); 32.27 (CH₂); 31.90 (CH₂); 31.42 (CH₂); 30.17 (CH₂); 29.68 (CH₂); 29.35 (CH₂); 25.99 (CH₂); 23.71

(CH₂); 22.67 (CH₂); 18.30 (CH₂); 16.91 (CH₂); 14.10 (CH₂); 0.32; -0.39; -5.16 (SiMe₃). **MS** (ESI, positive ion 200 eV): calc'd for (C₃₀H₄₄O₃Si₂Na)⁺ 531.27, found 531.36.

4-deuterium-6,7,8,9 tetrahydro-5H-benzo[7]annulen-5-one (1-D₁)

50 mL flask containing α -benzosuberone (1 g, 6.24 mmol), [(cyclooctadiene)(pyridine)(tricyclohexylphosphine)iridium(I)hexafluorophosphate] (251 mg, 0.31 mmol) in CH₂Cl₂ (30 mL) containing deuterium oxide (20 drops) was evacuated, flushed with deuterium, and stirred for 92 h at room temperature. The crude mixture was quenched with an aqueous NaHCO₃ solution, then extracted with Et₂O (240 mL), washed with brine, dried over Na₂SO₄ and concentrated to a brown oil (1g, 100%). The deuteration incorporation $\geq 92\%$.

¹H NMR (300 MHz, CDCl₃) δ 7.72 (d, 0.08H, J = 11.3 Hz); 7.43 (t, 1H, J = 11 Hz); 7.30 (d, 1H, J = 11 Hz); 7.21 (d, 1H, J = 11 Hz); 2.94 (t, 2H, J = 8.4 Hz); 2.74 (t, 2H, J = 9.9 Hz); 1.96-1.76 (m, 4H). **¹³C NMR** (75 MHz, CDCl₃) δ 206.21; 141.27; 138.77; 132.16; 129.65; 126.52; 40.85; 32.52; 25.23; 20.91.

9-bromo-1-deutero-6,7-dihydro-5H-benzo[7]annulene-8-carbaldehyde

This compound was prepared using the same experimental procedure than 9-bromo-6,7-dihydro-5H-benzo[7]annulene-8-carbaldehyde, starting for 1g from **1-D₁** (1 g, 6.24 mmol), PBr₃ (2.2 mL, 24.3 mmol), DMF (2.8 mL, 39.3 mmol) in 18 mL of anhydrous CH₂Cl₂. Chromatography on silica gel (hexane/ether 20:80) gives the deutero-carbaldehyde (870 mL, 345 mmol, 55%).

¹H NMR (300 MHz, CDCl₃) δ 10.22 (s, 1H); 7.66 (d, 0.08H, J = 9 Hz); 7.35 (d, 1H, J = 9 Hz); 7.25-7.22 (t, 1H, J = 11 Hz); 2.61 (t, 2H, J = 6.8 Hz); 2.24 (t, J = 8.76 Hz); 2.17 (q, 4H, 6.87Hz). **¹³C NMR** (50 MHz, CDCl₃) δ 192.43; 152.5; 140.32; 139.21; 138.99; 138.37; 130.39; 129.58; 128.77; 126.48; 33.68; 31.79; 22.51.

(1R*,2S*)-1-(1-deutero-9-bromo-6,7-dihydro-5H-benzo[7]annulen-8-yl)-4-trimethylsilyl-but-3-yne-1,2-diol and (1R*,2R*)-1-(1-deutero-9-bromo-6,7-dihydro-5H-benzo[7]annulen-8-yl)-4-trimethylsilyl-but-3-yne-1,2-diol (2-D₁)

A solution of *n*-butyllithium (3.56 mL, 1.5 equiv, 1.45 M in hexane) was added to a dried round-bottom flask containing 3-[(1-methoxy-1-methyl-ethoxy)-prop-1-ynyl]trimethylsilane (8 g, 5.97 mmol, 1.5 equiv) in freshly distilled THF (10 mL) at -78°C. The reaction was stirred 30 min at this temperature and was added *via cannula* at a solution of 9-bromo-1-deutero-6,7-dihydro-5H-benzo[7]annulene-8-carbaldehyde (870 mg, 3.45 mmol, 1 equiv) in THF (10 mL). The mixture was stirred for 30 min at -78°C and then allowed to warm up to rt for one hour. Then the mixture was quenched by addition of saturated aqueous NaHCO₃ (25 mL). After extraction with Et₂O, the combined organic layers were washed with water, brine, dried over Na₂SO₄ and concentrated *in vacuo*. The alcohols were deprotected by dissolving this oil in methanol (25 mL) containing a catalytic quantity of PPTS. The solution was stirred over night (18 hours) at rt and quenched with the addition of water (5 mL). The mixture was extracted with Et₂O and the combined extracts were washed with water, brine and dried over Na₂SO₄. The two diastereoisomers were separated by chromatography on silica gel (AcOEt/DCM/Hex, 5:40:55) to afford compounds *anti* (*unlike*) (330 mg, 0.66 mmol) and *syn* (*like*) (107 mg, 0.28 mmol) as clear brown solid for a global yield of 37 % and a ratio of 3 / 1.

Compound *syn* (*like*)

R_f = 0.25 (AcOEt/DCM/Hex: 5:40:55)

¹H NMR (200 MHz, CDCl₃) δ 7.57 (d, 0,1H, *J* = 7,1 Hz); 7.36-7.18 (m, 3H, H_{arom}); 5.12 (t ap, 1H, *J*_{H-10,H-11} = 4.8 Hz); 4.67 (t ap, 1H, *J*_{H-10,H-11} = 4.8 Hz); 2.71-2.58 (m, 4H); 2.31-2.03 (m, 4H including 2x OH); 0.20 (s, 9H, SiMe₃). **¹³C NMR** (75 MHz, CDCl₃) δ 140.01 (C-9); 139.9 (C-9a); 129.44 (C_{arom}, coupling with deuterium); 128.45 (C_{arom}); 128.23 (C_{arom}); 126.16 (C_{arom}); 120.81 (C_{quat}); 103.12 (C-11); 92.04 (C-12); 78.04 (C-11); 65.32 (C-10); 34.94 (CH₂); 31.28; (CH₂); 25.34 (CH₂); -0.27 (SiMe₃). **IR** (FTR, film): ν = 3402; 2949; 2182; 1698; 1635; 1556; 1454; 1388; 1264; 1059; 977; 851; 755; 683 cm⁻¹. **MS** (ESI, positive ion 90 eV): calc'd for (C₁₈H₂₂DBrO₂SiNa)⁺ 402.0610, found 401.9697.

Compound *anti* (*unlike*)

Rf = 0.20 (AcOEt/DCM/Hex: 5:40:55)

1H NMR (200 MHz, $CDCl_3$) δ 7.58 (d, 0.1H, $J = 7.3$ Hz); 7.35-7.14 (m, 3H, H_{arom}); 5.17 (d, 1H, $J_{H-10,H-11} = 8$ Hz); 4.68 (d, 1H, $J_{H-10,H-11} = 8$ Hz); 3.09-2.58 (m, 4H); 2.32-1.90 (m, 4H including 2x OH); 0.20 (s, 9H, $SiMe_3$). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 140.17 (C-9); 139.54 (C-9a, coupling with deuterium); 129.51 (C_{arom}); 128.23 (C_{arom}); 128.10 (C_{arom}); 125.89 (C_{arom}); 118.86 (C_{quat}); 103.12 (C-13); 92.05 (C-12); 76.62 (C-11); 64.82 (C-10); 34.98 (CH_2); 31.85 (CH_2); 25.73 (CH_2); -0.37 ($SiMe_3$). **IR** (FTR, film): $\nu = 3394$; 3059; 2927; 2857; 2177; 1616; 1452; 1408; 1339; 1250; 1094; 1052; 1014; 899; 845; 762; 685 cm^{-1} . **MS** (ESI, positive ion 90 eV): calc'd for $(C_{18}H_{22}DBrO_2SiNa)^+$ 402.0610, found 401.9705.

(1Z,2R,3S)-1-[trimethylsilyl]methylene]-1a-deutero-10-vinyl-1,2,3,4,5,6-hexahydrobenzo[e]azulene-2,3-diol (17-D₁)

To a solution of (1R*,2S*)-1-(5-bromo-4-deutero-8,9-dihydro-7H-benzocycloheptene-6-yl)-4-trimethylsilylbut-3-yn-1,2-diol (**2-D₁**) (50 mg, 1 equiv, 0,131 mmol) in dried benzene (5 mL), was added $Pd(PPh_3)_4$ (15 mg, 0.1 equiv) and tributylstannylethylene (62 mg, 1.5 equiv). The mixture was purged 20 min with argon and heated at 95°C under argon during 22 hours. The reaction is followed by TLC (Et_2O /Hex 30:70, anisaldehyde). The mixture was cooled to room temperature, diluted in Et_2O , treated with active *charcoal*, filtrated over *celite*, and concentrated to dryness. The crude product was purified by flash chromatography on silica gel (elution with Et_2O /Hex 30:70) to afford 60 mg of two inseparable atropoisomer (51%). The two forms are in equilibrium (ratio 6/4).

Rf = 0.33 et 0.35 (Et_2O /Hex: 30/70) for the two atropoisomers.

1H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, 1H, $J_{ortho} = 7.7$ Hz, H-9); 7.28-7.14 (m, 2H, H-7 and H-8); 6.70 (dd, 1H, maj, $J_{H-11,H-12a} = 10.9$ Hz, $J_{H-11,H-12b} = 17.4$ Hz, H-11 of one atropoisomer); 6.57 (dd, 1H, min, $J_{H-11,H-12a} = 10.9$ Hz, $J_{H-11,H-12b} = 17.4$ Hz, H-11 of the other atropoisomer); 5.63 (d, 1H, $J_{H-11,H-12b} = 17.4$ Hz, H-12b); 5.20 (s, 0.1H, H-1a); 5.13 (2x d ap t, 1H, $J_{H-11,H-12a} = 10.9$ Hz, H-12a of the two atropoisomer); 4.83-4.63 (m, 2H, H-1 and H-2); 2.77 (d, 1H, $J = 8.2$ Hz, CH_2); 2.53-2.06 (m,

7H, including OH); 0,15 (s, 9H, SiMe₃). ¹³C NMR (50 MHz, CDCl₃) δ 159.63 (C_{quat}); 157.25 (C_{quat}); 150.69 (C_{quat}); 150.32 (C_{quat}); 142.17 (C_{quat}); 141.62; 140.90 (C_{quat}); 137.52 (C_{quat}); 137.03 (C_{quat}); 128.51 (CH); 128.59 (CH); 128.21 (CH); 127.99 (CH); 127.87 (CH); 127.44 (CH); 123.76 (CH); 123.45; 122.94 (CH); 76.23 (C-2); 74.99 (C-2); 72.41 (C-3); 71.58 (C-3); 33.66 (CH₂); 33.15 (CH₂); 32.69 (CH₂); 32.54 (CH₂); 32.32 (CH₂); 24.09 (CH₂); 22.23 (CH₂); 0.07 (SiMe₃). IR (FTR, film): ν = 3410; 2945; 2927; 2845; 1703; 1410; 1249; 1096; 950; 843; 750 cm⁻¹. HRMS (ESI, positive ion 160 eV): calc'd for (C₂₀H₂₃DO₂SiNa)⁺: 350.1661, found 349.1731.

(1Z,2R,3S)-1-[1,3-bis(trimethylsilyl)prop-2-ynylidene]-10-deutero-1,2,3,4,5,6-hexahydrobenzo[e]azulene-2,3-diol (39-D₁)

To a solution of (1R*,2S*)-1-(5-bromo-4-deutero-8,9-dihydro-7H-benzocycloheptene-6-yl)-4-trimethylsilylbut-3-yn-1,2-diol (**2-D₁**) (20 mg, 1 equiv, 0,053 mmol) in dried benzene (2 mL), was added Pd(PPh₃)₄ (75 mg, 0.1 equiv) and trimethyl-tributylstannylethynylsilane (30 mg, 1.5 equiv). The mixture was purged 20 min with argon and irradiated under microwave during 20min. The reaction was followed by TLC (Et₂O/Hex 30:70, anisaldehyde). The mixture is cooled to room temperature, diluted in Et₂O, treated with active *charcoal*, filtrated over *celite*, and concentrated to dryness. The crude product was purified by flash chromatography on silica gel (elution with Et₂O/Hex 30:70) to afford 10 mg of two inseparable atropoisomer (47%).

R_f = 0.30 and 0.40 (60/40 Et₂O/Hex) for the two atropoisomers

¹H NMR (300 MHz, CDCl₃) δ 7.18 (m, 3H_{arom}); 4.70 (m, 1H, H-1); 4.59 (m, 1H, H-2); 2.65-2.63 (m, 2H, CH₂); 2.50-2.03 (m, 6H, including 2x OH); 0.31 (s, 9H, H-11); 0.07 (s, 9H, SiMe₃). ¹³C NMR (50 MHz, CDCl₃) δ 159.14 (C_{quat}); 156.90 (C_{quat}); 152.62 (C_{quat}); 151.99 (C_{quat}); 141.65 (C_{quat}); 141.43 (C_{quat}); 141.08 (C_{quat}); 137.71 (C_{quat}); 135.41 (C_{quat}); 132.79 (C_{quat}); 132.66 (C_{quat}); 130.66 (C_{arom}); 129.34 (C_{arom}); 128.83 (C_{arom}); 128.58 (C_{arom}); 128.29 (C_{arom}); 128.22; 128.11; 127.86; 127.43; 126.43; 123.44; 123.35; 122.96; 76.22 (C-2 of one atropoisomer); 74.97 (C-2 of the other atropoisomer); 71.69 (C-3 of one atropoisomer); 71.50 (C-3 of the other atropoisomer); 33.64 (CH₂); 32.97 (CH₂); 32.76 (CH₂); 32.51 (CH₂); 30.32; 29.69; 24.12 (CH₂); 22.21 (CH₂); 0.081 (C-11); 0.00 (SiMe₃). HRMS (ESI, positive ion 120eV): calc'd for (C₂₃H₃₁DO₂Si₂Na)⁺ 420.1870, found 420.1813.

References of Supporting Information

(1) Suffert, J. *J. Org. Chem.* **1989**, *54*, 509-510

- (2) The program nameiPro (ACD/Name version 5.5.5.5) was used to name the different compounds.
- (3) Brakta, M.; Doyle Daves G. Jr. *J. Chem. Soc, Perkin Transactions I* **1992**, 15, 1883-4.
- (4) (a) Betzer, J.F.; Ardisson, J.; Lallemand, J.Y; Pancrazi, A. *Tetrahedron Lett.* **1997**, 38, 2279-82.
- (b) Betzer, J.F.; Delalogue, F.; Muller, B.; Pancrazi, A.; Prunet, J. *J. Org. Chem.* **1997**, 62, 7768-80.
- (5) Rim, C.; Son, D. Y. *Org. Lett.* **2003**, 5, 3443-3