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Synthesis of new steroid analogues by samarium diiodide induced cyclisations of γ-naphthyl 1,3-diones

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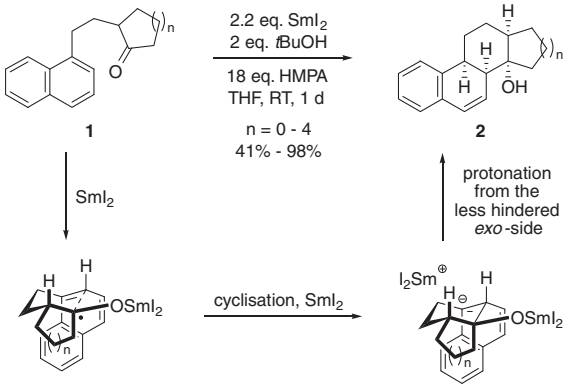
Dedicated to Professor Henri Kagan on the occasion of his 80th birthday.

ABSTRACT

We present the synthesis of new steroid analogues via samarium diiodide mediated intramolecular ketyl–aryl coupling reactions of γ-naphthyl-substituted 1,3-diones. From previous experiments with γ-naphthyl monoketones high stereoselectivities with the 'unnatural' *cis*/*cis* annulation of rings B/C/D were expected. Surprisingly, we observed the formation of two diastereomers with *cis*- and *trans*-fused rings B and C of the tetracyclic skeleton. The diastereoselectivity proved to be strongly dependent on the amount of the proton source employed in the reaction. A rationale for this unexpected behaviour is discussed. In addition, we observed a smooth aluminium chloride induced cyclisation of one of the γ-naphthyl-substituted 1,3-diones to furnish an equilenine precursor. Another cyclisation product was converted by Grob-fragmentation into a naphthannulated cyclononane derivative.

1. Introduction

Kagan et al. introduced samarium diiodide as a selective and versatile electron-donating reagent for organic synthesis.[1] It allows for mild reaction conditions and often furnishes products with high diastereoselectivity.[2] Our group has discovered the ability of samarium diiodide to promote intramolecular reductive ketyl–aryl coupling reactions furnishing interestingly functionalised dearomatised products.[3] Subsequently, we have systematically studied the scope and limitations of these processes. γ-Aryl ketones,[4] their nitrogen analogues prepared from aniline derivatives[5] as well as ketones with indole, pyrrole,[6] and quinoline[7] moieties in γ-position were successfully employed in these samarium diiodide induced intramolecular ketyl–aryl couplings. Furthermore, the influence of substituents on the arene moiety has been explored in detail.[4a] Reactions of simple γ-naphthyl monoketones **1** yielded steroid-like skeletons **2** as single diastereomers with 'unnatural' *cis*/*cis* annulation of rings B/C and C/D (Scheme 1).[8] The excellent diastereoselectivity in these reactions can be explained by a six-membered chair-like transition state in which the bulky samarium alcoholate group occupies an equatorial position. A second electron transfer followed by regioselective protonation from the less hindered *exo*-side affords compounds **2**. Surprisingly, when we exposed γ-naphthyl 1,3-diones to our protocol, in addition to the expected *cis*/*cis*-isomers we isolated significant amounts of the corresponding *trans*/*cis*-isomers.[9] Herein we describe in full detail the role of the proton source on the diastereoselectivity of samarium diiodide mediated intramolecular ketyl–aryl couplings of γ-naphthyl-substituted 1,3-diones.



Scheme 1. Diastereoselective cyclisations of γ-naphthyl monoketones **1** to steroid analogues **2**.[8]

2. Results and discussion

2.1. Synthesis of γ-naphthyl-substituted 1,3-diones

Starting from commercially available tetralone **3a** and 6-methoxytetralone **3b** γ-naphthyl-substituted 1,3-diones **7a**, **7b** and **7c** were prepared in four steps. Addition of vinylmagnesium bromide to the tetralone derivative was followed by a Pd-catalysed allylic substitution with 2-methylcyclopentane-1,3-dione or 2-methylcy-

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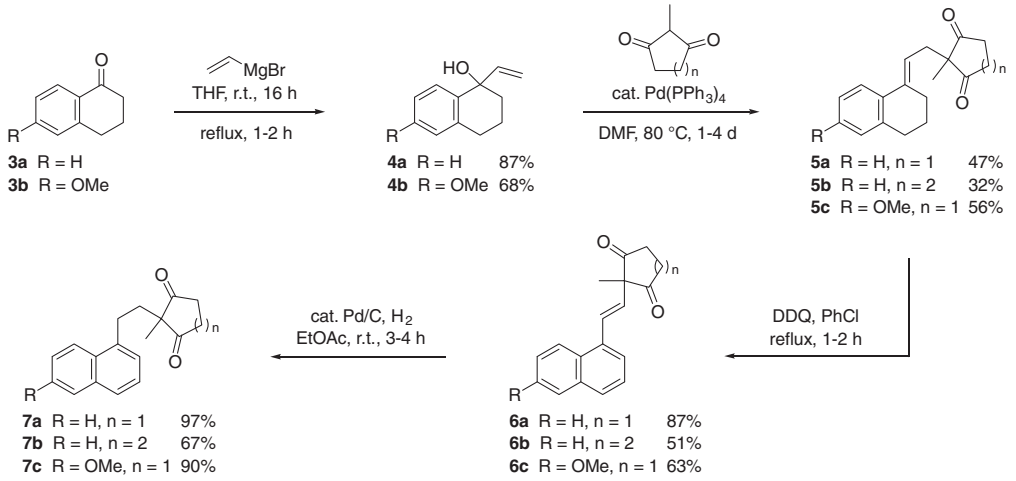
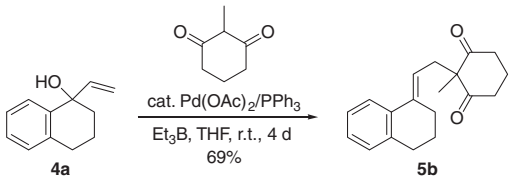


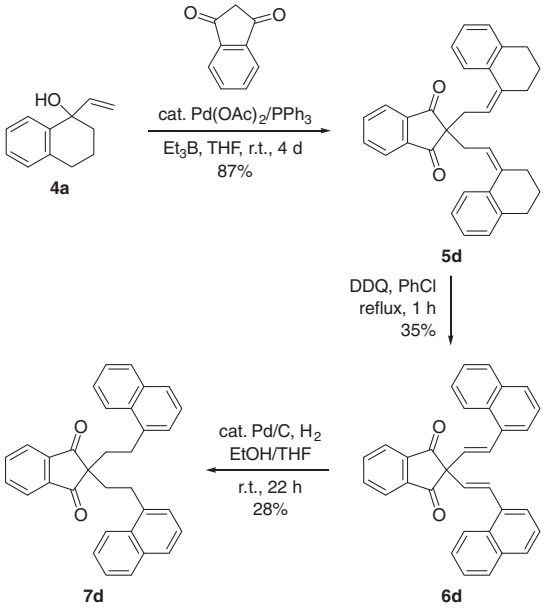
Scheme 2. Synthesis of γ-naphthyl-substituted 1,3-diones **7a**–**7c**.

clohexane-1,3-dione in DMF at 80 °C.[10] Oxidation of **5** with DDQ[11] and subsequent hydrogenation of the double bond in **6** yielded the desired 1,3-diones **7** (Scheme 2). The outcome of the reduction strongly depended on the amount and the reactivity of the palladium catalyst as well as on the reaction time. Too much Pd/C or long reaction times led to partial reduction of the naphthyl moiety. To improve the yield for the Pd-catalysed allylic substitution, we also used alternative reaction conditions with Et_3B in THF at room temperature.[12] Reaction of the six-membered 1,3-dione proceeded smoothly to give **5b** in 69% yield (Scheme 3), whereas the five-membered 1,3-dione did not show significant reactivity under these conditions, presumably due to its lower solubility in THF.



Scheme 3. Alternative reaction conditions for the allylic substitution to product **5b**.

We also prepared γ,γ′-dinaphthyl-substituted dione **7d** by a similar sequence (Scheme 4). The conditions for the oxidation and reduction steps have not been optimised. In the latter we isolated in addition to 28% of **7d** 34% of the mono-hydrogenated compound and 14% of starting material **6d**.



Scheme 4. Synthesis of γ,γ′-dinaphthyl-substituted 1,3-dione **7d**.

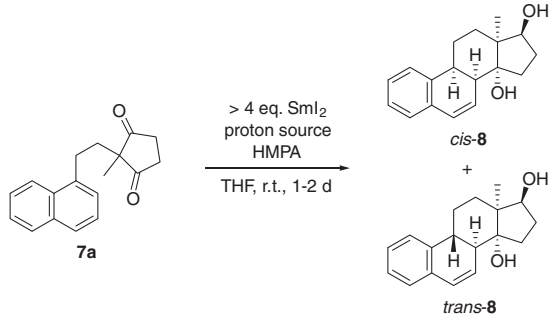
2.2. Reactions with samarium diiodide

The reaction of 1,3-dione **7a** was conducted with 5.5 equiv of SmI_2, 36 equiv of HMPA and varying amounts of the respective proton source (*t*BuOH, MeOH, PhOH or H_2O) in THF (Table 1). With 8 equiv of *t*BuOH we isolated 74% of a 56:44-mixture of the epimers *cis*-**8** and *trans*-**8** (entry 1). Herein *cis* and *trans* refer in all products to the relative configuration of rings B and C of the tetracyclic steroid-like skeleton. With 4 equiv of *t*BuOH the preference for the *cis*-isomer could be improved to 64:36 (entry 2). Changing the proton source to MeOH or PhOH did not show any positive effect on the selectivity (entries 3 and 4). With 2 or 1 equiv of *t*BuOH the selectivity was enhanced, but the yield of steroid analogue **8** dropped to 43%[‡] and 55%, respectively, when we employed our standard procedure A (entries 5 and 6), which consisted in addition of a solution of the starting material **7a** and *t*BuOH in THF to a solution of SmI_2 and HMPA in THF. On the other hand, when we premixed the SmI_2/HMPA/THF-solution with *t*BuOH before adding a solution of **7a** in THF the yield was maintained at approximately 70% and the selectivity increased to 83:17 and 91:9, respectively (procedure B, entries 7 and 8). Remarkably, with 6 equiv of H_2O we found 11% and 6% of two different isomers of *ipso*-coupling product **9** (Scheme 5), in addition to 26% of a 55:45-mixture of *cis*-**8** and *trans*-**8**.[§] The relative configuration of compounds **9** could not be determined with certainty. The *ipso*-attack of samarium-ketyls to arenes has been observed before by Tanaka et al.[13] and by our group.[4a] With 1 equiv of water (entry 10) we obtained **8** with 73% yield and a diastereomeric ratio of 90:10 a similar result as with 1 equiv of *t*BuOH. Nevertheless, we recommend the use of *t*BuOH as a proton source, as the reaction proceeds slightly cleaner; since less by-products are formed the purification is considerably easier. Without any proton source a second intramolecular cyclisation is ob-

[‡] Only 20 equiv instead of 36 equiv of HMPA were applied. This may be the reason for the lower yield of 43% compared with 55% for entry 6.

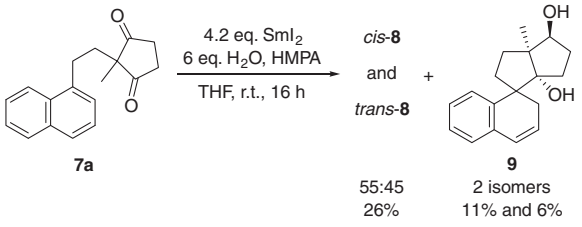
[§] In this experiment we used 4.2 equiv of SmI_2 and 28 equiv of HMPA.

Table 1
Influence of the proton source on the diastereomeric ratio during the synthesis of steroid analogues *cis*-**8** and *trans*-**8**



Entry	Proton source	Procedure	Ratio *cis*-**8**:*trans*-**8**	Yield
1	8 equiv *t*BuOH	A	56:44	74%
2	4 equiv *t*BuOH	A	64:36	74%
3	4 equiv MeOH	A	58:42	not purified
4	4 equiv phenol	A	53:47	not purified
5	2 equiv *t*BuOH	A	70:30	43%
6	1 equiv *t*BuOH	A	95:5	55%
7	2 equiv *t*BuOH	B	83:17	67%
8	1 equiv *t*BuOH	B	91:9	70%
9	6 equiv H_2O	A	55:45	26%
10	1 equiv H_2O	B	90:10	73%

Procedure A: a solution of **7a** and the proton source in THF was added to a solution of SmI_2 and HMPA in THF. Procedure B: a solution of **7a** in THF was added to a solution of SmI_2, HMPA and the proton source in THF.



Scheme 5. *ipso*-Coupling to **9** during transformation of 1,3-dione **7a** with SmI_2 in the presence of water (Table 1, entry 9).

served leading to a novel pentacyclic skeleton (Fig. 1).[9] In all these reactions the mass balance was nearly quantitative and starting material **7a** was completely consumed. As by-products we isolated uncyclised β-hydroxyketones and *cis*- and *trans*-1,3-diols, which are formed by simple reduction of the two carbonyl groups.

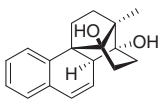
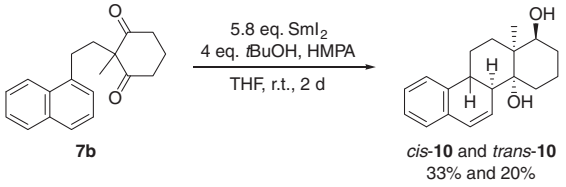
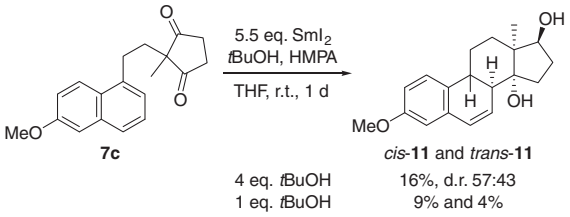


Figure 1. Pentacyclic product generated by reactions of **7a** with SmI_2 without proton source.[9]

The reaction of the homologous 1,3-dione **7b** with SmI_2 and 4 equiv of *t*BuOH proceeded more slowly. After 2 days we isolated 33% of *cis*-**10**, 20% of *trans*-**10** and 25% of starting material **7b** was recovered (Scheme 6). Additionally, we found 13% and 7% of two unknown diastereomeric by-products, which might occur from intramolecular pinacol coupling and subsequent fragmentation



Scheme 6. Synthesis of steroid analogues *cis*-**10** and *trans*-**10**.



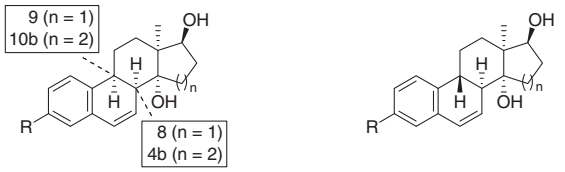
Scheme 7. Synthesis of methoxy-substituted steroid analogues *cis*-**11** and *trans*-**11**.

and reduction.[14] Longer reaction times did not lead to complete conversion of the starting material; no simple reduction of **7b** to the corresponding β-hydroxyketones or 1,3-diols was observed in this case.

As most of physiologically active steroid derivatives bear an oxygen substituent in 3-position of ring A, we applied our cyclisation protocol to methoxy-substituted γ-naphthyl 1,3-dione **7c** (Scheme 7). As expected for donor-substituted arenes,[4a] the yields were considerably lower. With 4 equiv of *t*BuOH as proton source we isolated only 16% of a 57:43-mixture of *cis*-**11** and *trans*-**11**. When we employed only 1 equiv *t*BuOH the preference for the *cis*-isomer could be enhanced to 69:31. As by-products again β-hydroxyketones and *cis*- and *trans*-1,3-diols were isolated.

The relative configurations of tetracyclic products *cis*-**8** and *trans*-**8** were determined via NOE NMR spectra and were unequivocally proven by X-ray analyses.[15] To differentiate between *cis*-**10** and *trans*-**10** or *cis*-**11** and *trans*-**11** we compared the coupling constants and the chemical shifts of the protons 8-H (4b-H) and 9-H

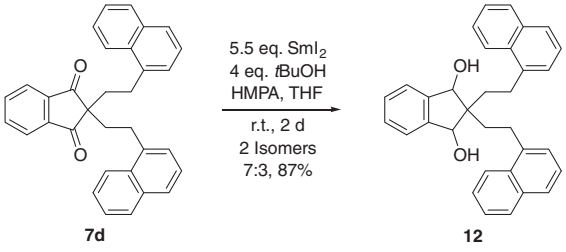
Table 2
Comparison of ^1H and ^{13}C NMR data of *cis*- and *trans*-configured steroid analogues **8**, **10** and **11**



Entry	Compound	8/4b-H (ppm)	9/10b-H (ppm)	C-8/4b (ppm)	C-9/10b (ppm)	$J_{8,9}$/$J_{4b,10b}$ (Hz)
1	*cis*-**8**	2.25	3.34	41.5	36.3	6.9
2	*trans*-**8**	2.19	2.63	44.9	39.3	15.4
3	*cis*-**10**	2.84	3.32	41.1	35.7	6.5
4	*trans*-**10**	2.57	2.75	44.6	37.1	15.9
5	*cis*-**11**	2.49	3.28	41.5	35.5	6.9
6	*trans*-**11**	2.15	2.56	45.2	38.7	15.2

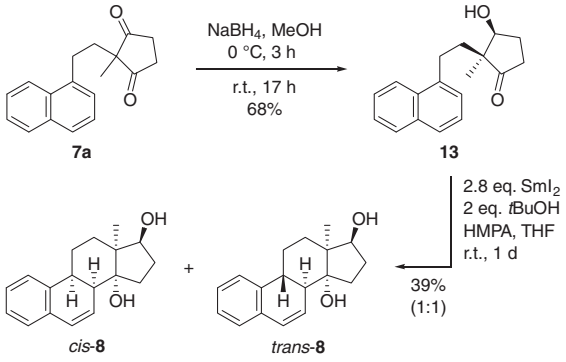
(10b-H) in the ^{1}H NMR spectra as well as the chemical shifts of the corresponding carbons in the ^{13}C NMR spectra (Table 2). The *cis*-isomers of **8**, **10** and **11** show coupling constants of 6.5–6.9 Hz between 8-H and 9-H or 4b-H and 10b-H, respectively, which correspond to dihedral angles of ~30–50°, whereas the *trans*-configuration with a dihedral angle of ~180° is confirmed by coupling constants in the range of 15.2–15.9 Hz. The chemical shifts of the two protons in the *cis*-isomers are located more downfield than in the corresponding *trans*-isomers, whilst the reverse is true for the two carbons C-8 and C-9 or C-4b and C-10b.[16]

A twofold intramolecular ketyl–aryl coupling of dione **7d** may generate an interesting product with eight annulated rings. Unfortunately, treatment of **7d** with SmI_2 only gave the simple reduction product **12** as a 7:3-mixture of two diastereomers in 87% yield (Scheme 8). The fairly high steric hindrance might suppress a cyclisation. Furthermore, the interaction of the $SOMO_{radical}/LUMO_{arene}$ might be less efficient in this example due to a higher energy gap: the ketyl radical is in conjugation with the adjacent aryl group and has thus a lower energy level.



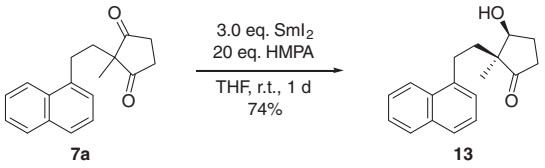
Scheme 8. Reaction of 1,3-dione **7d** with SmI_2.

To get further insight into the stereoselectivity of the protonation step we synthesised β-hydroxyketone **13**. Selective reduction of one of the carbonyl moieties in **7a** with $NaBH_4$ afforded 68% of **13** (Scheme 9) and 18% of its diastereomer *epi*-**13** (not shown). The relative configuration was determined by NOE measurements. Conversion of **13** with 2.8 equiv SmI_2 and 2 equiv of *t*BuOH yielded 39% of a 1:1-mixture of *cis*-**8** and *trans*-**8** hence providing a result similar to entry 1 (Table 1).



Scheme 9. Reaction of β-hydroxyketone **13** with SmI_2.

The reaction of 1,3-dione **7a** with 3.0 equiv samarium diiodide without any proton source yielded 74% of β-hydroxyketone **13** (Scheme 10) together with 14% of a 2:1 mixture of **13** and *epi*-**13** as well as 4% of the tetracyclic compound *cis*-**8**. Surprisingly, the pentacyclic product (Fig. 1) was not formed in this experiment.



Scheme 10. Reaction of 1,3-dione **7a** with 3 equiv of SmI_2 without proton source.

2.3. Discussion

The striking differences of the stereoselectivities of the monoketone cyclisations (Scheme 1) with that of the 1,3-diones described in this report must have its origin in the presence of the second carbonyl group. In an attempt to explain the variation of the diastereoselectivities[¶] we should have a look at the conformations of the conceivable intermediates before cyclisation, ketyls **A**, **B** or **C** (Scheme 11). In ketyl **A** the second carbonyl moiety is still present, **B** is a diketyl[‖,17] or a radical/anion, whereas in **C** the second carbonyl group is already fully reduced to a samarium alcoholate or the corresponding alcohol. After the cyclisation a second electron is transferred by SmI_2 to yield either benzylic anions **D**, **E** or **F** with SmI_2^+ as 'counterion'. Protonation of these anions from the less hindered *exo*-side (backside of the drawing in Scheme 11) leads to the expected *cis*-**8** as product.

For *endo*-protonation, leading to the unexpected *trans*-product, a pre-coordination of *t*BuOH via Sm(II) or Sm(III) to the carbonyl oxygen in **D** or by the samarium alcoholates in **E** and **F** may be decisive. Alternatively, intramolecular *endo*-protonation of alcohols **E** and **F** may also give *trans*-**8**. If more equivalents of *t*BuOH or other proton sources are present in the reaction mixture the equilibria are shifted to these pre-coordinated species or to the alcohols **E** and **F** and hence *endo*-protonation is more likely than with lower amounts of proton sources.

In the reaction of β-hydroxyketone **13** with SmI_2, we can be sure that **F** is an intermediate. Since 3 equiv of protons are present in this reaction (two from *t*BuOH, one from **13**) we would expect a ~2:1 mixture of *cis*-**8** and *trans*-**8** according to the results in Table 1. Instead the ratio is 1:1, which supports the possibility of an intramolecular protonation of anion **F**.

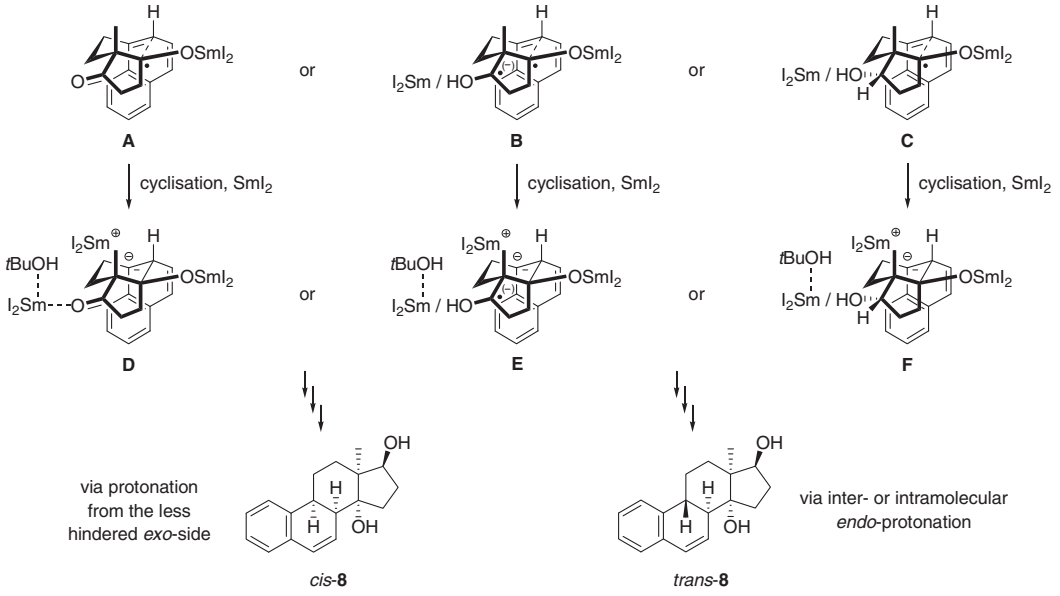
The experiment with 1,3-dione **7a**, 3 equiv of SmI_2 and without *t*BuOH (Scheme 10) provided almost no cyclisation product. Possibly, the equilibrium is either at the side of anion **G** and 1 equiv of SmI_2 (which may be coordinated to the carbonyl group in **G**) or at the side of anion/ketyl radical **H** (Scheme 12). Both, **G** and **H**, can afford alcohols **13** or *epi*-**13** after protonation during aqueous work-up. Although our conclusions are still speculative this experiment provides some evidence for the pathways via **B**/**E** or **C**/**F** as illustrated in Scheme 11.

2.4. Cyclisation with $AlCl_3$ and Grob-fragmentation

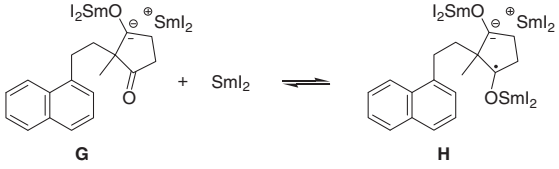
In several unsuccessful attempts to remove the methyl group in **7c** we observed the formation of steroid analogues **14** and **15**. The two products were obtained in good yield when **7c** was subjected to an excess of $AlCl_3$ in MeCN (Scheme 13). Compounds **14** and **15** are known precursors of the mare hormone equilenine which is

[¶] We assume that the protonation at the discussed benzylic position is irreversible, since the acidity of the proton sources should be considerably higher than that of the benzylic C–H. Thus, the diastereoselectivity is not under thermodynamic but under kinetic control.

[‖] Experiments from Flowers[17] indicate that *t*BuOH (other than MeOH, EtOH, PhOH) may not be sufficiently acidic to protonate the samarium ketyl of acetophenone. Nevertheless, we assume that in our case *O*-protonation of the samarium ketyl moiety should be possible due to a slightly higher basicity of the involved alcoholate.



Scheme 11. Possible mechanistic pathways for the cyclisation and stereoselective protonation of compound **7a**.



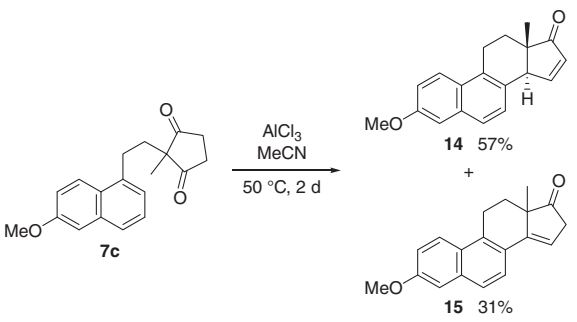
Scheme 12. Supposed equilibrium in the reaction of **7a** with 3 equiv of SmI_2 without proton source.

part of a commercially used steroid mixture for hormone replacement therapy and isolated from the urine of pregnant mares.[18]

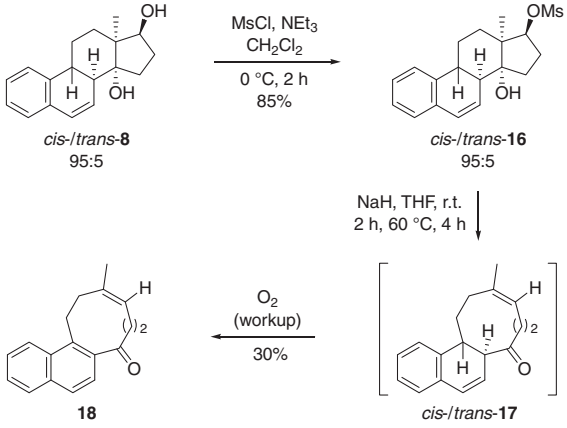
To investigate the ability of compounds with structure **8** to undergo fragmentation reactions generating medium-sized rings we selectively mesylated the secondary hydroxyl group of **8** (Scheme 14). Grob-fragmentation of mesylate **16** promoted by deprotonation with sodium hydride stereoselectively led to *Z*-configured nine-membered ring compound **18** (reaction conditions not optimised). Apparently, an aromatisation occurred during the work-up of the reaction mixture. The *Z*-configuration of the double bond in **18** is expected according to the fragmentation mechanism and it was proved by NOE experiments.

3. Conclusion

In samarium diiodide mediated intramolecular ketyl–aryl coupling reactions of γ-naphthyl-substituted 1,3-diones the second carbonyl group (or the resulting hydroxyl group) has a remarkable



Scheme 13. Cyclisation of **7c** with $AlCl_3$ to steroid derivatives **14** and **15**.



Scheme 14. Synthesis and stereoselective Grob-fragmentation of mesylate **16** leading to naphthannulated cyclononane derivative **18**.

effect on the protonation step of the reaction. While the samarium intermediates derived from γ-aryl- and γ-naphthyl-substituted monoketones were exclusively protonated from the less hindered *exo*-side, with γ-naphthyl-substituted 1,3-diones protonation can occur from both sides. We attempted to analyse the role of the proton source with regard to *exo*- versus *endo*-protonation. The highest diastereomeric ratios were achieved with only 1 equiv of *t*BuOH providing the *cis*/*cis*-annulated products in ratios up to 95:5. The reductive cyclisation protocol described here allowed a smooth and fairly efficient entry to novel steroid analogues. It should be mentioned that this method induces dearomatisation[19] of one of the two rings of the naphthyl moiety leading to compounds with a styrene subunit which allows smooth further functionalisations.[8,9] The briefly studied Grob-fragmention of compounds such as **8** deserves further investigation since it may allow a straightforward route to functionalised medium-sized ring compounds like **18**.

4. Experimental section

4.1. General

Reactions were generally performed under argon in flame dried flasks. Solvents and reagents were added by syringe. Solvents were

dried using standard procedures. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone under argon. 1,2-Diiodoethane was dried at 50 °C for 3 h in vacuo and stored at 4 °C. Hexamethylphosphoramide was distilled from calcium hydride and stored over molecular sieves (4 Å) under an atmosphere of argon. (CAUTION: *HMPA has been identified as a carcinogenic reagent. Appropriate glove protection is required during handling. Reactions and chromatography should be performed in a well-vented hood.*) SmI_2 was either freshly prepared (see procedure for *cis*-**8**/*trans*-**8**) or taken from a previously prepared 0.1 M stock solution. Products were purified by flash chromatography on silica gel (230–400 mesh, Merck or Fluka) or HPLC (Nucleosil 50-5). Unless otherwise stated, yields refer to analytical pure samples. NMR spectra were recorded on Bruker (AC 250, AC 500) and JOEL (Eclipse 500) instruments. Chemical shifts are reported relative to TMS (^{1}H: δ = 0.00 ppm) and $CDCl_3$ (^{13}C: δ = 77.0 ppm). Integrals are in accordance with assignments; coupling constants are given in Hertz. All ^{13}C spectra are proton-decoupled. For detailed peak assignments 2D spectra were measured. IR spectra were measured with an FT-IRD spectrometer Nicolet 5 SXC. MS and HRMS analyses were performed with Finnigan MAT 711 (EI, 80 eV, 8 kV), MAT CH7A (EI, 80 eV, 3 kV), CH5DF (FAB, 3 kV) and Varian Ionspec QFT-7 (ESI-FT ICRMS) instruments. Elemental analyses were carried out with CHN-Analyzer 2400 (Perkin Elmer), Vario EL or Vario EL III (Elementar). Melting points were measured with a Reichert apparatus Thermovar and are uncorrected.

4.2. Preparation of a 0.1 M stock solution of SmI_2

Sm metal (40 mesh, 2.71 g, 18.0 mmol) and I_2 (3.81 g, 15.0 mmol) were placed under argon in a flame dried 250 mL flask equipped with a three way adapter. THF (150 mL) was added and the mixture was vigorously stirred until the deep blue colour of SmI_2 appeared (2–5 h). For storage in the dark, the flask was wrapped by an alumina foil.

4.3. 2-[(2*E*)-2-(3,4-Dihydronaphthalen-1(2*H*)-ylidene)ethyl]-2-methylcyclopentane-1,3-dione 5a

Tetralone derivative **4a** (9.76 g, 56.0 mmol) and 2-methylcyclopentane-1,3-dione (7.53 g, 67.2 mmol) were dissolved in DMF (112 mL) under an atmosphere of argon, $Pd(PPh_3)_4$ (575 mg, 0.560 mmol) was added and the mixture was stirred at 80 °C for 24 h. CH_2Cl_2 (800 mL) was added and the solution was washed with water (3 × 100 mL) and brine (2 × 100 mL) and dried with Na_2SO_4. The solvent was removed under reduced pressure to afford the crude product as a solution in DMF. The solution was diluted with EtOAc (300 mL), washed with brine (5 × 20 mL) and dried with Na_2SO_4. The solvent was removed under reduced pressure. Column chromatography on silica gel (hexane/EtOAc 8:1) afforded 7.10 g (47%) of **5a** as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.18 (s, 3H, Me), 1.79 (quint., *J* = 6.6 Hz, 2H, 3″-H), 2.46 (t, *J* = 6.6 Hz, 2H, 2″-H), 2.57 (d, *J* = 8.2 Hz, 2H, 1′-H), 2.69–2.79 (m, 6H, 4-H, 5-H, 4″-H), 5.77 (t, *J* = 8.2 Hz, 1H, 2′-H), 7.05–7.18 (m, 3H, Ar), 7.42–7.47 (m, 1H, Ar) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 18.9 (q, Me), 23.2, 26.3, 30.2, 34.9 (4t, C-1′, C-2″, C-3″, C-4″), 35.5 (t, C-4, C-5), 56.9 (s, C-2), 116.1 (d, C-2′), 123.7, 125.9, 127.2, 128.9 (4d, Ar), 135.4, 137.6, 138.5 (3s, C-1″, Ar), 216.7 (s, C=O) ppm. IR (neat): ν = 3060–2840 (=CH, C–H), 1725 (C=O), 1640–1570 (C=C) cm^{-1}. EA: Calcd for $C_{18}H_{20}O_2$ (268.4): C, 80.56; H, 7.51. Found: C, 80.21; H, 7.52.

4.4. 2-[(2*E*)-2-(3,4-Dihydronaphthalen-1(2*H*)-ylidene)ethyl]-2-methylcyclohexane-1,3-dione 5b

Method 1: Similar to the procedure described for **5a**; 2-methylcyclohexane-1,3-dione (1.30 g, 10.3 mmol), tetralone derivative **4a** (1.50 g, 8.61 mmol), $Pd(PPh_3)_4$ (99 mg, 0.086 mmol), DMF (17 mL), 80 °C, 4 d. Product **5b** (770 mg, 32%) was isolated as a yellow solid, starting material **4a** (822 mg, 55%) was reisolated as a colourless oil.

Method 2: To a solution of tetralone derivative **4a** (2.00 g, 11.5 mmol) in THF (57 mL) was added 2-methylcyclohexane-1,3-dione (1.74 g, 13.8 mmol), $Pd(OAc)_2$ (128 mg, 0.570 mmol), PPh_3 (307 mg, 1.17 mmol) and Et_3B (1 M in THF, 27.6 mL, 27.6 mmol). The reaction mixture was stirred at rt for 4 d. Then satd aq $NaHCO_3$ solution (65 mL) was added, the organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 65 mL). The combined organic layers were washed with brine (1 × 10 mL) and dried with Na_2SO_4. Column chromatography on silica gel (hexane/EtOAc 9:1) afforded **5b** (2.22 g, 69%) as a yellow solid. Mp: 65 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.27 (s, 3H, Me), 1.78 (quint., *J* = 6 Hz, 2H, 3″-H), 1.81–1.87 (m, 1H, 5-H^1), 1.90–1.98 (m, 1H, 5-H^2), 2.46 (t, *J* = 5.7 Hz, 2H, 2″-H), 2.56–2.64 (m, 4H, 4-H, 6-H), 2.68 (d, *J* = 7.7 Hz, 2H, 1′-H), 2.72 (t, *J* = 6.3 Hz, 2H, 4″-H), 5.70 (t, *J* = 7.6 Hz, 1H, 2′-H), 7.02–7.05 (m, 1H, Ar), 7.08–7.11 (m, 2H, Ar), 7.42–7.45 (m, 1H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 17.3 (t, C-5), 19.5 (q, Me), 22.9 (t, C-3″), 26.3 (t, C-2″), 30.0 (t, C-4″), 35.6 (t, C-1′), 38.0 (t, C-4, C-6), 64.9 (s, C-2), 117.1 (d, C-2′), 123.5, 125.7, 126.7, 128.5 (4d, Ar), 135.4, 137.2, 137.4 (3s, Ar, C-1″), 210.0 (s, C=O) ppm. IR (KBr): ν = 3060–2835 (=CH, C–H), 1725 (C=O), 1695 (C=O), 1485–1025 (=C–H, C–H) cm^{-1}. HRMS (ESI): Calcd for $C_{19}H_{22}O_2 \cdot H^+$: 283.1698. Found: 283.1691.

4.5. 2-[(2*E*)-2-(6-Methoxy-3,4-dihydronaphthalen-1(2*H*)-ylidene)-ethyl]-2-methylcyclopentane-1,3-dione 5c

Similar to the procedure described for **5a**; tetralone derivative **4b** (1.87 g, 9.16 mmol), 2-methylcyclopentane-1,3-dione (1.23 g, 11.0 mmol), $Pd(PPh_3)_4$ (106 mg, 0.092 mmol), DMF (25 mL), 80 °C, 3 d. **5c** (1.54 g, 56%) was isolated as a yellow solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.17 (s, 3H, Me), 1.26 (t, *J* = 6.8 Hz, 2H, 2″-H), 1.77 (quint., *J* = 6.4 Hz, 2H, 3″-H), 2.43 (t, *J* = 5.9 Hz, 2H, 4″-H), 2.55 (d, *J* = 8.2 Hz, 2H, 1′-H), 2.68–2.78 (m, 4H, 4-H, 5-H), 5.64 (t, *J* = 8.2 Hz, 1H, 2′-H), 6.60 (d, *J* = 2.7 Hz, 1H, 5″-H), 6.69 (dd, *J* = 2.7, 8.7 Hz, 1H, 7″-H), 7.40 (d, *J* = 8.7 Hz, 1H, 8″-H) ppm.[20]

4.6. 2,2-Bis[(2*E*)-2-(3,4-dihydronaphthalen-1(2*H*)-ylidene)-ethyl]-1*H*-indene-1,3(2*H*)-dione 5d

Similar to the procedure described in method 2 for **5b**; tetralone derivative **4a** (2.50 g, 14.3 mmol), indane-1,3-dione (1.05 g, 7.17 mmol), $Pd(OAc)_2$ (162 mg, 0.722 mmol), PPh_3 (378 mg, 1.44 mmol) Et_3B (1 M in THF, 17.2 mmol, 17.2 mL), THF (36 mL), rt, 4 d. **5d** (2.87 g, 87%) was isolated as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.75 (quint., *J* = 6.4 Hz, 4H, 3″-H), 2.49, 2.67 (dt and t, *J* = 1.6, 6.4 Hz, *J* = 6.4 Hz, 4H each, 2″-H, 4″-H), 2.82 (d, *J* = 8.0 Hz, 4H, 1′-H), 5.68 (t, *J* = 8.0 Hz, 2H, 2′-H), 6.93–6.98 (m, 4H, Ar), 7.02 (dt, *J* = 1.3, 7.3 Hz, 2H, Ar), 7.10 (dd, *J* = 1.0, 7.9 Hz, 2H, Ar), 7.68–7.72 (m, 2H, Ar), 7.87–7.91 (m, 2H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 23.1 (t, C-3″), 26.2, 30.1 (2t, C-2″, C-1′), 33.4 (t, C-4″) 59.0 (s, C-2), 116.8 (d, C-2′), 122.8, 123.7, 125.7, 126.8, 128.6, 135.6 (6d, Ar), 135.7 (s, C-1″), 137.4, 138.0, 142.2 (3s, Ar), 203.9 (s, C=O) ppm. IR (KBr): ν = 3060–2835 (=CH, C–H), 1745 (C=O), 1710 (C=O), 1595 (C=C), 1480 (C=C) cm^{-1}. EA: Calcd for $C_{33}H_{30}O_2$ (458.6): C, 86.43; H, 6.59. Found: C, 86.36; H, 6.44.

4.7. 2-Methyl-2-[(*E*)-2-(1-naphthyl)ethenyl]cyclopentane-1,3-dione 6a

Compound **5a** (7.10 g, 26.5 mmol) and DDQ (12.1 g, 53.2 mmol) were suspended in chlorobenzene (140 mL) and stirred under reflux for 90 min. The mixture was filtered through a pad of silica

gel (hexane/EtOAc 4:1) and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (hexane/EtOAc 9:1) to afford 5.11 g (77%) of **6a** as yellow oil. A small scale reaction (2.15 mmol) yielded **6a** in 87%. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.41 (s, 3H, Me), 2.70–3.11 (m, 4H, 4-H, 5-H), 6.02 (d, J = 16.4 Hz, 1H, 1′-H), 7.25 (d, J = 16.4 Hz, 1H, 2′-H), 7.41 (t, J = 7.7 Hz, 1H, Ar), 7.45–7.56 (m, 3H, Ar), 7.75–7.87 (m, 2H, Ar), 7.95–8.03 (m, 1H, Ar) ppm. ^{13}C NMR (68 MHz, $CDCl_3$): δ = 18.9 (q, Me), 35.0 (t, C-4, C-5), 59.9 (s, C-2), 123.4, 123.8, 125.3, 125.8, 126.2, 128.4, 128.5, 128.8, 129.9 (9d, Ar, CH=), 130.9, 133.4, 133.5 (3s, Ar), 213.3 (s, C=O) ppm. IR (neat): ν = 3100–2940 (=CH, C–H), 1720 (C=O) cm^{-1}. MS (EI, 80 eV, 110 °C): m/z (%) = 264 (100) [M]$^+$, 208 (48), 179 (70), 178 (57), 165 (94), 155 (35), 152 (38), 128 (32), 127 (31), 89 (35), 55 (38), 43 (45). HRMS (EI): Calcd for $C_{18}H_{16}O_2$: 264.11503. Found: 264.11387.

4.8. 2-Methyl-2-[(*E*)-2-(1-naphthyl)ethenyl]cyclohexane-1,3-dione 6b

Similar to the procedure described for **6a**; **5b** (382 mg, 1.35 mmol), DDQ (613 mg, 2.70 mmol), chlorobenzene (7.6 mL), reflux, 135 min. Product **6b** was isolated as a yellow solid (192 mg, 51%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.52 (s, 3H, Me), 1.85 (ttd, J = 4.9, 9.6, 14.1 Hz, 1H, 5-H^1), 2.21 (quint.d, J = 6.2, 14.1 Hz, 1H, 5-H^2), 2.63 (ddd, J = 4.9, 6.4, 16.2 Hz, 2H, 4-H^1, 6-H^1), 2.96 (ddd, J = 5.9, 10.2, 16.2 Hz, 2H, 4-H^2, 6-H^2), 6.22 (d, J = 15.9 Hz, 1H, 1′-H), 7.14 (d, J = 15.9 Hz, 1H, 2′-H), 7.42 (t, J = 7.8 Hz, 1H, Ar), 7.47–7.53 (m, 3H, Ar), 7.79 (d, J = 8.1 Hz, 1H, Ar), 7.84 (dd, J = 2.3, 7.2 Hz, 1H, Ar), 7.94 (dd, J = 1.2, 7.8 Hz, 1H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 17.7, 18.0 (q and t, 2-Me, C-5), 38.2 (t, C-4, C-6), 69.4 (s, C-1), 123.4, 123.9, 125.4, 126.0, 126.4, 128.6, 128.7, 130.0, 131.5 (9d, Ar, C-1′, C-2′), 131.0, 133.5, 133.7 (3s, Ar), 207.4 (s, C=O) ppm. IR (KBr): ν = 3050–2940 (=CH, C–H), 1710 (C=O) cm^{-1}. HRMS (ESI): Calcd for $C_{19}H_{18}O_2{\cdot}H^+$: 279.1385. Found: 279.1403.

4.9. 2-[(*E*)-2-(6-Methoxy-1-naphthyl)ethenyl]-2-methylcyclopentane-1,3-dione 6c

Similar to the procedure described for **6a**; **5c** (1.30 g, 4.38 mmol), DDQ (1.99 g, 8.76 mmol) chlorobenzene (23 mL), reflux, 60 min. Product **6c** was isolated as a yellow solid (812 mg, 63%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.41 (s, 3H, Me), 2.75–3.08 (m, 4H, 4-H, 5-H), 3.92 (s, 3H, OMe), 6.01 (d, J = 15.5 Hz, 1H, 1′-H), 7.12–7.21* (m, 2H, Ar), 7.21* (d, J = 15.5 Hz, 1H, 2′-H), 7.34–7.42 (m, 2H, Ar), 7.68 (dd, J = 2.7, 6.4 Hz, 1H, Ar), 7.90 (d, J = 9.1 Hz, 1H, Ar) ppm; *signals overlap.

4.10. 2,2-Bis[(*E*)-2-(1-naphthyl)ethenyl]-1*H*-indene-1,3(2*H*)-dione 6d

Similar to the procedure described for **6a**; **5d** (301 mg, 0.656 mmol) DDQ (596 mg, 2.63 mmol), chlorobenzene (6.5 mL), reflux, 2 h. Product **6d** (104 mg, 35%) was isolated as a red-brown viscous oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.47 (d, J = 15.5 Hz, 2H, 1′-H), 7.42 (t, J = 7.7 Hz, 2H, Ar), 7.44–7.54 (m, 4H, Ar), 7.61 (d, J = 6.4 Hz, 2H, Ar), 7.65 (d, J = 15.5 Hz, 2H, 2′-H), 7.78 (d, J = 8.2 Hz, 2H, Ar), 7.83 (dd, J = 2.5, 6.7 Hz, 2H, Ar), 7.95 (dd, J = 3.2, 5.9 Hz, 2H Ar), 8.09 (dd, J = 2.7, 6.4 Hz, 2H, Ar), 8.15 (dd, J = 3.6, 5.9 Hz, 2H, Ar) ppm.

4.11. 2-Methyl-2-[2-(1-naphthyl)ethyl]cyclopentane-1,3-dione 7a

Compound **6a** (5.11 g, 19.3 mmol) was dissolved in EtOAc (250 mL) and Pd/C (10% wt, 411 mg, 0.368 mmol Pd) was added. Hydrogen was bubbled through the mixture for 40 min, then it was stirred for additional 155 min under H_2 atmosphere. Filtration through a pad of Celite followed by column chromatography on silica gel (hexane/EtOAc 9:1→3:1) afforded 5.01 g (97%) of dione **7a** as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.21 (s, 3H, Me), 2.04–2.13 (m, 2H, 1′-H), 2.66–2.96 (m, 6H, 2′-H, 4-H, 5-H), 7.25 (d, J = 6.4 Hz, 1H, Ar), 7.36 (t, J = 7.7 Hz, 1H, Ar), 7.43–7.59 (m, 2H, Ar), 7.71 (d, J = 7.3 Hz, 1H, Ar), 7.84 (d, J = 8.2 Hz, 1H, Ar), 7.95 (d, J = 8.2 Hz, 1H, Ar) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.0 (q, Me), 28.2 (t, C-1′), 35.2 (t, C-4, C-5), 36.1 (t, C-2′), 56.8 (s, C-2), 123.4, 125.4, 125.6, 126.16, 126.22, 127.2, 128.7 (7d, Ar), 131.6, 133.8, 136.9 (3s, Ar), 216.3 (s, C=O) ppm. IR (neat): ν = 3060–2870 (=CH, C–H), 1720 (C=O), 1595, 1510 (C=C) cm^{-1}. MS (EI, 80 eV, 80 °C): m/z (%) = 266 (12) [M]$^+$, 155 (17), 154 (100), 153 (20), 141 (33), 129 (14), 115 (18), 69 (11), 43 (13), 41 (19). HRMS (EI): Calcd for $C_{18}H_{18}O_2$: 266.13068. Found: 266.13107. EA: Calcd for $C_{18}H_{18}O_2$ (266.3): C, 81.17; H, 6.81. Found: C, 81.09; H, 6.90.

4.12. 2-Methyl-2-[2-(1-naphthyl)ethyl]cyclohexane-1,3-dione 7b

Similar to the procedure described for **7a**; **6b** (141 mg, 0.507 mmol), Pd/C (10% wt, 27 mg, 0.025 mmol Pd), EtOAc (17 mL), 4 h. Product **7b** (95 mg, 67%) was isolated as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.34 (s, 3H, Me), 1.90–1.96 (m, 2H, 5-H), 2.15–2.20 (m, 2H, 1′-H), 2.61–2.71 (m, 4H, 4-H, 6-H), 2.82–2.87 (m, 2H, 2′-H), 7.27 (dd, J = 1.1, 7.0 Hz, 1H, Ar), 7.35 (dd, J = 7.0, 8.2 Hz, 1H, Ar), 7.44 (ddd, J = 1.1, 7.0, 8.2 Hz, 1H, Ar), 7.53 (ddd, J = 1.1, 7.0, 8.2 Hz, 1H, Ar), 7.68 (d, J = 8.2 Hz, 1H, Ar), 7.81 (dd, J = 1.1, 8.2 Hz, 1H, Ar), 8.05 (d, J = 8.2 Hz, 1H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 17.5, 21.0 (q and t, 2-Me, C-5), 28.4 (t, C-1′), 37.5 (t, C-2′), 38.0 (t, C-4, C-6), 65.3 (s, C-2), 123.5, 125.5*, 126.0, 126.1, 126.8, 128.6 (6d, Ar), 131.6, 133.8, 137.4 (3s, Ar), 210.1 (s, C=O) ppm; *signal has higher intensity. IR (neat): ν = 3065–2875 (=CH, C–H), 1725 (C=O), 1695 (C=O), 1595 (C=C), 1510 (C=C) cm^{-1}. EA: Calcd for $C_{19}H_{20}O_2$ (280.4): C, 81.40; H, 7.19. Found: C, 80.82; H, 7.09.

4.13. 2-[2-(6-Methoxy-1-naphthyl)ethyl]-2-methylcyclopentane-1,3-dione 7c

Similar to the procedure described for **7a**; **6c** (859 mg, 2.92 mmol), Pd/C (10% wt, 124 mg, 0.177 mmol Pd), EtOAc (30 mL), 3 h. Product **7c** (781 mg, 90%) was isolated as a pale yellow solid. Mp: 91 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.20 (s, 3H, Me), 2.08 (m_c, 2H, 1′-H), 2.65–2.92 (m, 6H, 4-H, 5-H, 2′-H), 3.92 (s, 3H, OMe), 7.09* (d, J = 7.1 Hz, 1H, 2″-H), 7.13 (d, J = 2.6 Hz, 1H, 5″-H), 7.21 (dd, J = 2.6, 9.3 Hz, 1H, 7″-H), 7.31 (t, J = 7.7 Hz, 1H, 3″-H), 7.61* (d, J = 8.4 Hz, 1H, 4″-H), 7.85 (d, J = 9.3 Hz, 1H, 8″-H) ppm; *assignment interchangeable.

4.14. 2,2-Bis[2-(1-naphthyl)ethyl]-1*H*-indene-1,3(2*H*)-dione 7d

To a suspension of Pd/C (10% wt, 12 mg, 0.012 mmol Pd) in EtOH (2 mL) was added a solution of **6d** (104 mg, 0.231 mmol) in EtOH (3 mL) und THF (3 mL). Hydrogen was bubbled through the mixture for 20 min, then stirring was continued under an atmosphere of H_2 for 22 h. Filtration over Celite and purification by preparative HPLC yielded **7d** (29 mg, 28%) as a yellow solid. Starting material **6d** (15 mg, 14%) was recovered and 36 mg (34%) of the mono-hydrogenated compound was isolated. Mp: 139–141 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.30 (m_c, 4H, 1′-H), 2.84 (m_c, 4H, 2′-H), 7.17 (dd, J = 1.0, 7.0 Hz, 2H, Ar), 7.29 (dd, J = 7.1, 8.2 Hz, 2H, Ar), 7.43 (ddd, J = 1.1, 6.9, 8.1 Hz, 2H, Ar), 7.51 (ddd, J = 1.4, 6.9, 8.4 Hz, 2H, Ar), 7.65 (br d, J = 8.2 Hz, 2H, Ar), 7.79 (dd, J = 0.7,

8.2 Hz, 2H, Ar), 7.88 (br d, J = 8.4 Hz, 2H, Ar), 7.91 (dd, J = 3.0, 5.6 Hz, 2H, Ar), 8.11 (dd, J = 3.1, 5.7 Hz, 2H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.5 (t, C-1′), 36.3 (t, C-2′), 58.7 (s, C-2), 123.2, 123.4, 125.4, 125.5, 126.1, 126.2, 127.0, 128.7, 131.5 (9d, Ar), 133.8, 136.0, 137.0, 142.5 (4s, Ar), 204.5 (s, C=O) ppm. IR (KBr): ν = 3060–2835 (=CH, C–H), 1740, 1705 (C=O), 1595 (C=C), 1510 (C=C) cm^{-1}. HRMS (ESI): Calcd for $C_{33}H_{26}O_2{\cdot}H^+$: 455.2011. Found: 455.2024.

4.15. *rac*-(8α,9α,13α,14α,17β)-Estra-1(10),2,4,6-tetraene-14,17-diol *cis*-8 and *rac*-(8α,9β,13α,14α,17β)-estra-1(10),2,4,6-tetraene-14,17-diol *trans*-8

Sm (180 mg, 1.20 mmol) and ICH_2CH_2I (310 mg, 1.10 mmol) were suspended in THF (8 mL) at rt and vigorously stirred until the deep blue colour of SmI_2 appeared; then HMPA (1.26 mL, 1.29 g, 7.20 mmol) and *t*BuOH (0.20 mL, 1 M in THF, 0.20 mmol) were added. Dione **7a** (52 mg, 0.20 mmol) was dissolved in THF (8 mL) and the solution was purged with argon for 30 min. The solution of **7a** was added via syringe to the SmI_2/HMPA/*t*BuOH solution. The mixture was stirred at rt over night. Satd aq. $NaHCO_3$ solution was added, the organic layer was separated and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with water and brine and dried with Na_2SO_4. The solvents were removed under reduced pressure. Column chromatography on silica gel (hexane/EtOAc 2:1) afforded a 91:9 mixture of isomers *cis*-**8** and *trans*-**8** (38 mg, 70%) as a colourless solid. Analytically pure samples of *cis*-**8** and *trans*-**8** were obtained by preparative HPLC.

cis-**8**: Mp: 167–169 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.12–1.21 (m, 2H, 16-H^1, OH), 1.16 (s, 3H, Me), 1.26* (ddd, J = 4.5, 10.1, 14.7 Hz, 1H, 15-H^1), 1.26* (s, 1H, OH), AB-signal (δ_A = 1.38, δ_B = 1.42, $J_{A,B}$ = 13.8 Hz, additional couplings of A, J = 3.1, 13.8 Hz, and B, J = 3.6, 3.6 Hz, 1H each, 12-H$_2$), 1.53 (ddd, J = 5.9, 12.5, 14.7 Hz, 1H, 15-H^2), 1.87–2.01 (m, 2H, 16-H^2, 11-H^1), 2.43 (qd, J = 3, 14.6 Hz, 1H, 11-H^2), 2.52 (dd, J = 6.1, 6.9 Hz, 1H, 8-H), 3.34 (br dd, J = 6, 6.9 Hz, 1H, 9-H), 4.17 (t, J = 8.5 Hz, 1H, 17-H), 6.14 (dd, J = 6.1, 9.8 Hz, 1H, 7-H), 6.59 (d, J = 9.8 Hz, 1H, 6-H), 7.02 (dd, J = 1.2, 7.4 Hz, 1H, 4-H), 7.14 (br t, J = 7.4 Hz, 1H, 3-H), 7.19 (dt, J = 1.2, 7.4 Hz, 1H, 2-H), 7.26 (br d, J = 7.4 Hz, 1H, 1-H) ppm; *signals overlap. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 16.5 (q, Me), 19.9 (t, C-11), 24.6 (t, C-12), 28.3 (t, C-16), 31.4 (t, C-15), 36.3 (d, C-9), 41.5 (d, C-8), 47.2 (s, C-13), 80.9 (d, C-17), 83.8 (s, C-14), 123.5 (d, C-1), 126.1 (d, C-3), 126.5 (d, C-4), 127.7 (d, C-2), 129.1 (d, C-7), 129.8 (d, C-6), 134.1, 136.3 (2s, C-5, C-10) ppm. IR (KBr): ν = 3325 (O–H), 3060–2830 (=CH, C–H), 1655–1570 (C=C) cm^{-1}. MS (EI, 80 eV, 90 °C): m/z (%) = 270 (82) [M]$^+$, 156 (31), 154 (72), 142 (40), 141 (55), 129 (59), 128 (100), 28 (51). HRMS (EI): Calcd for $C_{18}H_{22}O_2$: 270.16199. Found: 270.16256.

trans-**8**: Mp: 176–178 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.07 (s, 3H, Me), 1.41 (dt, J = 3.8, 13.6 Hz, 1H, 12-H^1), 1.56–1.72 (m, 6H, 11-H^1, 12-H^2, 15-H$_2$, 16-H^1, OH), 2.16–2.34 (m, 4H, 8-H, 11-H^2, 16-H^2, OH), 2.63 (ddd, J = 3.7, 11.9, 15.4 Hz, 1H, 9-H), 4.32 (t, J = 8.6 Hz, 1H, 17-H), 6.17 (dd, J = 2.0, 9.7 Hz, 1H, 7-H), 6.57 (dd, J = 2.9, 9.7 Hz, 1H, 6-H), 7.08 (dd, J = 1.6, 7.1 Hz, 1H, 4-H), 7.17–7.21 (m, 1H, 3-H), 7.22 (dt, J = 1.6, 6.9 Hz, 1H, 2-H), 7.25–7.29 (m, 1H, 1-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 16.6 (q, Me), 23.2 (t, C-11), 28.4 (t, C-12), 28.8 (t, C-15), 30.0 (t, C-16), 39.3 (d, C-9), 44.9 (d, C-8), 47.7 (s, C-13), 80.9 (d, C-17), 83.1 (s, C-14), 123.5 (d, C-1), 126.0 (d, C-4), 126.4 (d, C-3), 127.3 (d, C-2), 129.0 (d, C-6), 129.4 (d, C-7), 134.1, 138.4 (2s, C-5, C-10) ppm. IR (KBr): ν = 3315 (O–H), 3060–2830 (=CH, C–H), 1660–1600 (C=C) cm^{-1}. MS (EI, 80 eV, 150 °C): m/z (%) = 270 (81) [M]$^+$, 157 (73), 155 (75), 142 (87), 141 (100), 129 (59), 128 (95), 115 (30), 97 (60), 43 (41), 41 (32), 28 (69). HRMS (EI): Calcd for $C_{18}H_{22}O_2$: 270.16199. Found: 270.16114.

4.16. *rac*-(1*S*,4a*R*,4b*S*,10b*S*,12a*S*)-12a-Methyl-1,3,4,4b,10b,11,12,12a-octahydrochrysene-1,4a(2*H*)-diol *cis*-10 and *rac*-(1*S*,4a*R*,4b*S*,10b*R*,12a*S*)-12a-methyl-1,3,4,4b,10b,11,12,12a-octahydrochrysene-1,4a(2*H*)-diol *trans*-10

According to the procedure described for *cis*-**8**/*trans*-**8**; dione **7b** (48 mg, 0.17 mmol), Sm (163 mg, 1.08 mmol), ICH_2CH_2I (279 mg, 0.99 mmol), *t*BuOH (66 μL, 53 mg, 0.72 mmol), HMPA (1.14 mL, 1.12 g, 6.49 mmol), THF (15 mL for preparation of SmI_2, 10 mL for the solution of **7b** and *t*BuOH), rt, 2 d. The crude product was filtered through silica gel, subsequent preparative HPLC afforded 16 mg (33%) of *cis*-**10** and 10 mg (20%) of *trans*-**10** as colourless solids.

cis-**10**: Mp: 166–169 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.08–1.16 (m, 3H, 12-H^1, 3-H^1, 4-H^1), 1.34 (s, 3H, Me), 1.43–1.48 (m, 1H, 4-H^2), 1.50–1.56 (m, 1H, 2-H^1), 1.63 (ddt, J = 2.4, 3.7, 13.7 Hz, 1H, 2-H^2), 1.68–1.79 (m, 2H, 12-H^2, 3-H^2), 2.12 (ddt, J = 4.1, 6.5, 14.7 Hz, 1H, 11-H^1), 2.38 (br d, J = 14.7 Hz, 1H, 11-H^2), 2.66 (br s, 1H, OH), 2.84 (t, J = 6.5 Hz, 1H, 4b-H), 2.88 (s, 1H, OH), 3.32 (t, J = 6.5 Hz, 1H, 10b-H), 3.43 (br s, 1H, 1-H), 6.07 (dd, J = 6.5, 9.8 Hz, 1H, 5-H), 6.64 (d, J = 9.8 Hz, 1H, 6-H), 7.02 (dd, J = 1.3, 7.4 Hz, 1H, Ar), 7.15 (br t, J = 7.4 Hz, 1H, Ar), 7.20 (dt, J = 1.5, 7.4 Hz, 1H, Ar), 7.24 (br d, J = 7.4 Hz, 1H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 15.0 (t, C-3), 17.1 (q, Me), 19.6 (t, C-11), 28.0 (t, C-4), 28.4 (t, C-2), 29.2 (t, C-12), 35.7 (d, C-10b), 40.9 (s, C-12a), 41.1 (d, C-4b), 77.5 (s, C-4a), 77.7 (d, C-1), 122.6, 125.9, 126.5, 127.7 (4d, Ar), 129.1 (d, C-5), 130.5 (d, C-6), 134.8, 137.4 (2s, Ar) ppm. IR (KBr): ν = 3235 (O–H), 3060–2835 (=CH, C–H), 1670–1570 (C=C) cm^{-1}. MS (EI, 80 eV, 140 °C): m/z (%) = 284 (24) [M]$^+$, 154 (37), 141 (49), 129 (34), 128 (100), 55 (38), 43 (59), 41 (35).

trans-**10**: Mp: 187–188 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21 (s, 3H, Me), 1.33–1.42 (m, 1H, 12-H^1), 1.54–1.66 (m, 2H, 3-H^1, 4-H^1), 1.69–1.75 (m, 1H, 2-H^1), 1.80–1.96 (m, 4H, 2-H^2, 4-H^2, 11-H^1, 12-H^2), 2.05 (tq, J = 3.8, 13.5 Hz, 1H, 3-H^2), 2.21–2.27 (m, 1H, 11-H^2), 2.51 (br s, 1H, OH), 2.57 (td, J = 2.5, 15.9 Hz, 1H, 4b-H), 2.71–2.78 (m, 1H, 10b-H), 3.34 (br s, 1H, OH), 3.57 (br s, 1H, 1-H), 6.17 (dd, J = 2.1, 9.8 Hz, 1H, 5-H), 6.53 (dd, J = 2.9, 9.8 Hz, 1H, 6-H), 7.04–7.07 (m, 1H, Ar), 7.16–7.22 (m, 2H, Ar), 7.23–7.26 (m, 1H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 15.4 (t, C-3), 17.5 (q, Me), 23.4 (t, C-11), 28.4 (t, C-2), 29.4 (t, C-4), 32.1 (t, C-12), 37.1 (d, C-10b), 40.8 (s, C-12a), 44.6 (d, C-4b), 75.9 (s, C-4a), 77.6 (d, C-1), 123.6, 125.9, 126.3, 127.0 (4d, Ar), 128.1 (d, C-6), 129.5 (d, C-5), 134.1, 138.2 (2s, Ar) ppm. IR (KBr): ν = 3375 (O–H), 3060–2855 (=CH, C–H), 1660–1570 (C=C) cm^{-1}. MS (EI, 80 eV, 100 °C): m/z (%) = 284 (73) [M]$^+$, 181 (20), 154 (64), 142 (51), 141 (80), 129 (41), 128 (100), 111 (21), 84 (21), 55 (25), 43 (30), 41 (18). HRMS (EI): Calcd for $C_{19}H_{24}O_2$: 284.17763. Found: 284.17778.

4.17. *rac*-(8α,9α,13α,14α,17β)-3-Methoxyestra-1(10),2,4,6-tetraene-14,17-diol *cis*-11 and *rac*-(8α,9β,13α,14α,17β)-3-methoxyestra-1(10),2,4,6-tetraene-14,17-diol *trans*-11

According to the procedure described for *cis*-**8**/*trans*-**8**; SmI_2 was taken from a previously prepared stock solution. Dione **7c** (190 mg, 0.641 mmol), SmI_2 (0.1 M in THF, 35 mL, 3.50 mmol), HMPA (4.1 mL, 4.1 g, 23 mmol), *t*BuOH (1 M in THF, 0.64 mL, 0.64 mmol; *t*BuOH was added to the SmI_2–HMPA solution before a solution of **7c** in THF was added), THF (10 mL, for the solution of **7c**). Column chromatography on silica gel (hexane/EtOAc 1:1) and preparative HPLC afforded 17 mg (9%) of *cis*-**11** and 7 mg (4%) of *trans*-**11** as colourless solids.

cis-**11**: Mp: 144–146 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 (s, 3H, 13-Me), 1.14–1.28 (m, 3H, OH, 15-H^1, 16-H^1), 1.32–1.44 (m,

3H, 12-H^2, OH), 1.57 (ddd, J = 5.7, 12.4, 14.9 Hz, 1H, 15-H^2), 1.89 (tdd, J = 5.1, 13.2, 14.6 Hz, 1H, 11-H^1), 1.96 (dtd, J = 5.7, 9, 13.2 Hz, 1H, 16-H^2), 2.39 (qd, J = 2.3, 14.6 Hz, 1H, 11-H^2), 2.49 (t, J = 6.5 Hz, 1H, 8-H), 3.28 (br t, J = 6 Hz, 1H, 9-H), 3.79 (s, 3H, OMe), 4.17 (t, J = 8.5 Hz, 1H, 17-H), 6.16 (dd, J = 6.5, 9.8 Hz, 1H, 7-H), 6.54 (d, J = 9.8 Hz, 1H, 6-H), 6.61 (d, J = 2.7 Hz, 1H, 4-H), 6.71 (dd, J = 2.7, 8.3 Hz, 1H, 2-H), 7.15 (d, J = 8.3 Hz, 1H, 1-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 16.4 (q, 13-Me), 20.0 (t, C-11), 24.4 (t, C-12), 28.1 (t, C-16), 31.3 (t, C-15), 35.5 (d, C-9), 41.5 (d, C-8), 47.1 (s, C-13), 55.2 (q, OMe), 80.8 (d, C-17), 83.8 (s, C-14), 112.1 (d, C-2), 112.6 (d, C-4), 124.4 (d, C-1), 128.3 (s, Ar), 129.8, 129.9 (2d, C-6, C-7), 135.7 (s, Ar), 158.0 (s, C-3) ppm. IR (KBr): ν = 3440, 3335 (O–H), 3045–2830 (=CH, C–H, OMe), 1640–1495 (C=C) cm^{-1}. MS (EI, 80 eV, 160 °C): m/z (%) = 300 (30) [M]$^+$, 171 (15), 159 (100), 158 (45), 144 (11), 128 (12), 115 (25), 55 (12), 43 (19), 41 (15). HRMS (EI): Calcd for $C_{19}H_{24}O_3$: 300.17254. Found: 300.17312.

trans-**11**: Mp: 169–171 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.06 (s, 3H, 13-Me), 1.40 (dt, J = 3.7, 13.7 Hz, 1H, 12-H^1), 1.52–1.70 (m, 6H, 11-H^1, 12-H^2, 15-H^1, 16-H^1, 2 × OH), 2.15 (td, J = 2.5, 15.2 Hz, 1H, 8-H), 2.17–2.34 (m, 3H, 11-H^2, 15-H^2, 16-H^2), 2.56 (ddd, J = 3.6, 11.9, 15.2 Hz, 1H, 9-H), 3.80 (s, 3H, OMe), 4.31 (t, J = 8.5 Hz, 1H, 17-H), 6.19 (dd, J = 2.1, 9.7 Hz, 1H, 7-H), 6.52 (dd, J = 2.9, 9.7 Hz, 1H, 6-H), 6.66 (d, J = 2.7 Hz, 1H, 4-H), 6.75 (dd, J = 2.7, 8.4 Hz, 1H, 2-H), 7.17 (d, J = 8.4 Hz, 1H, 1-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 16.6 (q, 13-Me), 23.4 (t, C-11), 28.3 (t, C-12), 28.7 (t, C-16), 29.8 (t, C-15), 38.7 (d, C-9), 45.2 (d, C-8), 47.6 (s, C-13), 55.3 (q, OMe), 80.8 (d, C-17), 83.0 (s, C-14), 111.9, 112.0 (2d, C-2, C-4), 124.4 (d, C-1), 128.9 (d, C-6), 130.1 (d, C-7), 130.6, 135.2 (2s, Ar), 158.3 (s, C-3) ppm. IR (KBr): ν = 3460 (O–H), 3030–2830 (=CH, C–H, OMe), 1630–1495 (C=C) cm^{-1}. MS (EI, 80 eV, 170 °C): m/z (%) = 300 (25) [M]$^+$, 184 (23), 172 (26), 171 (31), 159 (44), 158 (30), 115 (27), 97 (30), 57 (26), 55 (42), 43 (100), 41 (52). HRMS (EI): Calcd for $C_{19}H_{24}O_3$: 300.17254. Found: 300.17224.

4.18. *rac*-(2*S*,3*S*)-3-Hydroxy-2-methyl-2-[2-(1-naphthyl)-ethyl]cyclopentanone 13 and *rac*-(2*R*,3*S*)-3-hydroxy-2-methyl-2-[2-(1-naphthyl)ethyl]cyclopentanone *epi*-13

To a solution of **7a** (350 mg, 1.31 mmol) in MeOH (8 mL) was added $NaBH_4$ (50 mg, 1.32 mmol) at 0 °C in portions of 10 mg over 3 h. After warming up to rt over night satd aq NH_4Cl solution (5 mL) was added. The organic layer was separated and the aqueous phase was extracted with Et_2O. The combined organic layers were dried with Na_2SO_4 and the solvent was removed in vacuo. Filtration over silica gel (hexane/EtOAc 2:1) and subsequent separation of the diastereomers with preparative HPLC (hexane/EtOAc 4:1) yielded 237 mg (68%) of **13** as a colourless solid and 64 mg (18%) of *epi*-**13** as a colourless oil.

Compound **13**: Mp: 102–103 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21 (s, 3H, Me), 1.46 (s, 1H, OH), 1.88–1.99 (m, 2H, 1′-H^1, 4-H^1), 2.02 (ddd, J = 5.6, 12.0, 14.0 Hz, 1H, 1′-H^2), 2.22–2.30 (m, 1H, 4-H^2), 2.35 (ddd, J = 4.4, 9.2, 19.0 Hz, 1H, 5-H^1), 2.51 (ddd, J = 8.9, 9.7, 19.0 Hz, 1H, 5-H^2), 3.10 (ddd, J = 5.6, 12.0, 13.4 Hz, 1H, 2′-H^1), 3.21 (ddd, J = 4.8, 12.0, 13.4 Hz, 1H, 2′-H^2), 4.16 (t, J = 4.1 Hz, 1H, 3-H), 7.35 (d, J = 7.0 Hz, 1H, Ar), 7.39 (dd, J = 7.0, 8.1 Hz, 1H, Ar), 7.47 (ddd, J = 1.4, 7.0, 8.1 Hz, 1H, Ar), 7.51 (ddd, J = 1.4, 7.0, 8.1 Hz, 1H, Ar), 7.72 (d, J = 8.1 Hz, 1H, Ar), 7.85 (d, J = 8.1 Hz, 1H, Ar), 8.08 (d, J = 8.1 Hz, 1H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 19.3 (q, Me), 27.4, 28.1, 31.7, 34.0 (4t, C-4, C-5, C-1′, C-2′), 53.1 (s, C-2), 77.6 (d, C-3), 123.7, 125.4, 125.5, 125.86, 125.88, 126.7, 128.7 (7d, Ar), 131.7, 133.9, 138.5 (3s, Ar), 220.8 (s, C-1) ppm. IR (KBr): ν = 3425 (O–H), 3060–2860 (=C–H, C–H), 1720 (C=O), 1595 (C=C), 1510 (C=C) cm^{-1}. MS (EI, 80 eV, 90 °C): m/z (%) = 268 (29) [M]$^+$, 154 (100), 141 (54), 115 (32), 113 (96), 43 (31), 41 (28), 28 (56). EA: Calcd for $C_{18}H_{20}O_2$ (268.4): C, 80.56; H, 7.51. Found: C, 80.18; H, 7.43.

Epi-**13**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.18 (s, 3H, Me), 1.79–1.88 (m, 2H, 1′-H), 1.89–1.96 (m, 1H, 5-H^1), 2.02 (br s, 1H, OH), 2.23 (m$_c$, 2H, 4-H^1, 5-H^2), 2.47–2.58 (m, 1H, 4-H^2), 2.96–3.06 (m, 1H, 2′-H^1), 3.08–3.17 (m, 1H, 2′-H^2), 4.33 (t, J = 5.7 Hz, 1H, 3-H), 7.30 (d, J = 6.9 Hz, 1H, Ar), 7.38 (t, J = 7.5 Hz, 1H, Ar), 7.48 (ddd, J = 1.2, 6.8, 7.6 Hz, 1H, Ar), 7.53 (ddd, J = 1.2, 6.8, 8.5 Hz, 1H, Ar), 7.71 (d, J = 8.2 Hz, 1H, Ar), 7.85 (d, J = 7.6 Hz, 1H, Ar), 8.00 (d, J = 8.5 Hz, 1H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.8 (q, Me), 27.5 (t, C-2′), 27.9 (t, C-5), 34.9 (t, C-4), 36.4 (t, C-1′), 53.4 (s, C-2), 75.8 (d, C-3), 123.4, 125.51, 125.54, 125.9, 126.0, 126.8, 128.8 (7d, Ar), 131.6, 133.9, 137.9 (3s, Ar), 220.3 (s, C-1) ppm. IR (neat): ν = 3450 (O–H), 3095–2875 (=CH, C–H), 1730 (C=O), 1595 (C=C), 1510 (C=C) cm^{-1}. HRMS (ESI): Calcd for $C_{18}H_{20}O_2{\cdot}H^+$: 269.1542. Found: 269.1541.

4.19. 3-Methoxyestra-1,3,5(10),6,8,15-hexaen-17-one 14 and 3-methoxyestra-1,3,5(10),6,8,14-hexaen-17-one 15

Compound **7c** (24 mg, 0.081 mmol) was added to a suspension of $AlCl_3$ (125 mg, 0.937 mmol) in acetonitrile (2.5 mL) and the mixture was stirred in a sealed tube at 50 °C for 2 d. Then EtOAc (50 mL) was added, the solution was washed with water (1 × 5 mL) and brine (1 × 5 mL) and dried with Na_2SO_4. Column chromatography (hexane/EtOAc 4:1) yielded **14** (13 mg, 57%) and **15** (7 mg, 31%) as colourless solids.

Compound **14**: Mp: 88–90 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.30 (s, 3H, Me), 1.65 (ddd, J = 4.1, 11.2, 13.2 Hz, 1H, 12-H^1), 2.24 (ddd, J = 4.2, 5.5, 13.2 Hz, 1H, 12-H^2), 2.53 (ddd, J = 4.2, 11.2, 16.1 Hz, 1H, 11-H^1), 3.17 (ddd, J = 4.1, 5.5, 16.1 Hz, 1H, 11-H^2), 3.92 (s, 3H, OMe), 3.93 (t, J = 2.5 Hz, 1H, 14-H), 6.14 (dd, J = 2.5, 5.6 Hz, 1H, 16-H), 7.13 (d, J = 2.7 Hz, 1H, 4-H), 7.17 (dd, J = 2.7, 9.2 Hz, 1H, 2-H), 7.38* (d, J = 8.4 Hz, 1H, 7-H), 7.59 (dd, J = 2.5, 5.6 Hz, 1H, 15-H), 7.65* (d, J = 8.4 Hz, 1H, 6-H), 7.88 (d, J = 9.2 Hz, 1H, 1-H) ppm; *assignment interchangeable. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 22.1 (t, C-11), 23.8 (q, Me), 33.2 (t, C-12), 47.2 (d, C-14), 54.7 (s, C-13), 55.3 (q, OMe), 106.6 (d, C-4), 118.7 (d, C-2), 124.9 (d, C-1), 125.9, 127.2 (2d, C-6, C-7), 129.3 (s, Ar), 130.5* (d, C-16), 130.5*, 133.6, 133.7 (3s, Ar), 157.3 (s, C-3), 165.3 (d, C-15), 214.7 (s, C=O) ppm; *signals overlap. IR (ATR): ν = 2980–2840 (=CH, C–H), 1700 (C=O), 1605 (C=C) cm^{-1}. HRMS (ESI): Calcd for $C_{19}H_{18}O_2{\cdot}Na^+$: 301.1205. Found: 301.1212.

Compound **15**: Mp: 148–150 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.19 (s, 3H, Me), 1.76 (dt, J = 6.3, 12.5 Hz, 1H, 12-H^1), 2.22 (ddd, J = 1.2, 5.9, 13.0 Hz, 1H, 12-H^2), 3.06 (dd, J = 3.0, 23.3 Hz, 1H, 16-H^1), 3.22 (ddd, J = 5.9, 12.3, 17.9 Hz, 1H, 11-H^1), 3.33–3.40* (m, 1H, 11-H^2), 3.37* (dd, J = 2.3, 23.3 Hz, 1H, 16-H^2), 3.93 (s, 3H, OMe), 6.27 (br t, J = 2.5 Hz, 1H, 15-H), 7.14 (d, J = 2.7 Hz, 1H, 4-H), 7.19 (dd, J = 2.7, 9.2 Hz, 1H, 2-H), 7.62, 7.64 (2d, J = 8.7 Hz, 1H each, 7-H, 6-H), 7.93 (d, J = 9.2 Hz, 1H, 1-H) ppm; *signals overlap. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 19.6 (q, Me), 22.9, 28.0 (2t, C-11, C-12), 42.2 (t, C-16), 49.2 (s, C-13), 55.3 (q, OMe), 107.1 (d, C-4), 115.0 (d, C-15), 118.6 (d, C-2), 123.2 (d, C-6), 125.3 (d, C-1), 125.9* (d, C-7), 125.9*, 127.4, 130.7, 134.6 (4s, Ar), 146.1 (s, C-14), 157.6 (s, C-3), 220.2 (s, C=O) ppm; *signals overlap. IR (ATR): ν = 3010–2850 (=CH, C–H), 1735 (C=O), 1600 (C=C) cm^{-1}. HRMS (ESI): Calcd for $C_{19}H_{18}O_2{\cdot}Na^+$: 301.1205. Found: 301.1205.

4.20. *rac*-(8α,9α,13α,14α,17β)-14-Hydroxyestra-1(10),2,4,6,-tetraen-17-yl methane sulfonate *cis*-16 and *rac*-(8α,9β,13α,14α,17β)-14-hydroxyestra-1(10),2,4,6,tetraen-17-yl methane-sulfonate *trans*-16

To a solution of *cis*-**8** and *trans*-**8** (95:5, 122 mg, 0.451 mmol) in CH_2Cl_2 (7 mL) were added NEt_3 (0.29 mL, 0.23 g, 2.3 mmol) and

MsCl (45 μL, 67 mg, 0.59 mmol) at 0 °C. After stirring for 2 h at 0 °C water (2 mL), brine (2 mL) and CH_2Cl_2 (20 mL) were added. The organic layer was separated and dried with Na_2SO_4. The solvent was removed under reduced pressure. Column chromatography (hexane/EtOAc 2:1) yielded a 95:5-mixture of *cis*-**16** and *trans*-**16** (133 mg, 85%) as colourless foam.

cis-**16**: ^{1}H NMR (500 MHz, $CDCl_3$, 95:5-mixture with *trans*-**16**): δ = 1.23 (s, 3H, Me), 1.33 (ddd, J = 3.6, 9.9, 14.0 Hz, 1H, 15-H^1), 1.39 (br s, 1H, OH), 1.43–1.56 (m, 3H, 12-H$_2$, 16-H^1), 1.61 (ddd, J = 5.9, 12.6, 14.0 Hz, 1H, 15-H^2), 1.90 (dtd, J = 5.0, 9.9, 13.1 Hz, 1H, 11-H^1), 2.11 (dtd, J = 5.9, 9.6, 13.4 Hz, 1H, 16-H^2), 2.39–2.45 (m, 1H, 11-H^2), 2.53 (dd, J = 6.2, 7.4 Hz, 1H, 8-H), 2.95 (s, 3H, OSO_2Me), 3.35 (t, J = 6.5 Hz, 1H, 9-H), 4.96 (dd, J = 6.8, 9.6 Hz, 1H, 17-H), 6.11 (dd, J = 6.2, 9.8 Hz, 1H, 7-H), 6.60 (d, J = 9.8 Hz, 1H, 6-H), 7.03 (dd, J = 1.2, 7.4 Hz, 1H, Ar), 7.15 (tt, J = 1.2, 7.3 Hz, 1H, Ar), 7.20 (dt, J = 1.2, 7.4 Hz, 1H, Ar), 7.25 (d, J = 7.4 Hz, 1H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$, 95:5-mixture with *trans*-**16**): δ = 16.0 (q, Me), 19.5 (t, C-11), 25.3 (t, C-12), 25.6 (t, C-16), 31.3 (t, C-15), 35.9 (d, C-9), 37.9 (q, OSO_2Me), 40.7 (d, C-8), 47.4 (s, C-13), 82.5 (s, C-14), 90.3 (d, C-17), 123.3, 126.2, 126.6, 127.9 (4d, Ar), 128.2 (d, C-7), 130.2 (d, C-6), 134.3, 135.9 (2s, Ar) ppm.

trans-**16**: ^{13}C NMR (126 MHz, $CDCl_3$, 5:95-mixture with *cis*-**16**): δ = 16.2 (q, Me), 22.8, 26.2, 28.9, 29.9 (4t, C-11, C-12, C-15, C-16), 37.9 (q, OSO_2Me), 38.9 (d, C-9), 44.2 (d, C-8), 47.9 (s, C-13), 81.9 (s, C-14), 90.0 (d, C-17), 123.4, 126.0, 126.5, 127.3 (4d, Ar), 128.5 (d, C-7), 129.2 (d, C-6), 133.8, 137.8 (2s, Ar) ppm.

cis-**16**/*trans*-**16**: IR (KBr): ν = 3550 (O–H), 3090–2800 (=CH, C–H), 1485–1175 (=CH, S=O, O–H, C–H) cm^{-1}. MS (EI, 80 eV, 70 °C): m/z (%) = 348 (100) [M$^+$], 252 (62), 250 (17), 235 (19), 234 (22), 219 (17), 209 (19), 154 (12), 141 (15), 43 (11). HRMS (EI): Calcd for $C_{19}H_{24}O_4S$: 348.13953. Found: 348.14110.

4.21. 11-Methyl-8,9,12,13-tetrahydro-7*H*-cyclonona[*a*]naphthalen-7-one 18

A 95:5 mixture of *cis*-**16** and *trans*-**16** (14 mg, 0.040 mmol) was dissolved in THF (1 mL), then NaH (~50% wt, 9 mg, 0.19 mmol) was added. The mixture was stirred at rt for 2 h, then at 60 °C for 2 h. NaH (~50% wt, 13 mg, 0.31 mmol) was added again and stirring was continued for additional 2 h at 60 °C. Water (1 mL) and EtOAc (35 mL) were added, the organic layer was separated, washed with brine (1 × 2 mL) and dried with Na_2SO_4. The solvent was removed under reduced pressure. Column chromatography (hexane/EtOAc 10:1) yielded **18** (3 mg, 30%) as colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.54 (s, 3H, Me), 2.31 (dt, J = 8.3, 12.6 Hz, 2H 9-H), 2.42 (t, J = 6.2 Hz, 2H, 12-H), 2.83–2.86 (m, 2H, 8-H), 3.29 (t, J = 6.2 Hz, 2H, 13-H), 5.25 (t, J = 8.3 Hz, 1H, 10-H), 7.24 (d, J = 8.4 Hz, 1H, 6-H), 7.50–7.59 (m, 2H, 2-H, 3-H), 7.73 (d, J = 8.4 Hz, 1H, 5-H), 7.85 (d, J = 8.0 Hz, 1H, 4-H), 8.10 (d, J = 8.4 Hz, 1H, 1-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 25.1 (q, Me), 25.4 (t, C-9), 26.1 (t, C-13), 31.1 (t, C-12), 45.7 (t, C-8), 121.5 (d, C-6), 122.7 (d, C-10), 124.3 (d, C-1), 126.2 (d, C-3), 126.4 (d, C-5), 126.8 (d, C-2), 128.8 (d, C-4), 131.8, 133.7, 135.2, 138.6 (4 s, Ar), 139.8 (s, C-11), 212.3 (s, C-7) ppm. IR (neat): ν = 3065–2855 (=CH, C–H), 1695 (C=O), 1595 (C=C), 1510 (C=C) cm^{-1}. MS (EI, 80 eV, 40 °C): m/z (%) = 250 (100) [M$^+$], 194 (24), 193 (27), 28 (26). HRMS (EI): Calcd for $C_{18}H_{18}O$: 250.13577. Found: 250.13670.

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