Stereoselective Synthesis of Structurally Simplified Cephalostatin Analogues by Multiple Heck Reactions and Their Biological Evaluation

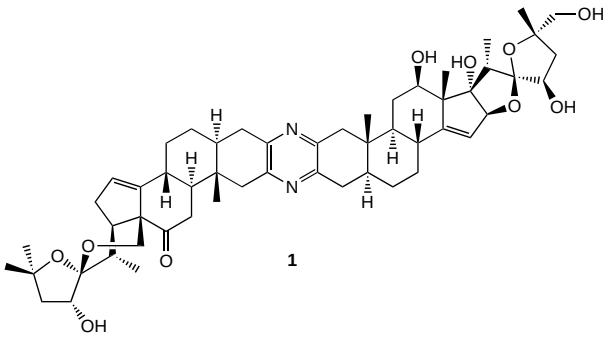
Lutz F. Tietze* and Wolf-Rüdiger Krahnert[a]

Abstract: The stereoselective synthesis of structurally simplified heptacyclic cephalostatin analogues **2**, **3**, **18**–**21**, **31**, **32** and **33** by multiple Heck reactions is described. The key step of the synthesis is a selective Heck reaction of hydrindene **7** with **12** and **25**, respectively at the vinyl bromide moiety followed by the introduction of a second molecule of **7** and a twofold intramolecular Heck reaction. The obtained bissteroidal heptacyclic compounds **2** and **3**, in which the central octahydrophenazine moiety of **1** is replaced by a benzene ring, contain an unusual *cis*-annulation of the two newly generated rings. The cytotoxicity of some of the derivatives was determined on human lung cancer cell line A 549 in HTFCA tests (*H*uman *t*umor *c*olony *f*orming *a*bility). They show a rather high activity with an ED_{50} in the micro molar range.

Keywords: cephalostatin · Heck reaction · natural products · palladium · steroids

Introduction

In 1988, Petit et al. isolated the unusual dimeric steroid derivative cephalostatin 1 (**1**) from the marine worm *Cephalodiscus gilchristi*.[1] The compound shows a remarkably high cytostatic activity with a GI_{50} value of about 2.20×10^{-9} M in an in vitro screening against the NCI 60 human cancer cell line.[2]



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To date, 19 cephalostatins are known, all of which show a high cytostatic activity. Together with the recently from the marine tunikate *Ritterella tokioka* isolated ritterazins[3–4] they belong to the family of steroidal alkaloids, with a backbone composed of two over a pyrazine ring connected steroids.[5]

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Clinical trials with cephalostatin **1** and **7** had to be stalled because of the lack of material which was mainly obtained from natural sources.[6] In view of this, synthesis of the cephalostatins has been the focus of a number of recent studies.[7–11] In 1998, Fuchs et al. have reported the first total synthesis of **1**.[6, 12–15] Considering its biological activity and its unusual bissteroidal structure as well as the lack of knowledge of its mode of action, we became interested in the synthesis of simplified analogues of **1**. In contrast to the work of Heathcock, Winterfeldt and Fuchs, who built up the backbone of cephalostatin from commercially available steroids, we herein describe a new approach to access the bissteroidal backbone using multiple Heck reactions.[16–20] In a convergent strategy the heptacycles **2** and **3** as simplified analogues of **1**, in which the central octahydrophenazine moiety is replaced by a benzene ring, were readily accessible by a twofold intramolecular Heck reaction of **4** and **5**, respectively. Retrosynthetic analysis of **4** and **5** led to tetrafunctionalised benzenes of type **6** and the hexahydro-1*H*-indene (**7**),[21–23] which can be obtained in a few steps from the Hajos–Wiechert ketone **8** (Scheme 1).[24] In addition to the synthesis, we also determined the cytotoxicity of the new analogues by performing HTFCA tests (*H*uman *t*umor *c*olony *f*orming *a*bility).

Results and Discussion

Synthesis of heptacycle 3 and its derivatives: The acid catalyzed reaction of dibromoterephthalaldehyde **9**[26] with ethylene glycol gave the monoacetal **10** together with the expected diacetal in a statistical distribution (see Scheme 2). The diacetal could be separated by column chromatography

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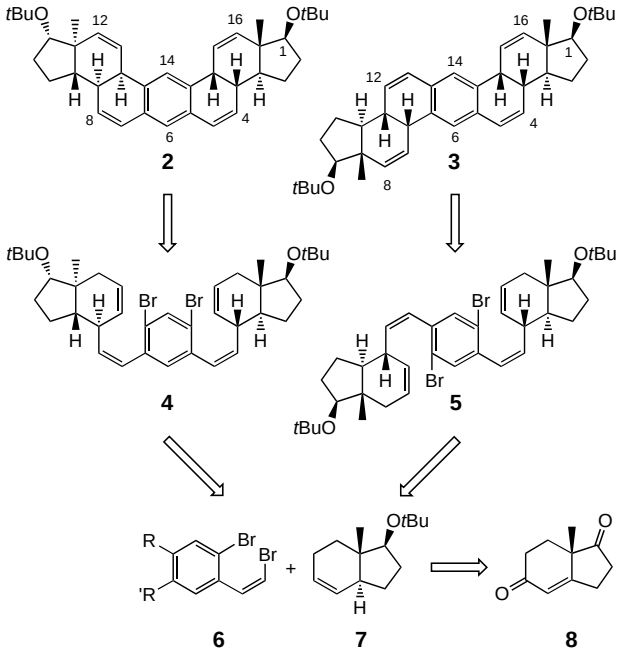
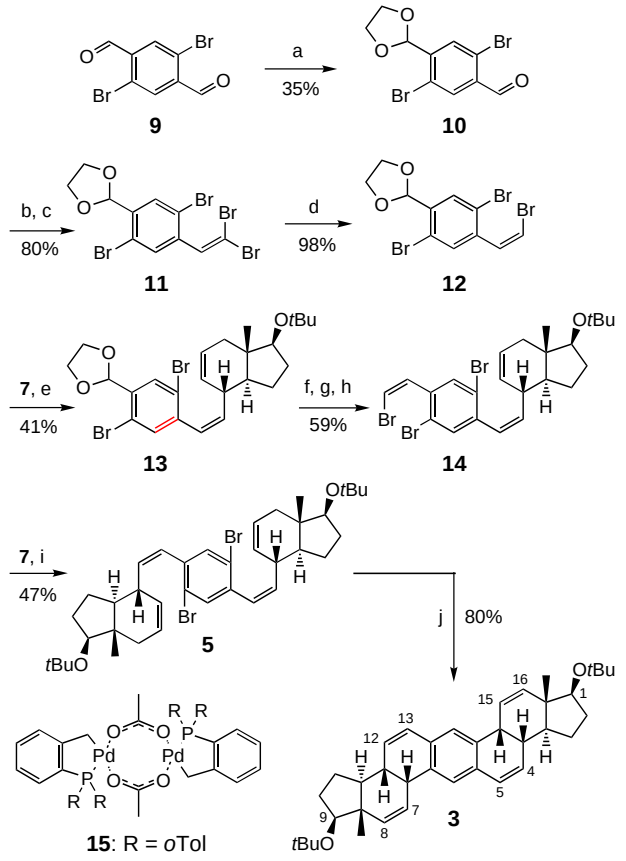


Scheme 1. Retrosynthesis of the simplified cephalostatin analogues **2** and **3**.



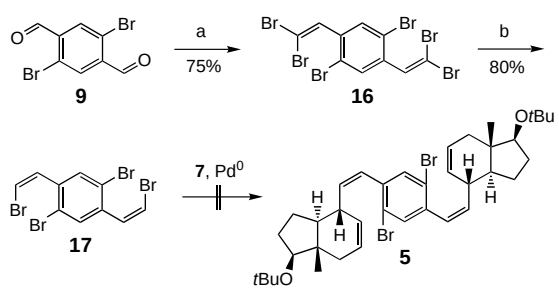
Scheme 2. Synthesis of the heptacycle **3**. a) $HOCH_2CH_2OH$, *p*TsOH, toluene, reflux; b) CBr_4, PPh_3, CH_2Cl_2, 0 °C; c) $HOCH_2CH_2OH$, *p*TsOH, toluene, reflux, 80 % (two steps); d) $[Pd(PPh_3)_4]$, nBu_3SnH, toluene, RT; e) $Pd(OAc)_2$, PPh_3, nBu_4NOAc, $DMF/CH_3CN/H_2O$ 1:1:0.2, 60 °C; f) HOAc, 80 °C, 74 %; g) CBr_4, PPh_3, CH_2Cl_2, 0 °C, 90 %; h) $[Pd(PPh_3)_4]$, nBu_3SnH, toluene, RT, 88 %; i) $Pd(OAc)_2$, PPh_3, nBu_4NCl, K_2CO_3, DMF/CH_3CN/H_2O 1:1:0.2, 60 °C; j) **15**, nBu_4NOAc, $DMF/CH_3CN/H_2O$ 1:1:0.2, 130–140 °C.

and was subsequently transformed back into **9**. Corey–Fuchs reaction[27–30] of **10** followed by selective debromination with nBu_3SnH[31–33] exclusively furnished the (*Z*)-2-bromoethenylbenzene **12** in 78 % overall yield. In the Heck reaction of **12** and hexahydro-1*H*-indene (**7**) we expected a selective reaction of the vinyl moiety since we had previously shown that vinyl bromides are more reactive in Pd^0-catalyzed reactions than bromoarenes.[17] Indeed, the bond formation seems to have occurred exclusively between the vinyl moiety and C-4 in **7** with complete facial selectivity *anti* to the angular methyl group to give **13** with 41 % yield; unreacted **7** could be recovered by chromatography. Neither a transformation at C-5 in **7** nor a formation of the homo coupled product of **12** or of diastereoisomers of **13** was observed. We assume that the high regioselectivity of the Heck reaction is due to a fast and reversible C–C bond formation between **7** and **12** followed by a fast elimination step when the Pd atom is located at C-5 of **7**. In the other case with the Pd atom at C-4 a slow elimination can be expected due to an unfavorable orientation of the Pd atom and the β-hydrogen.

To improve efficiency, we also tried to perform a Heck reaction of hydrindene **7** and the deprotected **12** containing an aldehyde moiety, which is accessible from **12** by hydrolysis of the acetal moiety. However, only decomposed material was obtained. For the introduction of a second molecule of hexahydro-1*H*-indene (**7**) we therefore hydrolyzed the acetal moiety in **13** using 80 % acetic acid and the obtained aldehyde was transformed into the (*Z*)-2-bromovinylbenzene derivative **14** in 59 % yield again using a sequence of a Corey–Fuchs reaction[27–30] and selective debromination.[31–33] Heck reaction of compound **14** with **7** then yielded the desired diindenylethenylbenzene **5** in 47 % yield again in a stereo- and regioselective way.

The following twofold intramolecular Heck reaction of **5** to give analogue **3** required a precise control of the reaction time and temperature. Thus, when **5** was reacted with catalytic amounts of the palladacycle **15**[34] at 130–140 °C for 1.5 h **3** could be obtained in 80 % yield. The conversion proceeded with high selectivity leading to the exclusive formation of an unusual *cis*-annelation of the two newly generated rings.

An even shorter way to **3** would be a double Heck reaction of hydrindene **7** and the bisvinyl bromide **17**, easily accessible from **9** via **16** (Scheme 3). However, all attempts to run this transformation resulted in a complete decomposition of **17** already after 30 min in the presence of any palladium catalyst.



Scheme 3. Twofold intramolecular Heck reaction of **17** and hydrindene **7** aimed at **5**: a) CBr_4, PPh_3, CH_2Cl_2, 0 °C; b) $[Pd(PPh_3)_4]$, nBu_3SnH, toluene, RT.

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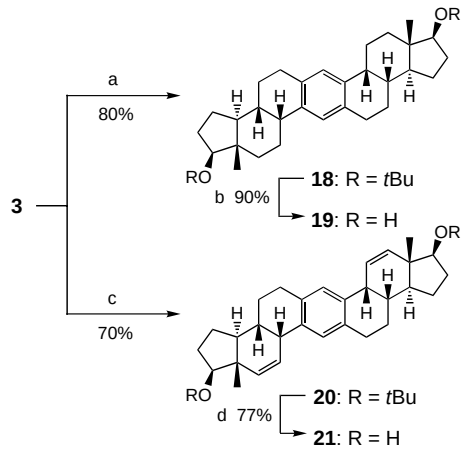
The decomposition of **17** was accompanied by the formation of a black solid, that was insoluble in any solvent.

The bissteroidal arene **3** could be further manipulated in several ways. Hydrogenation with 10% Pd on charcoal furnished **18**, which was subsequently treated with trimethyliodosilane (TMSI) to yield diol **19** (Scheme 4). On the other hand, hydrogenation of **3** using the Wilkinson catalyst led to the tetra-hydrogenated heptacycle **20**, which was again deprotected with TMSI to give diol **21**.

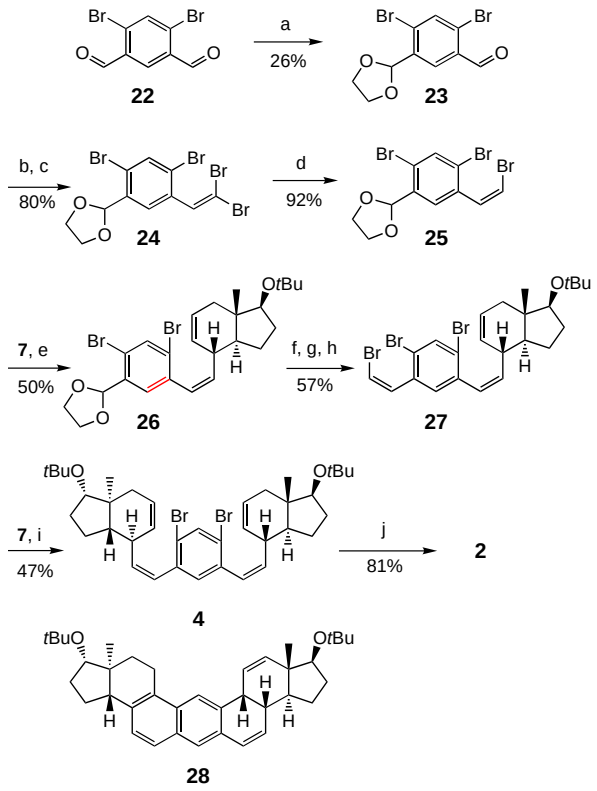


Scheme 4. Hydrogenation and deprotection of heptacycle **3**. a) 10 mol% 10% Pd/C, H_2 (3 bar), EtOAc, RT; b) TMSI, CH_2Cl_2, RT; c) [$(PPh_3)_3RhCl$], H_2 (3 bar), EtOAc/MeOH 1:1, RT; d) TMSI, CH_2Cl_2, RT.

The high chemoselectivity in the homogenous hydrogenation of **3** is probably due to a conformational effect in **3** where the angular 8a- and 16a-methyl groups shield the β-face of the $\Delta^{7,8}$- and $\Delta^{15,16}$-double bonds. The α-face of these double bonds is shielded by the bended molecule structure (see Figure 1 b).

Synthesis of heptacycle 2 and its derivatives: Reaction of dialdehyde **22** with ethylene glycol yielded the monoacetal **23** together with the corresponding diacetal, which was separated by column chromatography and transformed back into **22**. A sequence of a Corey–Fuchs reaction[27–30] followed by palladium-catalyzed debromination with nBu$_3$SnH[31–33] gave the desired (*Z*)-vinyl bromide **25** selectively (see Scheme 5). The Heck reaction between **25** and hydrindene **7** was carried out under similar conditions as described for vinyl bromide **12** with the difference that only a twofold excess of hydrindene **7** is necessary to achieve a yield of 50% of Heck product **26**. Again the bond formation takes place between the vinyl moiety of **25** and C-4 in **7** under formation of only one diastereoisomer.

The acetal moiety in **26** was hydrolyzed using pyridinium *p*-toluenesulfonate (PPTS) in acetone/water. Under these conditions the reaction proceeds slower than in case of hydrolysis of acetal **13** but with a substantially better yield. Corey–Fuchs reaction[27–30] followed by selective debromination[31–33] gave the (*Z*)-2-bromovinylbenzene derivative **27** in 69% yield (two steps). Heck reaction of **27** and hydrindene **7** proceeded with the expected high stereo- and regioselectivity and yielded diindenylethenylbenzene **4** in 47% yield.



Scheme 5. Synthesis of heptacycle **2**. a) $HOCH_2CH_2OH$, *p*TsOH, toluene, reflux; b) CBr_4, PPh_3, CH_2Cl_2, $-20\,^\circ C$; c) $HOCH_2CH_2OH$, *p*TsOH, toluene, reflux, 80% (two steps); d) [$Pd(PPh_3)_4$], nBu$_3$SnH, toluene, RT; e) $Pd(OAc)_2$, PPh_3, nBu$_4$NOAc, DMF/CH_3CN/H_2O 1:1:0.2, 60 °C; f) PPTS, acetone/H_2O 2:1, reflux, 83%; g) CBr_4, PPh_3, CH_2Cl_2, $-20\,^\circ C$, 75%; h) [$Pd(PPh_3)_4$], nBu$_3$SnH, toluene, RT, 92%; i) $Pd(OAc)_2$, PPh_3, nBu$_4$NCl, K_2CO_3, DMF/CH_3CN/H_2O 1:1:0.2, 60 °C; j) **15**, Ag_3PO_4, DMF/CH_3CN/H_2O 1:1:0.2, 120 °C.

Surprisingly, under the conditions described for the reaction of **5** the twofold intramolecular Heck reaction of **4** led to the desired heptacyclic product **2** in only 32% yield. The main product of this reaction was heptacycle **28** which was obtained in 67% yield. Its formation can be explained as a result of a readdition and elimination of the intermediately formed H-Pd-Br species at one of the two newly generated double bonds. However, it is known that in palladium catalyzed reactions silver salts might suppress the migration of double bonds.[35, 36] We were therefore pleased to find out that the twofold intramolecular Heck reaction of **4** using palladacycle **15**[34] and Ag_3PO_4[37, 38] instead of Bu_4NOAc as base led to the exclusive formation of heptacycle **2** in 81% yield without migration of any double bond.

However, **2** is also accessible via a shorter, more efficient synthetic route which failed for the synthesis of **3**. Transformation of the dialdehyde **22** in a twofold Corey–Fuchs reaction[27–30] followed by a twofold palladium catalyzed debromination reaction[31–33] yields (*Z*)-di(bromoethenyl)benzene **30** selectively in an overall yield of 44% (Scheme 6). In contrast to **17**, the bis(bromovinyl)arene **30** reacted with hydrindene **7** in the presence of a catalytic amount of $Pd(OAc)_2$ and a base system consisting of nBu$_4$NCl and K_2CO_3 at 60 °C to furnish the desired diindenylethenylbenzene **4** in 13% yield, which was then transformed into **2**.

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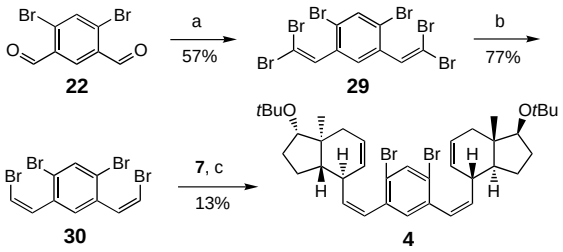
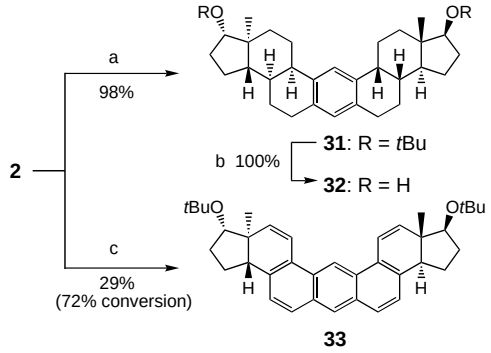


Scheme 6. Twofold intramolecular Heck reaction of **30** and hydrindene **7**. a) CBr_4, PPh_3, CH_2Cl_2, 0 °C; b) $[Pd(PPh_3)_4]$, nBu_3SnH, toluene, RT; c) $Pd(OAc)_2$, PPh_3, nBu_4NOAc, DMF/CH_3CN/H_2O 1:1:0.2, 60 °C.

Hydrogenation of heptacycle **2** using $PtO_2 \cdot H_2O$, 50 bar hydrogen pressure and a protic solvent system furnished the octahydro analogue **31** and deprotection of **31** by reaction with TMSI led to the corresponding diol **32** (Scheme 7). A selective hydrogenation of **2** using the Wilkinson catalyst as in the case of **3** was not possible. The reaction of **2** with 10% Pd on charcoal led in absence of a hydrogen atmosphere to the formation of **33**, which contains an equilenin substructure. Compound **33** was obtained as an inseparable mixture together with substrate **2**, since the reaction was not complete after six days and was therefore stopped.



Scheme 7. Hydrogenation and dehydrogenation of heptacycle **2**. a) 10 mol% $PtO_2 \cdot H_2O$, H_2 (50 bar), MeOH/EtOAc 1:1, RT; b) TMSI, CH_2Cl_2, RT; c) 10% Pd/C, MeOH, 50 °C.

The structures of the newly formed compounds were determined by NMR spectroscopy. In addition, X-ray analyses were performed from **20** and **31** (Figure 1).[39] As examples, the ^{1}H NMR data of **2**–**5** as well as of **13** and **26** are discussed.

For the angular methyl group in **13** a singlet at $\delta = 0.65$ and for 4-H a multiplet at $\delta = 2.82$ is found. NOESY experiments confirmed that 4-H is *cis*-orientated to the methyl group. Further signals are observed at $\delta = 3.46$ as triplet with $J =$ 8.8 Hz for 1-H, at $\delta = 5.48$ as doublet of doublet with $J = 11.5$ and 11.0 Hz for 1′-H and at $\delta = 6.36$ as doublet with $J =$ 11.5 Hz for 2′-H. The coupling constants indicate that the double bond has a *Z*-configuration. The two aromatic hydrogens resonate at $\delta = 7.43$ and 7.76. The ^{1}H NMR spectrum of **26** is nearly identical; here the aromatic hydrogens resonate at $\delta = 7.51$ and 7.77. Also the ^{1}H NMR spectra of **5** and **4** are very similar with the only difference that the integration of the

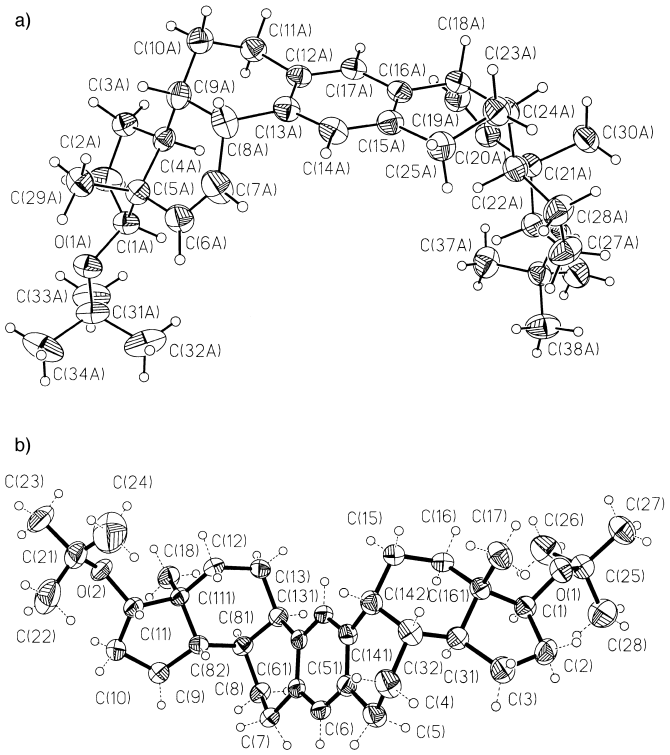


Figure 1. X-ray structure of a) **20** and b) **31**.

signals for the hydrindene moiety is twice as high and the signals for the acetal moiety in **13** and **26** are missing. Thus, the angular methyl groups resonate at $\delta = 0.66$ and 0.61, respectively, the hydrogens at the acyclic double bonds in **5** as a doublet of a doublet at $\delta = 5.47$ with $J = 11.2$ and 11.0 Hz and as a doublet at $\delta = 6.38$ with $J = 11.2$ Hz and for **4** as a doublet of a doublet at $\delta = 5.44$ with $J = 11.2$ and 11.0 Hz and at $\delta =$ 6.34 as doublet with $J = 11.2$ Hz. The only significant difference between the ^{1}H NMR spectra of **5** and **4** are the singlet at $\delta = 7.46$ found for the aromatic hydrogens of **5** and the two singlets at $\delta = 7.13$ and 7.78 for those of **4**.

Due to the symmetric structure of **3** and **2** again only one set of signals is found for the rings A,B,C and E,F,G in these compounds. As before, for the two aromatic hydrogens in **3** only one singlet is observed at $\delta = 6.86$, whereas two singlets at $\delta = 6.60$ and 7.18 are found for the corresponding hydrogens in **2**.

All other resonances are very similar with the exception of those for the angular methyl groups at $\delta = 0.61$ and 0.85, respectively. For the hydrogens at the O*t*Bu group multiplets are found at $\delta = 3.45$ and 3.47 and at the benzylic double bonds, doublets of doublets at $\delta = 5.80$ and 5.82 with $J = 9.6/$ 9.7 and 5.9/6.1 Hz as well as doublets at $\delta = 6.32$ and 6.30 with $J = 9.6/9.7$ Hz.

The proof for the *cis*-annulation of rings BC and EF demonstrated for **2** is given by a coupling constant of $J =$ 6.9 Hz for the hydrogens 13a-H and 14b-H at $\delta = 3.70$, whereas the *trans* orientation of rings AB and FG is indicated by a coupling constant of $J = 11.8$ Hz of the signal for 3b-H and 8a-H at $\delta = 2.63$.

The *cis* orientation of the rings BC and EF in **18** is confirmed by NOESY experiments.

Biological evaluation of analogues 19, 21, and 32: The cytotoxicities of the new structurally simplified cephalostatin analogues were determined by performing a HTFA tests (*H*uman *t*umor *c*olony *f*orming *a*bility). For this purpose, 10^2 to 10^5 human lung cancer cells of the line A549 were placed in six-well multiplates and cultivated in a culture medium that contained 90% DMEM (Dulbeco's modified Eagle's medium) and 10% FCS (fetal calf serum). After 24 h of cultivation, the medium was removed, and the cells were incubated with different concentrations of the synthesized analogues dissolved in DMSO/culture medium for 24 h. The remaining cells were cultivated for a further 8–9 days at 37 °C in air with a CO_2 content of 7.5% and dyed with Löfflers methylene blue; finally the relative colony-forming rate was determined.[40]

Since we only had a restricted amount of **19** and **21** for the determination of the cytotoxicity, we were just able determine effective dosage ranges (ED_{50}) for these two compounds, which are 1–100 μM for **19** and 13–130 μM for **21**. The effective dosage value for **32** is $ED_{50} = 59$ μM.[41] Though the observed cytotoxicities of the analogues **19**, **21** and **32** are not in the range of those found for the natural cephalostatins, they are still remarkably high since the compounds do not contain any obviously toxic functionalities as the well known and clinically used alkylating anticancer agent cyclophosphamide, which has an ED_{50} value of 251 μM against the same cell line.

Conclusion

With the synthesis of **2** and **3** as well as of their derivatives, we have developed a short entrance to structurally simplified cephalostatin analogues starting from simple molecules. Some of the analogues synthesized show a remarkably high cytotoxicity against the human cancer cell line A549, which encourages us to undertake further investigations in this area. Thus, application of the developed method to heterocyclic arenes and further substituted hydrindenes should allow the preparation of more complex symmetrical and unsymmetrical cephalostatin analogues.

Experimental Section

General: All reactions were performed in oven-dried glassware under an argon atmosphere. Solvents were degassed by the freeze–pump–thaw methology. TLC chromatography was performed on precoated aluminium silica gel SIL G/UV_{254} plates (Macherey, Nagel Co.), and silica gel 32–63 (0.032–0.064 mm) (Macherey, Nagel Co.) was used for column chromatography. Melting points: Mettler FP61. Optical rotations: Perkin–Elmer 241. IR: Bruker IFS25. UV/Vis: Perkin–Elmer Lambda 9. NMR: Varian VXR-200 (200 MHz, ^{1}H), Bruker AM-300 (300 MHz, 75 MHz, for ^{1}H and ^{13}C, respectively), Varian VXR-500 (500 MHz, 125 MHz, for ^{1}H and ^{13}C, respectively), Varian Unity Inova-600 (600 MHz, 150 MHz, for ^{1}H and ^{13}C, respectively). For ^{1}H and ^{13}C NMR, $CDCl_3$ as solvent, TMS as internal standard. Chemical shifts are reported on the δ scale. Signals are quoted as s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet) and br (broad). MS: Varian MAT 731. Elemental analysis: Mikroanalytisches Labor des Institutes für Organische Chemie der Universität Göttingen.

2,5-Dibromo-4-[1,3]dioxolan-2-ylbenzaldehyde (10): A suspension of 2,5-dibromobenzene-1,4-dicarbaldehyde (30.9 g, 106 mmol), ethylene glycol (5.92 mL, 6.57 g, 106 mmol) and *p*TsOH·H_2O (101 mg, 0.53 mmol) in toluene (430 mL) was heated under reflux for 1.5 h. After cooling the mixture was washed with water (100 mL) and brine (100 mL), dried over $NaSO_4$ and the solvent was removed in vacuo. Purification of the residue by column chromatography (*n*-pentane/CH_2Cl_2 2:1) furnished **10** (12.3 g, 36.6 mmol, 35%) as a white solid together with the corresponding diacetal (10.1 g, 26.6 mmol, 25%) and 2,5-dibromobenzene-1,4-dicarbaldehyde (8.96 g, 30.7 mmol, 29%). Analytical data for **10**: $R_f = 0.34$ (*n*-pentane/CH_2Cl_2 2:1); m.p. 112 °C; UV/Vis (CH_3CN): λ_{max} (lg ε) = 224.0 (4.422), 252.0 (3.996), 313.0 nm (3.297); IR (KBr): $\tilde{\nu} = 2902, 1695, 1085, 1055$ cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 4.06–4.22$ (m, 4H), 6.03 (s, 1H), 7.86 (s, 1H), 8.07 (s, 1H), 10.26 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 65.66$, 101.4, 122.4, 125.4, 133.0, 134.0, 134.6, 143.7, 190.1; MS (70 eV, EI): *m*/*z* (%): 335.8 (58) $[M]^+$, 306.8 (11) $[M - CHO]^+$, 290.8 (24) $[M - C_2H_5O]^+$, 262.8 (20) $[M - C_3H_5O_2]^+$, 254.9 (37) $[M - Br]^+$, 73.0 (100) $[C_3H_5O_2]^+$; elemental analysis calcd (%) for $C_{10}H_8Br_2O_3$ (336.0): C 35.75, H 2.40; found C 35.75, H 2.37.

1,4-Dibromo-2-(2,2-dibromovinyl)-5-[1,3]dioxolan-2-ylbenzene (11): A solution of PPh_3 (15.9 g, 60.7 mmol) in CH_2Cl_2 (50 mL) was added slowly to a solution of CBr_4 (10.1 g, 15.2 mmol) in CH_2Cl_2 (50 mL) at 0 °C. After stirring the reaction mixture for 1 h benzaldehyde **10** (5.10 g, 15.2 mmol) in CH_2Cl_2 (80 mL) was added within 10 min. Stirring was continued for 1 h at 0 °C followed by 1 h at room temperature. The reaction mixture was concentrated in vacuo until a precipitation of triphenylphospine oxide was seen and then purified by column chromatography (*n*-pentane/CH_2Cl_2 3:1) to yield a mixture of **11** and the corresponding deprotected benzaldehyde.

This mixture was dissolved in toluene (100 mL), ethylene glycol (3.40 mL, 3.77 g, 60.7 mmol) and *p*TsOH·H_2O (14.5 mg, 76.2 μmol) were added and the reaction mixture was heated under reflux for 5 h with a Dean–Stark tube. After cooling down it was washed with water (50 mL) and brine (50 mL), dried over Na_2SO_4. The solvent was removed in vacuo to yield **11** (5.94 g, 12.1 mmol, 80%) as white solid. $R_f = 0.25$ (*n*-pentane/CH_2Cl_2 3:1); m.p. 113 °C; UV/Vis (CH_3CN): λ_{max} (lg ε) = 212.0 (4.353), 263.0 nm (3.982); IR (KBr): $\tilde{\nu} = 2889, 1597, 1360$ cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 4.03–4.20$ (m, 4H), 6.02 (s, 1H), 7.43 (s, 1H), 7.79 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 65.59, 94.59, 101.7, 121.3, 122.0, 131.8, 134.2, 135.0, 138.1, 138.3$; MS (70 eV, EI): *m*/*z* (%): 491.6 (52) $[M]^+$, 446.5 (14) $[M - C_2H_5O]^+$, 410.6 (83) $[M - Br]^+$, 337.7 (12) $[M - Br - C_3H_5O_2]^+$, 330.8 (17) $[M - 2 \times Br]^+$; elemental analysis calcd (%) for $C_{11}H_8Br_4O_2$ (491.8): C 26.86, H 1.64; found C 27.17, H 1.75.

1,4-Dibromo-2-[(*Z*)-2-bromovinyl]-5-[1,3]dioxolan-2-ylbenzene (12): $[Pd(PPh_3)_4]$ (4.00 mol%, 938 mg, 0.81 mmol) was added to a solution of **11** (10.0 g, 20.3 mmol) in degassed toluene (120 mL) and the solution was stirred until homogeneous. Then *n*Bu_3SnH (5.92 mL, 6.50 g, 22.3 mmol) was added dropwise at room temperature and the solution was stirred for 1.5 h. *n*-Pentane (120 mL) was added to the reaction mixture, it was washed with water (100 mL) and brine (100 mL), dried over Na_2SO_4 and the solvents were removed in vacuo. Purification by column chromatography (*n*-pentane/CH_2Cl_2 3:1) furnished **12** (8.21 g, 19.9 mmol, 98%) as white solid. $R_f = 0.18$ (*n*-pentane/CH_2Cl_2 3:1); m.p. 76 °C; UV/Vis (CH_3CN): λ_{max} (lg ε) = 214.5 nm (4.311); IR (KBr): $\tilde{\nu} = 2887, 1609, 1354$ cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 4.03–4.21$ (m, 4H), 6.04 (s, 1H), 6.65 (d, $J = 7.9$ Hz, 1H), 7.13 (d, $J = 7.9$ Hz, 1H), 7.80 (s, 1H), 7.96 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 65.55, 101.8, 111.0, 121.0, 122.6, 130.9, 131.7, 134.3, 137.3, 137.9$; MS (70 eV, EI): *m*/*z* (%): 411.7 (24) $[M]^+$, 366.7 (8) $[M - C_2H_5O]^+$, 332.8 (51) $[M - Br]^+$, 288.8 (9) $[M - Br - C_2H_4O]^+$, 260.8 (12) $[M - Br - C_3H_4O_2]^+$; elemental analysis calcd (%) for $C_{11}H_9Br_3O_2$ (412.9): C 32.00, H 2.20; found C 31.96, H 2.18.

(−)-(1*S*,3a*S*,4*S*,7a*S*)-1-*tert*-Butoxy-4-{(*Z*)-2-[2,5-dibromo-4-([1,3]dioxolan-2-yl)phenyl]vinyl}-7a-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-indene (13): A solution of **12** (79 mg, 191 μmol), hydrindene **7** (10 mg, 48 μmol) and *n*Bu_4NOAc (116 mg, 384 μmol) in degassed DMF/CH_3CN/H_2O (1:1:0.2, 1 mL) was heated to 60 °C. At 50 °C PPh_3 (20 mol%, 10.0 mg, 38.4 μmol) and $Pd(OAc)_2$ (10 mol%, 4.30 mg, 19.1 μmol) were added and the mixture was heated at 60 °C for 21 h. After cooling down it was diluted with Et_2O (10 mL), washed with water (2 × 5 mL) and the combined aqueous layers were washed with Et_2O (2 × 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, the solvent was removed in vacuo and the residue purified by column chromatography (*n*-pentane/CH_2Cl_2 1:1) to yield **13** (10.6 mg, 19.6 μmol, 41%) as colorless oil. $R_f = 0.30$ (*n*-pentane/CH_2Cl_2 1:1); $[\alpha]_D^{20} = -8.7°$ ($c = 1$ in $CHCl_3$); UV/Vis (CH_3CN): λ_{max} (lg ε) = 207.0 (4.342), 224.0 (4.333), 345.0 nm (2.561); IR (KBr):

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$\tilde{\nu}$ = 2968, 2883, 1589, 1387 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.65 (s, 3H), 1.11 (s, 9H), 1.10–1.20 (m, 1H), 1.27–1.44 (m, 2H), 1.58–1.67 (m, 1H), 1.77–1.88 (m, 2H), 1.99 (ddt, J = 17.5, 5.2, 1.8 Hz, 1H), 2.80–2.89 (m, 1H), 3.47 (t, J = 8.8 Hz, 1H), 4.02–4.19 (m, 4H), 5.39 (d, J = 10.0 Hz, 1H), 5.48 (dd, J = 11.5, 11.0 Hz, 1H), 5.68 (ddt, J = 10.0, 5.0, 2.2 Hz, 1H), 6.00 (s, 1H), 6.36 (d, J = 11.5 Hz, 1H), 7.43 (s, 1H), 7.76 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.44, 24.77, 28.71, 30.43, 38.72, 38.80, 41.19, 46.23, 65.52, 65.64, 72.22, 80.53, 101.9, 120.92, 122.95, 127.7, 127.8, 128.2, 131.6, 134.3, 136.5, 137.7, 140.2; MS (70 eV, EI): m/z (%): 540.0 (7) $[M]^+$, 483.9 (100) $[M-C_4H_8]^+$, 465.9 (12) $[M-C_3H_6O_2]^+$, 385.0 (10) $[M-Br-C_3H_6O_2]^+$, 57.0 (69) $[C_4H_9]^+$; HRMS: calcd for $C_{25}H_{32}Br_2O_3$: 538.0718; found 538.0718; elemental analysis calcd (%) for $C_{25}H_{32}Br_2O_3$ (540.3): C 55.57, H 5.97; found C 55.31, H 5.88.

(−)-2,5-Dibromo-4-{(*Z*)-2-[(1*S*,3a*S*,4*S*,7a*S*)-1-*tert*-butoxy-7a-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-inden-4-yl]vinyl}benzaldehyde (13a): A solution of acetal **13** (500 mg, 92.5 μmol) in 80% acetic acid (20 mL) was heated at 80 °C for 2 h. After cooling down it was diluted with Et_2O (10 mL) followed by addition of a saturated solution of $NaHCO_3$ until the end of the gas formation. The organic layer was washed with water (10 mL) and brine (10 mL), dried over Na_2SO_4 and the solvent was removed in vacuo. Purification of the residue by column chromatography furnished **13a** (34.0 mg, 68.5 μmol, 74%) as colorless oil. R_f = 0.46 (*n*-pentane/Et_2O 20:1); $[\alpha]_D^{20}$ = −32.8° (c = 1 in $CHCl_3$); UV/Vis (CH_3CN): λ_{max} (lg ε) = 221.5 (4.206), 283.0 nm (3.911); IR (KBr): $\tilde{\nu}$ = 3009, 2971, 2874, 1692 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.67 (s, 3H), 1.13 (s, 9H), 1.00–2.12 (m, 7H), 2.77–2.97 (m, 1H), 3.49 (t, J = 8.0 Hz, 1H), 5.42 (d, J = 10.0 Hz, 1H), 5.61 (dd, J = 11.5, 11.0 Hz, 1H), 5.74 (ddt, J = 10.0, 5.0, 2.5 Hz, 1H), 6.43 (d, J = 11.5, 1H), 7.56 (s, 1H), 8.10 (s, 1H), 10.26 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.36, 24.80, 28.70, 30.41, 38.67, 39.02, 41.19, 46.13, 72.28, 80.41, 123.7, 124.8, 127.4, 127.6, 128.3, 132.8, 133.5, 135.1, 139.1, 145.0, 190.1; MS (70 eV, EI): m/z (%): 496 (2) $[M]^+$, 440 (56) $[M-C_4H_8]^+$, 343 (8) $[M-C_4H_9O-Br]^+$, 57 (100) $[C_4H_9]^+$; HRMS: calcd for $C_{23}H_{28}Br_2O_2$: 494.0456; found 494.0456; elemental analysis calcd (%) for $C_{23}H_{28}Br_2O_2$ (496.3): C 55.66, H 5.69; found C 55.90, H 5.68.

(−)-(1*S*,3a*S*,4*S*,7a*S*)-1-*tert*-Butoxy-4-{(*Z*)-2-[2,5-dibromo-4-(2,2-dibromovinyl)phenyl]vinyl}-7a-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-indene (13b): A solution of PPh_3 (235 mg, 895 μmol) in CH_2Cl_2 (0.4 mL) was added slowly to a solution of CBr_4 (148 mg, 447 μmol) in CH_2Cl_2 (0.4 mL) at 0 °C. After stirring of the reaction mixture for 30 min, benzaldehyde **13a** (111 mg, 224 μmol) in CH_2Cl_2 (0.4 mL) was added within 10 min. Stirring was continued for 1 h at 0 °C followed by 1 h at room temperature. The reaction mixture was concentrated in vacuo until a precipitation of triphenylphospine oxide was seen and then purified by column chromatography (*n*-pentane/CH_2Cl_2 6:1) to yield **13b** (131 mg, 201 μmol, 90%) as colorless oil. R_f = 0.49 (*n*-pentane/CH_2Cl_2 6:1); $[\alpha]_D^{20}$ = −22.3° (c = 0.7 in $CHCl_3$); UV/Vis (CH_3CN): λ_{max} (lg ε) = 229.5 (4.241), 272.0 nm (4.062); IR (KBr): $\tilde{\nu}$ = 2972, 1642, 1598 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.69 (s, 3H), 1.09–1.73 (m, 4H), 1.14 (s, 9H), 1.78–1.94 (m, 2H), 1.97–2.09 (m, 1H), 2.83–2.96 (m, 1H), 3.50 (t, J = 8.2 Hz, 1H), 5.42 (d, J = 10.0 Hz, 1H), 5.53 (dd, J = 11.2, 11.0 Hz, 1H), 5.72 (ddt, J = 10.0, 5.0, 2.5 Hz, 1H), 6.38 (d, J = 11.2 Hz, 1H), 7.46 (s, 1H), 7.49 (s, 1H), 7.85 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.42, 24.84, 28.75, 30.48, 38.74, 38.85, 41.24, 46.23, 72.29, 80.52, 93.86, 121.3, 122.5, 127.7, 127.9, 128.1, 133.6, 133.9, 135.1, 135.6, 139.5, 137.9; MS (70 eV, EI): m/z (%): 651.7 (2) $[M]^+$, 595.7 (10) $[M-C_4H_8]^+$, 496.8 (10) $[M-C_4H_9O-HBr]^+$, 57.1 (100) $[C_4H_9]^+$; HRMS: calcd for $C_{24}H_{28}Br_4O$: 647.8874; found 647.8874; elemental analysis calcd (%) for $C_{24}H_{28}Br_4O$ (652.1): C 44.20, H 4.33; found C 44.48, H 4.57.

(−)-(1*S*,3a*S*,4*S*,7a*S*)-1-*tert*-Butoxy-4-{(*Z*)-2-[2,5]-dibromo-4-((*Z*)-2-bromovinyl)phenyl]vinyl}-7a-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-indene (14): $[Pd(PPh_3)_4]$ (4.00 mol%, 30.0 mg, 25.8 μmol) was added to a solution of **13b** (420 mg, 644 μmol) in degassed toluene (3.8 mL) and the solution was stirred until homogeneous. Then nBu$_3$SnH (179 μL, 197 mg, 676 μmol) was added dropwise at room temperature and the solution was stirred for 1.5 h. *n*-Pentane (5 mL) was added to the reaction mixture, it was washed with water (5 mL) and brine (5 mL), dried over Na_2SO_4 and the solvents were removed in vacuo. Purification by column chromatography (*n*-pentane/Et_2O, 100:1) furnished **14** (323 mg, 564 μmol, 88%) as colorless oil. R_f = 0.20 (*n*-pentane/Et_2O, 100:1), $[\alpha]_D^{20}$ = −39.3° (c = 0.8 in $CHCl_3$); UV/Vis (CH_3CN): λ_{max} (lg ε) = 226.5 (4.401), 266.5 nm (4.214); IR (KBr): $\tilde{\nu}$ = 2971, 1461, 1197 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.67 (s, 3H), 1.08–1.71 (m, 4H), 1.15 (s, 9H), 1.76–1.92 (m, 2H), 1.95–2.06 (m, 1H), 2.83–2.96 (m, 1H), 3.47 (t, J = 8.2 Hz, 1H), 5.41 (d, J = 10.0 Hz, 1H), 5.50 (dd, J = 11.2, 11.0 Hz, 1H), 5.69 (ddt, J = 10.0, 5.0, 2.5 Hz, 1H), 6.37 (d, J = 11.2 Hz, 1H), 6.60 (d, J = 8.0 Hz, 1H), 7.12 (d, J = 8.0 Hz, 1H), 7.48 (s, 1H), 8.02 (s, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 11.41, 24.82, 28.73, 30.48, 38.73, 38.80, 41.21, 46.24, 72.25, 80.53, 110.2, 122.0, 122.2, 127.77, 127.79, 128.2, 130.8, 133.6, 133.9, 134.8, 137.7, 139.1; MS (70 eV, EI): m/z (%): 573.7 (4) $[M]^+$, 517.7 (9) $[M-C_4H_8]^+$, 497.7 (11) $[M-C_4H_{10}O]^+$, 418.9 (11) $[M-C_4H_{10}O-Br]^+$, 339.9 (2) $[M-C_4H_{10}O-2\times Br]^+$, 57.1 (52) $[C_4H_9]^+$; HRMS: calcd for $C_{24}H_{29}Br_3O$: 571.9748; found 571.9748; elemental analysis calcd (%) for $C_{24}H_{29}Br_3O$ (573.2): C 50.29, H 5.10; found C 50.54, H 5.03.

(−)-1,4-Dibromo-2,5-bis{(*Z*)-2-[(1*S*,3a*S*,4*S*,7a*S*)-1-*tert*-butoxy-7a-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-inden-4-yl]vinyl}benzene (5): A solution of **14** (40.0 mg, 69.8 μmol), hydrindene **7** (29.0 mg, 140 μmol), K_2CO_3 (24.0 mg, 174 μmol) and nBu$_4$NCl (19.0 mg, 69.8 μmol) in degassed DMF/CH_3CN/H_2O (1:1:0.2, 1 mL) was heated to 50 °C when PPh_3 (20 mol%, 3.70 mg, 14 μmol) and $Pd(OAc)_2$ (10 mol%, 1.60 mg, 6.98 μmol) were added with stirring; afterwards the mixture was stirred at 60 °C for 5 h. After cooling the reaction mixture was diluted with Et_2O (10 mL), washed with water (2 × 5 mL) and the combined aqueous layers were washed with Et_2O (2 × 5 mL). Then the combined organic layers were washed with brine, dried over Na_2SO_4, the solvent was removed in vacuo and the residue was purified by column chromatography (*n*-pentane/CH_2Cl_2 3:1) to yield **5** (23.0 mg, 32.8 μmol, 47%) as colorless oil. R_f = 0.33 (*n*-pentane/CH_2Cl_2 3:1); $[\alpha]_D^{20}$ = −21.2° (c = 0.25 in $CHCl_3$); UV/Vis (CH_3CN): λ_{max} (lg ε) = 226.0 (4.299), 260.0 nm (4.030); IR (KBr): $\tilde{\nu}$ = 2972, 1730, 1643, 1465 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.66 (s, 6H), 1.12 (s, 18H), 1.07–1.72 (m, 8H), 1.75–1.91 (m, 4H), 2.00 (dd, J = 17.0, 5.0 Hz, 2H), 2.83–2.97 (m, 2H), 3.46 (t, J = 8.5 Hz, 2H), 5.40 (d, J = 10.0 Hz, 2H), 5.47 (dd, J = 11.2, 11.0 Hz, 2H), 5.67 (ddt, J = 10.0, 5.0, 2.5 Hz, 2H), 6.38 (d, J = 11.2 Hz, 2H), 7.46 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.34, 24.88, 28.74, 30.52, 38.73, 38.75, 41.28, 46.24, 72.24, 80.58, 122.1, 127.6, 127.9, 128.5, 133.8, 137.4, 137.8; MS (70 eV, EI): m/z (%): 700.0 (10) $[M]^+$, 643.9 (7) $[M-C_4H_8]^+$, 625.9 (8) $[M-C_4H_{10}O]^+$, 587.8 (12) $[M-2\times C_4H_8]^+$, 569.9 (14) $[M-C_4H_8-C_4H_{10}O]^+$, 57.1 (100) $[C_4H_9]^+$; HRMS: calcd for $C_{38}H_{52}Br_2O_2$: 698.2334; found 698.2334.

(−)-(1*S*,3a*S*,3b*S*,6b*R*,8a*S*,9*S*,11a*S*,11b*S*,14b*R*,16a*S*)-1,9-Di-*tert*-butoxy-8a,16a-dimethyl-2,3,3a,3b,6b,8a,10,11,11a,11b,14b,16a-dodecahydro-di-1*H*-indeno[4,5-a:4,5-h]anthracene (3): A solution of **5** (100 mg, 143 μmol), nBu$_4$NOAc (215 mg, 714 μmol) and *trans*-di(μ-acetato)-bis[*ortho*-(di-*ortho*-tolylphosphino)benzyl]dipalladium(II) (**15**; 5.00 mol%, 6.54 mg, 7.14 μmol) in degassed DMF/CH_3CN/H_2O (1:1:0.2, 5 mL) was heated for 1.5 h at 130–140 °C in a preheated oil bath. After cooling down, water (15 mL) was added and the reaction mixture was extracted with Et_2O (2 × 20 mL). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. Removal of the solvent and chromatographic purification (*n*-pentane/CH_2Cl_2 5:1) yielded **3** (62.0 mg, 115 μmol, 80%) as colorless oil. R_f = 0.32 (*n*-pentane/CH_2Cl_2 5:1); $[\alpha]_D^{20}$ = −39.0° (c = 0.2 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.86 (s, 6H), 1.11 (s, 18H), 1.35–1.57 (m, 6H), 1.69–1.89 (m, 4H), 2.62–2.69 (m, 2H), 3.45 (dd, J = 8.7, 6.6 Hz, 2H), 3.67 (dd, J = 5.6, 4.4 Hz, 2H), 5.80 (dd, J = 9.6, 5.9 Hz, 2H), 6.04 (d, J = 10.0 Hz, 2H), 6.12 (dd, J = 10.0, 4.4 Hz, 2H), 6.32 (d, J = 9.6 Hz, 2H), 6.86 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.94, 22.84, 28.72, 31.89, 33.92, 37.47, 41.84, 44.69, 72.33, 76.22, 125.0, 125.3, 128.8, 129.2, 131.8, 134.6, 135.9; MS (70 eV, EI): m/z (%): 538.5 (38) $[M]^+$, 481.4 (25) $[M-C_4H_9]^+$, 425.4 (10) $[M-C_4H_8-C_4H_9]^+$, 407.3 (18) $[M-C_4H_9-C_4H_{10}O]^+$, 57.1 (100) $[C_4H_9]^+$; HRMS: calcd for $C_{38}H_{50}O_2$ 538.3811; found 538.3810.

1,4-Dibromo-2,5-di(2,2-dibromovinyl)benzene (16): A solution of PPh_3 (16.6 g, 63.2 mol) in CH_2Cl_2 (60 mL) was added slowly to a solution of CBr_4 (10.5 g, 31.6 mmol) in CH_2Cl_2 (87 mL) at 0 °C. After stirring of the reaction mixture for 30 min, terephthalaldehyde **9** (2.57 g, 7.89 mmol) in CH_2Cl_2 (118 mL) was added within 10 min. Stirring was continued for 1 h at 0 °C followed by 1 h at room temperature. The reaction mixture was concentrated in vacuo until triphenylphospine oxide precipitated, and subsequently purified by column chromatography (*n*-pentane) to yield **16** (3.57 g, 5.91 mmol, 75%) as white solid. R_f = 0.51 (*n*-pentane); m.p. 176 °C; UV/Vis (CH_3CN): λ_{max} (lg ε) = 223.0 (4.106), 276.0 nm (3.864); IR (KBr): $\tilde{\nu}$ = 3014, 1604, 863, 632 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.44 (s, 2H), 7.85 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 94.39, 121.3, 133.4, 134.7, 137.3; MS (70 eV, EI): m/z (%): 603.7 (100) $[M]^+$, 522.8 (9) $[M-Br]^+$, 443.8 (27) $[M-2\times Br]^+$, 364.9 (6) $[M-3\times Br]^+$, 283.9 (32) $[M-4\times Br]^+$, 124.1

(20) $[M-6\times Br]^+$; elemental analysis calcd (%) for $C_{10}H_4Br_6$ (603.6): C 19.90, H 0.67; found C 20.19, H 0.69.

1,4-Dibromo-2,5-di[(*Z*)-2-bromovinyl]benzene (17): $[Pd(PPh_3)_4]$ (8.00 mol%, 140 mg, 121 μmol) was added to a solution of **16** (912 mg, 1.51 mmol) in degassed toluene (100 mL) and the solution was stirred until homogeneous. Then nBu$_3$SnH (0.88 mL, 968 mg, 3.32 mmol) was added dropwise at room temperature and the solution was stirred for 3.5 h. n-Pentane (100 mL) was added and the mixture was washed with water (50 mL), brine (50 mL), dried over Na_2SO_4 and the solvents were removed in vacuo. Purification by column chromatography (n-pentane) furnished **17** as white solid (536 mg, 1.20 mmol, 80%). $R_f=0.40$ (n-pentane); m.p. 121 °C; UV/Vis (CH_3CN): λ_{max} (lg ε) = 225.0 (4.277), 270.0 nm (4.116); IR (KBr): $\tilde{\nu}=3080$, 1772, 1619 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=6.66$ (d, $J=8.1$ Hz, 2H), 7.14 (d, $J=8.1$ Hz, 2H), 8.04 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta=110.8$, 122.0, 130.8, 133.8, 136.1; MS (70 eV, EI): m/z (%): 445.9 (100) $[M]^+$, 364.9 (64) $[M-Br]^+$, 286.0 (39) $[M-2\times Br]^+$, 206.1 (15) $[M-2\times Br-HBr]^+$, 126.1 (30) $[M-4\times Br]^+$; elemental analysis calcd (%) for $C_{10}H_6Br_4$ (445.8): C 26.94, H 1.36; found C 27.18, H 1.40.

(+)-(1*S*,3a*S*,3b*R*,6b*R*,8a*S*,9*S*,11a*S*,11b*R*,14b*R*,16a*S*)-1,9-Di-*tert*-butoxy-8a,16a-dimethyl-2,3,3a,3b,4,5,6b,7,8,8a,10,11,11a,11b,12,13,14b,15,16,16a-eicosahydro-di-1*H*-indeno[4,5-*a*:4,5-*h*]-anthracene (18): A solution of freshly prepared **3** (9.0 mg, 17 μmol) and 10% Pd on charcoal (10 mol% Pd, 1.8 mg, 1.7 μmol) in ethyl acetate (1 mL) was stirred under a hydrogen atmosphere (3 bar) for 16 h at room temperature. The solvent was removed in vacuo and the residue was purified by column chromatography (n-pentane/CH_2Cl_2 5:1) to furnish **18** (7.3 mg, 13.3 μmol, 80%) as colorless oil. $R_f=0.32$ (n-pentane/CH_2Cl_2 5:1); $[\alpha]_D^{20}=+20.8°$ ($c=0.4$ in C_6H_6); ^{1}H NMR (500 MHz, C_6D_6): $\delta=0.87$ (s, 18H), 0.91–1.00 (m, 2H), 0.93 (s, 6H), 1.21–1.33 (m, 4H), 1.42–1.66 (m, 8H), 1.70–1.79 (m, 4H), 1.84 (ddt, $J=14.5$, 4.3, 4.3 Hz, 2H), 1.88–1.94 (m, 2H), 2.33 (d, $J=14.5$ Hz, 2H), 2.56 (t, $J=7.9$ Hz, 2H), 2.64 (ddd, $J=15.8$, 4.0, 4.0 Hz, 2H), 2.79–2.89 (m, 2H), 2.90 (br s, 2H), 7.21 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.64$, 23.94, 24.63, 26.26, 26.35, 28.71, 31.17, 33.22, 34.49, 38.23, 41.87, 43.30, 71.77, 80.53, 127.3, 135.3, 136.0; MS (70 eV, EI): m/z (%): 546.4 (100) $[M]^+$, 489.3 (43) $[M-C_4H_9]^+$, 472.3 (18) $[M-C_4H_{10}O]^+$, 433.3 (7) $[M-C_4H_8-C_4H_9]^+$, 415.3 (22) $[M-C_4H_9-C_4H_{10}O]^+$; HRMS: calcd for $C_{38}H_{58}O_2$: 546.4437; found 546.4436.

(−)-(1*S*,3a*S*,3b*R*,6b*R*,8a*S*,9*S*,11a*S*,11b*R*,14b*R*,16a*S*)-1,9-Dihydroxy-8a,16a-dimethyl-2,3,3a,3b,4,5,6b,7,8,8a,10,11,11a,11b,12,13,14b,15,16,16a-eicosahydro-di-1*H*-indeno[4,5-*a*:4,5-*h*]anthracene (19): A solution of **18** (7.2 mg, 13 μmol) and trimethylsilyliodide (TMSI) (4.7 μL, 6.9 mg, 34 μmol) in CH_2Cl_2 (1 mL) was stirred for 18 h at room temperature. Methanol (0.1 mL) and brine (5 mL) were added to the reaction mixture. Then it was extracted with ethyl acetate (3 × 5 mL), the combined organic layers were dried over Na_2SO_4, evaporated in vacuo and the residue was purified by column chromatography (n-pentane/EtOAc 1:1) to furnish **19** (5.2 mg, 12 μmol, 90%) as colorless oil. $R_f=0.34$ (n-pentane/EtOAc 1:1); $[\alpha]_D^{20}=-96.4°$ ($c=0.25$ in $CHCl_3$); ^{1}H NMR (500 MHz, CD_2Cl_2): $\delta=0.83$ (s, 6H), 1.00 (ddd, $J=13.3$, 13.3, 3.5 Hz, 2H), 1.25–1.45 (m, 6H), 1.53 (ddd, $J=13.3$, 3.5, 3.5 Hz, 2H), 1.56–1.82 (m, 8H), 1.86–2.07 (m, 6H), 2.32 (dd, $J=14.6$, 2.0 Hz, 2H), 2.55 (ddd, $J=16.5$, 5.4, 2.0 Hz, 2H), 2.73 (ddd, $J=16.5$, 12.7, 5.4 Hz, 2H), 2.90 (br s, 2H), 3.50 (t, $J=8.2$ Hz, 2H), 7.00 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=10.83$, 23.57, 24.87, 25.85, 26.07, 30.31, 33.01, 34.59, 37.98, 41.99, 43.48, 82.20, 127.1, 135.3, 135.4; MS (70 eV, EI): m/z (%): 434.3 (100) $[M]^+$, 375.2 (3) $[M-H_2O-CH_3-C_2H_2]^+$, 334.1 (2) $[M-H_2O-2\times CH_3-2\times C_2H_2]^+$, 321.2 (4) $[M-2\times CH_3-C_2H_2-C_3H_5O]^+$, 57.0 (4) $[C_3H_5O]^+$; HRMS: calcd for $C_{30}H_{42}O_2$: 434.3185; found 434.3184.

(−)-(1*S*,3a*S*,3b*S*,6b*R*,8a*S*,9*S*,11a*S*,11b*S*,14b*R*,16a*S*)-1,9-Di-*tert*-butoxy-8a,16a-dimethyl-2,3,3a,3b,4,5,6b,8a,10,11,11a,11b,12,13,14b,16a-hexadecahydro-di-1*H*-indeno[4,5-*a*:4,5-*h*]anthracene (20): A solution of freshly prepared **3** (20.6 mg, 38.2 μmol) and $[(PPh_3)_3RhCl]$ (10 mol%, 3.54 mg, 3.83 μmol) in methanol/ethyl acetate (1:1, 2.75 mL) was stirred under a hydrogen atmosphere (3 bar) for 13 h at room temperature. The solvent was removed in vacuo and the residue was purified by column chromatography (n-pentane/CH_2Cl_2 5:1) to furnish **20** (14.5 mg, 26.7 μmol, 70%) as white solid. $R_f=0.33$ (n-pentane/CH_2Cl_2 5:1); m.p. 151 °C; $[\alpha]_D^{20}=-271.8°$ ($c=0.8$ in C_6H_6); ^{1}H NMR (500 MHz, C_6D_6): $\delta=1.05$ (s, 18H), 1.09 (s, 6H), 1.27–1.39 (m, 2H), 1.44–1.61 (m, 6H), 1.61–1.69 (m, 2H), 1.70–1.82 (m, 4H), 2.27 (m, 2H), 2.52 (ddd, $J=15.8$, 4.4, 4.4 Hz, 2H), 2.75 (ddd, $J=15.8$, 11.5, 4.4 Hz, 2H), 3.21 (dd, $J=7.5$, 7.5 Hz, 2H), 3.48 (dd, $J=4.4$, 4.4 Hz, 2H), 6.10 (dd, $J=9.8$, 4.2 Hz, 2H), 6.16 (d, $J=9.8$ Hz, 2H), 7.14 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=15.44$, 23.24, 25.83, 26.14, 28.78, 31.90, 32.21, 39.55, 42.56, 45.09, 72.16, 77.04, 128.6, 129.3, 135.0, 136.4, 135.4; MS (70 eV, EI): m/z (%): 542.5 (76) $[M]^+$, 485.4 (100) $[M-C_4H_9]^+$, 429.3 (24) $[M-C_4H_8-C_4H_9]^+$, 411.3 (26) $[M-C_4H_9-C_4H_{10}O]^+$, 57.0 (24) $[C_4H_9]^+$; HRMS: calcd for $C_{38}H_{54}O_2$: 542.4124; found 542.4123.

(1*S*,3a*S*,3b*S*,6b*R*,8a*S*,9*S*,11a*S*,11b*S*,14b*R*,16a*S*)-1,9-Dihydroxy-8a,16a-dimethyl-2,3,3a,3b,4,5,6b,8a,10,11,11a,11b,12,13,14b,16a-hexadecahydro-di-1*H*-indeno[4,5-*a*:4,5-*h*]anthracene (21): Reaction of **20** (6.7 mg, 12 μmol) with TMSI (3.4 μL, 4.9 mg, 25 μmol) as described for **19** gave **21** (4.1 mg, 9.5 μmol, 77%) as colorless oil. $R_f=0.45$ (n-pentane/EtOAc 1:1); ^{1}H NMR (500 MHz, CD_2Cl_2): $\delta=0.87$ (s, 6H), 1.34–1.82 (m, 14H), 1.99–2.13 (m, 2H), 2.28–2.38 (m, 2H), 2.48 (ddd, $J=16.1$, 4.1, 4.1 Hz, 2H), 2.70 (ddd, $J=16.1$, 8.1, 8.1 Hz, 2H), 3.49 (br s, 2H), 3.69 (t, $J=8.0$ Hz, 2H), 5.97 (dd, $J=10.0$, 3.6 Hz, 2H), 6.01 (d, $J=10.0$ Hz, 2H), 6.98 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=14.31$, 22.88, 25.61, 25.66, 31.53, 31.96, 39.32, 42.77, 45.06, 78.10, 128.7, 130.2, 134.6, 135.2, 136.1; MS (70 eV, EI): m/z (%): 430.3 (100) $[M]^+$, 412.3 (4) $[M-H_2O]^+$, 371.3 (2) $[M-H_2O-CH_3-C_2H_2]^+$, 57.1 (16) $[C_3H_5O]^+$, 43.0 (11) $[C_2H_3O]^+$; HRMS: calcd for $C_{30}H_{38}O_2$: 430.2872; found 430.2871.

2,4-Dibromo-5-[1,3]dioxolan-2-ylbenzaldehyde (23): Reaction of 2,4-dibromobenzene-1,5-dicarbaldehyde (55.0 g, 188 mmol), ethylene glycol (10.5 mL, 11.7 g, 188 mmol) and pTsOH·H$_2$O (0.5 mol%, 179 mg, 9.41×10^{-4} mol) in toluene (765 mL) as described for **10** gave **23** (16.3 g, 48.5 mmol, 26%) as a white solid together with the corresponding diacetal (25.7 g, 67.7 mmol, 36%) and 2,4-dibromobenzene-1,5-dicarbaldehyde (19.8 g, 67.8 mmol, 36%). Analytical data for **23**: $R_f=0.25$ (n-pentane/CH_2Cl_2 2:1); m.p. 112 °C; UV/Vis (CH_3CN): λ_{max} (lg ε) = 222.5 (4.318), 263.5 (4.170), 297.5 nm (3.256); IR (KBr): $\tilde{\nu}=2903$, 2884, 1692 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=4.02-4.23$ (m, 4H), 6.04 (s, 1H), 7.91 (s, 1H), 8.11 (s, 1H), 10.30 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=65.57$, 101.6, 127.2, 128.8, 129.8, 132.5, 137.55, 137.57; MS (70 eV, EI): m/z (%): 335.9 (40) $[M]^+$, 334.9 (60) $[M-H]^+$, 306.9 (7) $[M-CHO]^+$, 290.9 (36) $[M-C_2H_5O]^+$, 262.9 (33) $[M-C_3H_5O_2]^+$, 73.1 (100) $[C_3H_5O_2]^+$; elemental analysis calcd (%) for $C_{10}H_8Br_2O_3$ (336.0): C 35.75, H 2.40; found C 35.75; H 2.25.

1,5-Dibromo-2-(2,2-dibromovinyl)-4-[1,3]dioxolan-2-ylbenzene (24): Reaction of CBr_4 (32.2 g, 97.0 mmol) in CH_2Cl_2 (100 mL), PPh_3 (50.9 g, 194 mmol) in CH_2Cl_2 (150 mL) and **23** (16.3 g, 48.5 mmol) in CH_2Cl_2 (150 mL) at −20 °C followed by reaction of the obtained mixture with ethylene glycol (27.1 mL, 30.1 g, 485 mmol) and pTsOH·H$_2$O (46 mg, 242 μmol) in toluene (350 mL) as described for **11** gave **24** as a white solid (19.1 g, 38.8 mmol, 80%). $R_f=0.19$ (n-pentane/CH_2Cl_2 3:1); m.p. 55 °C; UV/Vis (CH_3CN): λ_{max} (lg ε) = 209.0 (4.450), 266.0 nm (4.098); IR (KBr): $\tilde{\nu}=3084$, 2885, 1375 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=4.01-4.20$ (m, 4H), 6.05 (s, 1H), 7.43 (s, 1H), 7.81 (s, 1H), 7.82 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta=65.50$, 93.90, 101.9, 123.1, 123.9, 129.2, 135.3, 135.5, 136.2, 136.3; MS (70 eV, EI): m/z (%): 491.8 (24) $[M]^+$, 446.7 (9) $[M-C_2H_5O]^+$, 410.8 (37) $[M-Br]^+$, 337.9 (8) $[M-Br-C_3H_5O_2]^+$, 73.1 (100) $[C_3H_5O_2]^+$; elemental analysis calcd (%) for $C_{11}H_8Br_4O_2$ (491.8): C 26.86, H 1.64; found C 27.09, H 1.60.

1,5-Dibromo-2-[(*Z*)-2-bromovinyl]-4-[1,3]dioxolan-2-ylbenzene (25): Reaction of **24** (15.0 g, 30.5 mmol), $[Pd(PPh_3)_4]$ (4.00 mol%, 1.41 g, 1.22 mmol) and nBu$_3$SnH (8.90 mL, 9.77 g, 33.6 mmol) in toluene (180 mL) as described for **12** gave **25** (11.6 g, 28.1 mmol, 92%) as white solid. $R_f=0.17$ (n-pentane/CH_2Cl_2 3:1); m.p. 65 °C; UV/Vis (CH_3CN): λ_{max} (lg ε) = 210.5 (4.337), 257.5 nm (4.021); IR (KBr): $\tilde{\nu}=2887$, 1615, 1325 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=4.02-4.22$ (m, 4H), 6.09 (s, 1H), 6.63 (d, $J=8.4$ Hz, 1H), 7.14 (d, $J=8.4$ Hz, 1H), 7.83 (s, 1H), 8.00 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta=65.46$, 102.0, 110.3, 122.6, 124.5, 129.2, 131.3, 136.2, 134.3, 136.0; MS (70 eV, EI): m/z (%): 411.7 (54) $[M]^+$, 366.9 (15) $[M-C_2H_5O]^+$, 333.0 (77) $[M-Br]^+$, 289.0 (9) $[M-Br-C_2H_4O]^+$, 260.9 (14) $[M-Br-C_3H_4O_2]^+$, 73.1 (100) $[C_3H_5O_2]^+$; elemental analysis calcd (%) for $C_{11}H_9Br_3O_2$ (412.9): C 32.00, H 2.20; found C 32.36, H 2.11.

(−)-(1*S*,3a*S*,4*S*,7a*S*)-1-*tert*-Butoxy-4-{(*Z*)-2-[2,4-dibromo-5-([1,3]dioxolan-2-yl)phenyl]vinyl}-7a-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-indene (26): Reaction of **25** (150 mg, 363 μmol), hydrindene **7** (151 mg, 727 μmol), nBu$_4$NOAc (274 mg, 908 μmol), PPh_3 (20 mol%, 19.0 mg, 72.7 μmol) and $Pd(OAc)_2$ (10 mol%, 8.20 mg, 36.3 μmol) in DMF/CH_3CN/H_2O (1:1:0.2, 5 mL) as described for **13** gave **23** as colorless oil (98.0 mg, 181 μmol, 50%).

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$R_f = 0.22$ (*n*-pentane/CH_2Cl_2 1:1); $[\alpha]_D^{20} = -11.6^\circ$ ($c = 0.5$ in $CHCl_3$); UV/Vis (CH_3CN): λ_{max} (lg ε) = 208.5 (4.482), 251.5 nm (4.123); IR (KBr): $\tilde{\nu}$ = 2971, 2876, 1584, 1389 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.63$ (s, 3H), 1.11 (s, 9H), 1.17–1.26 (m, 1H), 1.29–1.44 (m, 2H), 1.60–1.69 (m, 1H), 1.79–1.89 (m, 2H), 1.99 (ddt, $J = 17.3$, 5.2, 1.4 Hz, 1H), 2.87–2.95 (m, 1H), 3.47 (t, $J = 8.5$ Hz, 1H), 4.01–4.06 (m, 4H), 5.39 (d, $J = 9.8$ Hz, 1H), 5.49 (dd, $J = 11.2$, 11.2 Hz, 1H), 5.67 (ddt, $J = 10.0$, 5.0, 2.5 Hz, 1H), 6.05 (s, 1H), 6.40 (d, $J = 11.2$ Hz, 1H), 7.51 (s, 1H), 7.77 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.37, 24.69, 28.71, 30.41, 38.66, 38.68, 41.20, 46.14, 65.31, 65.57, 72.25, 80.52, 102.1, 121.1, 124.9, 127.6, 128.1, 128.4, 129.4, 135.8, 136.8, 135.9, 137.3; MS (70 eV, EI): *m*/*z* (%): 540.1 (10) $[M]^+$, 483.0 (19) $[M - C_4H_9]^+$, 461.2 (34) $[M - Br]^+$, 403.1 (100) $[M - Br - C_4H_8]^+$, 73.0 (56) $[C_3H_5O_2]^+$, 57.0 (88) $[C_4H_9]^+$; HRMS: calcd for $C_{25}H_{32}Br_2O_3$: 538.0718; found 538.0718.

(−)-2,4-Dibromo-5-{(*Z*)-2-[(1*S*,3a*S*,4*S*,7a*S*)-1-*tert*-butoxy-7a-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-inden-4-yl]vinyl}benzaldehyde (26a): A solution of **26** (4.19 g, 7.76 mmol) and pyridinium *p*-toluenesulfonate (585 mg, 2.33 mmol) in acetone/water (2:1, 100 mL) was heated under reflux for 4.5 d. The solvents were removed in vacuo and diethyl ether (100 mL) was added. The organic phase was washed with brine, dried over Na_2SO_4 and evaporated in vacuo. Purification by column chromatography (*n*-pentane/Et_2O 30:1) furnished **26a** (3.21 g, 6.47 mmol, 83%) as colorless oil and **26** (163 mg, 302 μmol, 4%). $R_f = 0.28$ (*n*-pentane/Et_2O 30:1); $[\alpha]_D^{20} = -11.0^\circ$ ($c = 0.8$ in $CHCl_3$); UV/Vis (CH_3CN): λ_{max} (lg ε) = 202.5 (4.259), 245.0 (4.331), 314.5 nm (3.350); IR (KBr): $\tilde{\nu}$ = 2972, 1698, 1575 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.60$ (s, 3H), 1.11 (s, 9H), 1.12–1.21 (m, 1H), 1.27–1.50 (m, 2H), 1.56–1.67 (m, 1H), 1.77–1.88 (m, 2H), 1.98 (dd, $J = 17.2$, 5.3 Hz, 1H), 2.73–2.81 (m, 1H), 3.46 (t, $J = 8.3$ Hz, 1H), 5.40 (d, $J = 9.6$ Hz, 1H), 5.55 (dd, $J = 11.2$, 11.2 Hz, 1H), 5.68 (ddt, $J = 9.7$, 5.0, 2.6 Hz, 1H), 6.35 (d, $J = 11.2$ Hz, 1H), 7.76 (s, 1H), 7.88 (s, 1H), 10.27 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.33, 24.77, 28.71, 30.42, 38.66, 38.89, 41.18, 46.11, 72.24, 80.48, 124.8, 127.1, 127.9, 128.0, 130.9, 131.2, 132.0, 137.0, 138.1, 138.4, 190.8; MS (70 eV, EI): *m*/*z* (%): 496.1 (4) $[M]^+$, 440.0 (41) $[M - C_4H_8]^+$, 343.1 (26) $[M - C_4H_9O - Br]^+$, 57.1 (100) $[C_4H_9]^+$; HRMS: calcd for $C_{23}H_{28}Br_2O_2$: 494.0456; found 494.0456; elemental analysis calcd (%) for $C_{23}H_{28}Br_2O_2$ (496.3): C 55.66, H 5.69; found C 55.70, H 5.31.

(−)-(1*S*,3a*S*,4*S*,7a*S*)-1-*tert*-Butoxy-4-{(*Z*)-2-[2,4-dibrom-5-(2,2-dibromovinyl)phenyl]vinyl}-7a-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-indene (26b): Reaction of CBr_4 (4.28 mg, 12.9 mmol) in CH_2Cl_2 (20 mL), PPh_3 (6.77 g, 25.8 mmol) in CH_2Cl_2 (20 mL) and benzaldehyde **26a** (3.20 g, 6.45 mmol) in CH_2Cl_2 (10 mL) at −20 °C as described for **13b** gave **26b** as colorless oil (3.14 g, 4.82 mmol, 75%). $R_f = 0.34$ (*n*-pentane/CH_2Cl_2 6:1); $[\alpha]_D^{20} = -5.2^\circ$ ($c = 0.5$ in $CHCl_3$); UV/Vis (CH_3CN): λ_{max} (lg ε) = 253.3 nm (4.283); IR (KBr): $\tilde{\nu}$ = 2971, 1196, 1078 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.58$ (s, 3H), 1.04–1.16 (m, 1H), 1.10 (s, 9H), 1.26–1.40 (m, 2H), 1.56–1.65 (m, 1H), 1.76–1.87 (m, 2H), 1.97 (dd, $J = 17.2$, 5.2 Hz, 1H), 2.89–2.96 (m, 1H), 3.45 (t, $J = 8.5$ Hz, 1H), 5.44 (d, $J = 9.6$ Hz, 1H), 5.48 (dd, $J = 11.0$, 11.0 Hz, 1H), 5.69 (ddt, $J = 9.6$, 5.4, 2.6 Hz, 1H), 6.35 (d, $J = 11.2$ Hz, 1H), 7.40 (s, 1H), 7.46 (s, 1H), 7.80 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.73, 24.60, 28.72, 30.36, 38.67, 38.92, 41.23, 46.27, 72.27, 80.50, 93.40, 121.5, 124.4, 127.9, 127.9, 128.3, 131.5, 134.8, 137.2, 135.7, 137.6; MS (70 eV, EI): *m*/*z* (%): 652.1 (5) $[M]^+$, 594.9 (23) $[M - C_4H_9]^+$, 577.9 (30) $[M - C_4H_{10}O]^+$, 497.0 (12) $[M - C_4H_{10}O - Br]^+$, 57.1 (100) $[C_4H_9]^+$; HRMS: calcd for $C_{24}H_{28}Br_4O$: 647.8874; found 647.8874; elemental analysis calcd (%) for $C_{24}H_{28}Br_4O$ (652.1): C 44.20, H 4.33; found C 43.95, H 4.06.

(−)-(1*S*,3a*S*,4*S*,7a*S*)-1-*tert*-Butoxy-4-{(*Z*)-2-[2,4]-dibromo-5-((*Z*)-2-bromovinyl)phenyl]vinyl}-7a-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-indene (27): Reaction of **26b** (3.20 g, 6.45 mmol), $[Pd(PPh_3)_4]$ (4.00 mol%, 223 mg, 1.93×10^{-4} mol) and nBu_3SnH (1.34 mL, 1.47 g, 5.06 mmol) in degassed toluene (26 mL) as described for **14** gave **27** (2.53 g, 4.41 mmol, 92%) as colorless oil. $R_f = 0.28$ (*n*-pentane/CH_2Cl_2 6:1); $[\alpha]_D^{20} = -36.3^\circ$ ($c = 0.8$ in $CHCl_3$); UV/Vis (CH_3CN): λ_{max} (lg ε) = 252.5 nm (4.622); IR (KBr): $\tilde{\nu}$ = 2972, 1576, 1197 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.62$ (s, 1H), 1.05–1.16 (m, 1H), 1.11 (s, 9H), 1.26–1.41 (m, 2H), 1.57–1.65 (m, 1H), 1.76–1.87 (m, 2H), 1.97 (dd, $J = 17.2$, 5.2 Hz, 1H), 2.98–3.04 (m, 1H), 3.46 (t, $J = 8.5$ Hz, 1H), 5.45 (d, $J = 9.8$ Hz, 1H), 5.48 (dd, $J = 11.0$, 11.0 Hz, 1H), 5.68 (ddt, $J = 9.7$, 5.5, 2.2 Hz, 1H), 6.37 (d, $J = 11.2$ Hz, 1H), 6.58 (d, $J = 8.0$ Hz, 1H), 7.09 (d, $J = 8.0$ Hz, 1H), 7.65 (s, 1H), 7.81 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.71, 24.60, 28.73, 30.39, 38.71, 38.85, 41.25, 46.36, 72.22, 80.56, 110.0, 122.1, 123.9, 127.6, 128.0, 128.5, 131.4, 131.6, 133.9, 136.8, 135.6, 137.42; MS (70 eV, EI): *m*/*z* (%): 574.3 (2) $[M]^+$, 517.3 (4) $[M - C_4H_9]^+$, 500.2 (4) $[M - C_4H_{10}O]^+$, 419.3 (4) $[M - C_4H_{10}O - Br]^+$, 57.1 (100) $[C_4H_9]^+$; HRMS: calcd for $C_{24}H_{29}Br_3O$ 569.9768; found 569.9768.

(+)-1,5-Dibromo-2,4-bis{(*Z*)-2-[(1*S*,3a*S*,4*S*,7a*S*)-1-*tert*-butoxy-7a-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-inden-4-yl]vinyl}benzene (4): 1. Reaction of vinyl bromide **27** (40.0 mg, 69.8 μmol), hydrindene **7** (29.0 mg, 140 μmol), K_2CO_3 (24.0 mg, 174 μmol), nBu_4NCl (19.0 mg, 69.8 μmol), PPh_3 (20 mol%, 3.70 mg, 14.0 μmol) and $Pd(OAc)_2$ (10 mol%, 1.60 mg, 6.98 μmol) in DMF/CH_3CN/H_2O (1:1:0.2, 1 mL) as described for **5** gave **4** (23.0 mg, 32.8 μmol, 47%) as colorless oil.

2. PPh_3 (20 mol%, 4.70 mg, 17.9 μmol) was added at 50 °C to a stirred solution of **30** (40.0 mg, 89.7 μmol), hydrindene **7** (75.0 mg, 359 μmol) and nBu_4NOAc (135 mg, 449 μmol) in degassed DMF/CH_3CN/H_2O (1:1:0.2, 1 mL) and $Pd(OAc)_2$ (10 mol%, 2.00 mg, 8.97 μmol), and the reaction mixture was heated at 60 °C for 18 h. After cooling the solution was diluted with Et_2O (10 mL), washed with water (2 × 5 mL) and the combined aqueous layers were extracted with Et_2O (2 × 5 mL). Then, the combined organic layers were washed with brine, dried over Na_2SO_4, the solvent was removed in vacuo and the residue purified by column chromatography (*n*-pentane/CH_2Cl_2 3:1) to give **4** (8.0 mg, 11.4 μmol, 13%) as colorless oil. $R_f = 0.31$ (*n*-pentane/CH_2Cl_2 5:1); $[\alpha]_D^{20} = +6.3^\circ$ ($c = 1$ in $CHCl_3$); UV/Vis (CH_3CN): λ_{max} (lg ε) = 239.0 nm (4.340); IR (KBr): $\tilde{\nu}$ = 2972, 1197, 1079 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.61$ (s, 6H), 1.02–1.17 (m, 2H), 1.11 (s, 18H), 1.22–1.47 (m, 4H), 1.57–1.66 (m, 2H), 1.75–1.88 (m, 4H), 1.98 (dd, $J = 17.2$, 5.0 Hz, 2H), 2.76–2.85 (m, 2H), 3.45 (t, $J = 8.4$ Hz, 2H), 5.40 (d, $J = 10.0$ Hz, 2H), 5.44 (dd, $J = 11.0$, 11.0 Hz, 2H), 5.66 (ddt, $J = 10.0$, 5.4, 2.1 Hz, 2H), 6.34 (d, $J = 11.2$ Hz, 2H), 7.13 (s, 1H), 7.78 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.49, 24.76, 28.74, 30.37, 38.71, 38.97, 41.12, 46.35, 72.22, 80.58, 122.5, 127.7, 128.1, 128.4, 131.6, 135.5, 136.8, 137.0; MS (70 eV, EI): *m*/*z* (%): 700.2 (8) $[M]^+$, 643.2 (10) $[M - C_4H_9]^+$, 587.1 (36) $[M - C_4H_8 - C_4H_9]^+$, 569.1 (34) $[M - C_4H_9 - C_4H_{10}O]^+$, 57.1 (100) $[C_4H_9]^+$; HRMS: calcd for $C_{38}H_{52}Br_2O_2$: 698.2334; found 698.2334; elemental analysis calcd (%) for $C_{38}H_{52}Br_2O_2$ (700.6): C 65.14, H 7.48; found C 65.02, H 7.31.

(−)-(1*S*,3a*S*,3b*S*,8a*S*,8b*S*,11*S*,11a*S*,13a*R*,14b*R*,16a*S*)-1,11-Di-*tert*-butoxy-11a,16a-dimethyl-2,3,3a,3b,8a,8b,9,10,11a,13a,14b,16a-dodecahydro-di-1*H*-indeno[4,5-*a*:4,5-*j*]anthracene (2): A solution of **4** (20.0 mg, 28.5 μmol), Ag_3PO_4 (31.0 mg, 74.2 μmol) and *trans*-di(μ-acetato)-bis[*orto*-(di-*ortho*-tolylphosphino)benzyl]dipalladium(II) **15** (5.00 mol%, 1.30 mg, 1.43 μmol) in degassed DMF/CH_3CN/H_2O (1:1:0.2, 1 mL) was heated for 1.5 h at 130 °C in a preheated oil bath. After the reaction mixture was cooled, water (10 mL) was added and the reaction mixture was extracted with Et_2O (2 × 10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent and chromatographic purification (*n*-pentane/CH_2Cl_2 5:1) yielded **2** (12.4 mg, 23.0 μmol, 81%) as colorless oil. $R_f = 0.33$ (*n*-pentane/CH_2Cl_2 5:1); $[\alpha]_D^{20} = -338.3^\circ$ ($c = 0.3$ in $CHCl_3$); UV/Vis (CH_3CN): λ_{max} (lg ε) = 222.0 (4.133), 250.5 (4.508), 257.0 (4.538), 270.0 (4.287), 281.5 nm (4.167); IR (KBr): $\tilde{\nu}$ = 2972, 1362, 1198 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.85$ (s, 6H), 1.10 (s, 18H), 1.34–1.53 (m, 6H), 1.68–1.77 (m, 2H), 1.78–1.88 (m, 2H), 2.63 (ddd, $J = 11.8$, 6.9, 6.9 Hz, 2H), 3.47 (dd, $J = 8.7$, 6.5 Hz, 2H), 3.70 (dd, $J = 6.9$, 6.9 Hz, 1H), 5.82 (dd, $J = 9.7$, 6.1 Hz, 2H), 6.04 (d, $J = 10.1$ Hz, 2H), 6.15 (dd, $J = 10.1$, 4.7 Hz, 2H), 6.30 (d, $J = 9.7$ Hz, 2H), 6.60 (s, 1H), 7.18 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.93, 22.82, 28.73, 31.80, 33.83, 38.20, 41.62, 44.74, 72.39, 76.21, 124.2, 125.4, 126.2, 129.5, 130.7, 136.1, 136.3; MS (70 eV, EI): m/z (%): 538.6 (56) $[M]^+$, 481.5 (54) $[M - C_4H_9]^+$, 425.5 (20) $[M - C_4H_9 - C_4H_8]^+$, 407.4 (34) $[M - C_4H_9 - C_4H_8 - H_2O]^+$, 57.1 (100) $[C_4H_9]^+$; HRMS: calcd for $C_{38}H_{50}O_2$: 538.3811; found 538.3811.

(1*S*,3a*S*,3b*S*,8b*R*,11*S*,11a*S*,14b*R*,16a*S*)-1,11-Di-*tert*-butoxy-11a,16a-dimethyl-2,3,3a,3b,8b,9,10,11a,12,13,14b,16a-dodecahydro-di-1*H*-indeno[4,5-*a*:4,5-*j*]anthracene (28): $R_f = 0.18$ (*n*-pentane/CH_2Cl_2 5:1); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.66$ (s, 3H), 0.90 (s, 3H), 1.10 (s, 9H), 1.18 (s, 9H), 1.38–1.88 (m, 8H), 2.07–2.20 (m, 3H), 2.69–2.77 (m, 2H), 3.11–3.30 (m, 2H), 3.47 (dd, $J = 8.9$, 6.2 Hz, 1H), 3.64 (t, $J = 7.8$ Hz, 1H), 3.82 (t, $J = 5.5$ Hz, 1H), 5.95 (dd, $J = 9.6$, 6.0 Hz, 1H), 6.10 (d, $J = 10.0$ Hz, 1H), 6.30 (dd, $J = 10.0$, 4.3 Hz, 1H), 6.55 (d, $J = 9.6$ Hz, 1H), 7.09 (d, $J = 8.4$ Hz, 1H), 7.34 (s, 1H), 7.53 (d, $J = 8.4$ Hz, 1H), 7.77 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 10.81, 15.08, 22.87, 23.84, 24.52, 28.71, 28.77, 31.79, 31.85, 34.33, 34.35, 38.79, 42.38, 42.45, 45.22, 46.53, 72.34, 72.39, 76.19, 79.96, 121.1, 124.4, 125.0, 125.51, 125.54, 127.0, 130.2, 130.5, 130.8, 131.5, 130.6, 136.1, 136.3, 136.4; MS (70 eV, EI): *m*/*z* (%): 538.3 (100) $[M]^+$, 481.2 (96) $[M - C_4H_9]^+$, 464.2 (36)

$[M - C_4H_8 - H_2O]^+$, 407.2 (6) $[M - C_4H_9 - C_4H_8 - H_2O]^+$, 57.0 (54) $[C_4H_9]^+$; HRMS: calcd for $C_{38}H_{50}O_2$: 538.3811; found 538.3810.

1,5-Dibromo-2,4-di(2,2-dibromovinyl)benzene (29): Reaction of CBr_4 (2.67 g, 8.04 mmol) in CH_2Cl_2 (15 mL), PPh_3 (4.22 g, 16.1 mmol) in CH_2Cl_2 (15 mL) and 2,4-dibromobenzene-1,5-dicarbaldehyde (**22**; 587 mg, 2.01 mmol) as described for **16** gave **29** (694 mg, 1.15 mmol, 57%) as white solid. $R_f = 0.54$ (*n*-pentane); m.p. 175 °C; UV/Vis (CH_3CN): λ_{max} (lg ε) = 207.5 (3.948), 262.5 nm (3.908); IR (KBr): $\tilde{\nu} = 3080, 1595, 1574, 1444\ cm^{-1}$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.43$ (s, 2H), 7.79 (s, 1H), 7.84 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 94.15, 123.3, 131.3, 135.3, 135.4, 136.0$; MS (70 eV, EI): *m*/*z* (%): 603.7 (70) $[M]^+$, 522.7 (2) $[M - Br]^+$, 443.9 (10) $[M - 2 \times Br]^+$, 364.9 (2) $[M - 3 \times Br]^+$, 284.0 (10) $[M - 4 \times Br]^+$; elemental analysis calcd (%) for $C_{10}H_4Br_6$ (603.6): C 19.90, H 0.67; C 20.22, H 0.67.

1,5-Dibromo-2,4-di[(*Z*)-2-bromovinyl]benzene (30): Reaction of **29** (623 mg, 1.03 mmol), $[Pd(PPh_3)_4]$ (8.00 mol%, 95.0 mg, 82.6 μmol) and nBu_3SnH (0.57 mL, 631 g, 0.57 mmol) in toluene (62 mL) as described for **17** gave **30** (354 mg, 794 μmol, 77%) as white solid. $R_f = 0.39$ (*n*-pentane); m.p. 108 °C; UV/Vis (CH_3CN): λ_{max} (lg ε) = 256.5 nm (4.313); IR (KBr): $\tilde{\nu} = 3080, 1620, 1572, 1318, 1045, 864, 666\ cm^{-1}$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 6.65$ (d, $J = 8.0$ Hz, 2H), 7.15 (d, $J = 8.0$ Hz, 2H), 7.86 (s, 1H), 8.14 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 110.3, 123.6, 131.2, 131.3, 134.2, 135.8$; MS (70 eV, EI): *m*/*z* (%): 445.9 (100) $[M]^+$, 365.0 (64) $[M - Br]^+$, 286.0 (40) $[M - 2 \times Br]^+$, 206.1 (21) $[M - 2 \times Br - HBr]^+$, 126.1 (40) $[M - 4 \times Br]^+$; elemental analysis calcd (%) for $C_{10}H_6Br_4$ (445.8): C 26.94, H 1.36; found C 27.15, H 1.49.

(−)-(1*S*,3a*S*,3b*R*,8a*R*,8b*R*,11*S*,11a*S*,13a*R*,14b*R*,16a*S*)-1,11-Di-*tert*-butoxy-11a,16a-dimethyl-2,3,3a,3b,4,5,7,8,8a,8b,9,10,11a,12,13,13a,14b,15,16,16a-eicosahydro-di-1*H*-indeno[4,5-*a*:4,5-*j*]anthracene (31): A solution of freshly prepared **2** (54.3 mg, 101 μmol) and $PtO_2 \cdot H_2O$ (10 mol%, 2.50 mg, 10.2 μmol) in methanol/ethyl acetate (1:1, 4 mL) was stirred under a hydrogen atmosphere (50 bar) for 15 h at room temperature. The solvent was removed in vacuo and the residue was purified by column chromatography (*n*-pentane/CH_2Cl_2 5:1) to furnish **31** (54 mg, 98.7 μmol, 98%) as white solid. $R_f = 0.14$ (*n*-pentane/CH_2Cl_2 5:1); m.p. 188 °C; $[\alpha]_D^{20} = -95.0°$ ($c = 0.5$ in $CHCl_3$); UV/Vis (CH_3CN): λ_{max} (lg ε) = 204.0 (4.730), 248.0 (2.932), 254.0 (2.970), 260.5 (2.970), 275.5 (3.204), 284.5 (3.235), 308.0 nm (2.447); IR (KBr): $\tilde{\nu} = 2971, 2925, 1198\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.96$ (s, 24H), 1.06–1.16 (m, 2H), 1.21–1.42 (m, 4H), 1.48–1.59 (m, 4H), 1.60–1.77 (m, 8H), 1.86–1.97 (m, 4H), 2.47 (d, $J = 14.5$ Hz, 2H), 2.57 (dd, $J = 16.8$, 4.7 Hz, 2H), 2.82 (m, 2H), 3.01 (t, $J = 8.0$ Hz, 4H), 6.88 (s, 1H), 7.67 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 11.40, 23.74, 24.96, 25.25, 25.67, 28.54, 30.86, 33.30, 34.20, 38.24, 41.41, 42.96, 71.68, 80.82, 123.9, 130.2, 134.4, 136.0$; MS (70 eV, EI): *m*/*z* (%): 546.6 (100) $[M]^+$, 489.5 (88) $[M - C_4H_9]^+$, 471.5 (27) $[M - C_4H_9 - H_2O]^+$, 433.4 (14) $[M - C_4H_8 - C_4H_9]^+$, 415.4 (40) $[M - C_4H_9 - C_4H_8 - H_2O]^+$; HRMS: calcd for $C_{38}H_{58}O_2$: 546.4437; found 546.4436.

(−)-(1*S*,3a*S*,3b*R*,8a*R*,8b*S*,11*S*,11a*S*,13a*R*,14b*R*,16a*S*)-1,11-Dihydroxy-11a,16a-dimethyl-2,3,3a,3b,4,5,7,8,8a,8b,9,10,11a,12,13,13a,14b,15,16,16a-eicosahydro-di-1*H*-indeno[4,5-*a*:4,5-*j*]anthracene (32): Reaction of **31** (20.0 mg, 36.6 μmol) with TMSI (10.0 μL, 14.6 mg, 73.1 μmol) as described for **19** gave **32** (16 mg, 36.8 μmol, 100%) as colorless oil. $R_f = 0.52$ (*n*-pentane/EtOAc 1:1); $[\alpha]_D^{20} = -90.8°$ ($c = 1.16$ in $CHCl_3$); ^1H NMR (500 MHz, CD_2Cl_2): $\delta = 0.83$ (s, 6H), 0.92 (dd, $J = 13.1$, 3.3 Hz, 2H), 1.18–1.28 (m, 4H), 1.28–1.41 (m, 2H), 1.43 (br s, 2H), 1.52 (ddd, $J = 12.6$, 3.3, 3.3 Hz, 2H), 1.59–1.66 (m, 2H), 1.71–1.81 (m, 4H), 1.88–1.98 (m, 4H), 2.04 (ddd, $J = 11.8$, 8.0, 3.8 Hz, 2H), 2.36 (dddd, $J = 14.7$, 5.4, 2.5, 2.5 Hz, 2H), 2.56 (d, $J = 16.5$ Hz, 2H), 2.66–2.76 (m, 2H), 2.96 (br s, 2H), 3.45 (dd, $J = 8.6$, 7.8 Hz, 2H), 6.75 (s, 1H), 7.31 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 11.27, 23.96, 25.28, 25.74, 26.22, 30.67, 33.44, 35.00, 38.60, 42.43, 43.92, 82.59, 124.6, 130.2, 135.2, 136.3$; MS (70 eV, EI): *m*/*z* (%): 434.3 (100) $[M]^+$, 375.2 (3) $[M - H_2O - CH_3 - C_2H_2]^+$, 334.2 (3) $[M - H_2O - 2 \times CH_3 - 2 \times C_2H_2]^+$, 321.2 (7) $[M - 2 \times CH_3 - C_2H_2 - C_3H_5O]^+$; HRMS: calcd for $C_{30}H_{42}O_2$: 434.3185; found 434.3184.

(1*S*,3a*S*,8b*S*,11*S*,11a*S*,16a*S*)-1,11-Di-*tert*-butoxy-11a,16a-dimethyl-2,3,3a,8b,9,10,11a,16a-octahydro-di-1*H*-indeno[4,5-*a*:4,5-*j*]anthracene (33): A solution of freshly prepared **2** (30.0 mg, 55.7 μmol) and 10% palladium on charcoal (20 mol% Pd, 1.17 mg, 11.4 μmol) in methanol (1 mL) was stirred for 6 d at 50 °C. The catalyst was removed by filtration through a short pad of celite. Evaporation of the solvent and purification of the residue by column chromatography gave an inseparable 1:1 mixture consisting of **33** (8.5 mg, 15.9 μmol, 29%) and **2** (8.6 mg, 15.9 μg, 29%). Analytical data for **33**: $R_f = 0.24$ (*n*-pentane/CH_2Cl_2 3:1); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.71$ (s, 6H), 1.25 (s, 18H), 1.67–1.80 (m, 2H), 1.95–2.13 (m, 4H), 2.20–2.32 (m, 2H), 3.09 (dd, $J = 12.5$, 7.3 Hz, 2H), 4.02 (dd, $J = 8.5$, 7.5 Hz, 2H), 6.54 (d, $J = 9.8$ Hz, 2H), 7.26 (d, $J = 8.6$ Hz, 2H), 7.36 (d, $J = 9.8$ Hz, 2H), 7.87 (d, $J = 8.6$ Hz, 2H), 8.36 (s, 1H), 8.89 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 10.46, 23.69, 28.84, 32.49, 44.92, 46.35, 72.61, 75.62, 115.2, 122.2, 123.5, 127.3, 127.4, 128.3, 129.0, 130.2, 135.1, 139.2$; MS (70 eV, EI): *m*/*z* (%): 534.4 (87) $[M]^+$, 459.2 (12) $[M - C_4H_9 - H_2O]^+$, 57.0 (100) $[M]^+$; $C_{38}H_{46}O_2$ (534.8).

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