

Enantioselective Synthesis of a Polyfunctionalized Tetracycle Related to Pentacyclic Triterpenes by Using an Anionic Cycloaddition Reaction

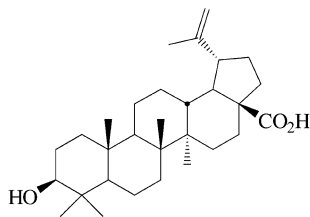
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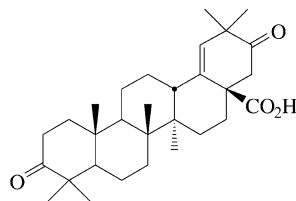
Dedicated to Professor *Duilio Arigoni* on the occasion of his 75th birthday

Herein we report a convergent enantioselective synthesis of a polyfunctionalized ABCD tetracycle by using an anionic cycloaddition reaction between a chiral bicyclic CD *Nazarov* intermediate (see **6**), derived from the (–)-*Weiland–Mischer* ketone, and an achiral cyclohexenone (see **5**) adequately functionalized to furnish the ring A of pentacyclic triterpenes (*Scheme 5*). The chiral bicyclic CD *Nazarov* intermediate forms ring B upon cycloaddition with the achiral cyclohexenone to yield an ABCD tetracycle with a *cis-anti-trans-anti-trans* configuration (see **4**). Further transformations on this adduct allowed reduction of the angular aldehyde function at C(10) to a Me group ($\rightarrow$ **17**) and introduction of an unsaturation at C(5)–C(6) by using the ketone function at C(7) ($\rightarrow$ **3**; *Scheme 6*).

Introduction. – Pentacyclic triterpenes such as betulinic acid (**1**), an anti-HIV and anti-cancer agent [1], and 3,21-dioxoolean-18-enoic acid (**2**), the first naturally occurring nonprotein inhibitor of Tie-2 kinase [2], have been derivatized [1][3] for studies on their bioactive functions and to enhance their potencies.



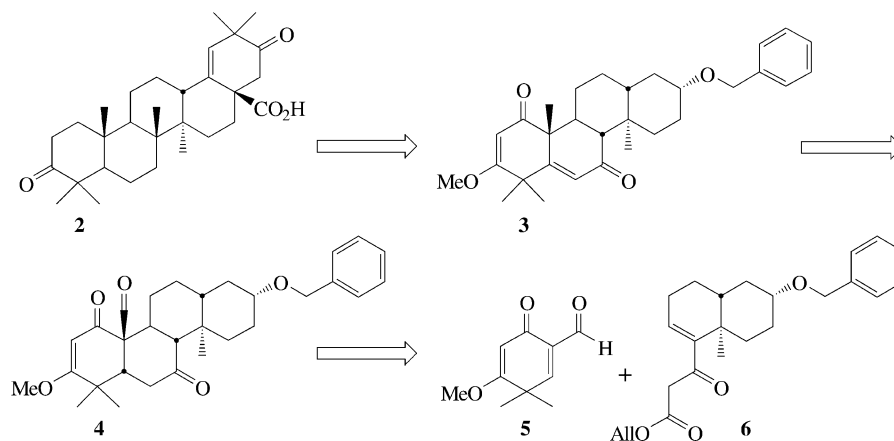
1 Betulinic acid



2 3,21-Dioxoolean-18-enoic acid

To fulfill the need for new analogs of these pentacyclic triterpenes, and to accomplish their total syntheses with a versatile strategy, we turned our attention to the novel anionic cycloaddition between the α,β -unsaturated β -keto ester **6** (*Nazarov* intermediate) derived from the (–)-*Weiland–Mischer* ketone (= (8*aR*)-3,4,8,8a-tetrahydro-8a-methylnaphthalene-1,6(2*H*,7*H*)-dione) and the adequately functionalized cyclohexenone **5** (*Scheme 1*). Anionic cycloaddition between an α,β -unsaturated β -keto ester, derived from the *Hajos–Parrish* ketone, and a cyclohexenone, leading to steroid-like compounds, have recently been successfully studied in our laboratory [4]. Retrosynthetic analysis of the ABCD ring of these pentacyclic triterpenes, which are

Scheme 1



basically the same for most pentacyclic triterpenes, led us to imagine that they might be derived from the tetracyclic enone **3**. This tetracycle **3** can be derived from tetracyclic aldehyde **4**, which can be formed *via* an enantioselective anionic cycloaddition between the bicyclic *Nazarov* reagent **6** and cyclohexenone **5**.

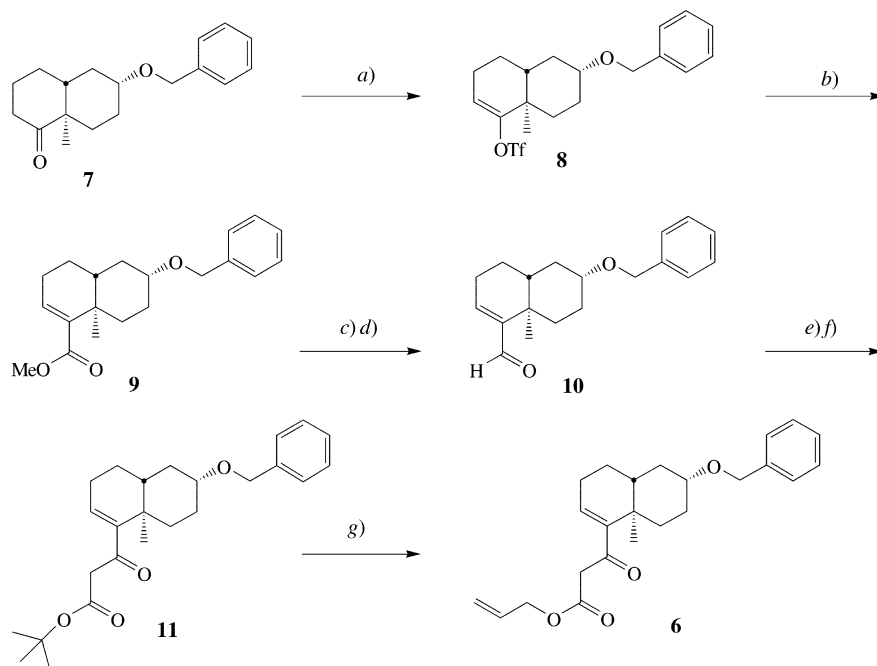
Results and Discussion. – β -Keto ester **6** was derived from the (–)-*Weiland–Mischer* ketone [5] by two approaches. The first one started with the formation of enol triflate **8** (Scheme 2) from the known (–)-ketone **7** [6], which was submitted to Pd-catalyzed carboxylation to yield ester **9** [7]. This ester was reduced to the alcohol, with Dibal-H, which was oxidized with *Dess–Martin* periodinane (= 1,1,1-tris(acetyloxy)-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one) to give aldehyde **10**. This aldehyde **10** was submitted to a *Reformatsky* addition of *tert*-butyl acetate. The resulting secondary alcohol was oxidized with *Dess–Martin* periodinane to give β -keto ester **11**, which was transesterified with allyl alcohol to yield β -keto ester **6** in 38% overall yield in seven steps starting from **7**.

Alternatively β -keto ester **6** can be synthesized from the known alcohol **12** [6] (Scheme 3). Removal of the ketal protecting group of **12** followed by sodium acetylide addition and *Rupe* rearrangement [8] yielded the enone **13** in good yield. The OH group of **13** was then protected as a benzyl ether with benzyl trichloroethanimidate [9]. The resulting enone **14** was then kinetically deprotonated with LiHMDS and added on allyl carbonocyanide [10] to afford β -keto ester **6** in 24% overall yield in five steps starting from **12**.

We found that aldehyde **5** (Scheme 4) was the best candidate to produce ring A of pentacyclic triterpenes *via* the anionic cycloaddition strategy [11]. The known enone **15** [12] was formylated followed by DDQ oxidation, or phenylseleno addition and oxidative elimination, to afford aldehyde **5** in good yield.

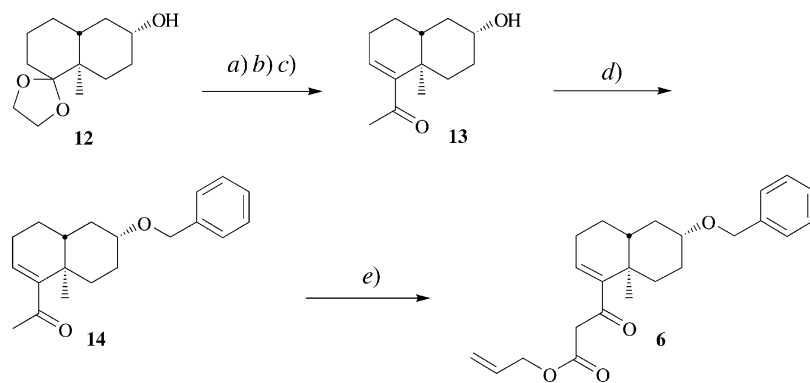
We attempted the anionic cycloaddition between β -keto ester **6** and cyclohexenone **5** under the standard conditions (Cs_2CO_3 , CH_2Cl_2 , room temperature) without any success. We then investigated other solvents and found that the use of AcOEt afforded

Scheme 2



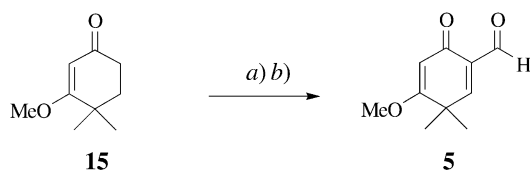
a) Ti_2O , *Proton Sponge*[®], CH_2Cl_2 ; 90%. b) K_2CO_3 , LiCl , MeOH , NMP (1-methylpyrrolidin-2-one), $[\text{PdCl}_2(\text{PPh}_3)_2]$, 200 psi CO , 130° ; 83%. c) Dibal-H (diisobutylaluminium hydride), CH_2Cl_2 , -78° ; 86%. d) *Dess–Martin* periodinane, CH_2Cl_2 , 0° ; 89%. e) $\text{tBuO}_2\text{CCH}_2\text{ZnBr}$, Et_2O , 0° to r.t.; 87%. f) *Dess–Martin* periodinane, CH_2Cl_2 , 0° ; 92%. g) DMAP (*N,N*-dimethylpyridin-4-amine), toluene, AlOH , 82%.

Scheme 3



a) 50% aq. H_2SO_4 soln., Et_2O ; 88%. b) Na , NH_3 (l), acetylene, Et_2O ; 83%. c) 1. HCO_2H , H_2SO_4 , r.t., then 90° ; 2. K_2CO_3 , MeOH ; 47%. d) $\text{CCl}_3\text{C}(=\text{NH})\text{OCH}_2\text{Ph}$, $\text{CF}_3\text{SO}_3\text{H}$, CH_2Cl_2 ; 77%. e) LiHMDS (lithium salt of 1,1,1,3,3,3-hexamethyldisilazane), NCCO_2All , THF ; 53% (90% corrected).

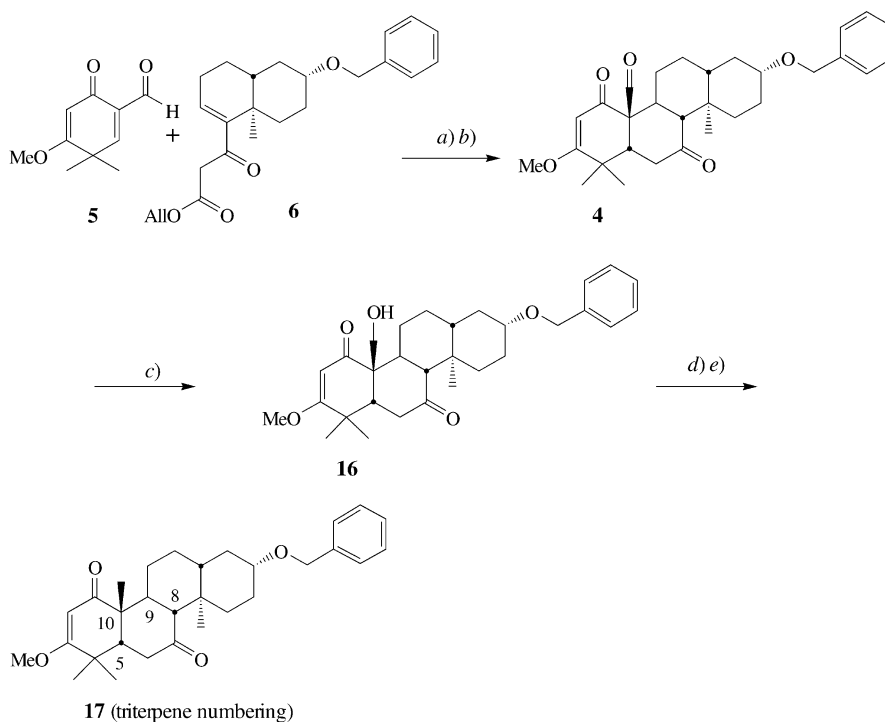
Scheme 4



a) MeONa, benzene, HCO₂Et, THF; 94%. *b)* 1. PhSeCl, pyridine, CH₂Cl₂; 2. 30% H₂O₂ soln., CH₂Cl₂ or DDO (4,5-dichloro-3,6-dioxocyclohexa-1,4-diene-1,2-dicarbonitrile), dioxane; 99%.

the desired cycloaddition product after 96 h (Scheme 5). Those conditions afforded aldehyde **4** as a single enantiomer after decarboxylation with [Pd(PPh₃)₄]. NaBH₄ Reduction of this aldehyde **4** yielded tetracyclic (hydroxymethyl)dione **16**. This tetracyclic hydroxy compound **16** was then converted to tetracycle **17** via formation of the corresponding phenyl carbonothioate followed by radical reduction [13]. The configurations of tetracycles **4**, **16**, and **17** were confirmed by spectral analysis.

Scheme 5



a) Cs₂CO₃, AcOEt, r.t., 96 h; 70%. *b)* [Pd(PPh₃)₄], morpholine, THF; 85%. *c)* NaBH₄, EtOH, THF, –78°, 99%. *d)* PhOC(=S)Cl, pyridine, CH₂Cl₂; 80%. *e)* Bu₃SnH, AIBN (2,2'-azobis[2-methylpropanenitrile]), toluene, reflux; 99%.

By using C_6D_6 as the solvent for the 1H -NMR analysis of **17**, we were able to assign the *d* at δ 1.75 ($J = 12.2$ Hz) to H–C(8) and the *dt* at δ 2.41 ($J = 3.8$ and 12.2 Hz) to H–C(9). COSY Experiments confirmed that these two protons were coupled with each other. We were then able to irradiate each of the four angular Me groups in a NOE difference experiment. We found that the *s* at δ 1.30 and 1.09 showed a NOE with the *dt* at δ 2.41 and had no effect on the *d* at 1.75 (Fig. 1). We also found that the *s* at δ 1.01 showed a NOE with the *d* at δ 1.75 and had no effect on the *dt* at δ 2.41. We were then able to assign the *s* at δ 1.01 to the angular Me group at C(10).

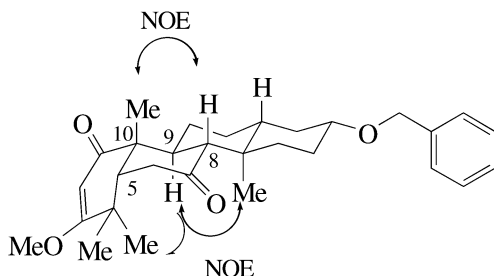


Fig. 1. Conformation and NOEs of **17**. Triterpene numbering.

Analysis of the anionic cycloaddition transition state showed that the α -approach of the cyclohexenone **5** to the (–)-keto ester **6** has a strong steric interaction between the angular Me group of β -keto ester **6** and the aldehyde function of cyclohexenone **5** (Fig. 2). This supports the proposal that the transition state with the lower energy barrier is the one where cyclohexenone **5** approaches from the β face of the β -keto ester **6** yielding tetracyclic aldehyde **4** after decarboxylation with $[Pd(PPh_3)_4]$.

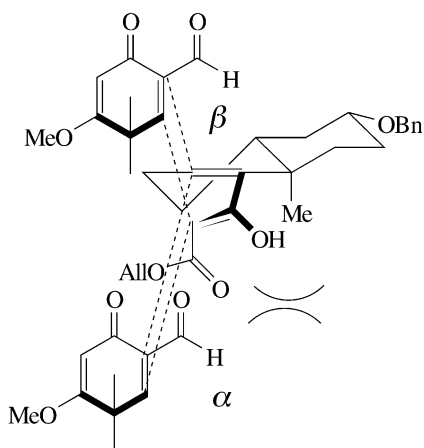
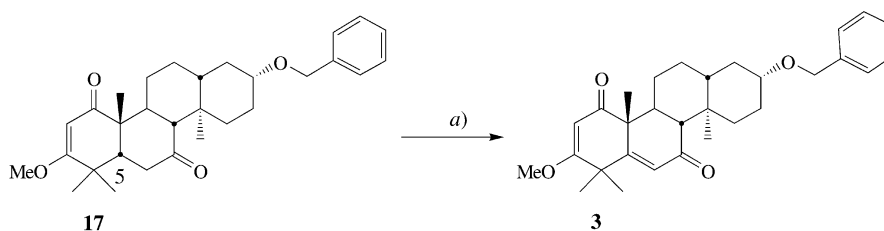


Fig. 2. Cyclohexenone approach to β -keto ester **6** (enol form) leading to the transition state of the anionic cycloaddition

Tetracycle **17** was then converted to tetracyclic enone **3** in a good yield by forming the lithium enolate of the C(7) ketone under kinetic control and trapping with $PhSeCl$ followed by oxidative elimination on treatment with hydrogen peroxide (Scheme 6). The synthesis of the polyfunctionalized tetracycle enone **3** tends to confirm that the anionic cycloaddition strategy will allow the synthesis of a variety of natural and

unnatural pentacyclic triterpenes. To reach this goal, one will have to introduce the angular Me group at C(8). Research in this direction is presently underway.

Scheme 6



a) 1. LiHMDS, CH_2Cl_2 , 0° , 2. PhSeCl , 3–30% aq. H_2O_2 soln., 99%.

A research chair from *BioChem Pharma Inc.* is gratefully acknowledged as well as financial support from *NSERC Canada* and *FCAR Québec*.

Experimental Part

General. All reactions were performed under N_2 with oven- or flame-dried glassware. Solvents were distilled and dried according to standard procedures. Anal. TLC: precoated glass plates (0.25 mm) with silica gel *Merck 60 F250*. Flash chromatography (FC): *Merck 230–400* mesh silica gel *60*. $[\alpha]_D$: *Perkin-Elmer 141* polarimeter, set at 589 nm; 10.0-cm cell. IR Spectra: *Perkin-Elmer 1600-FT-IR* spectrometer; in cm^{-1} . ^1H - and ^{13}C -NMR Spectra: *Bruker AC-300* spectrometer; referenced with respect to the residual signals of the solvent; δ in ppm, J in Hz. MS: *ZAB-1F* micromass spectrometer.

(4*a*R,6*R*,8*a*S)-3,4,4*a*,5,6,7,8,8*a*-Octahydro-8*a*-methyl-6-(phenylmethoxy)naphthalen-1-ol *Trifluoromethanesulfonate* (**8**). *Trifluoromethanesulfonic acid anhydride* (2.4 ml, 14.1 mmol) was added at 0° to a soln. of ketone **7** (2.26 g, 8.3 mmol) and *Proton Sponge*[®] (2.31 g, 10.8 mmol) in CH_2Cl_2 (100 ml). The mixture was warmed to r.t. and stirred for 16 h. The reaction was then quenched with sat. aq. NaHCO_3 soln. and extracted 4 times with CH_2Cl_2 . The combined org. phase was dried (MgSO_4) and evaporated and the crude product purified twice by FC (AcOEt /hexanes 1:4, R_f 0.66): **8** (3.02 g, 90%). Yellow oil. IR (film): 3030, 2940, 2866, 1674, 1411, 1247, 1209, 1142, 997, 877. ^1H -NMR (300 MHz, CDCl_3): 7.40–7.18 (*m*, 5 arom. H); 5.59 (*t*, $J = 4.3$, =CH); 4.57 (*s*, PhCH_2O); 3.47–3.38 (*m*, CH_2OCH); 2.29–2.16 (*m*, $\text{CH}_2\text{CH}=\text{}$); 2.09–2.01 (*m*, $(\text{CH}_2)_2\text{CHC}$); 1.90–1.81 (*m*, CH_2); 1.62–1.26 (*m*, 6 H, CH_2); 1.13 (*s*, Me). ^{13}C -NMR (75 MHz, CDCl_3): 118.47 (*q*, $J = 319$); 156.4; 138.7; 128.4; 127.9; 127.6; 115.5; 77.1; 70.1; 41.8; 38.0; 33.4; 32.1; 27.3; 24.2; 24.1; 17.1. CI-MS: 422 ($[M + \text{NH}_4]^+$), 313 ($[M - \text{C}_7\text{H}_7]^+$). HR-MS: 422.1603 ($\text{C}_{19}\text{H}_{27}\text{F}_3\text{NO}_4\text{S}^+$; calc. 422.1613).

(4*a*R,6*R*,8*a*S)-3,4,4*a*,5,6,7,8,8*a*-Octahydro-8*a*-methyl-6-(phenylmethoxy)naphthalene-1-carboxylic Acid Methyl Ester (**9**). K_2CO_3 (2.07 g, 15 mmol), LiCl (490 mg, 11.3 mmol), and MeOH (6.1 ml, 150 mmol) were added to a soln. of **8** in NMP (80 ml). This mixture was purged with CO, and then dichlorobis(triphenylphosphine)palladium (100 mg, 0.15 mmol) was added. The mixture was then placed under a 200-psi atmosphere of CO at 130° for 24 h in a *Parr* bomb. The bomb was then cooled down to r.t. and the pressure released. After addition of aq. sat. NH_4Cl soln. (200 ml) and brine (200 ml), the mixture was extracted with Et_2O /hexanes 1:1. The org. phase was dried (MgSO_4) and evaporated and the crude product purified by FC (AcOEt /hexanes 1:4; R_f 0.6): **9** (975 mg, 83%). Colorless oil. IR (film): 3028, 2933, 2861, 1711, 1248, 1218, 1106, 1073. ^1H -NMR (300 MHz, CDCl_3): 7.37–7.24 (*m*, 5 arom. H); 6.69 (*t*, $J = 3.7$, =CH); 4.56 (*s*, PhCH_2O); 3.69 (*s*, MeO); 3.42–3.33 (*m*, CH_2OCH); 2.36 (*dt*, $J = 13.2, 3.7$, $(\text{CH}_2)_2\text{CHC}$); 2.25–2.20 (*m*, $\text{CH}_2\text{CH}=\text{}$); 2.00–2.93 (*m*, 1 H, CH_2 ax.); 1.87–1.80 (*m*, 1 H, CH_2 ax.); 1.63–1.32 (*m*, 5 H, CH_2); 1.19 (*s*, Me); 1.09 (*td*, $J = 13.6, 3.9$, 1 H, $\text{PhCH}_2\text{OCHCH}_2$ eq.). ^{13}C -NMR (75 MHz, CDCl_3): 167.7; 140.3; 139.0; 138.5; 128.4; 127.6; 127.4; 77.6; 69.9; 51.2; 41.5; 36.0; 34.2; 33.4; 28.0; 26.3; 24.6; 17.9. EI-MS: 315 ($[M + \text{H}]^+$), 314 (M^+), 283 ($[M - \text{OMe}]^+$), 223 ($[M - \text{C}_7\text{H}_7]^+$). HR-MS: 314.1889 ($\text{C}_{20}\text{H}_{26}\text{O}_3^+$; calc. 314.1882).

(4*a*R,6*R*,8*a*S)-3,4,4*a*,5,6,7,8,8*a*-Octahydro-8*a*-methyl-6-(phenylmethoxy)naphthalene-1-carboxaldehyde (**10**). At -78° , 1*M* Dibal-H in CH_2Cl_2 (6.8 ml, 6.8 mmol) was added dropwise to **9** in CH_2Cl_2 (50 ml). The reaction was monitored by TLC until completion. Then MeOH (15 ml) was added, the mixture warmed to r.t., 1*M*

HCl added, and the mixture extracted with CH_2Cl_2 . The combined org. phase was dried (MgSO_4) and evaporated and the crude product purified by FC (AcOEt/hexanes 1:4; R_f 0.20): corresponding naphthalene-1-methanol (778 mg, 86%). Colorless oil. IR (film): 3403, 3029, 2930, 2861, 1453, 1358, 1090, 1072, 1016, 735, 698. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 7.38–7.22 (*m*, 5 arom. H); 5.56 (*t*, $J = 3.4$, =CH); 4.57 (*s*, PhCH_2O); 4.10 (*q*, CH_2OH); 3.44–3.34 (*m*, CH_2OCH); 2.13–2.09 (*m*, $\text{CH}_2\text{CH=}$); 2.05–1.95 (*m*, $(\text{CH}_2)_2\text{CHC}$); 1.86–1.79 (*m*, CH_2); 1.62–1.35 (*m*, 6 H, OH, CH_2); 1.28 (*dt*, $J = 13.3$, 3.9, 1 H, $\text{PhCH}_2\text{OCHCH}_2$ eq.); 1.04 (*s*, Me). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 145.9; 139.0; 128.4; 127.6; 127.4; 122.6; 77.7; 69.9; 63.5; 41.1; 36.1; 34.4; 33.8; 28.0; 25.5; 25.2; 18.9. EI-MS: 286 (M^+), 268 ($[M - \text{H}_2\text{O}]^+$), 195 ($[M - \text{C}_7\text{H}_7]^+$). HR-MS 286.1938 ($\text{C}_{19}\text{H}_{26}\text{O}_2^+$; calc. 286.1933).

Dess–Martin periodinane (1.49 g, 3.51 mmol) was added at 0° to a soln. of the naphthalene-1-methanol (see above; 670 mg, 2.34 mmol) in CH_2Cl_2 (100 ml). The mixture was then warmed to r.t. and stirred for 45 min. The mixture was diluted with hexanes (100 ml) and filtered through a silica-gel pad, which was eluted with AcOEt/hexanes 3:7. The soln. was evaporated and the residue purified by FC (AcOEt/hexanes 1:4; R_f 0.50): **10** (665 mg, 89%). Colorless oil. IR (film): 3030, 2972, 2933, 2863, 1686, 1455, 1358, 1191, 1105, 1073, 736, 698. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 9.33 (*s*, CHO); 7.37–7.25 (*m*, 5 arom. H); 6.62 (*t*, $J = 3.7$, =CH); 4.57 (*s*, PhCH_2O); 3.44–3.34 (*m*, CH_2OCH); 2.69 (*dt*, $J = 13.5$, 6.3, $(\text{CH}_2)_2\text{CHC}$); 2.43–2.37 (*m*, $\text{CH}_2\text{CH=}$); 2.03–1.96 (*m*, 1 H, CH_2 ax.); 1.89–1.82 (*m*, 1 H, CH_2 ax.); 1.65–1.31 (*m*, 5 H, CH_2); 1.13–1.07 (*m*, 4 H, Me, OCHCH_2 ax.). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 194.2; 152.8; 149.9; 139.0; 128.4; 127.5; 127.4; 77.4; 69.9; 41.4; 35.7; 33.9; 32.6; 27.8; 27.5; 24.4; 17.1. CI-MS: 302 ($[M + \text{NH}_4]^+$), 290 ($[272 + \text{NH}_4]^+$), 285 ($[M + \text{H}]^+$), 273 ($[272 + \text{H}]^+$), 193 ($[M - \text{C}_7\text{H}_7]^+$), 181 ($[272 - \text{C}_7\text{H}_7]^+$). HR-MS 285.1848 ($\text{C}_{19}\text{H}_{25}\text{O}_2^+$ ($[M + \text{H}]^+$) calc. 285.1854).

(4aR,6R,8aS)-3,4,4a,5,6,7,8,8a-Octahydro-8a-methyl- β -oxo-6-(phenylmethoxy)naphthalene-1-propanoic Acid 1,1-Dimethylethyl Ester (**11**). The Reformatsky reagent was prepared as follows: *tert*-butyl bromoacetate (2.6 ml, 17.6 mmol) was added to a suspension of Zn pieces (1.35 g, 20.6 mmol) in Et_2O (60 ml). A crystal of I_2 was added, and the mixture was heated to reflux. When the reaction turned milky, the reflux was continued for further 2 h and then cooled to r.t. The concentration of the organozinc in Et_2O was ca. 0.25M. This zinc enolate of *tert*-butyl acetate soln. (25 ml, 6.22 mmol) was added at 0° to a soln. of **10** (510 mg, 1.8 mmol) in Et_2O (25 ml). The mixture was then warmed to r.t. and stirred for 3 h. The mixture was quenched with sat. aq. NH_4Cl soln. and extracted with Et_2O (3×50 ml). The combined org. phase was dried (MgSO_4) and evaporated and the crude product purified by FC (AcOEt/hexanes 1:4; R_f 0.33): corresponding β -hydroxy ester (718 mg, 87%). Colorless oil. IR (film): 3436, 3062, 2975, 2932, 2863, 1727, 1454, 1366, 1150, 1073, 737, 698. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 7.36–7.24 (*m*, 5 arom. H); 5.70 (*t*, $J = 3.9$, =CH); 4.58–4.52 (*m*, PhCH_2O , CHOH); 3.42–3.35 (*m*, CH_2OCH); 2.87 (*s*, OH); 2.63–2.40 (*m*, $\text{CH}_2\text{COO}t\text{Bu}$); 2.16–1.79 (*m*, 5 H, CH, CH_2); 1.56–1.40 (*m*, 15 H, $t\text{Bu}$, CH_2); 0.97 (*s*, Me). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 172.2; 147.1; 139.0; 128.3; 127.5; 127.4; 123.1; 81.0; 77.6; 69.9; 65.8; 43.3; 41.3; 36.6; 34.7; 33.8; 28.1; 28.0; 25.6; 25.2; 18.8. EI-MS: 344 ($[M - \text{C}_4\text{H}_9]^+$). HR-MS 344.1992 ($\text{C}_{21}\text{H}_{28}\text{O}_4^+$; $[M - \text{C}_4\text{H}_9]^+$; calc. 344.1987).

Dess–Martin periodinane (1.49 g, 3.51 mmol) was added to a 0° soln. of the β -hydroxy ester (see above; 530 mg, 1.33) in CH_2Cl_2 (50 ml). The mixture was warmed to r.t. and stirred for 45 min. The resulting soln. was diluted with hexanes (50 ml) and filtered through silica gel, which was eluted with AcOEt/hexanes 3:7. The soln. was evaporated and the residue purified by FC (AcOEt/hexanes 1:4; R_f 0.47): **11** (486 mg, 92%). Colorless oil. IR (film): 3029, 2976, 2932, 2863, 1731, 1672, 1455, 1366, 1310, 1252, 1154, 1073, 737, 698. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 7.36–7.24 (*m*, 5 arom. H); 6.62 (*t*, $J = 3.9$, =CH); 4.56 (*s*, PhCH_2O); 3.57 (*d*, $J = 15.3$, 1 H, COCH_2CO); 3.47 (*d*, $J = 15.3$, 1 H, COCH_2CO); 3.42–3.32 (*m*, CH_2OCH); 2.47 (*dt*, $J = 13.4$, 3.7, $(\text{CH}_2)_2\text{CHC}$); 2.33–2.27 (*m*, $\text{CH}_2\text{CH=}$); 1.99–1.92 (*m*, 1 H, CH_2 ax.); 1.85–1.79 (*m*, 1 H, CH_2 ax.); 1.65–1.29 (*m*, 14 H, $t\text{Bu}$, CH_2); 1.17 (*s*, Me); 1.02 (*td*, $J = 3.8$, 13.7, 1 H, $\text{PhCH}_2\text{OCHCH}_2$ eq.). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 194.2; 167.4; 148.6; 140.8; 139.0; 128.3; 127.5; 127.4; 81.5; 77.5; 69.9; 48.4; 41.5; 36.6; 34.2; 32.9; 28.0; 27.9; 26.7; 24.3; 17.8. EI-MS: 398 (M^+), 342 ($[M - \text{C}_4\text{H}_8]^+$), 251 ($[M - \text{C}_4\text{H}_8 - \text{C}_7\text{H}_7]^+$). HR-MS 398.2451 ($\text{C}_{25}\text{H}_{34}\text{O}_4^+$; calc. 398.2457).

(4aR,6R,8aS)-3,4,4a,5,6,7,8,8a-Octahydro-8a-methoxy- β -oxo-6-(phenylmethoxy)naphthalene-1-propanoic Acid Prop-2-enyl Ester (=Nazarov Intermediate; **6**). DMAP (6 mg, 0.05 mmol) was added to a soln. of **11** (78 mg, 0.20 mmol) in toluene (4 ml) and allyl alcohol (1 ml). The mixture was refluxed for 16 h and then filtered through silica gel, which was eluted with AcOEt/hexanes 3:7. The soln. was evaporated and the residue purified by FC (AcOEt/hexanes 1:4; R_f 0.36): **6** (61 mg, 82%). Colorless oil. IR (film): 3085, 3029, 2930, 2859, 1742, 1673, 1455, 1358, 1073, 737, 698. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 12.30 (*s*, OH (enol)); 7.36–7.24 (*m*, 5 arom. H); 6.62 (*t*, $J = 3.8$, =CH); 5.97–5.84 (*m*, $\text{CH}_2\text{CH=CH}_2$); 5.36–5.21 (*m*, $\text{CH}_2\text{CH=CH}_2$); 5.09 (*s*, CH=(enol)); 4.62 (*dt*, $J = 5.8$, 1.4, =CHCH $_2\text{O}$); 4.56 (*s*, PhCH_2O); 3.66 (*d*, $J = 2.5$, COCH_2CO); 3.40–3.32 (*m*, CH_2OCH); 2.44 (*dt*, $J = 13.3$, 3.7, $(\text{CH}_2)_2\text{CHC}$); 2.34–2.28 (*m*, $\text{CH}_2\text{CH=}$); 1.99–1.94 (*m*, 1 H, CH_2 ax.); 1.85–1.79 (*m*, 1 H, CH_2 ax.); 1.61–1.20 (*m*, 6 H, CH_2); 1.17 (*s*, Me); 1.05 (*td*, $J = 4.0$, 13.6, 1 H, $\text{PhCH}_2\text{OCHCH}_2$ eq.). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 193.6; 167.7; 148.7; 141.2; 139.0; 131.7; 128.3; 127.6; 127.4; 118.7; 69.9; 65.8; 46.7; 41.5; 36.7;

34.2; 32.9; 29.7; 27.9; 26.7; 24.3; 17.8. EI-MS: 382 (M^+), 291 ($[M - C_7H_7]^+$). HR-MS: 382.2150 ($C_{24}H_{30}O_4^+$; calc. 382.2144).

1-[(4aR,6R,8aS)-3,4,4a,5,6,7,8,8a-Octahydro-6-hydroxy-8a-methylnaphthalen-1-yl]ethanone (13). A 50% aq. H_2SO_4 soln. (15 ml) was added to a soln. of alcohol **12** (2.6 g, 11.5 mmol) in Et_2O (100 ml). The mixture was stirred for 30 min and decanted. The Et_2O phase was dried ($MgSO_4$) and evaporated and the crude product purified by FC (hexanes/AcOEt 6:4; R_f 0.13): corresponding alkoxy ketone (1.84 g, 88%). IR (film): 3391, 2933, 2862, 1705, 1469, 1451, 1364, 1342, 1308, 1273, 1144, 1107, 1052, 1026. 1H -NMR (300 MHz, $CDCl_3$): 3.60–3.50 (*m*, $CHOH$); 2.68–2.56 (*m*, 1 H); 2.22–2.16 (*m*, 1 H); 2.06–1.97 (*m*, 2 H); 1.89–1.84 (*m*, 1 H); 1.79–1.36 (*m*, 9 H); 1.10 (*s*, Me). ^{13}C -NMR (75 MHz, $CDCl_3$): 215.9; 70.3; 47.6; 43.7; 37.4; 36.7; 30.8; 30.7; 27.4; 26.2; 15.7. EI-MS: 182 (M^+). HR-MS: 182.1312 ($C_{11}H_{18}O_2^+$, M^+ ; calc. 182.1307).

Sodium (2 g, 88.4 mmol) was dissolved in NH_3 (l) (200 ml) at -70° . Acetylene was then bubbled through the soln. until the blue color disappeared. The soln. of the alkoxy ketone (see above; 1.61 g, 8.85 mmol) in Et_2O (20 ml) was added slowly to this sodium acetylide soln. Then the NH_3 (l) was evaporated. The resulting soln. was quenched with sat. aq. NH_4Cl soln. and extracted with Et_2O and the extract dried ($MgSO_4$) and evaporated: diol mixture (1.52 g, 83%) that was used without further purification. The diol mixture (1.52 g, 7.35 mmol) was dissolved in formic acid (26 ml), and 2 drops of conc. H_2SO_4 soln. were added. This soln. was stirred at r.t. for 2 h, heated to 90° for 10 min, then cooled to 0° , and quenched with H_2O . The pH was adjusted to 12 with KOH, the soln. extracted with CH_2Cl_2 , the extract dried ($MgSO_4$) and evaporated, and the crude product dissolved in MeOH (40 ml). H_2O (2.6 ml) and K_2CO_3 were added, and this soln. was stirred for 1 h. After completion of formate hydrolysis, this soln. was evaporated, the residue dissolved in CH_2Cl_2 , the CH_2Cl_2 soln. washed with H_2O , dried ($MgSO_4$), and evaporated, and the crude product purified by FC (hexanes/AcOEt 6:4; R_f 0.15): **13** (714 mg, 47%). IR (film): 3368, 2930, 2861, 1665, 1618, 1457, 1422, 1370, 1243, 1064, 1031, 944. 1H -NMR (300 MHz, $CDCl_3$): 6.63 (*t*, $J = 3.9$, $CH=CC=O$); 3.63–3.59 (*m*, $CHOH$); 2.47 (*dt*, $J = 9.6, 3.7$, 1 H); 2.32–2.24 (*m*, 1 H); 2.23 (*s*, $MeC=O$); 1.84–1.81 (*m*, 1 H); 1.80–1.66 (*m*, 2 H); 1.56–1.35 (*m*, 5 H); 1.14 (*s*, $MeC(C)_3$); 0.99 (*td*, $J = 17.4, 3.9, 1$ H). ^{13}C -NMR (75 MHz, $CDCl_3$): 200.1; 149.3; 139.8; 71.0; 41.5; 37.3; 36.2; 33.1; 31.3; 27.9; 26.6; 24.3; 17.8. EI-MS: 208 (M^+), 193 ($[M - CH_3]^+$), 190 ($[M - H_2O]^+$). HR-MS: 208.1457 ($C_{13}H_{20}O_2^+$, M^+ ; calc. 208.1463).

1-[(4aR,6R,8aS)-3,4,4a,5,6,7,8,8a-Octahydro-8a-methyl-6-(phenylmethoxy)naphthalen-1-yl]ethanone (14). Benzyl trichloroethanimidate (1.28 ml, 6.83 mmol) and then trifluoromethanesulfonic acid (152 μ l, 1.72 mmol) were added at 0° to a soln. of **13** (714 mg, 3.43 mmol) in CH_2Cl_2 (100 ml). The soln. was stirred for 1 h, then quenched with sat. $NaHCO_3$ soln. and extracted with CH_2Cl_2 . The extract was dried ($MgSO_4$) and evaporated, and the crude product purified by FC (hexanes/AcOEt 9:1; R_f 0.4): **14** (782 mg, 77%). $[\alpha]_D^{20} = -79.3$ ($c = 1.11$, toluene). IR (film): 2931, 2860, 1668, 1455, 1366, 1355, 1243, 1220, 1108, 1090, 1073, 1226. 1H -NMR (300 MHz, $CDCl_3$): 7.35–7.28 (*m*, 5 arom. H); 6.63 (*t*, $J = 4.0$, $CH_2CH=CCOMe$); 4.56 (*s*, $PhCH_2O$); 3.38–3.31 (*m*, $CHOCH_2Ph$); 2.48 (*dt*, $J = 13.4, 3.7$, CH_2CHCH_2CHOH); 2.32–2.26 (*m*, 2 H); 2.24 (*s*, $MeCO$); 2.00–1.91 (*m*, 1 H); 1.85–1.78 (*m*, 1 H); 1.62–1.23 (*m*, 10 H); 1.16 (*s*, $MeC(C)_3$); 0.95 (*td*, $J = 17.4, 3.9, 1$ H). ^{13}C -NMR (75 MHz, $CDCl_3$): 200.0; 149.3; 139.8; 139.0; 128.3; 127.5; 127.3; 77.5; 69.8; 41.7; 36.5; 34.2; 33.2; 28.0; 27.9; 26.6; 24.5; 17.8. EI-MS: 298 (M^+). HR-MS: 298.1937 ($C_{20}H_{26}O_2^+$, M^+ ; calc. 298.1933).

Nazarov Intermediate **6**. At -78° , 1M LiHMDS in THF (8.34 ml) was added to a soln. of **14** (2.48 g, 8.34 mmol) in THF (100 ml). The soln. was stirred at -78° for 2 h. Then, a soln. of allyl carbonocyanidate (924 mg, 8.34 mmol) in THF (10 ml) was added. The resulting soln. was stirred for 15 min, neutralized with sat. NH_4Cl soln., warmed to r.t., and extracted with Et_2O . The extract was washed with brine, dried ($MgSO_4$), and evaporated and the crude product purified by FC (hexanes/AcOEt 95:5): **6** (1.68 g, 53%) and starting **14** (918 mg, 37%). **6**: $[\alpha]_D^{20} = -19.0$ ($c = 1.00$, $CDCl_3$). IR (film): 2933, 2863, 1742, 1672, 1620, 1495, 1454, 1420, 1358, 1304, 1273, 1197, 1144, 1073, 992, 936. 1H -NMR (300 MHz, $CDCl_3$): 12.13 (*s*, 0.07 H, OH (enol)); 7.36–7.24 (*m*, 5 arom. H); 6.62 (*t*, $J = 3.8$, $HC=CC=O$); 5.97–5.84 (*m*, $CH_2CH=CH_2$); 5.36–5.21 (*m*, $CH_2CH=CH_2$); 4.62 (*dt*, $J = 5.8, 1.4$, $OCH_2CH=CH_2$); 4.56 (*s*, $PhCH_2O$); 3.66 (*d*, $J = 2.5$, $O=CCH_2C=O$); 3.40–3.32 (*m*, $CHOCH_2Ph$); 2.44 (*dt*, $J = 13.3, 3.7$, $CCH(CH_2)_2$); 2.34–0.86 (*m*, 11 H); 1.17 (*s*, Me). ^{13}C -NMR (75 MHz, $CDCl_3$): 193.6; 167.7; 148.7; 141.2; 139.0; 131.7; 128.3; 127.6; 127.4; 118.7; 69.9; 65.8; 46.7; 41.5; 36.7; 34.1; 32.9; 29.7; 27.9; 26.7; 24.3; 17.8. EI-MS: 382 (M^+). HR-MS: 382.2134 ($C_{24}H_{30}O_4^+$, M^+ ; calc. 382.2144).

4-Methoxy-3,3-dimethyl-6-oxocyclohexa-1,4-diene-1-carboxaldehyde (5). MeOH (818 μ l, 20.2 mmol) was added to a suspension of NaH (60% in oil; 826 mg, 20.2 mmol) in benzene (100 ml). This NaOMe soln. was cooled to 0° , then a soln. of **15** (2.83 g, 18.4 mmol) in THF (50 ml) was added slowly. The soln. was stirred for 10 min, and ethyl formate (10.4 ml, 128.8 mmol) was added slowly. The mixture was warmed to r.t. and stirred for 12 h. H_2O (100 ml) was then added, and the org. phase was extracted once with an aq. 1M NaOH. The aq. phase was acidified to pH 6 at 0° and extracted with AcOEt, the extract dried ($MgSO_4$) and evaporated, and the

crude product purified by FC (hexanes/AcOEt 2 : 8): corresponding aldehyde (3.15 g, 94%). IR (film): 2967, 2931, 2894, 2844, 1723, 1642, 1598, 1567, 1471, 1436, 1418, 1388, 1364, 1237, 1199, 1176, 1152, 1131, 1019, 993, 971, 956, 868, 838, 825, 679, 584, 559. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 13.86 (s, OH); 7.17 (s, CHOH); 5.22 (s, $\text{O}=\text{CCH}=\text{C}$); 3.70 (s, MeO); 2.26 (s, CH_2); 1.11 (s, 6 H, 2 Me). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 192.4; 183.1; 161.4; 106.0; 99.0; 56.2; 38.5; 36.9; 25.4 (2C). EI-MS: 182 (M^+). HR-MS 182.0947 ($\text{C}_{10}\text{H}_{14}\text{O}_3^+$, M^+ ; calc. 182.0943).

At 0°, pyridine (1.67 ml, 20.2 mmol) was added to a soln. of PhSeCl (3.68 g, 19.3 mmol) in CH_2Cl_2 (100 ml) and the resulting soln. was stirred for 10 min. A soln. of the aldehyde (see above; 3.35 g, 18.4 mmol) in CH_2Cl_2 (100 ml) was added dropwise to the PhSeCl soln. The mixture was then warmed to r.t., stirred for 2 h, quenched with 1M aq. HCl, and extracted with CH_2Cl_2 . The extract was dried (MgSO_4) and evaporated and the crude product was dissolved in CH_2Cl_2 (50 ml). To the CH_2Cl_2 soln., 30% H_2O_2 soln. (10 ml) was added, and the mixture was stirred for 15 min at r.t. H_2O (50 ml) was then added, the resulting soln. extracted with CH_2Cl_2 , the extract washed with brine, dried (Na_2SO_4), decanted, and evaporated and the residue triturated in Et_2O /hexanes 1 : 1 **5** (3.24 g, 99%).

Alternatively, DDQ (4.69 g, 21 mmol) was added to a soln. of the aldehyde (see above; 3.76 g, 21 mmol) in dioxane (70 ml), and the mixture was stirred for 5 min. Then pentane (210 ml) was added and the solid filtered and dried under vacuum. The crude product was then triturated in Et_2O /hexanes 1 : 1: **5** (3.76 g, 99%). IR (film): 3020, 2931, 2879, 1702, 1648, 1620, 1584, 1464, 1410, 1386, 1360, 1221, 1174, 1102, 986, 934, 844, 727, 683, 629, 509. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 10.21 (s, $\text{CH}=\text{O}$); 7.31 (s, $\text{CH}=\text{CC}=\text{O}$); 5.56 (s, $\text{CH}=\text{COMe}$); 3.77 (s, MeO); 1.34 (s, 6 H, 2 Me). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 190.3; 186.9; 180.0; 157.4; 130.5; 101.0; 56.1; 40.2; 25.1 (2C). EI-MS: 180 (M^+), 181 ($[M+H]^+$), 165 ($[M-\text{CH}_3]^+$). HR-MS: 180.0782 ($\text{C}_{10}\text{H}_{12}\text{O}_3^+$, M^+ ; calc. 180.0786, 165.0554 ($\text{C}_9\text{H}_9\text{O}_3^+$, $[M-\text{Me}]^+$; calc. 165.0552).

(4aR,4bS,6aR,8R,10aR,10bR,12aR)-1,4,4a,4b,5,6,7,8,9,10,10a,10b,11,12,12a-Hexadecahydro-2-methoxy-1,1,10a-trimethyl-4,11-dioxo-8-(phenylmethoxy)chrysene-4a-carboxaldehyde (**4**). A soln. of **5** (75 mg, 416 μmol) in AcOEt (5 ml) was added to a soln. of **6** (159 mg, 416 μmol) and Cs_2CO_3 (136 mg, 416 μmol) in AcOEt (5 ml). The mixture was then stirred at r.t. for 96 h. The resulting soln. was filtered through silica gel, which was washed with AcOEt. The soln. was evaporated and the crude product dissolved in THF (30 ml). Morpholine (110 μl , 1.246 mmol) and a catalytic amount of $[\text{Pd}(\text{PPh}_3)_4]$ were added. The mixture was stirred at r.t. for 1 h and then filtered through silica gel, which was washed with AcOEt. The soln. was evaporated and the crude product purified by FC (toluene/AcOEt 9 : 1): **4** (139 mg, 70%). IR (film): 2934, 2862, 1709, 1642, 1606, 1455, 1354, 1222, 1203, 1135, 1094, 1027, 989, 912, 847, 733, 699. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 9.86 (d, $J = 1.6$, $\text{CH}=\text{O}$); 7.35–7.24 (m, 5 arom. H); 5.34 (s, $\text{MeOC}=\text{CH}$); 4.54 (s, PhCH_2O); 3.73 (s, $\text{MeOC}=\text{C}$); 3.38–3.28 (m, $(\text{CH}_2)_2\text{CHOCH}_2\text{Ph}$); 2.71–2.64 (m, 2 H); 2.57–2.34 (m, 4 H); 1.93–0.85 (m, 10 H); 1.23 (s, Me); 1.18 (s, Me); 0.94 (s, Me). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 209.4; 201.3; 197.1; 181.7; 139.1; 128.3; 127.6; 127.4; 99.5; 77.2; 69.8; 61.6; 58.7; 56.3; 44.2; 41.7; 40.9; 39.6; 36.7; 36.5; 34.4; 29.7; 28.7; 28.0; 27.9; 23.9; 11.2; 11.1. EI-MS: 478 (M^+). HR-MS: 180.0782 ($\text{C}_{10}\text{H}_{12}\text{O}_3^+$, M^+ ; calc. 180.0786), 478.2708 ($\text{C}_{30}\text{H}_{38}\text{O}_3^+$, $[M-\text{Me}]^+$; calc. 478.2719).

(4aR,4bS,6aR,8R,10aR,10bR,12aR)-4b,5,6,6a,7,8,9,10,10a,10b,12,12a-Dodecahydro-4a-(hydroxymethyl)-2-methoxy-1,1,10a-trimethyl-8-(phenylmethoxy)chrysene-4,11(1H,4aH)-dione (**16**). A soln. of **4** (23 mg, 48 μmol) in THF (3 ml) was added at 0° to a soln. of NaBH_4 (1.8 mg, 48 μmol) in MeOH (1.5 ml). The mixture was stirred at 0° for 1 h, then concentrated, diluted with AcOEt, washed with H_2O , dried (MgSO_4), and evaporated. The crude product was then purified by FC (hexanes/AcOEt 3 : 7): **16** (23 mg, 99%). $[\alpha]_D^{20} = -29.8$ ($c = 0.91$, toluene). IR (film): 3414, 2931, 2852, 1704, 1640, 1614, 1454, 1360, 1218, 1069, 733. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 7.39–7.23 (m, 5 arom. H); 5.33 (s, $\text{MeOC}=\text{CHC}=\text{O}$); 4.60 (d, $J = 11.5$, 1 H, CH_2OH); 4.53 (s, PhCH_2O); 3.73 (d, $J = 11.5$, 1 H, CH_2OH); 3.71 (s, MeO); 3.36–3.26 (m, CHOCH_2Ph); 2.80–0.71 (m, 17 H); 1.22 (s, Me); 1.20 (s, Me); 0.96 (s, Me). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 209.9; 201.4; 181.1; 139.0; 128.3; 127.5; 127.4; 99.9; 69.8; 60.4; 59.3; 56.0; 53.4; 44.8; 41.9; 40.8; 39.6; 39.2; 36.9; 36.6; 34.4; 30.0; 28.7; 28.3; 28.1; 27.9; 24.4; 11.3. EI-MS: 480 (M^+). HR-MS: 480.2886 ($\text{C}_{30}\text{H}_{40}\text{O}_3^+$, M^+ ; calc. 480.2876).

(4aR,4bS,6aR,8R,10aR,10bR,12aR)-4b,5,6,6a,7,8,9,10,10a,10b,12,12a-Dodecahydro-2-methoxy-1,1,4a,10a-tetramethyl-8-(phenylmethoxy)chrysene-4-11(1H,4aH)-dione (**17**). A soln. of **16** (250 mg, 548 μmol), pyridine (177 μl , 2.19 mmol), phenyl carbonochloridothioate (303 μl , 2.19 mmol), and a catalytic amount of DMAP in CH_2Cl_2 (25 ml) was stirred for 16 h. The mixture was then evaporated and the crude product purified by FC (hexanes/AcOEt 8 : 2): corresponding carbonothioate (268 mg, 80%). $^1\text{H-NMR}$ (300 MHz, CDCl_3): 7.41–7.07 (m, 10 arom. H); 5.41 (d, $J = 10.7$, 1 H, $\text{CH}_2\text{OC}(=\text{S})\text{OPh}$); 5.37 (s, $\text{MeOC}=\text{CH}$); 4.80 (d, $J = 10.7$, 1 H, $\text{CH}_2\text{OC}(=\text{S})\text{OPh}$); 4.54 (s, PhCH_2O); 3.72 (s, $\text{MeOC}=\text{CH}$); 3.36–3.29 (m, CHOCH_2Ph); 2.80–0.76 (m, 16 H); 1.22 (s, Me); 1.20 (s, Me); 0.97 (s, Me). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 209.1; 196.6; 194.6; 180.3; 160.1; 153.2; 138.9; 129.5; 128.3; 127.6; 127.4; 126.6; 121.8; 99.7; 71.6; 69.8; 59.6; 56.1; 51.1; 44.7; 42.6; 40.8; 39.8; 39.4; 37.1;

36.5; 34.3; 29.7; 28.4; 28.1; 27.9; 24.4; 11.3. EI-MS: 617 ($[M+H]^+$). HR-MS: 617.2939 ($C_{37}H_{44}O_6S^+$, $[M+H]^+$; calc. 617.2937).

A catalytic amount of AIBN and freshly distilled Bu_3SnH (98 μ l, 368 μ mol) were added to a soln. of the carbonothioate (see above; 151 mg, 245 μ mol) in toluene (10 ml). The mixture was degassed and then refluxed for 2 h. The mixture was evaporated and the crude product purified by FC (hexanes/AcOEt 8:2): **17** (114 mg, 99%). $[\alpha]_D^{20} = -32.5$ ($c = 1.00$, toluene). IR (film): 2925, 2849, 1704, 1643, 1616, 1455, 1355, 1220, 1196, 1132, 1091, 1067, 1026, 985, 850. 1H -NMR (300 MHz, $CDCl_3$): 7.33–7.22 (*m*, 5 arom. H); 5.29 (*s*, $MeOC=CHC=O$); 4.54 (*s*, $PhCH_2O$); 3.69 (*s*, MeO); 3.37–3.27 (*m*, $CHOCH_2Ph$); 2.77 (*dt*, $J = 13.5, 3.5$, $CCH(CH_2)_2$); 2.67–2.52 (*m*, 2 H); 2.29 (*td*, $J = 11.7, 3.6, 1$ H); 2.11 (*dd*, $J = 6.3, 2.7, 1$ H); 1.93–0.76 (*m*, 11 H); 1.38 (*s*, Me); 1.17 (*s*, Me); 1.16 (*s*, Me); 0.97 (*s*, Me). 1H -NMR (300 MHz, C_6D_6 ; triterpene numbering): 7.65–7.14 (*m*, 5 arom. H); 5.36 (*s*, $MeOC=CHC=O$); 4.55 (*s*, $PhCH_2O$); 3.35–3.24 (*m*, $CHOCH_2Ph$); 3.19 (*dt*, $J = 13.4, 3.7$, $CCH(CH_2)_2$); 2.96 (*s*, MeO); 2.49 (*d*, $J = 15.6, 1$ H, $CH_2(6)C=O$); 2.41 (*td*, $J = 12.2, 3.8$, $CH_2CH(9)CHC=O$); 2.25 (*dd*, $J = 15.6, 7.1, 1$ H, $CH_2(6)C=O$); 2.06–0.70 (*m*, 11 H); 1.75 (*d*, $J = 12.2$, $CHCH(8)C=O$); 1.42–0.98 (*m*, 3 H); 1.30 (*s*, Me); 1.09 (*s*, Me); 1.01 (*s*, $Me-C(10)$). ^{13}C -NMR (75 MHz, $CDCl_3$): 210.3; 201.2; 179.7; 139.0; 128.4; 127.5; 127.4; 127.3; 99.2; 69.7; 59.2; 55.9; 50.6; 48.3; 44.8; 41.1; 39.9; 39.7; 36.6; 34.4; 28.7; 28.6; 27.9; 26.8; 17.5; 13.6; 11.5. EI-MS: 464 (M^+). HR-MS: 464.2916 ($C_{30}H_{40}O_4^+$, M^+ ; calc. 464.2926).

(4aR,4bS,6aR,8R,10aR,10bR)-4b,5,6,6a,7,8,9,10,10a,10b-Decahydro-2-methoxy-1,1,4a,10a-tetramethyl-8-(phenylmethoxy)chrysene-4,11(1H,4aH)-dione (**3**). At 0°, 1M LiHMDS (1.51 ml) was added to a soln. of **17** (140 mg, 302 μ mol) in CH_2Cl_2 (10 ml). The soln. was stirred at 0° for 5 min, then $PhSeCl$ (290 mg, 1.51 mmol) was added. After 30 min, the mixture was quenched with sat. aq. NH_4Cl soln., warmed to r.t., and extracted with CH_2Cl_2 . The extract was dried (Na_2SO_4) and decanted. A 30% aq. H_2O_2 soln. (500 μ l) was then added to the org. soln., and the mixture was stirred for 10 min and washed with H_2O . The org. phase was dried (Na_2SO_4), decanted, and evaporated and the crude product purified by FC (hexanes/AcOEt 8:2): **3** (139 mg, 99%). IR (film): 2982, 2929, 2861, 1664, 1612, 1452, 1350, 1201, 1148, 1084, 990, 754. 1H -NMR (300 MHz, $CDCl_3$): 7.35–7.21 (*m*, 5 arom. H); 5.99 (*s*, $(C)_3C=CHC=O$); 5.30 (*s*, $MeOC=CHC=O$); 4.55 (*s*, $PhCH_2O$); 3.73 (*s*, MeO); 3.40–3.31 (*m*, $CHOCH_2Ph$); 2.89 (*dt*, $J = 3.6, 3.5$, $CCH(CH_2)_2$); 2.43–0.96 (*m*, 11 H); 1.42 (*s*, Me); 1.38 (*s*, 2 Me); 0.88 (*s*, Me). 1H -NMR (300 MHz, C_6D_6 ; triterpene numbering): 7.65–7.15 (*m*, 5 arom. H); 6.15 (*s*, $C(5)=CHC=O$); 5.23 (*s*, $MeOC=CHC=O$); 4.56 (*s*, $PhCH_2O$); 3.49 (*dt*, $J = 13.6, 3.8$, $CCH(CH_2)_2$); 3.42–3.89 (*m*, $CHOCH_2Ph$); 2.92 (*s*, MeO); 2.74–2.56 (*m*, 3 H); 2.20–0.82 (*m*, 8 H); 1.95 (*d*, $J = 12.6, 1$ H); 1.35 (*s*, Me); 1.21 (*s*, Me); 1.15 (*s*, Me); 1.03 (*s*, Me). ^{13}C -NMR (75 MHz, $CDCl_3$): 200.7, 199.3, 176.7, 167.0, 139.1, 128.4, 128.3, 127.5, 127.3, 126.3, 99.2, 69.7, 56.3, 55.9, 50.0, 45.3, 41.9, 40.9, 37.9, 37.5, 34.7, 30.0, 28.8, 28.4, 28.1, 25.7, 21.1, 12.3. EI-MS: 462 (M^+). HR-MS: 462.2779 ($C_{30}H_{38}O_4^+$, M^+ ; calc. 462.2770).

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