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# First total syntheses of (±)-3-aza-11-selena and (±)-3-aza-11-tellura steroids

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ABSTRACT

An efficient synthesis of 11-selena and 11-tellura steroids bearing a pyridine as an A ring was achieved via an intramolecular Diels–Alder cycloaddition of *o*-quinodimethanes, which were generated from a 3-azabicyclo[4.2.0]octa-1,3,5-trien-7-one ketal. The major isomer matches the *trans-anti-trans* ring configuration of natural products. Finally, the vinyl groups of the synthesized 11-hetero steroids have been oxidized by the Wacker process in good yields. The characteristic $^{1}H$ and $^{13}C$ NMR spectroscopic features of the synthesized compounds are reported.



## 1. Introduction

Steroids constitute an extensive and important class of biologically active polycyclic compounds that are widely used for therapeutic purposes.[1] Despite decades of research, the total synthesis of steroid nuclei by improved strategies continues to receive considerable attention. Numerous methods have been exploited for the total synthesis of steroids, which are widely distributed in nature and which possess practical medical importance.

Recently hetero steroids have received much attention for pharmacological interest[2] and their structure have been widely studied.[3]

This is particularly the case for aza steroids due to the presence of a nitrogen atom, which is known to give rise to biologically interesting properties.[4] For example, anti-bacterial[5] and neuromuscular-blocking activities[6] have been found for some aza steroids. Though many aza steroids have been reported, curiously and much to our surprise, 3-aza-1,3,5(10)-trieno steroids have been reported only once and it was not a total synthesis.[7] Nevertheless, a steroidal pyridine-*N*-oxide proved to be a potent inhibitor of the enzyme 5α-reductase (5AR), which catalyzes the conversion of testosterone to the more potent androgen dihydrotestosterone.[8]

Recently, we have described the first total syntheses of 11-selena[9] and 11-tellura[10] steroids based on our general strategy for elaborating the steroid skeleton.[11] This strategy involved the intramolecular cycloaddition of *o*-xylylenes to generate the BC ring system, which was developed by Oppolzer and Kametani.[12] We were now interested by the syntheses of 11-selena and 11-tellura steroids possessing a pyridine as an A ring using our general approach for elaborating the steroidal skeleton. To the best of our knowledge, there are no total syntheses described in the literature though their biological potential. Indeed, compounds containing selenium can possess biological properties and have been used as antiviral, antihypertensive, anti-bacterial, or chemopreventive anticancer agents.[13] There are several reports in the literature describing the antitumoral activity of selenium compounds via apoptosis in cancer cells induced by the generation of ROS in a pro-oxidant fashion.[14] Likewise, organotellurium compounds have attracted a great deal of attention because of their synthetic utility.[15]

We report herein the first total syntheses of 3-aza-11-selena and 3-aza-11-tellura steroids. We show that we can introduce by our method two heteroatoms at two key positions of the steroidal skeleton. We report here the full details of the study and we make a comparative study on the selectivity of the key thermolysis reaction between 11-hetero steroids and 3,11-dihetero steroids (Scheme 1).

## 2. Results and discussion

In 2005, we have reported the synthesis of a 3-aza-7-iodobicyclo[4.2.0]octa-1,3,5-triene **2** (Scheme 2).[16] The key step of this synthesis is the [2+2] cycloaddition of a 3,4-didehydropyridine and a ketene dialkyl acetal leading to 3-azabicyclo[4.2.0]octa-1,3,5-

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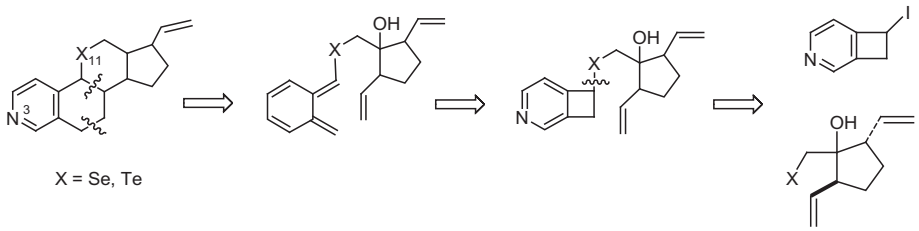
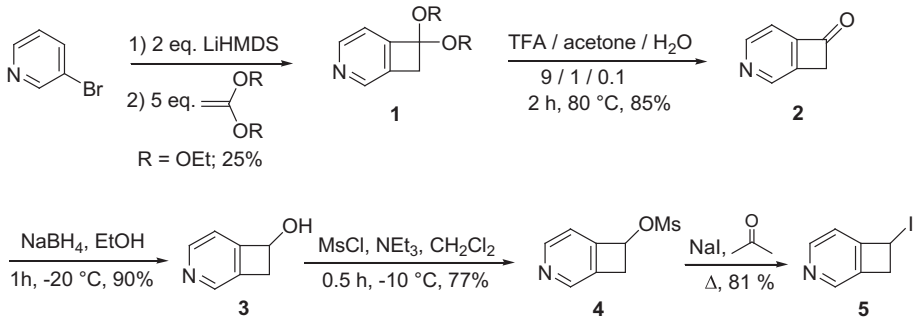



**Scheme 1.** Retrosynthetic pathway.

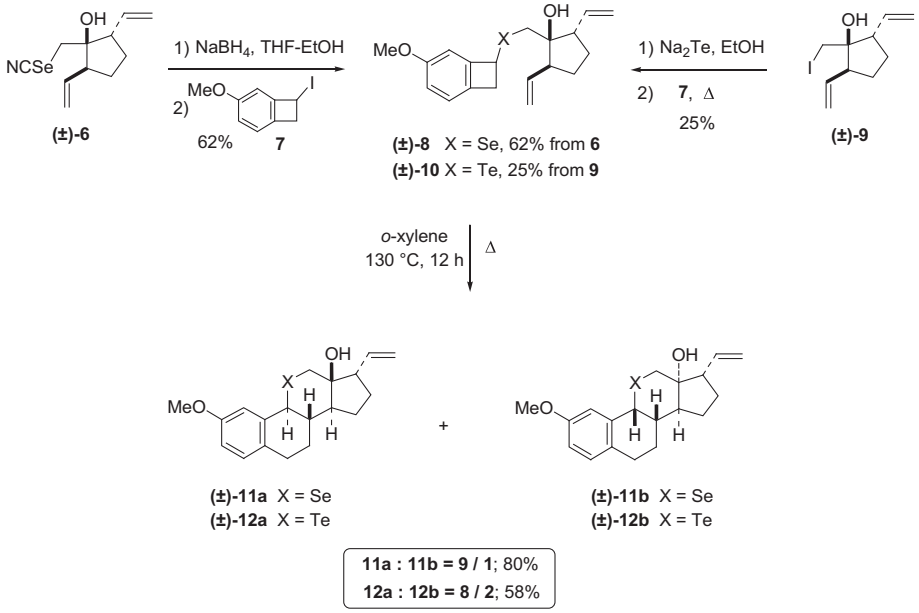



**Scheme 2.** Synthesis of 3-aza-7-iodo-bicyclo[4.2.0]octa-1,3,5-triene **2**.

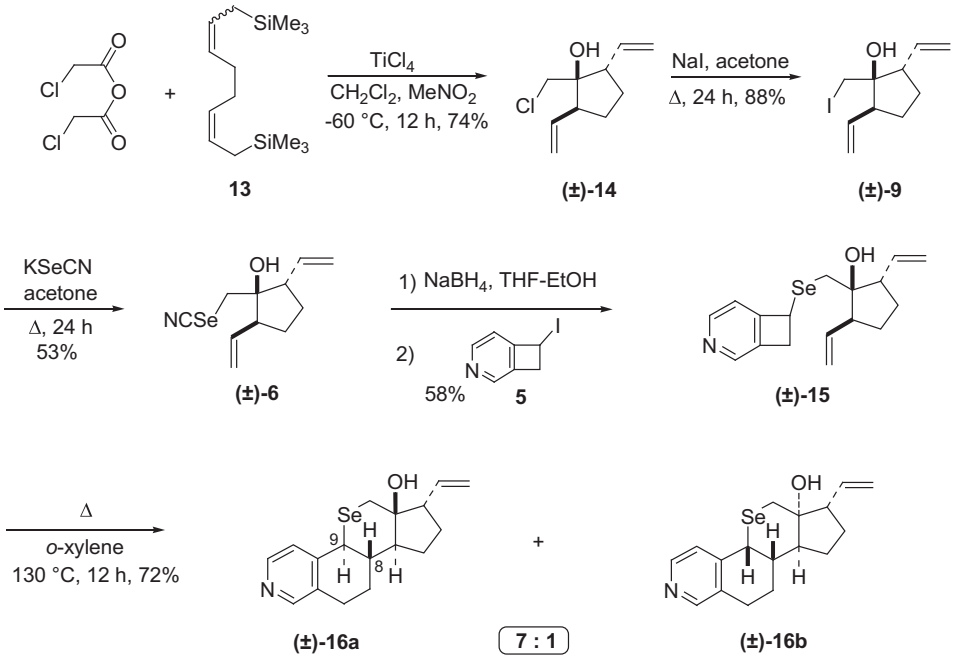
trien-7-one ketal **1**. Cycloaddition proceeded regioselectively. After deprotection of the ketal, 4-azabenzocyclobutenone **2** was reduced with $NaBH_4$ in ethanol to the corresponding azabenzocyclobutenol **3**. This latter was converted to the corresponding iodide **5** via its mesylate **4**. Thus, iodobenzocyclobutene **5** was obtained in 12% overall yield.

We recently described the first total syntheses of 11-selena[9] and 11-tellura-1,3,5(10) trieno steroids[10] (Scheme 3). Our strategy is based on an intramolecular Diels–Alder cycloaddition of *o*-quinodimethanes, which are generated by thermal ring opening of a benzocyclobutene.[11]

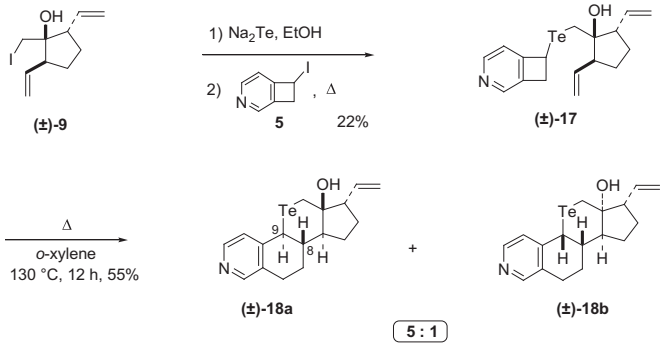
As a continuation of our synthetic and stereochemical studies on heterocyclic steroidal systems containing two heteroatoms, a similar strategy was used to obtain firstly 3-aza-11-selena-1,3,5(10)-trieno steroids (Scheme 4) and secondly 3-aza-11-tellura-1,3,5(10)-trieno steroids (Scheme 5). Thus, the starting iodhydrine **9** was easily accessible by a procedure reported previously by us[9] via a treatment with NaI of **14**, prepared by condensation of BISTRO **13** with chloroacetic anhydride. Iodhydrine **9** was dissolved in acetone containing potassium selenocyanate[17] and heated under reflux for 48 h, to give selenocyanate **6** in 53% yield. This latter, dissolved in tetrahydrofuran/ethanol, was treated with $NaBH_4$ at room temperature for 24 h, then the reductive product generated in this manner has been alkylated in situ with 3-aza-7-iodo-bicyclo[4.2.0] octa-1,3,5-triene **5**, leading to (±)-cyclobutene **15**. Thermolysis of **15** afforded a mixture of two selena steroids **16a** and **16b** in 72% yield and a 7/1 ratio, which were easily separable by flash chromatography on silica gel.




**Scheme 3.** Synthesis of 11-selena steroids **11** and 11-tellura steroids **12**.




**Scheme 4.** Synthesis of 3-aza-11-selena steroids **16**.




**Scheme 5.** Synthesis of 3-aza-11-tellura steroids **18**.

We turned then our attention to the synthesis of 3-aza-11-tellura-1,3,5(10)-trieno steroids (Scheme 5). Thus, iodhydrine **9** was dissolved in dry ethanol containing sodium telluride[18] and heated under reflux for 48 h, to give an intermediate, which was alkylated in situ with 3-aza-7-iodo-bicyclo[4.2.0]octa-1,3,5-triene **5**, providing a convenient way to produce the key intermediate **17**. This latter, sensitive to oxygen, was used in the following step without further purification. Thermolysis of (±)-cyclobutene **17** yielded a 5/1 mixture of two diastereoisomers **18a** and **18b** in a 55% overall yield. These tellura steroids were separated by flash chromatography on silica gel and stored under an argon atmosphere (Scheme 5).

The torquoselectivity in the electrocyclic conversion of benzocyclobutenes into *o*-xylylenes has been previously discussed.[19] Generally, a pronounced preference for outward rotation is observed in the case of electron-donating substituents borne by the benzocyclobutene.

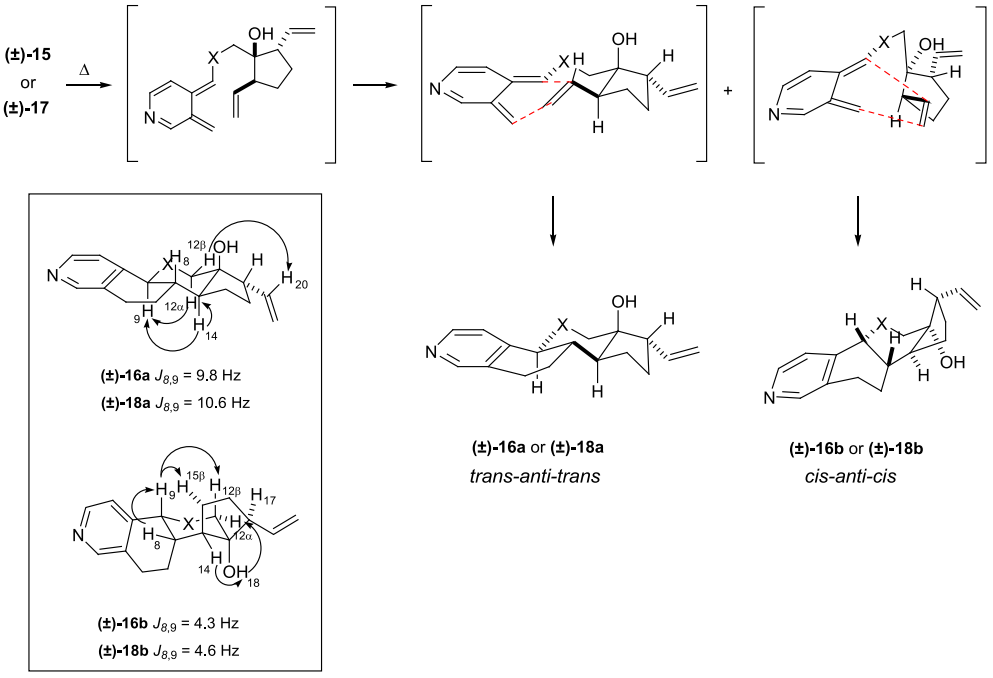
The relative stereochemistry of our new dihetero steroids **16** and **18** has been determined by a series of 1D NMR, COSY and NOESY experiments (400 MHz). The steroids **16a**/**18a** and **16b**/**18b** have, respectively, a *trans-anti-trans* and a *cis-anti-cis* ring fusion. Interestingly, in the two cases the main product **16a**/**18a** matches the *trans-anti-trans* ring fusion configuration of natural products. Phase mode NOESY experiments (Scheme 6) confirm the vicinal relationship between the axial protons H-(9), H-(14), H-(12$\alpha$) of the tetracycle **16a** or **18a**, indicating the C/D trans ring junction. No cross peak has been observed between H-(8) and H-(14). On the other hand, the trans relationship between H-(8) and H-(9) was confirmed by the vicinal coupling constant $^{3}J_{H(8)-H(9)}$ of the order of 10 Hz. The cycloadducts **16a** and **18a** result from an *exo* approach of the (*E*)-*o*-xylylene intermediate during the cyclization.

In the case of **16b** or **18b**, NOESY cross peaks have been observed between H-(15$\beta$), H-(9) and H-(12$\beta$). A similar interaction proved the *syn* relationship H-(14) and OH-(18). Finally, the doublet signal of H-(9) corresponds to a cis relationship with H-(8) ($J \sim 4.5$ Hz). The steroid **16b** or **18b**, which exhibits *cis-anti-cis* ring fusion stereochemistry comes from a cycloaddition process involving the vinyl group *syn* to the benzocyclobutene moiety. This steroid could result from an *endo* approach of the (*E*)-*o*-xylylene intermediate.

It is worth pointing out the similarity of the results between 11-hetero steroids and 3,11-dihetero steroids. The isomer's ratio observed by introducing a heteroatom at the three-position is quite the same (Schemes 3–5), and on top of that in favour of the isomer matching the *trans-anti-trans* ring fusion of natural product. So, interesting is to note the good stereoselectivity of the thermolysis step, the relative configurations of five stereogenic centres were controlled during the cycloaddition process. To the best of our knowledge, there is no total synthesis of such compounds reported in the literature.

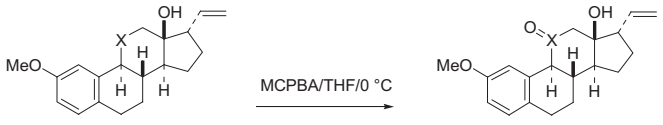
Having achieved the stereoselective formation of the steroid carbocyclic framework, we turned then our attention to the introduction of an acetyl group present in numerous steroids at the C-17 position. Wacker-type oxidation is well established as a synthetic organic reaction.[20]

As reported previously on thia steroids[21] and more recently on selena[9] steroids **11** and tellura[10] steroids **12**, the Wacker-type oxidation applied on these compounds always failed to give the desired ketone. To overcome this problem, selenium or tellurium atoms were firstly oxidized using common oxidants[22] before doing the Wacker oxidation. So, we undertook several attempts on steroids **11a** and **12a**, matching the *trans-anti-trans* ring fusion of natural products. Thus, fair yields (15–30%) were obtained with hydrogen peroxide ($H_2O_2$/$CH_3COOH$/0 °C), *tert*-butyl hydroperoxide (*t*-BuOOH/EtOH/0 °C) or



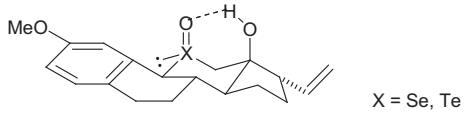

**Scheme 6.** Stereochemistry of major and minor isomers **16** and **18**.

ozone ($O_3$/−80 °C). On the other hand, oxidation of selenide **11a** and telluride **12a** to the corresponding selenoxide **19** and telluroxide **20** was effected with MCPBA[23] at low temperature in good yields. And (Scheme 7) to undergo clean oxidation, it was necessary to use THF rather than $CH_2Cl_2$ as the solvent.




**Scheme 7.** Synthesis of selenoxide **19** and telluroxide **20**.

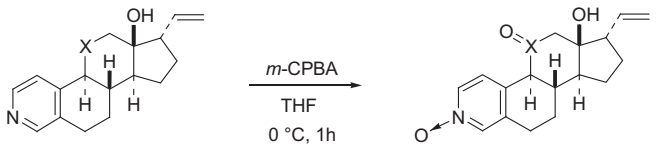
It is worth pointing out that no elimination reaction occurred and our selenoxides were stables. Moreover, we observed the formation of only one isomer, which is the axial isomer. Indeed, this result was not surprising since our steroids possess a hydroxyl substituent at the 13β position. So, we are in the case in which the oxygen atom of the selenoxide or telluroxide gave a hydrogen bond with a close acidic hydrogen atom (Scheme 8). Interesting is also to note that similar results of oxidation were obtained for the two series.




**Scheme 8.** Stereochemistry of **19** and **20**.

In the case of dihetero steroids **16a** and **18a** (Scheme 9), during this reaction the nitrogen atom of the pyridyl ring was also oxidized. Thus, the use of 3-chloroperbenzoic acid in THF at 0 °C led to the corresponding *N*-oxide steroids **21** and **22** in good yields. Here too, a single product was observed. We are in the same conditions as those described above for the aromatic analogous.

Selenoxides **19** and **21** and telluroxides **20**, **22** showed the characteristic spectroscopic data (see Experimental section). In particular, in the $^{13}C$ NMR spectra, carbons (C-9 and C-12) bearing




**Scheme 9.** Synthesis of selenoxide **21** and telluroxide **22**.

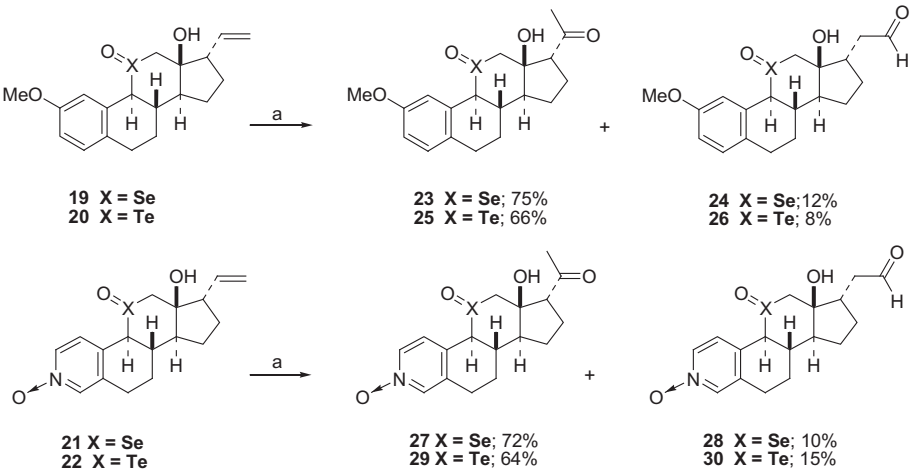
the heteroatom are deshielded on passing from selenides or tellurides to the corresponding selenoxides or telluroxides.

Having transformed our steroids into their corresponding oxides, we turned then our attention to the Wacker-type oxidation. Indeed, terminal olefins can be regarded as masked methyl ketones. The Wacker process, using palladium acetate/benzoquinone in the presence of perchloric acid,[24] was first applied to 11-hetero steroids **19** and **20**, and then to 3,11-dihetero steroids **21** and **22** matching the *trans-anti-trans* ring fusion of natural products (Scheme 10). Thus, in the two cases, oxidation of the 17α-vinyl groups according to the Miller and Wayner procedure, afforded the expected 17α-acetyl derivatives in good yields. However, minor amounts of the unexpected terminal aldehydes resulting from an *anti*-Markovnikov hydroxypalladation were obtained besides ketones.[25]

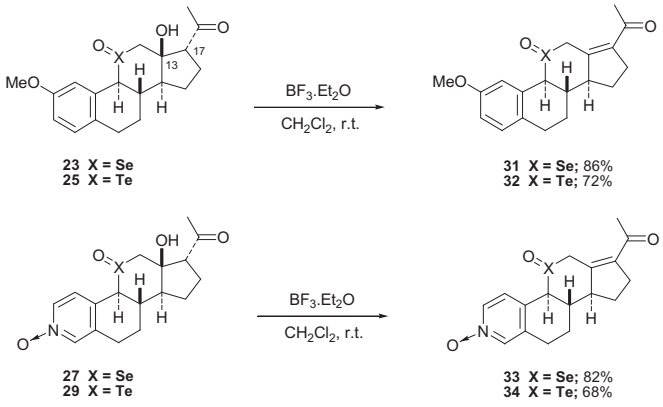
Finally, in order to develop novel steroids matching various functionalities, and particularly to introduce different substituents at C-13 via conjugate additions, we decided to create an unsaturation between C-13 and C-17 (Scheme 11). Thus, reaction of steroids **23**, **25**, **27** and **29** with $BF_3 \cdot Et_2O$[26] in dichloromethane led to the corresponding α,β-unsaturated ketones **31**, **32**, **33** and **34**, respectively, in good yields.

## 3. Conclusion

In summary, we have shown herein that our strategy is compatible with the synthesis of a wide range of steroids and particularly steroids possessing a pyridine as an A ring and a selenium or a tellurium atom in a biologically important position of the steroidal skeleton. Otherwise, the functionalisation realized on our




**Scheme 10.** Wacker-type oxidation of selenoxides and telluroxides.




**Scheme 11.** Synthesis of α,β-unsaturated ketones **31**, **32**, **33** and **34**.

steroids allows us to envisage the introduction of numerous functionalities and particularly a methyl group at C-13. We are currently pursuing our research towards more complex target systems.

## 4. Experimental section

### 4.1. General

All reactions were performed under an argon atmosphere in oven-dried glassware. Dichloromethane was freshly distilled from $P_2O_5$ and tetrahydrofuran (THF) over sodium/benzophenone. Other reagents and solvents were obtained from commercial sources and used as received. Flash column chromatography (FC): Merck 230–400 mesh silica gel; EtOAc, $Et_2O$ and petroleum ether as eluents. Thin-layer chromatography (TLC): *Macherey–Nagel* silica gel UV254 analytical plates; detection either with UV, or by dipping in revealing solution. $^1H$ and $^{13}C$ NMR spectra were recorded at 25 °C in $CDCl_3$ solutions at 500 or 300, and 125 or 75 MHz, respectively, using a Bruker Advance DPX 500 or AC300 spectrometers. Chemical shift $\delta$ in parts per million relative to $CDCl_3$ (signals for residual $CHCl_3$ in the $CDCl_3$: 7.24 ppm for $^1H$ NMR and 77.16 ppm (central) for $^{13}C$ NMR).

(±)-1-*Chloromethyl*-2,5-*divinylcyclopentol*[27] **14** and 1-*iodo*-5-*methoxybenzocyclo-butene*[28] **7** are prepared according to the previously described procedure.

*4.1.1. 4-Azabenzocyclobuten-1-one (**2**).* A mixture of 3-bromopyridine (1 equiv), lithium hexamethyl disilazide (LiHMDS) (2 equiv) and 2-methylen-1,3-dioxepane (2 equiv) in THF (approximatively 3 mL/mmol of bromopyridine) was stirred at reflux. The reaction was monitored by TLC. The reaction mixture was allowed to cool to room temperature and poured carefully onto crushed ice. The product was extracted with ether and the combined ether extracts were then washed with water and brine and dried over anhydrous $MgSO_4$. Removal of the solvent left a brown oil. Hydrolysis of the ketal was effected by stirring the brown oil in a THF/water/HCl mixture (89/10/1) until completion of the reaction (TLC). The residue was diluted and extracted with $CH_2Cl_2$. The combined extracts were then washed with water and brine and dried over anhydrous $MgSO_4$. Removal of the solvent and purification by flash chromatography (petroleum ether/ethyl acetate: 5/5) afforded the pure azabenzocyclobutenone (55% yield for the two steps) as a colourless oil. IR (film, $cm^{-1}$): 2965, 1732, 1456. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=8.89 (1H, s), 8.72 (1H, d, $J$=4.7 Hz), 7.15 (1H, d, $J$=4.7 Hz), 4.11 (2H, s). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$=187.7, 155.7, 149.3, 145.9, 144.9, 113.5, 53.5. HRMS (EI): calcd for $C_7H_5NO$ 119.0371, found 119.0374.

*4.1.2. 4-Azabenzocyclobuten-1-ol (**3**).* A flask equipped with a magnetic stirring bar and an argon outlet was charged with $NaBH_4$ (1.27 g, 33.6 mmol) and absolute ethanol. The solution was cooled at −20 °C and then the azabenzocyclobutenone **2** (4 g, 26 mmol) was added. After completion of the reaction (TLC), it was quenched by the addition of aqueous saturated $NH_4Cl$ and extracted with $CH_2Cl_2$ (3×20 mL). The extracts were dried over $MgSO_4$, filtered and then concentrated under vacuum. The residue was chromatographed on silica gel (diethyl ether: 100%) to give pure alcohol **3** (3.6 g, 90% yield) as an oil. IR (film, $cm^{-1}$): 3385, 2923, 1604, 1470. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=8.28 (1H, d, $J$=4.5 Hz), 8.14 (1H, s), 7.08 (1H, dd, $J$=4.5, 1.2 Hz), 5.28 (1H, dd, $J$=4.7, 1.9 Hz), 3.62 (1H, dd, $J$=14.5, 4.7 Hz), 3.11 (1H, d, $J$=14.5 Hz). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$=158.3, 147.3, 143.5, 138.8, 117.6, 70.8, 41.7. HRMS (EI): calcd for $C_7H_7NO$ 121.0528, found 121.0530.

*4.1.3. Mesylate of 4-azabenzocyclobuten-1-yle (**4**).* A solution of **3** (0.56 g, 4.62 mmol) in anhydrous $CH_2Cl_2$ (10 mL) was cooled to −10 °C and $NEt_3$ freshly distilled (1.3 mL, 9.24 mmol) and mesyl chloride (0.54 mL, 6.93 mmol) were added. After stirring 1 h, the mixture was hydrolysed with water and extracted with $CH_2Cl_2$ (3×20 mL). The organic layer was washed with a saturated solution

of NaCl (10 mL), dried over $MgSO_4$ and then concentrated under vacuum. The residue was chromatographed on silica gel (AcOEt: 100%) to afford 0.71 g (77% yield) of **4** as a solid. Mp=110 °C; IR (film, $cm^{-1}$): 2931, 1601, 1476. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=8.62 (1H, d, $J$=4.7 Hz), 8.47 (1H, s), 7.26 (1H, dd, $J$=4.7, 1.3 Hz), 5.91 (1H, dd, $J$=4.5, 1.9 Hz), 3.84 (1H, dd, $J$=14.9, 4.5 Hz), 3.55 (1H, d, $J$=14.9 Hz). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$=151.3, 148.8, 144.5, 138.1, 118.4, 73.8, 39.3, 38.5. HRMS (EI): calcd for $C_8H_9NO_3S$ 199.0303, found 199.0307.

*4.1.4. 1-Iodo-4-azabenzocyclobutene (**5**).* To a stirred solution of mesylate **4** (1.36 g, 6.82 mmol) in anhydrous acetone (30 mL) under argon was added NaI (2.04 g, 13.64 mmol). The mixture was stirred 24 h at reflux then cooled to room temperature, filtered over Celite and concentrated under vacuo. The residue was purified by flash chromatography on silica gel (diethyl ether: 100%) to give **5** (1.27 g, 81% yield) as a yellowish solid. Mp=62 °C; IR (film, $cm^{-1}$): 2925, 1607, 1586. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=8.57 (1H, d, $J$=4.8 Hz), 8.28 (1H, s), 7.02 (1H, d, $J$=4.8 Hz), 5.46 (1H, dd, $J$=4.7, 2.1 Hz), 4.00 (1H, dd, $J$=15.0, 4.7 Hz), 3.56 (1H, d, $J$=15.0 Hz). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$=156.4, 149.1, 143.8, 138.3, 117.5, 44.7, 11.1. HRMS (EI): calcd for $C_7H_6IN$ 230.9545, found 230.9548.

*4.1.5. (±)-1-Iodomethyl-2,5-divinylcyclopentol (**9**).* To a stirred solution of alcohol **14** (1.5 g, 8 mmol) in anhydrous acetone (30 mL) under argon was added NaI (2.4 g, 13.64 mmol). The mixture was stirred 24 h at reflux then cooled to room temperature, filtered over Celite and concentrated under vacuo. The residue was purified by flash chromatography on silica gel (diethyl ether: 100%) to give **9** (1.95 g, 88% yield) as a yellowish solid. Mp=123 °C; IR (film, $cm^{-1}$): 3410, 2960, 1362, 1064. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=5.74 (m, 2H), 5.03 (m, 2H), 3.21 (m, 2H), 2.28 (m, 2H), 2.04 (br s, 1H), 1.65 (m, 2H), 1.38 (m, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$=137.6, 137.2, 116.1, 115.9, 84.7, 52.9, 51.6, 27.9, 25.1, 15.2. HRMS (EI): calcd for $C_{10}H_{15}IO$ 278.0168, found 278.0171.

*4.1.6. (±)-1-Selenocyanomethyl-2,5-divinylcyclopentanol (**6**).* Iodhydrine **9** (0.5 g, 1.8 mmol) and potassium selenocyanate (0.27 g, 1.8 mmol) in acetone (30 mL) were heated under reflux for 24 h. After evaporation of the solvent, the product was dissolved in diethyl ether (20 mL). The solution was washed with saturated brine and with water (10 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent left a residue, which was chromatographed on silica gel, eluted with petroleum ether/diethyl ether: 7/3. Compound **6** was isolated in 53% yield (0.24 g) as an oil. IR (film, $cm^{-1}$): 3348, 2931, 2150, 1651, 1386. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=5.76 (m, 2H), 5.04 (m, 2H), 2.32 (m, 2H), 2.02 (br s, 1H), 1.60 (s, 2H), 1.65 (m, 2H), 1.40 (m, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$=138.2, 137.4, 116.3, 115.7, 101.4, 81.5, 66.9, 53.6, 50.6, 28.6, 24.2. HRMS (EI): calcd for $C_{11}H_{15}NOSe$ 257.0319, found 257.0325.

*4.1.7. (±)-1-(4-Methoxybenzocyclobuteneselanylmethyl)-2,5-divinylcyclopentanol (**8**).* Selenocyanate (1.32 mmol, 0.2 g) derivative **6** was dissolved in anhydrous EtOH (5 mL), under argon. The solution was cooled at 0 °C and $NaBH_4$ (0.04 g, 4.36 mmol) was added. After stirring at this temperature for 4 h, 0.49 g (4.36 mmol) of *t*-BuOK and 4.71 mmol of 1-iodobenzocyclobutene **7** was added. After stirring at room temperature for 24 h, the resulting mixture was hydrolysed with a saturated solution of $NH_4Cl$ (20 mL). The aqueous layer was extracted with $Et_2O$ (3×25 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/ether: 9.5/0.5) to afford **8** (0.82 g, 62% yield) as an oil. IR (film, $cm^{-1}$): 3447, 2940, 2128, 1608. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=6.95 (d, $J$=8.2 Hz, 1H), 6.78 (d, $J$=2.0 Hz, 1H), 6.59 (dd, $J$=8.2, 2.0 Hz, 1H), 5.64 (m, 2H), 5.05 (m, 4H), 3.69 (s, 3H), 3.12–2.90 (m, 3H), 2.43 (m, 2H), 1.72–1.38 (m, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$=159.8, 146.2, 138.9, 137.7, 134.1, 124.1, 116.8, 116.5, 115.8, 107.5, 82.7, 55.4, 54.3, 51.3, 44.2, 39.0, 38.4, 28.9, 27.8. HRMS (EI): calcd for $C_{19}H_{24}O_2Se$ 364.0942, found 364.0947.

*4.1.8. (±)-1-(4-Methoxybenzocyclobutenetellanylmethyl)-2,5-divinylcyclopentanol (**10**).* A mixture of powdered tellurium (130 mg, 1.02 mmol), Rongalite (sodium hydroxy-methane sulfinate) (340 mg) and aqueous sodium hydroxide (70 mg in 1 mL of water) was stirred at 60 °C for 2 h under argon, to produce sodium telluride. The wine-coloured solution was evaporated to dryness under reduced pressure. To the pale-yellow residue was added a solution of iodhydrine **9** (100 mg, 0.36 mmol) in dry ethanol (2 mL). The mixture was heated under reflux for 24 h, then 1-iodo-5-methoxybenzocyclobutene **7** was added (0.12 g, 0.46 mmol) and heated under reflux 24 h. The reaction was quenched by the addition of a 10% ammonium sulfate solution (5 mL), and the organic layer was extracted with diethyl ether (3×20 mL). The ethereal extract was washed with water (10 mL), dried over anhydrous sodium sulfate, and evaporated, to give crude cyclobutene **10**, which was stored under an argon atmosphere. This latter was used in the following step without further purification. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=7.02 (d, $J$=8.1 Hz, 1H), 6.76 (d, $J$=2.0 Hz, 1H), 6.64 (dd, $J$=8.1, 2.0 Hz, 1H), 5.58 (2H, m), 5.01 (4H, m), 3.68 (s, 3H), 3.10–2.85 (m, 3H), 2.45 (m, 2H), 1.68–1.36 (m, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$=157.8, 142.2, 136.9, 137.0, 128.7, 128.6, 115.8, 115.6, 112.8, 109.5, 81.9, 55.6, 54.6, 51.1, 44.6, 39.1, 27.9, 27.6, 25.4.

*4.1.9. (±)-1-(4-Azabenzocyclobuteneselanylmethyl)-2,5-divinylcyclopentanol (**15**).* Compound **6** (1.32 mmol, 0.3 g) was dissolved in anhydrous EtOH (5 mL) under argon. The solution was cooled at 0 °C and $NaBH_4$ (0.06 g, 1.59 mmol) was added. After stirring at this temperature for 4 h, 0.18 g (1.59 mmol) of *t*-BuOK and 1.72 mmol of azabenzocyclobutene **5** were added. After stirring at room temperature for 24 h, the resulting mixture was hydrolysed with a saturated solution of $NH_4Cl$ (10 mL). The aqueous layer was extracted with $Et_2O$ (3×25 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/ether: 9.5/0.5) to afford **15** (0.25 g, 58% yield) as an oil. IR (film, $cm^{-1}$): 3447, 2940, 2128, 1608. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=8.46 (1H, d, $J$=4.8 Hz), 8.24 (1H, d, $J$=2.0 Hz), 7.05 (1H, d, $J$=4.8 Hz), 5.74 (m, 2H), 5.02 (m, 4H), 4.54 (1H, dd, $J$=5.1, 2.4 Hz), 3.58 (1H, dd, $J$=12.8 Hz), 3.14 (1H, dd, $J$=14.6 Hz), 2.73 (1H, d, $J$=12.8 Hz), 2.54 (1H, m), 2.35 (1H, m), 2.13–1.41 (4H, m). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$=155.5, 148.1, 143.3, 139.2, 138.6, 137.4, 117.0, 115.9, 82.8, 54.2, 54.6, 45.6, 39.3, 38.5, 28.6, 27.4. HRMS calcd for $C_{17}H_{21}NOSe$ 335.0788, found 335.0793.

*4.1.10. (±)-1-(4-Azabenzocyclobutenetellanylmethyl)-2,5-divinylcyclopentanol (**17**).* Using the same procedure described above for compound **10**, reaction of 1 g (3.6 mmol) of **9** and 1 g (4.3 mmol) of **5** gave, after purification, 0.3 g (22%) of **17** as an oil. IR (film, $cm^{-1}$) 3447, 2940, 1608. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$=8.52 (d, $J$=6.1 Hz, 1H), 8.48 (br s, 1H), 7.19 (d, $J$=6.1 Hz, 1H), 5.65 (2H, m), 5.03 (4H, m), 3.68 (s, 3H), 3.12–2.88 (m, 3H), 2.25 (m, 2H), 1.62–1.38 (6H, m). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$=152.4, 148.8, 146.2, 138.9, 137.6, 135.5, 117.9, 117.7, 115.6, 82.3, 54.6, 52.3, 45.3, 39.1, 38.2, 28.6, 27.4.

### 4.2. Experimental procedure for the preparation of 16 and 18

A solution of **15** or **17** (3 mmol) in *o*-xylene (40 mL) was stirred under argon at 130 °C. The progress of the reaction was followed by TLC analysis. After cooling at room temperature, the solvent was removed under reduced pressure (1 mmHg). The resulting oil was purified by flash chromatography on silica gel (petroleum ether/diethyl ether: 1/1 to 2/8).

*4.2.1. (±)-(8β,9α,14α)-3-Aza-17α-vinyl-11-selenagona-1,3,5(10)-trien-13β-ol (**16a**).* Yield, 0.6 g (63%). Oil. IR (film, $cm^{-1}$): 3352, 2981, 1370, 1048. $^1H$ NMR (300 MHz, $CDCl_3$): δ=8.29 (br s, 2H), 7.41 (d, *J*=5.1 Hz, 1H), 5.61 (m, 1H), 5.00 (m, 2H), 3.64 (d, *J*=10.9 Hz, 1H), 3.26 (s, 1H), 2.95 (d, *J*=13.4 Hz, 1H), 2.77 (m, 3H), 2.68 (d, *J*=13.4 Hz, 1H), 2.17 (m, 1H), 2.01 (m, 1H), 1.82 (m, 2H), 1.56 (m, 4H), 1.43 (m, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=150.9, 147.6, 144.0, 139.6, 132.5, 122.4, 116.1, 76.8, 53.6, 51.2, 47.8, 42.1, 40.2, 28.2, 27.4, 26.9, 26.4. HRMS (EI): calcd for $C_{17}H_{21}NOSe$ 335.0788, found 335.0792.

*4.2.2. (±)-(8β,9β,14α)-3-Aza-17α-vinyl-11-selenagona-1,3,5(10)-trien-13α-ol (**16b**).* Yield, 90 mg (9%). Oil. IR (film, $cm^{-1}$): 3353, 2982, 1374, 1038. $^1H$ NMR (300 MHz, $CDCl_3$): δ=8.39 (d, *J*=5.2 Hz, 1H), 8.31 (s, 1H), 7.85 (d, *J*=5.2 Hz, 1H), 5.29 (m, 1H), 4.88 (m, 2H), 3.76 (d, *J*=4.3 Hz, 1H), 2.76 (m, 2H), 2.65 (td, *J*=9.0, 2.9 Hz, 1H), 2.46 (m, 1H), 2.37 (d, *J*=13.5 Hz, 1H), 2.32 (d, *J*=13.5 Hz, 1H), 2.12 (m, 1H), 2.03 (m, 1H), 1.92 (m, 1H), 1.87 (m, 1H), 1.57 (m, 1H), 1.34 (m, 1H), 1.29 (td, *J*=11.9, 7.4 Hz, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=150.2, 147.7, 144.4, 139.1, 131.5, 123.1, 115.5, 76.7, 53.6, 42.1, 41.8, 37.2, 35.3, 27.3, 26.7, 26.3, 25.6. HRMS (EI): calcd for $C_{17}H_{21}NOSe$ 335.0788, found 335.0794.

*4.2.3. (±)-(8β,9α,14α)-3-Aza-17α-vinyl-11-telluragona-1,3,5(10)-trien-13β-ol (**18a**).* Yield, 0.53 g (46%). Oil. IR (film, $cm^{-1}$): 3352, 2981, 1370, 1048. $^1H$ NMR (300 MHz, $CDCl_3$): δ=8.36 (d, *J*=4.9 Hz, 1H), 8.31 (br s, 1H), 7.41 (d, *J*=4.9 Hz, 1H), 5.61 (m, 1H), 5.02 (m, 2H), 3.89 (d, *J*=10.0 Hz, 1H), 2.82 (m, 2H), 2.70 (m, 1H), 2.24 (m, 1H), 2.01 (m, 1H), 1.86 (m, 2H), 1.65 (d, *J*=11.4 Hz, 1H), 1.53 (m, 4H), 1.32 (d, *J*=11.4 Hz, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=150.0, 147.4, 145.1, 138.6, 131.1, 119.6, 115.3, 75.3, 50.6, 49.1, 39.8, 32.6, 28.5, 27.2, 25.2, 24.9, 24.8. HRMS (EI): calcd for $C_{17}H_{21}NOTe$ 385.0685, found 385.0692.

*4.2.4. (±)-(8β,9β,14α)-3-Aza-17α-vinyl-11-telluragona-1,3,5(10)-trien-13β-ol (**18b**).* Yield, 0.1 g (9%). Oil. IR (film, $cm^{-1}$) 3353, 2982, 1374, 1038. $^1H$ NMR (300 MHz, $CDCl_3$): δ=8.37 (d, *J*=4.5 Hz, 1H), 8.33 (s, 1H), 7.45 (d, *J*=4.5 Hz, 1H), 5.89 (m, 1H), 5.15 (m, 2H), 3.97 (d, *J*=4.6 Hz, 1H), 2.79 (m, 2H), 2.66 (m, 1H), 2.13 (m, 1H), 1.94 (m, 3H), 1.68 (d, *J*=11.2 Hz, 1H), 1.48 (m, 4H), 1.25 (d, *J*=11.2 Hz, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=150.0, 147.4, 145.1, 138.6, 131.1, 119.6, 115.3, 75.3, 50.6, 49.1, 39.8, 32.6, 28.5, 27.2, 25.2, 24.9, 24.8. HRMS (EI): calcd for $C_{17}H_{21}NOTe$ 385.0685, found 385.0691.

### 4.3. Experimental procedure for the preparation of selenoxides 16, 18 and telluroxides 20, 22

Compounds **11a**, **12a**, **16a** and **18a** (2.6 mmol) were dissolved in anhydrous THF (15 mL), under argon. The solution was cooled at 0 °C and *m*-CPBA (1.28 g, 5.2 mmol) was added. After stirring at this temperature for 1 h, the mixture was hydrolysed with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with $CH_2Cl_2$ (3×25 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (typically eluting with petroleum ether/ethyl acetate: 9/1 to 8/2) to give a major diastereoisomer 19β, 20β, 21β, or 22β.

*4.3.1. (±)-(8β,9α,14α)-2-Methoxy-17α-vinyl-11-selenagona-1,3,5(10)-trien-13β-ol-11-oxide (**19**).* Yield, 0.9 g (92%). Oil. IR (neat) 3401, 2927, 1610, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 7.05 (d, *J*=2.5 Hz, 1H), 7.04 (d, *J*=8.2 Hz, 1H), 6.75 (dd, *J*=2.5, 8.2 Hz, 1H), 5.66 (br s, 1H), 5.58 (m, 1H), 5.02 (m, 2H), 3.74 (s, 3H), 3.48 (d, *J*=10.4 Hz, 1H), 2.70 (m, 3H), 1.80 (m, 8H), 1.46 (d, *J*=14.2 Hz, 1H), 1.31 (d, *J*=14.2 Hz, 1H). $^{13}C$ NMR ($CDCl_3$): 158.4, 138.6, 138.4, 131.1, 130.8, 116.3, 113.8, 112.4, 78.9, 64.5, 55.3, 55.2, 51.5, 43.5, 37.5, 28.4, 27.3, 26.5, 25.2. HRMS (EI): calcd for $C_{19}H_{24}O_3Se$ 380.0891, found 380.0895.

*4.3.2. (±)-(8β,9α,14α)-2-Methoxy-17α-vinyl-11-telluragona–1,3,5(10)-trien-13β-ol-11-oxide (**20**).* Yield, 0.95 g (85%). Oil. IR (neat) 3401, 2927, 1610, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 7.03 (d, *J*=8.2 Hz, 1H), 6.95 (d, *J*=2.6 Hz, 1H), 6.82 (dd, *J*=2.6, 8.2 Hz, 1H), 5.78 (m, 1H), 5.22 (m, 2H), 3.76 (s, 3H), 3.87 (d, *J*=10.6 Hz, 1H), 2.75 (m, 3H), 1.80 (m, 8H), 1.54 (d, *J*=12.8 Hz, 1H), 1.36 (d, *J*=12.8 Hz, 1H). $^{13}C$ NMR ($CDCl_3$): 157.3, 139.8, 137.6, 130.2, 128.8, 115.7, 114.8, 111.4, 76.8, 67.5, 55.9, 55.0, 53.6, 42.6, 36.2, 28.1, 27.6, 26.6, 22.2. HRMS (EI): calcd for $C_{19}H_{24}O_3Te$ 430.0788, found 430.0792.

*4.3.3. (±)-(8β,9α,14α)-3-Aza-17α-vinyl-11-selenagona-1,3,5(10)-trien-13β-ol-11-oxide (**21**).* Yield, 0.82 g (86%). Oil. IR (neat) 3353, 2982, 1374, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 8.16 (d, *J*=1.2 Hz, 1H), 8.02 (dd, *J*=1.2, 6.9 Hz, 1H), 7.86 (d, *J*=6.9 Hz, 1H), 5.72 (1H, m), 4.96 (2H, m), 3.36 (d, *J*=11.1 Hz, 1H), 3.28 (d, *J*=13.9 Hz, 1H), 3.16 (d, *J*=13.9 Hz, 1H), 2.69 (2H, m), 2.32 (2H, m), 1.95 (2H, m), 1.88 (1H, m), 1.56 (1H, m), 1.38 (3H, m). $^{13}C$ NMR ($CDCl_3$): 140.0, 138.9, 137.4, 136.9, 125.6, 124.3, 116.1, 78.0, 63.1, 54.6, 48.7, 37.2, 35.1, 27.6, 26.4, 24.4, 24.9. HRMS calcd for $C_{17}H_{21}NO_3Se$ 367.0687, found 367.0691.

*4.3.4. (±)-(8β,9α,14α)-3-Aza-17α-vinyl-11-telluragona-1,3,5(10)-trien-13β-ol-11-oxide (**22**).* Yield, 0.84 g (78%). Oil. IR (neat) 3353, 2982, 1374, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 7.96 (1H, d, *J*=7.2 Hz), 7.90 (1H, s), 7.38 (1H, d, *J*=7.2 Hz), 5.65 (1H, m), 5.01 (2H, m), 4.04 (1H, d, *J*=11.5 Hz), 2.81 (2H, m), 1.44 (4H, m), 2.68 (1H, m), 1.83 (2H, m), 1.72 (1H, d, *J*=11.2 Hz), 1.48 (1H, d, *J*=11.2 Hz), 1.61 (2H, m). $^{13}C$ NMR ($CDCl_3$): 141.4, 139.2, 137.9, 136.1, 134.6, 124.1, 115.2, 76.6, 51.4, 48.2, 36.5, 32.7, 28.9, 27.4, 26.1, 24.7, 24.2. HRMS calcd for $C_{17}H_{21}NO_3Te$ 417.0584, found 417.0589.

### 4.4. General procedure for the Wacker-type oxidation

A 25 mL three-necked flash equipped with an argon inlet, a magnetic stirring bar and a septum cap was charged with Pd $(OAc)_2$ (0.02 g, 0.09 mmol) and benzoquinone (0.088 g, 0.82 mmol). A solution of $CH_3CN/H_2O$ (7/1) (10.2 mL) and $HClO_4$ (0.3 M) is added. The resulting solution was stirred at room temperature for 1 h and steroid **19**, **20**, **21** or **22** (0.9 mmol) is then added. The reaction mixture is stirred at this temperature for 2 h and hydrolysed with a NaOH solution (30%). The aqueous phase is extracted with ether, and the organic layers are dried ($MgSO_4$), filtered and evaporated. After purification by flash chromatography, the corresponding ketones **23** ($CH_2Cl_2$/MeOH: 99/1 to 95/5), **25** ($CH_2Cl_2$/MeOH: 97/3), **27** ($CH_2Cl_2$/MeOH: 99/1) or **29** ($CH_2Cl_2$/MeOH: 95/5 to 9/1) and aldehydes **24**, **26**, **28** or **30** are obtained.

*4.4.1. (±)-(8β,9α,14α)-2-Methoxy-17α-acetyl-11-selenagona-1,3,5(10)-trien-13β-ol-11-oxide 23 from **19**.* Yield, 0.27 g (75%). Oil. IR (neat) 3317, 2930, 1703, 1609, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 7.03 (d, *J*=2.4 Hz, 1H), 7.02 (d, *J*=8.6 Hz, 1H), 6.75 (dd, *J*=2.4, 8.6 Hz, 1H), 5.80 (br s, 1H), 3.75 (s, 3H), 3.64 (d, *J*=10.9 Hz, 1H), 3.15 (dd, *J*=3.1, 9.6 Hz, 1H), 2.75 (m, 2H), 2.19 (s, 3H), 1.80 (m, 8H), 1.52 (d, *J*=14.1 Hz, 1H), 1.36 (d, *J*=14.1 Hz, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=210.8, 158.3, 131.2, 130.4, 129.6, 114.1, 112.2, 80.4, 64.1, 62.2, 55.2, 51.8, 43.6, 36.5, 30.3, 28.1, 26.6, 26.1, 22.7. HRMS (EI): calcd for $C_{19}H_{24}O_4Se$ 396.084, found 396.0843.

*4.4.2. (±)-(8β,9α,14α)-2-Methoxy-17α-(2-oxoethyl)-11-selenagona-1,3,5(10)-trien-13β-ol-11-oxide **24** from **19**.* Yield, 0.043 g (12%). IR (neat) 3431, 1638, 1264, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 9.71 (s, 1H), 7.24 (d, *J*=2.3 Hz, 1H), 7.03 (d, *J*=8.6 Hz, 1H), 6.76 (dd, *J*=2.3, 8.2 Hz, 1H), 5.69 (br s, 1H), 3.76 (s, 3H), 3.50 (d, *J*=11.3 Hz, 1H), 2.80 (m, 2H), 2.15 (m, 2H), 1.72 (m, 8H), 1.58 (d, *J*=13.7 Hz, 1H), 1.36 (d, *J*=13.7 Hz, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=201.2, 158.3, 131.0, 131.1, 130.4, 114.1, 112.3, 81.9, 64.6, 55.5, 51.6, 48.7, 47.5, 44.5, 30.6, 28.5, 27.9, 26.6, 23.8. HRMS (EI): calcd for $C_{19}H_{24}O_4Se$ 396.084, found 396.0843.

*4.4.3. (±)-(8β,9α,14α)-2-Methoxy-17α-acetyl-11-telluragona-1,3,5 (10)-trien-13β-ol-11-oxide **25** from **20**.* Yield, 0.265 g (66%). Oil. IR (neat) 2930, 1705, 1609, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 7.74 (d, *J*=2.1 Hz, 1H), 7.02 (d, *J*=8.5 Hz, 1H), 6.81 (dd, *J*=2.1, 8.5 Hz, 1H), 4.23 (br s, 1H), 4.15 (d, *J*=10.9 Hz, 1H), 3.76 (s, 3H), 3.18 (dd, *J*=2.8, 10.3 Hz, 1H), 2.82 (m, 2H), 2.19 (s, 3H), 1.85 (m, 8H), 1.58 (d, *J*=14.0 Hz, 1H), 1.34 (d, *J*=14.0 Hz, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=210.6, 158.2, 131.0, 130.5, 129.7, 114.0, 112.0, 81.4, 64.2, 62.1, 55.4, 51.9, 44.8, 34.9, 30.4, 28.5, 26.56, 26.2, 22.1. HRMS (EI): calcd for $C_{19}H_{24}O_4Te$ 446.0737, found 446.0743.

*4.4.4. (±)-(8β,9α,14α)-2-Methoxy-17α-(2-oxoethyl)-11-telluragona-1,3,5(10)-trien-13β-ol-11-oxide **26** from **20**.* Yield, 0.032 g (8%). Oil. IR (neat) 1640, 1265, 910, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 9.70 (s, 1H), 7.75 (d, *J*=2.4 Hz, 1H), 7.04 (d, *J*=8.5 Hz, 1H), 6.83 (dd, *J*=2.4, 8.5 Hz, 1H), 5.30 (br s, 1H), 3.77 (s, 3H), 3.90 (d, *J*=10.3 Hz, 1H), 2.84 (m, 2H), 2.28 (m, 2H), 1.83 (m, 8H), 1.56 (d, *J*=13.7 Hz, 1H), 1.32 (d, *J*=13.7 Hz, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=200.3, 157.9, 130.0, 130.3, 126.5, 115.4, 112.9, 79.4, 67.1, 59.1, 55.5, 50.7, 47.5, 42.8, 36.6, 28.9, 28.9, 26.7, 22.8. HRMS (EI): calcd for $C_{19}H_{24}O_4Te$ 446.0737, found 446.0744.

*4.4.5. (±)-(8β,9α,14α)-3-Aza-17α-acetyl-11-selenagona-1,3,5(10)-trien-13β-ol-11-oxide **27** from **21**.* Yield, 0.25 g (72%). Oil. IR (neat) 3424, 1709, 1269, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 8.13 (d, *J*=1.7 Hz, 1H), 8.07 (dd, *J*=1.7, 7.0 Hz, 1H), 7.89 (d, *J*=7.0 Hz, 1H), 3.53 (d, *J*=10.9 Hz, 1H), 3.15 (dd, *J*=2.5, 9.2 Hz, 1H), 2.74 (2H, m), 2.18 (3H, s), 1.72 (8H, m), 1.64 (d, *J*=13.8 Hz, 1H), 1.36 (d, *J*=13.8 Hz, 1H). $^{13}C$ NMR ($CDCl_3$): 210.2, 138.6, 137.3, 136.9, 125.8, 78.1, 63.9, 61.9, 59.8, 49.2, 34.4, 32.0, 26.1, 25.4, 25.0, 22.7. HRMS (EI): calcd for $C_{17}H_{21}NO_4Se$ 383.0636, found 383.0641.

*4.4.6. (±)-(8β,9α,14α)-3-Aza-17α-(2-oxoethyl)-11-selenagona-1,3,5 (10)-trien-13β-ol-11-oxide **28** from **21**.* Yield, 0.035 g (10%). Oil. IR (neat) 3430, 1640, 907, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 9.62 (s, 1H), 8.13 (d, *J*=1.7 Hz, 1H), 8.08 (dd, *J*=1.7, 7.0 Hz, 1H), 7.92 (d, *J*=7.0 Hz, 1H), 3.47 (d, *J*=11.1 Hz, 1H), 2.74 (m, 2H), 2.60 (m, 2H), 2.33 (m, 2H), 1.75 (m, 7H), 1.51 (d, *J*=13.8 Hz, 1H), 1.28 (d, *J*=13.8 Hz, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=202.8, 138.6, 136.4, 137.9, 125.6, 124.8, 78.3, 63.7, 59.5, 48.8, 48.0, 47.1, 34.7, 28.3, 26.5, 24.9, 22.6. HRMS (EI): calcd for $C_{17}H_{24}NO_4Se$ 383.0636, found 383.0639.

*4.4.7. (±)-(8β,9α,14α)-3-Aza-17α-acetyl-11-telluragona-1,3,5(10)-trien-13β-ol-11-oxide **29** from **22**.* Yield, 0.25 g (64%). Oil. IR (neat) 3425, 1708, 1265, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 8.11 (d, *J*=1.9 Hz, 1H), 8.07 (dd, *J*=1.9, 7.5 Hz, 1H), 7.89 (d, *J*=7.5 Hz, 1H), 3.18 (dd, *J*=2.8, 10.3 Hz, 1H), 3.13 (d, *J*=10.9 Hz, 1H), 2.84 (2H, m), 2.19 (3H, s), 1.76 (8H, m), 1.59 (d, *J*=13.7 Hz, 1H), 1.38 (d, *J*=13.7 Hz, 1H). $^{13}C$ NMR ($CDCl_3$): 209.9, 138.9, 137.6, 136.8, 126.1, 77.9, 64.2, 61.8, 59.5, 48.8, 34.6, 32.2, 26.4, 25.8, 25.2, 22.6. HRMS (EI): calcd for $C_{17}H_{21}NO_4Te$ 433.0533, found 433.0538.

*4.4.8. (±)-(8β,9α,14α)-3-Aza-17α-(2-oxoethyl)-11-telluragona-1,3,5 (10)-trien-13β-ol-11-oxide **30** from **22**.* Yield, 0.06 g (15%). Oil. IR (neat) 3430, 1640, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 9.72 (s, 1H), 8.15 (d, *J*=2.1 Hz, 1H), 8.06 (dd, *J*=2.1, 8.2 Hz, 1H), 7.91 (d, *J*=8.2 Hz, 1H), 3.17 (d, *J*=10.3 Hz, 1H), 2.81 (m, 2H), 2.29 (m, 3H), 1.76 (m, 9H), 1.56 (d, *J*=13.7 Hz, 1H), 1.31 (d, *J*=13.7 Hz, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=201.8, 138.9, 136.6, 137.8, 125.8, 124.3, 78.1, 63.2, 59.1, 48.2, 47.9, 47.2, 34.6, 28.1, 26.6, 24.3, 22.2. HRMS (EI): calcd for $C_{17}H_{21}NO_4Te$ 433.0533, found 433.0539.

### 4.5. Experimental procedure for the preparation of 31, 32, 33 and 34

A solution of **23**, **25**, **27** or **29** (0.5 mmol) and $BF_3{\cdot}Et_2O$ (1.5 mmol, 0.19 mL) in anhydrous $CH_2Cl_2$ (5 mL) was stirred under argon at room temperature during 12 h. The mixture was hydrolysed with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with $CH_2Cl_2$ (3×25 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/ethyl acetate: 6/4) to give **31**, **32**, **33** or **34**.

*4.5.1. (±)-(8β,9α,14α)-2-Methoxy-17-acetyl-11-selenagona-1,3,5 (10),13(17)-tetraene-11-oxide **31**.* Yield, 0.16 g (86%). Oil. IR (neat) 3432, 1692, 905, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 7.76 (d, *J*=2.6 Hz, 1H), 7.00 (d, *J*=8.5 Hz, 1H), 6.78 (dd, *J*=2.6, 8.5 Hz, 1H), 3.75 (s, 3H), 3.12 (d, *J*=11.1 Hz, 1H), 2.76 (m, 5H), 2.32 (m, 1H), 2.21 (s, 3H), 2.18 (d, *J*=15.5 Hz, 1H), 2.08 (m, 2H), 1.86 (d, *J*=15.5 Hz, 1H), 1.72 (m, 1H), 1.43 (m, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=197.8, 157.7, 142.3, 139.2, 130.8, 130.4, 126.6, 115.5, 113.4, 65.6, 55.2, 54.7, 52.2, 44.3, 33.2, 30.6, 28.8, 27.3, 27.1. $C_{19}H_{22}O_3Se$ (378.07): C 60.48, H 5.88; found C 60.09, H 6.12.

*4.5.2. (±)-(8β,9α,14α)-2-Methoxy-17-acetyl-11-telluragona-1,3,5 (10),13(17)-tetraene-11-oxide **32**.* Yield, 0.15 g (72%). Oil. IR (neat) 3385, 1696, 1610, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 8.05 (d, *J*=8.7 Hz, 1H), 6.75 (dd, *J*=2.8, 8.7 Hz, 1H), 6.65 (d, *J*=2.8 Hz, 1H), 3.76 (s, 3H), 3.19 (d, *J*=10.9 Hz, 1H), 2.78 (m, 5H), 2.31 (m, 1H), 2.24 (s, 3H), 2.12 (d, *J*=15.1 Hz, 1H), 2.06 (m, 2H), 1.88 (d, *J*=15.1 Hz, 1H), 1.70 (m, 1H), 1.44 (m, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=197.9, 159.4, 142.5, 140.2, 139.4, 130.6, 117.8, 114.9, 112.9, 65.1, 55.2, 54.6, 52.4, 44.1, 33.0, 30.0, 29.8, 27.4, 26.3. $C_{19}H_{22}O_3Te$ (428.06): C 53.57, H 5.21; found C 53.12, H 5.76.

*4.5.3. (±)-(8β,9α,14α)-3-Aza-17-acetyl-11-selenagona-1,3,5(10),13 (17)-tetraene-11-oxide **33**.* Yield, 0.15 g (82%). Oil. IR (neat) 3509, 1690, 1510, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 8.09 (d, *J*=1.8 Hz, 1H), 8.07 (dd, *J*=1.8, 7.6 Hz, 1H), 7.82 (d, *J*=7.6 Hz, 1H), 2.98 (d, *J*=10.9 Hz, 1H), 2.78 (2H, m), 2.19 (3H, s), 2.09 (d, *J*=14.1 Hz, 1H), 1.87 (d, *J*=14.1 Hz, 1H), 1.75 (8H, m). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=196.8, 146.2, 141.9, 139.9, 138.2, 137.4, 137.1, 126.2, 54.9, 50.7, 48.2, 42.3, 33.6, 32.1, 29.8, 28.9, 25.3. $C_{17}H_{19}NO_3Se$ (365.05): C 56.05, H 5.26; found C 55.79, H 5.62.

*4.5.4. (±)-(8β,9α,14α)-3-Aza-17-acetyl-11-telluragona-1,3,5(10),13 (17)-tetraene-11-oxide **34**.* Yield, 0.14 g (68%). Oil. IR (neat) 3395, 2975, 1696, 820 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): 8.05 (d, *J*=1.6 Hz, 1H), 8.02 (dd, *J*=1.6, 7.5 Hz, 1H), 7.86 (d, *J*=7.5 Hz, 1H), 3.02 (d, *J*=11.1 Hz, 1H), 2.77 (2H, m), 2.18 (3H, s), 1.98 (d, *J*=14.4 Hz, 1H), 1.89 (d, *J*=14.4 Hz, 1H), 1.76 (8H, m). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ=196.5, 145.9, 142.0, 139.6, 138.3, 137.4, 137.1, 126.0, 54.1, 49.6, 46.2, 42.1, 33.4, 30.9, 29.1, 27.9, 25.6. $C_{17}H_{19}NO_3Te$ (415.04): C 49.45, H 4.64; found C 49.01, H 4.98.

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