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A Gold-Catalyzed Domino Process to the Steroid Framework

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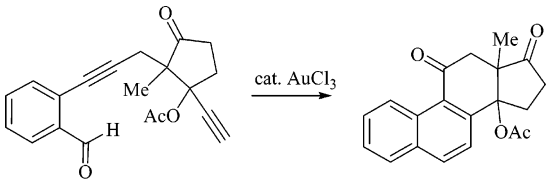

The facile formation of the B and C ring of *rac*-desoxyequilenin and of a chrysenone derivative in just one preparative step is demonstrated, applying a gold-catalyzed domino process, which involves a benzopyrylium cation as the key intermediate and an intramolecular [3 + 2] cycloaddition as the key step.

Introduction

Gold as precious metal is known for being rather inert, a fact that might have somewhat hampered the development of gold catalysts. This has dramatically changed in recent years, and meanwhile it is clearly justified to claim that an eldorado for homogeneous catalysis has been found:[1] gold salts are now established as highly active catalysts, especially as soft and carbophilic Lewis acids. We became interested in a domino process, which transforms *o*-alkynyl-substituted aromatic aldehydes and ketones to annulated ring systems via intermediary benzopyrylium cations, featuring a fascinating 1,5-migration of the carbonyl oxygen. Initially found to proceed under Brønsted acid catalysis,[2] this process became broadly applicable under the moderate reaction conditions with gold, platinum, and copper salts as catalysts.[3] Recently, we succeeded in the total synthesis of heliophenanthrone,[4] a tricyclic ring system, prompting us to extend this synthetic method to the steroid framework. Herein we report on the synthesis of angular fused tetracyclic rings, including 3-desoxyequilenin (**1**), a steroid isolated from the urine of pregnant mares in 1945 by Prelog and Fuehrer and possessing a moderate estrogenic activity.[5]

Results and Discussion

The retrosynthetic analysis for the synthesis of 3-desoxyequilenin (**1**) is depicted in Scheme 1. In the key transformation of this synthesis—from **3** to **2**—rings B and C should be built up in a single preparative step. Ring D was planned to be introduced via cyclopentanone **5**, substituted with an ethynyl and a propargyl group. Ring A is derived from bromobenzaldehyde **4**. Since both diastereoisomers of **2** should lead to the natural product **1** in the final transformation, we decided to use a mixture of the diastereoisomers of **5** for the approach to racemic 3-desoxyequilenin (*rac*-**1**).

The bisalkyne coupling component **5** was efficiently synthesized in three steps from cyclopentadione **6** (Scheme 2). The C-alkylation with propargyl bromide proceeded smoothly in 80% yield, in accord with a known procedure.[6] Trimethylsilyl acetylene was metalated with *n*-BuLi and classically added to one of the chemically equivalent keto groups to give **7** in 84%

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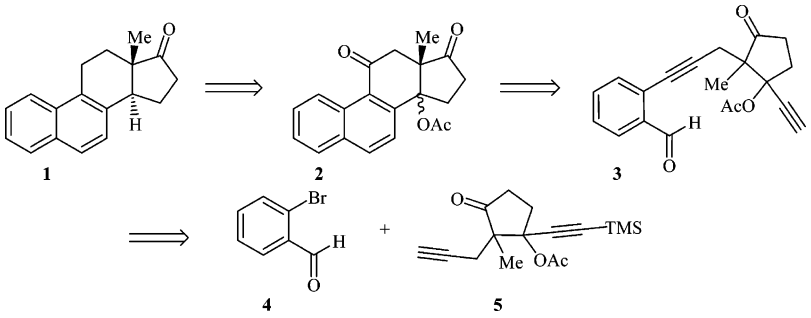
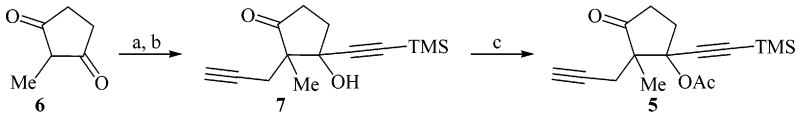
SCHEME 1. Retrosynthetic Analysis for the Synthesis of 3-Desoxyequilenin (1)

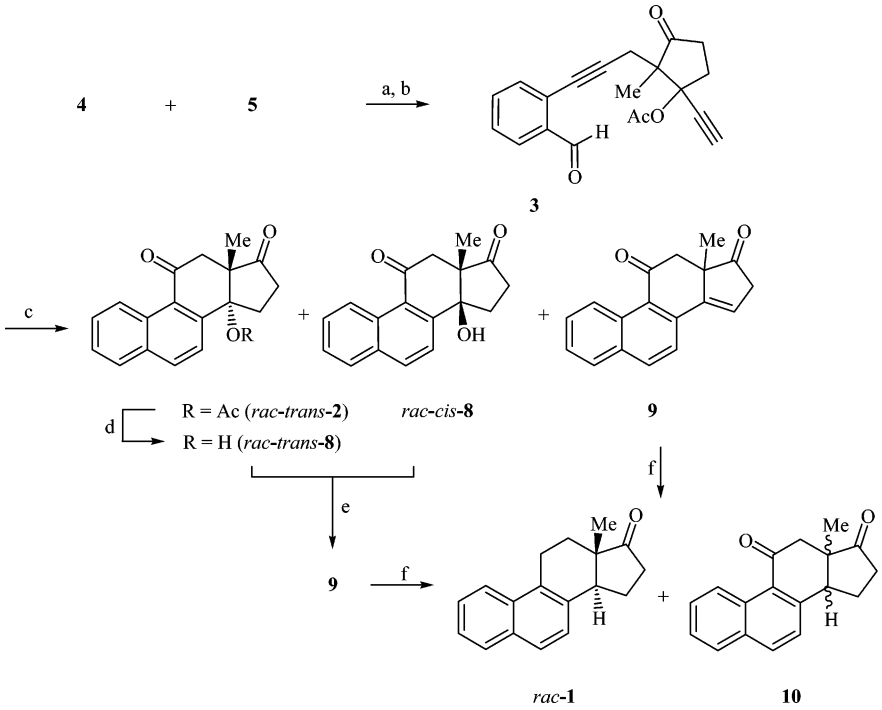


SCHEME 2. Preparation of Diyne 5[a]



[a] Conditions: (a) propargyl bromide, NaOH, H_2O, rt, 80%; (b) TMS acetylene, *n*-BuLi, −70 °C, THF, 84%; (c) $(AcO)_2O$, TEA, DMAP, rt, 85%.

SCHEME 3. Synthesis of Racemic 3-Desoxyequilenin (*rac*-1)[a]



[a] Conditions: (a) $PdCl_2(PPh_3)_2$ (2 mol %), CuI (2 mol %), TEA, 80 °C, 88%; (b) KF, THF, MeOH, rt, 92%; (c) $AuCl_3$ (3 mol %), MeCN, 80 °C, *rac-trans*-**2** (62%), *rac-cis*-**8** (7%), **9** (22%); (d) K_2CO_3, THF, MeOH, rt, 86%; (e) $KHSO_4$, $(AcO)_2O$, 100 °C, 71%; (f) H_2 (2.5 bar), Pd/C, EtOAc, *rac*-**1** (57%), **10** (36%) (diastereomeric mixture of *cis*-**10** and *trans*-**10**).

yield and a diastereomeric ratio of nearly 1:1 (determined by ^{1}H NMR).[7] Subsequent acetylation of the alcohol functionality gave the desired coupling component **5** in 85% yield.[8]

Compound **5** was coupled with aryl bromide **4** in a Sonogashira reaction,[9] followed by the cleavage of the TMS group with KF in THF/methanol, resulting in an overall yield of 81% of **3** (ratio of diastereoisomers 1:1.57).[10] For the gold chloride catalyzed cyclization of the functionalized aldehyde **3**, we anticipated the formation of a mixture of the two diastereoisomers of tetracycle **2**. Surprisingly, *cis*-**2** was completely missing in the crude product according to ^{1}H NMR analysis. Instead, the *trans*-annulated isomer *rac-trans*-**2** was isolated as the main product, accompanied by *rac-cis*-**8**—the hydrolization product of *cis*-**2**—and by the elimination product **9**, reflecting subtle steric or stereoelectronic influences on the reactivity of *cis*- and *trans*-**2**. The *trans*-configuration of the latter isomer was crucial for the identification of the subsequent products and therefore

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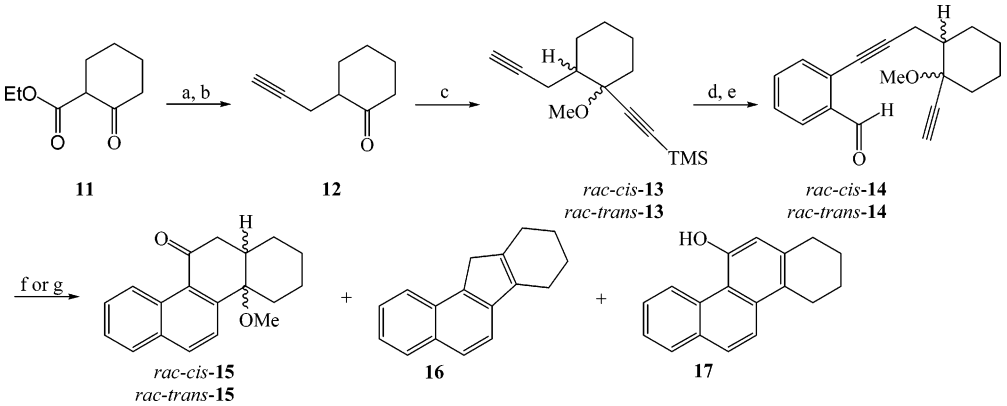
SCHEME 4. Synthesis of *rac-cis*-15 and *rac-trans*-15[a]



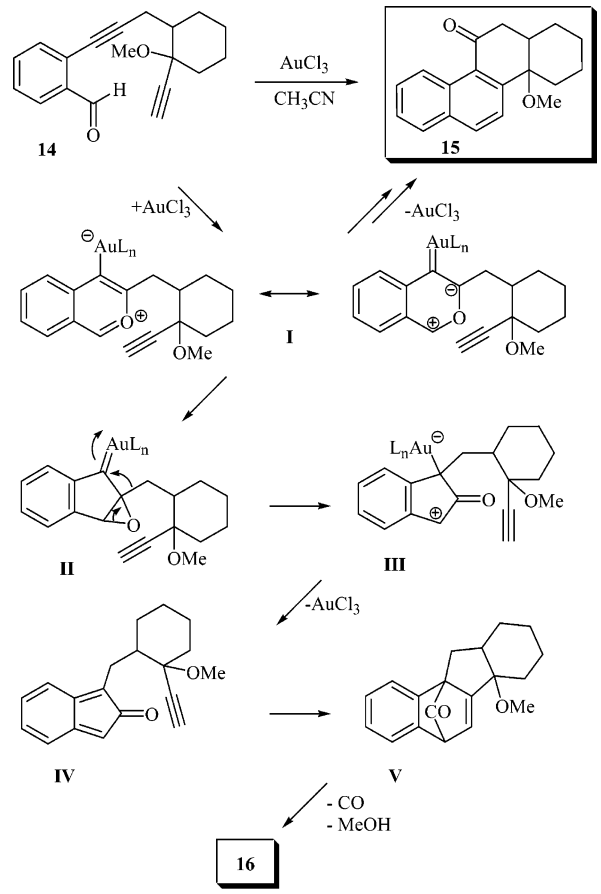
[a] Conditions: (a) KO*t*Bu, HO*t*Bu, propargyl bromide, rt, 86%; (b) LiI·$2H_2O$, 2,4,6-trimethylpyridine, 180 °C, 54%; (c) TMS acetylene, *n*-BuLi, −70 °C, MeI, THF, rt, 62%; (d) $PdCl_2(PPh_3)_2$ (2 mol %), CuI (2 mol %), TEA, 80 °C, 85% (*cis*), 88% (*trans*); (e) K_2CO_3, THF, MeOH, rt, 91%; (f) $AuCl_3$ (5 mol %), MeCN, 80 °C, transformation of *rac-cis*-**14** leads to *rac-cis*-**15** (27%), **16** (13%), **17** (15%), *rac-trans*-**14** leads to *rac-trans*-**15** (52%), **16** (10%), **17** (17%); (g) $AuCl_3$ (5 mol %), toluene, 120 °C (in a sealed tube), transformation of *rac-cis*-**14** generates *rac-cis*-**15** (77%), **16** (0%), **17** (0%), transformation of *rac-trans*-**14** generates *rac-trans*-**15** (75%), **16** (0%), **17** (0%).

was confirmed by a NOESY experiment due to the correlations observed between the methyl group and H-12 as well as H-15. In accord with this result, the correlation between the methyl group and the acetate functionality was missing.

Saponification of *rac-trans*-**2** with K_2CO_3 in THF/methanol gave *rac-trans*-**8** in 86% yield,[11] confirming the identity of *rac-trans*-**8** by comparison of the ^{1}H NMR spectra. The hydroxy groups of *rac-trans*-**8** and *rac-cis*-**8** were eliminated with $KHSO_4$ in acetic anhydride as solvent to give the β,γ-unsaturated ketone **9**.[12] Hydrogenation of **9** in ethyl acetate over palladium-on-charcoal at 2.5 bar hydrogen pressure gave racemic 3-desoxyequilenin (*rac*-**1**) and a diastereomeric mixture of **10** in 57 and 36% yield, respectively.[13]

To demonstrate the generality of the annulation method, we tested the synthesis of chrysenone *rac-cis*- and *rac-trans*-**15** as another tetracyclic product according to Scheme 4. C-Alkylation of the cyclic β-ketoester **11** with propargyl bromide and subsequent hydrolytic decarboxylation according to standard procedures gave the cyclohexanone **12** in an overall yield of 46%,[14] whereas the direct propargylation of cyclohexanone proved to be unsuccessful in terms of synthetic utility.[15] Preparation of the two diastereoisomers *rac-cis*-**13** and *rac-trans*-**13** in a ratio of 1.76:1 was achieved with a one-pot procedure by addition of lithiated trimethylsilyl acetylene to the keto functionality and quenching with methyl iodide;[7] the two diastereoisomers *rac-cis*-**13** and *rac-trans*-**13** were separated by flash column chromatography in 62% overall yield. The Sonogashira coupling reaction with 2-bromobenzaldehyde (**4**)[9] followed by cleavage of the TMS group with K_2CO_3 in THF/methanol provided *rac-cis*-**14** in 77% and *rac-trans*-**14** in 80% yield.[16] Surprisingly, the gold-catalyzed domino process let to the formation of three products when carried out in acetonitrile at 80 °C; besides the expected annulation products *rac-cis*-**15** and *rac-trans*-**15** (with low to moderate yields of 27 and 52%), phenolic compound **17** and the annulated fluorene **16** were identified as byproducts.[17] Changing to toluene as solvent and increasing the reaction temperature to 120 °C completely suppresses formation of these byproducts; instead, the chrysenones *rac-cis*-**15** and *rac-trans*-**15** were isolated with satisfactory yields above 75%. The relative configurations of both were identified by NOE experiments with the methine proton. However, the remarkable formation of **16**, which obviously involves a CO extrusion step, calls for a mechanistic interpretation (Scheme 5):

SCHEME 5. Proposed Mechanism for the Formation of 15 and 16



The double annulation process most probably proceeds through the benzopyrylium cation **I**, which results from the nucleophilic

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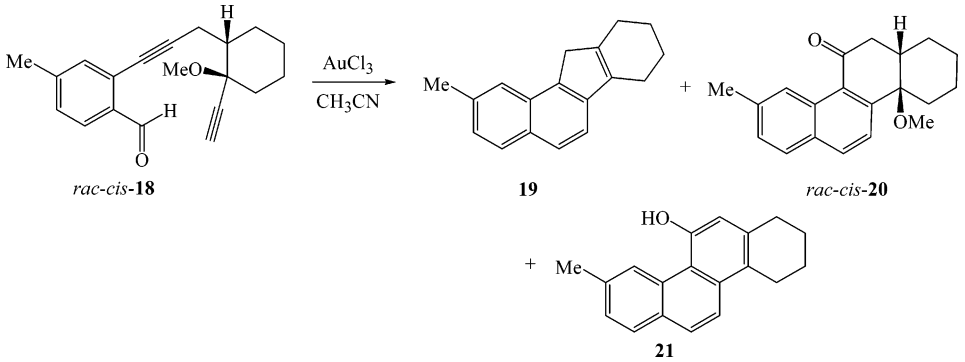
SCHEME 6. Synthesis of 19, *rac-cis*-20, and 21[a]



rac-cis-**18** **19** *rac-cis*-**20** **21**

[a] $AuCl_3$ (5 mol %), MeCN, 80°C, **19** (7%), *rac-cis*-**20** (47%), **21** (4%).

attack of the carbonyl oxygen at the alkyne, activated by the Lewis acidic gold salt. A subsequent intramolecular Huisgen-type [3 + 2] cycloaddition of the second alkyne followed by a rearrangement reaction leads to the aromatized final product **15**, in analogy to the calculations of Straub.[18] As a mechanistic pathway to the fluorene derivative **16**, we suggest an intramolecular ring closure of the dipolar intermediate **I** to oxirane **II** with a gold−carbene complex functionality.[19] A somewhat speculative rearrangement could lead to **III**, which should liberate the active catalyst under formation of the *o*-quinoid ketone **IV**. An intramolecular Diels−Alder reaction with the second alkyne moiety would lead to cycloadduct **V**, which should undergo the thermodynamically favorable extrusion of carbon monoxide and the final elimination of methanol to the observed byproduct **16**. To confirm the regioselectivity of the proposed mechanism, we synthesized model substrate *rac-cis*-**18**, equipped with a diagnostic methyl group (Scheme 6). The result of the gold-catalyzed annulation reaction corresponds to the mechanistic Scheme 5 because the methyl group indeed ends up at the 2-position of the fluorene derivative **19**, proven by two-dimensional NMR spectroscopy (HMBC correlation between the carbon of the methyl group at C-2 and H-1 and H-3 and by the absence of a cross signal between C-6 and H-11). The CO extrusion was confirmed with an indicator paper, which was soaked with an aqueous $PdCl_2$ solution; its color turned from brown to black upon contact with the gas phase above the reaction mixture.

Conclusion

The total syntheses of *rac*-3-desoxyequilenin and of a chrysenone derivative were accomplished via a gold-catalyzed domino process, which achieves a high degree of complexity in just one preparative step. This result demonstrates the usefulness of this method for the construction of tetracyclic ring systems as important structural framework of natural products, such as steroids.

Experimental Section

***trans*-14-Acetoxy-13-methyl-13,14,15,16-tetrahydro-12*H*-cyclopenta[*a*]phenanthrene-11,17-dione (*rac-trans*-2), *cis*-14-Hydroxy-13-methyl-13,14,15,16-tetrahydro-12*H*-cyclopenta[*a*]-phenanthrene-11,17-dione (*rac-cis*-8), and 13-Methyl-13,16-dihydro-12*H*-cyclopenta[*a*]phenanthrene-11,17-dione (9).** In a screw-capped flask, 385 mg (1.20 mmol) of **3** and 11 mg (36 μmol) of $AuCl_3$ were dissolved in 50 mL of acetonitrile. The mixture was stirred at 80 °C for 3 h and, after cooling to room temperature, filtered through a short pad of silica (eluent: ethyl acetate). After evaporation of the solvents, the residue was fractionated by flash chromatography (SiO_2, petroleum ether/ethyl acetate 3:1); 1st fraction (R_f = 0.33): 70 mg (22%) of **9** as colorless crystals (mp 109−111 °C); 2nd fraction (R_f = 0.19): 240 mg (62%) of *rac-trans*-**2** as colorless crystals (mp 55 °C); 3rd fraction (R_f = 0.09): 30 mg (7%) of *rac-cis*-**8** as colorless crystals (mp 170 °C). *rac-trans*-**2**: IR (KBr) $\tilde{\nu}$ 3056 (w), 2976 (w), 2935 (w), 1745 (vs), 1680 (s), 1430 (m), 1369 (m), 1236 (s), 1143 (m), 1078 (w), 1029 (m), 830 (m), 757 (m), 672 (w) cm^{-1}; UV (acetonitrile) λ_{max} (log ϵ) 316 (3.75), 308 (3.84), 234 (4.18) nm; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.24 (s, 3H), 2.10 (s, 3H), 2.11 (m, 1H), 2.59 (m, 1H), 2.65−2.79 (m, 2H), 3.00 (d, J = 14.6 Hz, 1H), 3.10 (d, J = 14.6 Hz, 1H), 7.55 (t, J = 7.8 Hz, 1H), 7.63−7.67 (m, 2H), 7.82 (d, J = 7.8 Hz, 1H), 8.08 (d, J = 8.8 Hz, 1H), 9.25 (d, J = 8.8 Hz, 1H); ^{13}C NMR {^1H} ($CDCl_3$, 100 MHz) δ 18.7, 21.6, 34.8, 35.2, 46.7, 53.4, 86.7, 123.0, 127.2, 127.3, 127.8, 128.2, 129.5, 129.8, 133.4, 135.5, 143.7, 169.9, 197.7, 215.3; MS (70 eV, EI) *m*/*z* (%) = 322 [M^+] (100), 280 (36), 262 (55), 238 (67), 220 (63), 196 (29), 178 (24), 165 (24), 152 (16), 127 (13), 73 (19), 43 (66). Anal. Calcd for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63. Found: C, 74.71; H, 5.49. *rac-cis*-**8**: IR (KBr) $\tilde{\nu}$ 3446 (s), 2951 (w), 2919 (w), 1750 (vs), 1648 (vs), 1590 (m), 1434 (m), 1209 (m), 1021 (m), 770 (m) cm^{-1}; UV (acetonitrile) λ_{max} (log ϵ) 318 (3.78), 308 (3.80), 242 (4.27), 224-(4.28) nm; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.97 (s, 3H), 2.01 (s, 1H), 2.59−2.76 (m, 4H), 2.63 (d, J = 18.4 Hz, 1H), 3.32 (dd, J = 18.3, 0.5 Hz, 1H), 7.52 (d, J = 8.3 Hz, 1H), 7.56 (td, J = 7.6, 1.0 Hz, 1H), 7.67 (td, J = 8.0, 1.0 Hz, 1H), 7.89 (d, J = 8.3 Hz, 1H), 8.12 (d, J = 8.3 Hz, 1H), 9.18 (d, J = 8.8 Hz, 1H); ^{13}C NMR {^1H} ($CDCl_3$, 100 MHz) δ 21.7, 29.8, 33.6, 42.4, 53.7, 79.5, 121.1, 126.7, 127.0, 127.4, 128.7, 129.5, 131.3, 134.5, 135.2, 142.7, 199.6, 216.0; MS (70 eV, EI) *m*/*z* (%) = 280 [M^+] (100), 262 (7), 221 (33), 207 (12), 197 (79), 178 (17), 165 (19), 152 (15), 127 (16). Anal. Calcd for $C_{13}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 77.41; H, 5.89. **9**: IR (KBr) $\tilde{\nu}$ 3062 (w), 2967 (w), 2928 (w), 1747 (vs), 1664 (vs), 1612 (m), 1590 (m), 1508 (m), 1428 (m), 1362 (m), 1213 (s), 1195 (m), 1149 (m), 1053 (m), 988 (m), 839 (m), 808 (s), 780 (m), 767 (m) cm^{-1}; UV (acetonitrile) λ_{max} (log ϵ) 327 (3.69), 277

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(4.22), 267 (4.25), 256 (4.26), 229 (4.25) nm; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.32 (s, 3H), 2.83 and 2.95 (d, J = 15.2 Hz, 2H), 3.21 and 3.42 (dd, J = 23.7, 2.5 Hz, 2H), 6.62 (t, J = 2.5 Hz, 1H), 7.53 (td, J = 7.3, 1.0 Hz, 1H), 7.66 (td, J = 7.8, 1.5 Hz, 1H), 7.72 (d, J = 8.6 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 8.04 (d, J = 8.6 Hz, 1H), 9.40 (d, J = 8.8 Hz, 1H); ^{13}C NMR {^{1}H} ($CDCl_3$, 100 MHz) δ 21.6, 42.7, 47.5, 52.6, 121.5, 121.8, 124.7, 126.9, 127.3, 128.6, 129.6, 131.2, 134.1, 135.4, 136.2, 144.6, 198.4, 216.5; MS (70 eV, EI) m/z (%) = 262 [M$^+$] (100), 234 (74), 219 (34), 206 (36), 191 (34), 178 (13), 165 (24), 117 (9), 101 (7), 89 (10). Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.43; H, 5.77.

***trans*-14-Hydroxy-13-methyl-13,14,15,16-tetrahydro-12*H*-cyclopenta[*a*]phenanthrene-11,17-dione (*rac-trans*-8).** A solution of 104 mg (0.75 mmol) of K_2CO_3 in 10 mL of methanol was added to 240 mg (0.75 mmol) of *rac-trans*-**2** in 10 mL of THF, and the mixture was stirred for 16 h. Fifteen milliliters of aqueous 1 N NH_4Cl was added, and the water layer was extracted three times with 20 mL of MTBE. The combined organic extract was dried over sodium sulfate. Evaporation of the solvents and flash chromatography of the residue (SiO_2, petroleum ether/ethyl acetate 2:1; R_f = 0.26) resulted in 180 mg (86%) of *rac-trans*-**8** as colorless crystals (mp 212 °C): IR (KBr) $\tilde{\nu}$ 3465 (s), 2977 (w), 2927 (w), 1727 (vs), 1654 (vs), 1591 (m), 1508 (m), 1362 (m), 1330 (m), 1218 (s), 1183 (m), 1067 (s), 971 (m), 828 (m), 759 (m) cm^{-1}; UV (acetonitrile) λ_{max} (log ϵ) 317 (3.76), 308 (3.82), 244 (4.21), 227 (4.23) nm; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.26 (s, 3H), 2.11 (s, 1H), 2.44−2.81 (m, 4H), 2.56 (d, J = 15.1 Hz, 1H), 2.94 (d, J = 14.9 Hz, 1H), 7.57 (td, J = 7.6, 1.0 Hz, 1H), 7.68 (td, J = 7.8, 1.5 Hz, 1H), 7.85 ("d", 1H), 7.89 (d, J = 8.8 Hz, 1H), 8.15 (d, J = 8.6 Hz, 1H), 9.34 (d, J = 8.8 Hz, 1H); ^{13}C NMR {^{1}H} ($CDCl_3$, 100 MHz) δ 14.6, 35.4, 35.5, 47.0, 57.2, 80.0, 123.4, 125.0, 127.0, 127.1, 128.5, 129.7, 130.3, 133.6, 136.2, 147.0, 196.6, 216.5; MS (70 eV, EI) m/z (%) = 280 [M$^+$] (100), 262 (6), 224 (87), 209 (16), 197 (34), 181 (17), 165 (17), 152 (17), 127 (25). Anal. Calcd for $C_{13}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 77.37; H, 5.70.

Elimination Reaction of 8 to 9. Ninety milligrams (0.32 mmol) of a mixture of *rac-trans*-**8** and *rac-cis*-**8** was dissolved in 4 mL of acetic anhydride; 109 mg (0.80 mmol) of $KHSO_4$ was added and the mixture was heated at 100 °C for 1 h. Ten milliliters of 5% aqueous $KHCO_3$ was added, and the water layer was extracted with MTBE. The combined organic extract was washed with brine and dried over sodium sulfate. Evaporation of the solvents and flash chromatography of the residue (SiO_2, petroleum ether/ethyl acetate 3:1; R_f = 0.35) gave 60 mg (71%) of **9** as colorless crystals (mp 109−111 °C).

***rac*-3-Desoxyequilenin (*rac*-1) and 13-Methyl-13,14,15,16-tetrahydro-12*H*-cyclopenta[*a*]phenanthrene-11,17-dione (10).** Fifty-five milligrams (0.21 mmol) of **9** was hydrogenated within 2.5 h at 2.5 bar of hydrogen pressure in ethyl acetate (10 mL) using 50 mg of 10% palladium-on-charcoal as catalyst. The mixture was filtrated, the solvent evaporated, and the residue was fractionated by flash chromatography (SiO_2, petroleum ether/ethyl acetate 3:1); 1st fraction (R_f = 0.52): 20 mg (36%) of **10** in the ratio 1:1.58 as colorless crystals (mp 146−149 °C); 2nd fraction (R_f = 0.20): 30 mg (57%) of *rac*-**1** as colorless crystals (mp 180 °C). *rac*-**1**: IR (KBr) $\tilde{\nu}$ 3046 (w), 2930 (s), 2865 (m), 1735 (vs), 1509 (m), 1459 (m), 1428 (m), 1369 (m), 1349 (m), 1287 (m), 1251 (m), 1063 (m), 1033 (m), 1014 (m), 820 (s), 764 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.82 (s, 3H), 1.91 (m, 1H), 2.04 (m, 1H), 2.24 (m, 1H), 2.42 (dd, J = 18.7, 9.1 Hz, 1H), 2.58 (m, 1H), 2.71 (dd, J = 19.2, 8.6 Hz, 1H), 3.21 (dd, J = 12.6, 6.0 Hz, 1H), 3.31−3.37 (m, 2H), 7.32 (d, J = 8.6 Hz, 1H), 7.46 (t, J = 7.8 Hz, 1H), 7.53 (td, J = 8.3, 1.3 Hz, 1H), 7.74 (d, J = 8.3 Hz, 1H), 7.84 (d, J = 7.8 Hz, 1H), 7.97 (d, J = 8.3 Hz, 1H); ^{13}C NMR {^{1}H} ($CDCl_3$, 100 MHz) δ 13.4, 22.0, 24.1, 29.3, 36.7, 47.1, 47.7, 123.4, 123.9, 125.2, 126.3, 126.8, 128.8, 131.0, 132.1, 132.6, 134.6, 219.9; MS (70 eV, EI) m/z (%) = 250 [M$^+$] (100), 235 (4), 207 (20), 193 (37), 178 (27), 165 (25), 113 (12), 98 (17), 89 (16), 76 (7). **10**: IR (KBr) $\tilde{\nu}$ 3021 (w), 2970 (w), 1745 (vs), 1662 (vs), 1594 (m), 1512 (m),-1335 (w), 1208 (m), 1132 (w), 1111 (w), 1038 (w), 1010 (w), 958 (w), 840 (m), 822 (m), 764 (m) cm^{-1}; UV (acetonitrile) λ_{max} (log ϵ) 317 (3.83), 308 (3.82), 246 (4.31), 220 (4.44) nm; ^{1}H NMR ($CDCl_3$, 400 MHz) double set of signals because of diastereoisomers (ratio 3:2) δ 0.86 and 1.29 (s, 3H), 2.12−2.24 (m, 1H), 2.39−2.77 (m, 4H), 2.92 and 2.94 (d, J = 13.8, 18.2 Hz, 1H), 2.35−3.44 (m, 1H), 7.38 and 7.41 (d, J = 8.6, 8.4 Hz, 1H), 7.53 ("t", 1H), 7.67 ("t", 1H), 7.83 and 7.87 (d, J = 7.6, 8.4 Hz, 1H), 8.03 and 8.09 (d, J = 8.3, 8.4 Hz, 1H), 9.30 and 9.31 (d, J = 8.8, 8.6 Hz, 1H); ^{13}C NMR {^{1}H} ($CDCl_3$, 100 MHz) δ 15.3, 20.4, 22.1, 28.5, 35.9, 37.7, 43.2, 49.0, 46.4, 48.4, 49.0, 50.4, 123.1, 126.7, 125.8, 127.0, 126.3, 126.5, 126.4, 126.6, 128.5, 128.7, 129.4, 129.5, 130.9, 131.4, 133.1, 133.4, 135.4, 135.4, 143.3, 145.6, 197.6, 198.7, 217.3, 218.0; MS (70 eV, EI) m/z (%) = 264 [M$^+$] (100), 236 (10), 221 (10), 208 (48), 196 (40), 178 (23), 165 (37), 152 (13), 76 (5).

***trans*-10a-Methoxy-6a,7,8,9,10,10a-hexahydro-6*H*-chrysen-5-one (*rac-trans*-15), 8,9,10,11-Tetrahydro-7*H*-benzo[*a*]fluorene (16), and 7,8,9,10-Tetrahydrochrysen-5-ol (17).** In a screw-capped flask, 135 mg (0.48 mmol) of *rac-trans*-**14** and 7.0 mg (23 μmol) of $AuCl_3$ were dissolved in 20 mL of acetonitrile. The mixture was stirred at 80 °C for 3 h and, after cooling to room temperature, filtered through a short pad of silica (eluent: ethyl acetate). After evaporation of the solvents, the residue was fractionated by flash chromatography (SiO_2, petroleum ether/ethyl acetate 20:1); 1st fraction (R_f = 0.73): 11 mg (10%) of **16** as colorless crystals (mp 81 °C); 2nd fraction (R_f = 0.30): 70 mg (52%) of *rac-trans*-**15** as colorless crystals (mp 105−107 °C); 3rd fraction (R_f = 0.13): 20 mg (17%) of **17** as colorless crystals (mp 189−190 °C). *rac-trans*-**15**: IR (KBr) $\tilde{\nu}$ 2929 (s), 2855 (s), 2823 (m), 1668 (vs), 1590 (m), 1460 (m), 1448 (m), 1367 (m), 1341 (m), 1231 (s), 1220 (s), 1199 (m), 1115 (s), 1071 (s), 1059 (s), 927 (m), 838 (s), 828 (s), 812 (s), 753 (vs) cm^{-1}; UV (acetonitrile) λ_{max} (log ϵ) 312 (3.91), 308 (3.98), 240 (4.52), 222 (4.57) nm; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.34 (m, 1H), 1.56 (m, 1H), 1.60−1.84 (m, 5H), 2.13 (m, 1H), 2.66 (dd, J = 18.1, 7.0 Hz, 1H), 2.79 (dd, J = 18.1, 10.6 Hz, 1H), 2.85 (m, 1H), 2.87 (s, 3H), 7.53 (td, J = 7.5, 1.0 Hz, 1H), 7.60−7.64 (m, 2H), 7.85 (d, J = 8.0 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 9.04 (d, J = 9.0 Hz, 1H); ^{13}C NMR {^{1}H} ($CDCl_3$, 100 MHz) δ 21.5, 25.5, 28.7, 29.2, 41.4, 42.5, 49.9, 73.8, 122.8, 126.6, 126.8, 128.1, 128.6, 129.6, 130.8, 132.5, 133.6, 145.8, 201.0; MS (70 eV, EI) m/z (%) = 280 [M$^+$] (100), 265 (15), 249 (67), 237 (14), 221 (33), 207 (20), 181 (79), 165 (25), 152 (20), 141 (12). Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.06; H, 7.25. **16**: IR (KBr) $\tilde{\nu}$ 3051 (m), 2929 (s), 2852 (m), 2826 (m), 1615 (w), 1513 (w), 1435 (m), 1397 (m), 1257 (m), 1209 (w), 1139 (m), 1022 (w), 943 (w), 820 (vs), 810 (vs), 744 (vs) cm^{-1}; UV (acetonitrile) λ_{max} (log ϵ) 316 (3.69), 304 (3.89), 296 (3.80), 248 (4.17), 218 (4.14) nm; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.85 (m, 4H), 2.52 (s, 4H), 3.56 (s, 2H), 7.34 (td, J = 7.5, 1.2 Hz, 1H), 7.44 (m, 2H), 7.76 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 8.3 Hz, 1H); ^{13}C NMR {^{1}H} ($CDCl_3$, 100 MHz) δ 22.6, 22.9, 23.5, 26.1, 39.6, 117.9, 123.5, 123.9, 126.0, 127.0, 129.0, 130.2, 131.4, 136.6, 138.7, 141.0, 143.7; MS (70 eV, EI) m/z (%) 220 [M$^+$] (100), 202 (6), 192 (51), 178 (15), 165 (12), 96 (5). Anal. Calcd for $C_{17}H_{16}$: C, 92.68; H, 7.32. Found: C, 92.30; H, 7.41. **17**: IR (KBr) $\tilde{\nu}$ 3520 (vs), 2929 (s), 2855 (m), 1621 (w), 1422 (w), 1391 (m), 1307 (m), 1221 (m), 1188 (m), 1111 (m), 850 (m), 807 (s), 755 (s) cm^{-1}; UV (acetonitrile) λ_{max} (log ϵ) 362 (3.62), 345 (3.53), 329 (3.30), 308 (3.93), 301 (3.94), 276 (4.28), 245 (4.29) nm; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.87 (m, 2H), 1.99 (m, 2H), 2.89 (t, J = 6.3 Hz, 2H), 3.11 (t, J = 6.3 Hz, 2H), 5.49 (s, 1H), 6.72 (s, 1H), 7.56 (td, J = 7.2, 1.2 Hz, 1H), 7.63 (td, J = 7.8, 1.5 Hz, 1H), 7.77 (d, J = 9.4 Hz, 1H), 7.88 (dd, J = 7.8, 1.3 Hz, 1H), 7.92 (d, J = 9.1 Hz, 1H), 9.64 (d, J = 8.6 Hz, 1H); ^{13}C NMR {^{1}H} ($CDCl_3$, 100 MHz) δ 22.9, 23.8, 26.3, 30.4, 114.5, 118.2, 122.1, 125.4, 125.6, 126.5, 128.2, 128.6, 128.6, 130.9, 132.0, 133.3, 135.9, 152.2; MS (70 eV, EI) m/z (%) = 248 [M$^+$] (100), 231 (5), 220 (26), 191 (10), 165 (7), 124 (7), 101 (12).

***cis*-10a-Methoxy-6a,7,8,9,10,10a-hexahydro-6*H*-chrysen-5-one (*rac*-*cis*-15), 8,9,10,11-Tetrahydro-7*H*-benzo[*a*]fluorene (16), and 7,8,9,10-Tetrahydrochrysen-5-ol (17).** In a screw-capped flask, 135 mg (0.48 mmol) of *rac*-*cis*-**14** and 7.0 mg (23 μmol) of $AuCl_3$ were dissolved in 20 mL of acetonitrile. The mixture was stirred at 80 °C for 3 h and, after cooling to room temperature, filtered through a short pad of silica (eluent: ethyl acetate). After evaporation of the solvents, the residue was fractionated by flash chromatography (SiO_2, petroleum ether/ethyl acetate 20:1); 1st fraction (R_f = 0.73): 14 mg (13%) of **16** as colorless crystals (mp 81 °C); 2nd fraction (R_f = 0.23): 37 mg (27%) of *rac*-*cis*-**15** as colorless crystals (mp 112 °C); 3rd fraction (R_f = 0.13): 18 mg (15%) of **17** as colorless crystals (mp 189−190 °C). *rac*-*cis*-**15**: IR (KBr) $\tilde{\nu}$ 2930 (s), 2858 (s), 2823 (m), 1665 (vs), 1616 (m), 1502 (m), 1446 (m), 1429 (m), 1357 (m), 1343 (m), 1267 (m), 1243 (m), 1223 (m), 1214 (m), 1181 (m), 1166 (m), 1098 (m), 1079 (s), 1066 (s), 839 (s), 799 (m), 757 (s) cm^{-1}; UV (acetonitrile) λ_{max} (log ϵ) 312 (3.37), 308 (3.41), 245 (3.88), 215 (4.15) nm; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.45−1.62 (m, 4H), 1.84−1.96 (m, 4H), 2.75 (dd, J = 15.6, 4.0 Hz, 1H), 2.84 (m, 1H), 3.06 (s, 3H), 3.07 (dd, J = 15.6, 13.5 Hz, 1H), 7.53 (t, J = 7.0 Hz, 1H), 7.64 (td, J = 8.5, 1.5 Hz, 1H), 7.70 (d, J = 9.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 9.0 Hz, 1H), 9.39 (d, J = 8.5 Hz, 1H); ^{13}C NMR {^1H} ($CDCl_3$, 100 MHz) δ 19.9, 21.7, 26.6, 34.8, 35.5, 43.7, 50.0, 78.0, 123.7, 126.6, 127.0, 128.0, 128.3, 128.9, 131.0, 133.3, 134.9, 149.9, 200.6; MS (70 eV, EI) *m*/*z* (%) = 280 [M^+] (100), 265 (12), 249 (52), 237 (27), 223 (38), 209 (25), 181 (59), 165 (29), 152 (24), 127 (13). Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.06; H, 7.25.

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Supporting Information Available: Experimental details of the syntheses of **3**, **5**, **7**, **13**, **14**, **18**−**21** as well as additional characterization data and spectra of all products. This material is available free of charge via Internet at http://pubs.acs.org.

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