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Diastereoselective routes towards the austrodorane skeleton based on pinacol rearrangement: synthesis of (+)-austrodoral and (+)-austrodoric acid

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Abstract—Efficient routes towards the austrodorane skeleton from the labdane diterpene (−)-sclareol (**22**) are described. The processes, based on pinacol rearrangement, take place with complete diastereoselectivity. Utilizing these, the marine nor-sesquiterpenes (+)-austrodoral (**1**) and (+)-austrodoric acid (**2**) have been prepared from **22**. Ketone **19**, a key intermediate in the synthesis of rearranged cytotoxic diterpene lactones, such as norrisolide (**3**), has also been prepared in moderate yield.

1. Introduction

Research into the chemical composition of marine organisms is one of the most exciting activities in the field of natural products chemistry, because of the incessant discovery of metabolites with novel chemical structures and potent biological activities.

Recently, Cimino's group reported the isolation of (+)-austrodoral (**1**) and the related (+)-austrodoric acid (**2**), with a new carbon skeleton, from the Antarctic nudibranch *Austrodoris kerguelenensis* (Fig. 1).[1] The unusual, rearranged perhydroindane moiety of this sesquiterpene skeleton, named 'austrodorane', is also present in the structure of the rearranged diterpene lactones norrisolide (**3**), a cytotoxic metabolite isolated from the nudibranch *Chromodoris norrisi*,[2] chromodorolides A (**4**) and B (**5**), found in the nudibranch *Chromodoris cavae*,[3] or the most recently reported chromodorolide C (**6**), isolated from an Aplysillid sponge.[4]

During the last few years, chemists have studied this type of marine metabolites not only because of their unusual

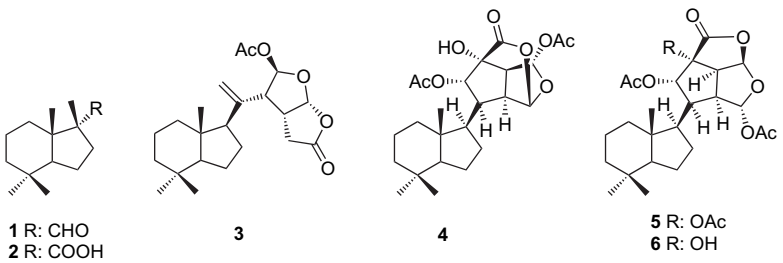

Figure 1. Austrodorane sesquiterpenes and structurally related spongiane diterpenes.

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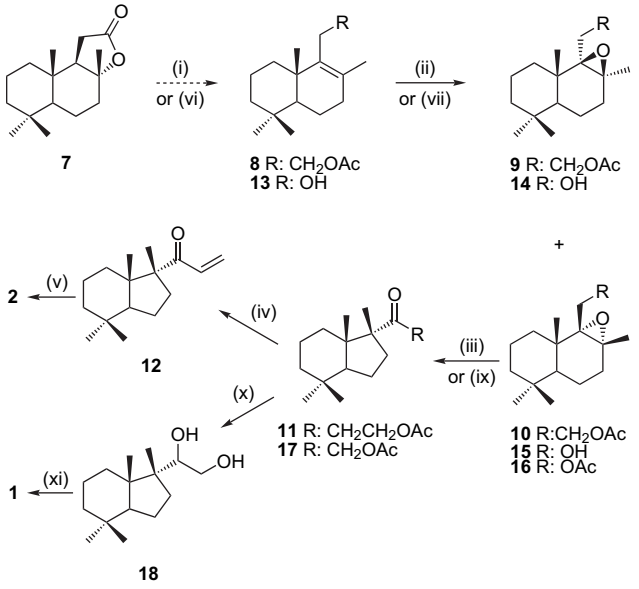
structures but also due to their biological properties and ecological significance. These substances, with toxic and antifeedant activities, are concentrated in the skin and constitute a 'chemical shell' possessed by the shell-less marine molluscs, named nudibranchs, against their natural predators.[5] Recent studies indicate that these metabolites are acquired from the nudibranch's diet, which generally includes sponges and bryozoans. Despite the still incompletely explored biology of this class of compounds, interesting biological properties including antifungal, antimicrobial, antifeedant, antitumour and PLA_2 inhibition, have been reported.[6]

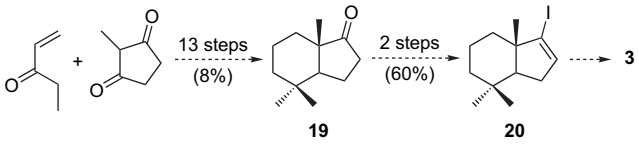
The scarcity of these metabolites in their natural sources and the observed fast degradation during the isolation of some of them, such as (+)-austrodoral (**1**), oblige us to develop suitable syntheses in order to study their structural and biological features. Cimino et al. developed a synthesis of (+)-austrodoric acid (**2**) starting from (+)-sclareolide (**7**). The key step was the rearrangement of epoxyester **10** to give ketoester **11** in 45% yield, after treatment with a complex Lewis acid, tris-(*p*-bromophenyl)-aminium-hexachloroantimonate; epoxidation of acetoxyalkene **8** led to a 3:1 mixture of stereoisomers **10** and **9** (Scheme 1).[7] After unsuccessful attempts to convert acid **2** into aldehyde **1**, these authors utilized a similar methodology to convert lactone **7** into (+)-austrodoral (**1**). The key step was again the isomerization of epoxyester **16** to ketoester **17**, which took place in good yields, under acidic conditions. In this case, epoxidation of drimane alcohol **13** gave a 3:1 mixture of stereoisomers **15** and **14** (Scheme 1).[8]



Scheme 1. Synthesis of austrodoral (**1**) and austrodoric acid (**2**) by Cimino's group. Reagents, conditions and yields: (i) Ref. 7, three steps (72% global yield); (ii) MCPBA, CH_2Cl_2, 0 °C, 1 h (90%); (iii) $RSbCl_6$, CH_2Cl_2, rt, 1 h (45%); (iv) NaH, THF, −78 °C→rt, 4 h (52%); (v) OsO_4, $NaIO_4$, *t*-BuOH, H_2O, 45 °C, 12 h (70%); (vi) Ref. 8, six steps (65% global); (vii) *o*-PPA, Et_2O, 0 °C, 12 h (75%); (viii) Ac_2O, pyridine, rt, 12 h (89%); (ix) $RSbCl_6$, CH_2Cl_2, rt, 2 h (87%) or FSO_3H, 2-nitropropane, −78 °C, 30 min (quant.); (x) $LiAlH_4$, Et_2O, rt, 3 h (98%); (xi) $NaIO_4$, THF, H_2O, rt, 3 h (quant.).

Publication of the above synthesis of (+)-austrodoric acid (**2**) prompted us to report our previous results on this subject.[9]

On the other hand, the perhydroindane moiety of norrisolide (**3**), which seems to play an important role in the biological activity of this type of compounds, has been synthesized through ketone **19**, prepared via asymmetric Robinson annulation (Scheme 2).[10] This ketone could also be synthesized starting from aldehyde **1** and/or acid **2**.



Scheme 2. Synthesis of the hydrindane core fragment of norrisolide (**3**).

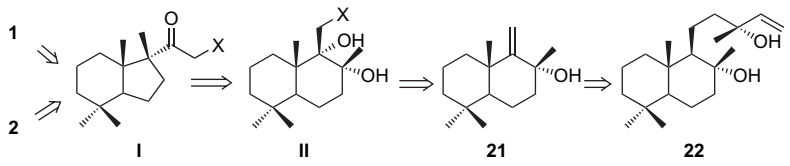
2. Results and discussion

During our research into the synthesis of bioactive marine metabolites from diterpenes we examined the recently isolated rearranged sesquiterpenes **1** and **2**, and other structurally related spongiane diterpenes, such as compound **3**. We planned the synthesis of (+)-austrodoral (**1**) and (+)-austrodoric acid (**2**) from (−)-sclareol (**22**), a labdane diterpene that is very abundant in *Salvia sclarea*. The key step involves the ring contraction through the pinacol rearrangement of diol **II**, leading to intermediate ketone **I**. Compounds **1** and **2** are obtained after oxidative degradation of ketone **I** (Scheme 3).

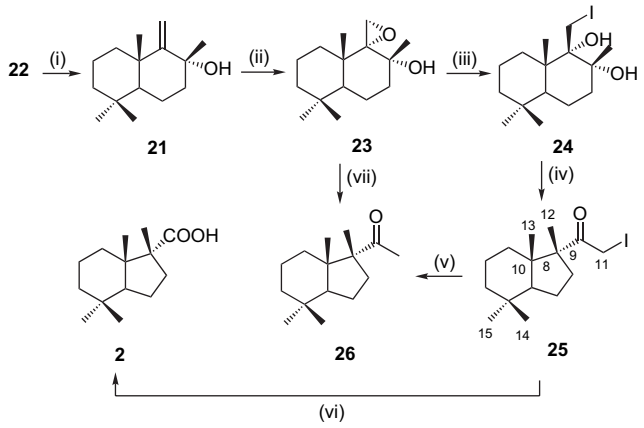
Scheme 4 shows a first approach to these compounds. The epoxidation of 9,11-drimen-8α-ol (**21**)[11,12] led quantitatively and with complete stereoselectivity to **23**, isolated as a crystalline solid. The behaviour of epoxy alcohol **23** against different Lewis acids was investigated: complex mixtures were obtained in all cases.

Crystalline iodohydrine **24** resulted by treating epoxide **23** with the PPh_3/I_2 system. The treatment of compound **24** with $BF_3 \cdot OEt_2$ gave the expected iodoketone **25** in high yield. All attempts at converting ketone **25** into acid **2** under the haloform reaction conditions, e.g., KI, I_2, KOH in dioxane, were unsuccessful, affording instead methyl ketone **26**. Even though these results seem to indicate that compound **26** would remain unreactive under the haloform conditions, due probably to the steric hindrance, the behaviour of this methyl ketone against these oxidizing reagents under more drastic conditions was assayed; methyl ketone **26** was recovered unaltered in all cases. Iodoketone **25** was converted in low yield into (+)-austrodoric acid (**2**) after prolonged reflux in DMSO. Interestingly, epoxide **23** was directly and quantitatively transformed into ketone **26**, by treating with PPh_3 and I_2 in CH_2Cl_2 under reflux. Scheme 5 shows a possible mechanism. The pinacol rearrangement of **24** induced by the phosphonium salt, would afford the iodoketone **25**, which would be reduced by iodide anion to give **26.**

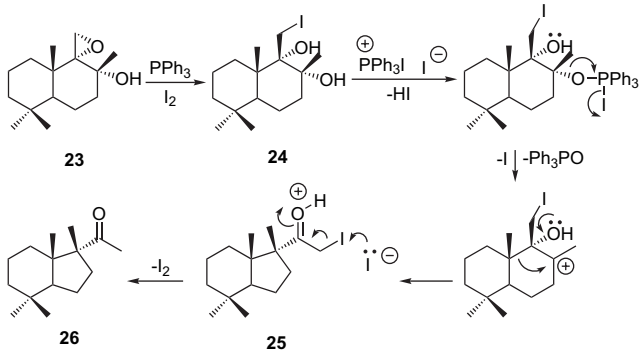
The hydroxyketone **28**, obtained after pinacol rearrangement of triol **27**, resulted in a most suitable precursor of acid **2** and also enabled us to obtain aldehyde **1** (Scheme 6). Compound **27**, which could not be synthesized from epoxide **23** by ring opening, was obtained in high yield and with complete stereoselectivity after cis-dihydroxylation of



Scheme 3. Retrosynthesis for **1** and **2** from (−)-sclareol (**22**).



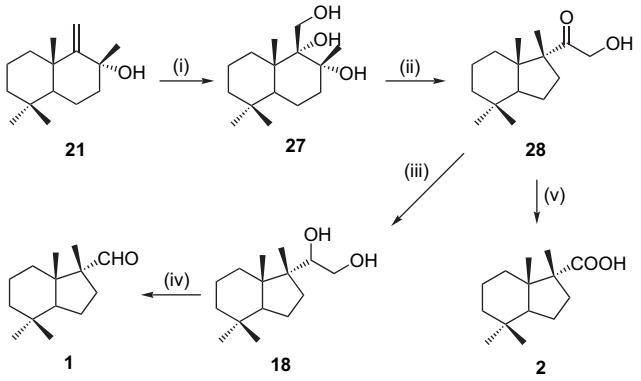
Scheme 4. Synthesis of austrodoric acid (**2**) from (−)-sclareol (**22**). Reagents, conditions and yields: (i) Ref. 12, four steps (59% global yield); (ii) MCPBA, CH_2Cl_2, rt, 1 h (quant.); (iii) PPh_3, I_2, CH_2Cl_2, rt, 30 min (quant.); (iv) $BF_3{\cdot}OEt_2$, CH_2Cl_2, rt, 15 min (92%); (v) I_2, KI, aq NaOH, dioxane, rt, 24 h (76%); (vi) DMSO, reflux, two days (30%); (vii) PPh_3, I_2, CH_2Cl_2, rt, 20 min, reflux, 2 h (88%).



Scheme 5. Possible mechanism for the direct transformation of **23** into **26**.

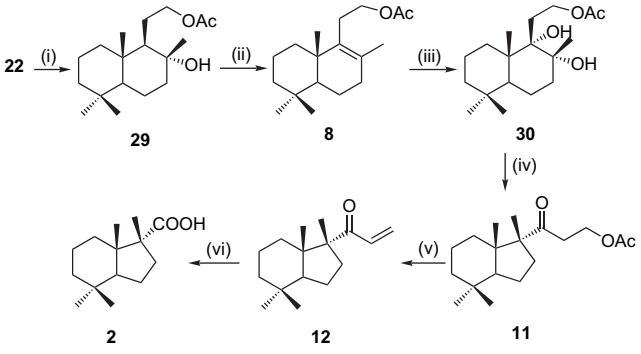
hydroxy alkene **21**. Treatment of triol **27** with $BF_3{\cdot}OEt_2$ led to ketone **28** in almost quantitative yield. Compound **28** was easily converted into (+)-austrodoral (**1**) via diol **18**. (+)-Austrodoric acid (**2**) was also obtained in high yield by treating the hydroxyketone **28** with $NaIO_4$.

After the successful ring contraction, via pinacol rearrangement of drimanediols **24** and **27**, we were interested in investigating the scope of this methodology in order to obtain terpenoids bearing a longer side chain on the pentacyclic moiety. Thus, we studied the behaviour of diol **30**, derived from acetoxyalkene **8**, whose efficient preparation from (−)-sclareol (**22**) had been previously reported by us (Scheme 7). Treatment of acetoxyalcohol **29**, obtained in a three-step sequence (60% overall yield) from **22**,[13] with PPh_3/I_2, utilizing a methodology recently described by our group,[14] afforded compound **8** in 87% yield. The cis-dihydroxylation of alkene **8** with OsO_4 also proceeded with



Scheme 6. A very efficient synthesis of compounds **1** and **2**, via drimanetriol **27**. Reagents, conditions and yields: (i) OsO_4, H_2O, *t*-BuOH, trimethylamine *N*-oxide, pyridine, reflux, 24 h (87%); (ii) $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0 °C→rt, 20 min (95%); (iii) $NaBH_4$, EtOH, rt, 15 min (97%); (iv) $Pb(OAc)_4$, CH_2Cl_2, rt, 45 min (92%); (v) $NaIO_4$, *t*-BuOH/H_2O, reflux, 12 h (91%).

complete stereoselectivity, affording diol **30** in 83% yield. Compound **30** underwent the expected rearrangement in high yield, under the same mild conditions utilized for diols **24** and **27**, to give the acetoxyketone **11**, which was efficiently converted into enone **12** after refluxing with DBU in benzene. Oxidative degradation of ketone **12** with $OsO_4/NaIO_4$ gave (+)-austrodoric acid (**2**).[7]

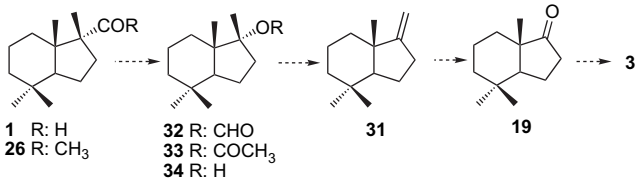


Scheme 7. Synthesis of acid **2** via acetoxyalkene **8**. Reagents, conditions and yields: (i) Ref. 13, three steps (60% global); (ii) Ref. 14; (iii) 0.2% aq OsO_4, Me_3NO, pyridine, *t*-BuOH, Ar, reflux, seven days (90%); (iv) $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0 °C→rt, 30 min (94%); (v) DBU, benzene, reflux, 12 h (95%); (vi) Ref. 7 (70%).

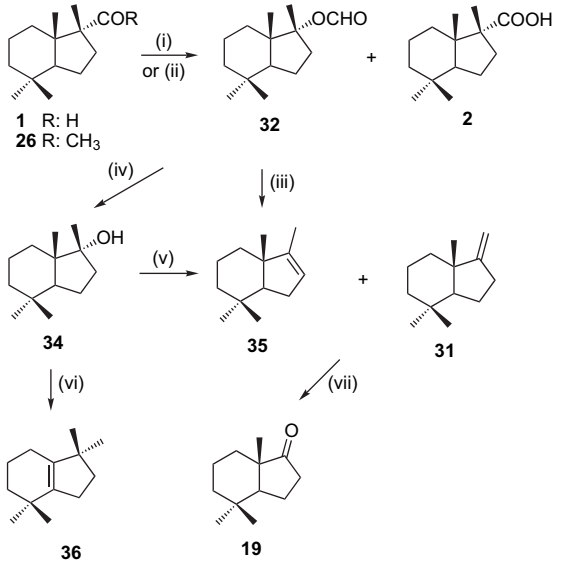
It should be noted that the obtention of acetoxyketone **11** from the epoxyester **10** described by Cimino's group took place in moderate yield, after treatment with the unusual tris-(*p*-bromophenyl)-aminium hexachloroantimonate (Scheme 1).[7] However, these authors reported a satisfactory result when the epoxyester **16** was transformed into ketone **17**, under similar conditions. The low yield attained for the desired rearranged product **11** could be due to cyclization side

reactions, which are most favoured in the precursor homodrimane epoxide **10**. In contrast with this, the pinacol rearrangement of the homodrimane diol **30**, reported here, did not suffer from this disadvantage and led satisfactorily to ketone **11**.

Finally, in view of the above successful obtention of austrodorane derivatives, such as compounds **1**, **2** and **26**, we planned a possible synthesis of ketone **19**, perhydroindane synthon of the spongiane diterpene (+)-norrisolide (**3**), starting from aldehyde **1** or ketone **26** (Scheme 8). Ketone **19** is obtained after oxidative degradation of exocyclic alkene **31**. Compound **31** results from the pyrolysis of formate **32** or acetate **33**, obtained after Baeyer–Villiger oxidation[15] of aldehyde **1** or methyl ketone **26**, or from the dehydration of the corresponding alcohol **34**. Scheme 9 summarizes the sequence from aldehyde **1** to ketone **19**. Treatment of aldehyde **1** with MCPBA in CH_2Cl_2 at reflux for 6 h gave a 45:55 mixture of formate **32** and acid **2**; this result is in agreement with the remarkable instability of aldehyde **1**, whose transformation into acid **2** by exposure of its solution to air had been reported in the previous studies.[7–9] When methyl ketone **26** was treated with MCPBA, under the same reaction conditions utilized for aldehyde **1**, no reaction was observed, the starting material being recovered; the same results were obtained by utilizing H_2O_2 and trifluorocacetic anhydride as oxidizing reagents.



Scheme 8. A possible synthesis of ketone **19**, precursor of spongiane diterpene (+)-norrisolide (**3**) from aldehyde **1** or ketone **26**.



Scheme 9. Synthesis of ketone **19** from austrodoral (**1**). Reagents, conditions and yields: (i) MCPBA, solid $NaHCO_3$, CH_2Cl_2, reflux, 6 h (**32**–**2**, 45:55, 80% from **1**; no reaction was observed starting from **26**); (ii) 90% H_2O_2, $(CF_3CO)_2O$, CH_2Cl_2, rt, 24 h; unaltered ketone **26** was recovered; (iii) collidine, reflux, 12 h (**35**–**31**, 4:1, 98%); (iv) KOH, MeOH, rt, 1 h (92%); (v) and (vi) see Table 1; (vii) 0.2% OsO_4, $NaIO_4$, *t*-BuOH, 45 °C, 5 h (30%).

Table 1. Reaction of alcohol **34** under different dehydration conditions

Entry	Conditions	Product(s) (%)
1	MsCl, Et_3N, 0 °C, 12 h	**35** (80)
2	$POCl_3$, Et_3N, −20 °C	**35**–**31**, 2:1 (82)
3	$SOCl_2$, Et_3N, −50 °C	**35**–**31**, 1.25:1 (78)
4	Amberlyst 15, CH_2Cl_2, rt, 4 h	**36** (98)

A 4:1 mixture of alkenes **35** and **31** was obtained when the formate **32** was refluxed with collidine. It should be emphasized that our previous studies concerning the ring A functionalization of terpenoids, through the pyrolysis of quaternary formates similar to **32**, revealed that this reaction was biased in favour of the corresponding exocyclic alkene.[15] The complete preference for the formation of the endocyclic regioisomer observed in this case must be attributed to the higher stability of endocyclic double bond in the cyclopentane ring. Then, the dehydration of alcohol **34**, resulting from the hydrolysis of ester **32**, was investigated; the most significant results are shown in Table 1. The best results were obtained with $SOCl_2$ at low temperature, which led to a 1:25:1 mixture of endocyclic **35** and exocyclic alkene **31** in good yield. Treatment of alcohol **34** with Amberlyst 15 in CH_2Cl_2 at room temperature led to the rearranged alkene **36**.[16] Finally, ketone **19** was obtained after treatment of the mixture **35**–**31** with $OsO_4/NaIO_4$. Unfortunately, although a suitable route towards the perhydroindane synthon of spongiane diterpenes from (−)-sclareol (**22**) could be expected to be achieved, the easy oxidation of aldehyde **1** together with the unfavourable formation of exocyclic alkene **31** diminishes the usefulness of this method.

3. Conclusions

In summary, very efficient strategies towards obtaining the austrodorane skeleton from (−)-sclareol (**22**) are reported. The processes, based on the pinacol rearrangement of the suitable diols take place with complete diastereoselectivity. Utilizing these, syntheses of (−)-austrodoral (**1**) and austrodoric acid (**2**) from **22** are described. Ketone **19**, a key intermediate in the synthesis of rearranged diterpene lactones, such as norrisolide (**3**), was also obtained in moderate yield.

4. Experimental

4.1. General

Routinely, dry organic solvents were stored under argon, over freshly activated molecular sieves. Dichloromethane (DCM) was dried over calcium hydride. Tetrahydrofuran (THF) and *tert*-butyl methyl ether (E) were dried over sodium-benzophenone ketyl. Methanol was distilled from magnesium at 760 Torr. Dimethylsulfoxide (DMSO) and ethanol were dried over 4 Å molecular sieves. Chromatography separations were carried out using conventional column on silica gel 60 (230–400 mesh) using hexane/MeO*t*-Bu (H/E) mixtures of increasing polarity. Infrared (IR) spectra were obtained using Perkin Elmer Spectrum Models 782 and 983G spectrophotometers with samples between sodium chloride plates or as potassium bromide pellets. Data are presented as the frequency of absorption

(cm^{-1}). Proton and carbon-13 nuclear magnetic resonance (^1H NMR or ^{13}C NMR) spectra were recorded on Varian 300, 400 and 500 spectrometers, chemical shifts are expressed in parts per million (δ scale) downfield from tetramethylsilane. Data are presented as follows: chemical shift, multiplicity (s=singlet, br s=broad singlet, d=doublet, t=triplet, m=multiplet), J=coupling constant in hertz (Hz). The signals of the ^{13}C NMR spectra were assigned utilizing DEPT experiments. HRMS were obtained on a trisector WG AutoSpecQ spectrometer. FAB spectra acquisition was performed with a 10,000 resolution and a relative error of 5 ppm.

4.1.1. 9α,11-Epoxydrimane-8α-ol (23). *m*-Chloroperoxybenzoic acid (MCPBA, 75%; 663 mg, 2.68 mmol) was added at 0 °C to a stirred solution of compound **21** (0.5 g, 2.25 mmol) in CH_2Cl_2 (15 mL) and the reaction was allowed to warm to room temperature for 1 h, then TLC indicated that no starting **21** remained. The reaction was quenched with satd aq Na_2SO_3 (2 mL) and stirred for an additional 30 min. Then, the mixture was poured into ether/water (40:10 mL), and the organic phase was washed with satd aq $NaHCO_3$ (9×10 mL) and brine. The organic phase was dried over Na_2SO_4 and concentrated to give pure **23** (535 mg, 99.9%) as a colourless oil. $[\alpha]_D$ −22.6 (*c* 0.67, $CHCl_3$); IR (KBr) ν 3521, 1775, 1729, 1465, 1386, 1173, 1078, 1054, 1009, 975, 948, 915, 842, 789, 675, 582 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.82 (d, J=4.5 Hz, 1H), 2.71 (d, J=4.5 Hz, 1H), 2.43 (br s, 1H), 1.91 (m, 1H), 1.68 (m, 1H), 1.45–1.35 (m, 9H), 1.32 (s, 3H), 1.16 (s, 3H), 0.86 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.33 (C), 69.27 (C), 51.2 (CH), 45.5 (CH_2), 42.1 (CH_2), 41.3 (CH_2), 38.1 (C), 33.6 (C), 32.9 (CH_3), 31.8 (CH_2), 25.7 (CH_3), 21.7 (CH_3), 20.4 (CH_3), 20.3 (CH_2), 18.0 (CH_2); EIMS *m/z* (rel int.): 238 [M+] (10), 159 (5), 147 (6), 139 (10), 123 (12), 119 (14), 111 (16), 109 (22), 105 (23), 95 (30), 91 (39); HRMS (FAB) *m/z* calcd for $C_{15}H_{26}O_2Na$ 261.1830; found 261.1822.

4.1.2. 11-Iododrimane-8α,9α-diol (24). Iodine (1.2 g, 4.72 mmol) was added to a solution of triphenylphosphine (1.2 g, 4.53 mmol) in CH_2Cl_2 (18 mL) and the mixture was stirred at room temperature for 5 min. A solution of epoxy alcohol **23** (0.6 g, 2.52 mmol) in CH_2Cl_2 (15 mL) was then added and the reaction mixture was further stirred at this temperature for 30 min, at which time TLC showed no **23**. The reaction was quenched with 10% aq $NaHSO_3$ (2 mL) and the mixture was vigorously stirred for 5 min. Then, the yellow mixture was diluted with ether (50 mL) and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated to give a crude product which was purified by flash chromatography column on silica gel (H/E, 9:1) to afford pure diol **24** (0.92 g, 99.8%) as a white solid. Mp 110 °C (dec); $[\alpha]_D$ +1.1 (*c* 0.84, $CHCl_3$); IR (KBr) ν 3510, 1459, 788, 752 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.74 (d, J=10.7 Hz, 1H), 3.63 (d, J=10.7 Hz, 1H), 3.16 (s, 1H), 3.14 (s, 1H), 2.54 (br s, 1H), 1.70–1.42 (m, 8H), 1.30–1.09 (m, 3H), 1.35 (s, 3H), 0.98 (s, 3H), 0.84 (s, 3H), 0.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 75.8 (C), 75.4 (C), 46.2 (CH), 43.7 (C), 41.0 (CH_2), 39.3 (CH_2), 33.8 (CH_2), 33.6 (CH_3), 33.4 (C), 25.4 (CH_3), 21.8 (CH_3), 19.5 (CH_2), 19.4 (CH_2), 17.7 (CH_3), 13.4 (CH_2); EIMS *m/z* (rel int.): 366 [M+] (4), 254 (15), 221 (29), 203 (20), 177 (30), 163 (22), 137 (47), 127 (30), 123 (36), 121 (28), 119 (22), 109 (61), 97 (26), 95 (71); HRMS (FAB) *m/z* calcd for $C_{15}H_{27}IO_2Na$ 389.0953; found 389.0961.

4.1.3. (5*S*,8*R*,10*S*)-9-(Iodomethyl)austrodor-9-one (25). $BF_3\cdot Et_2O$ (0.40 mL, 3.16 mmol) was added at 0 °C to a stirred solution of compound **24** (0.58 g, 1.58 mmol) in CH_2Cl_2 (15 mL) and the cooling bath was removed. After stirring for 15 min at this temperature, TLC showed no remaining starting material. Then, satd aq $NaHCO_3$ (2 mL) was added slowly, and the mixture was extracted with ether (2×30 mL). The organic phase was washed with water, brine, dried over Na_2SO_4 and concentrated to give pure **25** (0.51 g, 92%) as a colourless solid. Mp 75–77 °C; $[\alpha]_D$ −12.6 (*c* 0.14 $CHCl_3$); IR (KBr) ν 1694, 1464, 1384, 1269, 1188, 1088, 1016, 999, 966, 788, 751 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.03 (d, J=11.9 Hz, 1H), 3.88 (d, J=11.9 Hz, 1H), 2.28 (m, 1H), 1.74–1.22 (m, 8H), 1.32 (s, 3H), 0.94 (ddd, J=13.1, 13.1, 4.2 Hz, 1H), 0.88 (s, 3H), 0.85 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.6 (C), 62.5 (C), 52.5 (CH), 47.1 (C), 40.9 (CH_2), 36.1 (CH_2), 33.8 (CH_3), 33.4 (CH_2), 32.6 (C), 21.7 (CH_2), 21.5 (CH_3), 21.1 (CH_3), 20.0 (CH_2), 15.6 (CH_3), 8.3 (CH_2); EIMS *m/z* (rel int.): 348 [M+] (1), 333 (3), 254 (8), 221 (25), 203 (18), 179 (26), 169 (10), 163 (16), 149 (8), 147 (10), 138 (18), 137 (100), 125 (14), 123 (61), 121 (21), 119 (12), 109 (54), 107 (26), 97 (20), 95 (88), 93 (24); HRMS (FAB) *m/z* calcd for $C_{15}H_{25}IONa$ 371.0848; found 371.0843.

4.1.4. Treatment of ketone 25 with I_2/KI in aq NaOH. Synthesis of (5*S*,8*R*,10*S*)-9-methylaustrodor-9-one (26). To a stirred mixture of **25** (125 mg, 0.36 mmol) and 4 N aq NaOH (2 mL) in 1,4-dioxane (5 mL), were added dropwise at room temperature aqueous solutions of iodine (10%; 2 mL) and KI (20%; 1 mL) for 15 min, and the reaction mixture was stirred for an additional 24 h. Then, it was quenched with 2 N HCl (4 mL) and diluted with ether (20 mL). The organic phase was washed with water and brine, dried over Na_2SO_4 and concentrated to afford a crude product which was purified by flash column chromatography on silica gel (H/E, 8:2) to afford pure methyl ketone **26** (61 mg, 76%) as a colourless oil. $[\alpha]_D$ −1.1 (*c* 0.62, $CHCl_3$); IR (KBr) ν 1773, 1697, 1464, 1365, 1258, 1208, 1082, 966, 788, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.25–2.10 (m, 2H), 2.04 (s, 3H), 1.65–1.15 (m, 8H), 1.13 (s, 3H), 0.90 (m, 1H), 0.83 (s, 3H), 0.82 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.2 (C), 61.7 (C), 52.4 (CH), 46.7 (C), 41.0 (CH_2), 35.9 (CH_2), 33.7 (CH_3), 33.2 (C), 32.5 (CH_2), 29.5 (CH_3), 21.7 (CH_2), 21.5 (CH_3), 20.8 (CH_3), 20.1 (CH_2), 15.9 (CH_3); EIMS *m/z* (rel int.): 222 [M+] (1), 165 (3), 155 (4), 145 (5), 141 (9), 135 (9), 127 (13), 121 (9), 105 (10), 95 (12), 91 (15), 83 (15), 79 (16), 69 (19), 67 (25), 55 (42); HRMS (FAB) *m/z* calcd for $C_{15}H_{26}ONa$ 245.1881; found 245.1877.

4.1.5. Treatment of 26 with I_2/KI in aq NaOH. To a stirred mixture of methyl ketone **26** (0.5 g, 2.25 mmol) and 4 N aq NaOH (10 mL) in 1,4-dioxane (25 mL) were added dropwise at room temperature aqueous solutions of iodine (10%; 10 mL) and KI (20%; 5 mL) for 15 min, and the reaction mixture was stirred at reflux for an additional 36 h. Following the same work-up described for compound **25**, the unaltered starting material was obtained.

4.1.6. Treatment of epoxy alcohol 23 with I_2 and PPh_3. Iodine (1 g, 3.93 mmol) was added to a solution of triphenylphosphine (1 g, 3.77 mmol) in CH_2Cl_2 (15 mL) and the mixture was stirred at room temperature for 3 min. A solution of epoxy alcohol **23** (0.5 g, 2.1 mmol) in CH_2Cl_2 (15 mL) was then added and the mixture was further stirred at reflux for 30 min, at which time TLC showed no **23**. The reaction was quenched with 10% aq $NaHSO_3$ (2 mL) and the mixture was vigorously stirred for 10 min, and then it was diluted with ether (50 mL) and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated to give a crude product which was purified by flash chromatography column on silica gel (H/E, 9:1) to afford pure ketone **26** (0.41 g, 88%) as a colourless syrup.

4.1.7. Austrodoric acid (2). A solution of iodoketone **25** (0.2 g, 0.57 mmol) in DMSO (6 mL) was stirred at reflux for two days. Then, the reaction mixture was diluted with ether (20 mL) and washed with water and brine. The organic phase was dried over Na_2SO_4 and evaporated to give a crude product which was purified by a chromatography column (H/E, 7:3) to afford acid **2** (39 mg, 30%) as a white solid. Mp 172–173 °C; $[\alpha]_D$ +4.4 (*c* 1.2, $CHCl_3$) [lit.:[7] −2.0 (*c* 0.15, $CHCl_3$). The MS, IR, ^1H and ^{13}C NMR data agreed with the literature data.[7]

4.1.8. Drimane-8α,9α,11-triol (27). To a solution of alcohol **21** (1.5 g, 6.75 mmol) in *t*-BuOH/H_2O (45:5 mL) were added trimethylamine *N*-oxide dihydrate (0.91 g, 8.19 mmol) and pyridine (0.2 mL) under argon atmosphere. The solution was stirred for 5 min at room temperature, and 2% aq OsO_4 (2.8 mL) was added and the reaction mixture was further stirred under the inert atmosphere at reflux for 24 h, at which time TLC indicated no remaining starting material. The solvent was evaporated to afford a crude product that was dissolved in ether (40 mL) and washed with water (3×10 mL) and brine. The organic phase was dried over Na_2SO_4 and concentrated to give pure **27** (1.5 g, 87%) as a white solid. $[\alpha]_D$ +1.46 (*c* 0.13, $CHCl_3$); IR (KBr) ν 3427, 1460, 1389, 1130, 1094, 1059, 989, 936, 828, 771, 668 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.08 (d, *J*=11.5 Hz, 1H), 3.78 (s, 1H, –OH), 3.73 (d, *J*=11.5 Hz, 1H), 3.69 (br s, 1H, –OH), 3.48 (br s, 1H, –OH), 1.72–1.14 (m, 9H), 1.43 (s, 3H), 0.94 (s, 3H), 0.89 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 78.1 (C), 76.3 (C), 63.5 (CH_2), 45.9 (CH), 41.6 (C), 41.3 (CH_2), 38.6 (CH_2), 33.7 (CH_3), 33.1 (C), 32.9 (CH_2), 25.5 (CH_3), 21.9 (CH_3), 19.6 (CH_2), 18.4 (CH_2), 17.3 (CH_3); EIMS *m*/*z* (rel int.): 139 [M+] (5), 128 (6), 116 (7), 111 (11), 105 (12), 96 (9), 93 (14), 91 (26), 85 (12), 81 (16), 79 (24), 77 (35), 75 (35), 65 (28), 63 (33), 56 (28), 55 (42), 54 (75), 48 (7); HRMS (FAB) *m*/*z* calcd for $C_{15}H_{28}O_3Na$ 279.1936; found 279.1928.

4.1.9. (5*S*,8*R*,10*S*)-9-(Hydroxymethyl)austrodor-9-one (28). $BF_3{\cdot}Et_2O$ (1.5 mL, 11.83 mmol) was added at 0 °C to a stirred solution of triol **27** (1.5 g, 5.86 mmol) in CH_2Cl_2 (30 mL) and the cooling bath was removed. After stirring for 20 min at this temperature, TLC showed no remaining starting material. Then, satd aq $NaHCO_3$ (3 mL) was added slowly, and the mixture was extracted with ether (2×50 mL). The organic phase was washed with water, brine, dried over Na_2SO_4 and concentrated to give pure hydroxyketone **28** (1.32 g, 95%) as a colourless oil. $[\alpha]_D$ −9.1 (*c* 0.76, $CHCl_3$); IR (film) ν 3472, 1694, 1464, 1384, 1284, 1233, 1164, 1093, 997, 794, 756 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.27 (d, *J*=18.5 Hz, 1H), 4.18 (d, *J*=18.5 Hz, 1H), 3.10 (br s, 1H), 2.20 (m, 1H), 1.80–1.12 (m, 10H), 1.12 (s, 3H), 0.92 (m, 1H), 0.91 (s, 3H), 0.85 (s, 3H), 0.84 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 216.4 (C), 67.4 (CH_2), 59.2 (C), 52.4 (CH), 47.7 (C), 40.8 (CH_2), 35.4 (CH_2), 33.8 (CH_3), 33.1 (CH_2), 30.9 (C), 21.9 (CH_2), 21.5 (CH_3), 19.9 (CH_2), 18.4 (CH_3), 16.1 (CH_3); HRMS (FAB) *m*/*z* calcd for $C_{15}H_{26}O_2Na$ 261.1830; found 261.1822.

4.1.10. (5*S*,8*R*,10*S*)-9-(Hydroxymethyl)austrodor-9-ol (18). Sodium borohydride (0.32 g, 8.42 mmol) was added to a stirred solution of hydroxyketone **28** (1.3 g, 5.46 mmol) in EtOH (10 mL) and the reaction mixture was stirred at room temperature for 15 min, at which time TLC showed no **28**. The reaction mixture was quenched with water (1 mL), the solvent was evaporated, and the crude product was diluted with ether (30 mL) and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated to give **18** (1.27 g, 97%) as a mixture of diastereoisomers (ratio 4:1); ^1H NMR (400 MHz, $CDCl_3$) data for the major product: δ 3.84 (dd, *J*=9.5, 3.1 Hz, 1H), 3.75 (dd, *J*=10.6, 3.3 Hz, 1H), 3.51 (dd, *J*=10.3, 9.5 Hz, 1H), 2.72 (br s, 2H), 2.16 (m, 2H), 1.69–1.14 (m, 8H), 1.03 (ddd, *J*=16.6, 13.7, 3.7 Hz, 1H), 0.90 (s, 3H), 0.87 (s, 3H), 0.85 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) data for the major product: δ 73.6 (CH), 62.9 (CH_2), 52.5 (CH), 48.9 (C), 45.8 (C), 40.4 (CH_2), 33.8 (CH_2), 33.3 (CH_3), 32.3 (C), 31.1 (CH_2), 20.6 (CH_2), 20.5 (CH_3), 19.1 (CH_2), 16.5 (CH_3), 15.3 (CH_3); IR (film) data for the mixture: ν 3300, 1458, 1381, 1235, 1061, 1002 cm^{-1}; EIMS *m*/*z* (rel int.) data for the mixture: 240 [M+] (3), 235 (11), 204 (10), 189 (14), 163 (32), 133 (19), 123 (65), 119 (40), 109 (87), 107 (78), 105 (69), 95 (100), 91 (85); HRMS (FAB) *m*/*z* calcd for $C_{15}H_{28}O_2Na$ 263.1987; found 263.1994.

4.1.11. Austrodoral (1). $Pb(OAc)_4$ (2.8 g, 6 mmol) was added to a solution of diol **18** (1 g, 4.16 mmol) in CH_2Cl_2 (25 mL) and the reaction mixture was stirred at room temperature for 45 min, at which time TLC showed no **18**. The reaction was quenched with 10% aq $NaHSO_3$ (2 mL) and the mixture was diluted with ether (50 mL) and washed with satd aq $NaHCO_3$ (3×10 mL), water and brine. The organic phase was dried over Na_2SO_4 and concentrated to give pure **1** (0.8 g, 92%) as a colourless oil. $[\alpha]_D$ +9.0 (*c* 0.4, $CHCl_3$) [lit.:[1] +5.0 (*c* 0.3, $CHCl_3$); lit.:[8] +18.3 (*c* 0.45, $CHCl_3$)]. The MS, ^1H and ^{13}C NMR data agreed with the literature data.[1,8]

4.1.12. Synthesis of acid 2 from hydroxyketone 28. $NaIO_4$ (0.54 g, 2.52 mmol) was added to a solution of compound 2**8** (0.7 g, 2.94 mmol) in *t*-BuOH/H_2O (25:4 mL) and the reaction mixture was stirred at reflux for 12 h, at which time TLC showed no 2**8**. Then, the solvent was evaporated, and the crude product was diluted with ether (40 mL) and washed with water and brine. The organic phase was dried over Na_2SO_4 and concentrated to give pure **2** (0.6 g, 91%) as a white solid.

4.1.13. 12-Acetoxy-13,14,15,16-tetranorlabd-8-ene (8). Iodine (1.8 g, 7.10 mmol) was added to a solution of

triphenylphosphine (1.85 g, 7.0 mmol) in CH_2Cl_2 (15 mL) and the mixture was stirred at room temperature for 5 min. A solution of acetoxyalcohol **29** (2 g, 6.75 mmol) in CH_2Cl_2 (15 mL) was then added and the reaction mixture was further stirred at room temperature for 2.5 h, at which time TLC showed no **29**. The reaction was quenched with 10% aq $NaHSO_3$ (2 mL) and the reaction mixture was vigorously stirred for 4 min. The yellow mixture was diluted with ether (50 mL) and washed with water and brine. The organic phase was dried over anhydrous Na_2SO_4 and concentrated to give a crude product which was purified by flash chromatography column on silica gel (H/E, 95:5) to afford **8** (1.65 g, 87%) as a colourless syrup. $[\alpha]_D$ +92.4 (*c* 0.7, $CHCl_3$) [lit.:[7] +117.1 (*c* 1.4, $CHCl_3$)]. The MS, IR, ^1H and ^{13}C NMR data agreed with the literature data.[7]

4.1.14. 12-Acetoxy-13,14,15,16-tetranorlabdane-8α,9α-diol (30). To a solution of **8** (1 g, 3.60 mmol) in *t*-BuOH (15 mL) were added trimethylamine *N*-oxide dihydrate (1.11 g, 10 mmol) and pyridine (0.5 mL) under argon atmosphere. After stirring for 5 min at room temperature, 2% aq OsO_4 (6 mL) was added and the reaction mixture was further stirred under inert atmosphere at reflux for seven days. 10% aq $NaHSO_3$ (3 mL) was added and the solvent was evaporated, then ether (40 mL) was added and the mixture was washed with 5% HCl (2×10 mL), water and brine. The organic phase was dried over Na_2SO_4 and concentrated to give a crude product which was purified by flash chromatography column on silica gel (H/E, 1:1) to give pure **30** (1.01 g, 90%). $[\alpha]_D$ 19.9 (*c* 2.95, $CHCl_3$); IR (film) ν 3492, 1719, 1459, 1365, 1253, 1099, 1030, 944, 753 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.37 (m, 2H), 2.96 (br s, 1H), 2.58 (br s, 1H), 2.13 (dd, *J*=14.8, 7.8 Hz, 1H), 2.06 (s, 3H), 1.90 (ddd, *J*=14.8, 7.6, 6.3 Hz, 1H), 1.35 (s, 3H), 0.96 (s, 3H), 0.91 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.4 (C), 80.1 (C), 75.6 (C), 63.2 (CH_2), 46.0 (CH), 43.3 (C), 41.5 (CH_2), 39.4 (CH_2), 33.9 (CH_3), 33.4 (C), 32.9 (CH_2), 30.2 (CH_2), 25.5 (CH_3), 22.0 (CH_3), 21.4 (CH_3), 20.0 (CH_2), 18.6 (CH_2), 17.3 (CH_3); EIMS *m*/*z* (rel int.): 312 [M+] (4), 294 (10), 276 (28), 179 (11), 157 (29), 123 (34), 109 (19), 97 (64), 69 (47), 55 (100); HRMS (FAB) *m*/*z* calcd for $C_{18}H_{32}O_4Na$ 335.2198; found 335.2205.

4.1.15. (5*S*,8*R*,10*S*)-9-(2-Acetoxyethyl)-austrodor-9-one (11). $BF_3{\cdot}Et_2O$ (45%, 0.62 mL, 4.89 mmol) was added at 0 °C to a stirred solution of **30** (0.67 g, 2.15 mmol) in CH_2Cl_2 (20 mL) and the cooling bath was removed. After stirring for 30 min, TLC showed no remaining starting material. Then satd aq $NaHCO_3$ (1 mL) was added slowly, and the mixture was extracted with ether (2×35 mL). The organic phase was washed with water, brine, dried over Na_2SO_4 and concentrated to give **11** (0.593 mg, 94%) as a yellow oil. $[\alpha]_D$ −2.7 (*c* 1.9, $CHCl_3$) [lit.:[7] −2.4 (*c* 1.6, $CHCl_3$)]. The MS, IR, ^1H and ^{13}C NMR data agreed with the literature data.[7]

4.1.16. (5*S*,8*R*,10*S*)-9-Vinylaustrodor-9-one (12). 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (520 mg, 3.42 mmol) was added to a stirred solution of acetoxyketone **11** (0.5 g, 1.70 mmol) in benzene (15 mL) and the mixture was stirred under reflux for 12 h, at which time TLC showed no **11**. Then, it was diluted with ether (30 mL) and washed with 1 M HCl, water and brine. The organic phase was dried over Na_2SO_4 and concentrated under vacuum to yield ketone **12** (378 mg, 95%) as a yellow syrup. $[\alpha]_D$ −13.5 (*c* 1.2, $CHCl_3$) [lit.:[7] −6.4 (*c* 0.3, $CHCl_3$)]. The MS, IR, ^1H and ^{13}C NMR data agreed with the literature data.[7]

4.1.17. Treatment of austrodoral (1) with MCPBA. Synthesis of (5*S*,8*R*,10*S*)-8-formyloxy-9-nor-austrodorane (32). *m*-Chloroperoxybenzoic acid (MCPBA, 75%; 1.3 g, 5.25 mmol) was added at 0 °C to a stirred suspension of austrodoral (**1**) (0.5 g, 2.40 mmol) and solid $NaHCO_3$ (0.43 g, 5.12 mmol) in CH_2Cl_2 (25 mL) and the reaction was stirred at reflux for 3 h, at which time TLC indicated no starting material remaining. The reaction was quenched with satd aq Na_2SO_3 (2 mL) and stirred for an additional 30 min. Then, it was poured into ether/water (50:10 mL), and the organic phase was washed with satd aq $NaHCO_3$ (10×15 mL) and brine, dried over Na_2SO_4 and concentrated to give a crude product which was purified by chromatography column (H/E, 75:15) to give formate **32** (194 mg, 36%) and acid **2** (236 mg, 44%). *Compound* ***32***: $[\alpha]_D$ −16.61 (*c* 0.49, $CHCl_3$); IR (film) ν 1771, 1718, 1575, 1467, 1426, 1379, 1216, 1187, 1149, 1087, 1019, 804, 728 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (s, 1H), 2.45 (m, 2H), 1.90–1.70 (m, 2H), 1.69–1.03 (m, 6H), 1.48 (s, 3H), 1.10 (m, 1H), 0.91 (s, 3H), 0.90 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4 (C), 94.9 (C), 51.5 (CH), 47.5 (C), 41.2 (CH_2), 33.8 (CH_3), 33.3 (CH_2), 33.2 (C), 30.6 (CH_2), 30.3 (C), 21.3 (CH_3), 20.6 (CH_2), 19.5 (CH_2), 18.5 (CH_3), 16.2 (CH_3); EIMS *m*/*z* (rel int.): 224 [M+] (4), 222 (9), 163 (26), 139 (15), 111 (32), 107 (45), 105 (36), 95 (20), 93 (35), 91 (57), 85 (100), 83 (100), 77 (42); HRMS (FAB) *m*/*z* calcd for $C_{14}H_{24}O_2Na$ 247.1674; found 247.1682.

4.1.18. Treatment of methyl ketone 26 with MCPBA. To a stirred mixture of methyl ketone **26** (100 mg, 0.45 mmol) and solid $NaHCO_3$ (100 mg, 1.19 mmol) in CH_2Cl_2 (10 mL) was added *m*-chloroperoxybenzoic acid (MCPBA, 75%; 260 mg, 1.05 mmol) and the reaction was stirred at reflux for 24 h. The reaction was quenched with satd aq Na_2SO_3 (1 mL) and stirred for an additional 30 min. Following the same work-up used to prepare **32**, the unaltered starting material was obtained.

4.1.19. Treatment of methyl ketone 26 with H_2O_2/$(CF_3CO)_2O$. To a cooled (0 °C) solution of trifluoroacetic anhydride (1 mL, 7.08 mmol) in CH_2Cl_2 (20 mL) was added a 90% solution of H_2O_2 (0.3 mL, 7.92 mmol) and the mixture was stirred at this temperature for 10 min. Then a solution of **26** (0.5 g, 2.25 mmol) in CH_2Cl_2 (10 mL) was added and the reaction mixture was stirred at room temperature for 24 h. Solid $NaHCO_3$ (420 mg, 5 mmol) was added and the reaction mixture was stirred for 15 min, then it was diluted with ether (50 mL), washed slowly with a solution of $NaHCO_3$ (3×15 mL), water, brine, dried (Na_2SO_4) and the solvent was evaporated to give the unaltered **26**.

4.1.20. Treatment of formate 32 with collidine. A solution of ester **32** (0.3 g, 1.34 mmol) in collidine (5 mL) was refluxed for 12 h, at which time TLC showed no **32**. Then, the reaction mixture was diluted with ether (25 mL) and washed with 2 N HCl (5×10 mL), water and brine. The

organic phase was dried over Na_2SO_4 and concentrated to give a mixture of alkenes **35** and **31** (234 mg, 98%) as a yellow oil (ratio 4:1).

4.1.21. (5*S*,8*R*,10*S*)-9-Nor-austrodor-8-ol (34). KOH (2 N) in MeOH (1 mL) was added to a solution of ester **32** (167 mg, 0.745 mmol) in MeOH (5 mL) and the mixture was stirred at room temperature for 1 h. The solvent was evaporated and the residue was diluted with ether (20 mL) and washed with water and brine. The organic phase was dried (Na_2SO_4) and the solvent was evaporated to give alcohol **34** (135 mg, 92%) as a colourless oil. $[\alpha]_D$ −3.56 (*c* 0.71, $CHCl_3$); IR (film) ν 3169, 1697, 1462, 1376, 1281, 1235, 1134, 1022, 919, 788, 751, 572 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.84–1.76 (m, 2H), 1.68–1.52 (m, 4H), 1.50–1.25 (m, 4H), 1.18 (s, 3H), 1.08 (ddd, *J*=13.1, 13.1, 4.9 Hz, 1H), 0.90 (s, 3H), 0.89 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 82.4 (C), 51.6 (CH), 47.1 (C), 41.4 (CH_2), 37.4 (CH_2), 33.9 (CH_3), 33.2 (C), 30.6 (CH_2), 23.0 (CH_3), 21.2 (CH_3), 20.5 (CH_2), 19.7 (CH_2), 16.9 (CH_3); EIMS *m*/*z* (rel int.): 196 [M+] (4), 191 (5), 189 (5), 179 (6), 165 (9), 147 (10), 141 (12), 127 (18), 119 (16), 115 (19), 105 (21), 95 (21), 91 (75), 79 (44), 77 (48), 69 (73), 55 (100); HRMS (FAB) *m*/*z* calcd for $C_{13}H_{24}ONa$ 219.1725; found 219.1719.

4.1.22. Dehydration of alcohol 34.

4.1.22.1. Treatment of alcohol 34 with mesyl chloride. Synthesis of (5*S*,10*S*)-9-nor-austrodor-7-ene (35). Mesyl chloride (0.2 mL) was added to a solution of compound **34** (0.1 g, 5.10 mmol) in Et_3N (5 mL) and the mixture was stirred at room temperature for 12 h, at which time TLC showed no **34**. H_2O (2 mL) was added and the mixture was extracted with ether (3×10 mL). The organic phase was washed with 2 N HCl (3×10 mL), water and brine, dried over Na_2SO_4 and the solvent evaporated to give alkene **35** (73 mg, 80%). $[\alpha]_D$ +2.36 (*c* 0.10, $CHCl_3$); IR (film) ν 1722, 1560, 1464, 1378, 1260, 1203, 1097, 1018, 856, 787, 695, 594 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.29 (br s, 1H), 1.97 (t, *J*=2 Hz, 1H), 1.94 (t, *J*=2 Hz, 1H), 1.81–1.37 (m, 6H), 1.12 (ddd, *J*=13, 13, 5 Hz, 1H), 1.59 (s, 3H), 0.96 (s, 3H), 0.88 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.6 (C), 122.3 (CH), 99.6 (C), 60.2 (CH), 41.6 (CH_2), 34.8 (CH_2), 33.2 (CH_3), 33.1 (C), 29.8 (C), 28.6 (CH_2), 21.4 (CH_3), 20.1 (CH_2), 16.7 (CH_3), 12.1 (CH_3); EIMS *m*/*z* (rel int.): 178 [M+] (2), 170 (5), 152 (7), 149 (10), 111 (13), 104 (16), 97 (23), 95 (22), 81 (40), 71 (51), 69 (63), 57 (80), 55 (100); HRMS (FAB) *m*/*z* calcd for $C_{13}H_{22}Na$ 201.1619; found 201.1623.

4.1.22.2. Treatment of alcohol 34 with phosphorus oxychloride. Phosphorus oxychloride (0.2 mL) was added to a solution of alcohol **34** (110 mg, 0.56 mmol) and triethylamine (3 mL) in dry CH_2Cl_2 (5 mL) at −20 °C and the reaction mixture was stirred at this temperature for 3 h, at which time TLC showed no **34**. The reaction mixture was poured into ice and extracted with ether (3×10 mL). The combined organic phase was washed with 2 N HCl (3×7 mL), water and brine, dried (Na_2SO_4) and the solvent was evaporated to give 82 mg (82%) of a mixture of regioisomers (5*S*,10*S*)-9-nor-austrodor-8(12)-ene (**31**) and **35** (ratio 1:2). *Selected ^1H and ^{13}C NMR chemical shifts (300 and 75 MHz, $CDCl_3$) for compound **31***: δ 4.52 (s, 1H), 4.53 (s, 1H) and 99.6 ppm (exocyclic methylene).

4.1.22.3. Treatment of alcohol 34 with thionyl chloride. $SOCl_2$ (0.1 mL, 1.37 mmol) was added slowly to a solution of **34** (170 mg, 0.858 mmol) and triethylamine (1 mL) in dry CH_2Cl_2 (10 mL) at −50 °C. The reaction mixture was stirred at this temperature under argon atmosphere for 1 h, at which time TLC showed no starting material. The reaction mixture was quenched with satd aq $NaHCO_3$ (1 mL) and the cooling bath was removed. The mixture was poured into ether/water (20:5 mL) and it was extracted with ether (2×15 mL). The organic phase was washed with 2 N HCl (3×10 mL), brine (3×10 mL), dried over Na_2SO_4 and the solvent evaporated to give a crude product which was purified by flash chromatography on silica gel (H/E, 95:5) affording a mixture of regioisomers **35** and **31** (119 mg, 78%) as a colourless oil (ratio 1.25:1).

4.1.22.4. Treatment of alcohol 34 with Amberlyst 15. Amberlyst 15 (0.5 g) was added to a solution of alcohol **34** (113 mg, 0.57 mmol) in CH_2Cl_2 (10 mL) and the mixture was stirred at room temperature for 4 h, at which time TLC showed no **34**. Then, it was filtered and the solvent was evaporated to give 13-nor-austrodor-5(10)-ene (**36**) (99 mg, 98%). IR (film) ν 1693, 1463, 1379, 1359, 1261, 1190, 1097, 100, 801, 749 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.09 (m, 2H), 1.72 (m, 2H), 1.51 (dt, *J*=6.0, 3.1 Hz, 2H), 1.49 (t, *J*=7.1 Hz, 2H), 1.31 (dt, *J*=6.0, 3.0 Hz, 2H), 0.88 (s, 6H), 0.87 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 139.4 (C), 138.6 (C), 38.2 (CH_2), 38.0 (CH_2), 30.9 (C), 29.8 (C), 27.0 (CH_2), 26.8 ($2CH_3$), 25.4 ($2CH_3$), 20.6 (CH_2), 19.1 (CH_2); EIMS *m*/*z* (rel int.): 178 [M+] (4), 163 (46), 149 (12), 138 (9), 123 (92), 109 (21), 107 (23), 95 (37), 91 (30), 87 (35), 82 (51), 81 (32), 79 (23), 69 (34); HRMS (FAB) *m*/*z* calcd for $C_{13}H_{22}Na$ 201.1619; found 201.1611.

4.1.23. Synthesis of (5*S*,10*S*)-9,12-dinor-austrodor-8-one (19). To a solution of the mixture of alkenes **35**–**31** (1.25:1) (0.5 g, 2.80 mmol) in *t*-BuOH/Water (8:1 mL) was added under argon atmosphere 2% aqueous solution of OsO_4 (1 mL). After stirring for 5 min at room temperature, sodium periodate (1.8 g, 8.41 mmol) was added and the mixture was stirred at 45 °C under an atmosphere of argon for 5 h. Water (5 mL) was added and the mixture was extracted with ether (2×15 mL), the combined ether was washed with water (3×10 mL) and brine. The organic phase was dried over Na_2SO_4 and concentrated to give a crude product which was chromatographed on silica gel (H/E, 9:1) to give pure **19** (150 mg, 30%) as a colourless oil. $[\alpha]_D$ +112.4 (*c* 0.9, CH_2Cl_2) [lit.:[10b] +107.0 (*c* 3.8, CH_2Cl_2)]. The MS, IR, ^1H and ^{13}C NMR data agreed with the literature data.[10b]

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Supplementary data

Copies of ^{1}H, ^{13}C NMR and DEPT spectra for compounds **1**, **2**, **11**, **12**, **23**–**28**, **30**, **32** and **34**–**36** are included as Supplementary data. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.09.016.

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