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Stille–Heck Coupling Sequences Applied in a Versatile New Access to Steroid Skeletons

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Abstract: A variety of enantiomerically pure steroidal compounds was synthesized utilizing a sequence of Stille and Heck cross-coupling reactions and subsequent thermal 6π-electrocyclizations. Highly chemoselective Stille couplings on the triflate moiety of several 2-bromocyclohex-1-enyl triflates with *cis*- and *trans*-fused bicyclo[4.3.0]-nonenylstannanes furnished the corresponding tricyclic bromobutadienes in good to excellent yields (70–97%). These were subjected to Heck reactions with *tert*-butyl acrylate to provide pentasubstituted tricyclic 1,3,5-hexatrienes. A significant increase in efficiency could be achieved by applying a novel protocol with a precatalyst on the basis of the palladacycle prepared from $Pd(OAc)_2$ and $P(o\text{-}Tol)_3$ with added triarylphosphines as co-ligands (73–90% yield). Upon heating to 205–215°C in decalin or to 140°C in toluene (for certain cases), these hexatrienes yielded (78–90%) various unsaturated steroid analogues as single diastereomers. A particular oxohexatriene, obtained after deprotection of an adjacent carbonyl group, underwent 6π-electrocyclization at the unusually low temperature of 140°C to yield (75%) an interesting 7-carboxyl-substituted steroidal dienone. Attempts to remove the remaining protecting groups from some of the other new steroidal compounds under acidic conditions furnished a novel 3-oxo-7-carboxyl steroid analogue and a 3-hydroxy-substituted steroidal diene. A novel estradiol derivative could be obtained in 69% yield from the synthesized steroidal dienone. Deprotection furnished the corresponding unprotected 7-carboxylestradiol in 81% yield.

Keywords: asymmetric catalysis · cross-coupling · palladium · pericyclic reactions · steroids

Introduction

Natural steroids and many of their analogues are important substances with a wide spectrum of biological activities. Many steroidal compounds are used as pharmaceuticals. Research directed at exploiting natural and new artificial steroids for the use as potential pharmaceuticals is therefore a highly promising approach in medicinal chemistry. However, therapies with steroidal compounds sometimes are accompanied by undesired physiological side effects. Appropriate structural modifications of these steroids can lead to improved pharmacological selectivities and therefore fewer or less intense physiological side effects,[1] but such modifications of natural steroids by synthetic methods are somewhat restricted to certain types of steroidal compounds and thereby also restricted to a narrow spectrum of biological activities.[2]

For a deeper understanding of the structure–activity relationships, investigations on a large number of structurally diverse steroids are necessary. These can best be obtained by total synthesis. Interestingly, many classical steroid syntheses are highly target oriented and often lead to a single compound.[2] In view of the demands of pharmaceutical research, an efficient diversity-oriented steroid synthesis would be of high interest. Such a diversity-oriented access to the steroid skeleton should be possible employing an appropriate modification of our previously reported Stille–Heck cross-coupling sequence.[3] In this, chemoselective Stille coupling on the triflate moieties of an array of bromoenol triflates **4** with different bicyclic alkenylstannes **5**, would furnish diverse bromobutadienes **3** which can be subjected to Heck reactions with various alkenes to produce

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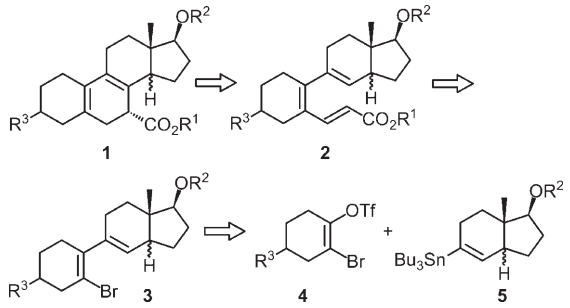
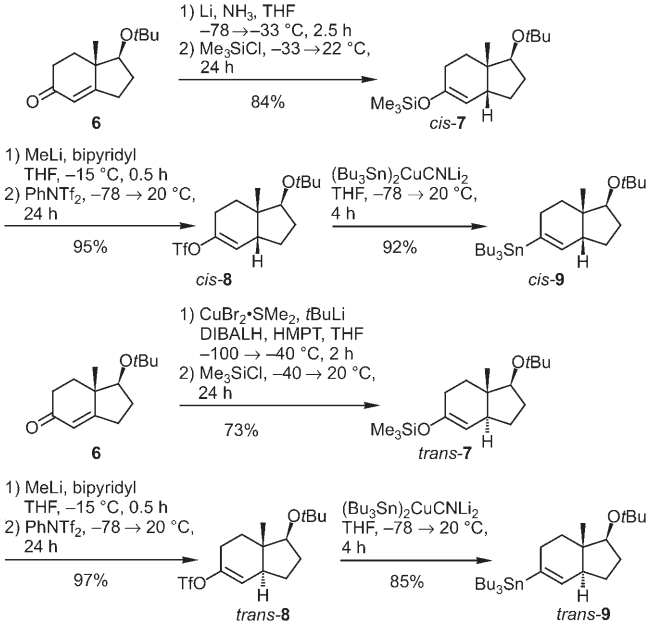


Scheme 1. Retrosynthetic concept for a novel access to the steroid skeleton.

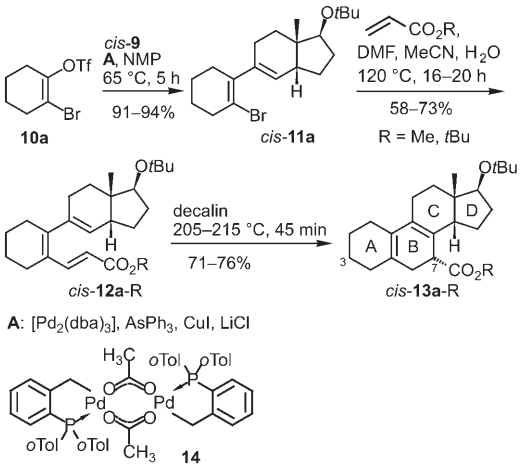
unsymmetrically substituted 1,3,5-hexatrienes **2**. The latter, in solution would be subjected to thermally induced 6π-electrocyclizations to yield various steroidal tetracycles of type **1** (Scheme 1).[4]

Results and Discussion

In order to be able to realize this new diversity-oriented access to steroid analogues,[5] an efficient synthesis for bicyclo[4.3.0]non-2-enylstannanes of type **9** had to be developed first. As most of the naturally occurring steroids have a *trans* CD-ring junction, the synthesis of the *trans*-bicyclo-[4.3.0]non-2-enylstannane *trans*-**9** was intended, but that of the *cis*-diastereomer *cis*-**9** was also pursued, since some pharmacologically interesting natural steroids do have a skeleton with a *cis* CD-ring junction. In fact, reduction of the easily accessible C,D-building block, the enantiomerically pure Hajos–Wiechert bicyclo[4.3.0]non-1-en-3-one **6**,[6] with lithium in liquid (Scheme 2) ammonia and subsequent trapping with trimethylsilyl chloride gave the *cis*-configured enol silyl ether *cis*-**7**.[7] The *trans*-diastereomer was obtained from **6** by reduction with the complex lithium hydridocuprate in situ generated from copper(II) bromide dimethyl sulfide complex, *tert*-butyllithium and dibutylaluminum hydride (DIBALH) as well as subsequent trapping with chlorotrimethylsilane.[8] The enol silyl ether *cis*-**7** and *trans*-**7** were converted to the corresponding enol triflates *cis*-**8** and *trans*-**8** by treatment with methyllithium first and then *N*,*N*-bis(trifluoromethanesulfonyl)aniline (95–97%). The enol triflates *cis*-**8** and *trans*-**8** with lithium cyano(bistributylstannyl)cuprate[9] gave the corresponding vinylstannanes *cis*-**9** and *trans*-**9** in high yields (92 and 85%, respectively). Direct trapping of the intermediate lithium enolates obtained in the reduction of **6** with lithium in liquid ammonia with *N*,*N*-bis(trifluoromethanesulfonyl)aniline required large amounts of this expensive reagent to achieve satisfactory yields, and therefore the longer route via the enol silyl ether *cis*-**7** is more economical. To achieve a high *trans*-diastereoselectivity in the hydridocuprate reduction, the bicyclononenone **6** had to be added to the reagent mixture at a very slow rate, but under optimized conditions, *trans*-**7** was obtained as the sole product. In order to optimize the cross-coupling conditions for the bicyclononenylstannanes *cis*-**9** and *trans*-**9** the first test reactions were performed with the unsubstituted 2-bromocyclohexenyl triflate **10a**,[3] for which an improved preparation was developed (see below), and *cis*-**9** with several catalytic systems on the basis of tetrakistriphenylphosphinepalladium(0), $Pd(OAc)_2$ with triphenylphosphine or other phosphine ligands, the Stille coupling of *cis*-**9** and **10a** furnished the bromodiene *cis*-**11a** only in low yields (5–30%) (Scheme 3).



Scheme 2. Synthesis of the novel enantiomerically pure bicyclo[4.3.0]-nonenylstannanes *cis*-**9** and *trans*-**9** starting from the bicyclic enone **6**.



Scheme 3. Testing the Stille–Heck sequence as an access to the steroid skeleton on the unsubstituted 2-bromocyclohexenol triflate **10a**.

However, with a precatalyst consisting of $[Pd_2(dba)_3]$, $AsPh_3$, LiCl and CuI in *N*-methylpyrrolidinone (NMP), *cis*-**11a** was obtained in an excellent yield of 91%. The choice of solvent turned out to be crucial, as the yield was significantly lower in DMF.

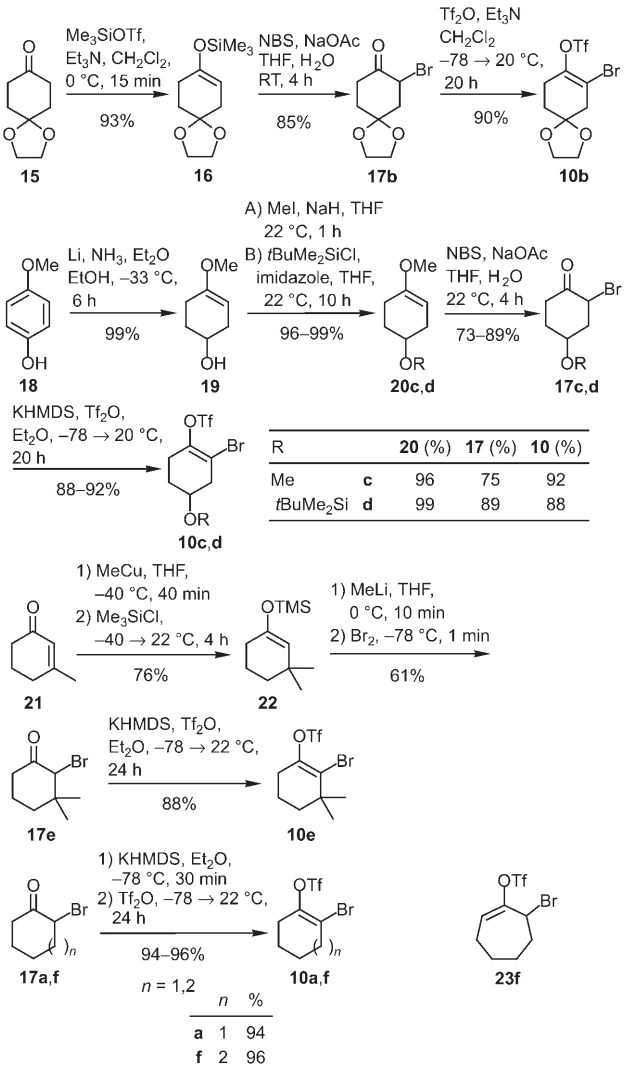
The first attempts to perform Heck reactions[10] of the bromodiene *cis*-**11a** with methyl- and *tert*-butyl acrylate using palladium(II) acetate and various phosphine ligands[11] also did not provide satisfactory yields (only 10–20%). Interestingly, when the palladacycle **14** was employed, the yield of the tricyclic 1,3,5-hexatrienes *cis*-**12a**-R could be increased to 58% (R = *t*Bu) and 73% (R = Me). However, these yields were only achieved with the addition of 2×8 mol% of the palladacycle **14**[12] no matter which solvent and base was employed. In all these reactions, even when a smaller overall amount of **14** was added in several portions, the yield did not increase, but a premature precipitation of palladium black occurred. The suggested colloidal palladium[12] did not seem to catalyze the reaction of the bromodiene *cis*-**11a** with methyl or *tert*-butyl acrylate towards *cis*-**12a**-R, but with smaller amounts of **14**, incomplete conversion of *cis*-**11a** was observed.

The pentasubstituted 1,3,5-hexatrienes *cis*-**12a**-R appeared to be reasonably well set up for 6π-electrocyclizations.[13] Indeed, heating in decaline at 210°C for only 45 min furnished the steroid analogues *cis*-**13a**-R in 71–76% yield. These products apparently arose from 6π-electrocyclizations with subsequent [1,5]-hydrogen shifts to provide the thermodynamically more stable products with the more highly substituted diene units. When the electrocyclization was performed at lower temperatures, much longer reaction times were required, for example, at a temperature of 160°C, the reaction mixture even after 20 h still contained the starting material *cis*-**12a**-R, the initial 6π-electrocyclization product along with *cis*-**13a**-R as well as significant amounts of side products.

Although these results were not ideal, they served as a basis for the development of a diversity-oriented approach to steroidal compounds with polar substituents at C-3 in the A-ring and a *trans*-junction of the C- and D-ring.

Towards this goal, a number of 4-substituted 2-bromocyclohexenyl triflates **10b-d** was prepared (Scheme 4) and tested in Stille–Heck coupling sequences. The synthesis of the bromoenol triflate **10b** with a protected carbonyl group in the appropriate position started with the monoethylene acetal of 1,4-cyclohexanedione **15** which was converted to the trimethylsilyl enol ether **16** (93% yield).[14] The latter was smoothly brominated with *N*-bromosuccinimide (NBS) to yield the α-bromoketone **17b** which proved to be rather unstable. At ambient temperature it readily undergoes elimination of hydrogen bromide and aromatization to the corresponding hydroquinone. However, in THF solution **17b** could be stored at 22°C for several hours. After rapid exchange of the solvent with methylene chloride, **17b** could be converted to the desired bromoenol triflate **10b** in 90% yield by treatment with trifluoromethanesulfonic acid anhydride in the presence of triethylamine.

The methoxy- and silyloxy-substituted bromocyclohexenyl triflates **10c,d** were prepared from *p*-methoxyphenol, starting with a Birch reduction,[15] bromination of the resulting cyclohexenyl ethers with NBS,[16] highly regioselective formation of the enolates with potassium hexamethyldisilazide



Scheme 4. Synthesis of various 2-bromocycloalkenyl triflates as building blocks for different steroidal tetracycles.

(KHMDS) and final trapping of them with trifluoromethanesulfonic acid anhydride.[17] The 3,3-dimethyl-2-bromocyclohexenyl triflate **10e** was synthesized from 3-methylcyclohex-2-enone (**21**) by addition of lithium dimethyl cuprate,[18] silylation of the resulting enolate, bromination of the enol silyl ether **22**[19] and trapping of the regioselectively formed potassium enolate with trifluoromethanesulfonic acid anhydride. The 2-bromocycloheptenyl triflate (**10f**) was obtained from 2-bromocycloheptanone[20] exploiting the highly regioselective formation of the potassium enolate with KHMDS, and its trapping with trifluoromethanesulfonic acid anhydride (Tf_2O). According to this protocol, the unsubstituted 2-bromocyclohexenyl triflate (**10a**) could also be prepared in much better yield (94%) than reported previously.[3] With LiHMDS and Tf_2O, the other regioisomeric **23f** was obtained with complete selectivity. It is noteworthy, that the more economical conditions for the generation of the enol triflates as employed for **10b** (Tf_2O, Et_3N) did not provide **10a** in good yield.

The best precatalyst in the Stille reactions[21] of the model system gave significantly poorer yields (70–76%) for the couplings of the functionalized 2-bromocyclohexenyl triflates **10b-d** with the bicyclononenylstannanes *cis*-**9** and *trans*-**9** (Table 1, entries 2,6,10). With an increased amount of $AsPh_3$ added, more side products were formed (Table 1, entry 3). Consequently, a catalyst system without $AsPh_3$ was tested, and indeed provided the desired bromodienes *cis*-**11b-d** in yields ranging from 85–97% (Table 1, entries 1,5,7) with a catalyst loading as low as 2.5 mol%. The excess of the alkenylstannane *cis*-**9** could be lowered from 1.20 to 1.05 equiv without a measurable drop in yields. Yet, the Stille coupling of the bromoenol triflate **10b** with the bicyclononenylstannane *trans*-**9** under the previously established conditions with $[Pd_2(dba)_3]\cdot CHCl_3$ or $[Pd_2(dba)_3]$ and CuI furnished the bromodiene *trans*-**11b** in an excellent yield of 95–96% (Table 1, entries 8,9). The bromodienes *cis*-**11c**,**d** and *trans*-**11c** were obtained as 1:1 mixtures of diastereomers since the bromoenol triflates **10c**,**d** were employed as racemates. In order to determine the beneficial role of the copper(I) cocatalyst,[22] the experiment without $AsPh_3$ was repeated also without added CuI, and this gave a significantly lower yield of 62% (Table 1, entry 4).

Table 1. Stille couplings of functionalized 2-bromo-1-trifluoromethanesulfonyloxycyclohexenes **10b–d** with bicyclononenylstannanes *cis*-**9** and *trans*-**9**.

Entry	Starting material	Product	Conditions[a] /[mol%]	Yield[b] (%)
1	**10b**	*cis*-**11b**	**A**/2.1	97
2	**10b**	*cis*-**11b**	**A**[c]/5.0	73
3	**10b**	*cis*-**11b**	**A**[d]/5.0	n.d.[e]
4	**10b**	*cis*-**11b**	**A**[f]/5.0	62
5	**10c**	*cis*-**11c**	**B**/3.0	85
6	**10c**	*cis*-**11c**	**A**[c]/5.0	76
7	**10d**	*cis*-**11d**	**B**/5.0	91
8	**10b**	*trans*-**11b**	**A**/2.5	95
9	**10b**	*trans*-**11b**	**B**/2.5	96
10	**10c**	*trans*-**11c**	**A**[c]/5.0	70

[a] **A**: $[Pd_2dba_3]\cdot CHCl_3$, CuI, LiCl, NMP, 65°C, 5–12 h; **B**: $[Pd_2dba_3]$, CuI, LiCl, NMP, 65°C, 5–12 h. [b] Isolated yields. [c] Plus 3.9 mol% of $AsPh_3$. [d] Plus 10 mol% of $AsPh_3$. [e] n.d. = not determined, complex mixture of various products. [f] Without CuI.

In accordance with the model sequence, Heck reactions of the substituted bromodienes *cis*-**11b-d** and *trans*-**11b**,**c** gave best yields with the palladacycle **14** as precatalyst and tetrabutylammonium acetate (TBAOAc) as base. However, high catalyst loadings (2×8 mol%) were required for full conversion of bromodienes *cis*-**11b** and *trans*-**11c** to provide the tricyclic hexatrienes *cis*-**12b** and *trans*-**12c** in 74 and 79% yield, respectively (Table 2, entries 2, 10). It was also detrimental that any attempted upscaling of these Heck reactions led to reduced yields. It was not a real help that one could operate several small scale reactors in parallel and do a combined work-up, which did provide, for example, the product *cis*-**12b** in a comparable yield of 72% (Scheme 5).

Table 2. Heck reactions of the bromodienes *cis*-**11b–d** and *trans*-**11b**,**c** with *tert*-butyl acrylates in the presence of the palladacycle **14** and added phosphine ligands performed at 105°C.

Entry	Starting material	Conditions[a] /[mol%]	Product	Solvent[b]	*t* [h]	Yield[c] (%)
1	*cis*-**11b**	**A**[d]/5.0	*cis*-**12b**	I	6	86
2	*cis*-**11b**	**E**[d]/2×8.0	*cis*-**12b**	I	12	74
3	*cis*-**11c**	**A**[d]/3.0	*cis*-**12c**	I	6	84
4	*cis*-**11d**	**D**[e]/3.0	*cis*-**12d**	II	4	73
5	*trans*-**11b**	**A**[d]/4.0	*trans*-**12b**	I	4	90
6	*trans*-**11b**	**B**[d]/4.0	*trans*-**12b**	I	8	78
7	*trans*-**11b**	**C**[d]/3.0	*trans*-**12b**	I	14	n.r.[f]
8	*trans*-**11b**	**A**[d]/2×4.0	*trans*-**12b**	II	8	80
9	*trans*-**11b**	**D**[e]/3.0	*trans*-**12b**	II	10	67
10	*trans*-**11c**	**E**[d]/2×8.0	*trans*-**12c**	I	12	79

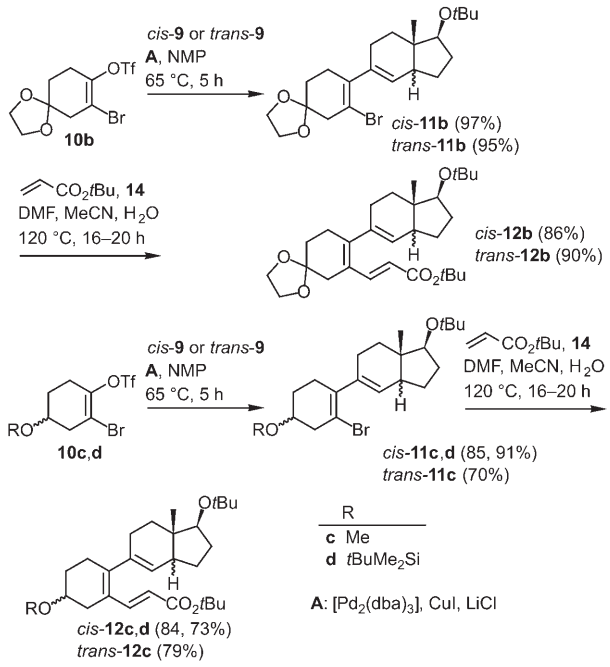
[a] **A**: **14**/P(*o*Tol)$_3$ 1:1; **B**: **14**/P(*o*Tol)$_3$ 1:2; **C**: = **14**/P(*o*Tol)$_3$ 1:3; **D**: **14**/dppb 1:1; **E**: **14**. [b] I: DMF/MeCN/H_2O 5:5:1; II: DMF/H_2O 10:1. [c] Isolated yields. [d] TBAOAc added. [e] NEt_3 added. [f] n.r. = no reaction.

In order to prevent the observed premature precipitation of palladium black, $[Pd_2(dba)_3]$ with added (*o*-Tol)$_3$P ligand in a molar ratio of 1:2 was tested, but did not improve the situation. However, with the palladacycle **14** and added (*o*-Tol)$_3$P in a molar ratio of 1:1, these Heck couplings of *cis*-**11b** and *cis*-**11c** to the tricyclic hexatrienes *cis*-**12b** and *cis*-**12c** could be achieved in 86 and 84% yield, respectively, even with a significantly lower catalyst load of 3–5 mol% (Table 2, entries 1, 3). The best solvent for such high yields turned out to be a mixture of DMF, MeCN and water in a ratio of 5:5:1.[23] The Heck couplings of the bromodiene *trans*-**11b** with *tert*-butyl acrylate also gave the best result with the palladacycle **14** and (*o*-Tol)$_3$P in the molar ratio of 1:1, and in spite of a catalyst load of 4 mol%, the 1,3,5-hexatriene *trans*-**12b** was obtained in an excellent yield of up to 90% (Table 2, entry 5).

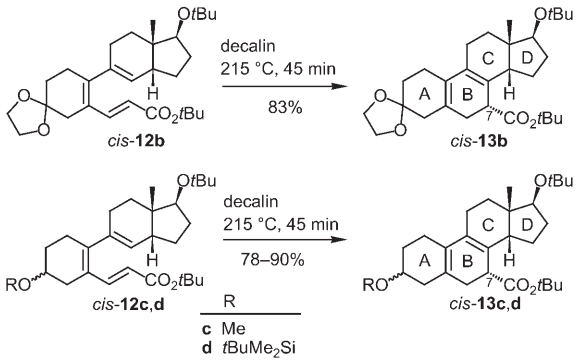
Employing the palladacycle **14** and the co-ligand (*o*-Tol)$_3$P in ratios smaller than 1:1 quickly led to a loss of activity, for example, with a ratio of 1:2 *trans*-**12b** was obtained in only 78% yield (Table 2, entry 6), and with an even lower ratio of 1:3 no progress of the reaction was observed (Table 2, entry 7).

Apparently, the influence of the copper(I) cocatalyst goes beyond simply acting as a ligand scavenger for $AsPh_3$.

All attempts to bring about the Stille coupling of the bromodimethylcyclohexenyl triflate **10e** and the 2-bromocycloheptenyl triflate **10f** with the bicyclononenylstannane *cis*-**9** under the optimized conditions only furnished complex mixtures which did contain the desired compounds, but also the products of a two-fold coupling on both the site of the triflate and that of the bromide leaving group. In this context, first experiments with less reactive catalytic systems delivered encouraging results.



Scheme 5. Stille–Heck coupling sequences of substituted bromoenol triflates **10b–d** with the bicyclononenylstannanes *cis*-**9** as well as *trans*-**9** and *tert*-butyl acrylate to establish an array of tricyclic 1,3,5-hexatrienes as precursors for various steroid analogues.



Scheme 6. Thermal 6π-electrocyclization of tricyclic 1,3,5-hexatrienes *cis*-**12** with a subsequent [1,5]-hydrogen shifts to furnish differently 3-substituted steroidal systems with a diene B-ring. For further details see Table 3.

Table 3. Thermal 6π-electrocyclization of tricyclic 1,3,5-hexatrienes *cis*-**12** with a subsequent [1,5]-hydrogen shift (see Scheme 6).

Entry	Starting material	Product	Solvent[a]	Yield (%)[b]
1	*cis*-**12b**	*cis*-**13b**	I	83
2	*cis*-**12c**	*cis*-**13c**	II	81[c]
3	*cis*-**12c**	*cis*-**13c**	I	78
4	*cis*-**12d**	*cis*-**13d**	I	90

[a] I: Decalin; II: Decalin plus 10% of DMF. [b] Isolated product. [c] Microwave heating.

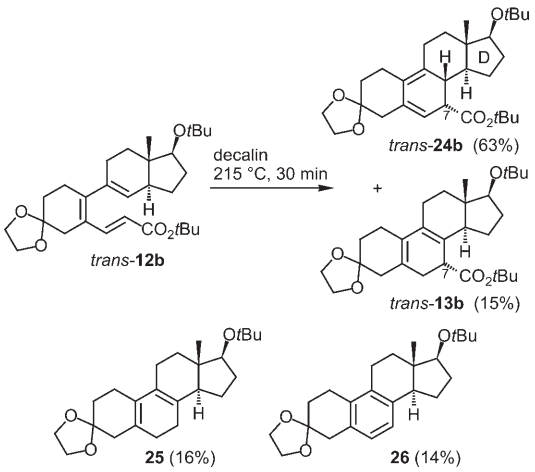
The catalyst stability appeared to be rather sensitive towards the solvent system. When the reaction was run in aqueous DMF, full consumption of the substrate to give an 80% yield of *trans*-**12b** was observed only after a second portion of 4.0 mol% of palladacycle **14** had been added (Table 2, entry 8).

Interestingly the combination of the palladacycle **14** and the bidentate co-ligand dppb in a molar ratio of 1:1 remained stable in aqueous DMF. With the significantly less expensive triethylamine as base and a catalyst load of 3.0 mol%, the hexatriene *trans*-**12b** was still obtained in a moderate yield of 67% (Table 2, entry 9). Under these same conditions, the bromodiene *cis*-**11d** gave the hexatriene *cis*-**12d** in 73% yield (Table 2, entry 4). It is noteworthy that best results in the Heck reactions were obtained with *tert*-butyl acrylate. Under the same conditions, the coupling with methyl acrylate provided the methyl ester corresponding to the 1,3,5-hexatriene *trans*-**12b** in only 44% yield. So far, with any other alkene than acrylic acid esters, only traces of the coupling products were detected.

For the thermal 6π-electrocyclizations of the substituted tricyclic hexatrienes **12b-d**, the conditions successfully applied for the unsubstituted hexatrienes *cis*-**12a**-R were tested. Indeed, the 1,3,4,5,6-pentasubstituted hexatrienes *cis*-**12b-d** upon heating in decalin at 205–215°C for 45 min cleanly underwent cyclization. The resulting tetracycles *cis*-**13b-d** actually were the apparently thermodynamically more stable products with the more highly substituted diene units resulting from a subsequent [1,5]-hydrogen shift (Scheme 6).[24] These steroid analogues were isolated in yields ranging from 81 to 90% (Table 3, entries 1, 2, 4). When *cis*-**12b** was heated at 215°C for only 30 min, a mixture of the expected 6π-electrocyclization product and *cis*-**13b** was obtained. Upon extended heating of this mixture, *cis*-**13b** was the sole product again. Microwave instead of conventional heating did not have a significant effect on the reaction rate and the resulting yield (Table 3, entry 2).

The steroid analogue *cis*-**13b** was obtained in diastereomerically pure form, whereas the 3-monosubstituted tetracycles *cis*-**13c** and *cis*-**13d** were formed as the expected 1:1 mixtures of two diastereomers, since the tricyclic hexatrienes *cis*-**13c,d** were 1:1 mixtures of diastereomers. The high diastereoselectivities in these thermal ring closures are due to a high degree of outward disrotational selectivity[25] in the 6π-electrocyclization processes.

Heating the 1,3,5-hexatriene *trans*-**12b** at 215°C for 30 min led to a separable mixture of the initial 6π-electrocyclization product *trans*-**24b** and the product of a subsequent [1,5]-hydrogen shift, *trans*-**13b** in a ratio of 4:1 (Scheme 7) in a total yield of 78% with 63% isolated yield of the main product *trans*-**24b**, which is preparatively satisfying (Table 4, entry 1). When a sample of *trans*-**13b** was heated in decalin at 215°C for 45 min, *trans*-**24b** was again the main product, which proves reversibility for the [1,5]-hydrogen shift in this case. Thus, by recycling *trans*-**13b**, complete transformation into *trans*-**24b** is possible. In view of the *trans* relationship of the hydrogen atoms on C8 and C14 and the *trans* CD-ring junction, this product *trans*-**24b** is



Scheme 7. Thermal 6π-electrocyclizations of the tricyclic 1,3,5-hexatriene *trans*-**12b** and subsequent transformations of the initial product.

Table 4. Thermal 6π-electrocyclizations of tricyclic *trans*-1,3,5-hexatrienones *trans*-**29** and *cis*-**29** with subsequent double bond migration (see Scheme 9).

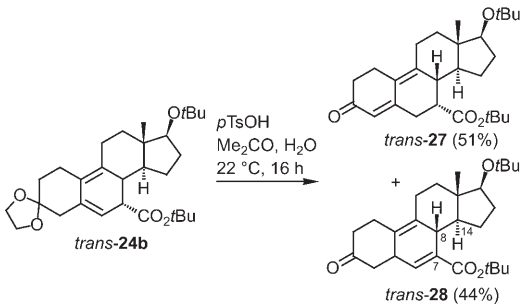
Entry	Starting material	Product	*T*/*t* [°C]/[h]	Solvent[a]	Yield (%)[b]
1	*trans*-**29**	*trans*-**27**	140/12	II	75
2	*trans*-**29**	*trans*-**27**	140/12	III	73
3	*trans*-**29**	*trans*-**27**	140/13	IV	55
4	*trans*-**29**	*trans*-**27**	205/0.75	I	27[c]
5	*cis*-**29**	*cis*-**27**	140/14	II	51

[a] I: decalin; II: toluene; III: dioxane; IV: DMF. [b] Isolated product. [c] Partial decomposition of the reaction mixture observed.

more closely related to the majority of naturally occurring steroids than *cis*-**13b**.

Variation of the temperature (190–260 °C) and extended heating (up to 90 min) of *trans*-**12b** did not significantly affect the ratio of the two regioisomers *trans*-**24b** and *trans*-**13b**, unlike the observation for the tricyclic hexatriene *cis*-**12b**. At 260 °C, however, the hexatriene *trans*-**12b** did not only furnish a mixture of the regioisomeric cyclohexadienes *trans*-**24b** and *trans*-**13b**, but also 16 and 14 %, respectively, of the tetracycles **25** and **26** which were formed by de-*tert*-butoxycarbonylation without and with subsequent aromatization, respectively, in the B-ring (Scheme 7). Upon heating the 1,3,5-hexatriene *trans*-**12c** at 215 °C for 45 min, a complex mixture of diastereomeric and regioisomeric tetracyclic products was obtained, but was not further investigated.

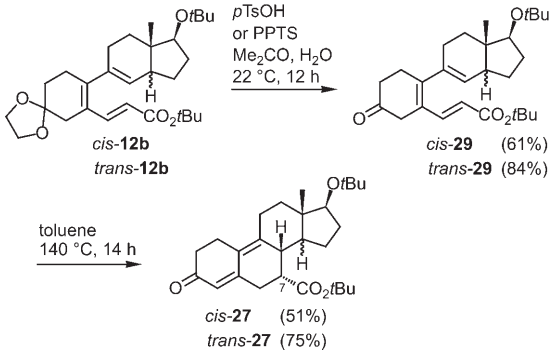
Treatment of the steroidal diene *trans*-**24b** with *p*-toluenesulfonic acid led to a mixture of the regioisomeric dienones *trans*-**27** and *trans*-**28**, which were isolated in 51 and 44 % yield, respectively. Both are products of an acid-catalyzed [1,3]-hydrogen shift (Scheme 8). The conjugated steroidal dienone *trans*-**27** is an interesting structure in that it is closely related to the pharmacologically important steroids such as Mifepriston. The regioisomeric dienone *trans*-**28** proved to be stable upon extended treatment with acids and further heating at 210 °C (Scheme 8).



Scheme 8. Acid-catalyzed cleavage of the dioxolane unit in *trans*-**24b** and subsequent rearrangements of the diene units in the B-ring.

Two of the steps in this new access to steroidal compounds with a *trans* CD-ring junction produced mixtures of isomers which required cumbersome chromatographic separation. The efficiency would definitely be better, if such separations could be avoided.

To increase the degree of thermodynamic control that apparently determines the ratio of the two regioisomers *trans*-**24b** and *trans*-**13b** formed upon heating of *trans*-**12b** (Scheme 7), the latter was modified by treatment with *p*-toluenesulfonic acid in acetone/H_2O to yield (84 %) the tricyclic hexatrienone *trans*-**29** without migration of the double bond from the β,γ- to the α,β-position (Scheme 9). This rearrangement, which is well known in steroid chemistry, was observed, when the bromodiene *trans*-**11b** was subjected to the same conditions. With pyridinium *p*-toluenesulfonate (PPTS) in acetone, the hexatrienone *cis*-**27** was obtained from *cis*-**29** in only 60 % yield, therefore *p*-toluenesulfonic acid was used preferentially for such transformations.



Scheme 9. Thermal 6π-electrocyclization of the hexatrienone *trans*-**29** to furnish the steroidal tetracycle *trans*-**27** with high selectivity. For further details see Table 4.

First attempts to cyclize the tricyclic hexatrienone *trans*-**29** in decalin solution by heating at 205 °C for 45 min led to the tetracyclic dienone *trans*-**27**, but only in a low yield of 27 % (Table 4, entry 5). Apparently, the tricyclic hexatrienone *trans*-**29** partially decomposed under these conditions. When the cyclization was performed at a temperature of 160 °C for

11 h, *trans*-**27** was formed in a significantly higher yield (59%).

The highest yield (75%) could be achieved by heating *trans*-**29** in toluene at a temperature of 140°C for 12 h (Table 4, entry 2; Scheme 9); below 100°C, the cyclization did not proceed to any extent. At 140°C, the cyclizations could also be performed in polar solvents such as dioxane (73% yield) and DMF, yet in the latter case with a significantly reduced yield of 55% (Table 4, entries 3, 4). Addition of a catalytic amount of the Lewis acid $ZnBr_2$ led to complete decomposition of the substrate *trans*-**29**.

Interestingly the thermal cyclization of the hexatrienone *cis*-**29** at 140°C required a longer time than that of the *trans* isomer *trans*-**29**, and the product *cis*-**27** was obtained in a yield of only 51% (Table 4, entry 6).

Figure 1

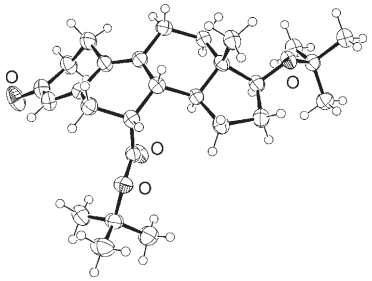
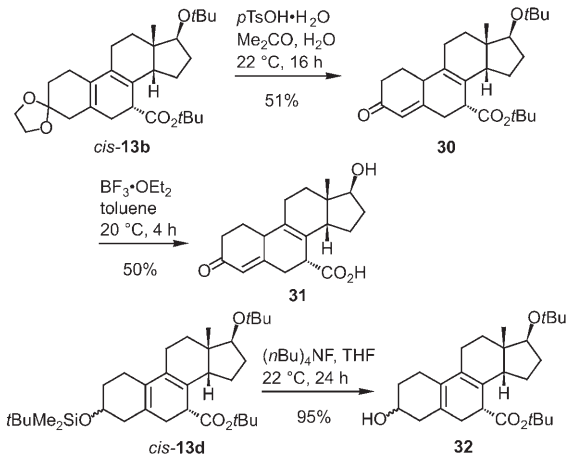


Figure 1. Structure of the steroid analogue *trans*-**27** in the crystal.[26]

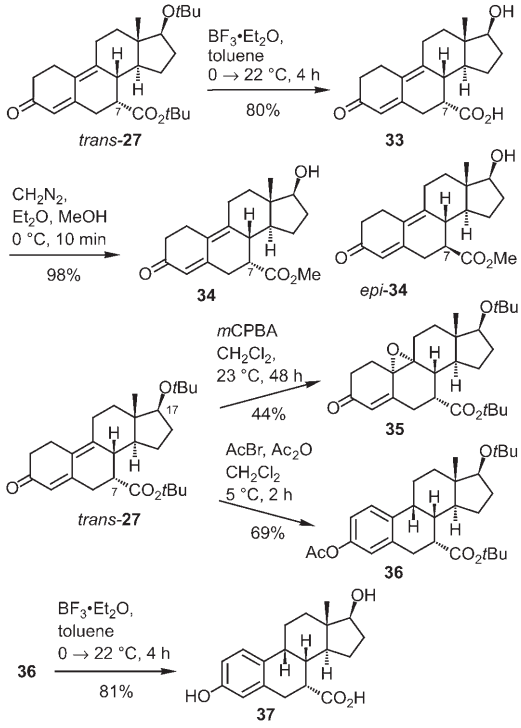
The cleavage of the dioxolane moiety in the tetracyclic diene *cis*-**13b** with *p*-toluenesulfonic acid furnished (51% yield) the steroidal dienone **30** with one isolated double bond, which did not migrate into the conjugated position as it was observed in the formation of *trans*-**27**. The unprotected steroidal carboxylic acid **31** could be obtained (50%) by reaction of **30** with boron trifluoride etherate in toluene (Scheme 10).



Scheme 10. Removal of protective groups in the steroid analogues *cis*-**13b** and *cis*-**13d**.

The trialkylsilyl group in the protected dihydroxysteroid *cis*-**13d** was easily removed with tetra-*n*-butylammonium-fluoride in tetrahydrofuran to provide the 3-hydroxy-substituted steroid **32** as a separable mixture of α- and β-diastereomers (Scheme 10). So far, all attempts to remove the *tert*-butyl protecting groups in **32** under various acidic conditions only led to decomposition of the substrate.[27]

Due to its structural analogy to pharmacologically important steroids, compound *trans*-**27** ought to be a promising object for biological testing and further exploitation as a versatile intermediate en route to other steroidal compounds. For biological investigations, however, the *tert*-butoxy groups had to be removed. Among the reagents tested, boron trifluoride etherate in toluene gave the best results, providing the free 7-hydroxycarbonyl steroid **33** in 80% yield (Scheme 11).



Scheme 11. Various steroid analogues obtainable from the steroidal dienone *trans*-**27**.

Pursuing the concept of "soft drugs",[30] the steroidal carboxylic acid **33** was converted with diazomethane into the methyl ester **34** for biological tests. It is noteworthy that the deprotection of the methyl ester analogue of the steroid *trans*-**27** under acidic conditions furnished the C-7 epimer of compound **34**.[31] Comparison of the X-ray crystal structure of *trans*-**27** with those of **33** and **37** verified, that acid assisted cleavage of the *tert*-butyl ester is fast enough to avoid a significant degree of epimerization at C-7 (Figure 1, Figure 2).

So far, the steroidal dienone *trans*-**27** successfully withstood all attempts to be cyclopropanated across the γ,δ-

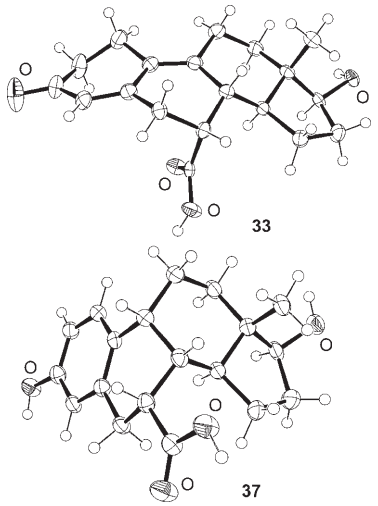


Figure 2. Structures of the 7-hydroxycarbonylsteroid **33**[28] and the 7-hydroxycarbonylestradiol **37**[29] in the crystal.

double bound. However, it could be epoxidized with *m*CPBA to give the steroidal epoxide *trans*-**35** in 44% yield. This compound is not only of interest as a potentially bioactive material, but also a possible starting material for the introduction of an angular methyl group at C-10 (Scheme 11).

Compound *trans*-**27** could be converted to the novel estradiol **36** by treatment with acetyl bromide and acetic anhydride. After treatment with boron trifluoride, the 7-hydroxycarbonylestradiol **37** was obtained in 81% yield. The estradiol analogue **36** is a C-9 epimer of naturally occurring estradiols. Biological investigations on such estradiol derivatives are rare, therefore this compound might be an interesting object for further research.[30]

All the steroidal products reported here were prepared from enantiomerically pure bicyclononenylstannanes *cis*-**9** and *trans*-**9** and thus they ought to be enantiomerically pure.

Conclusion

The Stille–Heck cross-coupling has proved to be a versatile synthetic tool which provides an efficient access to steroidal compounds. By utilizing differently substituted 2-bromocyclohexenyl triflates **10b-d** and the two bicyclononenylstannanes *cis*-**9** and *trans*-**9** an array of steroid analogues with 3-oxo as well as 3-hydroxyl functionalities with *cis*- and *trans*-C,D-ring junction has been prepared. All of the new steroid analogues carry a carboxyl group at the 7-position, which may be beneficial for their biological activities.[32] The successful deprotection of selected new steroidal compounds has furnished sufficient amounts for biological testing.

Experimental Section

General methods: ^{1}H NMR: Bruker AM 250 (250 MHz), Bruker AMX 300 (300 MHz). Chemical shifts in $CDCl_3$ and in C_6D_6 are reported as δ values relative to chloroform ($\delta = 7.26$) or benzene ($\delta = 7.20$) as internal reference. ^{13}C NMR: Bruker AW 250 (62.9 MHz). Chemical shifts in $CDCl_3$ are reported as δ values relative to chloroform ($\delta = 77.0$) or benzene ($\delta = 128$); the multiplicity of the signals was determined by the DEPT (62.9 MHz) and APT (75.6 MHz) technique and quoted as (+) for CH_3 and CH groups, (−) for CH_2 groups and (C_{quat}) for quaternary carbon atoms (DEPT) or (−) for quaternary carbon atoms (APT). IR spectra: Bruker IFS 66. Low-resolution EI mass spectra: Finnigan MAT 95, ionizing voltage 70 eV. High-resolution mass spectra: Finnigan MAT 95; preselected ion peak matching at $R \approx 10000$ to be within ± 2 ppm of the exact masses. Caution was exercised when optical rotations were measured in benzene. Elemental analyses: Mikroanalytisches Labor des Instituts für Organische und Biomolekulare Chemie der Universität Göttingen (Germany). Melting points are uncorrected. Solvents for extraction and chromatography were of technical grade and distilled before use. Flash chromatography was performed using Merck Kieselgel 60 (200–400 mesh). Aluminum oxide (ICN Alumina N, Super I) was obtained from ICN Biomedicals. Unless otherwise specified, aluminum oxide was deactivated with 5% of water. TLC analyses were performed using Macherey-Nagel precoated plates, 0.25 mm, Alugram Sil G/UV_{254} (I) and Merck silica gel 60 F_{254} precoated aluminum sheets (II). All reactions were carried out under an atmosphere of dry nitrogen or argon in oven- and/or flame-dried glassware. Unless otherwise specified, solutions of NH_4Cl, NaCl, Na_2SO_3 and $NaHCO_3$ were saturated aqueous solutions. Benzene, decalin, toluene, THF and diethyl ether were distilled from sodium/benzophenone. Dichloromethane was distilled from CaH_2. (1,4-Dioxaspiro[4.5]dec-7-en-8-yloxy)trimethylsilane (**16**),[14] 1-methoxycyclohexene-4-ol (**19**),[15] *tert*-butyl-(4-methoxycyclohex-3-enyloxy)dimethylsilane (**20d**),[16] 2-bromocycloheptanone (**17f**),[20] 2-bromo-3,3-dimethylcyclohexanone (**17e**),[19] 2-bromo-4-(*tert*-butyldimethylsilyloxy)cyclohexanone (**17d**),[16] (1*S*,3a*S*,7a*S*)-(1-*tert*-butoxy-7a-methyl-2,3,3a,6,7,7a-hexahydro-1*H*-inden-5-yloxy)trimethylsilane (*trans*-**7**),[7] *N,N*-bis(trifluoromethanesulfonyl)aniline[33] were prepared as described in the literature.

General procedure for the synthesis of α-bromocyclohexanones (GP 1): To a solution of NBS (1.30–1.50 equiv) and sodium acetate (0.100 equiv) in THF/water 1:1 was added dropwise at 0 °C the respective trimethylsilylenol ether (1.00 equiv). The reaction mixture was warmed to ambient temperature and stirred for the stated time. It was treated with Na_2SO_3 solution (10%) until decolorization. The reaction mixture was extracted with diethyl ether twice. The combined organic phases were washed with sat. $NaHCO_3$ solution, water and brine, then dried over $MgSO_4$. After concentration in vacuo the crude material were either used without further purification or purified by column chromatography (CC) on silica gel.

General procedure for the synthesis of bromoenol triflates (GP 2): To a solution of the respective α-bromocycloalkanone (1.00 equiv) and NEt_3 (3.00–5.00 equiv) in dichloromethane was added dropwise trifluoromethanesulfonic acid anhydride (1.05–1.30 equiv) in dichloromethane at −78 °C. The reaction mixture was slowly warmed to ambient temperature and stirred for a total of 20–24 h. After treatment with sat. $NaHCO_3$ solution, the aqueous phase was extracted with diethyl ether. Then the combined organic layers were washed with water and brine. After concentration in vacuo the residue was purified by CC on silica gel.

General procedure for the synthesis of bromoenol triflates (GP 3): To a solution of the respective α-bromocycloalkanone (1.00 equiv) in diethyl ether was slowly added potassium hexamethyldisilazide in toluene (1.05–1.20 equiv) at −78 °C. After 1 h, trifluoromethanesulfonic acid anhydride (1.05–1.30 equiv) was added dropwise. The reaction mixture was slowly warmed to ambient temperature and stirred for a total of 20–24 h. The reaction mixture was poured into pentane and washed with sat. $NaHCO_3$ solution. The aqueous phase was extracted with pentane, then the combined organic phases were washed with sat. $NaHCO_3$ solution, water and brine. After drying over $MgSO_4$ and concentration in vacuo the residue was purified by CC on silica gel.

General procedure for the synthesis of the bicyclic enol triflates (GP 4): The trimethylsilylenol ether (1.00 equiv) was slowly added at −15 °C to a solution of methyllithium (1.05–1.15 equiv) in THF. Before stirring the resulting solution for 1 h, 2–5 crystals of 4,4′-bipyridyl were added until

the solution turned red. After cooling the solution to −78 °C, *N,N*-bis(trifluoromethanesulfonyl)aniline (1.15 equiv) in THF was added. The mixture was warmed to ambient temperature within 12 h and continuously stirred for 10 h, then poured into diethyl ether. The organic layer was washed with NaOH solution (5 %) and water. The combined aqueous phases were extracted with diethyl ether. After drying the combined organic layers over $MgSO_4$, the solvent was removed in vacuo and the residue was subjected to CC on silica gel.

General procedure for the preparation of the bicyclo[4.3.0]nonenylstannanes (GP 5): *n*-Butyllithium (2.60 equiv, 2.36 M in hexane) was added at −78 °C to a solution of diisopropylamine (2.60 equiv) in THF, and the mixture was stirred for 30 min. To the resulting solution was added tributyltin hydride (2.20 equiv) and stirring was continued for 30 min before copper(I) cyanide was added in one portion. The reaction mixture was warmed to −50 °C until a yellow solution had formed, and this was treated with the respective enol triflate (1.00 equiv) in THF. The resulting solution was warmed to −25 °C and continuously stirred for 2 h. The reaction mixture was poured into pentane, and the mixture was washed with NH_3 solution (10 %), water and brine, then dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in ethyl acetate, and the solution was treated with silver(I) acetate (3.00 equiv) for 2 h at ambient temperature, using an unsealed vessel. The reaction mixture was filtered through Celite, washed with water, brine and dried over $MgSO_4$. After concentration in vacuo, the residue was purified by CC on neutral aluminum oxide (deactivated with 5 % of water).

General procedure for Stille couplings of bicycloalkenylstannanes with bromoenol triflates (GP 6): A screw-cap Pyrex bottle containing a magnetic stirring bar, was charged with a solution of the respective bromoenol triflate (1.00 equiv) and the bicycloalkenylstannane (1.10–1.30 equiv) in *N*-methylpyrrolidone (NMP). After purging the solution with argon in an ultrasonic bath for 5 min, $[Pd_2(dba)_3]\cdot CHCl_3$ (2.00–5.00 mol %), LiCl (3.00 equiv) and CuI (2.00–5.00 mol %) were added. Before carefully sealing the bottle with the screw cap, the resulting solution was again purged with argon in an ultrasonic bath for 5 min. The reaction mixture was stirred vigorously for 12 h at 65 °C. After having cooled down to ambient temperature, the reaction mixture was poured into diethyl ether and washed with NH_3 solution (5 %) and water. The combined aqueous phases were extracted with diethyl ether, and the combined organic layers were vigorously stirred with sat. KF solution for 45 min. The combined organic phases were dried over $MgSO_4$ and concentrated in vacuo. If necessary, the residue was adsorbed on silica gel and purified by CC on silica gel.

General procedure for Heck couplings of bromobutadienes with alkenes (GP 7): A screw-cap Pyrex bottle containing a magnetic stirring bar, was charged with the respective bromodiene (1.00 equiv), nBu_4NOAc or NEt_3 as described (2.50–3.00 equiv), the alkyl acryate (5.00–10.0 equiv) and the stated solvent system. After purging the resulting solution with argon in an ultrasonic bath for 5 min, *trans*-di(μ-acetato)bis[*o*-(di-*o*-tolylphosphanyl)benzyl]dipalladium(II) (**14**) (2.00–4.00 mol %) and the stated ligand (2.00–8.00 mol %) was added, and the mixture again purged with argon in an ultrasonic bath for 5 min. After carefully sealing the bottle with a screw cap, the mixture was slowly heated to 105 °C and stirred for 4–8 h at this temperature. After cooling to ambient temperature, the reaction mixture was poured into diethyl ether and NH_3 solution (5 %). The organic layer was washed with water, and the combined aqueous phases were extracted with diethyl ether. The combined organic layers were washed with brine and dried over $MgSO_4$. After concentration in vacuo the residue was subjected to CC on silica gel.

General procedure for the selective cleavage of dioxolane protective groups (GP 8): To a solution of the respective hexatriene in acetone and water (10.0–20.0 equiv) was treated with *p*-toluenesulfonic acid (0.30–0.60 equiv), and the mixture purged with argon before sealing the reaction vessel. After stirring the solution for 12–20 h at ambient temperature, the acid was neutralized with a few drops of sat. $NaHCO_3$ solution. The reaction mixture was concentrated in vacuo, and the residue was dissolved in diethyl ether. The organic layer was washed with sat. $NaHCO_3$ and the aqueous phase was back-extracted with diethyl ether. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The residue was subjected to CC on silica gel.

General procedure for the thermal 6π-electrocyclization of the unsymmetrically substituted 1,3,5-hexatrienes in solution (GP 9): In a screw-cap Pyrex bottle, the inside of which had been treated with hexamethyldisilane in acetone, containing a magnetic stirring bar, the respective hexatriene was dissolved in the stated solvent, and the solution was purged with argon in an ultrasonic bath for 5 min. The bottle was sealed with a screw cap and placed in a prewarmed oil bath. The solution was stirred for the given time and the stated temperature. After cooling the reaction mixture to ambient temperature, the solvent was removed in vacuo, and the residue was subjected to CC on silica gel.

General procedure for the cleavage of *tert*-butyl esters and *tert*-butyl ethers (GP 10): $BF_3\cdot Et_2O$ (0.500–3.00 equiv) was slowly added to a solution of the respective steroidal compound (1.00 equiv) in toluene at 0 °C. After the addition was complete, the mixture was warmed to ambient temperature and stirred for the stated time. The reaction mixture was treated with methanol/water 10:1 and concentrated in vacuo. The residue was subjected to CC on silica gel or the product was recrystallized from the stated solvent.

(1*S*,3a*R*,7a*S*)-(1-*tert*-Butoxy-7a-methyl-2,3,3a,6,7,7a-hexahydro-1*H*-inden-5-yloxy)trimethylsilane (*cis*-7): To a mixture of THF (130 mL) and liquid NH_3 (150 mL) was added lithium wire (748 mg, 108 mmol), and the mixture was stirred for 30 min at −78 °C. The α,β-unsaturated ketone **6** (10.0 g, 45.0 mmol) and aniline (0.500 mL, 5.10 g, 5.48 mmol) in THF (20 mL) were added dropwise to the resulting deep blue solution. The mixture was warmed to −33 °C and stirred for 2.5 h. In order to destroy excessive lithium, isoprene was added dropwise until the reaction mixture remained colorless. After removal of the volatile components in vacuo, the residue was dissolved in THF (100 mL), and the resulting mixture was cooled to −78 °C. Chlorotrimethylsilane (17.1 mL, 135 mmol) was added dropwise, and the reaction mixture was stirred for 3 h. After slowly warming to −20 °C, triethylamine (45.5 g, 450 mmol) was added, and then the mixture was warmed to ambient temperature and stirred for a total of 12 h. It was poured into diethyl ether (200 mL), washed with water (3×75 mL), the combined aqueous phases were back-extracted with diethyl ether (2×80 mL), and the combined organic layers were dried over $MgSO_4$. After removal of the solvents in vacuo, the residue was purified by CC on silica gel (100 g, pentane/diethyl ether 10:1) to yield the product *cis*-**7** as a colorless oil (11.3 g, 84 %). $R_f = 0.48$; IR (film): $\tilde{\nu} = 2971, 2930, 2874, 1667, 1643, 1601, 1560, 1507, 1465, 1457, 1437, 1388, 1363, 1292, 1254, 1195, 1094, 1078, 1025, 960, 869, 845, 668\ cm^{-1}$; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 0.18$ [s, 9H, $(CH_3)_3Si$], 0.90 (s, 3H, CH_3), 1.18 [s, 9H, $C(CH_3)_3$], 1.32–1.63 (m, 3H), 1.91–2.22 (m, 6H), 3.60 (t, $^3J = 7.3$ Hz, 1H, 3-H), 4.75–4.80 (m, 1H, 4-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, APT): $\delta = 0.3$ [+, 3C, $Si(CH_3)_3$], 20.7 (+, CH_3), 26.8 (−, CH_2), 28.7 [+, 3C, $C(CH_3)_3$], 29.7 (−, CH_2), 30.5 (−, CH_2), 33.0 (−, CH_2), 41.9 (−, C_{quat}, C-7a), 43.5 (+, CH, C-3a), 72.4 [−, C_{quat}, $C(CH_3)_3$], 76.2 (+, CH, C-1), 109.2 (+, CH, C-4), 148.5 (−, C_{quat}, C-5); MS (70 eV): *m/z* (%): 296 (5) [M^+], 281 (1), 239 (100) [$M^+ - C_4H_9$], 225 (5), 195 (4), 182 (7), 168 (19), 143 (24), 111 (3), 97 (11), 93 (3), 73 (10), 57 (10) [$C_4H_9^+$], 41 (2); HRMS: *m/z*: calcd for $C_{17}H_{32}O_2Si$: (296.5): 296.2195 (correct HRMS).

(+)-(3*S*,3a*S*,7a*R*)-3-*tert*-Butoxy-3a-methyl-2,3,3a,4,5,7a-hexahydro-1*H*-inden-6-yl trifluoromethanesulfonate (*cis*-8): According to GP 4, the trimethylsilylenol ether *cis*-**7** (8.80 g, 29.7 mmol) in THF (20 mL) was treated with methyllithium (687 mg, 31.3 mmol) in THF (100 mL), 4,4′-bipyridyl (20 mg, 0.13 mmol) and *N,N*-bis(trifluoromethanesulfonyl)aniline (12.7 g, 35.6 mmol) in THF (40 mL). Work-up with diethyl ether (75 mL), sodium hydroxide (15 mL, 5 %) and water (2×15 mL), and extraction of the aqueous phases with diethyl ether (2×30 mL) yielded after CC on silica gel (65 g, pentane/diethyl ether 20:1) the product *cis*-**8** as a colorless oil (10.1 g, 95 %). $R_f = 0.42$; IR (film): $\tilde{\nu} = 2974, 2926, 2853, 1688, 1419, 1364, 1247, 1209, 1144, 1057, 1015, 884, 616\ cm^{-1}$; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 0.97$ (s, 3H, CH_3), 1.15 [s, 9H, $C(CH_3)_3$], 1.22–1.40 (m, 2H), 1.43–1.75 (m, 2H), 1.92–2.17 (m, 2H), 2.26–2.39 (m, 3H), 3.58 (t, $^3J = 6.8$ Hz, 1H, 3-H), 5.63 (m, 1H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): $\delta = 20.2$ (+, CH_3), 24.7 (−, CH_2), 28.2 (−, CH_2), 28.6 [+, 3C, (C-

(CH_3)$_3$], 30.2 (−, CH_2), 32.6 (−, CH_2), 42.1 (C_{quat}, C-3a), 43.4 (+, CH, C-7a), 72.8 [C_{quat}, $C(CH_3)_3$], 75.7 (+, CH, C-3), 118.0 (q, ^1J=320 Hz, C_{quat}, CF_3), 122.1 (+, CH, C-7), 147.6 (C_{quat}, C-6); MS (70 eV): *m/z* (%): 300 (6) [$M^+-C_4H_8$], 282 (18) [$M^+-OH-C_4H_9$], 256 (4), 243 (2), 167 (5), 149 (5), 121 (3), 113 (8), 91 (3), 59 (4), 57 (100) [$C_4H_9^+$], 41 (6); elemental analysis calcd (%) for $C_{15}H_{23}F_3O_4S$: (356.5): C 50.55, H 6.50; found C 50.28, H 6.55.

(+)-(3*S*,3a*S*,7a*S*)-3-*tert*-Butoxy-3a-methyl-2,3,3a,4,5,7a-hexahydro-1*H*-inden-6-yl trifluoromethansulfonate (*trans*-8): According to GP 4, the trimethylsilylenol ether *trans*-**7** (14.0 g, 47.2 mmol) in THF (40 mL) was treated with methyllithium (1.08 g, 49.4 mmol) in THF (200 mL), 4,4′-bipyridyl (40 mg, 0.26 mmol) and *N,N*-bis(trifluoromethanesulfonyl)aniline (20.1 g, 56.3 mmol) in THF (80 mL). Work-up with diethyl ether (100 mL), NaOH solution (25 mL, 5%) and water (2×35 mL) and extraction of the aqueous phases with diethyl ether (2×45 mL) yielded, after CC on silica gel (100 g, pentane/diethyl ether 20:1), the product *trans*-**8** as a colorless oil (16.2 g, 97%). R_f=0.42; $[\alpha]_D^{20}$ = +57 (c=1.49, C_6H_6); IR (film): $\tilde{\nu}$=2981, 2936, 1670, 1466, 1420, 1391, 1361, 1248, 1223, 1194, 1146, 1121, 1077, 1044, 1017, 991, 942, 893, 877, 838, 811, 764, 613 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.82 (s, 3H, CH_3), 1.16 [s, 9H, $C(CH_3)_3$], 1.38–1.73 (m, 4H), 1.83–2.14 (m, 2H), 2.19–2.53 (m, 3H), 3.48 (dd, ^3J=9.8, ^3J=7.2 Hz, 1H, 3-H), 5.62–5.71 (m, 1H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=10.9 (+, CH_3), 24.0 (−, CH_2), 26.3 (−, CH_2), 28.6 [+, 3C, $C(CH_3)_3$], 31.8 (−, CH_2), 32.7 (−, CH_2), 42.1 (C_{quat}, C-3a), 42.9 (+, CH, C-7a), 72.5 [C_{quat}, $C(CH_3)_3$], 78.1 (+, CH, C-3), 118.2 (C_{quat}, ^1J=318 Hz, CF_3), 119.4 (+, CH, C-7), 149.0 (C_{quat}, C-6); EI-MS (70 eV): *m/z* (%): 354 (1), 299 (6) [$M^+-C_4H_9$], 282 (14) [$M^+-OH-C_4H_9$], 256 (3), 243 (1), 167 (5), 149 (6), 113 (4), 91 (3), 57 (100) [$C_4H_9^+$], 41 (8); elemental analysis calcd (%) for $C_{15}H_{23}F_3O_4S$: (356.5): C 50.55, H 6.50; found C 50.35, H 6.74.

(3*S*,3a*S*,7a*R*)-3-*tert*-Butoxy-3a-methyl-1,2,3,3a,4,5,7a-hexahydro-1*H*-inden-6-yltributylstannane (*cis*-9): According to GP 5, diisopropylamine (1.69 g, 16.7 mmol) in THF (100 mL), *n*-butyllithium (7.00 mL, 16.5 mmol, 2.36 M in hexanes), tributyltin hydride (4.07 g, 14.0 mmol), copper(I) cyanide (626 mg, 6.99 mmol) and the bicyclic enol triflate *cis*-**8** (2.26 g, 6.35 mmol) in THF (5 mL), after work-up with pentane (100 mL), NH_3 solution (30 mL, 10%), water (2×30 mL), brine (25 mL), treatment of the crude product with silver(I) acetate (3.18 g, 19.1 mmol) in ethyl acetate (80 mL) and CC on neutral aluminum oxide (40 g, pentane) gave *cis*-**9** as a colorless oil (2.92 g, 92%). R_f=0.48 (pentane/diethyl ether 20:1); IR (film): $\tilde{\nu}$=2957, 2925, 2871, 1609, 1464, 1418, 1387, 1376, 1361, 1292, 1198, 1072, 1020, 902, 874, 689 cm^{-1}; ^{1}H NMR (250 MHz, C_6D_6): δ=0.82–1.04 (m, 15H, *n*Bu-CH_3, *n*Bu-CH_2), 1.13 (s, 3H, CH_3), 1.15 [s, 9H, $C(CH_3)_3$], 1.24–1.79 (m, 16H), 1.89–2.16 (m, 2H), 2.18–2.27 (m, 1H), 2.33 (m, 2H), 3.66 (t, ^3J=6.8 Hz, 1H, 3-H), 5.85–5.95 (m, 1H, 7-H); ^{13}C NMR (62.9 MHz, C_6D_6, DEPT): δ=9.3 (−, 3C, *n*Bu-CH_2), 14.0 (+, 3C, *n*Bu-CH_3), 21.8 (+, CH_3), 27.8 [+, 3C, $C(CH_3)_3$], 28.9 (−, 3C, *n*Bu-CH_2), 29.1 (−, CH_2), 29.3 (−, CH_2), 29.7 (−, 3C, *n*Bu-CH_2), 31.1 (−, CH_2), 32.8 (−, CH_2), 42.2 (C_{quat}, C-3a), 46.2 (+, C-7a), 72.4 [C_{quat}, $C(CH_3)_3$], 76.7 (+, C-3), 137.4 (C_{quat}, C-6), 142.7 (+, C-7); EI-MS (70 eV): *m/z* (%): 443/442/441/440/439/438/437 (16/24/100/44/83/33/46) [$M^+-C_4H_9$], 387/386/385/384/383/382/381 (1/2/13/5/16/5/6) [$M^+-C_4H_9-C_4H_8$], 331/330/329/327/326/325/324 (2/1/12/4/11/4/5) [$M^+-C_4H_9-2C_4H_8$], 293/292/291/290/289/288/287 (1/1/6/3/5/2/3) [S*n*Bu$_3^+$], 237/236/235/234/233/232/231 (1/1/4/2/3/2/1) [$SnBu_2H^+$], 179/178/177/176/175 (2/1/4/1/2) [$SnBu^+$], 136 (2) [$M^+-SnBu_3-C_4H_8-CH_3$], 122/121/120/119/118/117 (1/5/2/4/2/3) [SnH^+], 91 (3), 57 (21) [*n*Bu$^+$], 41 (3); elemental analysis calcd (%) for $C_{26}H_{50}OSn$ (497.37): C 62.78, H 10.13; found C 62.80, H 10.06.

(+)-(3*S*,3a*S*,7a*S*)-3-*tert*-Butoxy-3a-methyl-2,3,3a,4,5,7a-hexahydro-1*H*-inden-6-yltributylstannane (*trans*-9): According to GP 5, diisopropylamine (3.69 g, 36.5 mmol) in THF (150 mL), *n*-butyllithium (15.1 mL, 36.5 mmol, 2.42 M in hexanes), tributyltin hydride (8.98 g, 30.9 mmol), copper(I) cyanide (1.38 g, 15.4 mmol) and the bicyclic enol triflate *trans*-**8** (5.00 g, 14.0 mmol) in THF (15 mL), after work-up with pentane (200 mL), NH_3 solution (50 mL, 10%), water (2×50 mL), brine (30 mL), after treatment of the crude product with silver(I) acetate (6.50 g, 39.0 mmol) in ethyl acetate (100 mL) and CC on neutral aluminum oxide (100 g, pentane) gave *trans*-**9** as a colorless oil (5.90 g, 85%). R_f=0.48 (pentane/diethyl ether 20:1); $[\alpha]_D^{20}$ = +42.5 (c=1.62, C_6H_6); IR (film): $\tilde{\nu}$=2976, 2956, 2928, 2872, 2847, 1606, 1461, 1419, 1383, 1359, 1337, 1290, 1251, 1195, 1117, 1070, 1021, 958, 897, 836, 689, 659 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.73 (s, 3H, CH_3), 0.82–1.01 (m, 14H, *n*Bu-CH_3, *n*Bu-CH_2), 1.14 [s, 9H, $C(CH_3)_3$], 1.22–1.40 (m, 7H, *n*Bu-CH_2), 1.42–1.58 (m, 7H, *n*Bu-CH_2), 1.65–1.83 (m, 2H), 1.89–2.16 (m, 2H), 2.20–2.41 (m, 4H), 3.43 (t, ^3J=6.8, ^3J=8.0 Hz, 1H, 3-H), 5.72 (m, 1H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=8.9 (−, 3C, *n*Bu-CH_2), 11.0 (+, CH_3), 13.7 (+, 3C, *n*Bu-CH_3), 24.6 (−, CH_2), 27.4 (−, 3C, *n*Bu-CH_2), 28.7 [+, 3C, $C(CH_3)_3$], 29.2 (−, 3C, *n*Bu-CH_2), 30.8 (−, CH_2), 31.15 (−, CH_2), 35.6 (−, CH_2), 41.5 (C_{quat}, C-3a), 44.8 (+, CH, C-7a), 72.1 [C_{quat}, $C(CH_3)_3$], 79.6 (+, CH, C-3), 138.3 (C_{quat}, C-6), 141.7 (+, CH, C-7); EI-MS (70 eV): *m/z* (%): 443/442/441/440/439/438/437 (16/24/100/44/83/33/46) [$M^+-C_4H_9$], 293/292/291/290/289/288/287 (1/1/6/3/5/2/3) [S*n*Bu$_3^+$], 239/237/236/235/234/233/232/231 (15/12/11/99/32/76/26/42) [$SnBu_2H^+$], 180/179/178/177/176/175 (11/88/83/53/26/12) [$SnBu^+$], 135 (5) [$M^+-SnBu_3-C_4H_9-CH_3$], 122/121/120/119/118/117 (1/5/26/20/12/10) [SnH^+], 91 (3), 57 (84) [Bu$^+$], 41 (22); elemental analysis calcd (%) for $C_{26}H_{50}OSn$ (497.37): C 62.78, H 10.13; found C 62.86, H 10.01.

1-Bromo-2-trifluoromethanesulfonyloxycyclohexene (10a): According to GP 3, α-bromocyclohexanone **17a** (1.00 g, 5.65 mmol) in diethyl ether (40 mL), potassium hexamethyldisilazide (13.6 mL, 6.80 mmol, 0.500 M in toluene) and trifluoromethanesulfonic acid anhydride (1.83 g, 6.50 mmol), after work-up with pentane (50 mL) and sat. $NaHCO_3$ solution (20 mL), extraction of the aqueous phases with pentane (2×35 mL) and purification by CC on silica gel (25 g, pentane) gave **10a** as a colorless oil (1.64 g, 94%), R_f=0.32. The analytical data were consistent with the ones previously reported.[3]

7-Bromo-1,4-dioxaspiro[4.5]dec-7-en-8-yl trifluoromethanesulfonate (10b): According to GP 2, α-bromocyclohexanone **17b** (3.00 g, 12.7 mmol), triethylamine (3.85 g, 38.1 mmol) in dichloromethane (45 mL), trifluoromethanesulfonic acid anhydride (4.28 g, 15.2 mmol) in dichloromethane (10 mL) at −78 °C, after work-up with diethyl ether (50 mL), sat. $NaHCO_3$ solution (30 mL), extraction of the aqueous phase with diethyl ether (2×40 mL) and CC on silica gel (30 g, pentane/diethyl ether 3:1) gave **10b** as a colorless oil (4.19 g, 90%). R_f=0.43; IR (film): $\tilde{\nu}$=2989, 2967, 2889, 1680, 1478, 1422, 1405, 1367, 1334, 1316, 1251, 1226, 1153, 1141, 1079, 1026, 945, 870, 851, 801, 766, 694, 621, 508 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.95 (t, ^3J=6.4 Hz, 2H, 9-H), 2.51–2.64 (m, 2H, 10-H), 2.81 (brs, 2H, 6-H), 3.92–4.07 (m, 4H, 2-H, 3-H); ^{13}C NMR (75.6 MHz, $CDCl_3$, APT): δ=26.6 (−, CH_2), 31.1 (−, CH_2), 44.3 (−, CH_2), 64.8 (−, 2C, CH_2, C-2, C-3), 106.3 (−, C_{quat}, C-7), 111.7 (−, C_{quat}, C-8) 118.2 (−, q, ^1J=315 Hz, C_{quat}, CF_3), 144.6 (−, C_{quat}, C-5); EI-MS (70 eV): *m/z* (%): 287 (3), 235/233 (95/100), 204 (3), 190/188 (8/9), 155 (6), 134/132 (23/25), 106/104 (15/15), 99 (20), 86 (12), 69 (85) [CF_3^+], 55 (36); DCI-MS (NH_3): *m/z* (%): 754/752/750 (45/83/40) [2*M*+NH_4^+], 403/401 (98/100) [*M*+NH_3+NH_4^+], 386/384 (28/29) [*M*+NH_4^+]; HRMS: *m/z*: calcd for $C_9H_{10}BrF_3O_5S$+Na (390.1): 388.9278 (correct HRMS).

2-Bromo-4-methoxy-1-trifluoromethanesulfonyloxycyclohexene (10c): According to GP 3, α-bromocyclohexanone **17c** (750 mg, 3.62 mmol) in diethyl ether (30 mL), potassium hexamethyldisilazide (8.69 mL, 4.35 mmol, 0.500 M in toluene) and trifluoromethanesulfonic acid anhydride (1.23 g, 4.36 mmol), after work-up with diethyl ether (60 mL), sat. $NaHCO_3$ solution (2×25 mL), extraction of the aqueous phases with pentane (2×35 mL) and CC on silica gel (30 g, pentane/diethyl ether 10:1) gave **10c** (1.12 g, 92%) as a colorless oil. R_f=0.44; IR (film): $\tilde{\nu}$=2984, 2958, 2898, 2878, 1677, 1597, 1560, 1493, 1477, 1453, 1422, 1401, 1368, 1332, 1270, 1251, 1206, 1141, 1078, 1024, 964, 943, 893, 851, 801, 765, 711, 693, 663, 621, 561, 507 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.90–2.07 (m, 2H, CH_2), 2.32–2.80 (m, 3H, CH_2), 2.82–2.92 (m, 1H, CH_2), 3.38 (s, 3H, CH_3), 3.58 (quin, ^3J=5.7 Hz, 1H, 4-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=25.4 (−, CH_2), 26.6 (−, CH_2), 39.7 (−, CH_2), 56.3 (+, CH_3), 74.1 (+, CH, C-4), 112.4 (C_{quat}, C-2), 119.2 (q, ^1J=326 Hz, C_{quat}, CF_3), 144.6 (C_{quat}, C-1); EI-MS (70 eV): *m/z* (%): 308/306 (2/2), 293 (1), 246 (3), 235/233 (100/99), 227 (34), 204 (4), 190/188 (12/11), 160 (6), 132 (15), 106 (2), 99 (11), 86 (22), 73 (14), 65 (10), 53 (5); HRMS: *m/z*: calcd for $C_8H_{10}BrF_3O_4S$ (339.1): 337.9435 (correct HRMS).

(3-Bromo-4-trifluoromethanesulfonyloxycyclohex-3-enyloxy)-*tert*-butyldimethylsilane (10d): According to GP 3, α-bromocyclohexanone **17d** (1.00 g, 3.26 mmol) in diethyl ether (30 mL), potassium hexamethyldisilazide (7.82 mL, 3.90 mmol, 0.500 M in toluene) and trifluoromethanesulfonic acid anhydride (1.10 g, 3.90 mmol), after work-up with pentane (40 mL) and sat. $NaHCO_3$ solution (20 mL), and extraction of the aqueous phases with pentane (2×30 mL). CC on silica gel (30 g, pentane/diethyl ether 5:1) gave **10d** as a colorless oil (1.25 g, 88%). R_f=0.67; IR (film): $\tilde{\nu}$=2947, 2835, 1653, 1559, 1521, 1472, 1449, 1419, 1248, 1215, 1138, 1114, 1033, 1018, 961, 866, 788, 766, 659, 640, 523 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ=0.06 (s, 6H, CH_3), 0.88 [m, 9H, $C(CH_3)_3$], 1.87 (m, 2H, CH_2), 2.27–3.89 (m, 4H, CH_2), 3.99–4.08 (m, 1H, 1-H); ^{13}C NMR (75.6 MHz, $CDCl_3$, APT): δ=−4.8 (+, 2C, CH_3), 17.9 [C_{quat}, $C(CH)_3$], 25.5 (−, CH_2), 25.63 [+, 3C, $C(CH)_3$], 30.4 (−, CH_2), 43.6 (−, CH_2), 65.9 (+, CH, C-1), 112.4 (−, C_{quat}, C-3) 118.8 (q, ^1J=319 Hz, −, C_{quat}, CF_3), 144,7 (−, C_{quat}, C-4); EI-MS (70 eV): *m/z* (%): 425/423 (1/1), 383/381 (60/54), 327 (1), 291 (2), 249/247 (96/88), 209 (7), 191 (14), 175/173 (20/18), 159/157 (53/54), 141 (50), 139 (20), 93 (10), 77 (63), 75/73 (100/100), 69 (37) [CF_3^+], 41 (26); HRMS: *m/z*: calcd for $C_{13}H_{22}BrF_3O_4SSi$+Na (462.3): 461.0039 (correct HRMS).

2-Bromo-3,3-dimethyl-1-trifluoromethanesulfonyloxycyclohexene (10e): According to GP 3, α-bromocyclohexanone **17e** (2.60 g, 12.7 mmol) in diethyl ether (80 mL), potassium hexamethyldisilazide (32.0 mL, 16.0 mmol, 0.500 M in toluene) and trifluoromethanesulfonic acid anhydride (3.95 g, 14.0 mmol), after work-up with pentane (50 mL) and sat. $NaHCO_3$ solution (20 mL), extraction of the aqueous phase with pentane (2×40 mL) and CC on silica gel (35 g, pentane/diethyl ether 20:1) gave **10e** as a colorless oil (3.75 g, 88%). R_f=0.37; IR (film): $\tilde{\nu}$=2970, 2946, 2873, 2857, 1660, 1473, 1428, 1417, 1401, 1388, 1366, 1342, 1242, 1228, 1198, 1148, 1138, 1118, 1054, 1007, 995, 981, 952, 894, 879, 853, 793, 769, 759, 664, 618, 608 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ=1.21 (s, 6H, CH_3), 1.65–2.88 (m, 4H, 4-H, 5-H), 2.40 (t, ^3J=7.2 Hz, 2H, 6-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=18.8 (−, CH_2), 28.7 (+, 2C, CH_3), 29.6 (−, CH_2), 37.8 (−, CH_2), 38.8 (C_{quat}, C-3), 118.7 (q, ^1J=311 Hz, C_{quat}, CF_3), 128.5 (C_{quat}, C-2), 145.1 (C_{quat}, C-1); EI-MS (70 eV): *m/z* (%): 337/335 (7/6), 322/320 (5/4), 256 (3), 202 (1), 177 (8), 162 (4), 146 (9), 123 (42), 107 (10), 95 (100), 81 (24), 69 (52) [CF_3^+], 53 (44); HRMS: *m/z*: calcd for $C_9H_{12}BrF_3O_3S$ (336.2): 335.9643 (correct HRMS).

1-Bromo-2-trifluoromethanesulfonyloxycycloheptene (10f): According to GP 3, α-bromocyclohexanone **17f** (2.00 g, 10.5 mmol) in diethyl ether (60 mL), potassium hexamethyldisilazide (25.2 mL, 12.6 mmol, 0.500 M in toluene) and trifluoromethanesulfonic acid anhydride (3.41 g, 12.1 mmol), after work-up with pentane (50 mL) and sat. $NaHCO_3$ solution (20 mL), extraction of the aqueous phases with pentane (2×40 mL) and CC on silica gel (30 g, pentane/diethyl ether 20:1) gave **10f** as a colorless oil (3.26 g, 96%). R_f=0.69; IR (film): $\tilde{\nu}$=2975, 2855, 2866, 1661, 1506, 1496, 1457, 1448, 1419, 1399, 1338, 1250, 1195, 1164, 1149, 1129, 1089, 1058, 1013, 999, 969, 926, 903, 874, 849, 815, 794, 782, 765, 688, 649, 629 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ=1.63–1.78 (m, 6H, CH_2), 2.49–2.60 (m, 2H, 3-H), 2.69–2.78 (m, 2H, 7-H); ^{13}C NMR (75.6 MHz, $CDCl_3$, APT): δ=24.0 (−, CH_2), 25.1 (−, CH_2), 29.3 (−, CH_2), 32.6 (−, CH_2), 37.5 (−, CH_2), 118.3 (q, ^1J=321 Hz, −, C_{quat}, CF_3), 119.3 (−, C_{quat}, C-2), 148.9 (−, C_{quat}, C-1); EI-MS (70 eV): *m/z* (%): 324/322 (2/2) [M^+], 191 (1/1), 163 (1), 147 (6), 119 (13), 109 (34), 91 (4), 82 (5), 81 (100), 69 (8) [CF_3^+], 67 (9), 55 (12), 41 (18); HRMS: *m/z*: calcd for $C_8H_{10}BrF_3O_3S$ (323.1): 321.9486 (correct HRMS).

(3′*S*,3a′*S*,7a′*R*)-7-Bromo-8-(1′-*tert*-butoxy-7a′-methyl-2′,3′,3a′,6′,7′,7a′-hexahydro-1′*H*-inden-5′-yl)-1,4-dioxaspiro[4.5]dec-7-ene (*cis*-11b): According to GP 6, bromoenol triflate **10b** (1.03 g, 2.81 mmol) and bicyclononenylstannane *cis*-**9** (1.46 g, 2.94 mmol) in NMP (10 mL) with $[Pd_2(dba)_3]$·$CHCl_3$ (64.1 mg, 61.2 μmol), LiCl (356 mg, 8.40 mmol) and CuI (13.3 mg, 70.0 μmol) after work-up with diethyl ether (100 mL), NH_3 solution (2×30 mL, 5%), water (30 mL), extraction with diethyl ether (2×50 mL), treatment with sat. KF solution (40 mL) and CC on silica gel (80 g, pentane/diethyl ether 10:1) gave *cis*-**11b** as a colorless wax (1.16 g, 97%). R_f=0.46; IR (film): $\tilde{\nu}$=2930, 2872, 2845, 1621, 1471, 1446, 1387, 1361, 1329, 1256, 1145, 1061, 1021, 954, 941, 872, 850 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ=0.93 (s, 3H, CH_3), 1.15 [s, 9H, $C(CH_3)_3$], 1.20–1.75 (m, 4H), 1.80 (t, ^3J=6.7 Hz, 2H, 5-H) 1.89–2.40 (m, 7H), 2.76 (s, 2H, 6-H), 3.72 (t, ^3J=6.8 Hz, 1H, 3′-H), 3.93–4.05 (m, 4H, 2-H, 3-H), 5.32–5.38 (m, 1H, 7′-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=21.1 (+, CH_3), 23.5 (−, CH_2), 26.9 (−, CH_2), 28.8 [+, 3C, $C(CH_3)_3$], 29.5 (−, CH_2), 30.0 (−, CH_2), 31.3 (−, CH_2), 32.6 (−, CH_2), 41.6 (−, CH_2), 43.8 (C_{quat}, C-7a′), 46.0 (+, CH, C-3a′), 64.6 (−, 2C, C-2, C-3), 72.5 [C_{quat}, C-$(CH_3)_3$], 75.9 (+, C-1′), 107.6 (C_{quat}, C-5), 113.3 (C_{quat}), 129.3 (+, C-5′), 136.8 (C_{quat}), 139.0 (C_{quat}); EI-MS (70 eV): *m/z* (%): 426/424 (2/2) [M^+], 370/368 (16/14) [M^+−C_4H_8], 289 (100) [M^+−Br−C_4H_8], 245 (10), 234 (34), 227 (9), 185 (16), 131 (14), 103 (18), 91 (15), 86 (26), 57 (62) [$C_4H_9^+$], 41 (25); HRMS: *m/z*: calcd for $C_{22}H_{33}BrO_3$ (425.4): 424.1613 (correct HRMS).

(3*S*,3a*S*,7a*R*)-6-(2′-Bromo-4′-methoxycyclohex-1′-enyl)-3-*tert*-butoxy-3a-methyl-2,3,3a,4,5,7a-hexahydro-1*H*-indene (*cis*-11c): According to GP 6, to the bromoenol triflate **10c** (500 mg, 1.47 mmol) and bicyclononenylstannane *cis*-**9** (879 mg, 1.77 mmol) in NMP (5.00 mL) with $[Pd_2(dba)_3]$ (40.4 mg, 44.1 μmol), LiCl (187 mg, 4.41 mmol) and CuI (8.40 mg, 44.1 μmol) after work-up with diethyl ether (75 mL), NH_3 solution (2×20 mL, 5%), water (20 mL), extraction with diethyl ether (2×35 mL), treatment with sat. KF solution (35 mL) and CC on silica gel (48 g, pentane/diethyl ether 10:1) gave *cis*-**11c** as a colorless wax (497 mg, 85%) with a diastereomeric ratio of 1:1 for the C-4′ epimers. R_f=0.29; IR (film): $\tilde{\nu}$=2976, 2929, 2906, 2871, 1621, 1462, 1440, 1387, 1360, 1257, 1197, 1099, 1077, 995, 938 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, distinguishable signals of diastereomers are marked with #): δ=0.90 (s, 3H, CH_3), 1.18 [s, 9H, $C(CH_3)_3$], 1.20–2.22 (m, 13H), 2.72–2.89 (m, 1H), 1.89–2.40 (m, 1H), 3.36 (s, 3H, OCH_3), 3.42–3.58 (m, 1H, 4′-H), 3.72 (m, 1H, 3-H), 5.28–5.36 (m, 1H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=21.1 (+, CH_3), 23.4 (−, CH_2), 23.5 (−, CH_2)#, 27.1 (−, CH_2), 27.3 (−, CH_2), 28.2 (−, CH_2), 28.3 (−, CH_2)#, 28.8 [+, 3C, $C(CH_3)_3$], 30.0 (−, CH_2), 32.4 (−, CH_2), 32.6 (−, CH_2)#, 41.5 (C_{quat}, C-3a), 41.7 (−, CH_2), 41.7 (−, CH_2)#, 43.8 (+, CH, C-7a), 56.0 (+, OCH_3), 72.4 [C_{quat}, $C(CH_3)_3$], 75.9 (+, C-3), 76.0 (+, C-4′), 76.1 (+, C-3), 114.2 (C_{quat}), 129.0 (+, C-7), 137.1 (C_{quat}), 139.4 (C_{quat}); EI-MS (70 eV): *m/z* (%): 398/396 (3/2) [M^+], 342/340 (21/19) [M^+−C_4H_8], 324/322 (27/27) [M^+−C_4H_8−H_2O], 261 (100) [M^+−Br−C_4H_8], 229 (44), 211 (21), 185 (16), 155 (11), 145 (16), 129 (26), 97 (19), 91 (17), 57 (63) [$C_4H_9^+$], 41 (18); HRMS: *m/z*: calcd for $C_{21}H_{33}BrO_2$ (397.4): 396.1663 (correct HRMS).

(3′*S*,3a′*S*,7a′*R*)-[3-Bromo-4-(1′-*tert*-butoxy-7a′-methyl-2′,3′,3a′,6′,7′,7a′-hexahydro-1′*H*-indene-5′-yl)cyclohex-3-enyloxy]-*tert*-butyldimethylsilane (*cis*-11d): According to GP 6, the bromoenol triflate **10d** (1.14 g, 2.60 mmol) and bicycloalkenylstannane *cis*-**9** (1.55 g, 3.12 mmol) in NMP (15.0 mL) with $[Pd_2(dba)_3]$ (71.6 mg, 78.0 μmol), LiCl (331 mg, 7.80 mmol) and CuI (17.3 mg, 90.8 μmol), after work-up with diethyl ether (100 mL), NH_3 solution (2×30 mL, 5%), water (40 mL), extraction with diethyl ether (2×50 mL), treatment with sat. KF solution (75 mL) and CC on silica gel (50 g, pentane/diethyl ether 20:1) gave *cis*-**11d** as a colorless wax (1.18 g, 91%) with a diastereomeric ratio of 1:1 for the C-1 epimers. R_f=0.44; IR (film): $\tilde{\nu}$=2979, 2930, 2953, 2871, 2855, 2812, 1635, 1609, 1473, 1464, 1443, 1388, 1377, 1361, 1293, 1258, 1251, 1227, 1200, 1109, 1091, 1042, 1024, 961, 938, 902, 873, 837, 810, 774, 690 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$ distinguishable signals of diastereomers are marked with #): δ=0.06 [s, 6H, $Si(CH_3)_2$], 0.91 [s, 9H, $SiC(CH_3)_3$], 0.98 (s, 3H, CH_3), 1.15 [s, 9H, $C(CH_3)_3$], 1.22–1.87 (m, 6H), 1.88–2.23 (m, 4H), 2.27–2.81 (m, 5H), 3.59–3.78 (m, 1H, 1-H), 3.87–4.04 (m, 1H, 1′-H), 5.30 (m, 1H, 4′-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=−4.7 [+, 2C, $Si(CH_3)_2$], 18.1 [C_{quat}, $SiC(CH_3)_3$], 21.1 (+, CH_3), 23.4 (−, CH_2), 23.5 (−, CH_2)#, 25.8 [+, 3C, $SiC(CH_3)_3$], 28.2 (−, CH_2), 28.3 (−, CH_2)#, 28.8 [+, 3C, $SiC(CH_3)_3$], 29.1 (−, CH_2), 30.0 (−, CH_2), 31.2 (−, CH_2), 31.34 (−, CH_2)#, 41.6 (C_{quat}, C-7a′), 43.8 (+, CH, C-3a′), 44.2 (−, CH_2)#, 45.4 (−, CH_2), 68.0 (+, CH, C-1), 68.1 (+, CH, C-1)#, 75.9 (+, CH, C-1′), 76.0 (+, CH, C-1′)#, 72.4 [C_{quat}, $C(CH_3)_3$], 72.6 [C_{quat}, $C(CH_3)_3$]#, 114.39 (C_{quat}), 114.44 (C_{quat})#, 128.8 (+, CH, C-4′), 128.9 (+, CH, C-4′)#, 137.26 (C_{quat}), 137.31 (C_{quat})#, 139.2 (C_{quat}); EI-MS (70 eV): *m/z* (%): 498/496 (6/10) [M^+], 441 (12), 424/422 (8/8), 383 (27), 361 (57), 310/308 (71/75), 303 (9), 229 (3), 185 (3), 143 (2), 91 (5), 75 (14), 57 (100), 41 (26); HRMS: *m/z*: calcd for $C_{26}H_{45}BrO_2Si$ (497.6): 496.2372 (correct HRMS).

(1′*S*,3a′*S*,7a′*S*)-7-Bromo-8-(1′-*tert*-butoxy-7a′-methyl-2′,3′,3a′,6′,7′,7a′-hexahydro-1′*H*-inden-5′-yl)-1,4-dioxaspiro[4.5]dec-7-ene (*trans*-11b): According to GP 6, the bromoenol triflate **10b** (1.03 g, 2.81 mmol) and bicyclononenylstannane *trans*-**9** (1.46 g, 2.94 mmol) in NMP (10 mL) with $[Pd_2(dba)_3]\cdot CHCl_3$ (73.0 mg, 70.5 μmol), LiCl (356 mg, 8.40 mmol) and CuI (14.0 mg, 73.5 μmol) after work-up with diethyl ether (100 mL), NH_3 solution (2×30 mL, 5%), water (30 mL), extraction of the combined aqueous phases with diethyl ether (2×50 mL), treatment with sat. KF solution (75 mL) and CC on silica gel (85 g, pentane/diethyl ether 10:1) gave *trans*-**11b** as a colorless wax (1.14 g, 95%). R_f=0.35; IR (film): $\tilde{\nu}$=2977, 2875, 2832, 1664, 1475, 1425, 1388, 1361, 1328, 1253, 1194, 1148, 1115, 1061, 1021, 954, 941, 892, 854 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ=0.81 (s, 3H, CH_3), 1.15 [s, 9H, $C(CH_3)_3$], 1.20–1.73 (m, 4H), 1.79 (t, ^3J=6.7 Hz, 2H, 9-H), 1.81–2.40 (m, 7H), 2.76 (s, 2H, 6-H), 3.72 (dd, ^3J=9.6, ^3J=7.1 Hz, 1H, 1′-H), 3.93–4.05 (m, 4H, 2-H, 3-H), 5.41 (d, ^3J=0.7 Hz, 1H, 4′-H); ^{13}C NMR (62.9 MHz, C_6D_6, DEPT): δ=11.6 (+, CH_3), 24.8 (−, CH_2), 25.2 (−, CH_2), 28.8 [+, 3C, $C(CH_3)_3$], 30.2 (−, CH_2), 31.9 (−, CH_2), 32.0 (−, CH_2), 34.3 (−, CH_2), 42.3 (−, CH_2), 43.6 (C_{quat}, C-7a′), 46.7 (+, CH, C-3a′), 64.4 (−, 2C, CH_2, C-2, C-3), 72.1 [C_{quat}, $C(CH_3)_3$], 79.5 (+, CH, C-1′), 108.0 (C_{quat}, C-5), 113.5 (C_{quat}), 126.3 (+, CH, C-4′), 138.5 (C_{quat}), 139.9 (C_{quat}); EI-MS (70 eV): *m/z* (%): 426/424 (36/32) [M^+], 370/368 (4/4) [$M^+-C_4H_8$], 289 (40) [$M^+-Br-C_4H_8$], 245 (4), 201 (4), 185 (10), 157 (6), 145 (5), 99 (12), 86 (20), 57 (100) [$C_4H_9^+$], 41 (25); HRMS: *m/z*: calcd for $C_{22}H_{33}BrO_3$ (425.4): 424.1615 (correct HRMS).

(3*S*,3a*S*,7a*S*)-6-(2′-Bromo-4′-methoxycyclohex-1′-enyl)-3-*tert*-butoxy-3a-methyl-2,3,3a,4,5,7a-hexahydro-1*H*-indene (*trans*-11c): According to GP 6, the bromoenol triflate **10c** (542 mg, 1.60 mmol) and bicyclononenylstannane *trans*-**9** (845 mg, 1.70 mmol) in NMP (5 mL) with $[Pd_2(dba)_3]\cdot CHCl_3$ (104 mg, 100 μmol), $AsPh_3$ (24 mg, 78 μmol), LiCl (192 mg, 4.53 mmol) and CuI (10 mg, 53 μmol), after work-up with diethyl ether (70 mL), NH_3 solution (2×25 mL, 5%), water (30 mL), extraction of the combined aqueous phases with diethyl ether (2×30 mL), treatment with sat. KF solution (45 mL) and CC on silica gel (47 g, pentane/diethyl ether 20:1) gave *trans*-**11c** as a colorless wax (443 mg, 70%) with a diastereomeric ratio of 1:1 for the C-4′ epimers. R_f=0.20; IR (film): $\tilde{\nu}$=2974, 2929, 2875, 2821, 1633, 1497, 1459, 1388, 1359, 1251, 1229, 1099, 1192, 1122, 1071, 972, 938 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, distinguishable signals of diastereomers are marked with #): δ=0.75 (s, 3H, CH_3), 1.11 [s, 9H, $C(CH_3)_3$], 1.18–2.38 (m, 13H), 2.40–2.58 (m, 1H), 2.71–2.88 (m, 1H), 3.32 (s, 3H, OCH_3), 3.44 (dd, ^3J=9.6, ^3J=7.1 Hz, 1H, 3-H), 3.40–3.53 (m, 1H, 4′-H), 5.36 (d, ^3J=0.6 Hz, 1H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=10.9 (+, CH_3), 24.3 (−, CH_2), 25.2 (−, CH_2), 27.1 (−, CH_2), 28.7 [+, 3C, $C(CH_3)_3$], 28.9 (−, CH_2), 29.0 (−, CH_2)#, 31.5 (−, CH_2), 33.8 (−, CH_2), 41.7 (C_{quat}, C-3a), 43.2 (+, CH, C-7a), 55.8 (+, OCH_3), 72.0 [C_{quat}, $C(CH_3)_3$], 79.2 (+, CH, C-3), 114.0 (C_{quat}), 114.1 (C_{quat})#, 125.6 (+, CH, C-7), 138.9 (C_{quat}), 139.1 (C_{quat}); EI-MS (70 eV): *m/z* (%): 398/396 (6/7) [M^+], 342/340 (18/18) [$M^+-C_4H_8$], 324/322 (20/20) [$M^+-C_4H_8-H_2O$], 283 (10), 261 (78) [$M^+-Br-C_4H_8$], 229 (34), 211 (20), 185 (16), 157 (11), 155 (8), 145 (18), 129 (22), 97 (13), 91 (27), 57 (100) [$C_4H_9^+$], 41 (29); HRMS: *m/z*: calcd for $C_{21}H_{33}BrO_2$: (397.4): 396.1664 (correct HRMS).

***tert*-Butyl (*E*)-(1″*S*,3a″*R*,7a″*S*)-3-[8′-(1″-*tert*-butoxy-7a″-methyl-2″,3″,3a″,6″,7″,7a″-hexahydro-1″*H*-indene-5″-yl)-1′,4′-dioxaspiro[4.5]dec-7′-ene-7′-yl]acrylate (*cis*-12b)**: According to GP 7, the bromodiene *cis*-**11b** (400 mg, 0.940 mmol) in DMF/CH_3CN/H_2O 5:5:1 (4.40 mL), the palladacycle **14** (44.1 mg, 47.0 μmol), tri-*o*-tolylphosphane (29.0 mg, 95.3 μmol), nBu_4NOAc (709 mg, 2.35 mmol) and *tert*-butyl acrylate (2.00 mL, 1.75 g, 13.7 mmol) after 6.5 h at 105 °C and work-up with diethyl ether (45 mL), water (2×15 mL), back-extraction with diethyl ether (20 mL), brine (15 mL) and CC on silica gel (35 g, pentane/diethyl ether 5:1) gave *cis*-**12b** as a colorless wax (382 mg, 86%). R_f=0.28; IR (film): $\tilde{\nu}$=2976, 2932, 2873, 1736, 1616, 1457, 1391, 1367, 1291, 1256, 1197, 1151, 1059, 985, 845, 736 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ=0.92 (s, 3H, CH_3), 1.17 [s, 9H, $C(CH_3)_3$], 1.22–1.42 (m, 4H), 1.46 [s, 9H, $CO_2C(CH_3)_3$], 1.51–1.73 (m, 5H), 1.76 (t, ^3J=7.5 Hz, 2H, 9′-H), 1.93–2.30 (m, 4H), 3.58 (t, ^3J=7.1 Hz, 1H, 1″-H), 3.96 (s, 4H, 2′-H, 3′-H), 5.33–5.42 (m, 1H, 4″-H), 5.61 (d, ^3J=16.7 Hz, 1H, 2-H), 7.58 (d, ^3J=16.7 Hz, 1H, 3-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=20.9 (+, CH_3), 25.0 (−, CH_2), 28.2 [+, 3C, $C(CH_3)_3$], 28.6 [+, 3C, $CO_2C(CH_3)_3$], 29.1 (−, CH_2), 29.3 (−, CH_2), 30.3 (−, CH_2), 30.9 (−, CH_2), 32.9 (−, CH_2), 35.6 (−, CH_2), 41.4 (C_{quat}, C-7a″), 44.3 (+, CH, C-3a″), 64.4 (−, CH_2, 2C, C-2′, C-3′), 72.5 [C_{quat}, $C(CH_3)_3$], 77.2 (+, CH, C-1″), 79.6 [C_{quat}, $CO_2C(CH_3)_3$], 107.7 (C_{quat}, C-5′), 116.9 (+, CH, C-2), 125.3 (C_{quat}), 131.5 (+, CH, C-4″), 135.0 (C_{quat}), 143.2 (+, CH, C-3), 148.4 (C_{quat}), 166.8 (C_{quat}, C=O); EI-MS (70 eV, EI): *m/z* (%): 472 (12) [M^+], 416 (22) [$M^+-C_4H_8$], 371 (20), 360 (30) [$M^+-2\times C_4H_8$], 359 (40) [$M^+-C_4H_9-C_4H_8$], 297 (13), 253 (14), 235 (8), 169 (6), 115 (9), 157 (9), 99 (28), 86 (24), 57 (100) [$C_4H_9^+$], 41 (28); elemental analysis calcd (%) for $C_{29}H_{44}O_5$ (472.7): C 73.69, H 9.32; found C 73.43, H 9.17.

***tert*-Butyl (*E*)-(1″*S*,3a″*R*,7a″*S*)-3-[2′-(1″-*tert*-butoxy-7a″-methyl-2″,3″,3a″,6″,7″,7a″-hexahydro-1*H*″-indene-5″-yl)-5′-methoxycyclohex-1′-enyl]acrylate (*cis*-12c)**: According to GP 7, the bromodiene *cis*-**11c** (380 mg, 0.956 mmol) in DMF/CH_3CN/H_2O 5:5:1 (5.0 mL), the palladacycle **14** (27.3 mg, 29.1 μmol) and nBu_4NOAc (586 mg, 1.94 mmol), tri-*o*-tolylphosphane (17.7 mg, 58.2 μmol) and *tert*-butyl acrylate (1.24 g, 1.42 mL, 9.70 mmol) after 4.5 h at 105 °C and work-up with diethyl ether (80 mL), water (2×20 mL), back-extraction with diethyl ether (30 mL), brine (15 mL) and CC on silica gel (40 g, pentane/diethyl ether 5:1) gave *cis*-**12c** as a colorless wax (358 mg, 84%) with a diastereomeric ratio of 1:1 for the C-5′ epimers. R_f=0.37; IR (film): $\tilde{\nu}$=2977, 2932, 2872, 1719, 1616, 1455, 1391, 1316, 1290, 1255, 1198, 1150, 1060, 983, 847, 737 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, distinguishable signals of diastereomers are marked with #): δ=0.92 (s, 3H, CH_3), 1.18 [s, 9H, $C(CH_3)_3$], 1.20–1.42 (m, 6H), 1.45 [s, 9H, $CO_2C(CH_3)_3$], 1.51–2.31 (m, 5H), 2.32–2.63 (m, 4H), 3.38 (s, 3H, OCH_3), 3.41–3.54 (m, 1H, 5′-H), 3.58 (t, ^3J=6.3 Hz, 1H, 1″-H), 5.35 (d, ^3J=3.7 Hz, 1H, 4″-H), 5.70 (d, ^3J=15.7 Hz, 1H, 2-H), 7.60 (d, ^3J=15.7 Hz, 1H, 3-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=20.9 (+, CH_3), 25.1 (−, CH_2), 26.9 (−, CH_2), 27.1 (−, CH_2)#, 28.2 [+, 3C, $C(CH_3)_3$], 28.4 (−, CH_2), 28.7 [+, 3C, $CO_2C(CH_3)_3$], 29.2 (−, CH_2), 29.2 (−, CH_2)#, 30.4 (−, CH_2), 31.1 (−, CH_2), 33.0 (−, CH_2), 33.0 (−, CH_2)#, 41.4 (C_{quat}, C-7a″), 44.3 (+, CH, C-3a″), 55.8 (+, OCH_3), 72.6 [C_{quat}, $C(CH_3)_3$], 75.3 (+, CH, C-1″), 75.3 (+, CH, C-1″)#, 77.3 (+, CH, C-5′), 79.6 [C_{quat}, $CO_2C(CH_3)_3$], 116.9 (+, C-2), 125.3 (C_{quat}), 131.1 (+, CH, C-4″), 131.2 (+, CH, C-4″)#, 135.3 (C_{quat}), 135.3 (C_{quat})#, 143.5 (+, CH, C-3), 149.1 (C_{quat}), 167.1 (C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 444 (2) [M^+], 388 (7) [$M^+-C_4H_8$], 332 (14) [$M^+-2\times C_4H_8$], 331 (18) [$M^+-C_4H_9-C_4H_8$], 311 (22), 299 (21), 282 (11), 255 (34), 237 (12), 157 (6), 143 (15), 138 (69), 109 (18), 96 (56), 81 (59), 67 (60), 57 (100) [$C_4H_9^+$], 41 (61); elemental analysis calcd (%) for $C_{28}H_{44}O_4$ (444.7): C 75.63, H 9.97; found C 75.47, H 9.69.

***tert*-Butyl (*E*)-(1″*S*,3a″*R*,7a″*S*)-3-[2′-(1″-*tert*-butoxy-7a″-methyl-2″,3″,3a″,6″,7″,7a″-hexahydro-1″*H*-indene-5″-yl)-5′-(*tert*-butyldimethylsilanyloxy)-cyclohex-1′-enyl]acrylate (*cis*-12d)**: According to GP 7, the bromodiene *cis*-**11d** (1.18 g, 2.37 mmol) in DMF/H_2O 10:1, the palladacycle **14** (66.5 mg, 71.1 μmol), tri-*o*-tolylphosphane (21.6 mg, 71.1 μmol), NEt_3 (719 mg, 7.11 mmol) and *tert*-butyl acrylate (1.52 g, 11.9 mmol) after 4 h at 105 °C and work-up with diethyl ether (100 mL), water (2×35 mL), back-extraction with diethyl ether (2×50 mL), brine (25 mL) and CC on silica gel (35 g, pentane/diethyl ether 20:1) gave *cis*-**12d** as a colorless wax (943 mg, 73%) with a diastereomeric ratio of 1:1 for the C-5′ epimers. R_f=0.36; IR (film): $\tilde{\nu}$=2977, 2952, 2929, 2855, 1750, 1646, 1437, 1388, 1362, 1287, 1257, 1196, 1150, 1043, 987, 939, 835, 747 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, distinguishable signals of diastereomers are marked with #): δ=0.04 [s, 6H, $Si(CH_3)_2$], 0.78 [s, 9H, $SiC(CH_3)_3$], 0.92 (s, 3H, CH_3), 1.17 [s, 9H, $C(CH_3)_3$], 1.34–1.42 (m, 2H), 1.47 [s, 9H, $CO_2C(CH_3)_3$], 1.51–1.83 (m, 5H), 1.91–2.31 (m, 6H), 2.32–2.47 (m, 2H), 3.58 (t, ^3J=6.7 Hz, 1H, 1″-H), 3.93 (m, 1H, 5′-H), 5.33 (m, 1H, 4″-H), 5.62 (d, ^3J=16.5 Hz, 1H, 2-H), 7.56 (d, ^3J=16.5 Hz, 1H, 3-H); ^{13}C NMR (75.6 MHz, $CDCl_3$, APT): δ=−5.0 [+, 2C, $Si(CH_3)_2$], 18.2 [−, C_{quat}, $SiC(CH_3)_3$], 20.9 (+, CH_3), 21.0 (+, CH_3)#, 25.2 (−, CH_2), 25.9 [+, 3C, $SiC(CH_3)_3$], 28.2 [+, 3C, $C(CH_3)_3$] 28.7 [+, 3C, $CO_2C(CH_3)_3$], 28.9 (−, CH_2), 29.0 (−, CH_2)#, 29.22 (−, CH_2), 29.24 (−, CH_2)#, 30.5 (−, CH_2), 31.3 (−, CH_2), 31.4 (−, CH_2)#, 33.0 (−, CH_2), 34.9 (−, CH_2), 35.0 (−, CH_2)#, 41.5 (−, C_{quat}, C-7a″), 44.35 (+, CH, C-3a″), 44.36 (+, CH, C-3a″)#, 67.4 (+, CH, C-5′), 67.5 (+, CH, C-5′)#, 72.57 [−, C_{quat}, $C(CH_3)_3$], 72.58 [−, C_{quat}, $C(CH_3)_3$]#, 77.3 (+, CH, C-1″), 79.7 [−, C_{quat}, $CO_2C(CH_3)_3$], 116.7 (+, CH, C-2), 125.47 (−, C_{quat}), 125.51 (−, C_{quat})#, 130.9 (+, CH, C-4″), 135.50 (−, C_{quat}), 135.54 (−, C_{quat})#, 143.66 (+, CH, C-3), 143.68 (+, CH, C-3)#,

149.0 (–, C_{quat}), 167.1 (–, C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 544 (8) [M^+], 488 (20) [$M^+-C_4H_8$], 447 (4), 432 (20) [$M^+-2\times C_4H_8$], 431 (36) [$M^+-C_4H_9-C_4H_8$], 385 (12), 356 (29), 311 (86), 299 (78), 255 (74), 237 (32), 195 (15), 143 (19), 91 (4), 75 (43), 57 (100) [$C_4H_9^+$]; HRMS: *m/z*: calcd for $C_{33}H_{56}O_4Si$ (544.9): 544.3948 (correct HRMS).

***tert*-Butyl (*E*)-(1″*S*,3a″*S*,7a″*S*)-3-[8′-(1″-*tert*-butoxy-7a″-methyl-2″,3″,3a″,6″,7″,7a″-hexahydro-1″*H*-indene-5″-yl)-1′,4′-dioxaspiro[4.5]dec-7′-ene-7′-yl]acrylate (*trans*-12b)**: According to GP 7, the bromodiene *trans*-**11b** (650 mg, 1.53 mmol) in DMF/CH_3CN/H_2O 5:5:1 (4.4 mL), the palladacycle **14** (57.3 mg, 61.1 μmol), tri-*o*-tolylphosphane (37.2 mg, 122 μmol), nBu$_4$NOAc (1.15 g, 3.83 mmol) and *tert*-butyl acrylate (2.00 mL, 1.75 g, 13.7 mmol) after 4 h at 105 °C and work-up with diethyl ether (80 mL), water (2×35 mL), back-extraction with diethyl ether (2×45 mL), brine (25 mL) and CC on silica gel (50 g, pentane/diethyl ether 5:1) gave *trans*-**12b** as a colorless wax (651 mg, 90 %). R_f=0.23; IR (film): $\tilde{\nu}$=2977, 2931, 2874, 1706, 1615, 1477, 1447, 1390, 1365, 1316, 1291, 1256, 1238, 1197, 1148, 1059, 989, 945, 864, 733 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.83 (s, 3H, CH_3), 0.86–1.04 (m, 1H), 1.15 [s, 9H, $C(CH_3)_3$], 1.20–1.44 (m, 2H), 1.48 [s, 9H, $CO_2C(CH_3)_3$], 1.48–1.71 (m, 2H), 1.78 (t, ^3J= 8.2 Hz, 2H, 9′-H), 1.83–2.25 (m, 4H), 2.36–2.52 (m, 4H), 3.49 (dd, ^3J= 9.0, ^3J=8.6 Hz, 1H, 1″-H), 3.91–4.09 (m, 4H, 2′-H, 3′-H), 5.39 (d, ^3J= 0.52 Hz, 1H, 4″-H), 5.65 (d, ^3J=16.4 Hz, 1H, 2-H), 7.63 (d, ^3J=16.4 Hz, 1H, 3-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=11.3 (+, CH_3), 24.4 (–, CH_2), 26.9 (–, CH_2), 28.2 [+, 3C, C(CH_3)$_3$], 28.7 [+, 3C, CO_2C-(CH_3)$_3$], 29.7 (–, CH_2), 31.0 (–, CH_2), 31.6 (–, CH_2), 33.9 (–, CH_2), 35.7 (–, CH_2), 41.7 (C_{quat}, C-7a″), 43.7 (+, CH, C-3a″), 64.5 (–, CH_2, 2C, C-2′, C-3′), 72.3 [C_{quat}, $C(CH_3)_3$], 79.2 (+, CH, C-1″), 79.8 [C_{quat}, $CO_2C(CH_3)_3$], 107.8 (C_{quat}, C-5′), 117.0 (+, CH, C-2), 125.7 (C_{quat}), 128.4 (+, CH, C-7″), 137.3 (C_{quat}), 143.2 (+, CH, C-3), 148.2 (C_{quat}), 167.1 (C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 472 (11) [M^+], 416 (50) [$M^+-C_4H_8$], 371 (19), 359 (31) [$M^+-C_4H_9-C_4H_8$], 327 (9), 313 (18), 253 (10), 235 (8), 209 (5), 169 (6), 159 (7), 129 (5), 99 (24), 86 (18), 57 (100) [$C_4H_9^+$], 41 (28); elemental analysis calcd (%) for $C_{29}H_{44}O_5$ (472.7): C 73.69, H 9.32; found C 73.91, H 9.10.

***tert*-Butyl (*E*)-(1″*S*,3a″*S*,7a″*S*)-3-[2′-(1″-*tert*-Butoxy-7a″-methyl-2″,3″,3a″,6″,7″,7a″-hexahydro-1″*H*-indene-5″-yl)-5′-methoxycyclohex-1′-enyl]acrylate (*trans*-12c)**: According to GP 7, the bromobutadiene *trans*-**11c** (250 mg, 0.629 mmol) in DMF/CH_3CN/H_2O 5:5:1 (2.0 mL), the palladacycle **14** (44.0 mg, 50.0 μmol), nBu$_4$NOAc (379 mg, 1.26 mmol) and *tert*-butyl acrylate (323 mg, 2.52 mmol) after 4 h at 105 °C and work-up with diethyl ether (70 mL), water (2×25 mL), back-extraction with diethyl ether (2×35 mL), brine (15 mL) and CC on silica gel (52 g, pentane/diethyl ether 5:1) gave *trans*-**12c** as a colorless wax (221 mg, 79 %) with a diastereomeric ratio of 1:1 for the C-5′ epimers. R_f=0.36; IR (film): $\tilde{\nu}$= 2975, 2929, 2822, 1703, 1615, 1458, 1390, 1364, 1313, 1288, 1254, 1194, 1148, 1103, 1071, 984, 897, 853, 732 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$, distinguishable signals of diastereomers are marked with #): δ=0.75–0.92 (m, 1H), 0.98 (s, 3H, CH_3), 1.12 [s, 9H, $C(CH_3)_3$], 1.16–1.38 (m, 3H), 1.45 [s, 9H, $CO_2C(CH_3)_3$], 1.49–2.22 (m, 11H), 3.10 (s, 3H, OCH_3), 3.11–3.31 (m, 2H, 5′-H, 1″-H), 5.38 (d, ^3J=0.4 Hz, 1H, 4″-H), 5.97 (d, ^3J= 14.9 Hz, 1H, 2-H), 7.60 (d, ^3J=14.9 Hz, 1H, 3-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=11.6 (+, CH_3), 24.8 (–, CH_2), 27.2 (–, CH_2), 27.3 (–, CH_2)$^{\#}$, 27.5 (–, CH_2), 27.6 (–, CH_2)$^{\#}$, 28.3 [+, 3C, C(CH_3)$_3$], 28.7 (–, CH_2), 28.8 (–, CH_2)$^{\#}$, 28.9 [+, 3C, $CO_2C(CH_3)_3$], 31.3 (–, CH_2), 32.0 (–, CH_2), 34.1 (–, CH_2), 34.2 (–, CH_2)$^{\#}$, 42.1 (C_{quat}, C-7a″), 43.7 (+, CH, C-3a″), 55.5 (+, OCH_3), 72.1 [C_{quat}, $C(CH_3)_3$], 75.0 (+, CH, C-1″), 75.3 (+, CH, C-1″)$^{\#}$, 79.2 (+, CH, C-5′), 79.3 (+, C-5′)$^{\#}$, 79.4 [C_{quat}, $CO_2C(CH_3)_3$], 117.4 (+, CH, C-2), 125.9 (C_{quat}), 126.0 (C_{quat})$^{\#}$, 128.2 (+, CH, C-4″), 128.2 (+, CH, C-4″)$^{\#}$, 138.1 (C_{quat}), 138.1 (C_{quat})$^{\#}$, 143.9 (+, CH, C-3), 148.9 (C_{quat}), 148.9 (C_{quat})$^{\#}$, 166.9 (C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 444 (4) [M^+], 388 (46) [$M^+-C_4H_8$], 356 (41), 331 (31) [$M^+-C_4H_9-C_4H_8$], 311 (92), 299 (38), 281 (30), 255 (36), 253 (46), 237 (29), 197 (18), 169 (51), 140 (43), 129 (16), 91 (11), 81 (6), 57 (100) [$C_4H_9^+$], 41 (27); elemental analysis calcd (%) for $C_{28}H_{44}O_4$ (444.7): C 75.63, H 9.97; found C 75.42, H 9.86.

***tert*-Butyl (+)-(7*R*,13*S*,14*R*,17*S*)-17-*tert*-butoxy-13-methyl-spiro(1′,3′-dioxolane[2′.3]-2,3,4,6,7,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene)-7-carboxylate (*cis*-13b)**: According to GP 9, *cis*-**12b** (125 mg, 0.265 mmol) in decalin (2.0 mL) was heated at 210 °C for 45 min to give, after purification by CC on silica gel (14 g, pentane/diethyl ether 5:1), *cis*-**13b** as a colorless wax (104 mg, 83 %). R_f=0.42; $[\alpha]_D^{20}$=+50 (c= 1.00, C_6H_6); IR (film): $\tilde{\nu}$=2975, 2930, 2870, 1721, 1456, 1391, 1366, 1253, 1196, 1148, 1061, 948 cm^{-1}; ^{1}H NMR (250 MHz, C_6D_6): δ=1.18 [s, 9H, C-(CH_3)$_3$], 1.22 (s, 3H, CH_3), 1.29–1.33 (m, 2H), 1.38 [s, 9H, $CO_2C(CH_3)_3$], 1.25–1.83 (m, 4H), 1.89 (t, ^3J=7.8 Hz, 2H, 1-H), 1.93–2.30 (m, 5H), 2.32–2.63 (m, 3H), 2.65–2.88 (m, 2H), 3.48 (t, ^3J=6.0 Hz, 1H, 17-H), 3.54–3.68 (m, 4H, C-4′, C-5′); ^{13}C NMR (62.9 MHz, C_6D_6, DEPT, HMBC, HSQC, NOESY, H,H-COSY): δ=20.1 (+, CH_3), 22.9 (–, CH_2), 24.4 (–, CH_2), 28.0 [+, 3C, C(CH_3)$_3$], 28.7 [+, 3C, $CO_2C(CH_3)_3$], 30.8 (–, CH_2), 30.9 (–, CH_2), 32.0 (–, CH_2), 32.1 (–, CH_2), 33.9 (–, CH_2), 41.2 (–, CH_2), 42.8 (C_{quat},C-13), 43.7 (+, CH, C-7), 47.6 (+, CH, C-14), 64.3 (–, CH_2, C-4′), 64.3 (–, CH_2, C-5′), 72.5 [C_{quat}, $C(CH_3)_3$], 79.5 [C_{quat}, $CO_2C(CH_3)_3$], 80.1 (+, CH, C-7), 108.2 (C_{quat}, C-3), 125.3 (C_{quat}), 127.5 (C_{quat}, 2C), 130.5 (C_{quat}), 172.7 (C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 472 (22) [M^+], 416 (46) [$M^+-C_4H_8$], 371 (15), 359 (100) [$M^+-C_4H_8-C_4H_9$], 297 (8), 253 (12), 169 (6), 157 (10), 99 (8), 57 (99) [$C_4H_9^+$], 41 (30); elemental analysis calcd (%) for $C_{29}H_{44}O_5$ (472.7): C 73.69, H 9.32; found C 73.97, H 8.97.

***tert*-Butyl (+)-(7*R*,13*S*,14*R*,17*S*)-17-*tert*-Butoxy-3-methoxy-13-methyl-2,3,4,6,7,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene-7-carboxylate (*cis*-13c)**: According to GP 9, *cis*-**12c** (120 mg, 0.270 mmol) in decalin (2.00 mL) at 210 °C for 45 min, after purification by CC on silica gel (18 g, pentane/diethyl ether 5:1) gave *cis*-**13c** as a colorless wax (94.1 mg, 78 %) with a diastereomeric ratio of 1:1 for the C-3 epimers. R_f=0.50; $[\alpha]_D^{20}$=+55 (c=0.100, C_6H_6); IR (film): $\tilde{\nu}$=2979, 2930, 2869, 1730, 1459, 1390, 1366, 1253, 1197, 1143, 1100 cm^{-1}; ^{1}H NMR (250 MHz, C_6D_6 (distinguishable signals of diastereomers are marked with #): δ=1.18 [s, 9H, C(CH_3)$_3$], 1.22 (s, 3H, CH_3), 1.26 (s, 3H, CH_3)$^{\#}$, 1.29–1.43 (m, 2H), 1.45 [s, 9H, $CO_2C(CH_3)_3$], 1.46–2.60 (m, 14H), 2.63–2.94 (m, 2H), 3.21 (s, 3H, OCH_3), 3.26 (s, 3H, OCH_3)$^{\#}$, 3.31–3.48 (m, 1H, H-3), 3.50 (t, ^3J=5.6 Hz, 1H, 17-H); ^{13}C NMR (62.9 MHz, C_6D_6, DEPT): δ=20.0 (+, CH_3), 20.2 (+, CH_3)$^{\#}$, 22.3 (–, CH_2), 22.9 (–, CH_2), 24.6 (–, CH_2)$^{\#}$, 27.5 (–, CH_2), 28.1 [+, 3C, C(CH_3)$_3$], 28.7 [+, 3C, $CO_2C(CH_3)_3$], 28.9 (–, CH_2)$^{\#}$, 30.8 (–, CH_2, 2C), 30.9 (–, CH_2)$^{\#}$, 32.3 (–, CH_2), 32.4 (–, CH_2)$^{\#}$, 33.8 (–, CH_2), 33.9 (–, CH_2)$^{\#}$, 36.4 (–, CH_2), 36.6 (–, CH_2)$^{\#}$, 42.8 (C_{quat}, C-13), 43.7 (+, C-7), 43.8 (+, C-7)$^{\#}$, 47.5 (+, C-14), 47.7 (+,C-14)$^{\#}$, 55.4 (+, OCH_3), 55.4 (+, OCH_3)$^{\#}$, 72.5 [C_{quat}, $C(CH_3)_3$], 72.5 [C_{quat}, C-(CH_3)$_3$]$^{\#}$, 75.0 (+, CH, C-3), 76.4 (+, CH, C-3)$^{\#}$, 79.4 [C_{quat}, $CO_2C(CH_3)_3$], 79.5 [C_{quat}, $CO_2C(CH_3)_3$]$^{\#}$, 79.8 (+, CH, C-17), 80.2 (+, CH, C-17)$^{\#}$, 124.9 (C_{quat}), 125.3 (C_{quat})$^{\#}$, 127.7 (C_{quat}, 2C), 127.9 (C_{quat}, 2C)$^{\#}$, 130.2 (C_{quat}), 130.5 (C_{quat})$^{\#}$, 172.7 (C_{quat}, C=O), 172.9 (C_{quat}, C=O)$^{\#}$; EI-MS (70 eV): *m/z* (%): 444 (29) [M^+], 388 (46) [$M^+-C_4H_8$], 331 (82) [$M^+-C_4H_8-C_4H_9$], 299 (60), 281 (16), 255 (38), 197 (15), 181 (6), 143 (26), 129 (6), 57 (100) [$C_4H_9^+$], 41 (24); elemental analysis calcd (%) for $C_{28}H_{44}O_4$ (444.7): C 75.63, H 9.97; found C 75.70, H 10.06.

***tert*-Butyl (7*R*,13*S*,14*R*,17*S*)-17-*tert*-Butoxy-3-(*tert*-butyldimethylsilanyloxy)-13-methyl-2,3,4,6,7,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene-7-carboxylate (*cis*-13d)**: According to GP 9, *cis*-**12d** (500 mg, 0.918 mmol) in decalin (15.0 mL) at 210 °C for 45 min, after purification by CC on silica gel (30 g, pentane/diethyl ether 20:1) gave *cis*-**13d** as a colorless wax (452 mg, 90 %) with a diastereomeric ratio of 1:1 for the C-3 epimers. R_f=0.41; IR (film): $\tilde{\nu}$=2972, 2956, 2930, 2858, 1721, 1472, 1463, 1389, 1367, 1281, 1255, 1196, 1150, 1087, 1062, 1005, 949, 933, 909, 870, 836, 814, 775, 733, 670, 647 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$, (distinguishable signals of diastereomers are marked with #): δ=0.04 [s, 6H, Si(CH_3)$_2$], 0.92 [s, 9H, SiC(CH_3)$_3$], 0.95 (s, 3H, CH_3), 1.18 [s, 9H, C-(CH_3)$_3$], 1.20–1.32 (m, 5H), 1.38 [s, 9H, $CO_2C(CH_3)_3$], 1.41–2.36 (m, 12H), 2.69–2.80 (m, 2H), 3.52 (t, ^3J=5.3 Hz, 1H, 17-H), 3.78 (m, 1H, 3-H), 3.88 (m, 1H, 3-H)$^{\#}$; ^{13}C NMR (75.6 MHz, C_6D_6, APT): δ=–4.6 [+, 2C, Si(CH_3)$_2$], 18.2 (+, CH_3), 19.5 (–, CH_2), 19.8 (–, CH_2)$^{\#}$, 22.4 (–, CH_2), 22.8 (–, CH_2)$^{\#}$, 24.8 (–, CH_2), 25.9 [+, 3C, SiC(CH_3)$_3$], 28.0 [+, 3C, C(CH_3)$_3$], 28.6 [+, 3C, ($CO_2C(CH_3)_3$], 30.3 (–, CH_2)$^{\#}$, 30.7 (–, CH_2), 31.7 (–, CH_2), 31.9 (–, CH_2)$^{\#}$, 32.6 (–, CH_2), 33.5 (–, CH_2), 33.8 (–, CH_2)$^{\#}$, 40.2 (–, CH_2), 40.4 (–, CH_2)$^{\#}$, 42.1 (–, C_{quat},C-13), 43.2 (+, CH, C-7), 43.7 (+, CH, C-7)$^{\#}$, 47.2 (+, CH, C-14), 47.6 (+, CH, C-14)$^{\#}$, 67.6 (+,CH, C-3)$^{\#}$, 68.6 (+,CH, C-3)$^{\#}$, 72.6 [–, C_{quat}, $C(CH_3)_3$], 72.7 [–, C_{quat}, $C(CH_3)_3$]$^{\#}$, 79.4 [–, C_{quat}, $CO_2C(CH_3)_3$], 79.8 [–, C_{quat}, $CO_2C(CH_3)_3$]$^{\#}$, 79.9 (+, CH, C-17), 80.0 (+, CH, C-17)$^{\#}$, 124.3 (–, C_{quat})$^{\#}$, 125.1 (–, C_{quat}),

127.48 (−, C_{quat}, 2C), 127.54 (−, C_{quat}, 2C)[#], 128.3 (−, C_{quat}), 130.1 (−, C_{quat})[#], 130.2 (−, C_{quat}), 173.3 (−, C_{quat}, C=O), 173.7 (−, C_{quat}, C=O)[#]; ESI-MS (MeOH): *m/z* (%): 1173 (1), 1143 (4), 1126 (10), 1112 (27), 1111 (40) [$2M$+Na^+], 1110 (14), 1109 (11), 1025 (2), 1009 (6), 645 (2), 583 (5), 569 (10), 568 (38), 567 (100) [M+Na^+], 565 (6), 465 (3); HRMS: *m/z*: calcd for $C_{33}H_{56}O_4Si$+H (545.8): 545.40190 (correct HRMS).

7-Bromo-1,4-dioxaspiro[4,5]decan-8-one (17b): According to GP 1, (1,4-dioxaspiro[4.5]dec-7-en-8-yloxy)trimethylsilane (**16**) (2.50 g, 11.0 mmol), NBS (2.34 g, 13.2 mmol), sodium acetate (108 mg, 1.32 mmol) in THF/water (100 mL) at ambient temperature for 3.5 h, after work-up with diethyl ether (2×75 mL), sat. $NaHCO_3$ solution (50 mL), water (50 mL) and brine (40 mL) gave **17b** as a colorless solid (2.20 g, 85%) which spontaneously decomposed after 10–20 min at ambient temperature. Alternatively, purification by CC on silica gel is possible (pentane/diethyl ether 2:1 + 1% MeOH). R_f=0.34; ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.98–2.15 (m, 2H, CH_2), 2.39 (m, 1H, CH_2), 2.56–2.77 (m, 3H, CH_2), 3.88–4.20 (m, 4H, OCH_2CH_2O), 4.81 (dd, ^3J=12.1, ^3J=6.6 Hz, 1H, 7-H). ^{13}C NMR (75.5 MHz, $CDCl_3$, DEPT): δ=36.15 (−, CH_2), 38.04 (−, CH_2), 45.98 (−, CH_2), 51.56 (+, CH, C-7), 65.43 (−, OCH_2CH_2O), 65.67 (−, OCH_2CH_2O), 108.47 (C_{quat}, C-5), 203.48 (C_{quat}, C-8).

2-Bromo-4-methoxycyclohexanone (17c): According to GP 1, 1,4-dimethoxycyclohexene (**20c**) (3.00 g, 21.1 mmol), NBS (4.10 g, 23.0 mmol), sodium acetate (218 mg, 2.66 mmol) in THF/water (90 mL) at ambient temperature for 3 h, after work-up with diethyl ether (2×80 mL), sat. $NaHCO_3$ (50 mL), water (50 mL) and brine (40 mL) gave **17c** as a yellow oil (3.17 g, 73%). R_f=0.44 (pentane/diethyl ether 2:1); IR (film): $\tilde{\nu}$= 2931, 1723, 1653, 1457, 1355, 1302, 1181, 1137, 1095, 1053, 926, 827, 786 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.86–2.36 (m, 3H, CH_2), 2.50–2.79 (m, 3H, CH_2), 3.38 (s, 3H, OCH_3), 3.70 (m, 1H, 4-H), 4.73 (dd, ^3J= 8.5, ^3J=5.5 Hz, 1H, 2-H); ^{13}C NMR (69.7 MHz, $CDCl_3$, DEPT): δ=30.2 (−, CH_2), 34.9 (−, CH_2), 41.7 (−, CH_2), 51.1 (+, CH, C-2), 56.2 (+, OCH_3), 74.2 (+, CH, C-4), 201.8 (C_{quat}, C-1); EI-MS (70 eV): *m/z* (%): 207/205 (11/13), 190 (1), 174 (2), 151 (4), 133 (3), 127 (100), 120 (1), 113 (4), 109 (2), 99 (16), 95 (30), 85 (58), 74 (82), 67 (68), 58 (24), 55 (72); HRMS: *m/z*: calcd for $C_7H_{11}BrO_2$ (207.1): 205.9943 (correct HRMS).

1,4-Dimethoxycyclohexene (20c): To a suspension of sodium hydride (400 mg, 10.0 mmol, 60% in mineral oil) in THF (45 mL) a solution of 1-methoxycyclohexene-4-ol (**19**) (1.00 g 7.81 mmol) in THF (15 mL) was added at 0°C, and the mixture was stirred for 10 min. After dropwise addition of methyl iodide (2.22 g, 15.6 mmol), the mixture was warmed to ambient temperature and stirred for 1 h. The reaction mixture was poured into diethyl ether (45 mL) and washed with water (2×20 mL). After extraction of the combined aqueous phases with diethyl ether (20 mL), the organic layers were dried over $MgSO_4$. The solvent was removed in vacuo, and the residue was purified by CC on silica gel (pentane/diethyl ether 1:1) to yield product **20c** as a colorless oil (1.07 g, 96%). R_f=0.73; IR (film): $\tilde{\nu}$=2928, 1669, 1617, 1576, 1559, 1540, 1533, 1521, 1447, 1385, 1354, 1322, 1298, 1247, 1208, 1171, 1158, 1104, 1058, 1027, 1003, 966, 930, 881, 873, 836, 788, 779, 715, 665 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.61–1.80 (m, 1H, CH_2), 1.81–1.95 (m, 1H, CH_2), 1.99–2.22 (m, 3H, CH_2), 2.31–2.42 (m, 1H, CH_2), 3.34 (m, 3H, OCH_3), 3.40 (m, 1H, 4-H), 3.49 (s, 3H, OCH_3), 4.43 (m, 1H, 2-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=25.4 (−, CH_2), 26.9 (−, CH_2), 29.0 (−, CH_2), 53.9 (+, OCH_3), 55.8 (+, OCH_3), 75.3 (+, CH, C-4), 89.6 (+, CH, C-2), 154.6 (C_{quat}, C-1); EI-MS (70 eV): *m/z* (%): 142 (39) [M^+], 127 (1) [M^+−CH_3], 111 (13) [M^+−OCH_3], 110 (28) [M^+−$HOCH_3$], 101 (12), 95 (4), 88 (5), 84 (100), 79 (9), 71 (6), 67 (7), 58 (8), 54 (12), 45 (8), 43 (52), 41 (20).

***tert*-Butyl (+)-(7*R*,8*R*,13*S*,14*S*,17*S*)-17-*tert*-butoxy-13-methylspiro(1′,3′-dioxolane[2′.3]-2,3,4,6,7,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene)-7-carboxylate (*trans*-24b), *tert*-butyl (7*R*,13*S*,14*S*,17*S*)-17-*tert*-butoxy-13-methylspiro(1′,3′-dioxolane[2′.3]-2,3,4,7,8,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene)-7-carboxylate (*trans*-13b)**: According to GP 9, *trans*-**12b** (40.0 mg, 0.0847 mmol) in decalin (2.00 mL) at 215°C for 30 min, after purification by CC on silica gel (25 g, pentane/diethyl ether 5:1) *trans*-**24b** (25.3 mg, 63%) and the regioisomer *trans*-**13b** (6.0 mg, 15%) were both obtained as colorless waxes.

trans-**24b**: R_f=0.36; $[\alpha]_D^{20}$=+27 (c=0.100, C_6H_6); IR (film): $\tilde{\nu}$=2978, 2930, 2870, 1729, 1477, 1456, 1388, 1391, 1366, 1255, 1197, 1165, 1098, 1062, 946, 906, 734 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$, H,H-COSY): δ= 0.72 (s, 3H, CH_3), 1.14 [s, 9H, $C(CH_3)_3$], 1.18–1.31 (m, 1H), 1.36 [s, 9H, $CO_2C(CH_3)_3$], 1.38–1.62 (m, 2H), 1.63–2.13 (m, 7H), 2.15–2.58 (m, 6H), 2.69 (t, ^3J=7.1 Hz, 1H, 7-H), 3.52 (t, ^3J=9.7 Hz, 1H, 17-H), 3.88–4.06 (m. 4H, 4′-H, 5′-H), 5.63 (m, 1H, 6-H); ^{13}C NMR (62.9 MHz, C_6D_6, DEPT, HSQC, HMBC, NOESY): δ=12.0 (+, CH_3), 24.4 (−, CH_2), 24.7 (−, CH_2), 28.1 [+, 3C, $C(CH_3)_3$], 28.8 [+, 3C, $CO_2C(CH_3)_3$], 31.6 (−, CH_2), 31.9 (−, CH_2), 34.6 (−, CH_2), 39.7 (−, CH_2), 41.2 (+, CH), 41.6 (+, CH), 42.0 (C_{quat}, C-13), 42.0 (−, CH_2), 43.5 (+, CH, C-14), 64.2 (−, CH_2, C-4′), 64.3 (−, CH_2, C-5′), 72.1 [C_{quat}, $C(CH_3)_3$], 79.2 [C_{quat}, $CO_2C(CH_3)_3$], 81.1 (+, CH, C-17), 108.3 (C_{quat}, C-3), 119.0 (+, CH), 126.9 (C_{quat}), 127.3 (C_{quat}), 134.8 (C_{quat}), 172.4 (C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 472 (38) [M^+], 416 (100) [M^+−C_4H_8], 371 (12), 359 (62) [M^+−C_4H_8−C_4H_9], 331 (7), 298 (8), 253 (5), 195 (4), 159 (6), 99 (8), 83 (11), 57 (44) [$C_4H_9^+$], 41 (8); elemental analysis calcd (%) for $C_{29}H_{44}O_5$ (472.7): C 73.69, H 9.32; found C 73.39, H 9.04.

trans-**13b**: R_f=0.45; IR (film): $\tilde{\nu}$=2977, 2932, 2867, 1725, 1477, 1456, 1383, 1362, 1245, 1197, 1154, 1099, 1078, 945, 901, 732 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.74 (s, 3H, CH_3), 0.78–1.01 (m, 1H), 1.17 [s, 9H, $C(CH_3)_3$], 1.22–1.35 (m, 1H), 1.41 [s, 9H, $CO_2C(CH_3)_3$], 1.48–2.52 (m, 15H), 2.73–2.84 (m, 1H, 7-H), 3.59 (dd, ^3J=9.0, ^3J=8.5 Hz, 1H, 17-H), 3.89–4.08 (m, 4H, C-4′, C-5′); ^{13}C NMR (62.9 MHz, C_6D_6, DEPT): δ= 11.4 (+, CH_3), 24.0 (−, 2C, CH_2), 24.7 (−, CH_2), 28.0 [+, 3C, $C(CH_3)_3$], 28.9 [+, 3C, $CO_2C(CH_3)_3$], 30.9 (−, CH_2), 31.5 (−, CH_2), 31.8 (−, CH_2), 39.1 (−, CH_2), 34.0 (−, CH_2), 40.5 (−, CH_2), 41.1 (+, CH, C-14), 42.0 (C_{quat}, C-13), 45.9 (+, C-7), 64.3 (−, CH_2, C-4′), 64.3 (−,CH_2, C-5′), 72.2 [C_{quat}, $C(CH_3)_3$], 77.7 (+, C-17), 80.0 [C_{quat}, $CO_2C(CH_3)_3$], 107.9 (C_{quat}, C-3), 124.5 (C_{quat}), 126.8 (C_{quat}), 127.1 (C_{quat}), 129.1 (C_{quat}), 173.4 (C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 472 (10) [M^+], 416 (22) [M^+−C_4H_8], 415 (21) [M^+−C_4H_9], 371 (7), 359 (100) [M^+−C_4H_8−C_4H_9], 313 (5), 298 (6), 269 (3), 253 (5), 233 (2), 195 (3), 99 (2), 83 (11), 57 (6) [$C_4H_9^+$], 41 (2); HRMS: *m/z*: calcd for $C_{29}H_{44}O_5$ (472.3): 472.3189 (correct HRMS).

***tert*-Butyl (13*S*,14*S*,17*S*)-17-*tert*-butoxy-13-methylspiro(1′,3′-dioxolane-[2′.3]-2,3,4,6,7,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene)-7-carboxylate (25), (13*S*,14*S*,17*S*)-17-*tert*-Butoxy-13-methylspiro(1′,3′-dioxolane[2′.3]-2,3,4,11,12,13,14,15,16,17-decahydro-1*H*-cyclopenta[*a*]phenanthrene) (26)**: According to GP 9, a solution of the hexatriene *trans*-**12b** (40 mg, 0.085 mmol) in decalin (1.0 mL) was heated to 260°C for 20 min. After purification of the residue by CC on silica gel (15 g, pentane/diethyl ether 10:1) besides minor amounts of the steroid analogues *trans*-**24b** and *trans*-**13b,** the tetracycles **25** (4.9 mg, 16%) and **26** (4.3 mg, 14%) were both obtained as colorless waxes.

Compound **25**: R_f=0.21; ^{1}H NMR (250 MHz, C_6D_6): δ=0.91 (s, 3H, CH_3), 1.20 [s, 9H, $C(CH_3)_3$], 1.21–1.73 (m, 6H), 1.75–2.11 (m, 7H), 2.13–2.43 (m, 4H), 2.47–2.78 (m, 2H), 3.41 (dd, ^3J=9.8, ^3J=7.6 Hz, 1H, 17-H), 3.89–4.02 (m, 4H, C-4′, C-5′); EI-MS (70 eV): *m/z* (%): 372 (87) [M^+], 315 (68) [M^+−C_4H_9], 253 (23), 230 (14), 202 (20), 169 (14), 155 (18), 129 (13), 99 (74), 83 (34), 57 (100) [$C_4H_9^+$], 41 (31).

Compound **26**: R_f=0.35; ^{1}H NMR (250 MHz, C_6D_6): δ=0.99 (s, 3H, CH_3), 1.21 [s, 9H, $C(CH_3)_3$], 1.32–1.75 (m, 4H), 1.92–2.30 (m, 4H), 2.55–2.65 (m, 2H), 2.69–2.92 (m, 3H), 3.00 (m, 2H, 4-H), 3.59 (t, ^3J=6.8 Hz, 1H, 17-H), 4.06 (s, 4H, C-4′, C-5′), 6.80–6.98 (m, 2H, Ar-H); EI-MS (70 eV): *m/z* (%): 370 (66) [M^+], 314 (82) [M^+−C_4H_8], 313 (100) [M^+−C_4H_9], 295 (62), 270 (24), 257 (43), 251 (64), 225 (12), 195 (19), 170 (18), 155 (22), 141 (12), 99 (10), 83 (3), 57 (56) [$C_4H_9^+$], 41 (16).

***tert*-Butyl (7*R*,8*R*,13*S*,17*S*,14*R*)-17-*tert*-butoxy-13-methyl-3-oxo-2,3,6,7,8,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene-7-carboxylate (*cis*-27)**: According to GP 9, *cis*-**29** (71 mg, 0.166 mmol) in toluene (1.0 mL) at 140°C for 14 h, after purification by CC on silica gel (15 g, pentane/diethyl ether 1:1) gave *cis*-**27** as a colorless wax (36 mg, 51%). R_f=0.32; IR (film): $\tilde{\nu}$=2948, 1733, 1674, 1623, 1496, 1464, 1387, 1362, 1253, 1229, 1192, 1164, 754, 689, 667 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.83 (s, 3H, CH_3), 1.14 [s, 9H, $C(CH_3)_3$], 1.18–1.35 (m, 2H), 1.38 [s, 9H, $CO_2C(CH_3)_3$], 1.40–2.00 (m, 6H), 2.30–2.74 (m, 8H), 2.88 (m, 1H), 3.52 (dd, ^3J=11.1, ^3J=7.4 Hz, 1H, 17-H), 5.69 (s, 1H, 4-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ=22.0 (+, CH_3), 22.3 (−, CH_2),

25.0 (−, CH_2), 25.6 (−, CH_2), 26.8 (−, CH_2), 28.1 [+, 3C, $C(CH_3)_3$], 28.8 [+, 3C, $CO_2C(CH_3)_3$], 32.1 (−, CH_2), 32.4 (−, CH_2), 36.8 (−, CH_2), 42.05 (+, CH, C-14), 42.11 (C_{quat}, C-13), 43.6 (+, CH, C-8), 44.8 (+, CH, C-7), 72.6 [C_{quat}, $C(CH_3)_3$], 80.2 [C_{quat}, $CO_2C(CH_3)_3$], 80.8 (+, CH, C-17), 122.0 (+, CH, C-4), 125.1 (C_{quat}), 144.7 (C_{quat}), 154.5 (C_{quat}), 172.2 (C_{quat}, OC=O), 199.6 (C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 428 (2) [M^+], 372 (35) [$M^+-C_4H_8$], 370 (1), 327 (7), 316 (100) [$M^+-2C_4H_8$], 298 (22), 271 (14), 253 (26), 213 (4), 206 (7), 171 (4), 159 (11), 129 (5), 91 (3), 84 (70), 57 (86) [$C_4H_9^+$], 41 (23); HRMS: *m/z*: calcd for $C_{27}H_{40}O_4$+H (429.6): 429.2999 (correct HRMS).

***tert*-Butyl (7*R*,8*R*,13*S*,14*S*,17*S*)-17-*tert*-butoxy-13-methyl-3-oxo-2,3,6,7,8,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene-7-carboxylate (*trans*-27)**: According to GP 9, *trans*-**29** (420 mg, 0.980 mmol) in toluene (10 mL) at 140 °C for 14 h, after purification by CC on silica gel (30 g, pentane/diethyl ether 1:1) gave *trans*-**27** as colorless crystals (317 mg, 75 %). Good quality crystals for X-ray diffraction were grown from pentane/diethyl ether 1:1 by slow evaporation of solvents at 23 °C. R_f = 0.29; m.p. 161–163 °C; $[\alpha]_D^{20}$ = −77 (*c* = 1.11, MeOAc); IR (KBr): $\tilde{\nu}$ = 2972, 2930, 1728, 1667, 1611, 1460, 1389, 1365, 1254, 1227, 1197, 1149, 1107, 1066, 1034, 903, 858 cm^{-1}; ^1H NMR (250 MHz, C_6D_6): δ = 0.89 (s, 3H, CH_3), 1.09 [s, 9H, $C(CH_3)_3$], 1.32 [s, 9H, $CO_2C(CH_3)_3$], 1.38–1.93 (m, 8H), 2.14–2.33 (m, 4H), 2.36–2.59 (m, 5H), 3.22 (t, ^3J = 8.3 Hz, 1H, 17-H), 5.83 (s, 1H, 4-H); ^{13}C NMR (75.6 MHz, C_6D_6, APT): δ = 10.8 (+, CH_3), 24.3 (−, CH_2), 25.8 (−, CH_2), 25.9 (−, CH_2), 28.0 [+, 3C, C-(CH_3)$_3$], 28.8 [+, 3C, $CO_2C(CH_3)_3$], 31.6 (−, CH_2), 34.1 (−, CH_2), 36.7 (−, CH_2), 37.4 (−, CH_2), 41.5 (+, CH), 42.1 (+, CH), 43.1 (−, C_{quat}, C-13), 45.9 (+, CH), 72.2 [−, C_{quat}, $C(CH_3)_3$], 79.9 [−, C_{quat}, $CO_2C(CH_3)_3$], 80.4 (+, CH, C-17), 123.5 (+, CH, C-4), 125.4 (−, C_{quat}), 142.7 (−, C_{quat}), 153.0 (−, C_{quat}), 171.5 (−, C_{quat}, OC=O), 197.3 (−, C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 428 (1) [M^+], 388 (2), 372 (44) [$M^+-C_4H_8$], 335 (1), 328 (4), 316 (20) [$M^+-2C_4H_8$], 271 (8), 253 (16), 225 (6), 211 (40), 195 (4), 159 (10), 147 (24), 119 (100), 104 (95), 77 (48), 57 (42) [$C_4H_9^+$], 44 (37).

***tert*-Butyl (8*R*,13*S*,14*S*,17*S*)-17-*tert*-butoxy-13-methyl-3-oxo-2,3,4,5,8,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[a]phenanthrene-7-carboxylate (*trans*-28)**: According to GP 8 *trans*-**24b** (30 mg, 0.064 mmol) in acetone (5.0 mL) with *p*-toluenesulfonic acid (5.0 mg, 26 μmol) at 36 h at ambient temperature after work-up with diethyl ether (35 mL), sat. $NaHCO_3$ solution (2×10 mL), back-extraction with diethyl ether (2× 15 mL) and CC on silica gel (10 g, pentane/diethyl ether 1:1) gave *trans*-**27** (14 mg, 51 %) as colorless crystals and *trans*-**28** as a colorless wax (12 mg, 44 %).

trans-**28**: R_f = 0.42; IR (film): $\tilde{\nu}$ = 2951, 1727, 1703, 1652, 1479, 1461, 1339, 1261, 1236, 1192, 1104, 752, 689 cm^{-1}; ^1H NMR (250 MHz, C_6D_6): δ = 0.98 (s, 3H, CH_3), 1.13 [s, 9H, $C(CH_3)_3$], 1.16–1.28 (m, 2H), 1.31 [s, 9H, $CO_2C(CH_3)_3$], 1.37–1.78 (m, 3H), 1.87–2.31 (m, 11H), 2.35–2.72 (m, 11H), 3.45 (t, ^3J = 7.6 Hz, 1H, 17-H), 5.57 (m, 1H, 6-H); ^{13}C NMR (62.9 MHz, C_6D_6, DEPT): δ = 11.9 (+, CH_3), 24.4 (−, CH_2), 25.7 (−, CH_2), 28.1 [+, 3C, $C(CH_3)_3$], 28.8 [+, 3C, ($CO_2C(CH_3)_3$], 31.7 (−, CH_2), 33.5 (−, CH_2), 38.8 (−, CH_2), 39.6 (−, CH_2), 40.9 (+, CH), 41.3 (+, CH), 42.0 (C_{quat},C-13), 43.6 (+, CH, C-14), 45.1 (−, CH_2), 72.1 [C_{quat}, $C(CH_3)_3$], 79.3 [C_{quat}, $CO_2C(CH_3)_3$], 81.0 (+, CH, C-17), 120.3 (+, CH), 127.2 (C_{quat}), 127.8 (C_{quat}), 134.0 (C_{quat}), 172.1 (C_{quat}, OC=O), 201.3 (C_{quat}, C=O); MS (70 eV): m/z (%): 428 (4) [M^+], 372 (20) [$M^+-C_4H_8$], 368 (27), 335 (18), 315 (41) [$M^+-C_4H_8-C_4H_9$], 263 (31), 271 (10), 258 (33), 211 (6), 172 (4), 159 (11), 99 (5), 82 (7), 57 (100) [$C_4H_9^+$], 41 (26).

***tert*-Butyl (*E*)-(1″*S*,3a″*R*,7a″*S*)-3-[2′-(1″-*tert*-Butoxy-7a″-methyl-2″,3″,3a″,6″,7″,7a″-hexahydro-1″*H*-inden-5″-yl)-5′-oxocyclohex-1′-enyl]acrylate (*cis*-29)**: According to GP 8, the hexatriene *cis*-**12b** (110 mg, 0.233 mmol) in acetone (15 mL) and water (150 μL, 8.33 mmol) with pyridinium *p*-toluenesulfonate (14.4 mg, 57.5 μmol) at 60 °C for 12 h, after work-up with diethyl ether (50 mL), sat. $NaHCO_3$ solution (2×15 mL) and back-extraction with diethyl ether (2×25 mL) and CC on silica gel (45 g, pentane/diethyl ether 3:1) gave *cis*-**29** as a colorless wax (60.4 mg, 61 %). R_f = 0.37; IR (film): $\tilde{\nu}$ = 2974, 2939, 2908, 2850, 1737, 1687, 1632, 1573, 1552, 1513, 1479, 1450, 1391, 1369, 1308, 1257, 1196, 1155, 1117, 1083, 1025, 738, 654 cm^{-1}; ^1H NMR (250 MHz, C_6D_6): δ = 1.11 (s, 3H, CH_3), 1.18 [s, 9H, $C(CH_3)_3$], 1.20–1.41 (m, 2H), 1.43 [s, 9H, $CO_2C(CH_3)_3$], 1.49–1.78 (m, 3H), 1.80–2.02 (m, 3H), 2.06 (m, 2H), 2.12–2.24 (m, 3H), 2.75 (s, 2H), 3.63 (t, ^3J = 7.7 Hz, 1H, 1″-H), 5.31 (m, 1H, 4″-H), 5.71 (d, ^3J = 15.2 Hz, 1H, 3-H), 7.83 (d, ^3J = 16.4 Hz, 1H, 2-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 21.4 (+, CH_3), 24.9 (−, CH_2), 28.18 [+, 3C, $CO_2C(CH_3)_3$], 28.19 [+, 3C, $C(CH_3)_3$], 28.8 (−, CH_2), 29.2 (−, CH_2), 29.5 (−, CH_2), 30.6 (−, CH_2), 35.0 (−, CH_2), 38.0 (−, CH_2), 39.7 (C_{quat}, C-7a″), 44.4 (+, CH, C-3a″), 72.6 [C_{quat}, $C(CH_3)_3$], 76.9 (+, CH, C-1″), 79.7 [C_{quat}, CO_2C-(CH_3)$_3$], 118.4 (+, CH, C-4″), 123.4 (C_{quat}), 132.4 (+, CH), 134.2 (C_{quat}), 142.1 (+, CH), 148.5 (C_{quat}), 166.7 (C_{quat}, OC=O), 207.00 (C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 428 (1) [M^+], 372 (10) [$M^+-C_4H_8$], 316 (32) [$M^+-2\times C_4H_8$], 298 (14), 278 (6), 253 (12), 234 (99), 233 (100), 222 (28), 179 (18), 165 (17), 157 (6), 131 (31), 103 (40), 77 (37), 57 (62) [$C_4H_9^+$], 41 (17); $C_{27}H_{40}O_4$ (428.6).

***tert*-Butyl (*E*)-(1″*S*,3a″*S*,7a″*S*)-3-[2′-(1″-*tert*-butoxy-7a″-methyl-2″,3″,3a″,6″,7″,7a″-hexahydro-1″*H*-inden-5″-yl)-5′-oxocyclohex-2′-enyl]acrylate (*trans*-29)**: According to GP 8, the hexatriene *trans*-**12b** (650 mg, 1.38 mmol) in acetone (45 mL) and water (300 μL, 16.7 mmol) with *p*-toluenesulfonic acid (141 mg, 741 μmol) at ambient temperature for 12 h, after work-up with diethyl ether (90 mL), sat. $NaHCO_3$ solution (2× 25 mL), back-extraction with diethyl ether (2×30 mL) and CC on silica gel (50 g, pentane/diethyl ether 3:1) gave *trans*-**29** as a colorless wax (497 mg, 84 %). R_f = 0.33; IR (film): $\tilde{\nu}$ = 2974, 2970, 2934, 1728, 1653, 1635, 1600, 1496, 1457, 1436, 1370, 1285, 1236, 1210, 1147, 1111, 1080, 1065, 1015, 950, 904, 844, 753, 695, 629 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.81 (s, 3H, CH_3), 1.18 [s, 9H, $C(CH_3)_3$], 1.47 [s, 9H, CO_2C-(CH_3)$_3$], 1.56–2.12 (m, 5H), 2.16–2.25 (m, 3H), 2.46–2.60 (m, 3H), 2.61–2.72 (m, 2H), 3.03 (s, 2H), 3.30 (dd, ^3J = 9.8, ^3J = 7.5 Hz, 1H, 1″-H), 5.43 (s, 1H, 4″-H), 5.62 (d, ^3J = 15.9 Hz, 1H, 1-H), 7.63 (d, ^3J = 15.9 Hz, 1H, 3-H); ^{13}C NMR (75.5 MHz, $CDCl_3$, APT): δ = 11.3 (+, CH_3), 24.4 (−, CH_2), 26.7 (−, CH_2), 28.2 [+, 3C, $C(CH_3)_3$], 28.7 [+, 3C, $CO_2C(CH_3)_3$], 30.0 (−, CH_2), 31.5 (−, CH_2), 33.8 (−, CH_2), 38.2 (−, CH_2), 39.9 (−, CH_2), 41.8 (−, C_{quat}, C-7a″), 43.7 (+, CH, C-3a″), 72.4 [−, C_{quat}, $C(CH_3)_3$], 79.1 (+, CH, C-1″), 80.2 [−, C_{quat}, $CO_2C(CH_3)_3$], 118.3 (+, CH, C-2), 125.8 (−, C_{quat}), 129.1 (+, CH), 136.6 (−, C_{quat}), 141.6 (+, CH), 148.4 (−, C_{quat}), 166.6 (−, C_{quat}, OC=O), 209.0 (−, C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 428 (1) [M^+], 388 (2), 372 (48) [$M^+-C_4H_8$], 327 (2), 316 (30) [$M^+-2\times C_4H_8$], 315 (24) [$M^+-C_4H_8-C_4H_9$], 297 (23), 269 (8), 253 (18), 227 (5), 213 (4), 165 (3), 159 (11), 129 (4), 91 (6), 57 (100) [$C_4H_9^+$], 41 (24); HRMS: *m/z*: calcd for $C_{27}H_{40}O_4$ (428.6): 428.2927 (correct HRMS).

Methyl (*E*)-(1″*S*,3a″*S*,7a″*S*)-3-[2′-(1″-*tert*-Butoxy-7a″-methyl-2″,3″,3a″,6″,7″,7a″-hexahydro-1″*H*-inden-5″-yl)-5′-oxocyclohex-1′-enyl]acrylate (*trans*-29-Me): According to GP 8, the hexatriene *trans*-**12b**-Me (520 mg, 1.21 mmol) in acetone (40 mL) and water (300 μL, 16.7 mmol) with *p*-toluenesulfonic acid (69.0 mg, 363 μmol) at ambient temperature for 13 h, after work-up with diethyl ether (80 mL), sat. $NaHCO_3$ solution (2× 25 mL), back-extraction with diethyl ether (2×40 mL) and CC on silica gel (50 g, pentane/diethyl ether 3:1) gave *trans*-**29**-Me as a colorless wax (254 mg, 54 %). R_f = 0.27; ^1H NMR (250 MHz, C_6D_6): δ = 0.93 (s, 3H, CH_3), 1.17 [s, 9H, $C(CH_3)_3$], 1.23–1.96 (m, 9H), 2.00–2.12 (m, 4H), 2.71 (s, 2H), 3.22 (t, ^3J = 7.2 Hz, 1H, 1″-H), 3.48 (s, 3H, OCH_3), 5.35 (s, 1H, 5″-H), 5.75 (d, ^3J = 15.2 Hz, 1H, 2-H), 8.00 (d, ^3J = 15.2 Hz, 1H, 3-H).

***tert*-Butyl (7*R*,13*S*,14*R*,17*S*)-17-*tert*-butoxy-13-methyl-3-oxo-2,3,6,7,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene-7-carboxylate (30)**: According to GP 8, *cis*-**13b** (350 mg, 0.740 mmol) in acetone (20 mL) and water (200 μL) with *p*-toluenesulfonic acid (45.0 mg, 236 μmol) at ambient temperature for 16 h, after work-up with diethyl ether (80 mL), sat. $NaHCO_3$ solution (2×25 mL) and back-extraction with diethyl ether (2×40 mL) and CC on silica gel (35 g, pentane/diethyl ether 1:1) gave, besides a fraction containing a complex mixture, a fraction consisting of the steroidal diene **30** as a colorless wax (161 mg, 51 %). R_f = 0.45; IR (film): $\tilde{\nu}$ = 2955, 2924, 2871, 1731, 1649, 1608, 1494, 1439, 1378, 1349, 1279, 1259, 1204, 1168, 1124, 1103, 1080, 1048, 973, 948, 912, 856, 800, 733 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.85 (s, 3H, CH_3), 1.11 [s, 9H, $C(CH_3)_3$], 1.15–1.42 (m, 2H), 1.31 [s, 9H, CO_2C-(CH_3)$_3$], 1.40–1.67 (m, 3H), 1.68–1.80 (m, 1H), 2.00–2.69 (m, 9H), 2.81–2.93 (m, 1H, 10-H), 3.09 (m, 1H, 7-H), 3.44 (dd, ^3J = 6.9, ^3J = 4.4 Hz, 1H, 17-H), 5.81 (s, 1H, 4-H); ^{13}C NMR (75.5 MHz, $CDCl_3$, APT): δ = 18.5 (+, CH_3), 25.2 (−, CH_2), 27.8 (−, CH_2), 28.0 [+, 3C, $C(CH_3)_3$], 28.5 [+, 3C,

$CO_2C(CH_3)_3$], 29.5 (–, CH_2), 30.1 (–, CH_2), 33.8 (–, CH_2), 36.2 (–, CH_2), 38.3 (–, CH_2), 41.6 (+, CH, C-14), 42.5 (–, C_{quat}, C-13), 46.5 (+, CH, C-10), 47.6 (+, CH, C-7), 72.8 [–, C_{quat}, $C(CH_3)_3$], 80.5 (+, CH, C-17), 80.9 [–, C_{quat}, $CO_2C(CH_3)_3$], 125.7 (+, CH, C-4), 128.7 (–, C_{quat}), 130.6 (–, C_{quat}), 163.6 (–, C_{quat}), 171.9 (–, C_{quat}, CO_2), 199.2 (–, C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 428 (1) [M^+], 372 (64) [$M^+-C_4H_8$], 315 (52) [$M^+-C_4H_8-C_4H_9$], 298 (10), 271 (15), 253 (6), 213 (5), 169 (4), 159 (5), 129 (6), 83 (4), 57 (100) [$C_4H_9^+$], 40 (24); HRMS: *m/z*: calcd for $C_{27}H_{40}O_4$+H (429.4): 429.30006 (correct HRMS).

(7*R*,13*S*,14*R*,17*S*)-17-Hydroxy-13-methyl-3-oxo-2,3,6,7,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene-7-carboxylic acid (31): According to GP 10, the steroid **30** (30 mg, 0.070 mmol) in toluene (2 mL) after treatment with BF_3·Et_2O (26.5 mg, 30 μL, 187 μmol) at 0 °C for 1 h, then at ambient temperature for 4 h, work-up and purification by CC on silica gel (10 g, diethyl ether/methanol 3:2) gave **31** as a colorless solid (11 mg, 50 %). R_f = 0.22; m.p. 193–196 °C; IR (KBr): $\tilde{\nu}$ = 2996, 2968, 2955, 2870, 2840, 1702, 1657, 1650, 1556, 1530, 1462, 1450, 1415, 1265, 1209, 1113, 1084, 1022, 922, 800, 774, 754 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.87 (s, 3H, CH_3), 1.17–1.40 (m, 4H), 1.50–1.69 (m, 2H), 1.72–1.86 (m, 1H), 1.99–2.44 (m, 5H), 2.46–2.75 (m, 2H), 2.81–2.93 (m, 1H), 3.17–3.28 (m, 1H), 3.69–3.79 (m, 2H, 17-H, 10-H), 4.89 (br s, 1H, 17-O*H*), 5.87 (s, 1H, 4-H); ^{13}C NMR (75.6 MHz, $CDCl_3$, APT): δ = 16.7 (+, CH_3), 24.98 (–, CH_2), 27.6 (–, CH_2), 28.5 (–, CH_2), 29.3 (–, CH_2), 31.9 (–, CH_2), 35.6 (–, CH_2), 38.2 (–, CH_2), 41.5 (+, CH, C-14), 44.0 (–, C_{quat}, C-13), 45.1 (+, CH, C-10), 45.9 (+, CH, C-7), 82.0 (+, CH, C-17), 125.8 (+, CH, C-4), 129.3 (–, C_{quat}), 129.9 (–, C_{quat}), 163.6 (–, C_{quat}), 176.1 (–, C_{quat}, CO_2H), 200.0 (–, C_{quat}, C=O); ESI-MS (MeOH): *m/z* (%): 1015 (6), 975 (5), 916 (5), 816 (2), 733 (10), 711 (10), 662 (18), 631 (40), 489 (4), 428 (6), 345 (16), 315 (100) [$M-H^+$], 271 (46), 249 (10).

***tert*-Butyl (+)-(7*R*,13*S*,14*R*,17*S*)-17-*tert*-butoxy-3-hydroxy-13-methyl-2,3,4,6,7,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene-7-carboxylate (32)**: To a solution of *cis*-**13d** (95.0 mg, 0.174 mmol) in THF (15.0 mL) was added tetra-*n*-butylammonium fluoride (1.00 mL, 1.00 mmol, 1.0 M in THF). The solution was stirred at ambient temperature for 24 h. The reaction mixture was poured into diethyl ether (35 mL) and washed with water (15 mL). After back-extraction of the aqueous phases with diethyl ether (2×20 mL), the combined organic layers were dried over $MgSO_4$, concentrated in vacuo, and the residue was purified by CC on silica gel (15 g, pentane/diethyl ether 2:1) to yield **32** as a colorless wax (71.3 mg, 95 %) with a diastereomeric ratio of 1:1 for the C-3 epimers. R_f = 0.21; IR (film): $\tilde{\nu}$ = 2972, 2930, 2838, 1684, 1653, 1623, 1559, 1506, 1472, 1457, 1419, 1363, 1248, 1196, 1142, 1084, 1069, 1040, 946, 907, 881, 800, 756, 734, 668, 648 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, distinguishable signals of diastereomers are marked with #): δ = 0.92 (s, 3H, CH_3), 1.18 [s, 9H, $C(CH_3)_3$], 1.40 [s, 9H, $CO_2C(CH_3)_3$], 1.45–1.69 (m, 5H), 1.73–1.82 (m, 2H), 1.87–2.40 (m, 11H), 3.50 (t, ^3J = 5.2 Hz, 1H, 17-H), 3.86 (m, 1H, 3-H), 4.02 (m, 1H, 3-H)#; ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.3 (+, CH_3), 19.5 (+, CH_3)#, 21.2 (–, CH_2), 22.5 (–, CH_2), 23.7 (–, CH_2), 28.0 [+, 3C, $C(CH_3)_3$], 28.6 [+, 3C, $CO_2C(CH_3)_3$], 30.3 (–, CH_2)#, 30.5 (–, CH_2), 30.6 (–, CH_2)#, 31.7 (–, CH_2), 32.1 (–, CH_2)#, 33.6 (–, CH_2), 33.7 (–, CH_2), 39.3 (–, CH_2)#, 39.8 (–, CH_2), 42.1 (C_{quat}, C-13), 43.2 (+, CH, C-14), 47.3 (+, CH, C-7)#, 47.4 (+, CH, C-7), 67.3 (+, CH, C-3), 72.7 [C_{quat}, $C(CH_3)_3$], 79.9 [C_{quat}, $CO_2C(CH_3)_3$], 80.1 (+, CH, C-17), 124.3 (C_{quat}), 127.4 (C_{quat}), 127.6 (C_{quat}), 130.5 (C_{quat}), 173.3 (C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 430 (1) [M^+], 374 (1), 350 (3), 315 (9), 298 (11), 297 (15), 251 (9), 235 (5), 195 (3), 155 (5), 127 (8), 111 (13), 97 (15), 85 (26), 71 (31), 59 (100), 57 (92) [$C_4H_9^+$], 41 (38); HRMS: *m/z*: calcd for $C_{27}H_{42}O_4$ + H^+ (431.6): 431.31546 (correct HRMS).

(–)-(7*R*,8*R*,13*S*,14*R*,17*S*)-17-Hydroxy-13-methyl-3-oxo-2,3,6,7,8,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene-7-carboxylic acid (33): According to GP 10, steroid *trans*-**27** (400 mg, 0.933 mmol) in toluene (60 mL) after treatment with BF_3·Et_2O (88.5 mg, 100 μL, 0.624 mmol) at 0 °C for 1 h then at ambient temperature for 4 h and work-up gave the crude product, which was precipitated from ethyl acetate (5 mL) and pentane (10 mL) to obtain the steroidal acid **33** as a colorless solid (237 mg, 80 %). Good quality crystals for X-ray diffraction were grown from ethyl acetate and pentane by slow diffusion of the solvents into each other at ambient temperature. R_f = 0.36 (EtOAc/MeOH 4:1); m.p. 228–229 °C; $[\alpha]_D^{20}$ = –28 (*c* = 0.980, MeOAc); IR (KBr): $\tilde{\nu}$ = 3334, 2963, 2859, 1717, 1635, 1464, 1394, 1352, 1210, 1146, 1050, 994, 869, 754 cm^{-1}; ^1H NMR (300 MHz, [D$_4$]-MeOH): δ = 0.91 (s, 3H, CH_3), 1.21 (m, 1H), 1.39–1.77 (m, 4H), 1.87–2.08 (m, 2H), 2.26 (m, 1H), 2.35–2.52 (m, 2H), 2.58–2.77 (m, 4H), 2.78–2.95 (m, 3H), 3.59 (t, ^3J = 9.3 Hz, 1H, 17-H), 5.67 (s, 1H, 4-H); ^{13}C NMR (75.6 MHz, [D$_4$]-MeOH, APT, HSQC, HMBC, NOESY): δ = 10.7 (+, CH_3), 24.2 (–, CH_2), 26.5 (–, CH_2), 26.9 (–, CH_2), 30.7 (–, CH_2), 34.4 (–, CH_2), 37.4 (–, CH_2), 37.7 (–, CH_2), 42.3 (+, CH, C-14), 42.6 (+, CH, C-8), 44.5 (–, C_{quat}, C-13), 47.5 (+, CH, C-7), 81.7 (+, CH, C-17), 123.0 (+, CH, C-4), 126.2 (–, C_{quat}), 146.5 (–, C_{quat}), 158.1 (–, C_{quat}), 176.6 (–, C_{quat}, CO_2H), 202.5 (–, C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 316 (100) [M^+], 298 (5), 271 (12), 253 (20), 213 (5), 211 (9), 197 (5), 171 (5), 169 (6), 159 (37), 155 (8), 129 (14), 115 (10), 93 (9), 91 (20), 77 (10), 55 (19), 44 (33), 41 (25).

Methyl (+)-(7*R*,8*R*,13*S*,14*S*,17*S*)-17-hydroxy-13-methyl-3-oxo-2,3,6,7,8,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene-7-carboxylate (34): To a solution of the steroidal acid **33** (79.9 mg, 0.253 mmol) in methanol (4.0 mL) was added dropwise diazomethane in diethyl ether (5.0 mL, 1.5 mmol, ca. 0.3 M) at 0 °C. After stirring the mixture for 10 min, the excess of diazomethane was quenched with acetic acid. The reaction mixture was poured into diethyl ether (40 mL) and washed with sat. $NaHCO_3$ solution (2×20 mL). After back-extraction of the combined aqueous phases with diethyl ether (2×30 mL), the combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, concentrated in vacuo, and the residue was purified by CC on silica gel (20 g, diethyl ether/methanol 10:1) to yield **34** as colorless crystals (82.0 mg, 98 %). Good quality crystals for X-ray diffraction were grown from diethyl ether by slow evaporation of the solvent at ambient temperature. R_f = 0.50; m.p. 209–212 °C; $[\alpha]_D^{20}$ = +6 (*c* = 0.53, EtOAc); IR (KBr): $\tilde{\nu}$ = 3221, 2950, 2935, 1718, 1652, 1456, 1387, 1373, 1278, 1250, 1164, 1105, 1048, 1032, 920, 853, 777 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.91 (s, 3H, CH_3), 0.99–1.39 (m, 2H), 1.41–1.63 (m, 3H), 1.71–1.99 (m, 3H), 2.05 (m, 1H), 2.17–2.78 (m, 9H), 3.28 (s, 3H, OCH_3), 3.51 (t, ^3J = 8.0 Hz, 1H, 17-H), 5.83 (s, 1H, 4-H); ^{13}C NMR (75.6 MHz, $CDCl_3$, APT): δ = 10.6 (+, CH_3), 23.4 (–, CH_2), 25.7 (–, CH_2), 26.1 (–, CH_2), 30.9 (–, CH_2), 32.4 (–, CH_2), 36.8 (–, CH_2), 37.2 (–, CH_2), 41.2 (+, CH, C-14), 41.5 (+, CH, C-8), 43.9 (–, C_{quat}, C-13), 46.7 (+, CH, C-7), 51.0 (s, OCH_3), 80.6 (+, CH, C-17), 123.4 (+, CH, C-4), 125.1 (–, C_{quat}), 143.9 (–, C_{quat}), 153.6 (–, C_{quat}), 172.8 (–, C_{quat}, CO_2Me), 198.4 (–, C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 330 (100) [M^+], 312 (1), 271 (29), 253 (24), 215 (4), 211 (11), 169 (5), 159 (47), 131 (10), 129 (12), 115 (9), 91 (12), 81 (4), 55 (9), 41 (10); HRMS: *m/z*: calcd for $C_{20}H_{26}O_4$ (330.4): 330.1831 (correct HRMS).

Methyl (+)-(7*S*,8*R*,13*S*,14*S*,17*S*)-17-hydroxy-13-methyl-3-oxo-2,3,6,7,8,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene-7-carboxylate (*epi*-34): According to GP 10, the steroid *trans*-**27**-Me (97.0 mg, 0.251 mmol) in toluene (5.0 mL), after treatment with BF_3·Et_2O (44.3 mg, 50.0 μL, 0.312 mmol) at 0 °C for 1 h, then at ambient temperature for 4 h, the crude product was poured into diethyl ether (30 mL), and the mixture washed with water (2×15 mL). After drying the organic phase over $MgSO_4$ and concentration in vacuo, the residue was purified by CC on silica gel (18 g, diethyl ether/methanol 100:1) to yield the steroid *epi*-**34** as a colorless solid (55 mg, 66 %). R_f = 0.22; m.p. 205–207 °C; $[\alpha]_D^{20}$ = +13 (*c* = 1.01, MeOAc); IR (KBr): $\tilde{\nu}$ = 2972, 2952, 2934, 2875, 1728, 1698, 1656, 1650, 1611, 1552, 1536, 1493, 1460, 1439, 1416, 1382, 1350, 1279, 1261, 1203, 1169, 1106, 1077, 1051, 1033, 974, 958, 857, 814, 780 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.88 (s, 3H, CH_3), 1.16–1.63 (m, 5H), 1.65–1.97 (m, 3H), 2.00–2.34 (m, 4H), 2.38–2.93 (m, 6H), 3.61 (s, 3H, OCH_3), 3.66 (t, ^3J = 7.5 Hz, 1H, 17-H), 5.65 (s, 1H, 4-H); ^{13}C NMR (75.6 MHz, $CDCl_3$, APT): δ = 10.3 (+, CH_3), 23.1 (–, CH_2), 25.6 (–, CH_2), 26.0 (–, CH_2), 30.5 (–, CH_2), 32.6 (–, CH_2), 36.2 (–, CH_2), 36.9 (–, CH_2), 40.9 (+, CH, C-14), 41.4 (+, CH, C-8), 43.5 (–, C_{quat}, C-13), 46.3 (+, CH, C-7), 51.6 (+, OCH_3), 80.8 (+, CH, C-17), 123.0 (+, CH, C-4), 125.1 (–, C_{quat}), 144.0 (–, C_{quat}), 154.0 (–, C_{quat}), 173.2 (–, C_{quat}, CO_2CH_3), 199.7 (–, C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 330 (100) [M^+], 312 (2), 286 (1), 271 (28), 253 (22), 211 (9), 169 (7), 159 (39), 129 (12), 91 (9), 59 (5), 55 (4), 41 (9); HRMS: *m/z*: calcd for $C_{20}H_{26}O_4$ (330.4): 330.1831 (correct HRMS).

***tert*-Butyl (7*R*,8*R*,9*R*,10*S*,13*S*,14*S*,17*S*)-17-*tert*-butoxy-13-methyl-3-oxo-2,3,6,7,8,11,12,13,14,15,16,17-dodecahydro-1*H*-19-oxacyclopropa[9,10]-cyclopenta[*a*]phenanthrene-7-carboxylate (35)**: To a solution of *trans*-**27** (78.2 mg, 0.182 mmol) in dichloromethane (2.0 mL) was added *m*-chloroperbenzoic acid (41.7 mg, 0.250 mmol) at ambient temperature, and the mixture was stirred for 48 h. The excess of *m*-chloroperbenzoic acid was quenched with sat. Na_2SO_3 solution (1 mL). The reaction mixture was poured into dichloromethane (25 mL) and the organic layer was washed with water (2×10 mL). After back-extraction of the combined aqueous phases with dichloromethane (20 mL), the combined organic layers were dried over $MgSO_4$, concentrated in vacuo, and the residue was purified by CC on silica gel (10 g, pentane/diethyl ether 1:2) to yield the steroidal epoxide **35** as a colorless wax (35.6 mg, 44 %). R_f=0.24; IR (film): $\tilde{\nu}$= 2972, 2931, 2872, 1724, 1675, 1653, 1617, 1472, 1457, 1388, 1363, 1254, 1227, 1195, 1154, 1106, 1068, 1034, 918 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=0.82 (s, 3H, CH_3), 1.11 [s, 9H, $C(CH_3)_3$], 1.38 [s, 9H, $CO_2C(CH_3)_3$], 1.39–1.55 (m, 3H), 1.57–1.80 (m, 2H), 1.83–2.09 (m, 3H), 2.11–2.22 (m, 3H), 2.27 (m, 1H), 2.30–2.40 (m, 2H), 2.45–2.56 (m, 1H), 2.73 (m, 1H), 2.86 (m, 1H), 3.52 (t, ^3J=7.2 Hz, 1H, 17-H), 6.09 (m, 1H, 4-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, APT): δ=10.2 (+, CH_3), 24.4 (−, CH_2), 25.2 (−, CH_2), 27.3 (−, CH_2), 28.0 [+, 3C, $C(CH_3)_3$], 28.7 [+, 3C, $CO_2C(CH_3)_3$], 30.8 (−, CH_2), 34.0 (−, CH_2), 34.1 (−, CH_2), 34.9 (−, CH_2), 36.9 (+, CH, C-14), 42.6 (−, C_{quat}, C-13), 42.9 (+, CH, C-8), 44.2 (+, CH, C-7), 59.1 (−, C_{quat}, C-9), 66.0 (−, C_{quat}, C-10), 72.4 [C_{quat}, $C(CH_3)_3$], 80.3 [C_{quat}, $CO_2C(CH_3)_3$], 80.5 (+, CH, C-17), 131.3 (+, CH, C-4), 156.7 (−, C_{quat}), 170.6 (−, C_{quat}, OC=O), 198.6 (−, C_{quat}, C=O); EI-MS (70 eV): *m/z* (%): 442 (1), 426 (4), 388 (32), 334 (3), 314 (10), 276 (7), 269 (11), 264 (44), 223 (8), 207 (12), 195 (9), 161 (12), 139 (8), 112 (21), 91 (9), 57 (100) [$C_4H_9^+$]; DCI-MS (NH_3): *m/z* (%): 906 (1) [2*M*+NH_4^+], 491 (5), 482 (7), 462 (70) [*M*+NH_4^+], 445 (100) [*M*+H^+], 406 (18), 344 (2), 276 (1), 150 (1); HRMS: *m/z*: calcd for $C_{27}H_{40}O_5$+H (445.6): 445.29499 (correct HRMS).

***tert*-Butyl (7*S*,8*R*,9*R*,13*S*,14*S*,17*S*)-3-acetoxy-17-*tert*-butoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene-7-carboxylate (36)**: To a solution of the steroid analogue *trans*-**27** (180 mg, 0.420 mmol) in dichloromethane (2.50 mL) was added at 0 °C acetic acid anhydride (286 mg, 2.80 mmol) and acetyl bromide (217 mg, 1.76 mmol). The mixture was stirred at 0 °C for 1.5 h, then poured into diethyl ether (40 mL), and the organic layer was washed with sat. $NaHCO_3$ solution (2×25 mL). The combined aqueous layers were back-extracted with diethyl ether (2×20 mL), the combined organic layers were dried over $MgSO_4$, concentrated in vacuo, and the residue was purified by CC on neutral aluminum oxide (15 g, pentane/diethyl ether 3:1) to yield the estradiol **36** as a colorless wax (137 mg, 69 %). R_f=0.27; IR (film): $\tilde{\nu}$=3050, 2969, 1700, 1667, 1653, 1635, 1559, 1496, 1490, 1457, 1437, 1419, 1387, 1363, 1204, 1153, 1112, 1080, 1030, 900, 736 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=0.84 (s, 3H, CH_3), 1.03 [s, 9H, $C(CH_3)_3$], 1.12–1.41 (m, 3H), 1.46 [s, 9H, $CO_2C(CH_3)_3$], 1.54–1.80 (m, 2H), 1.88–2.10 (m, 1H), 2.27 (s, 3H, $COCH_3$), 2.23–2.36 (m, 2H), 2.59–2.70 (m, 2H), 2.84–3.00 (m, 2H), 3.05 (m, 2H), 3.18 (t, ^3J=6.9 Hz, 1H, 17-H), 6.82–6.91 (m, 2H, Ar-H), 7.29–7.36 (d, ^3J=8.7 Hz, 1H, Ar-H); ^{13}C NMR (75.6 MHz, $CDCl_3$, APT): δ=11.3 (+, CH_3), 21.2 (−, CH_2), 23.8 (−, CH_2), 24.7 (−, CH_2), 27.7 (−, CH_2), 28.0 [+, 3C, $C(CH_3)_3$], 28.7 [+, 3C, $CO_2C(CH_3)_3$], 30.7 (−, CH_2), 32.4 (−, CH_2), 36.6 (−, CH_2), 40.3 (+, CH), 40.7 (+, CH), 43.3 (−, C_{quat}, C-13), 44.3 (+, CH), 72.2 [−, C_{quat}, $C(CH_3)_3$], 80.2 [−, C_{quat}, $CO_2C(CH_3)_3$], 80.4 (+, CH, C-17), 119.3 (+, CH, Ar-C), 122.0 (+, CH, Ar-C), 127.5 (+, CH, Ar-C), 135.3 (−, C_{quat}), 137.9 (−, C_{quat}), 148.3 (−, C_{quat}), 167.7 [−, C_{quat}, $CO_2C(CH_3)_3$], 173.6 (−, C_{quat}, H_3CCO_2); EI-MS (70 eV): *m/z* (%): 470 (1) [M^+], 414 (1) [M^+−C_4H_8], 357 (13), 339 (8), 297 (3), 269 (3), 209 (1), 190 (2), 157 (2), 149 (6), 122 (5), 111 (9), 97 (12), 83 (14), 69 (24), 59 (52), 57 (100) [$C_4H_9^+$], 41 (53); DCI-MS (NH_3): *m/z* (%): 959 (2), 520 (4), 488 (100) [*M*+NH_4^+], 446 (6), 374 (3); HRMS: *m/z*: calcd for $C_{29}H_{42}O_5$ (470.6): 470.3032 (correct HRMS).

(−)-(7*S*,8*R*,9*R*,13*S*,14*S*,17*S*)-3,17-Dihydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene-7-carboxylic acid (37): According to GP 10, estradiol **36** (90.1 mg, 0.191 mmol) in toluene (10 mL) after treatment with BF_3·Et_2O (147 mg, 0.130 mL, 1.04 mmol) at 0 °C for 1 h, then at ambient temperature for 4 h, work-up and purification by CC on silica gel (12 g, chloroform/ethyl acetate/methanol 5:5:1) gave **37** as a colorless solid (49.0 mg, 81 %). Good quality crystals for X-ray diffraction were grown from ethyl acetate and pentane by slow diffusion of the solvents into each other at ambient temperature. R_f=0.41; m.p. 170–171 °C; $[\alpha]_D^{20}$=−12 (*c*=0.500, MeOH); IR (KBr): $\tilde{\nu}$=3342, 3061, 3027, 2953, 2929, 2876, 2856, 1726, 1706, 1648, 1618, 1500, 1441, 1371, 1335, 1244, 1213, 1172, 1159, 1111, 1073, 1048, 1023, 982, 958, 858, 820, 790 cm^{-1}; ^1H NMR (250 MHz, [D_4]-MeOH): δ=1.04 (s, 3H, CH_3), 1.42–1.84 (m, 5H), 1.97–2.29 (m, 3H), 2.46–2.60 (m, 1H), 2.81–3.30 (m, 5H), 3.54 (t, ^3J=8.1 Hz, 1H, 17-H), 6.71–6.82 (s, 2H, Ar-H), 7.32 (d, ^3J= 7.8 Hz, 1H, Ar-H); ^{13}C NMR (69.2 MHz, [D_4]-MeOH, APT): δ=11.7 (+, CH_3), 24.2 (−, CH_2), 26.0 (−, CH_2), 29.0 (−, CH_2), 30.3 (−, CH_2), 33.5 (−, CH_2), 38.9 (+, CH), 41.3 (+, CH), 41.9 (+, CH), 44.6 (+, CH), 45.2 (C_{quat}, C-13), 82.4 (+, CH, C-17), 115.0 (+, CH, Ar-C), 116.8 (+, CH, Ar-C), 128.6 (+, CH, Ar-C), 129.4 (C_{quat}, Ar-C), 138.6 (C_{quat}, Ar-C), 156.2 (C_{quat}, C-Ar), 179.2 (C_{quat}, C=O); DCI-MS (NH_3): *m/z* (%): 351 (4) [*M*+NH_3+NH_4^+], 334 (100) [*M*+NH_4^+], 290 (6), 271 (2), 242 (5), 200 (4), 169 (2), 145 (5), 134 (14), 94 (5), 84 (1).

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[1] D. Refojo, A. C. Liberman, F. Holsboer, E. Arzt, *Immunol. Cell Biol.* **2001**, *79*, 385–394.

[2] a) S. N. Anachenko, I. V. Torgov, *Tetrahedron Lett.* **1963**, 1553–1558; b) N. Cohen, B. L. Banner, W. F. Eichel, D. R. Parrish, G. Saucy, J. M. Cassal, W. Meier, A. Fürst, *J. Org. Chem.* **1975**, *40*, 681–685; c) S. J. Danishefsky, P. Cain, *J. Am. Chem. Soc.* **1976**, *98*, 4975–4983; d) G. H. Posner, C. Switzer, *J. Am. Chem. Soc.* **1986**, *108*, 1239–1244; e) S. Takano, M. Moriya, K. Ogasawara, *Tetrahedron Lett.* **1992**, *33*, 1909–1910; f) R. B. Woodward, F. Sondheimer, D. Taub, *J. Am. Chem. Soc.* **1951**, *73*, 405–407; g) H, Nemoto, N. Matsuhashi, M. Imaizumi, M. Nagai, K. Fukumoto, *J. Org. Chem.* **1990**, *55*, 5625–5631; h) C. D. Dzierba, K. S. Zandi, T. Möllers, K. J. Shea, *J. Am. Chem. Soc.* **1996**, *118*, 4711–4712; i) K. C. Nicolaou, D. Vourloumis, N. Winssinger, P. S. Baran, *Angew. Chem.* **2000**, *112*, 46–126; *Angew. Chem. Int. Ed.* **2000**, *39*, 44–122; j) L. Funk, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1980**, *102*, 5253–5261; k) K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1979**, *101*, 215–217; l) Y. Zang, E. Negishi, *J. Am. Chem. Soc.* **1989**, *111*, 3454–3456; m) E. Negishi, *Pure Appl. Chem.* **1992**, *64*, 323–334; n) Y. Zang, G. Wu, G. Agnel, E. Negishi, *J. Am. Chem. Soc.* **1990**, *112*, 8590–8592; o) L. F. Tietze, T. Nöbel, M. Specha, *Angew. Chem.* **1996**, *108*, 2385–2386; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2259–2261; p) L. F. Tietze, T. Nöbel, M. Specha, *J. Am. Chem. Soc.* **1998**, *120*, 8971–8977.

[3] a) P. v. Zezschwitz, F. Petry, A. de Meijere, *Chem. Eur. J.* **2001**, *7*, 4035–4046.

[4] H. W. Sünnemann, A. de Meijere, *Angew. Chem.* **2004**, *116*, 913–915; *Angew. Chem. Int. Ed.* **2004**, *43*, 895–897.

[5] For an alternative approach to certain steroidal compounds with an assembly of the B-ring by two consecutive Heck couplings, see refs. [2o,p] as well as: L. F. Tietze, S. Peterson, *Eur. J. Org. Chem.* **2001**, 1619–1624, and references therein.

[6] a) U. Eder, G. Sauer, R. Wiechert, *Angew. Chem.* **1971**, *83*, 492–493; *Angew. Chem. Int. Ed. Engl.* **1971**, *10*, 496–497; b) Z. G. Hajos, D. R. Parrish, *J. Org. Chem.* **1974**, *39*, 1612–1614; c) Z. G. Hajos, D. R. Parrish, *Org. Synth.* **1985**, *63*, 26–36.

[7] U. Groth, T. Köhler, T. Taapken, *Tetrahedron* **1991**, *47*, 7583–7592.

[8] J. E. Mc Murry, W. J. Scott, *Tetrahedron Lett.* **1983**, *24*, 979–982.

[9] S. R. Gilbertson, C. A. Challener, M. E. Bos, W. D. Wulff, *Tetrahedron Lett.* **1988**, *29*, 4795–4798.

[10] For reviews on the Heck reaction see: a) S. Bräse, A. de Meijere, in *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: A. de Meijere, F. Diederich), Wiley VCH, Weinheim, **2004**, pp. 217–315; b) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009–3066; c) C. Amatore, M. Azzabi, A. Jutand, *J. Am. Chem. Soc.* **1991**, *113*, 1670–1678; d) S. Bräse, A. de Meijere, in *Handbook of Organopalladium Chemistry for Organic Synthesis* (Eds.: E. Negishi, A. de Meijere), Wiley, New York, **2002**, pp. 1179–1208, 1223–1254; e) A. de Meijere, F. E. Meyer, *Angew. Chem.* **1994**, *106*, 2473–2506; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2379–2411.

[11] Heck coupling protocols on the basis of $Pd(OAc)_2$ and phosphane ligands as triphenylphosphane, other trisarylphosphanes as tris-*o*-tolylphosphane and tris-*n*-butylphosphane with different solvent systems and bases were investigated.

[12] The palladacycle **14** was prepared from $Pd(OAc)_2$ and $(o\text{Tol})_3P$: a) W. A. Herrmann, C. Brossmer, K. Öfele, C.-P. Reisinger, T. Priermeier, M. Beller, H. Fischer, *Angew. Chem.* **1995**, *107*, 1989–1992; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1844–1848; b) W. A. Herrmann, C. Brossmer, K. Öfele, C.-P. Reisinger, T. Priermeier, M. Beller, *Chem. Eur. J.* **1997**, *3*, 1357–1364; for reviews on the application of palladacycles in Heck couplings see: c) J. Dupont, C. S. Consorti, J. Spencer, *Chem. Rev.* **2005**, *105*, 2527–2571; d) W. A. Herrmann, V. P. W. Böhm, C.-P. Reisinger, *J. Organomet. Chem.* **1999**, *576*, 23–41; e) V. Farina, *Adv. Synth. Catal.* **2004**, *346*, 1553–1582.

[13] a) T. L. Gilchrist, R. J. Summersell, *J. Chem. Soc. Perkin Trans. 1* **1988**, 2595–2601; b) R. v. Essen, D. Frank, H. W. Sünnemann, D. Vidovic, J. Magull, A. de Meijere, *Chem. Eur. J.* **2005**, *11*, 6583–6592.

[14] W. J. Kerr, M. Mc Laughlin, A. J. Morrison, P. L. Pauson, *Org. Lett.* **2001**, *3*, 2945–2948.

[15] J. A. Marshall, G. A. Flynn, *Synth. Commun.* **1979**, *9*, 123–127.

[16] K. A. Parker, H. J. Kim, *J. Org. Chem.* **1992**, *57*, 752–755.

[17] When the enolate was generated from **17d** with LiHMDS the non-desired regioisomer of **10d** (compare **23f**) was formed highly regioselectively upon trapping with Tf_2O. Yet, under these same conditions, the methyl ether derivative **17c** was converted into the desired bromoenol triflate **10c** without observing significant amounts of the non-desired regioisomer.

[18] C. R. Johnson, T. J. Marren, *Tetrahedron Lett.* **1987**, *28*, 27–30.

[19] P. L. Stotter, K. A. Hill, *J. Org. Chem.* **1973**, *38*, 2576–2578.

[20] R. K. Sehgal, R. K. Koenigsberger, T. J. Howard, *J. Org. Chem.* **1975**, *40*, 3073–3078.

[21] For reviews on the Stille reaction see: a) T. N. Mitchell in *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, **2004**, pp. 167–202; b) V. Farina, V. Krishnamurthy, W. J. Scott in *The Stille Reaction Organic Reactions* (Ed.: L. A. Paquette), Wiley, New York, **1997**; c) T. N. Mitchell, *Synthesis* **1992**, 803–815; d) M. Kosugi, K. Fugami in *Handbook of Organopalladium Chemistry for Organic Synthesis* (Eds.: E. Negishi, A. de Meijere), Wiley, New York, **2002**, pp. 263–284.

[22] V. Farina, S. Kapüdia, B. Krishnan, C. Wang, L. S. Liebeskind, *J. Org. Chem.* **1994**, *59*, 5905–5911.

[23] The beneficial role of water as a co-solvent in Heck reactions has previously been established. a) N. A. Bumagin, N. P. Andryukhova, I. P Beletskaya, *Izv. Akad. Nauk USSR, Ser. Khim.* **1988**, 1449–1450; *Bull. Acad. Sci. USSR Div. Chem. Sci. (Engl. Transl.)* **1988**, *37*, 1285; b) T. Jeffery, *Tetrahedron Lett.* **1994**, *35*, 3051–3054.

[24] The structures were confirmed by $^1H,^1H$ NOESY experiments in which interactions within the steroid analogue *cis*-**13b** between the protons of the methyl group at C-13 and the proton at C-14 as well as between the proton at C-14 with the proton at C-7 were detected. Within the steroid *trans*-**24b** interactions between the methyl group at C-13 and the proton at C-8 could be observed and also interactions between the proton at C-7 with the proton at C-8 and the proton at C-14 with one proton at C-15 were found.

[25] a) B. M. Trost, P. G. McDougal, *J. Org. Chem.* **1984**, *49*, 458–468; this rotational selectivity has also been termed torquoselectivity, cf. b) E. A. Kallel, Y. Wang, D. C. Spellmeyer, K. N. Houk, *J. Am. Chem. Soc.* **1990**, *112*, 6759–6763; c) J. D. Evanseck, B. E. Thomas IV, D. C. Spellmeyer, K. N. Houk, *J. Org. Chem.* **1995**, *60*, 7134–7141.

[26] CCDC-618817 (*trans*-**27**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif/

[27] a) A. J. Robinson, I. DeLucca, S. Drummond, G. A. Boswell, *Tetrahedron Lett.* **2003**, *44*, 4801–4804; b) G. H. Rasmusson, G. F. Reynolds, T. Utne, R. B. Jobson, L. Raymond, *J. Med. Chem.* **1984**, *27*, 1690–1701.

[28] CCDC-618818 (**33**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif/

[29] CCDC-618819 (**37**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif/

[30] a) D. C. Labaree, J. X. Zhang, H. A. Harris, C. O'Connor, T. Y. Reynolds, R. B. Hochberg, *J. Med. Chem.* **2003**, *46*, 1886–1904; b) N. Bodor, *Trends Pharmacol. Sci.* **1982**, *3*, 53–56; c) J. L. Bowler, J. Timothy, J. D. Pittam, A. Wakeling, *Steroids* **1989**, *54*, 71–100.

[31] The methyl ester analogue of compound *trans*-**27** was obtained along the same synthetic pathway, using the less cleanly and efficiently reacting methyl acrylate instead of *tert*-butyl acrylate in the Heck reaction.

[32] R. M. Weier, L. M. Hofmann, *J. Med. Chem.* **1975**, *18*, 817–821.

[33] J. B. Hendrickson, R. Bergeron, *Tetrahedron Lett.* **1973**, *14*, 4607–4610.

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