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STUDIES TOWARD THE TOTAL SYNTHESIS OF POLYOXYGENATED LABDANES: PRELIMINARY APPROACHES

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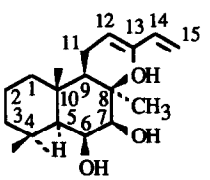
Summary- Using the keto-ester **3** as a starting material, methods are developed for the successive introduction of hydroxy groups at C-6, C-7 and C-8 of a decalin system, as well as for elaboration of a C-9 pentadiene chain in a preliminary approach to the total synthesis of trihydroxylabdadienes

Within recent years, there has been high interest in the total synthesis of certain polyoxygenated diterpenes, most notably forskolin,[1] because of their biological activities and scarcity from plant sources In this context, we have undertaken the synthesis of crotomachlin, a labdane diterpene from the East African plant *Croton macrostachyus*, reported by I Kubo to possess, *in vitro*, antilipoxygenase activity [2] Kubo initially assigned structure **1** to this substance Subsequently and independently, F Bohlman reported the isolation, from the leaves of *Koanophyllon conglobatum*, of a substance having the same physicochemical properties to which he assigned the structure **2**, epimeric to **1** at C-8 [3] In order to determine the correct structure of this natural product, we have explored the total synthesis of these two compounds



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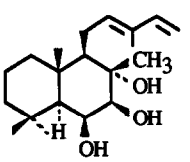


2

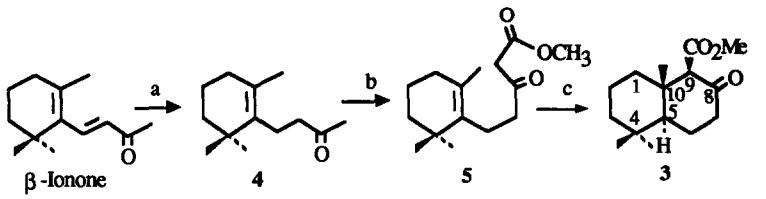
In this first paper, we describe our approaches to these substances Specifically, we report methods for the generation of the diene chain at C-9 of a decalin system, and tactics which permit the introduction of hydroxy groups at C-6, C-7 and C-8 of the same system

I- Preparation of useful intermediates

Our starting material, keto-ester **3**, could be synthesized from geraniol in a 20% yield by White's procedure,[4] or from β-ionone in a 46% yield by the three step sequence described in Scheme 1

Selective reduction of the α,β double bond of β-ionone was achieved using tri-*n*-butyltin hydride[5] to give γ,δ unsaturated ketone **4** This underwent Claisen condensation with dimethyl carbonate and sodium hydride to yield the keto-ester **5**, which was cyclised to **3** with tin tetrachloride

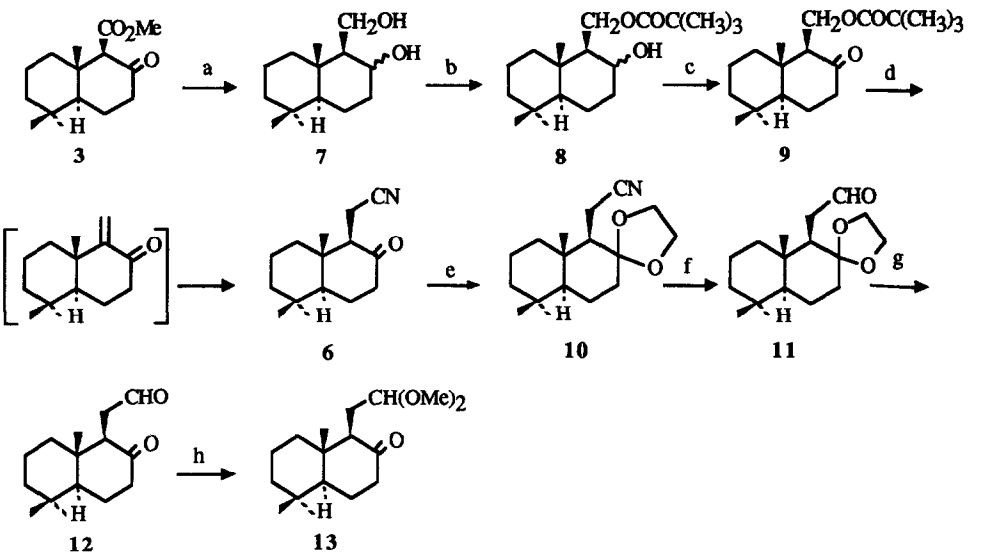
Scheme 1



a) Bu_3SnH, 1 eq , AIBN cat , 60°, 91%, b) $(MeO)_2CO$, excess, NaH, 1 eq , toluene, reflux, 97%, c) $SnCl_4$, 2 eq , CH_2Cl_2, -20° to rt, 12 h, 52%

Keto-ester **3** was transformed to cyanoketone **6**[6] through the reaction sequence depicted in Scheme 2

Scheme 2



a) $LiBH_4$, 2 eq, THF, reflux, 94%, b) $ClCOC(CH_3)_3$, 1 2 eq, py, 24 h, rt , 90%, c) Dess-Martin periodinane, 1 2 eq, CH_2Cl_2, 15 min, rt, 80%, d) KCN, 3 eq, DMSO, 90°, 12 h, 85%, e) $SiMe_3OCH_2CH_2OSiMe_3$, 1 1 eq, TMS triflate, cat, CH_2Cl_2, rt, 90%, f) DIBAH, 1.2 eq, toluene, 0°, 76%, g) HCl, acetone, quantitative, h) $(MeO)_3CH$, 3 eq, MeOH, $CeCl_3$ 7 H_2O, 1 2 eq, rt, 78%

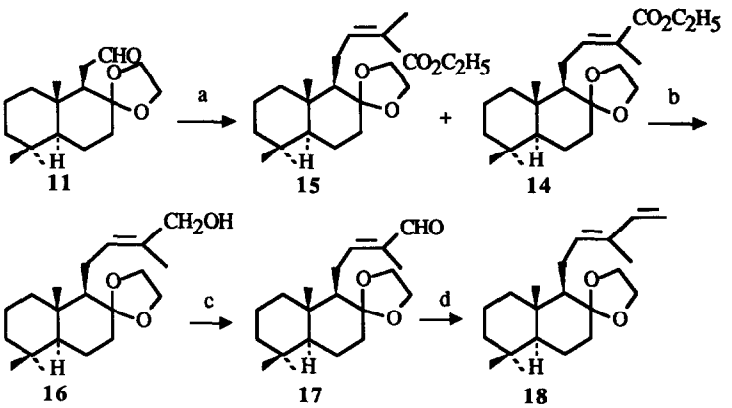
Thus, reduction with lithium borohydride in THF gave diols **7** Selective monotosylation of diols **7** at the primary hydroxyl was not successful, but the monopivalate **8** could be obtained in good yield. Oxidation of the secondary alcohol with CrO3/pyridine[7] or Dess-Martin periodinane[8] gave ketone **9** which provided the key cyanoketone **6**[6], in a 93% yield when treated with potassium cyanide in DMSO[9] at 90°C β-elimination of the ester and subsequent Michaël addition of cyanide ion could explain this result

Cyanoketone **6** could be transformed to a number of useful intermediates Thus, conversion of **6** to the dioxolane[10] **10**, followed by DIBAH reduction[11] in toluene at 0°C gave aldehyde **11.** Following acid hydrolysis of the dioxolane, selective protection of the aldehyde function in **12** with trimethyl orthoformate in methanol using cerium trichloride catalyst[12] gave the ketoacetal **13** Compounds **6, 11** and **13** represent useful intermediates for the synthesis of various diterpenes

II-Introduction of the diene side chain

Aldehyde **11** was employed to construct the diene side chain Our attempts to add the entire four carbon atoms in a single step were unsuccessful Therefore, we developed the four-step sequence depicted in Scheme 3 Wittig-Horner-Emmons condensation between **11** and the sodio derivative of ethyl diethylphosphonopropionate gave the E ester **14** in 76% yield, easily separated from its Z-isomer **15**, formed in 20% yield Lithium aluminium hydride reduction in ether transformed ester **14** to alcohol **16.** Dess-Martin periodinane converted the latter to aldehyde **17**, which with methylene triphenylphosphorane gave the desired diene **18**

Scheme 3



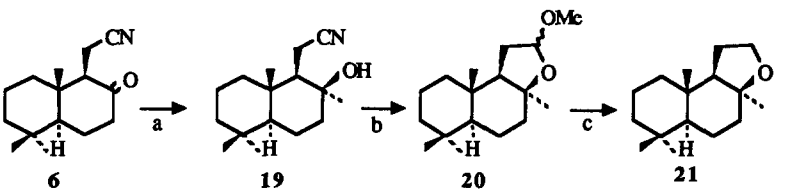
a) ethyl 2-sodio-2-diethylphosphonopropionate, 2 eq, toluene, reflux, 76%, b) $LiAlH_4$, 2 eq, ether, 0°C, 94%, c) periodinane, 1 2 eq, CH_2Cl_2, 30 min, rt, then 3 M NaOH, ether, 95%, d) methylene triphenyl phosphorane, 3 eq, THF, rt, 67%

III- Functionalisation of B ring

Modification of the B-ring was first explored by reaction of cyanoketone **6** with methyl lithium or methyl magnesium bromide, as shown in Scheme 4 Nucleophilic attack at C-8 from the less-hindered α face[13] gave

carbinol **19**, which was transformed to the acetal **20** by reduction with DIBAH followed by treatment with acidic methanol DIBAH reduction of **20** gave the known *iso*-ambrox **21** [14]

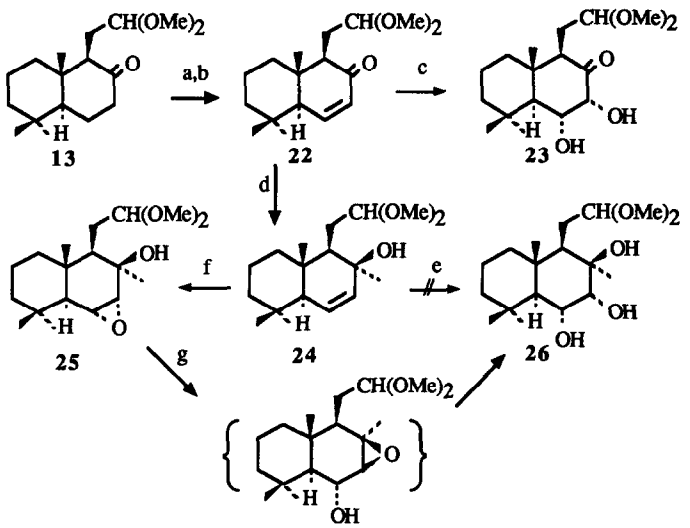
Scheme 4



a) MeLi, 2 eq , ether, -10°C, 1 h 85% or MeMgBr, 3 eq , ether, rt, 3 h 85%, b) DIBAH, 2 eq , toluene, 1 h, 0°C, then 0.1 N methanolic HCl, 85% c) DIBAH, 2 eq , toluene, 0°C, 6h, 87%

At this point, we transformed ketoacetal **13**, by the Saegusa oxidation[15] to the enone **22**. This could be osmylated with stoichiometric OsO_4 in pyridine to give keto diol **23** in a 30% yield. Reaction of enone **22** with methyl lithium gave the 8 β carbinol **24** Although the latter was inert to OsO_4, it did react with MCPBA to give epoxide **25** This underwent Payne rearrangement, in low yield, with potassium hydroxide in DMSO, to give ultimately the triol **26**, as shown in Scheme 5

Scheme 5



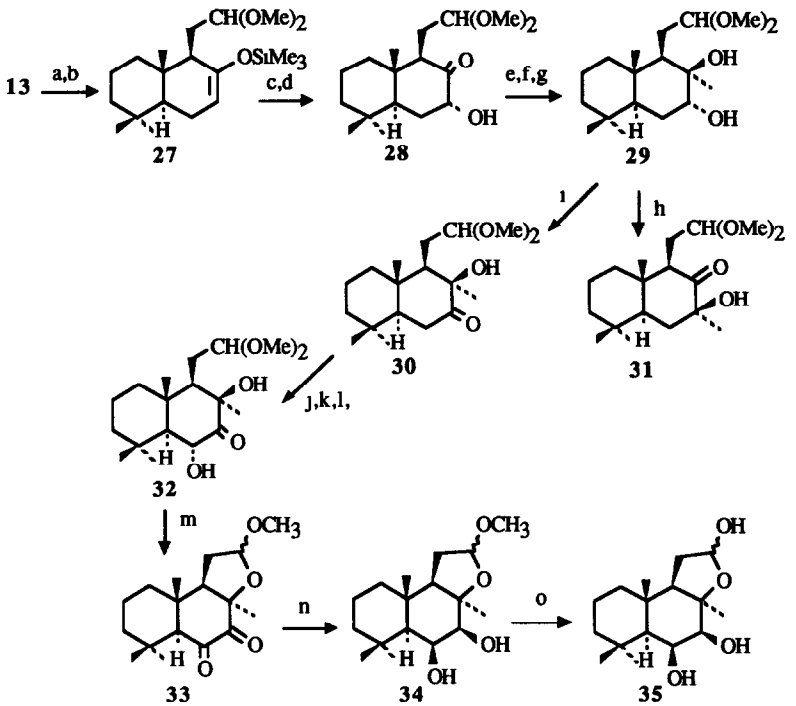
a) LDA, 3 eq, THF, -78°C, then $ClSiMe_3$, 1 2 eq; , b) $PdOAc_2$, MeCN, rt, 75%; c) OsO_4, 1 eq, py, 10 d, 54%, d) MeLi, 1 eq, ether, 0°C, 85%, e) OsO_4, 1 eq, py, rt, recovered starting material, f) MCPBA, 1 2 eq, CH_2Cl_2, 65%, g) KOH pellets, H_2O-DMSO 15/85, 60°C, 12%

A more fruitful sequence is depicted in Scheme 6 Ketoacetal **13** was converted to its trimethyl silyl enol ether **27**. Oxidation of **27** with MCPBA and desilylation introduced the 7α-hydroxyl, **28**, in 66% yield After silylation of the alcohol, addition of methyl lithium and desilylation produced the 7α, 8β-diol **29** The α-OH was

oxidised by Swern reagent[16] to give 7-ketone **30** When the oxidation was performed with Collins reagent,[7] the rearranged ketol **31** was obtained instead Structure **31** was confirmed by high field NMR which showed a methine (C-H) rather than a methylene (CH_2) α to the ketone function

At this point, the ketone **30** was converted to its trimethylsilyl enol ether[17] which was then oxidized with MCPBA and desilylated to yield the 6α, 8β-dihydroxy-7-ketone **32** Although C-6 oxidation of **32** failed with various reagents, Jones oxidation transformed **32** to the 6, 7-diketone cyclic acetal **33** Reduction of this diketone with sodium borohydride gave the 6β, 7β-dihydroxy acetal **34**, easily cleaved to the hemiacetal **35**

Scheme 6



a) LDA, 3 eq, THF, -78°C, b) $ClSiMe_3$, 1 2 eq, THF, -78°C to rt, 96%; c) MCPBA, 1 2 eq, CH_2Cl_2, rt, d) nBU_4NF, THF, 66%, e) $ClSiMe_3$, Et_3N, THF, rt, 63%, f) MeLi, 1 2 eq, ether, 0°C, g) nBu_4NF, THF, rt, 72%, h) CrO_3/py, 3 eq, CH_2Cl_2, rt, 61%, i) ClCOCOCl, 1 2 eq, DMSO, 2 eq, CH_2Cl_2, -78°C, 30 min, then Et_3N, 3 eq, -78°C to rt, 49%, j) LDA, 3 eq, THF, -78°C, 1h then $ClSiMe_3$, 1 eq, -78°C to rt, k) MCPBA, 1 2 eq, CH_2Cl_2, rt , l) nBu_4NF, THF, 50%, m) Jones reagent, 2 eq, acetone, 86%, n) $NaBH_4$, excess, EtOH, 80%, o) HCO_2H, H_2O%, 70%

At this stage, we had finally secured the 6β, 7β, 8β-trioxygenated B-ring system represented by target structure **1** From the above results, we were able to develop convenient strategies for the syntheses of both compounds **1** and **2**, to be reported in the next paper

Acknowledgements

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Experimental

Melting points were determined in capillary tubes and are uncorrected IR spectra were determined with a PERKIN-ELMER 257 or a NICOLET FT-IR 205 spectrometers, UV spectra with a PERKIN-ELMER Lambda 205 spectrometer ^1H NMR spectra were measured in $CDCl_3$ (unless otherwise stated) with TMS as internal reference, chemical shifts δ were expressed in ppm, coupling constants in Hz They were recorded on VARIAN T-60, BRUKER WP-200, BRUKER AC-250 or BRUKER WM-400 instruments ^{13}C NMR spectra were recorded on Bruker AC-250 Mass spectra (MS) were run on AEI MS-50 or AEI MS-9 spectrographs Diethyl ether and tetrahydrofuran were distilled from sodium-benzophenone ketyl, dichloromethane from phosphorous pentoxide, toluene from sodium, acetonitrile from calcium hydride Other solvents and reagents were purified by standard procedures as necessary Column chromatography was performed on Merck Kieselgel 60, flash column chromatography on Merck Kieselgel 60H Analytical thin layer chromatography was performed using Kieselgel pre-coated foils Usual work-up means that water was added to the reaction mixture which was then extracted three times with CH_2Cl_2 The combined organic layers were washed with brine, dried over Na_2SO_4 or $MgSO_4$ and evaporated The natural product numbering system was adopted for ^1H and ^{13}C assignments for the decahydronaphtalene derivatives, but systematic nomenclature was used for compound **5** The described products are racemates, however, to point out the relative configurations of their substituents they are represented as 4α, 4β, 10β- trimethyl- (5α-H)- decahydronaphtalene derivatives

Dihydro-β-ionone, 4.

Neat β-ionone (15 g, 78 mmol), Bu_3SnH (25 g, 86 mmol), AIBN (140 mg) were mixed and held at 80°C, overnight, under an Argon atmosphere The crude cool reaction mixture was poured onto a silica gel column Elution with CH_2Cl_2 gave essentially pure dihydro-β-ionone **4**, (14 g, 91%), as a tan oil, IR $\nu_{C=O}$ 1705 cm^{-1}, ^1H NMR, 200 MHz, δppm 0 95 (6H, *s*, CH_3-1), 1 40 (2H, *m*, CH_2), 1 54 (3H, *s*, CH_3-5), 1 54 (2H, *m*, CH_2), 1 88 (2H, *m*, CH_2), 2 12 (3H, *s*, $COCH_3$), 2 20 (2H, *m*, CH_2), 2 48 (2H, *m*, CH_2)

Methyl 5[2',6',6'-trimethylcyclohex-1'-enyl]-3-ketopentanoate, 5.

NaH (3 5 g of 50% suspension in oil, 73 mmol) was added to a solution of **4** (14 g, 72 mmol) and diethyl carbonate (17 g, 144 mmol) in toluene (150 mL) The stirred reaction mixture was held at 100°C for 3 h, under an Argon atmosphere Upon cooling, a mixture of ether (250 mL), concentrated HCl (35 mL) and water (85 mL) was carefully added After vigourous stirring, the organic layer and a subsequent ether extract of the aqueous phase were combined, dried ($MgSO_4$) and evaporated to yield **5** (17 6 g, 97%), as a colorless oil, $C_{15}H_{24}O_3$ calc % C 71 39, H 9 59, O 19 02, found C 71 16, H 9 85, O 18 98, IR $\nu_{C=O}$ 1705 cm^{-1}, ^1H NMR, 200 MHz, δppm 1 09 (6H, *s*, CH_3), 1 50 (2H, *m*, CH_2), 1 67 (3H, *s*, CH_3), 1 67 (2H, *m*, CH_2), 2 0 (2H, *m*, CH_2), 2 39 (2H, *m*, CH_2), 2 70 (2H, *m*, CH_2), 3 57 (2H, *s*, CH_2-2), 3 85 (3H, *s*, OCH_3),

9β-Carbomethoxy-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalen-8-one, 3.

$SnCl_4$ (12 7 g, 47 mmol) was added to a solution of **5** (11 5 g, 45 6 mmol) in CH_2Cl_2 (1 l).at 0°C The solution was stirred for 12 h at room temperature and then, washed three times with aqueous HCl (150 mL of 2 N solution), dried over Na_2SO_4 and evaporated Column chromatography on silica gel of the residue, by elution with heptane-ethyl acetate 95/5, gave **3** (6 g, 52%), as an oil crystallizing upon standing, m p 82-83°,$C_{15}H_{24}O_3$, calc % C 71 39, H 9 59, O 19 02, found C 71 41, H 9 85, O 19 11, MS, EI M^+ 252, IR $\nu_{C=O}$ 1705 cm^{-1}, ^1H NMR, 400 MHz, δppm 0 88 (3H, *s*, CH_3), 0 96 (3H, *s*, CH_3), 1 16 (3H, *s*, CH_3), 1 26 (2H, *m*, CH_2), 1 56 (6H, *m*, CH_2), 1 77 (1H, *dd*, J=13, J'=5, H-5), 2 05 (1H, *m*, part of CH_2), 2 36 (1H, *m*, H-7α), 2 52 ((1H, *ABdd*, J=15, J'=5, J''=2, H-7β), 3 23 (1H, *s*, H-9), 3 70 (3H, *s*, OCH_3)

8ξ-hydroxy-9β–hydroxymethyl-4α, 4β,10β-trimethyl-(*trans*)-decahydronaphtalene, 7.
$LiBH_4$ (3 g, 13 6 mmol) was carefully added to a solution of **3** (35 g, 13 8 mmol) in THF (500 mL) at 0°C. The stirred mixture was then refluxing for 18 h After cooling, MeOH (20 mL) and H_2O were added. Extraction with ether furnished **7** as mixture of diastereomers Cristallization in acetone gave pure 8β-OH (15.3 g), m.p 148°C, $C_{14}H_{26}O_2$, calc·% C 74 28, H 11 58, O 14 14, found C 74 30, H 11 61, O 13.97, MS, EI: M^+226, m/z 208, ^1H NMR, 400 MHz, δppm. 0 88 (3H, *s*, CH_3), 0 90 (3H, *s*, CH_3), 1 14 (3H, *s*, CH_3), 3.85 and 3.96 (2H, *ABX*, J_{AB}=11.5, J_{AX}=4 5, J_{BX}=8, CH_2OH), 4 27 (1H, *q*, J=3, H-8α) Mother liquors were filtered through silica gel column to give **7** (14 4 g), as diastereomeric mixture, (total yield 29 7 g, 94%).

8ξ-hydroxy-9β-pivaloyoxymethyl-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalene, 8.
Pyvaloyl chloride (7.9 g, 66 mmol) was added to **7** as mixture of diastereomers (12.41 g, 55 mmol) in pyridine (50 ml) After 24 h at room temperature, aqueous $NaHCO_3$ and ether were added to the solution. The organic layer was separated, the aqueous phase was extracted twice with ether and the combined ether fractions were washed with brine, dried over $MgSO_4$ and evaporated to give **8**, (13 6 g, 80%), oil, which was used without further purification, MS, EI· M^+310, m/z 295, 292, 225, 208

9β-pivaloyloxymethyl-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalen-8-one, 9.
Dess-Martin periodinane[8] (11 32 g, 26 mmol) was added portionwise to a stirred solution of **8** (6.9 g, 22 mmol) in CH_2Cl_2 (100 ml) and the mixture was stirred at room temperature Upon completion of the reaction monitored by TLC, ether (300 ml) aqueous $NaHCO_3$ and aqueous $Na_2S_2O_7$ were added and the mixture was stirred for 1 h. The organic layer was separated, washed with brine and evaporated to give **9** (5 8 g, 85%), after purification by flash chromatography, oil, $C_{19}H_{32}O_3$, calc % C 73 98, H 10 46, O 15 56, found· C 73 72, H 10 75, O 15 54, MS, EI M^+ 308, m/z 295, 223 (M-COC$(CH_3)_3$, 206 (M-HOOCC$(CH_3)_3$), IR $\nu_{C=O}$ 1720 cm^{-1}, 1150, (C-0), 1280, 1355, 1390 (CH_3), 1460, 1480 cm^{-1}, ^1H NMR, 250 MHz, δppm 0 70 (3H, *s*, CH_3), 0.86 (3H, *s*, CH_3), 0 96 (3H, *s*, CH_3), 1 13 (9H, *s*, CH_3), 1 15-1 8 (7H, *m*, CH) 2 03 (2H, *m*, CH) 1 20-1 45 (5H, *m*, CH) 3 85 and 3 96 (2H, *ABX*, J_{AB}=11, J_{AX}=4, J_{BX}=7, CH_2O)

8-Keto-9β-cyanomethyl-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalene, 6.
A solution of **9** (7 g, 22 7 mmol) and KCN (4 5 g, 69 mmol) in DMSO (300 mL) were warmed at 90°C overnight, under an Argon atmosphere After cooling, addition of aqueous $NaHCO_3$ was followed by extraction with ether The organic phase was washed five times with water, dried ($MgSO_4$) and evaporated Flash chromatography of the residue, with CH_2Cl_2 as eluent, gave **6** (4 76 g, 90%) m.p 82-83° (ether), $C_{15}H_{23}NO$, calc % C 77 20, H 9 94, N 6 00, O 6 86, found C 77 09, H 10 06, N 6 10, O 7 04, MS, EI M^+ 233, m/z 218, ^1H NMR, 400 MHz, δppm 0 73 (3H, *s*, CH_3), 0 88 (3H, *s*, CH_3), 0 99 (3H, *s*, CH_3), 1 66 (1H, *dd*, J=14, J'=5, H-5), 2 38 and 2 56 (2H, *ABXY*, J_{AB}=14, $J_{7a\text{-}6a}$=14, $J_{7a\text{-}6e}$=7, $J_{7e\text{-}6a}$=4, $J_{7e\text{-}6e}$=2, CH_2-7), 2 23 and 2 74 (2H, *ABX*, J_{AB}=16, J_{AX}=8, J_{BX}=4, CH_2CN), 2.59 (1H, *dd*, J=3, J'=8, H-9); ^{13}C NMR δ ppm 10 73 (CH_2-11), 13 82 (CH_3-17), 18 47 (CH_2-2), 21 40 (CH_3-19), 23 10 (CH_2-6), 33 35 (CH_3-18), 33 72 (C-4), 39 01 (CH_2-1), 41 08 (CH_2-3)[a], 41 37 (CH_2-7)[a], 53 31 (CH-5), 60 22 (CH-9), 119 58 (CN), 207 55 (C=O) [a] tentative assignment that may be reversed

8-Ethylenedioxy-9β-cyanomethyl-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalene, 10.
TMSTfO (0 1 mL) was added to a stirred solution of **6** (18 g, 77 mmol) and bistrimethylsilyloxyethane (17 3 g, 84 mmol) in CH_2Cl_2 (200 mL) The solution was held for 12 h at room temperature and then, washed with aqueous $NaHCO_3$, dried (Na_2SO_4) and evaporated to yield **10** (19 g, 90%), as a colorless oil crystallizing upon standing, $C_{17}H_{27}NO_2$, calc % C 73 60, H 9 81 found C 73 59, H 10 21, MS, EI M^+ 277, m/z 267, 179, 99, ^1H NMR, 200 MHz, δppm 0 88 (3H, *s*, CH_3), 0 91 (6H, *s*, CH_3), 2 23 and 2 43 (J_{AB}=18, J_{AX}=5, J_{BX}=7, CH_2CN), 4 03 (4H, *m* ,OCH_2CH_2O)

8-Ethylenedioxy-9β-carbaldehydemethyl-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalene, 11.
DIBAH (3 8 mL of 1M solution in toluene, 1 2 eq) was added to a solution of **10** (0 887 g, 3.20 mmol) in toluene (10 mL) at 0°C under an Argon atmosphere The solution was stirred for 30 min at 0°C and then, MeOH (1 mL) and 10% aqueous H_2SO_4 (10 mL) were added Aqueous phase was extracted three times with ether (20 mL) Organic phase was washed successively with 10% aqueous H_2SO_4, water and aqueous $NaHCO_3$ and dried (Na_2SO_4) Evaporation of the solvents and flash chromatography of the crude extract, with CH_2Cl_2 as eluent, gave **11** (0 685 g, 76%), as a colorless oil, $C_{17}H_{28}O_3$, calc % C 72 82, H 10 06, O 17 12 , found C

72.81, H 10.28, O 16.85, MS, EI: M^+ 280, m/z 265, 252, 99; ^1H NMR, 400 MHz, δppm. 0.83 (3H, *s*, CH_3), 0 89 (3H, *s*, CH_3), 0.90 (3H, *s*, CH_3), 1 93 (1H, *dd*, J=10, J'=3, H-5), 2.10 (1H, *dd*, J=10, J'=3, H-9) 2.15 (1H, *A* from *ABXY*, J_{AB}=16, J_{AX}=3, J_{BX}=0, H-11a), 2.31 (1H, *B* from *ABXY*, J_{AB}=16, J_{AX}=10, J_{BX}=5, H-11b), 3.56 (1H, *q*, J=5), 3.76 (1H, *q*, J=5), 3 96 (1H, *q*, J=5) and 3.98 (1H, *q*, J=5) for OCH_2CH_2O, 9.41 (1H, *d*, J=5, CHO).

9β-carbaldehydemethyl-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalen-8-one, 12.
A solution of **11** (1 g, 3 57 mmol) in acetone (10 mL) and 10% aqueous HCl (1 mL) was kept overnight at room temperature. Aqueous $NaHCO_3$ solution was added and the products were extracted with CH_2Cl_2 The organic phase was washed, dried (Na_2SO_4) and evaporated to yield **12** (0.840 g, quantitative) as a colorless oil; MS, EI: M^+ 236, ^1H NMR, 250 MHz, δppm. 0.73 (3H, *s*, CH_3), 0 85 (3H, *s*, CH_3), 0.97 (3H, *s*, CH_3), 1 22 (3H, *m*, CH), 1.4-1 8 (5H, *m*, CH), 2-2 52 (4H, *m*, CH), 2 88-3 (2H, *m*, CH), 9.75 (1H, *s*, CHO).

9β-[1'-Dimethoxyethyl]-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalen-8-one, 13.
A solution of **12** (1 g, 3 57 mmol) in MeOH (10 mL) was treated by $(MeO)_3CH$ (2.8 mL, 25 mmol) and $CeCl_3$, 7 H_2O (1.33 g, 3 57 mmol) for 3 h, at room temperature. Usual work-up gave **13** (932 mg, 78%), as a colorless oil, $C_{17}H_{30}O_3$, calc.% C 72 30, H 10 71, O 17 00 , found C 72 35, H 10.65, O 16 86,, MS, EI M^+ 282, m/z 251, 89, 75, ^1H NMR, 250 MHz, δppm. 0 70 (3H, *s*, CH_3), 0.85 (3H, *s*, CH_3), 0 95 (3H, *s*, CH_3), 1.2 (3H, *m*, CH), 1 3-1 7 (5H, *m*, CH), 2.0 (2H, *m*, CH), 2.2 (1H, *m*, CH), 2.4 (1H, *m*, CH), 3.16 (3H, *s*, OCH_3), 3 25 (3H, *s*, OCH_3), 4.26 (1H, *dd*, J=8, J'=4, H-12)

Unsaturated esters 14 and 15.
A solution of aldehyde-dioxolane **11** (167 mg, 0 6 mmol) in toluene (3 mL) was added, at 0°C, under an Argon atmosphere, to a solution of ethyl 2-sodio-phosphonopropionate (from ethyl 2-diethylphosphono-propionate, 285 mg, 1.2 mmol, and HNa, 28 mg, 1 2 mmol) in toluene (3 mL) The mixture was refluxed for 1 h. Standard work-up and flash chromatography (gradient heptane/ethyl acetate) gave pure **14** (156 mg, 71%), fraction as 1/1 mixture of **14** and **15** (20 mg) and pure **15** (34 mg, 15%)

8-ethylenedioxy-9β-[(E)-2'-carbethoxy-2'-butenyl]-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalene, 14: colorless oil, $C_{22}H_{36}O_4$, calc.% C 72.49, H 9 95, O 17 56 , found. C 72 72, H 10 05, O 17 32,, MS, EI M^+ 282, m/z 251, 89, 75, MS, EI M^+ 364, m/z 349, 319, 224, 99; IR $\nu_{C=O}$ 1700 cm^{-1}, 1260 cm^{-1} (C-O), 1640 cm^{-1} (C=C), UV $\lambda_{max\ nm}$ 224, ε 14 210; ^1H NMR, 400 MHz, δppm. 0 84 (3H, *s*, CH_3), 0.89 (3H, *s*, CH_3), 0 94 (3H, *s*, CH_3), 1.29 (3H, *t* , J=7, $CH_2\underline{CH_3}$), 1 83 (3H, *s*, CH_3-13), 3 70 (1H, *q*, J=7), 3 88 (1H, *q*, J=7), 3 96 (1H, *q*, J=7) and 4 01 (1H, *q*, J=7) for OCH_2CH_2O, 4 19 (2H, *q*, J=7, $\underline{CH_2}CH_3$), 6 88 (1H, *t*, J=7, H-12)

8-ethylenedioxy-9β-[(Z)-2'-carbethoxy-2'-butenyl]-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalene, 15 colorless oil, ^1H NMR, 400 MHz, δ ppm 0 81 (3H, *s*, CH_3), 0 91 (3H, *s*, CH_3), 0 93(3H, *s*, CH_3), 1.30 (3H, *t* , J=7, $CH_2\underline{CH_3}$), 1 86 (3H, *s*, CH_3-13), 3 68 (1H, *q*, J=7), 3 85 (1H, *q*, J=7), 3 96 (1H, *q*, J=7) and 4 01 (1H, *q*, J=7) for OCH_2CH_2O, 4 19 (2H, *q*, J=7, $\underline{CH_2}CH_3$), 6 07 (1H, *t* J=7, H-12)

8-ethylenedioxy-9β-[(E)-2'-hydroxymethyl-2'-butenyl]-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalene, 16.
Lithium aluminium hydride (16 mg, 0 42 mmol) was added to a solution of **14** (150 mg, 0 42 mmol) in anhydrous ether (5 mL) at 0°C.The mixture was stirred for 30 min at room temperature. Usual work-up gave **16** (125 mg, 94%), m p 108°C (acetone), $C_{20}H_{34}O_3$, calc % C 74 49, H 10 63, O 14 88, found· C 74 72, H 10 80, O 14 89, MS, EI M^+ 322, m/z 307, 305, 304, 263, 221, 99, ^1H NMR, 400 MHz, δppm. 0 83 (3H, *s*, CH_3), 0 88 (3H, *s*, CH_3), 0 92 (3H, *s*, CH_3), 1 69 (3H, *s*, CH_3-13), 3 98 (2H, *s*, CH_2OH), 3 75 (1H, *q*, J=7), 3 88 (1H, *q*, J=7), 4 10 (1H, *q*, J=7) and 4 11 (1H, *q*, J=7) (OCH_2CH_2O), 5 51 (1H, *m* , H-12), ^{13}C NMR δ ppm 13 70 (CH_3-16), 14 59 (CH_3-17), 18 66 (CH_2-2), 19 91 (CH_2-11), 21 80 (CH_3-19), 21 96 (CH_2-6), 33 26 (C-4), 33 68 (CH_3-18), 36 27 (CH_2-1), 39 37 (C-10), 39 78 (CH_2-3)[a], 42 02 (CH_2-7)[a], 55 36 (CH-5), 58 29 (CH-9), 63 21 and 54 01 (OCH_2CH_2O), 69 12 (CH_2OH-14), 111 52 (C-8), 129 65 (CH-12) 132 22 (C-13) [a] tentative assignment that may be reversed

8-ethylenedioxy-9-[(E)-2'-carbaldehyde-2'-butenyl]-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalene, 17.
Dess-Martin periodinane[8] (254 mg, 0 6 mmol)was added to a solution of **16** (161 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) The mixture was stirred for 30 min at room temperature Then, ether (10 mL) and 2M aqueous NaOH (2

mL) were poured and the mixture was stirred for further 30 min Extraction with ether afforded **17** (152 mg, 95%), MS EI· M^+ 320, m/z, IR $\nu_{C=O}$ 1640 cm^{-1} ; UV $\lambda_{max.nm}$ 235, ε 15400; ^1H NMR, 400 MHz, δppm: 0 84 (3H, *s*, CH_3), 0 90 (3H, *s*, CH_3), 0 97 (3H, *s*, CH_3), 1 75 (3H, *s*, CH_3-13), 3.66 (1H, *q*, J=7), 3.86 (1H, *q*, J=7), 3.96 (1H, *q*, J=7) and 3.98 (1H, *q*, J=7) for OCH_2CH_2O, 6.62 (1H, *t*, J-6 Hz, H-12) 9.3 (1H, *s*, CHO).

8-ethylenedioxy-9-[(E)-3'methyl-1',3'-pentadienyl]-4,4',10-trimethyl-(*trans*)-decahydronaphtalene, 18.

A solution of **17** (45 mg, 0 14 mmol) in THF (2 mL) was added to a solution of methylene triphenylphosphorane (from triphenylphosphonium bromide, 100 mg, 0.28 mmol and 0 17 mL of 1 6 M solution of n-BuLi in hexane) in THF/hexane, under an Argon atmosphere, at room temperature The mixture was stirred for 2 h Usual work-up followed by silica gel column chromatography gave **18** (30 mg, 67%), as a colorless oil, $C_{21}H_{34}O_2$, calc %· C 79 19, H 10 76, O 10.05 , found C 79 04, H 10 68, O 9 93; MS, EI M^+ 282, m/z 251, 89, 75, MS EI M^+ 318, m/z 303, 221, 180, 99 (base peak), UV $\lambda_{max\ nm}$ 231, ε 23 380, ^1H NMR, 400 MHz, δppm· 0 86 (3H, *s*, CH_3), 0 90 (3H, *s*, CH_3), 0 96 (3H, *s*, CH_3), 1 76 (3H, *s*, CH_3-13), 3 70 (1H, *q*, J=7), 3.88 (1H, *q*, J=7), 3 95 (1H, *q*, J=7) and 4 03 (1H, *q*, J=7) for OCH_2CH_2O, 4 88 (1H, *d*, J= 12.6, H-15a), 5 04 (1H, *d*, J=20, H-15b), 5 60 (1H, *t*, J=6 6, H-12), 6 35 (1H, *dd*, J=20, J'=12 6, H-14)

9β-cyanomethyl-8β-hydroxy-4α,4β,8α,10β-tetramethyl-(*trans*)-decahydronaphtalene, 19.

A solution of MeLi (0.3 mL of a 3M solution in ether, 0 9 mmol) was added, at -78°C, to a solution of **6** (100 mg, 0 42 mmol) in anhydrous ether (3 mL), under an Argon atmosphere The reaction mixture was stirred for 30 min. Quenching with aqueous NH_4Cl was followed by extraction with ether The organic layer was washed, dried ($MgSO_4$) and evaporated to give **19** (91 mg, 85%), m p 107° (hexane), $C_{16}H_{27}ON$, calc.% C 77.06, H 10 91, N 5 62, O 6.42 found C 76 85, H 10 94, N 5 36, O 6 51, MS, EI M^+ 249, m/z 234, 216, 179, 164, 96, ^1H NMR, 400 MHz, δppm 0 83 (3H, *s*, CH_3), 0 90 (3H, *s*, CH_3), 0 91 (3H, *s*, CH_3), 1 30 (3H, *s*, 8-CH_3), 1 55 (12H, *m*, $W_{1/2\ H}$=233 Hz, 5 CH_2 and 2 CH), 2 30 and 2 60 (2H, *ABX*, J_{AB}=18, J_{AX}=3, J_{BX}=7 5, CH_2-11)

12-methoxy-isoambrox, 20.

DIBAH (0 7 mL of 1M in toluene, 0 7 mmol) was added to a solution of **19** (80 mg, 0 32 mmol) in toluene (5 mL), at 0°C, under an Argon atmosphere The mixture was stirred for 1 h and then, MeOH (1 mL) and 10% aqueous H_2SO_4 (5 mL) were added Aqueous phase was extracted three times with ether (20 mL). Organic phase was washed successively with 10% aqueous H_2SO_4, water and aqueous $NaHCO_3$ and dried ($MgSO_4$) Evaporation of the solvents gave a residue which was dissolved in MeOH (5 mL) and HCl (0 5 mL of 1M solution) was added The mixture was held at room temperature for 30 min After neutralization with aqueous $NaHCO_3$, usual work-up, followed by flash chromatography, of the crude extract gave **20** (72 mg, 85%), mixture of epimers at C-12, as a colorless oil, $C_{17}H_{30}O_2$, calc % C 76 64, H 11 35, O 12 01 found C 76 70, H 11 13, O 12 17, ^1H NMR, 200 MHz, δppm 0 86 (6H, *s*, CH_3), 0 91 (3H, *s*, CH_3), 1 23 (3H, *s*, 8-CH_3), 2 06 (2H, *m*, CH_2-11), 3 36 (3H, *s*, OCH_3), 4 93 (1H, m, H-12)

dl-*iso*-Ambrox, 21.

DIBAH (0 5 mL of 1M in toluene, 0 5 mmol) was added to a solution of **20** (70 mg, 0 26 mmol) in toluene (5 mL), at room temperature, under an Argon atmosphere The mixture was stirred for 6 h and then, MeOH (1 mL) and 10% aqueous H_2SO_4 (5 mL) were added The aqueous phase was extracted three times with ether (20 mL) The organic phase was washed successively with 10% aqueous H_2SO_4, water and aqueous $NaHCO_3$ and dried (Na_2SO_4) Evaporation of the solvents and flash chromatography of the residue gave **21** (54 mg, 87%), as a colorless oil, MS, EI M^+ 236, m/z 221, ^1H NMR, 250 MHz, δppm 0 87 (3H, *s*, CH_3), 0 90 (3H, *s*, CH_3), 0 91 (3H, *s*, CH_3), 1 06 (3H, *s*, 8-CH_3), 2 06 (2H, *m*, CH_2-11), 3 70 (1H, *q*, J=7 5, H-12), 3 78 (1H, *m*, H-12) [14]

9β-[1'-Dimethoxyethyl]-4α,4β,10β-trimethyl-(*trans*)-1,3,5,8-octahydronaphtalen-8-one, 22.

A solution of LDA (6 mL of 1M solution in THF/hexane) was added to a solution of **13** (380 mg, 1 35 mmol) in THF (10 mL), at -78°C, under an Argon atmosphere The reaction was stirred for 30 min at -78°C and then freshly distillated $ClSiMe_3$ (0 4 mL, 3 1 mmol) was added The mixture was stirred and warmed up from -78°C to room temperature Usual work-up and filtration on a Florisil column gave the crude trimethylsilyl enol ether, (286 mg, 60%, 0 8 mmol) which was treated in CH_3CN solution (6 mL) with $Pd(OAc)_2$ (215 mg, 0 96 mmol), at room temperature, for 3 h The mixture was poured on a silica gel column Elution with CH_2Cl_2 gave **22** (170 mg, 75%), m p 62-63°C (heptane), $C_{17}H_{28}O_3$, calc % C 72.82, H 10 06, O 17 12 found C 72 71, H 9 88, O 17 01, MS EI M^+ 280, IR $\nu_{C=O}$ cm^{-1} 1700 cm^{-1}, ^1H NMR, 200 MHz, δppm 0 79 (3H, *s*, CH_3), 0 90 (3H, *s*, CH_3), 1 03 (3H, *s*, CH_3), 1 29 (2H, *m*, $W_{1/2H}$=30 Hz, CH), 1 54, (3H, *m*, $W_{1/2H}$=30 Hz, CH), 1 72 (1H, *m*,

$W_{1/2H}$=20 Hz, CH), 1.97 (2H, *m*, $W_{1/2H}$=40 Hz, CH), 2 27 (2H, *m*, $W_{1/2H}$=18 Hz, CH), (3.27 (3H, *s*, OCH_3), 3 37 (3H, *s*, OCH_3), 4 61 (1H, *dd*, J=8, J'=5, H-12), 6.05 (1H, part A of *ABX*, J_{AB}=11, J_{AX}=4, H-7), 6 92 (part B of ABX, J_{AB}=11, J_{BX}=3, H-6).

9β-[1'-Dimethoxyethyl]-6α-7α-dihydroxy-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalen-8-one, 23.

OsO_4 (140 mg, 0 55 mmol) was added to a solution of **22** (155 mg, 0 55 mmol) in pyridine (2 mL) The mixture was kept for 10 days in the dark, then, 10% aqueous Na_2SO_3 (4 mL) and pyridine (2 mL) were added and the mixture was stirred for 2 h. Extraction with CH_2Cl_2 and filtration on silica gel column gave **23** (93 mg, 54%), MS EI M^+ 314, m/z 313, 282, ^1H NMR, 60 MHz, δppm. 0 80 (3H, *s*, CH_3), 1 0 (3H, *s*, CH_3), 1 10 (3H, *s*, CH_3), 3 18 (3H, *s*, OCH_3), 3 20 (3H, *s*, OCH_3), 3 83 (1H, *d*, J=5, H-7), 4 16 (1H, *t*, J=5, H-6)

9β-[1'-Dimethoxyethyl]-8β-hydroxy-4α,4β,8α,10β-tetramethyl-(*trans*)-1,3,5,8-octahydronaphtalene, 24.

A solution of methyl magnesium bromide (1 mL of 3M ethereal solution) was added to a solution of **22** (167 mg, 0 6 mmol) in ether at 0°C, under an Argon atmosphere The mixture was stirred for 30 min at room temperature After addition of aqueous NH_4Cl, extraction with ether gave **24** (133 mg, 85%°), as a colorless oil, MS EI M^+ 296, ^1H NMR, 60 MHz, δppm 0 83 (6H, *s*, CH_3), 0 90 (3H, *s*, CH_3), 1 16 (3H, *s*, 8-CH_3), 3 23 (3H, *s*, OCH_3), 3.26 (3H, *s*, OCH_3), 4 36 (1H, *dd*, J=7, J'=4, H-12), 5 50 (2H, *s*, H-6 and H-7)

9β-[1'-Dimethoxyethyl]-8β-hydroxy-6α,7α-epoxy-4α,4β,8α,10β-tetramethyl-(*trans*)-decahydronaphtalene, 25.

MCPBA (517 mg of 80% material, 2 39 mmol) was added to a solution of **24** (709 mg, 2 39 mmol) in CH_2Cl_2 (30 mL) the mixture was stirred, overnight, at room temperature The solution was successively washed with aqueous $Na_2O_7S_2$, aqueous $NaHCO_3$, dried (Na_2SO_4)and evaporated to give **25** (492 mg, 65%), MS EI m^+ 312, ^1H NMR, 200 MHz, δppm 0 89 (3H, *s*, CH_3), 0 94 (3H, *s*, CH_3), 1 02 (3H, *s*, CH_3), 1 30 (3H, *s*, CH_3), 3 0 (1H, *d*, J=4, H-7), 3 10 (1H, *t*, J=4, H-6), 3 30 (3H, *s*, OCH_3), 3 33 (3H, *s*, OCH_3), 4 35 (1H, *dd*, J=8, J'=4, H-12).

9β-[1'-Dimethoxyethyl]-6α,7α, 8β-trihydroxy-4α,4β,8α,10β-tetramethyl-(*trans*)-decahydronaphtalene, 26

Epoxide **25** (100 mg, 0 32 mmol) was dissolved in a 0 3 N solution of KOH in DMSO/H_2O 85/15 (10 mL) The solution was warmed for 2 h at 110°C under an Argon atmosphere. After cooling, water was added. The reaction mixture then was extracted three times with ether The combined organic layers were washed five times with H_2O, dried ($MgSO_4$) and evaporated Chromatography of the residue gave **26** (13 mg, 12%), oil, MS EI M^+ 330, ^1H NMR, 200 MHz, δppm 0 98 (3H, *s*, CH_3), 1 05 (3H, *s*, CH_3), 1 13 (3H, *s*, CH_3), 1 30 (3H, *s*, CH_3), 3 38 (3H, *s*, OCH_3), 3 40 (3H, *s*, OCH_3), 3 60 (1H, *d*, J=4, H-7), 4 20 (1H, *t*, J=4, H-6), 4 43 (1H, *t*, J=5, H-12)

9β-[1'-Dimethoxyethyl]-7α-hydroxy-4α,4β,10β-trimethyl-(*trans*)-decahydronaphtalen-8-one, 28.

A solution of **13** (2 28 g, 8 mmol) in THF (20 mL) was added to a solution of LDA (40 mL of 1M solution in THF/hexane), at -78°C, under an Argon atmosphere and the mixture was stirred for 30 min Freshly distillated $ClSiMe_3$ (2 mL, 16 mmol) was added The mixture was stirred during warming from -78°C to room temperature Usual work-up and filtration of the crude extract on a Florisil column gave trimethyl silyl enol ether **27** (2 72 g, 95%, 7 6 mmol) which was reacted in CH_2Cl_2 solution (30 mL) with MCPBA (1 72 g of 80% material, 7 6 mmol), for 2 h, at room temperature The reaction mixture was successively washed with aqueous $Na_2O_7S_2$, aqueous $NaHCO_3$ and H_2O Evaporation of the organic phase gave a residue which was treated in THF solution with nBu$_4$NF (2 4 g, 7 6 mmol) Usual work-up and chromatography of the crude extract afforded **28** (1 62 g, 66%), as a colorless oil, $C_{17}H_{20}O_4$, calc % C 68 42, H 10 13, O 21 45 found C 68 24, H 10 09, O 21 65, MS EI M^+ 298, ^1H NMR, 200 MHz, δppm 0 60 (3H, *s*, CH_3), 0 83 (3H, *s*, CH_3), 0 93 (3H, *s*, CH_3), 3 15 (3H, *s*, OCH_3), 3 23 (3H, *s* OCH_3), 3 95 (1H, *t*, J=3, H-7), 4 21 (1H, *dd*, J=5, J'=8, H-12)

9β-[1'-Dimethoxyethyl]-7α, 8β-dihydroxy-4α,4β, 8α,10β-tetramethyl-(*trans*)-decahydronaphtalene, 29.

Freshly distillated $ClSiMe_3$ (0 5 mL, 4 mmol) was added to a solution of **28** (1 04 g, 3,5 mmol) and Et_3N (1 5 mL, 1 07 mmol) in CH_2Cl_2 (10 mL) The mixture was stirred overnight at room temperature Extraction and filtration on a Florisil column gave the corresponding O-silylated compound (815 mg, 63%, 2 2 mmol) which was dissolved in anhydrous ether (50 mL), cooled at 0°C and a solution of MeLi (3 mL of 1 5 M ethereal

solution) was added, under an Argon atmosphere The mixture was stirred for 2 h at room temperature. Usual work-up gave a crude product which was treated in THF solution (20 mL) by *n*Bu4NF (800 mg, 2.5 mmol), overnight, at room temperature. Extraction with ether and chromatography of the crude extract afforded **29** (791 mg, 72%), m p 130°C (acetone), $C_{18}H_{34}O_4$, calc % : C 68.75, H 10.90, O 20 25 found. C 68.80, H 10.80, O 20 38, MS EI no M^+, m/z 282 (M-MeOH), 250 (282-MeOH), 75 ($CH(OMe)_2$; ^1H NMR, 200 MHz, δppm· 0 70 (3H, *s*, CH_3), 0 75 (3H, *s*, CH_3), 0 80 (3H, *s*, CH_3), 1 10 (3H, *s*, CH_3), 2.46 (1H, *dd*, J=12, J'=2, H-9), 3 23 (6H, *s*, OCH_3), 3.50 (1H, *t*, J=3, H-7), 4 26 (1H, *t*, J=6, H-12)

9β-[1'-Dimethoxyethyl]-8β-hydroxy-4α,4β,8α,10β-tetramethyl-(*trans*)-decahydronaphtalen-7-one, 30.

A solution of DMSO (0 9 mL, 12 8 mmol) in anhydrous CH_2Cl_2 (15 mL) was slowly added to a solution of $(ClCO)_2$ (0.5 mL, 5 8 mmol) in CH_2Cl_2 (15 mL), at -78°C, under an Argon atmosphere. After 5 min, **29** (1 6 g, 5 1 mmol) in anhydrous CH_2Cl_2 (15 mL) was then slowly added.The mixture was stirred for 15 min at -78°C and then Et_3N (3 6 mL, 25 mmol) was added The reaction was warmed to room temperature and after quenching with water, usual work-up followed by flash chromatography gave **30** (795 mg, 49%) and starting material **29** (279 mg, 17%) Ketone **30**, m p 108-109° (acetone), $C_{18}H_{32}O_4$, calc % C 69 19, H 10.32, O 20.48, found: C 68 91, H 10 32, O 20 62; MS CI (isobutane)· no MH^+, 281 (MH^+-MeOH), 249 (281-MeOH); MS CI (NH3) 330 (MNH_4^+), 312 (330-H_2O), 298 (330-MeOH), 266 (298-MeOH), IR $\nu_{C=O}$ 1700 cm^{-1}, ^1H NMR, 200 MHz, δppm 0 56 (3H, *s*, CH_3), 0 80 (3H, *s*, CH_3), 0 83 (3H, *s*, CH_3), 1 26 (3H, *s*, CH_3), 2 38 and 2.60 (2H, *ABX*, J_{AB}=16, J_{AX}=8,J_{BX}=13, CH_2-6), 3 26 (3H, *s*, OCH_3), 3 31 (3H, *s*, OCH_3), 3 70 (1H, *s*, OH), 4 70 (1H, *dd*, J=8, J'=3, H-12)

9β-[1'-Dimethoxyethyl]-7β-hydroxy-4α,4β,7α,10β-tetramethyl-(*trans*)-decahydronaphtalen-8-one, 31.

A solution of **29** (100 mg, 0 3 mmol) in CH_2Cl_2 (5 mL) was added to a suspension of Collins reagent[8] (1 mmol, from CrO_3, 100 mg, added to cold pyridine, 5 mL), at 0°C The mixture was stirred for 3 h and then was poured on a silica gel column Elution with CH_2Cl_2 gave **31** (61 mg, 61%), as a tan oil, MS CI (isobutane) no MH^+, 281 (MH^+- MeOH), 249 (281-MeOH), ^1H NMR, 200 MHz, δppm 0 60 (3H, *s*, CH_3), 0 83 (3H, *s*, CH_3), 0 90 (3H, *s*, CH_3), 1 33 (3H, *s*, CH_3), 2 46 (1H, *dd*, J=12, J'=2, H-9), 3 20 (3H, *s*, OCH_3), 3 30 (3H, *s*, OCH_3), 4 10 (1H, *s*, OH), 4 26 (1H, *dd*, J=4, J'=8, H-12)

9β-[1'-Dimethoxyethyl]-6α-8β-dihydroxy-4α,4β,8α,10β-tetramethyl-(*trans*)-decahydronaphtalen-7-one, 32.

A solution of **30** (690 mg, 2 21 mmol) in THF (10 mL) was added to a solution of LDA (11 mL of 1M solution in THF/hexane) at -78°C, under an Argon atmosphere. The mixture was stirred for 30 min and then freshly distillated $ClSiMe_3$ (0 6 mL, 4 4 mmol) was added The mixture was warmed to room temperature After quenching with aqueous NH_4Cl, usual work-up and filtration on a Florisil column gave crude trimethylsilyl enol ether which was dissolved in CH_2Cl_2 (15 mL) MCPBA (526 mg of 80% material, 2 4 mmol) was added and the mixture was stirred for 3 h, at room temperature The solution was washed with aqueous $Na_2O_7S_2$, aqueous $NaHCO_3$, dried (Na_2SO_4) and evaporated The residue was dissolved in THF (10 mL) and *n*Bu4NF (835 mg, 2 6 mmol) was added The mixture was held at room temperature for 2 5 h Extraction with ether and chromatography of the crude extract gave starting ketone **30** (63 mg, 9%) and **32** (364 mg, 50%), m p 140-141° (acetone), $C_{17}H_{30}O_4$, calc % C 68 42, H 10 18, O 21 45, found C 68 35, H 10 38, O 21 27, MS IC (isobutane) no MH^+, 297 (MH^+-MeOH), 279 (297-H_2O), 265 (281-MeOH), 247 (265-H_2O), MS IC (NH3) 346 (MNH_4^+), 314 (346-MeOH), 282 (314-MeOH), IR $\nu_{C=O}$ 1700 cm^{-1}, ^1H NMR, 200 MHz, δppm 1 10 (3H, *s*, CH_3), 1 12 (3H, *s*, CH_3), 1 13 (3H, *s*, CH_3), 1 47 (3H, *s*, CH_3), 3 40 (3H, *s*, OCH_3), 3 41 (3H, *s*, OCH_3), 4 44 (1H, *t*, J=6, H-12), 4 73 (1H, *d*, J=12, H-6), 4 81 (1H, *s*, OH)

(8β,9β,d)-[2'-methoxytetrahydrofuryl]-4α,4β,8α,10β-tetramethyl-(*trans*)-decahydronaphtalen-6-7-dione, 33.

Four drops of Jones reagent were added to a solution of **32** (100 mg, 0 3 mmol) in acetone (5 mL) Upon completion of the reaction monitored by TLC, MeOH (0 2 mL) and H_2O were added Extraction with CH_2Cl_2 and flash chromatography of the crude extract gave **33** (77 mg, 86%), as an unstable oil, as 2/1 mixture of epimers at C-12, $C_{17}H_{26}O_4$, MS EI M^+ 294, m/z 279 (M-31), 266 (M-C=O), IR $\nu_{C=O}$ 1720 cm^{-1}, ^1H NMR, 200 MHz, δppm 0 90 (min) and 0 96 (maj) (3H, *s*, CH_3), 1 03 (min) and 1 10 (maj) (3H, *s*, CH_3), 1 23 (min) and 1 26 (maj) (3H, *s*, CH_3), 1 46 (3H, *s*, 8-CH_3), 3 38 (3H, *s*, OCH_3), 5 06 (1H, *dd*, J=6, J'=3, H-12)

(8β,9β,d)-[2'-methoxytetrahydrofuryl]-6β,7β-dihydroxy-4α,4β,8α,10β-tetramethyl-(*trans*)-decahydronaphtalene, 34.
$NaBH_4$ (14 mg, 0.4 mmol) was added to a solution of **33** (54 mg, 0.18 mmol) in EtOH (1 mL). The mixture was stirred at room temperature. Upon completion of the reaction monitored by TLC, addition of H_2O and extraction with CH_2Cl_2 gave **34** (43 mg, 80%), as a 2/1 mixture of epimers at C-12, $C_{17}H_{30}O_4$, calc %: C 68 42, H 10 13, O 21.45, found C 68.39, H 10 05, O 21 72; MS EI· M^+ 298, m/z 283 (M-15), 264 (M-18-15), ^1H NMR, 200 MHz, δppm 0 96 (maj.) and 1.0 (min.) (3H, *s*, CH_3), 1 0 (3H, *s*, CH_3), 1.15 (maj.) and 1 06 (min.) (3H, *s*, CH_3), 1.48 (min) and 1.55 (maj.) (3H, *s*, 8-CH_3), 3 31 (min) and 3 33 (maj.) (3H, *s*, OCH_3), 3 95 (min.) and 4.06 (maj.) (1H, *t*, J=5, H-6), 5 0 (1H, 2*dd*, H-12)

(8β,9β,d)-[2'-hydroxytetrahydrofuryl]-6β,7β-dihydroxy-4α,4β,8α,10β-tetramethyl-(*trans*)-decahydronaphtalene, 35.
A solution of **34** (87mg, mmol) in HCOOH (0.7 mL) and H_2O (0 3 mL) was held at room temperature for 2 h Solid $NaHCO_3$ was added and the solution was extracted with CH_2Cl_2 to give **35** (75 mg, 90%), as a colorless oil, $C_{16}H_{28}O_4$, calc.%. C 67 57, H 9 92, O 22.50; found· C 67.78, H 10 02, O 22.34, MS, EI M^+ 284, m/z 269, 251, ^1H NMR, 250 MHz, $CDCl_3/CD_3OD$, δppm 0.92 (3H, *s*, CH_3), 1 12 (3H, *s*, CH_3), 1 19 (3H, *s*, CH_3), 1 44 (3H, *s*, 8-CH_3), 3.34 (1H, *d*, J=4, H-7), 4 19 (1H, *dd*, J=4, J'=2, H-7), 5 46 (1H, *t*, J=6, H-12)

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