Supplementary Material (ESI) for Chemical Communications

Bio-inspired Polyene Cyclization: Synthesis of Tetracyclic Terpenoids Promoted by Steroidal Acetal-$SnCl_4$

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General

Experiments involving moisture and/or air sensitive components were performed in oven-dried glassware. Commercial solvents and reagents were used without further purification with the following exceptions: THF was freshly distilled from sodium wire, CH_2Cl_2 (DCM) was freshly distilled from CaH_2, and dried Et_2O was taken from solvent purification system (PS-400-5, innovative technology Inc.). HPLC grade isopropanol was used without further purification. Aldehyde was distilled before used.

Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 precoated silica gel plate (0.2 mm thickness). Subsequent to elution, plates were visualized using UV radiation (254 nm) on Spectroline Model ENF-24061/F 254 nm. Further visualization was possible by staining with basic solution of potassium permanganate or acidic solution of ceric molybdate, followed by heating on a hot plate.

Flash chromatography was performed using Merck silica gel 60 with distilled solvents. Columns were typically packed as slurry and equilibrated with hexane prior to use.

Infrared spectra were recorded on a Shimadzu IR Prestige-21 FT-IR Spectrometer. Liquid samples were examined as film between NaCl or KBr salt plates.

Proton nuclear magnetic resonance (^{1}H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectroscopy were performed on a Bruker Advance 300, 400 and 500 NMR spectrometers. Chemical shifts ^{1}H NMR spectra are reported as in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-*d* (7.264, singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublet of doublets); ddd (doublet of doublets of doublets); dddd (doublet of doublets of doublets of doublets); dt (doublet of triplets); m (multiplets) and etc. The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported as a *J* value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) are reported as in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-*d* (7.03, triplet). *ee* was determined by chiral HPLC analysis.

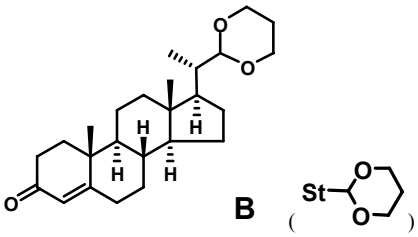
Low resolution mass spectrum analysis was performed on Finnigan polaris Q, GCMS XP mass spectrometer (Thermo Electron Corporation). High resolution mass spectral analysis (HRMS) was performed on Finnigan MAT 95 XP mass spectrometer (Thermo Electron Corporation).

X-ray crystallogphy analysis was performed on Bruker X8 APEX X-Ray diffractometer.

Optical rotation was measured using a JASCO P-1030 Polarimeter equipped with a sodium vapor lamp at 589 nm. Concentration is denoted as *c* and was calculated as grams per deciliters (g / 100mL) whereas the solvent in indicated in parentheses (*c*, solvent).

1. General procedure for preparation of acetals

Acetals were synthesized according to the method developed by R. Noyori[1] and modified method developed by Masaaki Kurihara.[2] Chiral cyclic acetal was synthesis as following: To a solution of StdCHO (329 mg, 1.0 mmol, 1.0 eq.) in DCM (5 mL) was added $(TMSO)_2R$ (221 mg, 1.0 mmol, 1.0 eq.). The reaction mixture was cooled to -78 ^{o}C prior to addition of TMSOTf (11 mg, 0.05 mmol, 0.05 eq.). The reaction was allowed to proceed at -78 ^{o}C for overnight before quenching with pyridine (2 mL). The mixture was diluted with DCM (30 mL), washed with water (20 mL) and brine (20 mL), and dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residual crude product was purified by flash column chromatography to afford the desired acetals.



(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((*S*)-1-(1,3-dioxan-2-yl)ethyl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[α]phenanthren-3(2*H*)-one (B) , white solid, 70% yield. $[\alpha]^{20.0}_{D}$ = 62.9 (*c* 1.89, $CHCl_3$)

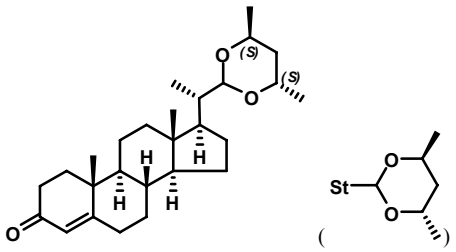
R*f*: 0.35 (Hexane : Ethyl Acetate = 4:1)

^{1}H NMR (400 MHz, $CDCl_3$): 5.59 (s, 1H), 4.36 (d, *J* = 1.78 Hz, 1H), 3.97 (dd, *J* = 11.14, 4.62 Hz, 2H), 3.65 (td, *J* = 12.21, 1.30 Hz, 1H), 3.58 (td, *J* = 11.85, 1.54 Hz, 1H), 1.07 (s, 3H), 0.89 (d, *J* = 6.75 Hz, 3H), 0.59 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.3, 171.3, 123.7, 103.6, 66.9, 66.8, 55.3, 53.7, 51.4, 42.3, 40.6, 39.3, 38.5, 35.6, 35.5, 33.9, 32.8, 31.9, 27.2, 25.9, 24.2, 20.9, 17.3, 12.4, 11.8

HRMS (ESI): *m*/*z* calculated for $C_{25}H_{38}O_3$ $[M]^+$: 386.2821, Found: 386.2815

FTIR (NaCl): ν 1672, 1614 cm^{-1}



C

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((S)-1-((4*S*,6*S*)-4,6-dimethyl-1,3-dioxan-2-yl)ethyl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[α]phenanthren-3(2*H*)-one (C), white solid, 85% yield. $[\alpha]^{20.0}_{D}$ = 49.9 (*c* 3.48, $CHCl_3$)

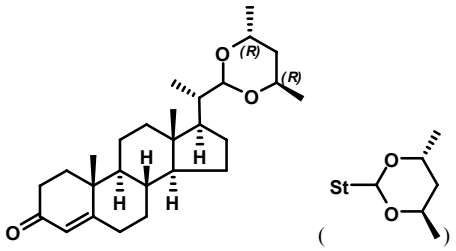
R*f*: 0.42 (Hexane : Ethyl Acetate = 4:1)

^{1}H NMR (400 MHz, $CDCl_3$): 5.71 (s, 1H), 4.79 (d, *J* = 1.96 Hz, 1H), 4.27 (quintet, *J* = 6.66 Hz, 1H), 3.84 (dtd, *J* = 17.65, 6.03, 2.24 Hz, 1H), 1.32 (d, *J* = 7.03 Hz, 3H), 1.17 (s, 3H), 1.16 (d, *J* = 6.88 Hz, 3H), 0.98 (d, *J* = 6.58 Hz, 3H), 0.69 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.7, 171.7, 123.8, 95.4, 67.9, 67.4, 55.3, 53.8, 51.7, 42.4, 40.6, 39.4, 38.6, 37.0. 35.8, 34.0, 32.9, 32.1, 27.3, 24.3, 22.0, 21.0, 17.4, 17.3, 12.5, 11.9

HRMS (ESI): *m*/*z* calculated for $C_{27}H_{42}O_3$ $[M]^+$: 414.3134, Found $[M+H]^+$: 415.3207

FTIR (NaCl): ν 1674, 1610 cm^{-1}



D

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((*S*)-1-((4*R*,6*R*)-4,6-dimethyl-1,3-dioxan-2-yl)ethyl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[α]phenanthren-3(2*H*)-one (D), white solid, 90% yield. $[\alpha]^{20.0}_{D}$ = 75.0 (*c* 1.95, $CHCl_3$)

R*f*: 0.42 (Hexane : Ethyl Acetate = 4:1)

^{1}H NMR (400 MHz, $CDCl_3$): 5.72 (s, 1H), 4.82 (s, 1H), 4.28 (quintet, *J* = 6.78 Hz, 1H), 3.96 (dtd, *J* = 17.32, 6.04, 1.48 Hz, 1H), 1.33 (d, *J* = 7.31 Hz, 3H), 1.19 (d, *J* = 6.16 Hz, 3H), 1.17 (s, 3H), 1.00 (d, *J* = 6.75 Hz, 3H), 0.70 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.7, 171.6, 123.8, 94.9, 67.7, 67.3, 55.3, 53.8, 51.6, 42.4, 40.5, 39.4, 38.6, 36.9,

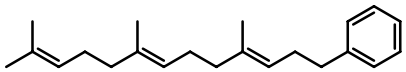
35.7, 35.7, 34.0, 32.9, 32.0, 27.1, 24.3, 22.0, 21.0, 17.4, 17.0, 12.2, 11.9

HRMS (ESI): *m*/*z* calculated for $C_{27}H_{42}O_3$ $[M]^+$: 414.3134, Found $[M+H]^+$: 415.3207

FTIR (NaCl): ν 1666, 1610 cm^{-1}

2. General procedure for preparation of polyene

The procedure was following the method developed by Martin Demuth.[3] To an oven-dried 100 mL round-bottom flask equipped with a magnetic stirring bar was added $[(Ph_3P)_4Pd]$ (0.289g, 0.25 mmol, 5 mol%) and dry THF (20 mL). The solution was cooled to 0 °C prior to addition of farnesyl bromide (1.36 mL, 5.0 mmol, 1.0 eq.). The solution was stirred for 5 minutes and was treated with the Grignard reagent (1.0 M in THF solution, 7.5 mL, 7.5 mmol, 1.5 eq.). The reaction mixture was allowed to proceed at room temperature for another 24 hours before quenching with ice water (30 mL). The aqueous layer was extracted with diethyl ether (2 × 30 mL), and the combined organic extracts were washed with water (30 mL) and brine (30 mL) and dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The residual crude product was purified by column chromatography to afford the desired product.



1

(3*E*,7*E*)-4,8,12-trimethyltrideca-3,7,11-trienyl)benzene (1), colorless oil, 87% yield.

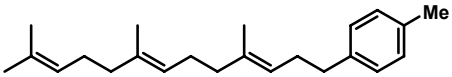
R_f: 0.91 (Hexane : Et_2O = 9:1)

^{1}H NMR (400 MHz, $CDCl_3$): 7.32–7.25 (m, 2H), 7.22–7.16 (m, 3H), 5.25–5.18 (m, 1H), 5.17–5.08 (m, 2H), 2.66 (t, *J* =7.88 Hz, 2H), 2.32 (q, *J* = 8.40 Hz, 2H), 2.09 (q, *J* = 6.60 Hz, 4H), 2.01 (q, *J* = 3.67 Hz, 4H), 1.71 (s, 3H), 1.62 (s, 6H), 1.64 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 142.4, 135.8, 135.0, 131.3, 128.5, 128.2, 125.7, 124.4, 124.2, 123.6, 39.8, 39.7, 36.2, 30.0, 26.8, 26.6, 25.7, 17.7, 16.0, 16.0

HRMS (EI): *m*/*z* calculated for $C_{22}H_{32}$ $[M]^+$: 296.2504, Found: 296.2494

FTIR (NaCl): ν 1662, 1494, 1452, 1373 cm^{-1}



1c

1-methyl-4-((3*E*,7*E*)-4,8,12-trimethyltrideca-3,7,11-trienyl)benzene (1c), colorless oil, 78% yield.

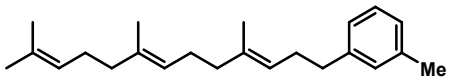
R_f: 0.91 (Hexane : Et_2O = 9:1)

^{1}H NMR (400 MHz, $CDCl_3$): 7.12–7.04 (m, 4H), 5.19 (td, *J* = 6.99, 0.95 Hz, 1H), 5.14–5.05 (m, 2H), 2.59 (dd, *J* = 9.59, 7.34 Hz, 2H), 2.31 (s, 3H), 2.32–2.23 (m, 2H), 2.13–2.02 (m, 4H), 2.02–1.92 (m, 4H), 1.68(s, 3H), 1.60 (s, 6H), 1.57 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 139.4, 135.7, 135.1, 135.0, 129.0, 128.9, 128.3, 124.4, 124.2, 123.8, 39.8, 39.7, 35.7, 30.1, 26.8, 26.6, 25.7, 21.0, 17.7, 16.0, 16.0

HRMS (EI): *m*/*z* calculated for $C_{23}H_{34}$ $[M]^+$: 310.2661, Found: 310.2650

FTIR (NaCl): ν 1514, 1448, 1377, 1107 cm^{-1}



1d

1-methyl-3-((3*E*,7*E*)-4,8,12-trimethyltrideca-3,7,11-trienyl)benzene (1d), colorless oil, 66% yield.

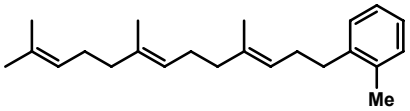
R_f: 0.91 (Hexane : Et_2O = 9:1)

^{1}H NMR (400 MHz, $CDCl_3$): 7.20–7.10 (m, 1H), 7.04–6.90 (m, 3H), 5.19 (td, *J* = 7.11, 1.33 Hz, 1H), 5.15–5.05 (m, 2H), 2.59 (dd, *J* = 9.71, 7.48 Hz, 2H), 2.32 (s, 3H), 2.33–2.23 (m, 2H), 2.13–2.02 (m, 4H), 2.02–1.93 (m, 4H), 1.68 (s, 3H), 1.56 (s, 6H), 1.51 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 142.4, 137.7, 135.7, 135.0, 131.3, 129.3, 128.1, 126.4, 125.5, 124.4, 124.2, 123.7, 39.8, 39.7, 36.1, 30.1, 26.8, 26.7, 25.7, 21.4, 17.7, 16.0, 16.0

HRMS (EI): *m*/*z* calculated for $C_{23}H_{34}$ $[M]^+$: 310.2661, Found: 310.2645

FTIR (NaCl): ν 1662, 1608, 1489, 1448, 1377 cm^{-1}



1e

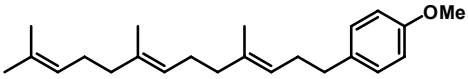
1-methyl-2-((3*E*,7*E*)-4,8,12-trimethyltrideca-3,7,11-trienyl)benzene (1e), colorless oil, 68% yield.

R_f: 0.91 (Hexane : Et_2O = 9:1)

^{1}H NMR (400 MHz, $CDCl_3$): 7.22–7.03 (m, 4H), 5.22 (t, *J* = 6.64 Hz, 1H), 5.16–5.04 (m, 2H), 2.60 (dd, *J* = 9.75, 7.37 Hz, 2H), 2.32 (s, 3H), 2.31–2.20 (m, 2H), 2.14–2.02 (m, 4H), 2.02–1.94 (m, 4^{13}C NMR (100 MHz, $CDCl_3$): 140.6, 135.9, 135.8, 135.0, 131.3, 130.1, 128.9, 125.9, 125.8, 124.4, 124.2, 123.8, 39.8, 39.8, 33.4, 28.7, 26.8, 26.6, 25.7, 19.3, 17.7, 16.0, 15.9

HRMS (EI): *m*/*z* calculated for $C_{23}H_{34}$ $[M]^+$: 310.2661, Found: 310.2646

FTIR (NaCl): ν 1490, 1448, 1377, 1107 cm^{-1}



1f

1-methoxy-4-((3*E*,7*E*)-4,8,12-trimethyltrideca-3,7,11-trienyl)benzene (1f), colorless oil, 60% yield.

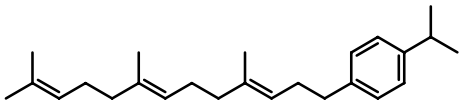
R_f: 0.91 (Hexane : Et_2O = 9:1)

^{1}H NMR (400 MHz, $CDCl_3$): 7.14–7.04 (m, 2H), 6.86–6.76 (m, 2H), 5.18 (td, *J* = 6.98, 1.05 Hz, 1H), 5.15–5.06 (m, 2H), 3.79 (s, 3H), 2.58 (dd, *J* = 9.32, 7.42 Hz, 2H), 2.32–2.23 (m, 2H), 2.05 (q, *J* = 7.23 Hz, 4H), 2.02–1.94 (m, 4H), 1.69 (s, 3H), 1.60 (s, 6H), 1.56 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 157.7, 135.7, 135.0, 134.6, 131.3, 129.3, 124.4, 124.2, 123.7, 113.6, 55.2, 39.7, 39.7, 35.2, 30.2, 26.8, 26.6, 25.7, 17.7, 16.0, 16.0

HRMS (EI): *m*/*z* calculated for $C_{23}H_{34}O$ $[M]^+$: 326.2610, Found: 326.2596

FTIR (NaCl): ν 1612, 1512, 1452, 1377, 1300, 1246, 1117, 1107, 1039 cm^{-1}



1g

1-methoxy-3-((3*E*,7*E*)-4,8,12-trimethyltrideca-3,7,11-trienyl)benzene (1g), colorless oil, 50% yield.

R_f: 0.91 (Hexane : Et_2O = 9:1)

^{1}H NMR (400 MHz, $CDCl_3$): 7.22–7.18 (m, 2H), 7.18–7.13 (m, 2H), 5.24 (td, *J* = 6.97, 0.93 Hz, 1H), 5.19–5.10

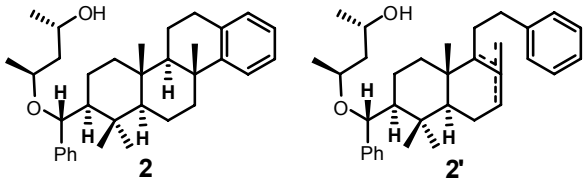
(m, 2H), 2.95–2.85 (m, 1H), 2.64 (dd, *J* = 9.64, 7.78 Hz, 2H), 2.33 (q, *J* = 7.78 Hz, 2H), 2.15–2.07 (m, 4H), 2.06–1.97 (m, 4H), 1.72 (s, 3H), 1.64 (s, 6H), 1.61 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 146.2, 139.8, 135.7, 135.0, 131.3, 128.4, 126.3, 124.5, 124.3, 123.9, 39.8, 39.7, 35.8, 33.7, 30.1, 26.8, 26.7, 25.8, 24.1, 17.7, 16.1, 16.0

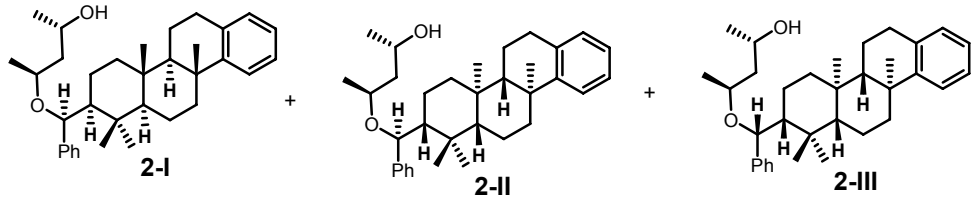
HRMS (EI): *m/z* calculated for $C_{25}H_{38}$ $[M]^+$: 338.2974, Found: not obtained.

FTIR (NaCl): ν 1512, 1448, 1381, 1361, 1107, 1055, 1018 cm^{-1}

3. Procedure for benzaldehyde chiral acetal cyclization and modification of cyclization products.



*Only the names and the data of the major products (like **2**) were provided. Three possible minor isomers of **2** shown as follow:*



(2*S*,4*S*)-4-((*R*)-phenyl((2*S*,4a*S*,4b*R*,10b*R*,12a*S*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)methoxy)pentan-2-ol (2)

To a solution of alkene **1** (30 mg, 0.1 mmol, 1.0 eq.) in DCM (2 mL) was added acetal (60 mg, 0.3 mmol, 3.0 eq.) at room temperature. The solution was cooled to -78 ^oC prior to addition of $SnCl_4$ (1.0 M in DCM, 0.2 mL, 2.0 eq.). The reaction was allowed to stir at -78 ^oC for 1 hour before quenching with saturated $NaHCO_3$ aqueous solution (5 mL).The mixture was gradually warmed up to room temperature and was allowed to stirred for another 1 hour. The aqueous layer was extracted with DCM (3 × 20 mL), and the combined organic layer was washed with water (20 mL), brine (20 mL) and dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residual crude product was purified by flash column chromatography. Cyclization product was obtained as white solid with 71% yield. It is a mixture of **2** and **2'** isomers. Isomer ratio was determined based on oxidative derivatives **3**.

R_f: 0.50 (Hexane : Ethyl Acetate = 4:1)

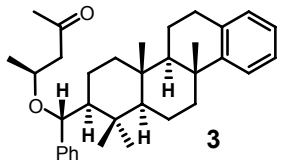
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.40–6.90 (m, 9H), 4.89 (s, 1H), 4.30–4.15 (m, 1H), 3.75–3.55 (m, 1H), 2.87 (dd, *J* = 17.39, 5.63 Hz, 1H), 2.80–2.65 (m, 1H), 2.50 (t, *J* = 8.69 Hz, 1H), 2.38 (dt, *J* = 12.62, 2.84 Hz, 1H), 1.21 (s, 3H), 1.18 (d, *J* = 6.61 Hz, 3H), 1.12 (s, 3H), 1.06 (d, *J* = 6.26 Hz, 3H), 0.98 (s, 3H), 0.94 (s, 3H), 0.83 (s, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): 150.3, 143.3, 135.2, 128.8, 128.6, 126.7, 126.3, 125.4, 124.9, 124.3, 81.2, 70.8, 64.2, 57.7, 55.8, 55.3, 44.3, 40.7, 39.8, 38.0, 37.7, 37.4, 30.8, 29.9, 26.1, 23.4, 19.3, 18.6, 17.9, 17.5, 16.3, 16.2

HRMS (CI): *m/z* calculated for $C_{34}H_{48}O_2$ $[M]^+$: 488.3654, Found: 488.3679

FTIR (NaCl): ν 3600, 1490, 1452, 1373, 1240 cm^{-1}



3

(*S*)-4-((*R*)-phenyl((2*S*,4a*S*,4b*R*,10b*R*,12a*S*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)methoxy)pentan-2-one (3)

To an oven-dried round-bottom flask equipped with a magnetic stirring bar was added PCC (65mg, 0.3 mmol, 3.0 eq.), 4 Å molecular sieve (0.1 g), silica gel (0.1 g) and DCM (10 mL). The mixture was allowed to cool to 0 ^{o}C and mixture of alcohol **2** and **2'** in DCM (2 mL) was added *via* syringe at 0 ^{o}C. The reaction mixture was gradually warmed to room temperature and was allowed to stir for another 12 hours. The mixture was filtered through a pad of silica gel and flushed with 100 mL DCM. The solution was concentrated *in vacuo*. The residual crude product was purified by flash column chromatography to afford compound **3** and compound **3'** as white solid in 60% (**3**) and 32% (**3'**).

Isomer ratio for **3**: 48:15:30:7

R_f: 0.62 (Hexane : Ethyl Acetate = 4:1)

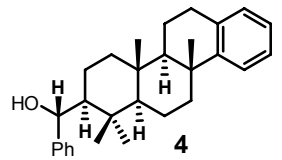
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.45–7.00 (m, 9H), 4.95 (s, 1H), 4.01 (dq, *J* = 18.14, 6.26 Hz, 1H), 2.98 (dd, *J* = 16.58, 5.32 Hz, 1H), 2.92–2.80 (m, 1H), 2.75 (dd, *J* =14.92, 6.88 Hz, 1H), 2.70–2.52 (m, 1H), 2.55–2.45 (m, 1H), 2.17 (s, 3H), 1.32 (s, 3H), 1.30 (d, *J* = 6.24 Hz, 3H), 1.26 (s, 3H), 1.11 (s, 3H), 1.08 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 207.8, 150.3, 143.8, 135.1, 128.9, 128.4, 128.2, 126.7, 125.8, 125.2, 124.6, 76.9, 69.3, 57.7, 56.3, 55.4, 51.4, 40.8, 39.9, 38.0, 37.7, 37.4, 31.4, 31.0, 30.2, 27.1, 26.2, 19.4, 19.2, 18.8, 18.0, 16.3

HRMS (CI): *m*/*z* calculated for $C_{34}H_{46}O_2$ $[M]^+$: 486.3498, Found: 486.3503

FTIR (NaCl): ν 1716, 1627, 1602, 1490, 1450, 1377, 1338, 1212, 1174 cm^{-1}



4

(*R*)-phenyl((2*S*,4a*S*,4b*R*,10b*R*,12a*S*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)methanol (4)

The procedure was following the method developed by Y. Yamamoto.[4] To a solution of ketone **3** (49 mg, 0.1 mmol, 1.0 eq.) in THF/MeOH (4 mL/2 mL) was added KOH aqueous solution (1 mL, 10.0 M). The reaction was allowed to stir at room temperature for 3 days. The reaction was quenched by pouring into HCl (1.0 M, 10 mL) and ice mixture. The mixture was extracted with DCM (3 × 20 mL) and combined organic layer was washed with saturated $NaHCO_3$ aqueous solution (10 mL), water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residual crude product was purified by flash column chromatography to afford the alcohol **4** as a white solid in 80% yield and isomer ratio 71:29.

R_f: 0.75 (Hexane : Ethyl Acetate = 4:1)

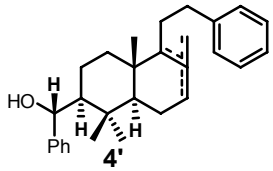
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.38–7.28 (m, 5H), 7.25–7.70 (m, 4H), 5.18 (s, 1H), 2.90 (dd, *J* = 17.45, 6.23 Hz, 1H), 2.81–2.69 (m, 1H), 2.41 (dt, *J* = 12.46, 2.74 Hz, 1H), 1.90–1.70 (m, 4H), 1.70–1.46 (m, 6H), 1.38–1.28 (m, 2H), 1.20 (s, 3H), 1.15 (s, 3H), 1.03 (s, 3H), 0.97 (s, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): 150.3, 146.2, 135.1, 128.8, 128.1, 126.5, 125.7, 125.4, 125.2, 124.6, 72.1, 57.6, 55.8, 55.3, 40.7, 39.5, 38.0, 37.7, 37.2, 30.9, 30.0, 26.1, 19.3, 18.7, 17.9, 16.2, 15.2,

HRMS (CI): *m*/*z* calculated for $C_{29}H_{38}O$ $[M]^+$: 402.2923, Found: 402.3064

FTIR (NaCl): ν 3444 (b), 1650, 1640 (b), 1635, 1602, 1489, 1468, 1386, 1367 cm^{-1}



4'

(*R*)-phenyl((2*S*,4a*S*,8a*S*)-1,1,4a,6-tetramethyl-5-phenethyl-1,2,3,4,4a,7,8,8a-octahydronaphthalen-2-yl)methanol (4')

white solid, yield: 70%

R_f: 0.75 (Hexane : Ethyl Acetate = 4:1)

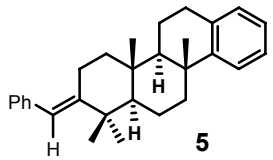
Mixture of isomers:

^{1}H NMR (400 MHz, $CDCl_3$): 7.50–6.70 (m, 9H), 5.20–5.15 (m, 1H), 5.15–5.07 (m, 1H), 2.98–2.84 (m, 1H), 2.80–2.65 (m, 1H), 1.20 (s, 3H), 1.50 (s, 3H), 1.03 (s, 3H), 0.97 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 150.2, 146.1, 135.1, 128.8, 128.4, 128.3, 128.2, 128.1, 126.5, 125.7, 125.5, 125.4, 124.6, 72.2, 57.6, 55.7, 55.3, 40.7, 39.5, 38.1, 37.7, 37.3, 30.9, 30.0, 26.2, 19.3, 18.8, 18.0, 16.2, 15.2

HRMS (CI): *m*/*z* calculated for $C_{29}H_{38}O$ $[M]^+$: 402.2933, Found $[M-H]^+$: 401.2849

FTIR (NaCl): ν 3414 (b), 1650, 1641 (b), 1450, 1435, 1379 cm^{-1}



5

(4a*S*,4b*R*,10b*R*,12a*R*,*E*)-2-benzylidene-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysene (5)

To a solution of alcohol **4** (40 mg, 0.1 mmol, 1.0 eq.) in Et_2O (4 mL) was added PBr_3 (0.03 mL, 0.3 mol, 3.0 eq.). The reaction was allowed to stir at room temperature for 6 hours. The reaction was then quenched by pouring into $NaHCO_3$ saturated solution (20 mL). The mixture was extracted with Et_2O (2 × 20 mL) and combined organic layer was washed with water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residual crude product was used directly for the next step reaction without further purification. The bromination product was azeotropically dried using THF (10 mL × 2) in a 25 mL round-bottom flask, then DMF was added to dissolve bromide. Solid *t*BuOK (0.1 g, 0.9 mmol, 9.0 eq.) was added to the DMF solution at room temperature and allowed to stir for 12 hours. The reaction was quenched by pouring into ice water (20 mL). The mixture was extracted with ethyl acetate (3 × 20 mL) and combined organic layer was washed with water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude residual was purified by flash column chromatography to afford the alkene **5** as a white solid in 50% yield.

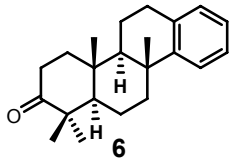
R_f: 0.88 (Hexane : Ethyl Acetate = 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): 7.38–7.00 (m, 9H), 6.41 (s, 1H), 2.95 (ddd, *J* = 16.88, 6.45, 1.90 Hz, 1H), 2.89–2.74 (m, 1H), 2.60–2.40 (m, 3H), 1.88–1.62 (m, 6H), 1.60–1.47 (m, 3H), 1.37–1.12 (m, 3H), 1.28 (s, 3H), 1.19 (s, 3H), 1.15 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): 151.0, 150.1, 139.5, 135.0, 128.9, 128.8, 128.0, 128.0, 125.7, 125.2, 124.6, 120.0, 55.2, 55.0, 41.4, 40.3, 40.0, 38.1, 37.8, 30.9, 29.2, 25.9, 23.2, 22.0, 20.3, 18.5, 17.5

HRMS (CI): *m/z* calculated for $C_{29}H_{36}$ $[M]^+$: 384.2817, Found: 384.1726

FTIR (NaCl): ν 1645, 1633 (b), 1489, 1446, 1380, 1361 cm^{-1}



6

(4a*S*,4b*S*,10b*S*,12a*S*)-1,1,4a,10b-tetramethyl-3,4,4a,4b,5,6,10b,11,12,12a-decahydrochrysen-2(1*H*)-one (6),

O_3.gas was bubbled into a solution of alkene **5** (38 mg, 0.1 mmol, 1.0 eq.) in DCM (10 mL) for 10 minutes at -78 ^oC. The reaction was then quenched by adding 0.3 mL of Me_2S at -78 ^oC and allowed to warm up to room temperature. The organic solvent was removed *in vacuo*. The residual crude product was purified by flash column chromatography to afford the ketone **6** as a colorless solid in 50% yield, 46% *ee*.

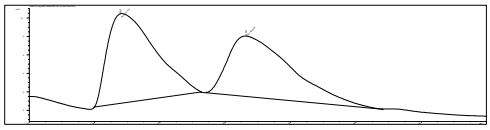
R_f: 0.68 (Hexane : Ethyl Acetate = 4:1)

^1H NMR (400 MHz, $CDCl_3$): 7.30–7.20 (m, 1H), 7.15–7.01 (m, 3H), 2.96 (dd, *J* = 16.67, 5.97 Hz 1H), 2.91–2.80 (m, 1H), 2.62–2.47 (m, 2H), 2.45 (dt, *J* = 12.35, 3.50 Hz, 1H), 2.07 (ddd, *J* = 12.83, 7.40, 4.55 Hz, 1H), 1.88–1.63 (m, 2H), 1.63–1.60 (m, 1H), 1.58–1.42 (m, 4H), 1.36 (dd, J = 11.44, 2.01 Hz, 1H), 1.24 (s, 3H), 1.11 (s, 3H), 1.10 (s, 3H), 1.04 (s, $3^{13}C$ NMR (100 MHz, $CDCl_3$): 217.8, 149.5, 134.8, 128.9, 125.8, 125.4, 124.6, 54.6, 54.4, 47.3, 39.7, 39.1, 37.9, 37.0, 34.0, 30.7, 26.7, 25.6, 21.0, 20.1, 18.6, 16.1

HRMS (CI): *m/z* calculated for $C_{22}H_{30}O$ $[M]^+$: 310.2297, Found: 310.1463

FTIR (NaCl): ν 1703, 1487, 1470, 1454, 1381 cm^{-1}

The enantiomeric excess was determined by HPLC analysis employing Daicel Chiral OJ and Daicel Chiral AD-H column in series (Hexane : *i*-propanol = 99.2 : 0.8, 1 mL/min): t_1 = 18.82 min (major) , t_2 = 23.17 min (minor)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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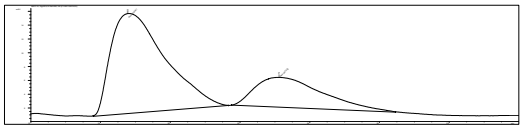
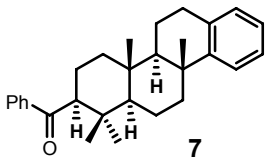
2	22.680	MM	2.2752	890.49487	6.52329	47.6645



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.823	MM	1.8074	1569.80664	14.47605	72.7812
2	23.170	MM	2.2675	587.07886	4.31509	27.2188



7

Phenyl((2*S*,4a*S*,4b*R*,10b*R*,12a*S*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)methanone (7)

To an oven-dried 25 mL round-bottom flask equipped with a magnetic stirring bar was added PCC (0.129 g, 0.6 mmol, 6.0 eq.), 4Å MS (0.3 g, oven-dried over 48 hours), silica gel (0.3 g, oven-dried over 48 hours) and DCM (10 mL). The mixture was allowed to cool to 0 ^oC and alcohol **4** (40 mg, 0.1 mmol, 1.0 eq.) in DCM (1 mL) was added dropwise. The reaction was gradually warmed up to room temperature and was allowed to stir for another 12 hours. The mixture was filtered through a pad of silica gel and flushed with 100 mL of ethyl acetate. The solution was concentrated *in vacuo*. The residual crude product was purified by flash column chromatography to afford the ketone as a colorless solid in 85% yield, 46% *ee*.

R_f: 0.78 (Hexane : Ethyl Acetate = 4:1)

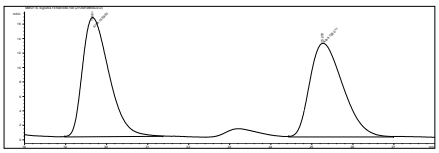
^{1}H NMR (300 MHz, $CDCl_3$): 7.99–7.89 (m, 2H), 7.58–7.49 (m, 1H), 7.48–7.39 (m, 2H), 7.34–7.00 (m, 4H), 3.31 (dd, J= 12.69, 3.00 Hz, 1H), 2.96 (dd, *J* = 16.04, 5.46 Hz, 1H), 2.91–2.76 (m, 1H), 2.43 (dt, *J* = 12.34, 3.00 Hz, 1H), 2.19–2.01 (m, 1H), 1.96 (dt, *J* = 12.87, 2.82 Hz, 1H), 1.90–1.46 (m, 7H), 1.38–1.15 (m, 2H), 1.22 (s, 3H), 1.02 (s, 3H), 1.00 (s, 3H), 0.88 (s, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): 204.5, 150.1, 139.1, 135.0, 132.6, 128.9, 128.5, 128.2, 125.7, 125.2, 124.6, 57.7, 55.4, 54.7, 40.6, 39.6, 38.1, 37.9, 37.3, 31.4, 30.9, 26.1, 22.6, 18.5, 18.3, 18.0, 16.7

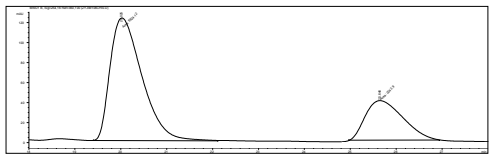
HRMS (CI): *m*/*z* calculated for $C_{29}H_{36}O$ $[M]^+$: 400.2766, Found: 400.1886

FTIR (NaCl): ν 1670, 1660 (b), 1595, 1577, 1487, 1469, 1446, 1379, 1377 cm^{-1}

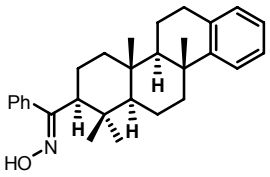
The enantiomeric excess was determined by HPLC analysis employing Daicel Chiral OD-H and Daicel Chiral AD-H column in series (Hexane : *i*-propanol = 99.2 : 0.8, 1 mL/min): t_1 = 20.03 min (major) , t_2 = 25.65 min (minor)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.661	MM	0.7468	738.96320	16.49185	50.4421
2	25.270	MM	0.9341	726.01111	12.95423	49.5579



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.025	MM	0.8051	5924.11719	122.63852	72.5283
2	25.646	MM	0.9475	2243.89551	39.47046	27.4717



(*Z*)-phenyl((2*S*,4a*S*,4b*R*,10b*R*,12a*S*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)methanone oxime

To a 25 mL round-bottom flask equipped with a magnetic stirring bar was added keone **7** (80 mg, 0.2 mmol, 1.0 eq.), NH_2OH HCl (0.14 g, 2.0 mmol, 10.0 eq), pyridine (1.0 mL) and EtOH (15 mL). The mixture was allowed to reflux for 24 hours. The reaction was cooled to room temperature and then diluted with 100 mL ethyl acetate. The solution was then washed with HCl (0.5 M, 50 mL × 2), water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residual crude product was purified by flash column chromatography to afford the ketone as a white solid in 69% yield.

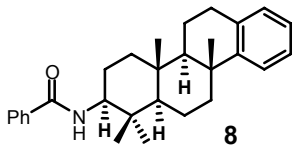
R_f: 0.58 (Hexane : Ethyl Acetate = 4:1)

^{1}H NMR (400 MHz, $CDCl_3$): 7.42–7.29 (m, 4H), 7.27–7.20 (m, 2H), 7.14–7.00 (m, 3H), 2.93 (dd, *J* = 16.94, 6.08 Hz, 1H), 2.87–2.75 (m, 1H), 2.46 (dd, *J* = 13.07, 2.58 Hz, 1H), 2.37 (dt, *J* = 12.33, 2.95 Hz, 1H), 2.10 (qd, *J* = 13.62, 3.31 Hz, 1H), 1.94 (dt, *J* = 12.89, 3.13 Hz, 1H), 1.88–1.60 (m, 5H), 1.50 (m, 2H), 1.30–1.20 (m, 1H), 1.18 (s, 3H), 1.06–0.95 (m, 1H), 0.94 (s, 3H), 0.86 (s, 3H), 0.83 (s, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): 161.4, 150.1, 136.0, 135.0, 128.8, 128.4, 128.0, 127.9, 125.7, 125.2, 124.6, 57.9, 55.9, 55.3, 40.6, 40.3, 38.1, 38.0, 37.7, 30.8, 30.4, 26.1, 24.3, 18.9, 18.4, 18.0, 16.5

HRMS (CI): *m*/*z* calculated for $C_{29}H_{37}NO$ $[M]^+$: 415.2875, Found: 415.2371

FTIR (NaCl): ν 3284, 1487, 1454, 1444, 1386, 1379, 1369, 1317 cm^{-1}



8

_N_-((2_S_,4aR,4b_R_,10bR,12a_R_)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)benzamide (8)

To a solution of oxime (42 mg, 0.1 mmol, 1.0 eq.) in Et_2O (15 mL) was added $SOCl_2$ (0.2 mL, 2.74 mmol, 27.4 eq.). The reaction was allowed to reflux for 3 hours. The condenser was removed and Et_2O was distilled away. The reaction was quenched by adding water (10 mL). The mixture was refluxed for overnight. DCM (40 mL) was added to dissolve organic compound and combined organic layer was washed with saturated $NaHCO_3$ aqueous solution (10 mL), water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residual crude product was purified by flash column chromatography to afford the amide **8** as white solid in 67% yield, 46% *ee*.

R_f: 0.53 (Hexane : Ethyl Acetate = 4:1)

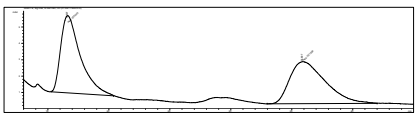
^{1}H NMR (400 MHz, $CDCl_3$): 7.80–7.70 (m, 2H), 7.55–7.40 (m, 3H), 7.35–7.20 (m, 1H), 7.20–7.00 (m, 3H), 5.96 (d, *J* = 9.44 Hz, 1H), 3.90 (ddd, *J* = 12.47, 9.98, 4.51 Hz, 1H), 2.94 (dd, *J* = 16.94, 6.00, 1H), 2.91–2.80 (m, 1H), 2.42 (dt, *J* = 12.18, 2.82 Hz, 1H), 1.93–1.50 (m, 9 H), 1.35–1.20 (m, 1H), 1.21 (s, 3H), 1.20–.1.14 (m, 2H), 0.98 (s, 3H), 0.96 (s, 3H), 0.92 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): 167.1, 149.9, 135.3, 135.0, 131.3, 128.9, 128.6, 126.8, 125.8, 125.3, 124.6, 56.9, 55.9, 55.0, 40.4, 38.7, 38.1, 38.0, 37.3, 30.7, 28.6, 26.0, 25.6, 19.11, 18.1, 16.5, 16.3

HRMS (CI): *m*/*z* calculated for $C_{29}H_{37}NO$ $[M]^+$: 415.2875, Found: 415.2907

FTIR (NaCl): ν 3373 (b), 1637, 1521, 1465, 1381, 1340, 1305 cm^{-1}

The enantiomeric excess was determined by HPLC analysis employing Daicel Chiral OB-H and Daicel Chiral AD-H column in series (Hexane : *i*-propanol = 80 : 20, 1 mL/min): t_1 = 16.66 min (minor) , t_2 = 36.18 min (major).



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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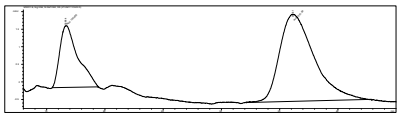
2	35.897	MM	3.3780	521.59607	2.57350	49.4572

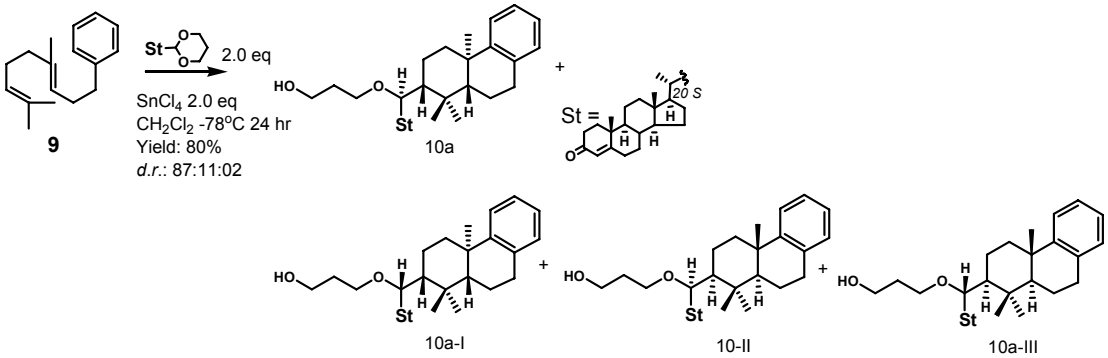


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.664	PM	1.8064	190.45557	1.75720	27.1685
2	36.181	MM	3.4356	510.55981	2.47678	72.8315

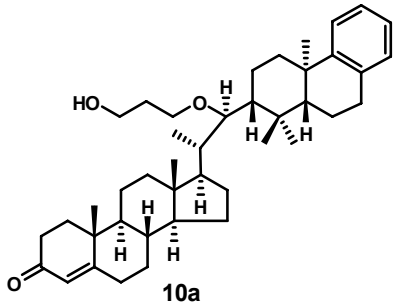
4. General procedure for steroidal aldehyde acetal cyclization reactions

*Only the names and the data of the major products (like **10a**) were provided.*

*For tricyclic cyclization, only two of the three possible minor isomers (**10a-I**, **10a-II** and **10a-III**) were detected from ^{1}H NMR.*



To a solution of alkene **9** (22.4 mg, 0.1 mmol, 1.0 eq.) in DCM (2 mL) was added acetal (78.0 mg, 0.2 mmol, 2.0 eq.) at room temperature. The solution was cooled to -78 ^{o}C prior to the addition of $SnCl_4$ (1.0 M in DCM, 0.2 mL, 2.0 eq.). The reaction was allowed to stir at -78 ^{o}C for 24 hours before quenching with saturated $NaHCO_3$ aqueous solution (5 mL).The mixture was gradually warmed up to room temperature and was allowed to stir for another 1 hour. The aqueous layer was extracted with DCM (3 × 20 mL), and the combined organic layer was washed with water (20 mL), brine (20 mL) and dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residual crude product was purified by flash column chromatography.



10a

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((1*R*,2*S*)-1-(3-hydroxypropoxy)-1-((2*R*,4a*R*,10a*R*)-1,1,4a-trimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-2-yl)propan-2-yl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (10a), white solid, 80% yield (mixture of isomers).

Isomer ratio: 87:11:2 (based on derivate aldehyde ^{1}H NMR integration).

R_f: 0.18 (Hexane : Ethyl Acetate = 4:1)

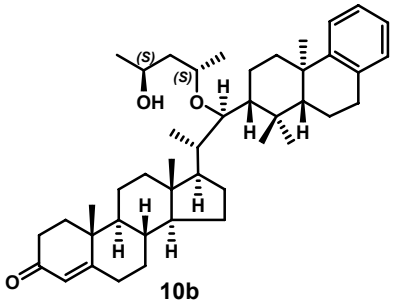
Major isomer:

^{1}H NMR (500 MHz, $CDCl_3$): 7.38–7.02 (m, 4H), 5.75 (s, 1H), 3.90–3.70 (m, 3H), 3.70–3.50 (m, 1H), 3.45–3.35 (m, 1H), 2.97 (dd, *J* = 17.03, 5.58 Hz, 1H), 2.90–2.80 (m, 1H), 1.23 (s, 3H), 1.20 (s, 3H), 1.20 (s, 3H), 0.95 (d, *J* = 6.80 Hz, 3H), 0.94 (s, 3H), 0.72 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.7, 171.6, 149.9, 135.0, 128.8, 125.7, 125.2, 124.5, 123.8, 80.6, 72.5, 63.1, 55.8, 53.7, 53.6, 53.3, 52.2, 45.1, 42.4, 39.6, 39.0, 38.6, 37.8, 37.3, 35.7, 35.7, 34.0, 32.9, 32.4, 32.0, 30.8, 29.5, 28.6, 25.2, 24.3, 21.0, 20.9, 19.2, 18.0, 17.4, 12.7, 11.7

HRMS (CI): *m*/*z* calculated for $C_{42}H_{62}O_3$ $[M]^+$: 614.4699, Found $[M-H]^+$: 613.4521

FTIR (NaCl): ν 3436 (b), 1658, 1616, 1448, 1436, 1377, 1265, 1230 cm^{-1}



10b

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((1*R*,2*S*)-1-((2*S*,4*S*)-4-hydroxypentan-2-yloxy)-1-((2*R*,4a*R*,10a*R*)-1,1,4a-trimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-2-yl)propan-2-yl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (10c), white solid, 85% yield (mixture of isomers).

Isomer ratio: 94:6 based on ^{13}C NMR, (^{13}C: 64.0 ppm). R_f: 0.15 (Hexane : Ethyl Acetate = 4:1)

Major isomer:

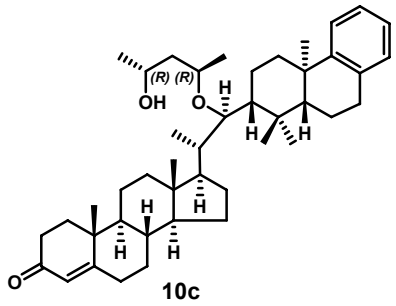
^{1}H NMR (500 MHz, $CDCl_3$): 7.33–7.20 (m, 2H), 7.15–7.00 (m, 2H), 5.73 (s, 1H), 4.30–4.23 (m, 1H), 3.88 (septet, *J* = 3.15 Hz, 1H), 3.53 (d, *J* = 3.15 Hz, 1H), 2.97 (dd, *J* = 17.15, 5.80 Hz, 1H), 2.90–2.80 (m, 1H), 1.28 (d, *J* = 6.28

Hz, 3H), 1.21 (d, *J* = 3.75 Hz, 3H), 1.20 (s, 6H), 1.17 (s, 3H), 0.93 (s, 3H), 0.89 (d, *J* = 6.97 Hz, 3H), 0.71 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.8, 171.7, 149.8, 135.0, 128.8, 125.7, 125.3, 124.4, 123.8, 75.4, 72.1, 64.0, 55.7, 54.1, 53.6, 52.7, 52.3, 46.2, 43.4, 42.3, 39.4, 39.3, 38.6, 37.8, 37.3, 35.6, 35.6, 33.9, 32.9, 32.0, 30.8, 29.4, 28.3, 25.4, 24.3, 23.6, 21.6, 21.0, 19.1, 18.0, 17.7, 17.4, 12.2, 11.6

HRMS (CI): *m*/*z* calculated for $C_{44}H_{66}O_3$ $[M]^+$: 642.5012, Found:642.5006

FTIR (NaCl): ν 3427 (b), 1662, 1616, 1448, 1417, 1373, 1330, 1305, 1269, 1228cm^{-1}



10c

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((1*R*,2*S*)-1-((2*R*,4*R*)-4-hydroxypentan-2-yloxy)-1-((2*R*,4a*R*,10a*R*)-1,1,4a-trimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-2-yl)propan-2-yl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (10b), white solid, 62% yield (mixture of isomers).

Isomer ratio: 93:7 based on ^{13}C NMR, (^{13}C: 77.9 ppm) Recrystallization yield: 30%, $[\alpha]^{20.0}_{D}$ = 13.9 (*c* 1.67, $CHCl_3$).

R_f: 0.18 (Hexane : Ethyl Acetate = 4:1)

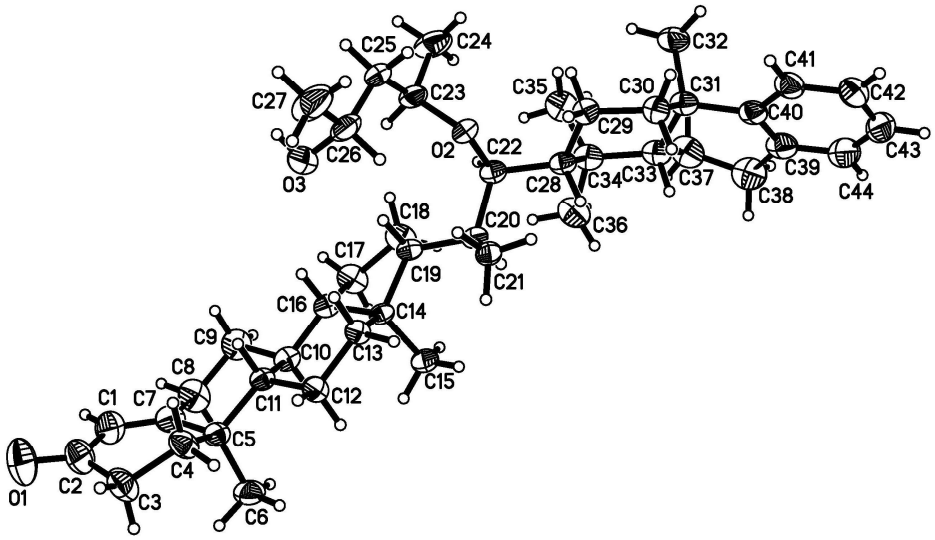
Major isomer:

^{1}H NMR (500 MHz, $CDCl_3$): 7.31–7.23 (m, 1H), 7.15–7.09 (m, 1H), 7.09–7.00 (m, 2H), 5.74 (s, 1H), 4.28–4.20 (m, 1H), 4.05–3.92 (m, 1H), 3.67 (d, *J* = 1.89 Hz, 1H), 2.96 (dd, *J* = 16.90, 5.89 Hz, 1H), 2.89–2.79 (m, 1H), 1.29 (d, *J* = 6.04 Hz, 3H), 1.22 (d, *J* = 5.97 Hz, 3H), 1.19 (s, 6H), 0.97 (d, *J* = 6.76 Hz, 3H), 0.97 (s, 3H), 0.96 (s, 3H), 0.71 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.8, 171.5, 149.9, 135.0, 128.8, 125.7, 125.2, 124.5, 123.8, 77.9, 74.5, 64.1, 55.8, 54.0, 53.7, 53.7, 52.4, 45.4, 44.1, 42.7, 39.7, 39.3, 38.6, 38.0, 37.8, 35.7, 35.6, 34.0, 32.9, 32.0, 30.8, 29.7, 28.7, 25.3, 24.4, 23.7, 22.0, 21.0, 19.1, 19.1, 18.1, 17.4, 13.4, 11.5

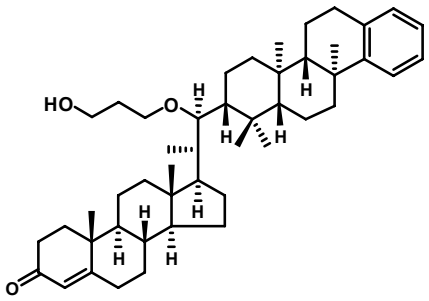
HRMS (CI): *m*/*z* calculated for $C_{44}H_{66}O_3$ $[M]^+$: 642.5012, Found: 642.5006

FTIR (NaCl): ν 3435 (b), 1666, 1614, 1448, 1417, 1375, 13321269. 1228 cm^{-1}



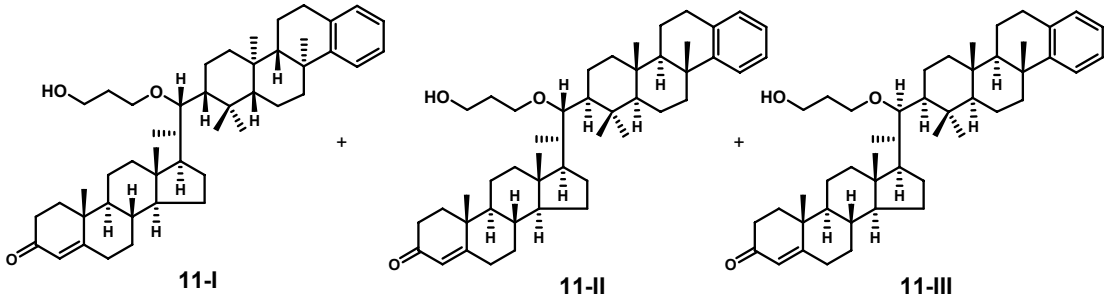
X ray structure of **10c,** 50% probability was chosen for the ellipsoids.

*For tetracyclization cyclization, the names and the NMR data of the major product (like **11)** were provided.*



11

*The other three possible minor isomers were shown as **11-I**, **11-II** and **11-III** (shown below).*



11-I **11-II** **11-III**

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((1*R*,2*S*)-1-(3-hydroxypropoxy)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-2-yl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (11), white solid, 73% yield (mixture of isomers).

R_f: 0.20 (Hexane : Ethyl Acetate = 4:1)

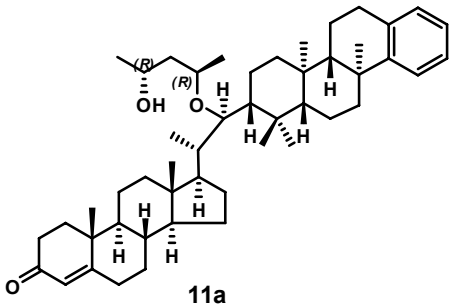
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.04–6.99 (m, 4H), 5.72 (s, 1H), 3.90–3.65 (m, 3H), 3.65–3.50 (m, 1H), 3.45–3.25 (m, 1H), 2.93 (dd, *J* = 16.89, 5.98 Hz, 1H), 2.86–2.74 (m, 1H), 1.19 (s, 3H), 1.16 (s, 3H), 0.92 (s, 3H), 0.91 (d, *J* = 6.56 Hz, 3H), 0.85 (s, 3H), 0.83 (s, 3H), 0.69 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): 199.80, 171.7, 150.2, 135.1, 128.8, 125.7, 125.1, 124.6, 123.8, 80.5, 72.6, 63.2, 57.9, 55.8, 55.4, 53.8, 53.6, 53.5, 53.4, 45.1, 42.3, 40.7, 40.0, 39.6, 38.6, 38.0, 37.6, 37.1, 35.5, 34.0, 32.9, 32.3, 32.0, 30.9, 29.3, 28.6, 26.2, 24.3, 21.0, 20.2, 19.1, 18.0, 17.9, 17.4, 16.6, 12.7, 11.7

HRMS (CI): *m*/*z* calculated for $C_{47}H_{70}O_3$ $[M]^+$: 682.5325, Found $[M-H]^+$: 681.4085

FTIR (NaCl): ν 3444 (b), 1662, 1614, 1450, 1448, 1435, 1379, 1361, 1246, 1215 cm^{-1}



11a

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((1*R*,2*S*)-1-((2*R*,4*R*)-4-hydroxypentan-2-yloxy)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4

a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-2-yl)-10,13-dimethyl-6,7 ,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (11a), white solid, 45% yield (mixture of isomers). Isomer ratio: 69:15:13:3 based on ^{13}C NMR, (^{13}C: 78.0 ppm).

R_f: 0.25 (Hexane : Ethyl Acetate = 4:1)

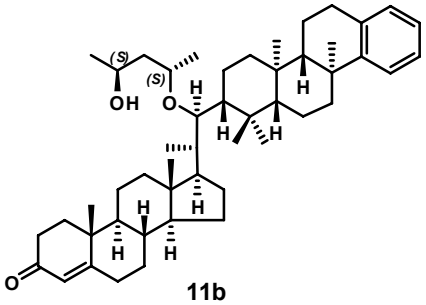
Major isomer:

^1H NMR (400 MHz, $CDCl_3$): 7.30–6.98 (m, 4H), 5.72 (s, 1H), 4.28–4.12 (m, 1H), 3.96–3.88 (m, 1H), 3.60 (d, *J* = 2.04 Hz, 1H), 2.92 (dd, *J* = 16.94, 5.71 Hz, 1H), 2.85–2.75 (m, 1H), 1.18 (d, *J* = 5.27 Hz, 6H), 0.95 (s, 3H), 0.93 (s, 3H), 0.92 (d, *J* = 3.64 Hz, 3H), 0.90 (s, 3H), 0.88 (s, 3H), 0.86 (s, 3H), 0.69 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.6, 171.5, 150.2, 135.1, 128.8, 125.6, 125.1, 124.5, 123.8, 78.0, 74.7, 64.1, 58.0, 55.8, 55.4, 54.0, 53.9, 53.7, 53.6, 44.1, 42.6, 40.7, 40.3, 39.7, 38.5, 38.0, 37.8, 37.4, 35.6, 35.6, 33.9, 32.9, 32.0, 30.8, 29.5, 28.6, 26.1, 24.3, 23.6, 21.3, 21.0, 19.1, 19.0, 18.1, 17.9, 17.4, 16.6, 13.3, 11.5

HRMS (CI): *m*/*z* calculated for $C_{49}H_{74}O_3$ $[M]^+$: 710.5638, Found: 710.4336

FTIR (NaCl): ν 3446 (b), 1672, 1610, 1450, 1377, 1228, 1217, 1120 cm^{-1}



11b

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((1*R*,2*S*)-1-((2*S*,4*S*)-4-hydroxypentan-2-yloxy)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4 a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-2-yl)-10,13-dimethyl-6,7 ,8,9,10,11,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3(2H)-one (11b), white solid, 50% yield (mixture of isomers). Isomer ratio: (71:12:9:8, based on ^{13}C NMR, (^{13}C: 75.4 ppm).

R_f: 0.25 (Hexane : Ethyl Acetate = 4:1)

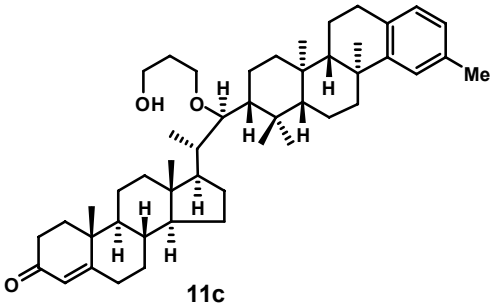
Major isomer:

^1H NMR (400 MHz, $CDCl_3$): 7.35–7.00 (m, 4H), 5.74 (s, 1H), 4.26 (sextet, *J* = 5.49 Hz, 1H), 3.86 (quintet, *J* = 2.82 Hz, 1H), 3.49 (d, *J* = 2.04 Hz, 1H), 2.95 (dd, *J* = 17.61, 6.13 Hz, 1H), 2.90–2.80 (m, 1H), 1.25 (d, *J* = 6.27 Hz, 3H), 1.22 (d, *J* = 5.09 Hz, 3H), 1.19 (s, 3H), 1.18 (s, 3H), .0.94 (s, 3H), 0.91 (d, *J* = 6.82 Hz, 3H), 0.86 (s, 3H), 0.85 (s, 3H), 0.72 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.7, 171.6, 150.2, 135.1, 128.8, 125.7, 125.2, 124.6, 123.8, 75.4, 72.1, 63.9, 58.1, 55.7, 55.4, 54.2, 53.6, 52.7, 46.3, 43.4, 42.3, 40.7, 40.3, 39.4, 38.6, 38.0, 37.6, 37.1. 35.7, 35.6, 34.0, 32.9, 32.0, 30.9, 29.3, 28.3, 26.2, 24.3, 23.6, 21.0, 20.9, 19.1, 18.0, 17.9, 17.6, 17.4, 16.8, 12.3, 11.6

HRMS (CI): *m*/*z* calculated for $C_{49}H_{74}O_3$ $[M]^+$: 710.5638, Found: 710.5564

FTIR (NaCl): ν 3600, 1666, 1610, 1452, 1440, 1452, 1375, 1300, 1215, 1122 cm^{-1}



11c

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((1*R*,2*S*)-1-(3-hydroxypropoxy)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,9,10b-pentamethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-2-yl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (11c), white solid, 66% yield (mixture of isomers).

R_f: 0.16 (Hexane : Ethyl Acetate = 4:1)

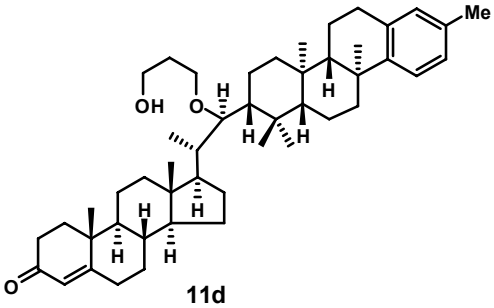
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.15–7.04 (m, 2H), 6.98–6.85 (m,1H), 5.75 (s, 1H), 3.86–3.73 (m, 3H), 3.61–3.55 (m, 1H), 3.40–3.36 (m, 1H), 3.10–3.00 (m, 1H), 2.91 (dd, J = 17.10, 6.58 Hz, 1H), 2.83–2.75 (m, 1H), 2.31 (s, 3H), 1.22 (s, 3H), 1.20 (s, 3H), 0.94 (d, J = 5.08 Hz, 3H), 0.91 (s, 3H), 0.88 (s, 3H), 0.86 (s, 3H), 0.72 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.6, 171.5, 150.1, 134.8, 132.0, 128.7, 126.1, 125.1, 123.8, 80.5, 72.5, 63.1, 57.9, 55.8, 55.6, 53.7, 53.6, 53.5, 45.1, 42.4, 40.8, 40.1, 39.6, 38.6, 38.0, 37.6, 37.1, 35.7, 34.0, 32.9, 32.4, 32.0, 30.5, 29.4, 28.6, 26.1, 24.3, 21.3, 21.0, 21.0, 20.2, 19.2, 18.0, 18.0, 17.4, 16.6, 12.7, 11.7

HRMS (CI): m/z calculated for $C_{48}H_{72}O_3$ $[M]^+$: 696.5481, Found: 696.5534

FTIR (NaCl): ν 3560, 1662, 1612, 1450, 1435, 1379, 1083, 1070 cm^{-1}



11d

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((1*R*,2*S*)-1-(3-hydroxypropoxy)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,8,10b-pentamethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-2-yl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (11d), white solid, 75% yield (mixture of isomers). No regioisomer of benzene ring was detected from ^{1}H NMR. See reference 4b in manuscript.

R_f: 0.16 (Hexane : Ethyl Acetate = 4:1)

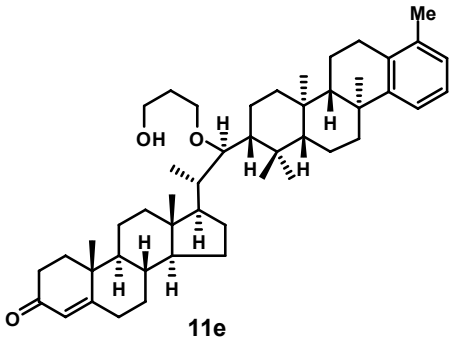
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.23–7.12 (m, 1H), 7.04–6.81 (m, 2H), 5.75 (s, 1H), 3.87–3.73 (m, 3H), 3.65–3.55 (m, 1H), 3.44–3.34 (m, 1H), 3.09–3.00 (m, 1H), 2.91 (dd, J = 16.92, 5.87 Hz, 1H), 2.85–2.73 (m, 1H), 2.29 (s, 3H), 1.21 (s, 3H), 1.20 (s, 3H), 0.93 (d, J = 6.33 Hz, 3H), 0.91 (s, 3H), 0.88 (s, 3H), 0.85 (s, 3H), 0.72 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.7, 171.6, 147.4, 134.9, 134.5, 129.4, 126.5, 124.5, 123.8, 80.5, 72.6, 63.2, 57.9, 55.7, 55.6, 53.7, 53.5, 53.4, 45.1, 42.3, 40.8, 40.0, 39.6, 38.5, 37.7, 37.5, 37.1, 35.6, 35.6, 34.0, 32.9, 32.3, 32.0, 30.8, 29.3, 28.5, 26.2, 24.3, 21.0, 20.8, 20.1, 19.1, 17.9, 17.9, 17.4, 16.6, 12.6, 11.7

HRMS (CI): m/z calculated for $C_{48}H_{72}O_3$ $[M]^+$: 696.5481, Found: 696.5385

FTIR (NaCl): ν 3600, 1662, 1612, 1450, 1435, 1379, 1332, 1269, 1215, 1188 cm^{-1}



11e

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((1*R*,2*S*)-1-(3-hydroxypropoxy)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,7,10b-pentamethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-2-yl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (11e), white solid, 76% yield (mixture of isomers).

R_f: 0.16 (Hexane : Ethyl Acetate = 4:1)

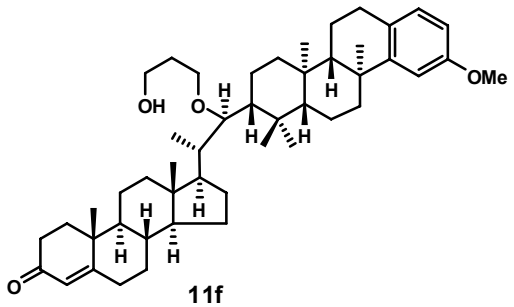
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.18–7.05 (m, 3H), 7.00–6.95 (m, 1H), 5.75 (s, 1H), 3.85–3.75 (m, 3H), 3.65–3.56 (m, 1H), 3.42–3.51 (m, 1H), 3.08–2.93 (m, 1H), 2.82 (dd, *J* = 17.42, 6.12 Hz, 1H), 2.70– 2.50 (m, 1H), 2.22 (s, 3H), 1.24 (s, 3H), 1.20 (s, 3H), 0.95 (s, 3H), 0.94 (d, *J* = 6.58 Hz, 3H), 0.88 (s, 3H), 0.85 (s, 3H), 0.72 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.6, 171.5, 150.3, 136.1, 133.7, 126.8, 125.5, 123.8, 122.4, 80.5, 72.5, 63.1, 57.8, 55.8, 54.9, 53.7, 53.6, 53.5, 45.2, 42.4, 41.1, 40.1, 39.6, 38.6, 38.1, 37.5, 37.1, 35.7, 35.7, 34.0, 32.9, 32.4, 32.0, 29.4, 28.7, 28.6, 26.2, 24.3, 21.0, 20.2, 19.9, 19.3, 18.0, 17.8, 17.4, 16.5, 12.7, 11.7

HRMS (CI): *m*/*z* calculated for $C_{48}H_{72}O_3$ $[M]^+$: 696.5481, Found: 696.5506

FTIR (NaCl): ν 3429, 1658, 1612, 1469, 1450, 1419, 1379, 1246, 1215 cm^{-1}



11f

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((1*R*,2*S*)-1-(3-hydroxypropoxy)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-9-methoxy-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-2-yl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (11f), white solid, 59% yield (mixture of isomers).

Major isomer:

R_f: 0.16 (Hexane : Ethyl Acetate = 4:1)

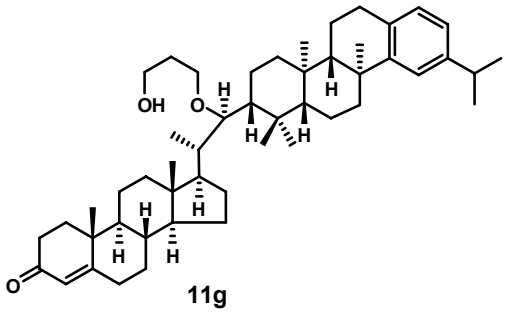
^{1}H NMR (400 MHz, $CDCl_3$): 7.17–6.94 (m, 1H), 6.88–6.63 (m, 2H), 5.74 (s, 1H), 3.85–3.75 (m, 3H), 3.78 (s, 3H), 3.65–3.55 (m, 1H), 3.44–3.35 (m, 1H), 3.08–3.00 (m, 1H), 2.87 (dd, *J* = 16.51, 5.81 Hz, 1H), 2.80–2.70 (m, 1H), 1.22 (s, 3H), 1.20 (s, 3H), 0.94 (s, 3H), 0.93 (d, *J* = 6.33 Hz, 3H), 0.91 (s, 3H), 0.85 (s, 3H), 0.71 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.7, 171.6, 157.6, 151.5, 127.4, 123.8, 113.7, 113.7, 110.2, 80.5, 72.6, 63.2, 57.8,

55.7, 55.3, 55.2, 53.7, 53.5, 53.4, 45.1, 42.3, 40.7, 40.0, 39.6, 38.5, 38.2, 37.5, 37.1, 35.6, 35.6, 34.0, 32.9, 32.3, 32.0, 30.0, 29.3, 28.5, 26.0, 24.3, 21.0, 20.1, 19.1, 18.0, 17.9, 17.4, 16.6, 12.6, 11.7.

HRMS (CI): *m/z* calculated for $C_{48}H_{72}O_4$ $[M]^+$: 712.5431, not obtained

FTIR (NaCl): ν 3460 (b), 1662, 1612, 1510, 1452, 1379, 1267, 1246, 1215, 1070 cm^{-1}



11g

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((1*R*,2*S*)-1-(3-hydroxypropoxy)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-9-isopropyl-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-2-yl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (11g), white solid, 71% yield (mixture of isomers).

R_f: 0.16 (Hexane : Ethyl Acetate = 4:1)

Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.20–7.05 (m, 2H), 7.00–6.90 (m, 1H), 5.73 (s, 1H), 3.85–3.70 (m, 3H), 3.65–3.50 (m, 1H), 3.42–3.32 (m, 1H), 2.96–2.75 (m, 2H), 1.25 (d, *J* = 4.61 Hz, 3H), 1.24 (s, 3H), 1.22 (d, *J* = 4.61 Hz, 3H), 1.18 (s, 3H), 0.93 (s, 3H), 0.92 (d, *J* = 5.30 Hz, 3H), 0.87 (s, 3H), 0.84 (s, 3H), 0.71 (s, 3H)

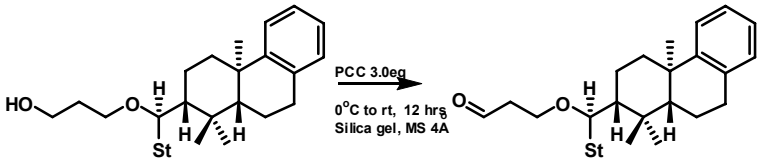
^{13}C NMR (100 MHz, $CDCl_3$): 199.7, 171.7, 150.0, 146.1, 132.5, 128.7, 123.8, 123.2, 122.6, 80.5, 72.5, 63.1, 57.9, 55.8, 55.5, 53.7, 53.6, 53.5, 45.2, 42.3, 40.7, 40.1, 39.6, 38.6, 38.1, 37.6, 37.1, 35.7, 35.7, 34.0, 34.0, 32.9, 32.4, 32.0, 30.5, 29.4, 28.6, 26.2, 24.2, 24.2, 24.1, 21.0, 20.2, 19.1, 18.0, 18.0, 17.4, 16.6, 12.7, 11.7

HRMS (CI): *m/z* calculated for $C_{50}H_{76}O_3$ $[M]^+$: 724.5794, not obtained

FTIR (NaCl): ν 3444, 1662, 1614, 1450, 1435, 1417, 1379, 1215 cm^{-1}

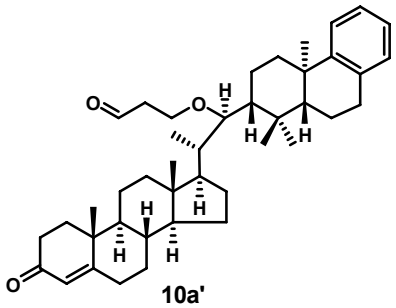
5. General procedure for oxidation of cyclization products.

For each cyclization reaction, only the product name and the NMR data of the major product was provided. Only one of the enantiomers' names was shown.



10a **10a'**

To an oven-dried round-bottom flask equipped with a magnetic stirring bar was added PCC (65mg, 0.3 mmol, 3.0 eq.), 4 Å molecular sieve (0.1 g), silica gel (0.1 g) and DCM (10 mL). A solution of alcohol **10a** (61 mg, 0.1 mmol, 1.0 eq. in 5 mL of DCM) mixture was added *via* syringe at 0 °C. The mixture was allowed to warm up to room temperature and stirred for 12 hours until reaction finished. The reaction solution was filtered through as pad of silica gel packed in sintered funnel and washed with 100 mL ethyl acetate. The filtrate was concentrated *in vacuo*. The residual crude product was purified by flash column chromatography to afford compound **10a'** as white solid.



10a'

3-((1*R*,2*S*)-2-((8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[α]phenanthren-17-yl)-1-((2*R*,4a*R*,10a*R*)-1,1,4a-trimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-2-yl)propoxy)propanal (10a'), white solid, 80% yield.

Isoemer ratio: 87:11:2 (CHO ^{1}H NMR integration)

R_f: 0.23 (Hexane : Ethyl Acetate = 4:1)

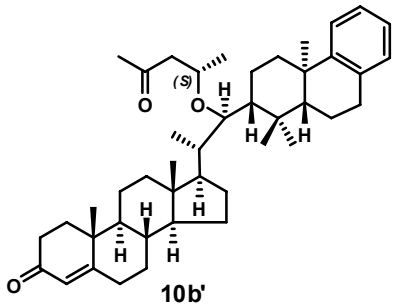
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 9.84 (t, *J* = 2.07 Hz, 1H), 7.29–7.22 (m, 1H), 7.16–7.09 (m, 1H), 7.09–7.00 (m, 2H), 5.73 (s, 1H), 3.87 (dt, *J* = 8.60, 5.87 Hz, 1H), 3.74 (dt, *J* = 9.12, 6.40 Hz, 1H), 3.42 (m, 1H), 2.95 (dd, *J* = 16.78, 5.87 Hz, 1H), 2.90–2.80 (m, 1H), 2.65–2.60 (m, 2H), 1.20 (s, 3H), 1.19 (s, 3H), .0.94 (s, 3H), 0.93 (s, 3H), 0.91 (d, *J* = 6.91 Hz, 3H), .0.70 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 201.9, 199.6, 171.6, 149.9, 135.0, 128.8, 125.7, 125.2, 124.5, 123.8, 80.0, 65.6, 55.8, 53.7, 53.5, 53.3, 52.2, 45.1, 44.5, 42.4, 39.6, 39.1, 38.6, 37.8, 37.3, 35.7, 35.6, 34.0, 33.0, 32.0, 30.9, 29.5, 28.6, 25.3, 24.3, 21.0, 20.8, 19.2, 18.0, 17.4, 12.5, 11.7

HRMS (CI): *m*/*z* calculated for $C_{42}H_{60}O_3$ $[M]^+$: 612.4542, Found: not obtained

FTIR (NaCl): ν 1654 (b), 1448, 1375, 1228, 1186, 1097 cm^{-1}



10b'

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-17-((1*R*,2*S*)-1-((*S*)-4-oxopentan-2-yloxy)-1-((2*R*,4a*R*,10a*R*)-1,1,4a-trimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-2-yl)propan-2-yl)-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one, white solid, 80% yield. Recrystallization yield: 40%. $[\alpha]^{20.0}_D$ = 72.7 (*c* 3.33, $CHCl_3$).

R_f: 0.25 (Hexane : Ethyl Acetate = 4:1)

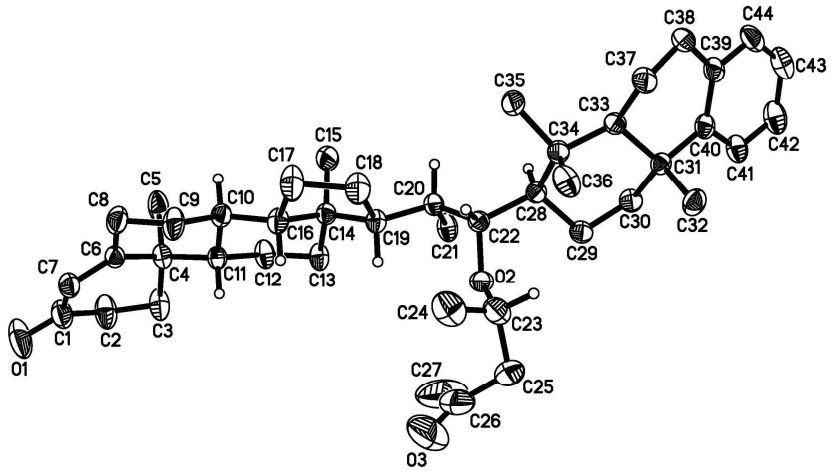
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.28–7.20 (m, 1H), 7.15–7.00 (m, 3H), 5.72 (s, 1H), 3.91 (sextet, *J* = 6.07 Hz, 1H), 3.48 (d, *J* = 2.87 Hz, 1H), 2.95 (dd, *J* = 17.20, 6.07 Hz, 1H), 2.89–2.80 (m, 1H), 2.69 (dd, *J* = 14.50, 5.23 Hz, 1H), 2.54 (dd, *J* = 14.67, 6.74 Hz, 1H), 2.21 (s, 3H), 1.19 (s, 3H), 1.17 (s, 3H), 1.15 (d, *J* = 5.83 Hz, 3H), 0.92 (s, 3H), 0.91 (s, 3H), 0.89 (d, *J* = 6.94 Hz, 3H), 0.70 (s, 3H)

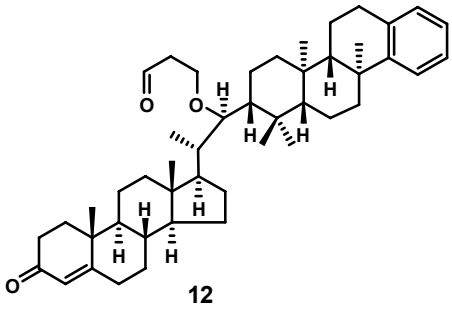
^{13}C NMR (100 MHz, $CDCl_3$): 208.5, 199.6, 171.6, 149.9, 135.0, 128.8, 125.6, 125.2, 124.4, 123.7, 74.6, 69.6, 55.8, 54.2, 53.7, 52.6, 52.3, 51.2, 46.4, 42.3, 39.5, 39.3, 38.5, 37.8, 37.4, 35.7, 35.6, 34.0, 32.9, 32.0, 32.0, 30.8, 29.4, 28.3, 25.3, 24.3, 21.3, 21.0, 19.7, 19.1, 18.0, 17.4, 12.3, 11.6

HRMS (CI): *m/z* calculated for $C_{44}H_{64}O_3$ $[M]^+$: 640.4855, Found $[M+H]^+$: 641.4820

FTIR (NaCl): ν 1712, 1660, 1620, 1448, 1371, 1332, 1228, 1168 cm^{-1}



X ray structure of **10b',** 50% probability was chosen for the ellipsoids.



12

3-((1*R*,2*S*)-2-((8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[a]phenanthren-17-yl)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propoxy)propanal (12), white solid, 68% yield. Isomer ratio: 66:18:10:6.

R_f: 0.25 (Hexane : Ethyl Acetate = 4:1),

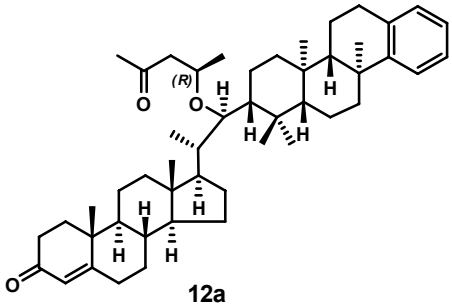
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 9.82 (t, *J* = 2.00 Hz, 1H), 7.31–6.96 (m, 4H), 5.72 (s, 1H), 3.91–3.76 (m, 1H), 3.76–3.64 (m, 1H), 3.40–3.30 (m, 1H), 2.93 (dd, *J* = 16.87, 5.62 Hz, 1H), 2.88–2.75 (m, 1H), 1.20 (s, 3H), 1.17 (s, 3H), 0.92 (s, 3H), 0.88 (d, *J* = 6.44 Hz, 3H), 0.85 (s, 3H), 0.83 (s, 3H), 0.69 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 202.1, 199.7, 171.6, 150.3, 135.1, 128.8, 125.7, 125.1, 124.6, 123.8, 80.0, 65.7, 57.9, 55.8, 55.4, 53.7, 53.5, 53.4, 45.2, 44.5, 42.3, 40.7, 40.1, 39.6, 38.6, 38.0, 37.6, 37.1, 35.7, 35.7, 34.0, 33.0, 32.0, 30.9, 29.3, 28.6, 26.1, 24.3, 21.0, 20.0, 19.1, 18.0, 17.9, 17.4, 16.6, 12.4, 11.7

HRMS (CI): *m/z* calculated for $C_{47}H_{68}O_3$ $[M]^+$: 680.5168, Found $[M+H]^+$: 681.4118

FTIR (NaCl): ν 1718, 1660, 1618, 1450, 1379, 1332, 1267, 1215 cm^{-1}



12a

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-17-((1*R*,2*S*)-1-((*R*)-4-oxopentan-2-yloxy)-1-((2*R*,4a*R*,4b*S*,10bS,12a*R*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-2-yl)-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (12a), white solid, 56% yield.

R_f: 0.25 (Hexane : Ethyl Acetate = 4:1)

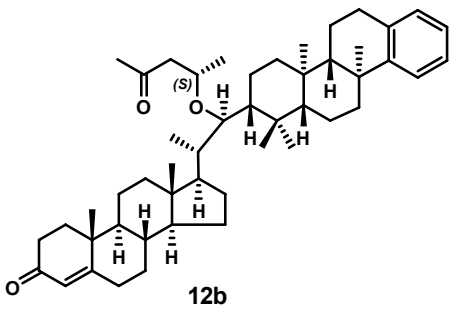
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.33–7.01 (m, 4H), 5.74 (s, 1H), 3.94 (sextet, *J* = 6.05 Hz, 1H), 3.51 (d, *J* = 2.47 Hz, 1H), 2.94 (dd, *J* = 17.32, 6.05 Hz, 1H), 2.88–2.79 (m, 1H), 2.74 (dd, *J* = 14.57, 4.95 Hz, 1H), 2.20 (s, 3H), 1.21 (s, 3H), 1.19 (s, 3H), 1.18 (d, *J* = 6.26 Hz, 3H), 0.93 (s, 3H), 0.89 (d, *J* = 6.52 Hz, 3H), 0.88 (s, 3H), 0.86 (s, 3H), 0.70 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 208.1, 199.6, 171.5, 150.2, 135.1, 128.8, 125.7, 125.1, 124.6, 123.8, 75.5, 70.8, 58.1, 55.8, 55.4, 54.1, 53.7, 53.4, 50.9, 45.9, 42.5, 40.7, 40.5, 39.6, 38.6, 38.0, 37.7, 37.6, 35.7, 35.6, 34.0, 32.9, 32.0, 31.8, 30.9, 29.5, 28.5, 26.2, 24.4, 21.0, 20.9, 20.7, 19.0, 18.2, 17.9, 17.4, 16.7, 12.8, 11.6,

HRMS (CI): *m*/*z* calculated for $C_{49}H_{72}O_3$ $[M]^+$: 708.5481, Found $[M+H]^+$: 709.4159

FTIR (NaCl): ν 1708, 1662, 1610, 1450, 1373, 1359 cm^{-1}



12b

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-17-((1*R*,2*S*)-1-((*S*)-4-oxopentan-2-yloxy)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-2-yl)-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (12b), colorless solid, 55% yield, recrystallization yield: 28%. $[\alpha]^{20.0}_D$ = 108.6, (*c* 0.57, $CHCl_3$).

R_f: 0.25 (Hexane : Ethyl Acetate = 4:1)

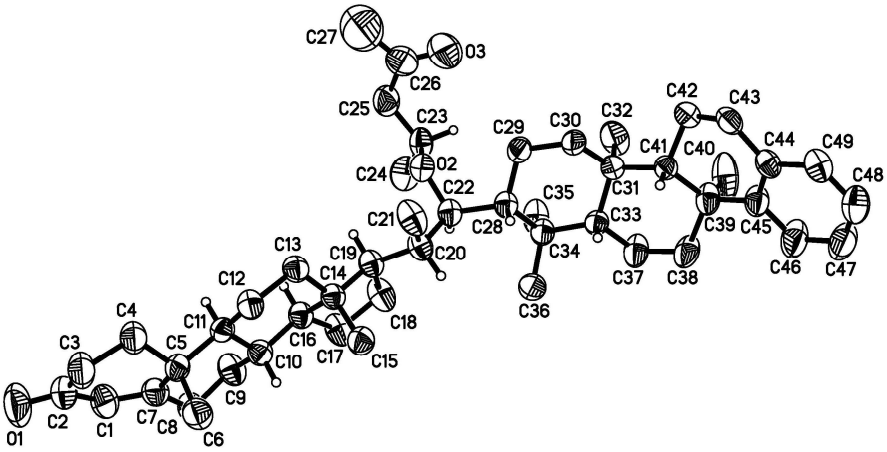
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.29–7.21 (m, 1H), 7.15–7.00 (m, 3H), 5.72 (s, 1H), 3.86 (sextet, *J* = 5.86 Hz, 1H), 3.43 (d, *J* =2.44 Hz, 1H), 2.92 (dd, *J* = 17.24, 6.02 Hz, 1H), 2.86–2.75 (m, 1H), 2.66 (dd, *J* = 14.31, 5.20 Hz, 1H), 2.51 (dd, *J* =14.64, 6.67 Hz, 1H), 2.20 (s, 3H), 1.20 (s, 3H), 1.17 (s, 3H), 1.23 (d, *J* = 5.66 Hz, 3H), 0.91 (s, 3H), 0.89 (d, *J* = 6.67 Hz, 3H), 0.84 (s, 3H), 0.82 (s, 3H), 0.69 (s, 3H)

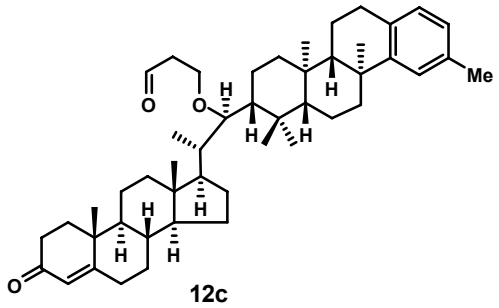
^{13}C NMR (100 MHz, $CDCl_3$): 208.6, 199.7, 171.6, 150.2, 135.1, 128.8, 125.6, 125.1, 124.5, 123.7, 74.5, 69.6, 58.1, 55.8, 55.4, 54.3, 53.7, 52.6, 51.2, 46.5, 42.3, 40.7, 40.3, 39.5, 38.6, 38.0, 37.6, 37.2, 35.7, 35.6, 34.0, 32.9, 32.0, 32.0, 30.8, 29.2, 28.2, 26.1, 24.3, 21.0, 20.6, 19.6, 19.0, 18.0, 17.9, 17.4, 16.7, 12.2, 11.6

HRMS (CI): *m/z* calculated for $C_{49}H_{72}O_3$ $[M]^+$: 708.5481, Found$[M+H]^+$: 709.4643

FTIR (NaCl): ν 1708, 1600, 1616, 1450, 1373, 1360 cm^{-1}



X ray structure of **12b**, 50% probability was chosen for the ellipsoids.



12c

3-((1*R*,2*S*)-2-((8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[α]phenanthren-17-yl)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,9,10b-pentamethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propoxy)propanal (12c), white solid, 95% yield. Isomer ratio: 66:17:14:3.

R_f: 0.25 (Hexane : Ethyl Acetate = 4:1).

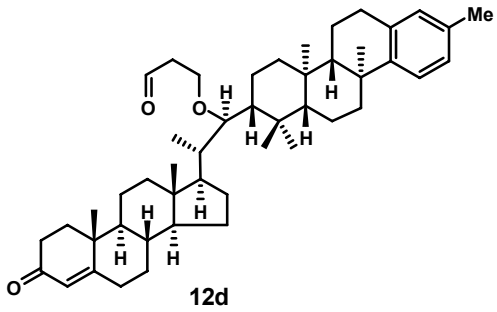
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 9.81 (t, *J* = 2.00 Hz, 1H), 7.12–7.00 (m, 2H), 6.95–6.85 (m, 1H), 5.73 (s, 1H), 3.90–3.76 (m, 1H), 3.75–3.65 (m, 1H), 3.35 (m, 1H), 2.89 (dd, *J* = 16.83, 6.18 Hz, 1H), 2.81–2.70 (m, 1H), 2.29 (s, 3H), 1.19 (s, 3H), 1.17 (s, 3H), 0.91 (s, 3H), 0.88 (d, *J* = 6.61 Hz, 3H), 0.85 (s, 3H), 0.83 (s, 3H), 0.69 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 202.0, 199.6, 171.5, 150.1, 134.8, 131.9, 128.7, 126.0, 125.1, 123.8, 79.9, 65.8, 57.9, 55.7, 55.5, 53.7, 53.5, 53.4, 45.2, 44.6, 42.3, 40.7, 40.1, 39.6, 38.5, 37.9, 37.5, 37.1, 35.6, 35.6, 34.0, 32.9,, 32.0, 30.4, 29.3, 28.5, 26.1, 24.3, 21.3, 21.0, 20.0, 19.1, 18.0, 18.0, 17.4, 16.5, 12.4, 11.7

HRMS (CI): *m/z* calculated for $C_{48}H_{70}O_3$ $[M]^+$: 694.5325, Found $[M+H]^+$: 695.4252

FTIR (NaCl): ν 1728, 1662, 1612, 1448, 1375, 1247 cm^{-1}



12d

3-((1*R*,2*S*)-2-((8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[α]phenanthren-17-yl)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,8,10b-pentamethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propoxy)propanal (12d), white solid, 80% yield. Isomer ratio: 73:14:12:1. No regioisomer of benzene ring was detected from ^{1}H NMR. See reference 4b in manuscript.

R_f: 0.25 (Hexane : Ethyl Acetate = 4:1)

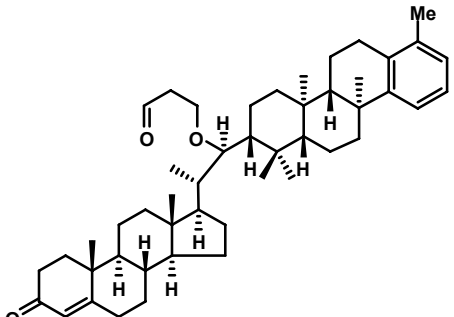
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 9.81 (t, *J* = 2.05 Hz, 1H), 7.21–7.10 (m, 1H), 7.00–6.77 (m, 2H), 5.72 (s, 1H), 3.90–3.76 (m, 1H), 3.75–3.50 (m, 1H), 3.35 (m, 1H), 2.88 (dd, *J* = 17.10, 5.65 Hz, 1H), 2.82–2.70 (m, 1H), 2.26 (s, 3H), 1.18 (s, 3H), 1.17 (s, 3H), 0.91 (s, 3H), 0.89 (d, *J* = 6.46 Hz, 3H), 0.85 (s, 3H), 0.82 (s, 3H), 0.69 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 202.1, 199.7, 171.7, 147.4, 135.0, 134.5, 129.4, 126.6, 124.5, 123.8, 78.0, 65.7, 57.9, 55.8, 55.6, 53.7, 53.5, 53.4, 45.2, 44.5, 42.3, 40.8, 40.1, 39.6, 38.6, 37.7, 37.5, 37.1, 35.7, 35.7, 34.0, 32.9, 32.0, 30.8, 29.3, 28.6, 26.2, 24.3, 21.0, 20.8, 20.0, 19.1, 18.0, 17.9, 17.4, 16.6, 12.5, 11.7

HRMS (CI): *m*/*z* calculated for $C_{48}H_{70}O_3$ $[M]^+$: 694.5325, Found $[M+H]^+$: 695.4450

FTIR (NaCl): ν 1726, 1668, 1612, 1450, 1379, 1332, 1228, 1215, 1097 cm^{-1}



12e

3-((1*R*,2*S*)-2-((8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[α]phenanthren-17-yl)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,7,10b-pentamethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propoxy)propanal (12e), white solid, 80% yield. Isomer ratio: 71:20:8:1.

R_f: 0.25 (Hexane : Ethyl Acetate = 4:1)

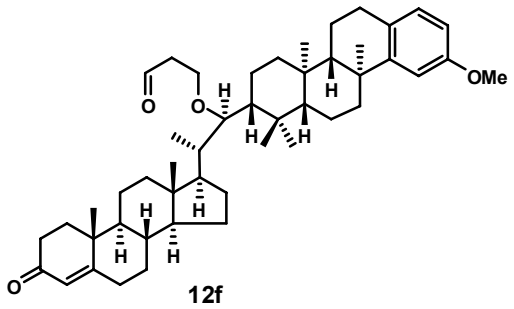
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 9.82 (t, *J* = 1.92 Hz, 1H), 7.19–6.90 (m, 3H), 5.73 (s, 1H), 3.92–3.76 (m, 1H), 3.75–3.60 (m, 1H), 3.40–3.30 (m, 1H), 2.79 (dd, *J* = 17.78, 5.83 Hz, 1H), 2.20 (s, 3H), 1.21 (s, 3H), 1.17 (s, 3H), 0.92 (s, 3H), 0.89 (d, *J* = 6.83 Hz, 3H), 0.85 (s, 3H), 0.82 (s, 3H), 0.69 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 202.1, 199.7, 171.7, 150.3, 136.1, 133.7, 126.8, 125.5, 123.8, 122.4, 80.0, 65.7, 57.8, 55.8, 54.9, 53.7, 53.5, 53.4, 45.2, 44.5, 42.3, 41.1, 40.1, 39.6, 38.6, 38.1, 37.4, 37.1, 35.7, 35.7, 34.0, 32.9, 32.0, 29.3, 28.7, 28.6, 26.2, 24.3, 21.0, 20.0, 19.9, 19.2, 18.0, 17.8, 17.4, 16.5, 12.4, 11.7

HRMS (CI): *m*/*z* calculated for $C_{48}H_{70}O_3$ $[M]^+$: 694.5325, Found $[M]^+$: 694.4215

FTIR (NaCl): ν 1724, 1662, 1612, 1450, 1379, 1269, 1188, 1112 cm^{-1}



12f

3-((1*R*,2*S*)-2-((8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[α]phenanthren-17-yl)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-9-methoxy-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propoxy)propanal (12f), white solid, 79% yield. Isomer ratio: 74:18:7:1.

R_f: 0.25 (Hexane : Ethyl Acetate = 4:1)

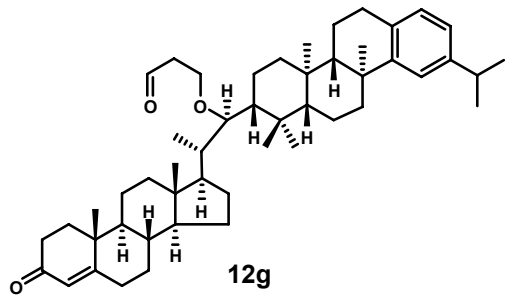
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 9.81 (s, 1H), 7.15–6.91 (m, 1H), 6.88–6.60 (m, 2H), 5.72 (s, 1H), 3.90–3.62 (m, 2H), 3.77 (s, 3H), 3.42–3.33 (m, 1H), 2.86 (dd, *J* = 17.13, 6.46 Hz, 1H), 2.79–2.66 (m, 1H), 1.19 (s, 3H), 1.17 (s, 3H), 0.90 (s, 3H), 0.88 (d, *J* = 6.19 Hz, 3H), .0.85 (s, 3H), 0.82 (s, 3H),. 0.68 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 202.0, 199.6, 171.6, 157.7, 151.5, 127.4, 123.8, 113.7, 110.7, 110.3, 80.1, 65.7, 57.9, 55.8, 55.3, 55.2, 53.7, 53.5, 53.4, 45.1, 44.5, 42.3, 40.7, 40.1, 39.6, 38.6, 38.2, 37.6, 37.1, 35.7, 35.7, 34.0, 32.9, 32.0, 30.0, 29.3, 28.6, 26.0, 24.3, 21.0, 20.0, 19.1, 18.0, 17.9, 17.4, 16.6, 12.4, 11.7

HRMS (CI): *m*/*z* calculated for $C_{48}H_{70}O_4$ $[M]^+$: 710.5274, Found $[M]^+$: 710.4492

FTIR (NaCl): ν 1724, 1662, 1612, 1510, 1452, 1246, 1215, 1097 cm^{-1}



12g

3-((1*R*,2*S*)-2-((8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[α]phenanthren-17-yl)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-9-isopropyl-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propoxy)propanal (12g), white solid, 90% yield. Isomer ratio: 64:20:14:2.

R_f: 0.25 (Hexane : Ethyl Acetate = 4:1)

Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 9.82 (t, *J* = 2.00 Hz, 1H), 7.17–7.03 (m, 2H), 6.99–6.91 (m, 1H), 5.72 (s, 1H), 3.90–3.63 (m, 2H), 3.42–3.30 (m, 1H), 2.95–2.72 (m, 2H), 1.23 (d, *J* = 3.76 Hz, 3H), 1.22 (s, 3H), 1.20 (d, *J* = 3.49 Hz, 3H), 1.17 (s, 3H), 0.91 (s, 3H), 0.88 (d, *J* = 6.71 Hz, 3H), 0.85 (s, 3H), 0.82 (s, 3H), .0.69 (s, 3H)

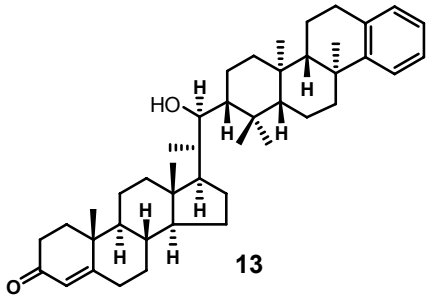
^{13}C NMR (100 MHz, $CDCl_3$): 202.2, 199.7, 171.6, 150.1, 146.1, 132.5, 128.7, 123.8, 123.2, 122.6, 80.0, 65.7, 57.9,

55.8, 55.5, 53.7, 53.5, 53.4, 45.2, 44.5, 42.3, 40.7, 40.1, 39.6, 38.6, 38.1, 37.6, 37.1, 35.7, 35.7, 34.0, 33.9, 32.9, 32.0, 30.5, 29.3, 28.6, 26.2, 24.3, 24.2, 24.1, 21.0, 20.0, 19.1, 18.0, 18.0, 17.4, 16.6, 12.5, 11.7

HRMS (CI): *m*/*z* calculated for $C_{50}H_{74}O_3$ $[M]^+$: 722.5638, Found [M+H]: 723.4851

FTIR (NaCl): ν 1724, 1662, 1612, 1450, 1419, 1379, 1269, 1188 cm^{-1}

6. Procedure for modification of steroidal aldehyde acetal cyclization products.



13

(8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-17-((1*R*,2*S*)-1-hydroxy-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-2-yl)-10,13-dimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[α]phenanthren-3(2*H*)-one (13)

A solution of **12a** (71 mg, 0.1 mmol 1.0 eq.) in DCM (3 mL) and MeCN (3 mL) was cooled to -40 °C prior to the addition of BCl_3 (1.0 M in DCM, 0.45 mL, 4.5 eq.). The reaction was allowed to proceed at -40 °C for 24 hours before quenching by pouring into water (5 mL). The aqueous layer was extracted with DCM (3 × 20 mL). The organic layer was combined, washed with water (20 mL) and brine (20 mL), and dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residual crude product was purified by flash column chromatography to afford the desired alcohol as white solid with 80% yield.

For *S* acetal product, 3.5 eq. BCl_3 was used and 85% yield was obtained.

R_f: 0.30 (Hexane : Ethyl Acetate = 4:1)

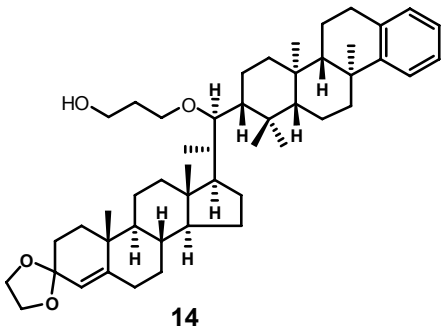
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.40–7.00 (m, 4H), 5.74 (s, 1H), 3.86 (m, 1H), 2.96 (dd, *J* = 17.13, 5.85 Hz, 1H), 2.90–2.79 (m, 1H), 2.73–2.63 (m, 1H), 2.62–2.54 (m, 1H), 2.50–2.24 (m, 5H), 2.10–2.20 (m, 4H), 1.22 (s, 3H), 1.20 (s, 3H), 1.20 (s, 3H), 0.95 (s, 3H), 0.94 (s, 3H), 0.86 (d, *J* = 3.86 Hz, 3H), 0.73 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 199.7, 171.6, 150.3, 135.1, 128.8, 125.7, 125.2, 124.6, 123.8, 71.0, 57.8, 55.7, 55.4, 53.7, 52.9, 52.4, 44.9, 42.2, 40.7, 39.6, 39.6, 38.6, 38.0, 37.6, 37.5, 35.7, 35.7, 34.0, 32.9, 32.0, 30.8, 29.1, 27.9, 26.2, 24.1, 21.0, 19.9, 19.2, 17.9, 17.4, 17.4, 16.8, 16.4, 11.8

HRMS (CI): *m*/*z* calculated for $C_{44}H_{64}O_2$ $[M]^+$: 624.4906, Found $[M+H]^+$: 625.4974

FTIR (NaCl): ν 3429 (b), 1660, 1616, 1450, 1435, 1379 cm^{-1}



14

3-((1*R*,2*S*)-2-((8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydrospir

o[cyclopenta[α]phenanthrene-3,2'-[1,3]dioxolane]-17-yl)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propoxy)propan-1-ol (14)

To a solution of **12** (680 mg, 1 mmol 1.0 eq.) in DCE (1,2-dichloroethane, 40 mL), CSA (camphorsulfonic acid, 23 mg, 0.1 mmol, 0.1 eq.) was added. The reaction mixture was refluxed for 24 hours with MS 4 Å as drying reagents. The reaction was then cooled to room temperature and quenched with saturated $NaHCO_3$ aqueous solution (40 mL). The aqueous layer was extracted with DCM (2 × 30 mL). The organic layer was combined, washed with water (30 mL) and brine (30 mL), and dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residual crude product was purified by flash column chromatography to afford the desired alcohol as white solid with 67% yield, double bond regioisomer ratio< 90:10. [5]

R_f: 0.25 (Hexane : Ethyl Acetate = 4:1)

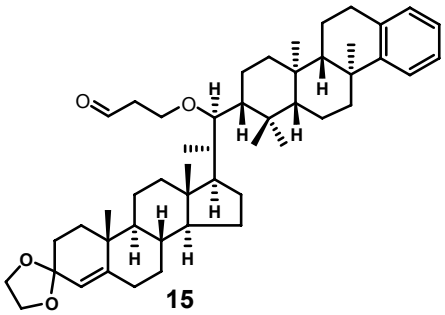
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.31–7.00 (m, 4H), 5.36 (s, 1H), 4.02–3.86 (m, 4H), 3.84–3.68 (m, 3H), 3.65–3.55 (m, 1H), 3.40–3.33(m, 1H), 3.02 (t, *J* = 5.55 Hz, 1H), 2.92 (dd, *J* = 16.67, 6.06 Hz, 1H), 2.86–2.74 (m, 1H), 2.57 (d, *J* = 12.87 Hz, 1H), 2.40 (d, *J* = 12.12 Hz, 1H), 2.38–2.20 (m, 1H), 2.11 (d, *J* = 13.88 Hz, 1H), 1.26 (s, 3H), 1.20 (s, 3H), 1.01 (s, 3H), 0.92 (s, 3H), 0.91 (d, *J* = 6.09 Hz, 3H), 0.85 (s, 3H), 0.66 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): 150.2, 140.2, 135.1, 128.8, 125.6, 125.1, 124.6, 122.1, 109.5, 80.6, 72.6, 64.5, 64.2, 63.3, 57.9, 56.6, 55.4, 53.7, 53.5, 49.5, 45.2, 42.3., 41.8, 40.7, 40.0, 39.7, 38.0, 37.6, 37.2, 36.7, 36.3, 35.5, 32.4, 32.0, 31.7, 31.0, 29.4, 29.3, 26.2, 24.5, 21.0, 20.2, 19.1, 18.9, 18.0, 17.9, 16.6, 11.7, 11.6

HRMS (CI): *m/z* calculated for $C_{49}H_{74}O_4$ $[M]^+$: 726.5587, Found $[M+H]^+$: 727.5504

FTIR (NaCl): ν 3462 (b), 1637, 1456, 1379, 1365, 1215, 1099 cm^{-1}



15

3-((1*R*,2*S*)-2-((8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydrospiro[cyclopenta[α]phenanthrene-3,2'-[1,3]dioxolane]-17-yl)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propoxy)propanal (15)

To an oven-dried round-bottom flask equipped with a magnetic stirring bar was added PCC (65mg, 0.3 mmol, 3.0 eq.), 4 Å molecular sieve (0.1 g), silica gel (0.1 g) and DCM (10 mL). A DCM solution of alcohol **14** (74 mg, 0.1 mmol, 1.0 eq.) was added *via* syringe at 0 ^oC. The mixture was allowed to warm up to room temperature and stirred for 12 hours until reaction completed. The reaction solution was filtered through as pad of silica gel packed in sintered funnel and washed with 100 mL ethyl acetate. The filtrate was concentrated *in vacuo*. Further purification was done by flash column chromatography. The compound **15** was obtained as white solid in 66% yield. Isomer ratio: 75:21:4.

R_f: 0.50 (Hexane : Ethyl Acetate = 4:1)

Major isomer:

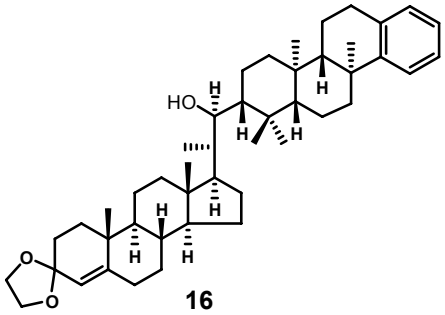
^{1}H NMR (400 MHz, $CDCl_3$): 9.81 (t, *J* = 2.04 Hz, 1H), 7.30–6.97 (m, 4H), 5.36 (s, 3H), 4.00–3.90 (m, 4H), 3.88–3.80 (m, 2H), 3.78–3.66 (m, 2H), 3.40–3.30 (m, 1H), 2.92 (dd, *J* = 17.21, 5.47 Hz, 1H), 2.86–2.74 (m, 1H),

2.65–2.50 (m, 3H), 2.40 (d, *J* = 11.51 Hz, 1H), 2.35–2.20 (m, 1H), 2.11 (d, *J* = 13.81 Hz, 1H), 1.26 (s, 3H), 1.19 (s, 3H), 1.01 (s, 3H), 0.91 (s, 3H), 0.88 (d, *J* = 6.10 Hz, 3H), 0.85 (s, 3H), 0.66 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 202.1, 150.3, 140.2, 135.1, 128.4, 125.7, 125.1, 124.6, 122.1, 109.5, 80.0, 65.7, 64.5, 64.2, 57.9, 56.6, 55.4, 53.6, 53.5, 49.6, 45.3, 44.5, 42.3, 44.5, 40.7, 40.1, 39.8, 38.0, 37.6, 37.1, 36.7, 36.3, 32.0, 31.8, 31.1, 29.4, 29.3, 28.6, 26.2, 24.5, 22.7, 21.1, 19.1, 18.9, 18.0, 17.9, 16.6, 12.6, 11.6

HRMS (CI): *m*/*z* calculated for $C_{49}H_{72}O_4$ $[M]^+$: 724.5431, Found $[M+H]^+$: 725.5483

FTIR (NaCl): ν 1718, 1647, 1454, 1379, 1363, 1259, 1101 cm^{-1}



16

(1*R*,2*S*)-2-((8*S*,9*S*,10*R*,13*S*,14*S*,17*R*)-10,13-dimethyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydrospiro[cyclopenta[α]phenanthrene-3,2'-[1,3]dioxolane]-17-yl)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-1-ol (16)

To a solution of ketone **15** (73 mg, 0.1 mmol, 1.0 eq.) in THF/MeOH (4 mL/2 mL) was added KOH aqueous solution (1 mL, 10.0 M). The reaction was allowed to stir at room temperature for 2 days. The reaction was quenched by pouring into HCl (0.5 M, 20 mL) at 0^{o}C. The mixture was extracted with DCM (3 × 20 mL) and combined organic layer was washed with saturated $NaHCO_3$ aqueous solution (10 mL), water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residual crude product was purified by flash column chromatography to afford the alcohol **16** as a white solid in 70% yield, double bond regioisomer ratio>96:4.[5]

R_f: 0.36 (Hexane : Ethyl Acetate = 4:1)

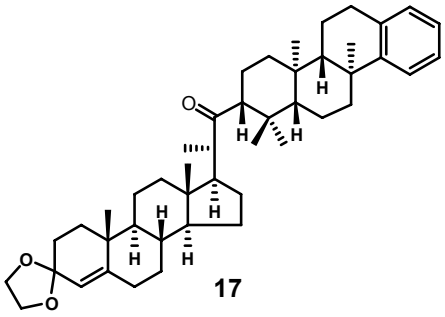
Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.30–6.93 (m, 4H), 5.34 (t, *J* = 1.95 Hz, 1H), 4.00–3.85 (m, 4H), 3.84 (m, 1H), 2.93 (dd, *J* = 16.69, 6.07 Hz, 1H), 2.88–2.74 (m, 1H), 2.60–2.50 (m, 2H), 2.40 (d, *J* = 10.62 Hz, 1H), 1.26 (s, 3H), 1.20 (s, 3H), 1.02(s, 3H), 1.02 (s, 3H), 0.93 (s, 3H), 0.83 (d, *J* = 4.31 Hz, 3H), 0.68 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 150.3, 140.2, 135.1, 128.8, 125.7, 125.1, 124.6, 122.2, 109.5, 71.0, 64.4, 64.2, 57.8, 56.6, 55.4, 52.9, 52.4, 49.6, 45.0, 42.2, 41.8, 40.7, 39.8, 39.7, 38.0, 37.6, 37.5, 36.6, 36.3, 32.0, 31.7, 31.1, 30.9, 29.1, 27.9, 26.2, 24.2, 21.1, 19.9, 19.2, 18.9, 17.9, 16.9, 16.4, 11.7, 11.7

HRMS (CI): *m*/*z* calculated for $C_{46}H_{68}O_3$ $[M]^+$: 668.5168, Found $[M+H]^+$: 669.5141

FTIR (NaCl): ν 3600, 1732, 1446, 1373, 1265 cm^{-1}



17

(*S*)-2-((8*S*,9*S*,10*R*,13S,14*S*,17R)-10,13-dimethyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydrospiro[cyclopenta[α]phenanthrene-3,2'-[1,3]dioxolane]-17-yl)-1-((2*R*,4a*R*,4b*S*,10b*S*,12a*R*)-1,1,4a,10b-tetramethyl-1,2,3,4,4a,4b,5,6,10b,11,12,12a-dodecahydrochrysen-2-yl)propan-1-one (17)

To an oven-dried round-bottom flask equipped with a magnetic stirring bar was added PCC (65mg, 0.3 mmol, 3.0 eq.), 4 Å molecular sieve (0.1 g), silica gel (0.1 g) and DCM (10 mL). A DCM solution of alcohol **16** (67 mg, 0.1 mmol, 1.0 eq.) was added *via* syringe at 0 ^{o}C. The mixture was allowed to warm up to room temperature and stirred for 12 hours until reaction completed. The reaction solution was filtered through a pad of silica gel packed in sintered funnel and washed with 100 mL ethyl acetate. The filtrate was concentrated *in vacuo*. Further purification was done by flash column chromatography. The compound **17** was obtained as white solid in 44% yield, recovered SM 25%, regioisomer ratio>88:12.[5]

R_f: 0.63 (Hexane : Ethyl Acetate = 4:1)

Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): 7.35–7.00 (m, 4H), 5.34 (m, 1H), 4.00–3.89 (m, 4H), 2.94 (dd, *J* = 17.23, 6.00 Hz, 1H), 2.88–2.75 (m, 1H), 2.70–2.60 (m, 1H), 2.55 (dd, *J* = 14.18, 2.63 Hz, 2H), 2.41 (dt, *J* = 12.56, 3.04 Hz, 1H), 2.12 (dd, *J* = 14.18, 2.23 Hz, 1H), 1.22 (s, 3H), 1.20 (s, 3H), 1.10 (s, 3H), 1.01 (d, *J* = 8.40 Hz, 3H), 0.93 (S, 3H), 0.90 (s, 3H), 0.70 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 217.1, 150.1, 140.1, 135.0, 128.8, 125.7, 125.2, 124.6, 122.2, 109.5, 64.4, 64.2, 60.5, 57.5, 55.9, 55.3, 51.8, 51.4, 49.7, 42.2, 41.8, 40.5, 39.7, 39.6, 38.0, 37.6, 37.1, 36.6, 36.1, 31.9, 31.8, 31.7, 31.1, 30.3, 29.7, 29.4, 29.3, 26.1, 24.6, 22.7, 21.0, 18.9, 18.1, 18.0, 16.4, 14.1

HRMS (CI): *m*/*z* calculated for $C_{46}H_{66}O_3$ $[M]^+$: 666.5012, Found $[M+H]^+$: 667.5096

FTIR (NaCl): ν 1703, 1672, 1641, 1445, 1367, 1311, 1247, 1199 cm^{-1}

7. References:

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