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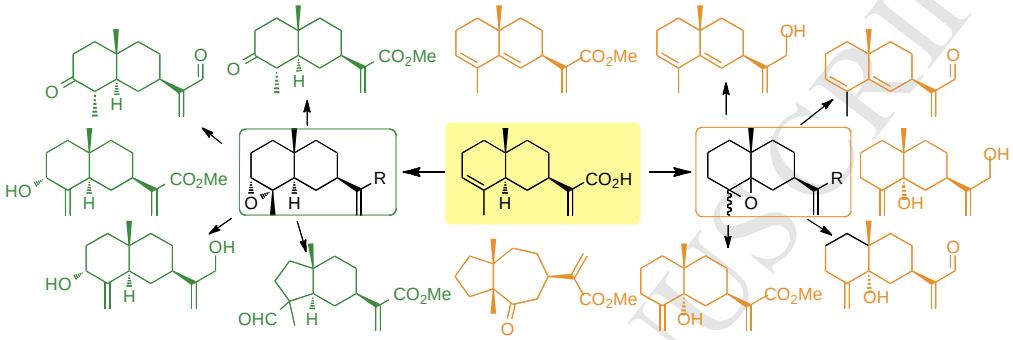

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Acid-promoted opening of 4,5- and 3,4-epoxy eudesmane scaffolds from α-isocostic acid

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ABSTRACT

The acid-catalyzed rearrangement of epoxide **3a** and **8a** derived from sesquiterpernic isocostic acid (**1**), the main component of *Dittrichia viscosa*, was studied using Lewis and Brönsted acids. Several new compounds were obtained with different selectivities depending on the catalyst used. These compounds were fully characterized by spectroscopic methods, and mechanistic explanations for their formation are proposed.

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1. Introduction

Eudesmane derivatives are widespread in the plant kingdom.[1] Among them, eudesmane acids have attracted considerable attention due to their wide spectrum of biological properties: for example, α-isocostic acid **1** (Figure 1) is the first natural product[2] exhibiting antifungal and antibacterial properties;[3] eudesmane acid derivatives feature antipyretic and anti-inflammatory activity[4] and hydrocostic acid is toxic for *Artemisia Salina* and has antifeedant activity against *Spodopetra Littoralis*.[5]

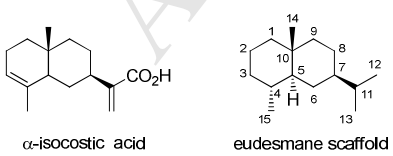


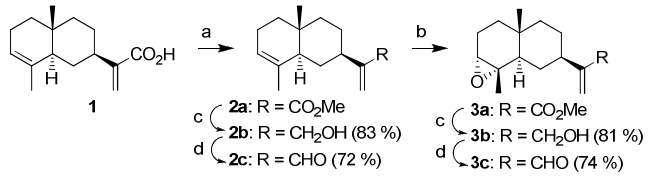
Fig. 1

Continuing with a research project based on the support of Moroccan plant resources,[6] we report herein the use of α-isocostic acid **1** extracted in enantiomerically pure form[7] from *Dittrichia viscosa* (L.) W. Greuter as a convenient starting material for the stereoselective synthesis of eudesmane derivatives.[6b,8] *Dittrichia viscosa* (L.) W. Greuter[9] is a tough plant that is widespread in the Mediterranean region. Considered as an invasive species and particularly abundant in wasteland areas, this perennial plant proved to be a rich source of sesquiterpenes with eudesmane scaffolds. It could accordingly be used as a renewable source of products. In view of the high biological potential of the eudesmane skeleton, we therefore envisaged synthesizing various analogues of α-isocostic acid and enlarging the library to eudesmanols and eudesmane aldehydes since they are also widely represented in nature[1,10] and can trigger other chemical transformations. We focused on epoxidation as a way to introduce diversity since these epoxides are prone to react with a large number of reagents.[11,12] Although the acid-catalyzed rearrangement of epoxides has been reported with $BF_3.Et_2O$ on a 4,5- and 3,4-epoxy eudesmane scaffold,[13] no comparative studies using different Lewis and Brönsted acids have been so far carried out. Prompted by this absence of precedents, we disclose herein the formation of various eudesmane derivatives via epoxidic intermediates.

2. Results and discussion

First the α-isocostic acid, extracted from *Dittrichia viscosa*, was esterified to facilitate its further manipulation (scheme 1). The ester function was straightforwardly reduced in aldehyde and alcohol to synthetize **2b**[14] and **2c**. Then **2a** in presence of *m*-chloroperbenzoic acid gave the expected product **3a** in 70 % yield as a unique diastereoisomer. The presence of the unsaturated ester was confirmed by IR, ^{1}H and ^{13}C NMR.

Unfortunately, the NOESY NMR proved unable to determine the relative configuration of the epoxide. However the broad singlet signal of H-3 at δ2.86 in ^{1}H NMR corroborates a pseudo-equatorial position of this proton. Furthermore, the attack of the epoxidating agent from the less sterically congested side of the double bond opposite to the C-7 unsaturated ester seemed to be the most expected. Finally, this hypothesis was confirmed by comparing our experimental data with the literature.[2c] Compound **3a** was next reduced in aldehyde and alcohol (**3b** and **3c**).



Scheme 1. Reagents and conditions: (a) $TMSCHN_2$, PhMe:MeOH (8:2), 0 °C, 3 h, 75 %; (b) *m*CPBA, DCM, rt, 3 h, 70 %; (c) DiBALH, dry PhMe, -20 °C, 2 h; (d) PDC, DCM, rt, 4 h.

Various acidic conditions were tested on **3a** to examine the reactivity of the epoxide (Table 1). We were pleased to observe that each condition selectively opened the epoxide without degradation giving access to original interesting bicyclic compounds. The reactions were performed at room temperature for 30 min in dichloromethane.

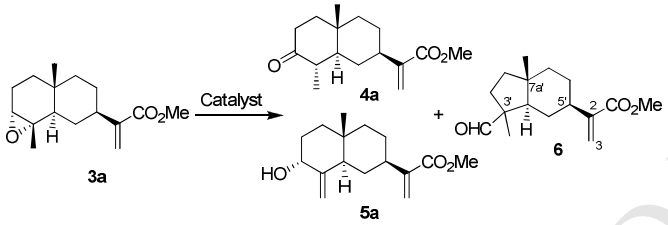
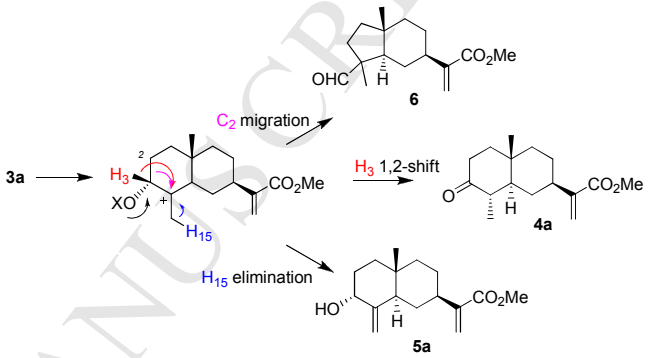


Table 1. Reaction of **3a** with different acids in CH_2Cl_2, at room temperature for 30 min.

Entry	Catalyst	**4a**	**5a**	**6**
1	$BF_3.Et_2O$	70 %	-	-
2	$InCl_3$	71 %	-	3 %
3	$ZnBr_2$	48 %	38 %	-
4	$Bi(OTf)_3$	-	56 %	35 %
5	PTSA	-	72 %	-
6	TFA	-	52 %	-
7	TfOH	63 %	-	-

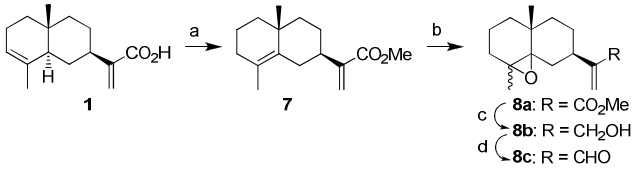
The ketone **4a** was formed selectively with $BF_3.Et_2O$ in 70 % yield. ^{13}C NMR confirmed the presence of the ketone with a quaternary signal at δ 213.2. The formation of **4a** can be explained in terms of a 1,2-shift of the proton from C-3 to C-4 in the carbocation that results after the acid-promoted cleavage of the epoxide (Scheme 2). The migration of H-3 is concomitant with the formation of the ketone. Satisfactorily, we noticed that only one diastereoisomer was obtained. The exact configuration was verified by an X-ray diffraction analysis of a single crystal of **4a**.[15] The same reactivity was observed with $InCl_3$. When $ZnBr_2$ was tested, **4a** was the major product isolated. However a new compound **5a** was formed. The appearance of an additional double bond signal in ^{1}H NMR (δ4.48 and 4.86) and 13C NMR (δ112.9 and 152.0) strongly corroborates the elimination of H-15 to stabilize the intermediate carbocation formed after the opening of the epoxide moiety. Furthermore, DEPT analysis confirmed the exocyclic position of the unsaturation. The axial position of the alcohol is highly probable considering the broad singlet signal of H-3 at δ 4.25 in ^{1}H NMR, which could corroborate an equatorial position of H-3. Then $Bi(OTf)_3$ was tested. Along with **5a**, which was the major product isolated, the aldehyde **6** was obtained in 35 % yield (entry 4). The aldehyde function was confirmed by ^{1}H and ^{13}C NMR with its characteristic signals at δ 9.36 and 203.1 respectively. Next, the skeleton of **6** was fully elucidated by the shielding effect observed for C-4 (δ 51.8 vs. 58.4 ppm) following the reduced electron withdrawing effect on C-4 of the aldehyde vs the oxiran. A carbocation 1,2-rearrangement reaction explained the ring contraction in which C-2 migrated to create a new bond with C-4. Traces of **6** were also observed by using $InCl_3$ as catalyst.



Scheme 2. Proposed mechanism for the formation of **4a**, **5a**, and **6**.

To compare the activities and selectivities, Brönsted acids were next examined. The unsaturated alcohol **5a** was mainly obtained with p-toluenesulfonic acid (PTSA) and trifluoroacetic acid (TFA). However, with a stronger acid such as triflic acid (TfOH), **4a** was synthesized as a single product (entry 7). No loss of reactivity was observed with Brönsted acids since the reaction was completed after 30 min at room temperature.

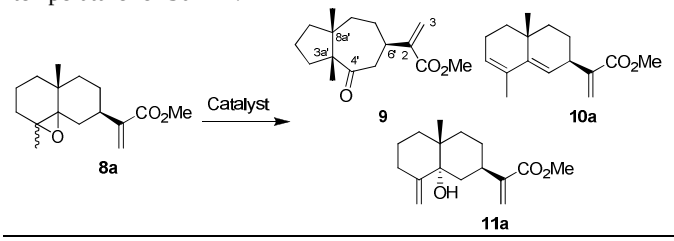
Then the same approach was tested on the 4,5-epoxy eudesmane scaffold (Scheme 3). Unfortunately, this time the epoxidation step gave access to a mixture of two diastereoisomers α:β in 4:3 proportions. Each isomer was clearly identified thanks to ^{1}H NMR comparison with the literature data.[16] King *et al.* described the (4α,5α) epoxide with H-7 at δ 2.54 whereas for the (4β,5β) epoxide H-7 appeared at δ 2.79. These two signals were indubitably present in our experimental data. The reaction was attempted at a lower temperature (0 °C and -78 °C) and with sodium acetate[12a] but except for a longer reaction time to obtain completion, the selectivity observed at room temperature remained unchanged.



Scheme 3. Reagents and conditions: (a) H_2SO_4, MeOH, 24 h, 85 %; (b) *m*CPBA, DCM, rt, 3 h, 70 %; (c) DiBALH, dry PhMe, -20 °C, 2 h, 82 %; (d) PDC, DCM, rt, 4 h ,75 %.

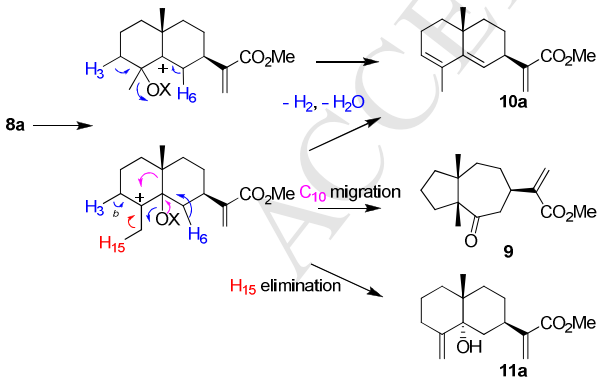
Thus, the reactivity of **8a** towards different acids to promote ring opening was studied. Its treatment with $BF_3.Et_2O$ in DCM at room temperature afforded the ketone **9** in 76% yield (Table 2).

Table 2. Reaction of **8a** with different acids in CH_2Cl_2, at room temperature for 30 min.



Entry	Catalyst	9	10a	11a
1	$BF_3.Et_2O$	76 %	-	-
2	$InCl_3$	47 %	47 %	
3	$ZnBr_2$	25 %	42 %	
4	$Bi(OTf)_3$	50 %	48 %	-
5	TfOH	46 %	43 %	
6	PTSA	-	38 %	60 %
7	TFA		36 %	28 %

It was fully characterized by NMR, IR and MS spectrometric analysis. The HRMS of **9** exhibited its $[M+H]^+$ at m/z 265.1801 corresponding to the correct molecular formula $C_{16}H_{25}O_3$. The IR spectrum showed the typical band for an α,β-conjugated ester (1725, 1620 cm^{-1}) and a band at 1710 cm^{-1}, which suggested the presence of a ketone embedded in a medium sized ring. The ^{13}C NMR spectrum confirmed the presence of these functionalities showing the corresponding signals at δ 214.8 (C-4'), 167.0 (C-1), 144.8 (C-2) and 123.9 (C-3). The stabilized carbocation intermediate went through a 1,2-rearrangement reaction, which explains the ring expansion. C-10 migrated to create a new bond with C-4 (Scheme 4). The 5,7-fused ring **9** was obtained as a single diastereoisomer. The *cis* ring junction was determined by X-ray diffraction analysis.[17] The methyl groups rigidified the bicyclic skeleton and induced a clear preference for *cis* fusion.[18] Then, the reaction of epoxide **8a** with $InCl_3$, $ZnBr_2$ and $Bi(OTf)_3$ afforded a mixture of the ketone **9** and triene **10a** in approximately a 1:1 ratio and up to 90% overall yield except for $ZnBr_2$ where a lower yield was noticed. The structure of the conjugated diene **10a** was established on the basis of its ^1H, ^{13}C NMR, and mass spectrometry.[19]

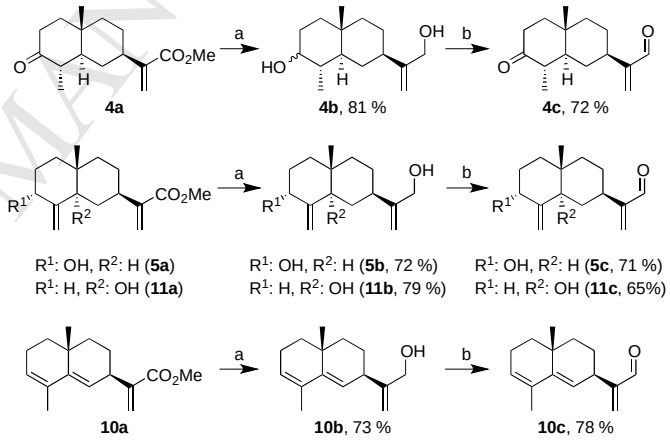


Scheme 4. Proposed mechanism for the formation of **9**, **10**, and **11**.

Two signals corresponding to olefinic protons appeared at δ 5.37 (H-6) and 5.54 (H-3). DEPT analysis underlined the presence of two tertiary carbons at δ 125.2 and 122.2 (C-3 and C-6 respectively) and two quaternary carbons indicating the existence of two trisubstituted double bonds. The new quaternary bridgehead carbon C-5 was assigned to a signal at δ 143.4 while C-4 appeared at δ 131.4. **10a** can be formed by the double elimination of dihydrogen and water from either C-4 or C-5 carbocation that results from the epoxide ring opening. As previously, TfOH exhibited a Lewis acid behavior type giving access to a separable mixture of **9** and **10a** (entry 5).

Finally when a catalytic amount of PTSA or TFA was used, the alcohol **11a** was isolated along with **10a**. The ^1H and ^{13}C NMR spectra of **11a** were identical to those reported in the literature.[20] The structure assigned to the eudesma methyl carboxylate **11a** and its absolute configuration were confirmed by X-ray diffraction analysis of a single crystal of **11a**.[21] A plausible mechanism is thought to involve the elimination of H-15 to form **11a**. In our case, only the α-OH isomer was isolated. We next postulated that **11a** might be an intermediate for the synthesis of **10a**. However when **11a** was left for a prolonged time in acidic conditions only degradation was observed making unlikely that **10a** arises from **11a**, its formation should come from a different epoxide diastereoisomer.

In order to broaden the scope of substrates, **4a**, **5a**, **10a** and **11a** were subjected to a reduction and mild oxidation sequence to synthesize the aldehyde and alcohol analogues (Scheme 5). With four new eudesmane derivatives in hand, their modifications in aldehydes and alcohols were attempted and gave successfully access to seven active enantiopure products, except for **4b**, which was isolated as an equimolar ratio of diastereoisomers.



Scheme 5 Reagents and conditions: (a) DiBALH, dry PhMe, -20 °C, 2 h; (b) PDC, DCM, rt, 4 h.

3. Conclusion

Finally, the acid-promoted epoxide opening of **3a** and **8a** derived from natural extracts of *Dittrichia viscosa* (L.) W. Greuter gave several interesting new products, which were successfully turned into alcohols and aldehydes to broaden the scope of structural diversities. The selectivity of this rearrangement was controlled by the nature of the catalyst and gave access to new chiral eudesmane derivatives. In general, the opening of the eudesmanic epoxide derivative with Lewis acid led to the formation of ketone by C-C breaking and hydroxyl oxidation whereas the use of Brönsted acid funneled the rearrangement toward a mixture of diene and unsaturated alcohols except for TfOH whose behavior was close to $BF_3.Et_2O$. In summary, 4,5- and 3,4-epoxy eudesmane scaffolds appeared to be an interesting source of new chiral intermediates. The salient features of their use are their facile formation from α-isocostic acid, which is readily available from the plant kingdom, and the variety of the products synthesized in a single step.

4. Experimental section

4.1 General remarks and methods

All reagents were purchased from commercial suppliers and were used without further purification The reactions were monitored by thin-layer chromatography (TLC) analysis using silica gel (60 F254) plates. Compounds were visualized by UV irradiation. Flash column chromatography was performed on silica gel 60 (230-400 mesh, 0.040-0.063 mm). Melting points (mp [°C]) were taken on samples in open capillary tubes and are uncorrected. 1H and 13C NMR spectra were recorded on a Bruker DPX 250 (13C, 62.9 MHz), Bruker avance II 250.13 (13C, 63 MHz), Bruker avance 400.13 (13C, 101MHz), or on a Bruker avance III HD nanobay 400.13 (13C, 101 MHz). Chemical shifts are given in parts per million from tetramethylsilane (TMS) as internal standard. The following abbreviations are used for the proton spectra multiplicities: b : broad, s: singlet, d: doublet, t: triplet, q: quartet, p: pentuplet, m: multiplet. Coupling constants (*J*) are reported in hertz (Hz). Multiplicities were determined by the DEPT 135 sequence. Attributions of protons and carbons were made with the help of HSQC and HMBC 2D NMRs. Eudesmane numbering of carbons was used instead of the IUPAC numbering. High-resolution mass spectra (HRMS (ESI)) were performed on a Maxis Bruker 4G by the "Federation de Recherche" ICOA/CBM (FR2708) platform.

5. Experimental data

General procedure for acid-promoted ring opening of epoxide

The epoxide (1 mmol) was diluted in CH_2Cl_2 (10 mL) and stirred at room temperature. Brönsted or Lewis acid (5 mol %) was added to the solution and the reaction mixture was stirred at room temperature for 30 min. After completion of the reaction, the reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with aqueous saturated solutions of $NaHCO_3$ (10 mL) and NaCl (10 mL). The organic layer was dried with $MgSO_4$, after filtration and concentration under reduced pressure the product was purified by flash chromatography on silica gel.

General procedure of DibAlH reduction

Under argon atmosphere at - 20°C, DiBAlH (1M in cyclohexane, 2.4 mL) was added to a solution of ester (1 mmol) in dry toluene (10 mL). After 2 hours, water (5mL) was added to the mixture, and the reaction was allowed to warm up to room temperature and left for 30 min. The mixture was then filtered through celite; Et_2O was used to rince the celite. The resulting filtrate was concentrated under reduced pressure providing a crude product, which was purified by flash chromatography over silica gel.

General procedure of PDC oxidation

Pyridinium dichromate (PDC) (1.1 mmol) was added over a solution of alcohol (1 mmol) in CH_2Cl_2 (10 mL). The resulting suspension was stirred at room temperature. After completion of the reaction, the mixture was filtered through celite. The filtrate was concentrated under reduced pressure. The crude residue was purified by flash chromatography over silica gel to provide the corresponding aldehyde.

5.1. α-isocostic acid (1).[2a]

$[\alpha]_D^{20}$ +10.4 (*c* 1.0, $CHCl_3$) lit $[\alpha]_D^{20}$ +8 (*c* 0.24, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$, 25°C) δ= 0.82 (s, 3H, H-14), 1.17-1.22 (q, 1H, *J* = 12.5 Hz, H-6β), 1.27 (dt, 1H, *J* = 4.1, 11.4 Hz, H-9α), 1.32-1.41 (m, 2H, H-8a, H-9β), 1.45 (t, 1H, *J* = 3.4, 6.2 Hz, H-1β), 1.50-1.68 (m, 2H, H-1α, H-8β), 1.61 (sa, 3H, H-15), 1.84-1.89 (da, 1H, *J* = 12.5 Hz, H-6α), 1.93-2.04 (m, 2H, 2H-2), 2.06-2.18 (m, 1H, H-5α), 2.53 (tt, 1H, *J* = 3.4, 11.8 Hz, H-7α), 5.31 (sa, 1H, H-3), 5.70 (sa, 1H, H-13α), 6.32 (sa, 1H, H-13β) ppm. ^{13}C NMR (250 MHz, $CDCl_3$, 25°C) δ = 16.1 (C-14), 21.6 (C-15), 23.4 (C-2), 27.9 (C-8), 29.8 (C-6), 32.7 (C-10), 38.2 (C-1), 40.6 (C-9), 40.8 (C-7), 47.3 (C-5), 121.5 (C-3), 125.6 (C-13), 135.2 C-4), 145.7 (C-11), 173.3 (C-12).

5.2. Methyl 2-[(2*R*,4a*R*,8a*R*)-4a,8-dimethyl-1,2,3,4,4a,5,6,8a-octahydronaphthalen-2-yl]acrylate (2a).[12e]

1 (200 mg, 0.85 mmol) was dissolved in a mixture of toluene-methanol (8:2, 10 mL). The solution was cooled to 0 °C and $TMSCHN_2$ (0.5 mL, 2M in diethyl ether) was then added. The reaction time was monitored by TLC. Once the reaction was complete, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel (petroleum ether/ ethyl acetate, 98:2) provided **2** (158 mg, 75 %) as a colorless oil; $[\alpha]_D^{20}$ +26.8 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.82 (s, 3H, H-14), 1.16 (dd, 1H, *J* = 12.4, 12.4 Hz), 1.29-1.41 (m, 3H), 1.44 (dd, 1H, *J* = 3.4, 2.9 Hz), 1.47-1.53 (m, 1H), 1.54-1.69 (m, 4H), 1.75-1.88 (m, 1H), 1.90-2.14 (m, 3H), 2.52 (ddd, 1H, *J* = 11.9 , 4.3, 4.0 Hz), 3.76 (s, 3H, OMe), 5.31 (bs, 1H, H-3), 5.56 (bs, 1H, H-13), 6.14 (bs, 1H, H-13); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 15.8 (C-15), 21.3 (C-14), 23.1 (C-2), 27.6 (C-8), 29.5 (C-6), 32.4 (C-10), 38.0 (C-1), 40.3 (C-9), 40.7 (C-7), 47.0 (C-5), 51.9 (OMe), 121.2 (C-3), 122.7 (C-13), 135.0 (C-4), 146.1 (C-11), 168.1 (C-12).

5.3. 2-[(2*R*,4a*R*,8a*R*)-4a,8-dimethyl-1,2,3,4,4a,5,6,8a-octahydronaphthalen-2-yl]prop-2-en-1-ol (2b).[14]

Following the general reduction with DiBAlH with **2a** (250 mg, 1 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 8/2) provided **2b** (184 mg, 83 %) as a colorless oil; $[\alpha]_D^{20}$ +15.7 (c 1.0, CH_2Cl_2). ^{1}H NMR (400.13 MHz, $CDCl_3$) δ = 0.81 (s, 3H, H-14), 1.09-1.55 (m, 7H), 1.55-1.68 (m, 6H), 1.75-1.85 (m, 1H), 1.89-2.07 (m, 2H), 4.15 (bs, 2H, H-12), 4.94 (s, 1H, H-13), 5.06 (q, 1H, *J* = 2.1 Hz, H-13), 5.31 (bs, 1H, H-3); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ = 15.6 (C-14), 21.1 (C-15), 22.9 (CH_2), 27.4 (CH_2), 29.4 (CH_2), 32.3 (C-10), 37.9 (CH_2), 40.3 (CH_2), 42.4 (C-7), 46.9 (C-5), 65.3 (C-12), 107.9 (C-13), 121.0 (C-3), 134.8 (C-4), 154.2 (C-11).

5.4. 2-[(2*R*,4a*R*,8a*R*)-4a,8-dimethyl-1,2,3,4,4a,5,6,8a-octahydronaphthalen-2-yl]acrylaldehyde (2c).

Following the general procedure of oxidation with PDC with 2b (83 mg, 0.38 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 9.5/0.5) provided 2c (59 mg, 72 %) as a colorless oil; $[\alpha]_D^{20}$ +6.4 (c 1.0, CH_2Cl_2). ^{1}H NMR (250.13 MHz, $CDCl_3$) δ= 0.83 (s, 3H, H-14), 1.00-1.54 (m, 8H), 1.54-1.69 (m, 6H), 1.73-1.85 (m, 1H), 1.91-2.16 (m, 3H), 2.49-2.64 (m, 1H), 5.31-5.38 (m, 1H, H-3), 6.00 (s, 1H, H-13), 6.30 (s, 1H, H-13), 9.55 (s, 1H, H-12); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 15.4 (C-14), 20.9 (C-15), 22.7 (C-2), 26.8 (C-8), 28.7 (C-6), 32.1 (C-10), 36.9 (C-1), 37.6 (C-9), 39.8 (C-7), 46.6 (C-5), 120.9 (C-3), 132.9 (C-13), 134.5 (C-4), 155.1 (C-11), 194.54 (C-12); HRMS (ESI): calcd. For $C_{15}H_{23}O$ $[M + H]^+$ 219.1742; found 219.1743.

5.5. Methyl 2-[(1a*R*,3a*S*,6*R*,7a*R*,7b*S*)-3a,7b-dimethyldecahydronaphtho[1,2-*b*]oxiren-6-yl]acrylate (3a).[2c]

To a solution of ester **2** (315 mg, 1.3 mmol) in dichloromethane (10 mL) was added m-chloroperbenzoic acid (220 mg, 1.3 mmol). The reaction mixture was stirred at room temperature for 3 hours then washed with a solution of sodium bisulfite (10%) (3 x 10 mL) and a solution of sodium hydrogen carbonate (5%) (10 mL). The aqueous phases were combined and extracted with DCM (3 x 10 mL). The organic phases were combined, washed with water (10 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography on silica gel. (petroleum ether/ ethyl

acetate 9.7/ 0.3) provided **3a** (236 mg, 70 %) as a colorless oil; $[\alpha]_D^{20}$ +10.7 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.83 (s, 3H, H-14), 1.03-1.22 (m, 7H), 1.33 (ddd, 1H, *J* = 13.4, 3.5, 3.3 Hz), 1.40-1.48 (m, 1H), 1.48-1.53 (m, 1H), 1.57 (dd, 1H, *J* = 13.4, 3.3 Hz), 1.77-1.84 (m, 1H), 1.87 (ddd, 1H, *J* = 12.1, 6.7, 3.1 Hz), 1.94 (dd, 1H, *J* = 15.1, 6.1 Hz), 2.43 (dddd, 1H, *J* = 12.1, 12.0, 3.9, 3.9 Hz), 2.86 (bs, 1H, H-3), 3.70 (s, 3H, CO_2Me), 5.50 (s, 1H, H-13), 6.09 (s, 1H, H-13); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 16.5 (C-14), 21.3 (C-15), 21.7 (CH_2), 27.3 (CH_2), 30.1 (CH_2), 31.6 (C-10), 34.8 (CH_2), 39.8 (CH_2), 40.7 (C-7), 48.2 (C-5), 52.1 (OMe), 58.8 (C-4), 61.1 (C-3), 123.1 (C-13), 145.5 (C-11), 168.0 (C-12); HRMS (ESI): calcd. For $C_{16}H_{25}O_3$ [M + H]$^+$ 265.1800; found 265.1798.

5. 6. 2-[(1a*R*,3a*S*,6*R*,7a*R*,7b*S*)-3a,7b-dimethyldecahydronaphtho[1,2-*b*]oxiren-6-yl]prop-2-en-1-ol (3b).

Following the general reduction with DiBAlH with **3a** (235 mg, 0.9 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 8/2) provided **3b** (170 mg, 81 %) as a colorless oil; $[\alpha]_D^{20}$+46.4 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.77 (s, 3H, H-14), 1.03-1.16 (m, 3H), 1.18 (s, 3H, H-15), 1.23 (d, 1H, *J* = 12.7 Hz), 1.34 (ddd, 1H, *J* = 13.4, 3.5, 3.1 Hz), 1.39-1.58 (m, 3H), 1.76-1.84 (m, 1H), 1-84-1.90 (m, 1H), 1.90-2.01 (m, 2H), 2.25 (bs, 1H, OH), 2.89 (s, 1H, H-3), 4.06 (s, 2H, H-12), 4.88 (s, 1H, H-13), 5.01 (s, 1H, H-13); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 16.4 (C-14), 21.2 (C-15), 21.6 (CH_2), 27.4 (CH_2), 30.0 (CH_2), 31.6 (C-10), 34.8 (CH_2), 39.8 (CH_2), 42.3 (C-7), 48.2 (C-5), 59.0 (C-4), 61.2 (C-3), 65.2 (C-12), 108.1 (C-13), 154.0 (C-11); HRMS (ESI): calcd. For $C_{15}H_{25}O_2$ [M + H]$^+$ 237.1850; found 237.1849.

5.7. 2-[(1a*R*,3a*S*,6*R*,7a*R*,7b*S*)-3a,7b-dimethyldecahydronaphtho[1,2-b]oxiren-6-yl]acrylaldehyde (3c).

Following the general procedure of oxidation with PDC with **3b** (181 mg, 0.8 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 9.5/0.5) provided **3c** (134 mg, 74 %) as a colorless oil; ($[\alpha]_D^{20}$ +4.3 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.80 (s, 3H, H-14), 1.06-1.26 (m, 7H), 1.36 (ddd, 1H, *J* = 13.3, 3.3, 3.3 Hz), 2.41-2.56 (m, 2H), 1.61 (dd, 1H, *J* = 13.4, 3.3 Hz), 1.75-1.82 (m, 1H), 1.83-1.94 (m, 1H), 1.95-2.01 (m, 1H), 2.48 (dddd, 1H, *J* = 11.9, 11.9, 4.2, 4.1), 2.89 (bs, 1H, H-3), 5.96 (s, 1H, H-13), 6.25 (s, 1H, H-13), 9.50 (s, 1H, H-12); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 16.4 (C-14), 21.2 (C-15), 21.7 (CH_2), 26.8 (CH_2), 29.4 (CH_2), 31.6 (CH_2), 34.8 (C-10), 37.5 (CH_2), 39.7 (C-7), 48.1 (C-5), 58.7 (C-4), 61.0 (C-3), 133.4 (C-13), 155.0 (C-11), 194.8 (C-12); HRMS (ESI): calcd. For $C_{15}H_{23}O_2$ [M + H]$^+$ 235.1689; found 235.1692.

5.8. Methyl 2-[(2*R*,4a*S*,8*S*,8a*S*)-4a,8-dimethyl-7-oxodecahydronaphthalen-2-yl]acrylate (4a).

Following the general procedure for acid-promote ring opening of epoxide with **3a** (225 mg, 0.9 mmol) and $BF_3.Et_2O$. Column chromatography on silica gel (petroleum ether/ ethyl acetate 8/2) provided **4a** (156 mg, 69 %) as a white solid; mp = 121 – 123 °C; $[\alpha]_D^{20}$ -1.9 (*c* 1.0, CH_2Cl_2). ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 1.00 (d, 3H, *J* = 6.5 Hz, H-15), 1.14 (s, 3H, H-14), 1.17-1.36 (m, 3H), 1.49-1.57 (m, 3H), 1.57-1.66 (m, 1H, H-5), 1.73-1.80 (m, 2H), 2.19-2.28 (m, 1H, H-4), 2.27-2.35 (m, 1H), 2.36-2.44 (m, 1H, H-7), 2.55 (dddd, 1H, *J* = 14.1, 14.1, 6.5, 0.9 Hz), 3.78 (s, 3H, OMe), 5.58 (s, 1H, H-13), 6.18 (s, 1H, H-13); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 11.3 (C-15), 16.5 (C-14), 27.0 (CH_2), 31.3 (CH_2), 33.5 (C-10), 38.1 (CH_2), 39.7 (C-7), 40.8 (CH_2), 41.3 (CH_2), 45.7 (C-4), 51.1 (C-5), 51.9 (OMe), 123.3 (C-13), 145.6 (C-11), 168.0 (C-12), 213.2 (C-3); HRMS (ESI): calcd. For $C_{16}H_{25}O_3$ [M + H]$^+$ 265.1800; found 265.1798.

5.9. (1*S*,4a*S*,7*R*,8a*S*)-7-(3-hydroxyprop-1-en-2-yl)-1,4a-dimethyldecahydronaphthalen-2-ol (4b).[2a]

Following the general reduction with DiBAlH with **4a** (165 mg, 0.6 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 6/4) provided **4b** (120 mg, 81 %) as a colorless oil; $[\alpha]_D^{20}$ -8.2 (*c* 1.0, $CHCl_3$) lit $[\alpha]_D^{20}$ -25 (*c* 1.4, $CHCl_3$); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.82 (s, 1.5 H, H-14), 0.83 (s, 1.5H, H-14), 0.87 (d, 1H, *J* = 6.7 Hz), 0.92 (d, 1H, *J* = 6.7 Hz), 0.95-1.29 (m, 5H), 1.30-1.68 (m, 7H), 1.68-1.81 (m, 1H), 1.82-1.99 (m, 1H), 2.19 (bs, 2H), 3.07 (ddd, 0.5H, *J* = 10.5, 10.3, 5.1 Hz), 3.72-3.77 (m, 0.5H), 4.07 (bs, 2H, H-12), 4.86 (bs, 1H, H-13), 4.99 (bs, 1H, H-13); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 15.0 (CH_3), 16.1 (CH_3), 16.1 (CH_3), 17.0 (CH_3), 27.2 (CH_2), 27.4 (CH_2), 29.1 (CH_2), 29.9 (CH_2), 30.0 (CH_2), 30.9 (CH_2), 33.3 (C-10), 33.6 (C-10), 35.3 (CH_2), 35.5 (CH), 39.3 (CH), 39.6 (CH_2), 41.7 (CH_2), 41.8 (CH_2), 41.9 (CH), 42.2 (CH), 43.1 (CH), 49.1 (CH), 65.0 (C-12), 65.0 (C-12), 72.3 (C-3), 107.5 (C-13), 107.8 (C-13), 154.2 (C-11), 154.4 (C-11); HRMS (ESI): calcd. For $C_{15}H_{26}LiO_2$ [M + Li]$^+$ 245.2091; found 245.2087.

5.10. 2-[(2*R*,4a*S*,8*S*,8a*S*)-4a,8-dimethyl-7-oxodecahydronaphthalen-2-yl]acrylaldehyde (4c).

Following the general procedure of oxidation with PDC with **4b** (90 mg, 0.4 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 8/2) provided **4c** (64 mg, 72 %) as a colorless oil; $[\alpha]_D^{20}$ +39.4 (*c* 1.0, CH_2Cl_2). ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 1.04 (d, 3H, *J*= 8.1 Hz; H-15), 1.13 (s, 3H, H-14), 1.16-1.39 (m, 2H), 1.40-1.67 (m, 5H), 1.68-1.83 (m, 2H), 2.18-2.31 (m, 1H), 2.32-2.43 (m, 1H, H-4), 2.45-2.56 (m, 1H, H-7), 2.57-2.74 (m, 1H), 5.99 (s, 1H, H-13), 6.28 (s, 1H, H-13), 9.51 (s, 1H, H-12); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 13.8 (C-15), 19.0 (C-14), 27.1 (CH_2), 31.3 (CH_2), 33.5 (C-10), 35.4 (CH_2), 36.9 (CH_2), 40.3 (C-7), 42.9 (CH_2), 46.5 (C-5), 49.2 (C-4), 133.5 (C-13), 154.8 (C-11), 194.8 (C-12), 216.0 (C-3); HRMS (ESI): calcd. For $C_{15}H_{23}O_2$ [M + H]$^+$ 235.1691; found 235.1692.

5.11. Methyl 2-[(2*R*,4a*S*,7*R*,8a*R*)-7-hydroxy-4a-methyl-8-methylenedecahydronaphthalen-2-yl]acrylate (5a)[2c] and methyl 2-[(3a*R*,5*R*,7a*S*)-3-formyl-3,7a-dimethyloctahydro-*1H*-inden-5-yl]acrylate (6).

Following the general procedure for acid-promote ring opening of epoxide with **3a** (478 mg, 1.8 mmol) and $Bi(OTf)_3$. Column chromatography on silica gel (petroleum ether/ ethyl acetate 6/4) provided **5a** (268 mg, 56 %) as a colorless oil and **6** (152 mg, 32%) as a colorless oil.

5a: $[\alpha]_D^{20}$ +35.3 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.60-0.73 (m, 3H, H-14), 1.15-1.29 (m, 2H), 1.32-1.64 (m, 5H), 1.66-1.90 (m, 4H), 2.33-2.46 (m, 1H, H-5), 2.47-2.62 (m, 1H, H-7), 3.72 (s, 3H, OMe), 4.25 (dd, 1H, *J* = 2.5, 2.4 Hz, H-3), 4.52 (s, 1H, H-15), 4.89 (s, 1H, H-15), 5.53 (s, 1H, H-13), 6.12 (s, 1H, H-13); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 15.8 (C-14), 27.4 (CH_2), 29.8 (CH_2), 29.9 (CH_2), 35.9 (CH_2), 36.1 (C-10), 39.9 (C-7), 40.9 (CH_2), 43.9 (C-5), 52.0 (OMe), 73.7 (C-3), 109.2 (C-15), 122.9 (C-13), 146.0 (C-11), 152.0 (C-4), 168.1 (C-12); HRMS (ESI): calcd. For $C_{16}H_{24}LiO_3$ [M + Li]$^+$ 271.1881; found 271.1880.

6: $[\alpha]_D^{20}$ -3.2 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 1.00 (s, 3H, Me-7a'), 1.07 (s, 3H, Me-3'), 1.12-1.56 (m, 5H), 1.60-1.71 (m, 4H), 1.76 (ddd, 1H, *J* = 12.4, 3.1, 3.1 Hz), 2.06-2.13 (m, 1H), 2.54 (dddd, 1H, *J* = 12.4, 12.4, 4.2, 4.2 Hz), 3.74 (s, 3H, OMe), 5.57 (s, 1H), 6.14 (d, 1H, *J* = 1.2 Hz), 9.36 (s, 1H). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 16.7 (Me-3'), 19.3 (Me-7a'),

27.4 (CH_2), 27.6 (CH_2), 33.6 (CH_2), 40.5 (CH_2), 40.7 (CH_2), 40.7 (C-5'), 42.5 (C-7a'), 51.3 (C-3a'), 51.9 (OMe), 53.0 (C-3'), 123,2 (C-3), 145.4 (C-2), 167.8 (C-1), 204.3 (CHO). HRMS (ESI+): calcd. For $C_{16}H_{25}O_3$ [M+H]+ 265,1798; found 265,1801.

5.12. (2*R*,4a*S*,7*R*,8a*R*)-7-(3-hydroxyprop-1-en-2-yl)-4a-methyl-1-methylenedecahydronaphthalen-2-ol (5b).[10e]

Following the general reduction with DiBAlH with **5a** (200 mg, 0.8 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 6/4) provided **5b** (130 mg, 72%) as a white crystal; $[\alpha]_D^{20}$ -16.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.67 (s, 3H, H-14), 1.16-1.38 (m, 3H), 1.38-1.62 (m, 4H), 1.63-1.84 (m, 3H), 2.01-2.11 (m, 1H), 2.19 (bs, 2H), 2.30-2.35 (m, 1H), 4.07 (s, 2H, H-12), 4.26 (dd, 1H, *J* = 2.9, 2.8 Hz, H-3), 4.54 (dd, 1H, *J* = 1.8, 1.7 Hz), 5.90 (bs, 2H), 5.01 (bs, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 15.8 (C-14), 27.5 (CH_2), 29.9 (CH_2), 30.0 (C-7), 35.9 (CH_2), 36.1 (C-10), 41.1 (CH_2), 41.7 (CH_2), 44.1 (C-5), 65.3 (C-12), 73.7 (C-3), 108.0 (CH_2), 109.2 (CH_2), 152.1 (C), 154.3 (C); HRMS (ESI): calcd. For $C_{15}H_{24}LiO_2$ $[M + Li]^+$ 243.1932; found 243.1931.

5.13. 2-[(2*R*,4a*S*,7R,8a*R*)-7-hydroxy-4a-methyl-8-methylenedecahydronaphthalen-2-yl]prop-2-enal (5c).

Following the general procedure of oxidation with PDC with **5b** (102 mg, 0.4 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 8/2) provided **5c** (71 mg, 71%) as a colorless oil; $[\alpha]_D^{20}$ -1.4 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.72 (s, 3H, H-14), 1.20-1.85 (m, 10H), 2.39-2.50 (m, 1H), 2.51-2.67 (m, 1H), 4.26-4.32 (m,1H), 4.54 (dd, 1H, *J* = 2.0, 2.0 Hz), 4.92 (bs, 1H), 5.97 (s, 1H), 6.27 (s, 1H), 9.51 (s, 1H, H-12); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 15.9 (C-14), 27.0 (CH_2), 29.4 (CH_2), 29.9 (CH_2), 35.9 (CH_2), 36.1 (C-10), 36.8 (C-7), 40.9 (CH_2), 43.9 (C-5), 73.8 (C-3), 109.4 (CH_2), 133.3 (CH_2), 152.0 (C), 155.3 (C), 195.0 (C-12); HRMS (ESI): calcd. For $C_{15}H_{21}O_2$ $[M + H]^+$ 233.1536; found 233.1536.

5.14. Methyl 2-[(2*R*,4a*R*)-4a,8-dimethyl-1,2,3,4,4a,5,6,7-octahydronaphthalen-2-yl]acrylate (7).[3, 13b]

1 (2g, 8.5 mmol) in methanol (30 mL) and H_2SO_4 (1 mL) was heated to reflux for 12 h. The reaction mixture was filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography on silica gel (hexane) providing **7** (1.5 g, 75 %) as the major isomer and as a yellow oil. $[\alpha]_D^{20}$ +41.2 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 1.05 (s, 3H, H-14), 1.22-1.42 (m, 4H), 1.46-2.04 (m, 10H), 2.32-2.43 (m, 1H), 2.63 (ddd, 1H, *J* = 13.6, 3.3, 2.2Hz), 3.76 (s, 3H, OMe), 5.56 (s, 1H, H-13), 6.16 (s, 1H, H-13); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ =19.2 (CH_2), 19.4 (C-15), 24.7 (C-14), 28.2 (CH_2), 31.5 (CH_2), 33.2 (CH_2), 34.6 (C-10), 40.3 (CH_2), 40.7 (C-7), 42.2 (CH_2), 51.8 (OMe), 122.5 (C-13), 125.2 (C-4), 134.4 (C-5), 145.8 (C-11), 167.9 (C-12); MS, m/z: 249 :$[M+H]^+$.

5.15. Methyl 2-(1a,4a-dimethyloctahydro-1aH-naphtho[1,8a-*b*]oxiren-7-yl)acrylate (8a).[16]

7 (160 mg, 0.6 mmol) was dissolved in dichloromethane (10 mL) then *m*-chloroperbenzoic acid (112 mg, 0.6 mmol) was added. The reaction mixture was stirred at room temperature for 3 hours then washed with a solution of sodium bisulfite (10%) (3 x 10 mL) and a solution of sodium hydrogen carbonate (5%) (10 mL). The aqueous phases were combined and extracted CH_2Cl_2 (3 x 10 mL). The resulted organic phases were finally washed with water (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography on silica gel (hexane / ethyl acetate: 9.8/0.2) providing **8a** (119 mg, 70%) in a 4/3 mixture of α and β as a colorless oil; $[\alpha]_D^{20}$ +17.8 (c 1.0, CH_2Cl_2). ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 1.08 (s, 1.8H, H-14), 1.25 (s, 1.2H, H-14), 1.35-2.01 (m, 15H), 2.56 (dddd, 0.6H, *J* = 12.1, 12.1, 3.8, 3.8 Hz, H-7α), 2.73-2.89 (m, 0.4H, H-7β), 3.76 (s, 1.2H, OMe), 3.77(s, 1.8H, OMe), 5.55 (s, 0.4H, H-13α), 5.58 (s, 0.6H, H-13β), 6.16 (bs, 0.4H, H-13β), 6.20 (s, 0.6H, H-13α); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 16.1 (CH_2), 16.8 (CH_2), 20.9 (CH_3), 21.0 (CH_3), 21.5 (CH_3), 23.2 (CH_3), 27.6 (CH_2), 28.9 (CH_2), 30.8 (CH_2), 31.3 (CH_2), 32.5 (CH_2), 33.4 (C-10), 33.9 (C-10), 34.0 (CH_2), 35.6 (CH_2), 35.9 (CH_2), 37.5 (CH_2), 38.1 (C-7), 38.8 (C-7), 51.8 (OMe), 51.9 (OMe), 63.3 (C-4), 64.4 (C-4), 68.6 (C-5), 69.4 (C-5), 123.0 (C-13), 123.3 (C-13), 144.5 (C-11), 145.3 (C-11), 167.6 (C-12); HRMS (ESI): calcd. For $C_{16}H_{25}O_3$ $[M + H]^+$ 265.1800; found 265.1798.

5.16. 2-(1a,4a-dimethyloctahydro-1a*H*-naphtho[1,8a-*b*]oxiren-7-yl)prop-2-en-1-ol (8b).

Following the general reduction with DiBAlH with **8a** (300 mg, 1.1 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 8/2) provided **8b** (220mg, 82 %) in a 4/3 mixture of α and β as a colorless oil; $[\alpha]D^{20}$ +12.3 (c 1.0, CH_2Cl_2). ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 1.04 (s, 1.2H, H-14), 1.06 (s, 1.8H, H-14), 1.22 (s, 1.8H, H-15), 1.30 (s, 1.2H, H-15), 1.33-1.95 (m, 12H), 4.09 (s, 2H, H-12), 4.89 (s, 1H, H-13), 5.03 (s, 1H, H-13); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 16.0 (CH_2), 16.7 (CH_2), 20.7 (CH_3), 21.0 (CH_3), 21.5 (CH_3), 23.2 (CH_3), 27.5 (CH_2), 27.7 (CH_2), 28.9 (CH_2), 31.2 (CH_2), 32.2 (CH_2), 33.4 (C-10) , 33.9 (C-10), 34.0 (CH_2), 35.5 (CH_2), 36.0 (CH_2), 37.6 (CH_2), 38.8 (C-7), 40.6 (C-7), 63.6 (C-4), 64.2 (C-4), 65.0 (C-12), 65.1 (C-12), 68.8 (C-5), 69.8 (C-5), 108.0 (C-13), 108.4 (C-13), 152.7 (C-11), 153.6 (C-11); HRMS (ESI): calcd. For $C_{15}H_{25}O_2$ $[M + H]^+$ 237.1848; found 237.1849.

5.17. 2-(1a,4a-dimethyloctahydro-1a*H*-naphtho[1,8a-*b*]oxiren-7-yl)acrylaldehyde (8c).

Following the general procedure of oxidation with PDC with **8b** (90 mg, 0.4 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 95/5) provided **8c** (68 mg, 75%) in a 4/3 mixture of α and β as a colorless oil; $[\alpha]_D^{20}$ +50.2 (c 1.0, CH_2Cl_2). ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 1.05 (s, 1.2H, H-14), 1.09 (s, 1.8H, H-14), 1.21 (s, 1.8H, H-15), 1.33 (s, 1.2H, H-15), 1.35-1.97 (m, 12H), 2.55 (dddd, 0.4H, *J* = 12.7, 12.5, 3.5, 3.0 Hz), 2.74-2.84 (m, 0.6H), 5.95 (s, 0.6H, H-13), 5.98 (s, 0.4H, H-13), 6.23 (s, 0.6H, H-13), 6.25 (s, 0.4H, H-13), 9.51 (s, 1H, H-12); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 16.3 (CH_2), 17.0 (CH_2), 21.0 (CH_3), 21.2 (CH_3), 21.7 (CH_3), 23.3 (CH_3), 27.2 (CH_2), 27.4 (CH_2), 29.1 (CH_2), 30.3 (CH_2), 31.5 (CH_2), 32.0 (CH_2), 33.3 (C-10), 33.7 (C-10), 34.1 (CH_2), 35.5 (C-7), 35.7 (C-7), 35.8 (CH_2), 36.1 (CH_2), 37.6 (CH_2), 63.4 (C-4), 64.6 (C-4), 68.6 (C-5), 69.5 (C-5), 133.2 (C-13), 133.5 (C-13), 154.1 (C-11), 154.6 (C-11), 194.6 (C-12), 194.6 (C-12); HRMS (ESI): calcd. For $C_{15}H_{23}O_2$ [M + H]+ 235.1692; found 235.1692.

5.18. Methyl 2-((3a*R*,6*R*,8a*R*)-3a,8a-dimethyl-4-oxodecahydroazulen-6-yl)acrylate (9).

Following the general procedure for acid-promote ring opening of epoxide with **8a** (260 mg, 1 mmol) and $BF_3.Et_2O$. Column chromatography on silica gel (petroleum ether/ ethyl acetate 9/1) provided **9** (198 mg, 76 %) as a yellow solid; mp = 45 - 47 °C, $[\alpha]_D^{20}$ -0.8 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 1.12 (s, 3H), 1.20 (s, 3H), 1.33-1.59 (m, 6H), 1.61-1.81 (m, 3H), 2.19-2.27 (m, 1H, H-5'), 2.35-2.49 (m, 1H), 2.58-2.73 (m, 1H, H-6'), 3.07 (dd, 1H, *J* = 12.5, 10.3 Hz, H-5'), 3.74 (s, 3H, OMe), 5.53 (s, 1H, H-3), 6.13 (d, 1H, *J* = 0.9 Hz, H-3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 21.4 (CH_2), 23.3 (CH_3), 23.7 (CH_3), 30.2 (C-7'), 36.1 (CH_2), 40.6 (CH_2), 41.7 (C-6'), 42.8 (C-8a'), 44.2 (C-5'), 46.0 (CH_2), 52.0 (OMe), 60.2 (C-3a'), 123.9 (C-3), 144.8

(C-2), 167.0 (C-1), 214.8 (C-4'); HRMS, Calcd for $C_{16}H_{25}O_3[M+H]^+$: 265.1798. Found: 265.1801.

5.19. Methyl 2-[(2*R*,4a*R*)-4a,8-dimethyl-2,3,4,4a,5,6-hexahydronaphthalen-2-yl]acrylate (10a) and methyl 2-[(2*R*,4a*R*,8a*R*]-8a-hydroxy-4a-methyl-8-methylenedecahydronaphthalen-2-yl)acrylateEudesma carboxylic (11a).[16]

Following the general procedure for acid-promote ring opening of epoxide with **8a** (1.35g, 5.1 mmol) and PTSA. Column chromatography on silica gel (petroleum ether/ ethyl acetate 8/2) provided **10a** (480 mg, 38 %) as a yellow oil and **11a** (810 mg, 60 %) as a white solid.

10a: $[\alpha]_D^{20}$ -137.3 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.99 (s, 3H; H-14), 1.37-1.47 (m, 3H), 1.48-1.61 (m, 3H), 1.74-1.79 (m, 3H), 1.94-2.05 (m, 1H), 2.05-2.13 (m, 1H), 2.15-2.35 (m, 1H), 3.37-3.48 (m, 1H), 3.76 (s, 3H, OMe), 5.37 (bs, 1H, H-6), 5.51-5.58 (m, 1H, H-3), 5.59 (dd, 1H, *J* = 1.2, 1.1 Hz, H-13), 6.17 (d, 1H, *J* = 1.3 Hz, H-13); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 20.5 (C-15), 23.2 (CH_2), 23.8 (C-14), 26.7 (CH_2), 32.6 (C-10), 37.5 (CH_2), 38.6 (CH_2), 39.3 (C-7), 52.1 (OMe), 122.2 (C-6), 124.0 (C-13), 125.2 (C-3), 131.4 (C-4), 143.4 (C), 146.0 (C), 167.9 (C-12); MS m/z: 247 :$[M+H]^+$; HRMS (ESI): calcd. For $C_{16}H_{23}O_2$ $[M + H]^+$ 247.1692; found 247.1692.

11a: mp = 97 – 99 °C, (lit 93 °C); $[\alpha]_D^{20}$ +82. (*c* 1.0, $CHCl_3$) lit $[\alpha]_D^{20}$ +99 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.89 (s, 3H, H-14), 1.01-1.11 (m, 1H), 1.14-1.30 (m, 1H), 1.51-1.72 (m, 6H), 1.76 (dd, 1H, *J* = 13.0, 12.8 Hz), 1.82-1.94 (m, 2H), 2.06-2.16 (m, 1H), 2.54-2.73 (m, 1H), 3.01-3.17 (m, 1H, H-7), 3.76 (s, 3H, OMe), 4.64 (dd, 1H, *J* = 1.5, 1.5 Hz, H-15), 4.80 (dd, 1H, *J* = 1.6, 1.5 Hz, H-15), 5.58 (dd, 1H, *J* = 1.3, 1.1 Hz, H-13), 6.17 (bs, 1H, H-13); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 20.3 (C-14), 22.6 (CH_2), 26.6 (CH_2), 32.0 (CH_2), 34.6 (CH_2), 35.1 (C-7), 35.2 (CH_2), 36.4 (CH_2), 38.2 (C-10), 52.1 (OMe), 75.8 (C-5), 107.9 (C-15), 123.3 (C-13), 146.1 (C-11), 152.2 (C-4), 168.2 (C-12); HRMS (ESI): calcd. For $C_{16}H_{25}O_3$ $[M + H]^+$ 265.1801; found 265.1798.

5.20. 2-[(2*R*,4a*R*)-4a,8-dimethyl-2,3,4,4a,5,6-hexahydronaphthalen-2-yl]prop-2-en-1-ol (10b).

Following the general reduction with DiBAlH with **10a** (258 mg, 1mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 8/2) provided **10b** (170 mg, 73%) as a colorless oil; $[\alpha]_D^{20}$ +8.5 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.98 (s, 3H, H-14), 1.28-1.65 (m, 6H), 1.75 (bs, 3H), 1.78-1.86 (m, 1H), 1.97-2.08 (m, 1H), 2.15-2.30 (m, 1H), 2.96-3.01 (m, 1H), 4.15 (s, 2H, H-12), 4.95 (s, 1H, H-6), 5.04 (bs, 1H, H-13), 5.41 (bs, 1H, H-13), 5.52 (bs, 1H, H-3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 20.5 (C-15), 23.2 (CH_2), 23.8 (C-14), 26.0 (CH_2), 32.6 (C-10), 37.5 (CH_2), 38.6 (CH_2), 41.8 (C-7), 65.0 (C-12), 109.3 (C-13), 122.7 (C-6), 125.2 (C-3), 131.5 (C-4), 143.2 (C-5), 154.0 (C-11); HRMS (ESI): calcd. For $C_{15}H_{23}O$ $[M + H]^+$ 219.1744; found 219.1743.

5.21. 2-[(2*R*,4a*R*)-4a,8-dimethyl-2,3,4,4a,5,6-hexahydronaphthalen-2-yl]acrylaldehyde (10c).

Following the general procedure of oxidation with PDC with **10b** (90 mg, 0.4 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 95/5) provided **10c** (70 mg, 78 %) as a yellow oil; $[\alpha]_D^{20}$ +42.6 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.99 (s, 3H, H-14), 1.37-1.56 (m, 6H), 1.76 (bs, 2H), 1.91-1.99 (m, 1H), 2.01-2.11 (m, 1H), 2.16-2.34 (m, 1H), 3.44 (dd, 1H, *J* = 9.4, 7.4 Hz, H-7), 5.32 (s, 1H, H-6), 5.51-5.57 (m, 1H, H-3), 5.99 (s, 1H, H-13), 6.27 (s, 1H, H-13), 9.59 (s, 1H, H-12); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 20.1 (C-15), 23.2 (CH_2), 23.5 (C-14), 25.8 (CH_2), 32.6 (C-10), 36.0 (C-7), 37.4 (CH_2), 38.4 (CH_2), 121.3 (C-6), 125.4 (C-3), 131.3 (C-4), 133.8 (C-13), 144.0 (C-5), 155.4 (C-11), 194.6 (C-12); HRMS (ESI): calcd. For $C_{15}H_{21}O$ $[M + H]^+$ 217.1586; found 217.1586.

5.22. (3*R*,4a*R*,8a*R*)-3-(3-hydroxyprop-1-en-2-yl)-8a-methyl-5-methylenedecahydronaphthalen-4a-ol (11b).[10c]

Following the general reduction with DiBAlH with **11a** (113 mg, 0.4 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 6/4) provided **11b** (80 mg, 79%) as a colorless oil; $[\alpha]_D^{20}$ +118.4 (*c* 1.0, $CHCl_3$), lit $[\alpha]_D^{20}$ +46.67 (*c* 0.11, $CHCl_3$); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.87 (s, 3H, H-14), 0.99-1.09 (m, 1H), 1.13-1.25 (m, 1H), 1.46-1.92 (m, 10H), 2.05-2.14 (m,1H), 2.51-2.68 (m, 2H), 4.06 (bs, 2H, H-12), 4.65 (dd, 1H, *J* = 1.6, 1.4 Hz), 4.79 (dd, 1H, *J* = 1.7, 1.6 Hz), 4.92 (bs, 1H), 5.03-5.07 (m, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ= 20.2 (C-14), 22.2 (CH_2), 26.7 (CH_2), 31.9 (CH_2), 34.6 (CH_2), 35.2 (CH_2), 35.8 (C-7), 36.1 (CH_2), 38.2 (C-10), 65.6 (C-12), 75.8 (C-5), 107.8 (CH_2), 108.6 (CH_2), 152.2 (C), 154.2 (C). HRMS (ESI): calcd. For $C_{15}H_{25}O_2$ $[M + H]^+$ 237.1856; found 237.1849.

5.23. 2-[(2*R*,4a*R*,8a*R*)-8a-hydroxy-4a-methyl-8-methylenedecahydronaphthalen-2-yl]acrylaldehyde (11c).

Following the general procedure of oxidation with PDC with **11b** (80 mg, 0.3 mmol). Column chromatography on silica gel (petroleum ether/ ethyl acetate 8/2) provided **11c** (52 mg, 65%) as a colorless oil; $[\alpha]_D^{20}$ +71.5 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250.13 MHz, $CDCl_3$) δ = 0.88 (s, 3H, H-14), 1.02 (d, 1H, *J* = 12.8 Hz), 1.16 (d, 1H, *J* = 13.5 Hz), 1.44-1.77 (m, 7H), 1.78-1.96 (m, 2H), 2.07 (d, 1H, *J* = 13.7 Hz), 2.54-2.71 (m, 1H), 3.00-3.19 (m, 1H, H-7), 4.58 (s, 1H, H-15), 4.76 (s, 1H, H-15), 5.98 (s, 1H, H-13), 6.28 (s, 1H, H-13), 9.50 (s, 1H, H-12); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ = 20.0 (C-14), 22.4 (CH_2), 25.7 (CH_2), 31.7 (C-7), 31.8 (CH_2), 34.2 (CH_2), 35.0 (CH_2), 35.5 (CH_2), 38.0 (C-10), 75.3 (C-5), 107.5 (C-15), 133.5 (C-13), 152.0 (C), 155.1 (C), 194.9 (C-12); HRMS (ESI): calcd. For $C_{15}H_{22}NaO_2$ $[M + Na]^+$ 257.1515; found 257.1512.

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