Studies on the Liverwort Sesquiterpene Alcohol Tamariscol. Synthesis and Absolute Configuration

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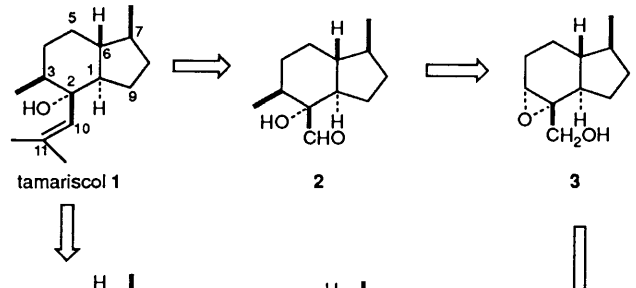
The relative configuration of the liverwort sesquiterpene alcohol (−)-tamariscol **1** has been confirmed by total synthesis and the absolute configuration has been established from the CD spectrum of the hydrindanone degradation product from (−)-**1**.

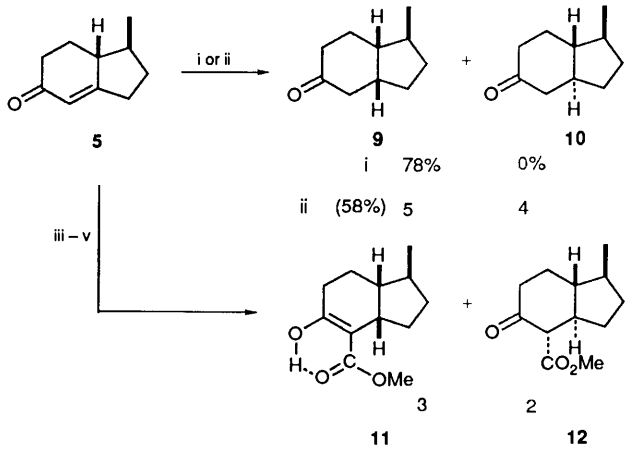
Liverworts are rich sources of various types of terpenoids and aromatic compounds which frequently show significant biological activity.[1] The absolute configuration of terpenoids isolated from the liverwort is either the same as or the opposite to that isolated from the higher plants.[1] Therefore it is very important to establish the absolute configuration of compounds isolated from this source. Tamariscol [(−)-**1**] is a sesquiterpene alcohol isolated from the liverwort *Frullania tamarisci* and its structure was determined by extensive high-resolution NMR techniques by Connolly and his group.[2] However, the stereochemistry has been revealed only by measurement of the coupling constants in its ^1H NMR spectra in the presence of a shift reagent and by comparison of the ^{13}C NMR data with those of known compounds. The absolute configuration of (−)-**1** has not been established. Since tamariscol (−)-**1** has a pleasant smell and may be useful in the preparation of perfumes and other additives,[3] we became interested in its absolute configuration as well as its total synthesis, the results of which also confirmed the relative stereochemistry. The stereoisomers of compound **1** as well as model compounds have been synthesized in order to estimate the quality of their odours. We now report our results on the synthesis and degradation of (−)-**1** to confirm the relative stereochemistry and to determine the absolute configuration of this compound.

Results and Discussion

Synthetic Plan.—Since the relative stereochemistry of tamariscol, (−)-**1**, has not been completely assigned, we planned to synthesize compound **1** from a compound with known stereochemistry and *via* a common intermediate which can be converted into all the possible isomers. The enone **5** having a secondary methyl group, and prepared from the indanone **6**, was chosen as the starting material, since its relative sterochemistry is known.[4] Epoxidation of an intermediate allyl alcohol followed by methylation was investigated first (Scheme 1). After several attempts, the synthetic route which includes the isomerization of ketone **7** was then studied. On the other hand, we synthesized the optically active compound starting from *l*-carvone **50**.



Scheme 1

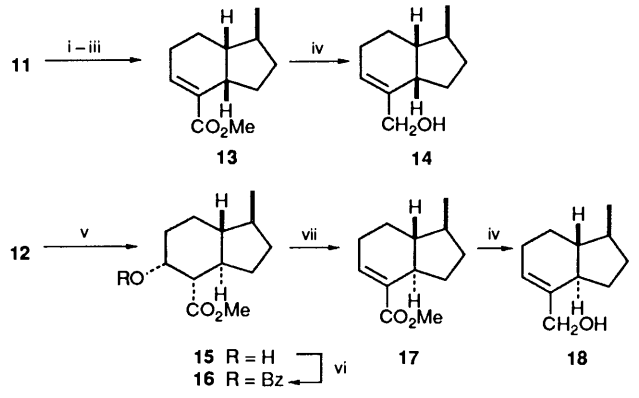


Scheme 2 *Reagents and conditions:* i, H_2, Pd–C, PhH; ii, Li, liq. NH_3; iii, Li, liq. NH_3, Bu^{t}OH; iv, CO_2, THF, −78 °C; CH_2N_2, Et_2O

1. *Epoxide Route.*[5]—When the enone **5** was subjected to catalytic hydrogenation (H_2, Pd–C, EtOH), the corresponding *cis*-isomer **9** was produced (78%), while a mixture of *cis*- and *trans*-isomer, **9** and **10**, was produced (58%) under Li–liq. NH_3 conditions (**9**:**10** 5:4) (Scheme 2). After the enone **5** had been treated with Li in liq. NH_3 and Bu^{t}OH, the solvents were removed under reduced pressure.[6] Dry tetrahydrofuran (THF) was added and the solution was treated with solid CO_2 (−78 °C to room temp.) overnight. Careful work-up and CH_2N_2 treatment gave the methyl esters **11** and **12** (3:2) after chromatographic separation. Since *trans*-fused system of the keto ester **12** could not be determined by examination of the 2-H [δ 3.23 (d, $J_{1,2}$ 12.3 Hz)] signal, further transformations of both the keto esters **11** and **12** into the ketones **22**, **25** and **30** were undertaken in order to elucidate the stereochemistry (Schemes 3–5).

Compound **11** (enol form) was converted into the α,β-unsaturated methyl ester **13** in three steps (i, $NaBH_4$–MeOH; ii, MsCl–Py; iii, 1,8-diazabicyclo[5.4.0]undec-7-ene(DBU)–PhH]. The ester **13** was reduced by $LiAlH_4$ to give the allyl alcohol **14** (Scheme 3). Compound **12** (keto form) was reduced by

L-Selectride to give an axial alcohol **15**, which was further converted into the benzoate **16** by treatment with benzoyl



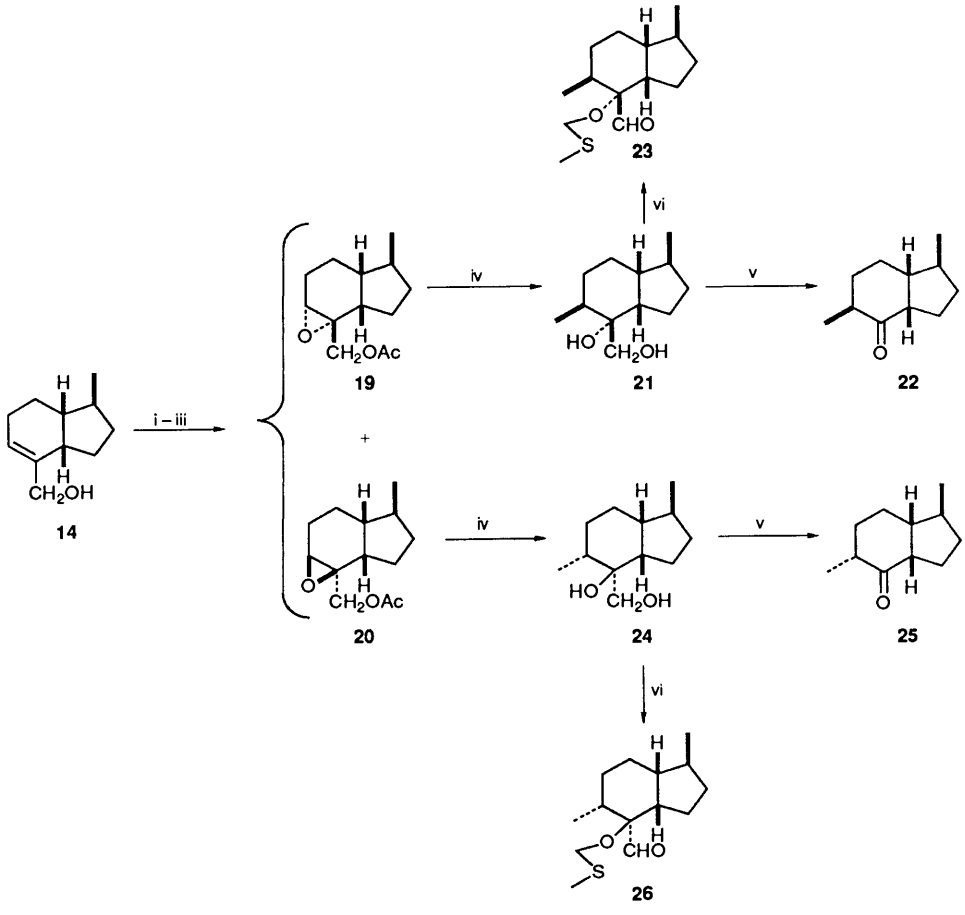
Scheme 3 *Reagents:* i, $NaBH_4$, MeOH; ii, MsCl, pyridine; iii, DBU, PhH; iv, $LiAlH_4$; v, L-Selectride; vi, BzCl, pyridine; vii, LDA

chloride in pyridine. This derivative was more easily used than the acetate or the mesyl ester, because the proton at C-3 resonated at lower field and was easily detected, and because compound **16** can be detected on TLC plates by UV light. Treatment of the benzoate **16** with lithium diisopropylamide (LDA) afforded α,β-unsaturated methyl ester **17**, which was reduced by $LiAlH_4$ to give the allyl alcohol **18**.

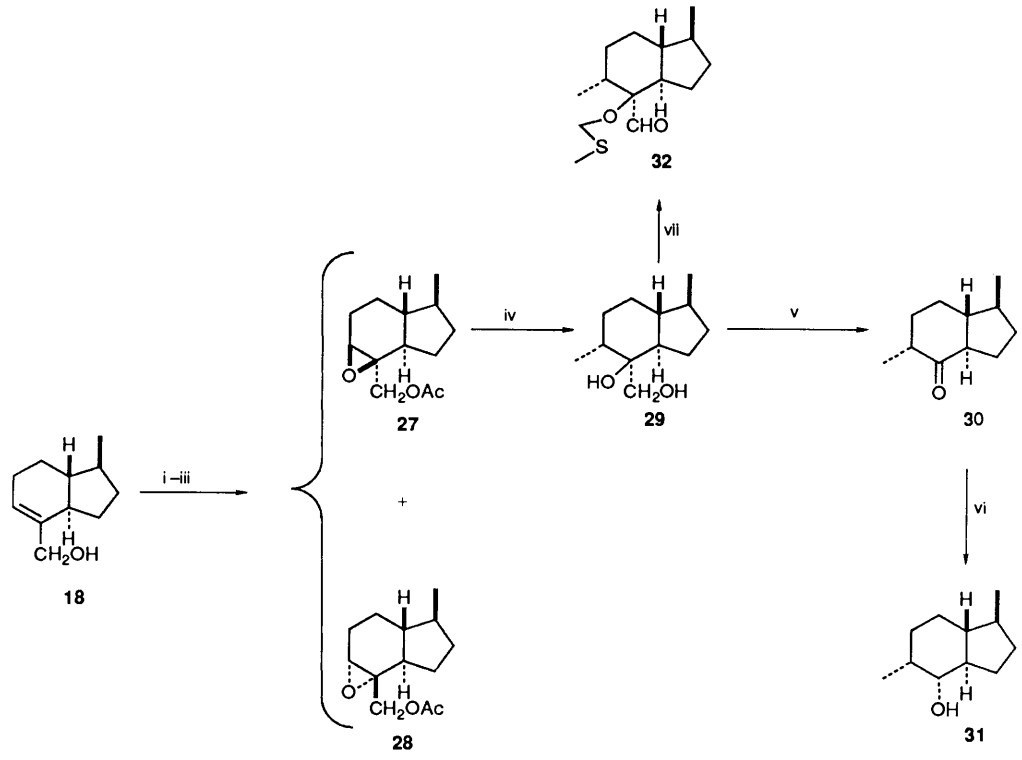
The allyl alcohol **14** was treated with *m*-chloroperbenzoic acid (MCPBA) followed by acetylation to afford both isomers of the epoxide acetates, which were separated by column chromatography over silica gel to give the epoxides **19** and **20**, although their stereochemistry was not clear at this stage (Scheme 4). Reaction of the epoxides **19** and **20** with Me_2CuLi gave diols **21** and **24**, respectively. When the diol **21** was oxidized with pyridinium chlorochromate (PCC), the ketone **22** was obtained, while the diol **24** gave ketone **25**. The proton (1-H) α to the carbonyl group of compound **22** appeared at δ 2.79 (q, *J* 8.4 Hz) and that of compound **25** at δ 2.70 (br t, *J* 6.4 Hz). The coupling patterns of these protons are quite different from each other and clearly show that they have *cis*-fused hydrindanone systems because they can change conformations due to the configuration of the methyl group at the 3-position. Hence, compound **22** adopts the steroidal conformation, while its isomer **25** the non-steroidal one.

The allyl alcohol **18** was converted into epoxides **27** and **28** by the same procedure described above (Scheme 5). The epoxide **27** afforded a diol **29** smoothly, while the epoxide **28** gave a complex mixture. The reason for the different behaviour between these epoxides was not clear, but we assume that the epoxide opening of **28** was not in a *trans*-diaxial fashion and hence that rearrangement might have occurred. The ketone **30** was obtained by PCC oxidation of the diol **29**. The proton (1-H) α to the carbonyl group of compound **30** resonated at δ 2.13 (dd, *J* 12.7, 10.3 and 7.3 Hz). The coupling pattern of 1-H of compound **30** is best explained as that of a *trans*-fused hydrindanone. The ketone **30** was further reduced by $LiAlH_4$ to afford the alcohol **31** [δ 3.23 (dd, *J* 10.5 and 4.6 Hz, 2-H)] as the sole product. The ^1H NMR spectrum of product **31** shows two couplings due to 3-H (axial–equatorial) and 1-H (axial–axial), indicating that the methyl group at the 3 position is α-axial.

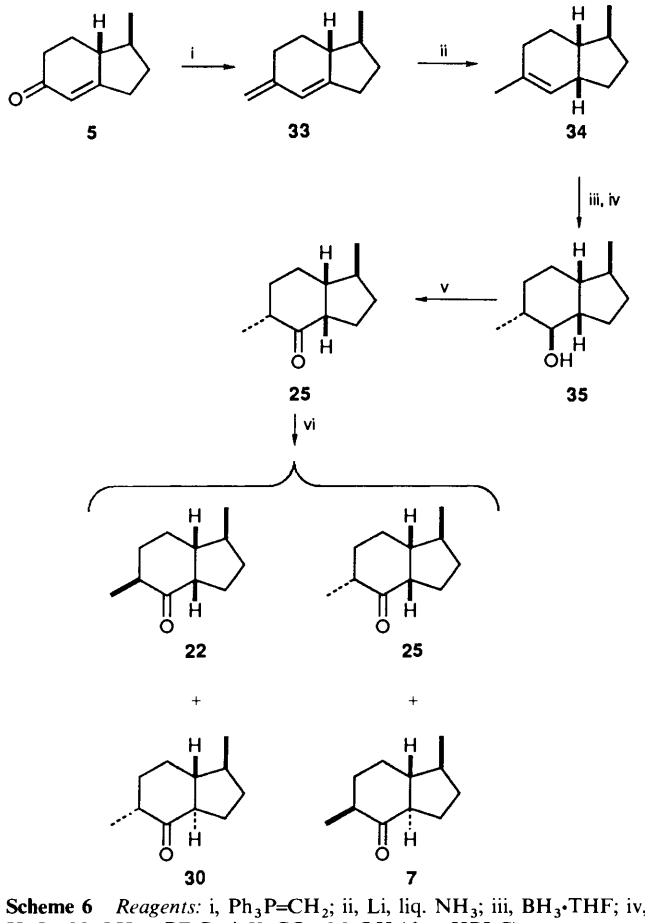
Since all the configurations for compounds **21**, **24** and **29** are clear now, each diol was subjected to oxidation and protection reaction [Me_2S, *N*-chlorosuccinimide (NCS)].[7] The methylthiomethoxy aldehyde **23** was allowed to react with the Wittig



Scheme 4 *Reagents:* i, MCPBA; ii, Ac_2O, pyridine; iii, SiO_2; iv, Me_2CuLi; v, PCC; vi, NCS, Me_2S



Scheme 5 *Reagents:* i, MCPBA; ii, Ac_2O, pyridine; iii, SiO_2; iv, Me_2CuLi; v, PCC; vi, $LiAlH_4$; vii, NCS, Me_2S



Scheme 6 *Reagents:* i, $Ph_3P{=}CH_2$; ii, Li, liq. NH_3; iii, BH_3·THF; iv, H_2O_2, NaOH; v, PDC; vi, K_2CO_3, MeOH (then HPLC)

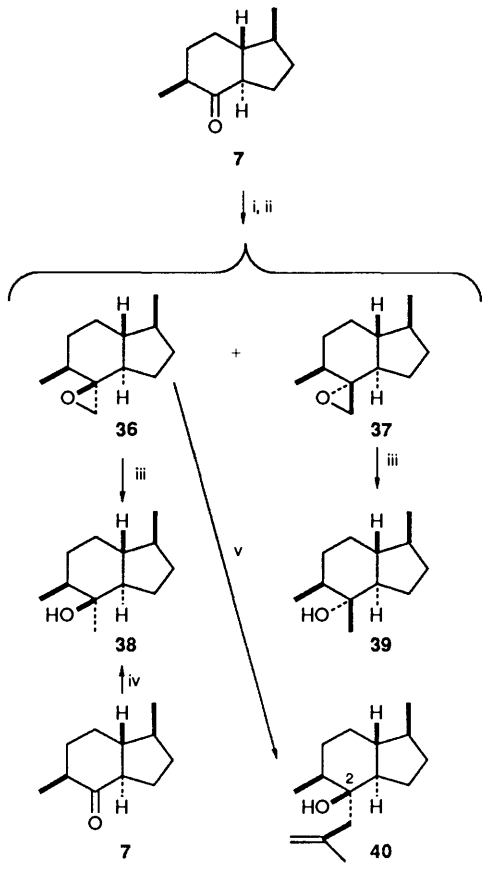
reagent in THF under a variety of conditions. No desired olefin was detected, but decomposition of the starting aldehyde was observed. In all cases the results were the same.

2. *Alkylation Route.*[8]—The enone **5** was subjected to Wittig reaction ($Ph_3\overset{+}{P}Me\ Br^-$–$Bu^nLi$) to afford the diene **33**[4] (Scheme 6), which was reduced (Li–liq. NH_3) to the *cis*-hydrindene **34**. Hydroboration–oxidation of the olefin **34** and pyridinium dichromate (PDC) oxidation gave the *cis*-hydrindanone **25**, whose spectral data were completely identical with those described above. Since MM2 calculations predicted the thermodynamic stability of the four hydrindanones to lie in the order **7** > **25** > **22** > **30**, the ketone **25** was subjected to isomerization conditions (K_2CO_3–MeOH). HPLC separation gave mainly 1-H/3-Me-*trans* isomers* **25** and **7** as well as small amounts of the corresponding *cis* isomers **22** and **30**. The spectral data of these latter two hydrindanones **22** and **30** were identical with those described above. Thus the ketone **7** was the missing *trans*-β-methylhydrindanone and its structure was explained quite reasonably by the ^1H NMR spectral data.

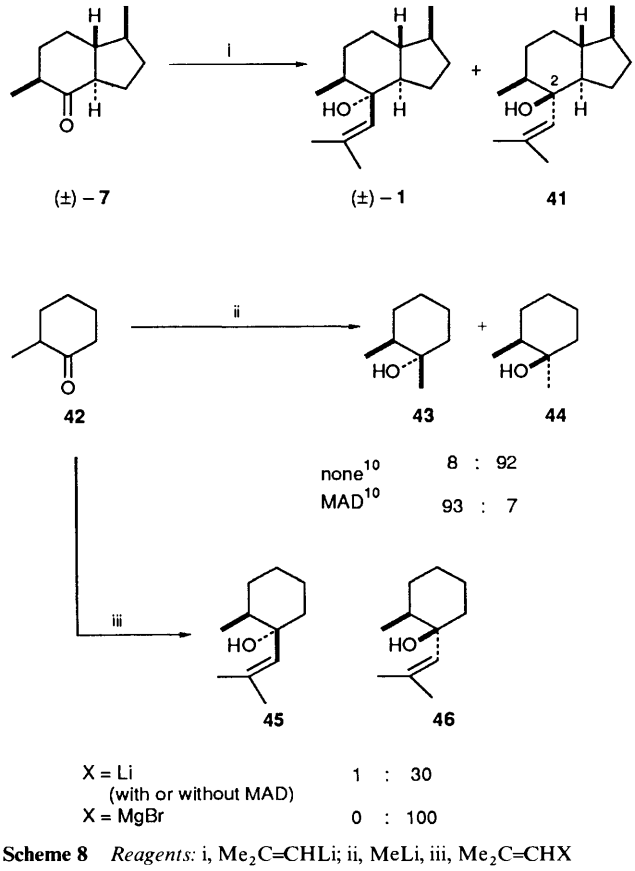
The ketone **7** was subjected to Wittig reaction ($Ph_3\overset{+}{P}Me\ Br^-$–$Bu^nLi$) followed by epoxidation (MCPBA) to give a mixture of epoxides **36** and **37** (Scheme 7). These isomers were separated by HPLC and the stereochemistry was assigned by the following reactions. Each epoxide was reduced by $LiAlH_4$ to give an alcohol, (**38**) or (**39**). The ketone **7** was methylated with MeLi to afford only one isomer of alcohol **38**, which was easily assigned as the β-axial alcohol, *i.e.* the *trans*-dimethyl alcohol, as demonstrated in the model studies (*vide infra*). Thus the less polar alcohol **38** was the axial alcohol and the epoxide **36** was β, while the more polar alcohol **39** was the equatorial alcohol and the epoxide **37** was α. Each epoxide was subjected to alkylation conditions (2-bromopropene–Bu^tLi–THF). However, only the β-epoxide **36** gave a ring-opened alcohol **40**. The α-epoxide **37** remained unchanged under the same conditions. This is again presumably due to the severe steric hindrance of the methyl group at the C-3 position.

Alkylation (MeLi) of 2-methylcyclohexanone **42** resulted in

* Tamariscol numbering



Scheme 7 *Reagents:* i, $Ph_3P{=}CH_2$; ii, MCPBA (then HPLC); iii, $LiAlH_4$; iv, MeLi; v, $CH_2{=}C(Li)Me$



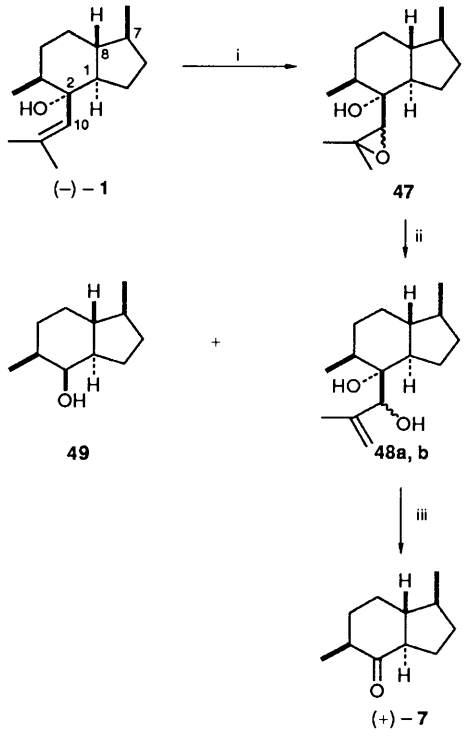
Scheme 8 *Reagents:* i, $Me_2C{=}CHLi$; ii, MeLi, iii, $Me_2C{=}CHX$

the formation of the *trans*-dimethyl alcohol **44** predominantly (Scheme 8)[9]. However, the addition of methylaluminium bis-(2,6-di-t-butyl-4-methylphenoxide) (MAD) or methylaluminium bis-(2,4,6-tri-t-butylphenoxide) (MAT)[10] dramatically changed the products, due to preco-ordination of the aluminium reagents. Although methylation of 2-methylcyclohexanone worked well, the reaction with 2-methylprop-1-enyllithium in the presence of MAD or MAT did not give the 'mini-tamariscol' **45** as a major product. Reaction of ketone **42** with the corresponding Grignard reagent gave only compound **46**.

The ketone (±)-**7** was alkylated with 2-methylprop-1-enyllithium to afford (±)-**1** and its isomer **41** in the ratio 1:50. The spectral data of the minor synthetic product were completely identical with those of the natural product **1**. Since attack from the axial face (β-side) was severely sterically hindered, the desired product was produced only in minute amounts even though, in the presence of MAD or MAT,[10] attack from the equatorial face predominated. Grignard reagent did not give good results.

These results show that racemic tamariscol [(±)-**1**] has been synthesized and that the relative configuration was confirmed as depicted in the formula.

3. *On the Absolute Configuration.*[8]—Tamariscol [(−)-**1**], $[\alpha]_D$ −20.5° (*c* 3.46 in $CHCl_3$),* isolated from the liverwort *F. tamarisci* collected in Taiwan, was subjected to oxidation by MCPBA to give a mixture of diastereoisomers **47** (Scheme 9).

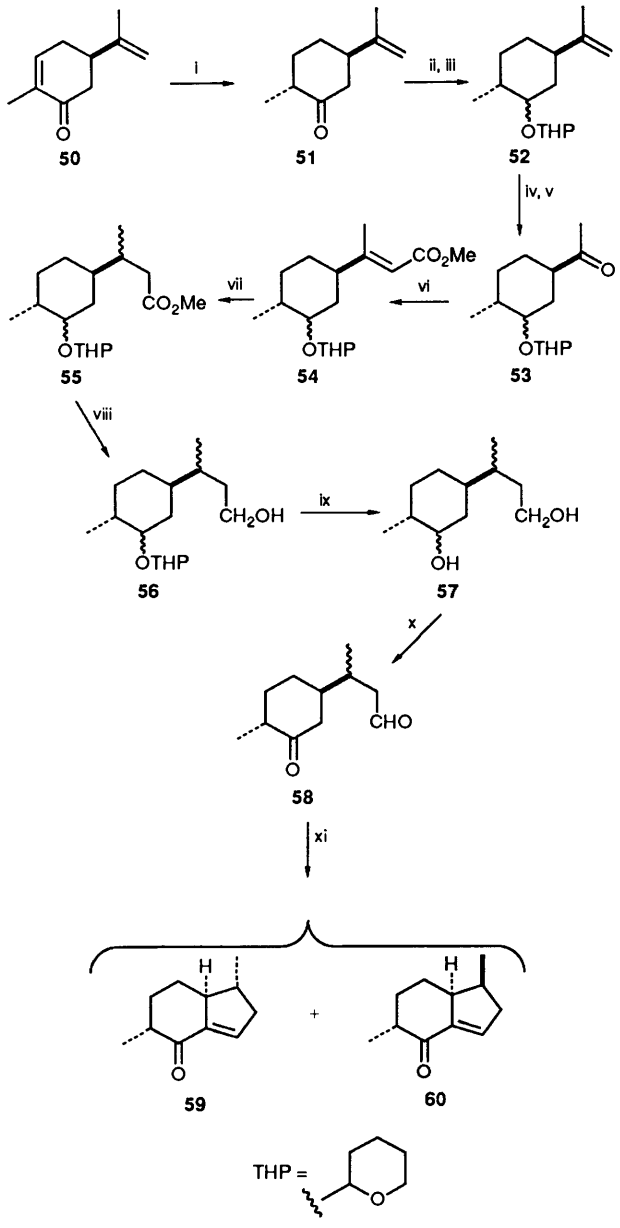


Scheme 9 *Reagents:* i, MCPBA; ii, $LiAlH_4$, PhH; iii, $NaIO_4$

The epoxides were treated with lithium aluminium hydride in dry benzene† under reflux to give a mixture of the diols **48a** and

* Although the original paper reports the specific rotation as $[\alpha]_D$ +19.7° ($CHCl_3$), our samples from Taiwan, $[\alpha]_D$ −20.5° ($CHCl_3$) or −22.6° (MeOH) and France, −17.4° (MeOH), both show negative values. It would be very interesting if both enantiomers were to exist in Nature, as precedented by frullanolide.[1] Dr. J. D. Connolly is now checking his results. We thank him for this information.

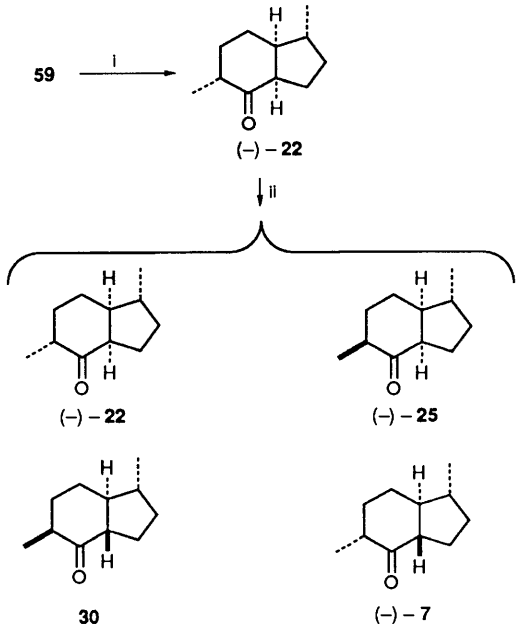
† Reaction in diethyl ether resulted only in complete recovery of the starting material.



Scheme 10 *Reagents and conditions:* i, NaTeH, EtOH; ii, $NaBH_4$; iii, dihydropyran, PPTS; iv, O_3; v, PPh_3; vi, $(MeO)_2P(O)CH_2CO_2Me$, NaH, PhH; vii, H_2, Pd–C; viii, $LiAlH_4$; ix, PPTS, MeOH; x, Swern oxidation; xi, $PhCO_2H$, Et_3N, PhH (then HPLC)

48b as well as an alcohol (**49**). The alcohol **49** was presumably formed through the ketone **7** by C–C bond fission of the diol **48** under the reaction conditions. The diols **48a** and **48b** were cleaved by sodium metaperiodate (aq. EtOH) to yield the hydrindanone (+)-**7**, $[\alpha]_D$ +10.1° (*c* 0.76 in $CHCl_3$).

l-Carvone **50** was reduced by NaHTe in EtOH to give *trans*-dihydrocarvone **51**,[11] which was reduced ($NaBH_4$) and protected as a tetrahydropyranyl (THP) ether (**52**) (Scheme 10). The isomers were not separated. Ozonolysis (CH_2Cl_2–PPh_3), Wittig reaction [NaH–$(MeO)_2POCH_2CO_2Me$], hydrogenation (H_2/Pd–C–AcOEt), reduction ($LiAlH_4$), deprotection [pyridinium toluene-*p*-sulphonate (PPTS)–MeOH], and Swern oxidation afforded a keto aldehyde (**58**). The keto aldehyde **58** was treated with $PhCO_2H$–Et_3N in benzene under reflux to give a mixture of enones **59** and **60**. Separation of this mixture was carried out by HPLC. The structure of each enone was assigned by analysis of the chemical shift of the secondary methyl group at the C-7 position* and this was finally confirmed by conversion into the ketone (−)-**7**. Hydrogenation (H_2–PtO_2–hexane) of the enone **59** yielded optically active *cis*-fused hydrindanone (−)-**22**, $[\alpha]_D$ −58.0° (*c* 1.3 in MeOH). The ketone (−)-**22** was treated with K_2CO_3–MeOH as before, followed by HPLC separation, to afford the optically active diastereoisomer (−)-**7**, $[\alpha]_D$ −14.3° (*c* 0.25 in $CHCl_3$), $[\theta]_{294}$ +3638 ($CHCl_3$), as well as the other three diastereoisomers (−)-**25**, (−)-**22** and **30** (the specific rotation of which was not measured due to the minute quantity of the sample isolated) (Scheme 11).



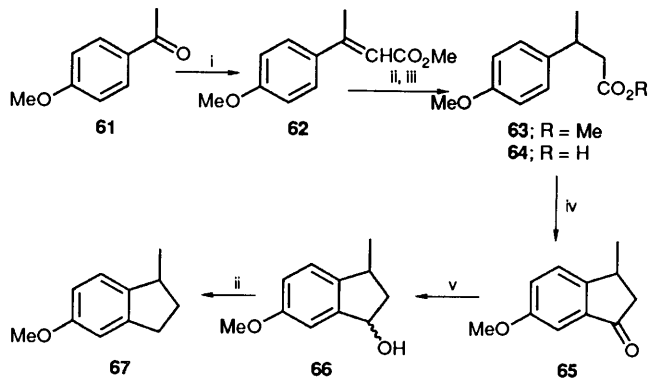
Scheme 11 *Reagents:* i, H_2, PtO_2; ii, K_2CO_3, MeOH (then HPLC)

The CD spectrum of (+)-**7** derived from natural (−)-tamariscol [(−)-**1**] showed a negative Cotton effect, $[\theta]_{294}$ −4389 ($CHCl_3$). These results show that the ketone (−)-**7** derived from (−)-carvone is enantiomeric to that derived from tamariscol (−)-**1**, indicating the absolute configuration of each chiral centre as shown in the formula, which was predicted from the back octant of ketone (+)-**7**. Thus the absolute configuration of natural (−)-tamariscol, $[\alpha]_D$ −20.5° ($CHCl_3$), which we have isolated has been shown to possess the absolute structure as shown in the formula (−)-**1**.

4. *Synthesis of the Hydrindenone* **5** *by an Alternative Route.*— Although there are many ways to prepare hydrindanone systems,[12] we needed to explore the most economical route to a particular hydrindenone. Martin and Clardy described the four-step synthesis of the enone **5** starting from 5-methoxyindan-1-one **6**.[4] However, this starting material is expensive. We have developed a new route to the enone **5** using cheaper materials.

Commercially available *p*-methoxyacetophenone **61** is an economical starting material for our synthesis (Scheme 12). Compound **61** was treated with trimethyl phosphonoacetate $[(MeO)_2P(O)CH_2CO_2Me]$ in dry benzene with sodium hydride as base to afford a mixture (*E* and *Z*) of the methyl ester **62** in 85%. The methyl ester was hydrogenated (H_2/Pd–C, MeOH) to give the dihydro methyl ester **63** in quantitative yield. The ester **63** was subjected to hydrolysis with KOH in aq. MeOH to give the corresponding acid **64** in 78% yield, which was then treated with polyphosphoric acid (PPA) at 90 °C for 10 min to yield the indanone **65** in 50% yield after column chromatographic separation. The indanone **65** was reduced

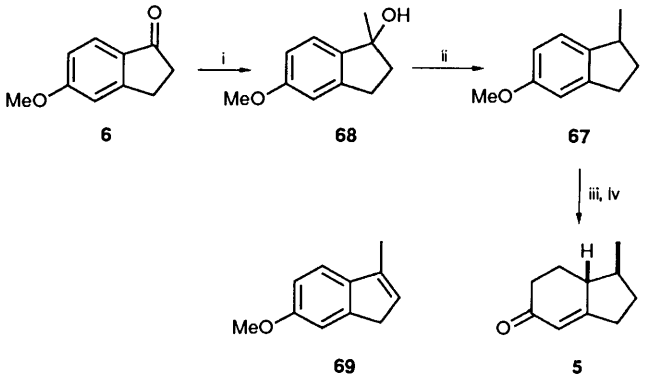
* Tamariscol numbering.



Scheme 12 *Reagents:* i, $(MeO)_2P(O)CH_2CO_2Me$, NaH; ii, H_2, Pd–C; iii, KOH; iv, PPA; v, $NaBH_4$

with $NaBH_4$ in methanol to afford a mixture of *cis* and *trans* alcohols **66** quantitatively, which mixture was not separated but was subjected to hydrogenolysis (H_2/Pd–C, MeOH) to give the indane **67** in 93%. The enone **5** was obtained by Birch reduction of compound **67**, followed by acid hydrolysis and isomerization, in 70% yield.

According to the literature,[4] 5-methoxyindan-1-one **6** was methylated by use of methylmagnesium iodide (Scheme 13).



Scheme 13 *Reagents:* i, MeMgI, Et_2O–THF; ii, H_2, Pd–C, PhH; iii, Li, liq. NH_3, Bu^tOH; iv, HCl, MeOH

This step is somewhat strange, because if a one molar equivalent or a small excess of reagent is used, the reaction product was a very complex mixture. The subsequent hydrogenation step did not give a good yield of the desired compound **67**. However the use of a large excess of reagent (more than 20-fold excess) smoothly gave the desired indanol **68** in excellent yield. In some cases the olefin **69** or a mixture of products **68** and **69** was produced. Hydrogenation of either **68** or **69** afforded the indane **67**

Although the published procedure[4] is short (four steps) (overall yield 35–68%), the starting material (compound **6**) is expensive and the methylation step sometimes causes problems. While our method of synthesis of the enone **5** requires a total of seven steps (overall yield 22%), the procedures are quite simple and very easy to carry out, although the yield of the cyclization step (**64** ⟶ **65**) is rather low.

Conclusions.—These studies have revealed that the relative and absolute stereostructure of (−)-tamariscol **1** is represented by the structure as depicted in the formula. In the course of these synthetic studies, the stereochemistry of reduction products or reductive alkylation products was investigated and all four possible hydrindanones were prepared and their thermodynamic stability was studied. Alkylation of a 2-methylcyclohexanone derivative showed very interesting behaviour, and severe steric hindrance determines the stereochemistry of the products.

Experimental

General.—IR spectra were measured on a Shimadzu IR-408 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM GX-400 or a FX-90Q spectrometer. Solvent used for NMR spectra was $CDCl_3$ unless otherwise stated and *J*-values are given in Hz. Mass spectra were measured on a JEOL JMS HX-100 spectrometer. A Chemcopak Nucleosil 50-5 (10 × 250 mm) column was used for HPLC (JASCO pump system). Silica gel 60 for column chromatography was purchased from Merck. THF, diethyl ether and toluene were distilled from sodium wire prior to use. Dichloromethane was distilled and stored over molecular sieves (3 Å).

1. *Epoxide Route*

Hydrogenation of the Enone **5**.—The enone **5** (50 mg) was hydrogenated in PhH (4 cm^3) in the presence of Pd–C (10 mg) to give the cis-*dihydro ketone* **9** (40.5 mg, 78%), ν_{max}(film)/cm^{-1} 1710; δ_H 1.05 (3 H, d, *J* 5.3); δ_C 19.3, 25.4, 32.8, 34.1, 37.5, 37.8, 39.4, 44.1, 44.7 and 214.2; *m/z* 152 (M^+), 137, 108, 95 and 81 (base) (Found: M^+, 152.1207. $C_{10}H_{16}O$ requires M, 152.1202).

Birch Reduction of the Enone **5**.—A solution of the enone **5** (303 mg) in dry diethyl ether (20 cm^3) was added into Li (121 mg) in liq. NH_3 (20 cm^3) at −78 °C. The mixture was refluxed for 1 h and solid NH_4Cl was added until the blue colour disappeared. The solvents were evaporated off and the mixture was extracted with diethyl ether. The usual work-up afforded a residue (318 mg), which was separated by column chromatography (PhH–EtOAc, gradient) and HPLC (Chemcopak 50-5; 15% EtOAc–hexane) to give the *cis*-dihydro ketone **9** (97 mg, 32%) and the trans-*dihydro ketone* **10** (79 mg, 26%). For compound **10**: ν_{max}(film)/cm^{-1} 1710; δ_H 1.04 (3 H, d, *J* 5.3); δ_C 18.6, 27.8, 29.5, 32.4, 37.9, 40.5, 46.7, 47.5, 51.8 and 211.6; *m/z* 152 (M^+), 137, 108, 95 and 81 (base) (Found: M^+, 152.1191. $C_{10}H_{16}O$ requires M, 152.1201).

Reductive Carboxylation of the Enone **5**.—Lithium (654 mg) was dissolved in liq. NH_3 (180 cm^3) and a solution of the enone **5** (4.7 g) and Bu^tOH (2.4 cm^3) in dry THF (130 cm^3) was added to the base cooled to −78 °C. The mixture was refluxed for 1 h and isoprene was added until the blue colour disappeared. The solvent was evaporated off under reduced pressure and the residue was dissolved in dry THF (150 cm^3). A large excess of solid CO_2 was added in one portion at −78 °C. The mixture was left overnight and diethyl ether was then added. The mixture at 0 °C, was carefully acidified by addition of 3 mol dm^{-3} HCl. The organic layer was separated and the aq. layer was extracted with diethyl ether (300 cm^3 × 2). The combined organic layers were washed successively with 1 mol dm^{-3} HCl and brine, dried over $MgSO_4$, filtered and evaporated to afford a residue, which was treated with diazomethane in diethyl ether. The residue (6.1 g) was separated by column chromatography over silica gel (EtOAc–hexane, gradient) to give the cis-*keto ester* **11** (1.21 g, 18.4%) and the trans-*keto ester* **12** (805 mg, 12.2%). For compound **11**: ν_{max}(film)/cm^{-1} 1650 and 1610; δ_H 1.00 (3 H, d, *J* 6.2), 3.75 (3 H, s) and 12.2 (1 H, s); δ_C 20.9, 24.6, 28.2, 33.3, 33.5, 36.4, 38.4, 44.9, 51.1, 101.1, 172.3 and 173.5; *m/z* 210 (M^+), 178, 149 (base), 122 and 81 (Found: M^+, 210.1250. $C_{12}H_{18}O_3$ requires M, 210.1256). For compound **12**: ν_{max}(film)/cm^{-1} 1740 and 1710; δ_H 1.04 (3 H, d, *J* 5.7), 3.23 (1 H, d, *J* 12.3) and 3.70 (3 H, s); δ_C 18.5, 27.8, 28.2, 32.3, 37.8, 40.5, 48.6, 50.6, 51.5, 63.1, 169.6 and 205.5; *m/z* 210 (M^+), 192, 122, 81 (base) and 51 (Found: M^+, 210.1255).

Preparation of the cis-*Methyl Ester* **13**.—To a stirred solution of the *cis*-keto ester **11** (1.3 g) in THF (20 cm^3)–MeOH (40 cm^3) was added $NaBH_4$ (480 mg). The mixture was stirred for 12 h at

0 °C. The solvent was evaporated off and the mixture was extracted with $CHCl_3$ (200 cm^3 × 2). The $CHCl_3$ layer was washed successively with water and brine, dried ovr $MgSO_4$, filtered and evaporated to afford a mixture of alcohols (1.27 g, 75%), ν_{max}/cm^{-1} 3400 and 1730; *m/z* 212 (M^+), 194, 184, 166, 152, 135 and 113 (base).

Mesyl chloride (0.12 cm^3) was added to a solution of triethylamine (0.72 cm^3) in dry diethyl ether (4 cm^3) at 0 °C and a solution of the mixture of the alcohols (181 mg) in diethyl ether (2 cm^3) was added to this mixture. The mixture was stirred for 4 h. Saturated aq. NH_4Cl (5 cm^3) was then added and the mixture was extracted with diethyl ether. The extract was washed successively with water and brine, dried over $MgSO_4$, filtered and evaporated to afford a mixture of mesyl esters (234 mg).

A solution of the mesyl esters (234 mg) in dry benzene (20 cm^3) was treated with DBU (0.55 cm^3) at room temperature for 4 h. The mixture was extracted with diethyl ether (100 cm^3 × 2) and the extract was washed successively with 1 mol cm^{-3} HCl and brine, dried over $MgSO_4$, filtered and evaporated to afford a residue (146 mg), which was purified by column chromatography over silica gel to give the cis-α,β-*unsaturated methyl ester* **13** (51 mg, 35.2%), ν_{max}(film)/cm^{-1} 1710; δ_H 1.00 (3 H, d, *J* 6.2), 3.72 (3 H, s) and 6.95 (1 H, td, *J* 4.2 and 1.1); δ_C 20.5, 24.2 (× 2), 32.2, 33.4, 37.6, 38.4, 44.8, 51.3, 134.5, 138.6 and 168.2; *m/z* 194 (M^+), 179, 163, 147 and 134 (base) (Found: M^+, 194.1306. $C_{12}H_{18}O_2$ requires M, 194.1306).

Preparation of the Allyl Alcohol **14**.—To a solution of the methyl ester **13** (280 mg) in dry diethyl ether (4 cm^3) was added $LiAlH_4$ (82 mg) and the mixture was stirred for 4 h at 0 °C. The usual work-up afforded the *allyl alcohol* **14** (227 mg, 98%), ν_{max}(film)/cm^{-1} 3300; δ_H 1.00 (3 H, d, *J* 5.9), 4.03 (2 H, m) and 5.69 (1 H, m); δ_C 20.5, 23.5, 25.5, 31.2, 33.8, 38.6, 38.9, 45.2, 66.4, 122.4 and 141.1; *m/z* 166 (M^+), 148 and 135 (base) (Found: M^+, 166.1360. $C_{11}H_{18}O$ requires M, 166.1358).

Preparation of the Alcohol **15**.—To a stirred solution of the ketone **12** (738 mg) in dry THF (17 cm^3) at −78 °C was added L-Selectride (1 mol dm^{-3} in THF; 3.5 cm^{-3}). The mixture was stirred for 5 h at the same temperature before addition of wet diethyl ether. The mixture was extracted with diethyl ether (200 cm^3 × 2) and the extract was washed successively with water and brine, dried over $MgSO_4$, filtered and evaporated to afford a residue (780 mg), which was purified by column chromatography over silica gel (AcOEt–hexane, gradient) to give the *alcohol* **15** (564 mg, 76%), ν_{max}/cm^{-1} 3450 and 1725; δ_H 0.97 (3 H, d, *J* 5.9), 2.21 (1 H, br d, *J* 11), 3.69 (3 H, s) and 4.21 (1 H, m); δ_C 18.4, 23.0, 27.9, 30.9, 32.1, 38.2, 40.9, 51.1, 52.5 (× 2), 66.6 and 175.6; *m/z* 212 (M^+), 194, 184, 152, 135, 113 (base) and 81 (Found: M^+, 212.1405. $C_{12}H_{20}O_3$ requires M, 121.1412).

Preparation of the Benzoate **16**.—A mixture of benzoyl chloride (0.7 cm^3), the alcohol **15** (623 mg), 4-dimethylaminopyridine (DMAP) (70 mg), and pyridine (5 cm^3) was stirred for 3 h at 0 °C. Water (1 cm^3) was added and the mixture was stirred for 1 h. The usual work-up afforded the *benzoate* **16** (592 mg, 64%), ν_{max}/cm^{-1} 1720; δ_H 1.01 (3 H, d, *J* 6.2), 2.46 (1 H, dd, *J* 11.6 and 2.9), 3.58 (3 H, s), 5.64 (1 H, m), 7.45 (3 H, m) and 8.00 (2 H, m); δ_C 18.6, 24.0, 28.6, 30.7, 31.3, 38.4, 41.8, 51.5, 52.1, 52.4, 71.0, 129.5 (× 4), 132.7 (× 2), 165.5 and 172.4; *m/z* 211 (M − 105), 194, 134, 105 and 77 (Found: M^+, 316.1677. $C_{19}H_{24}O_4$ requires M, 316.1675).

Preparation of the trans-α,β-*Unsaturated Methyl Ester* **17**.—A solution of the benzoate **16** (592 mg) in dry THF (2 cm^3) was treated with LDA prepared from diisopropylamine (0.32 cm^3), Bu^nLi (1.6 mol dm^{-3}; 1.25 cm^3), and THF (4 cm^3). The mixture was stirred for 4 h at room temperature. The usual work-up afforded a residue (595 mg), which was purified by column chromatography over silica gel (AcOEt–hexane, gradient) to give the *ester* **17** (220 mg, 60%) and the benzoate **16** (137 mg recovery). For compound **17**: ν_{max}(film)/cm^{-1} 1710; δ_H 0.99 (3 H, d, *J* 5.9), 3.70 (3 H, s) and 6.82 (1 H, m); δ_C 18.5, 24.9, 27.8, 28.0, 31.9, 37.3, 43.8, 51.0, 51.2, 134.3, 139.7 and 167.7; *m/z* 194 (M^+), 179, 163, 135 (base), 134, 119 and 95 (Found: M^+, 194.1310. $C_{12}H_{18}O_2$ requires M, 194.1307).

Preparation of the trans-*Allyl Alcohol* **18**.—The ester **17** (257 mg) was reduced by $LiAlH_4$ (63 mg) in diethyl ether (12 cm^3) at room temperature for 3 h. The usual work-up afforded the alcohol **18** (200 mg, 91%), ν_{max}(film)/cm^{-1} 3300; δ_H 1.00 (3 H, d, *J* 5.7), 4.05 (2 H, br s) and 5.56 (1 H, m); δ_C 18.7, 25.9, 26.3, 26.9, 32.1, 37.6, 45.2, 51.4, 65.4, 122.5 and 140.7; *m/z* 166 (M^+), 148 and 135 (base) (Found: M^+, 166.1357. $C_{11}H_{18}O$ requires M, 166.1358).

Preparatuion of the Epoxy Acetates **19** *and* **20**.—A solution of the alcohol **14** (20 mg) in dichloromethane (0.5 cm^3) was treated with MCPBA (36 mg) at 0 °C for 6 h. The usual work-up afforded a mixture of epoxides (22.4 mg), ν_{max}(film)/cm^{-1} 3400; *m/z* 182 (M^+), 165, 164, 151 (base) and 81.

The mixture of epoxides was treated with Ac_2O (0.5 cm^3) and pyridine (0.5 cm^3) at room temperature for 4 h. The usual work-up afforded a residue (96 mg), which was separated by column chromatography over silica gel (EtOAc–hexane, gradient) to give the α-*epoxy acetate* **19** (36 mg, 33%) and the β-*epoxy acetate* **20** (40 mg, 37%). For compound **19**: ν_{max}(film)/cm^{-1} 1740; δ_H 0.96 (3 H, d, *J* 6.4), 2.09 (3 H, s) and 3.20 (1 H, d, *J* 1.5); δ_C 20.6, 20.8, 23.1, 24.1, 27.5, 33.4, 37.3, 41.1, 43.4, 58.0, 59.1, 67.8 and 170.6; *m/z* 182 $(M - 42)^+$, 164, 81 and 43 (base) [Found: $(M^+ - 42)$ 182.1307. $C_{11}H_{18}O_2$ requires *m/z* 182.1307]. For compound **20**; ν_{max}(film)/cm^{-1} 1740; δ_H 0.94 (3 H, d, *J* 5.7), 2.09 (3 H, s), 3.13 (1 H, m), 3.76 (1 H, d, *J* 12.1) and 4.44 (1 H, d, *J* 12.1); δ_C 19.4, 20.0, 20.7, 21.3, 29.0, 34.1, 37.0, 38.5, 42.5, 56.2, 59.6, 67.1 and 170.6; *m/z* 182 $(M - 42)^+$, 164, 121, 81 and 43 (base) [Found: $(M - 42)^+$, 182.1309].

Preparation of the cis-β-*Methyl Diol* **21**.—MeLi (1 mol dm^{-3} in Et_2O; 5 cm^3) was added into a suspension of CuI (472 mg) in diethyl ether (5 cm^3) at 0 °C and the mixture was stirred for 10 min. A solution of the epoxy acetate **19** (79 mg) in diethyl ether (1 cm^3) was added to the mixture at −78 °C and the mixture was then stirred for 60 h at room temperature. Saturated aq. NH_4Cl (5 cm^3) was added and the mixture was extracted with diethyl ether (30 cm^3 × 2). The extract was washed successively with water and brine, dried over $MgSO_4$, filtered and evaporated to afford the *diol* **21** (70 mg), ν_{max}(film)/cm^{-1} 3450; δ_H 0.95 (6 H, d, *J* 6.8) and 3.66 (2 H, m); δ_C 15.1, 22.3, 24.2, 27.3, 30.4, 31.3, 35.2, 39.3, 43.0, 46.5, 64.4 and 75.4; *m/z* 198 (M^+), 167 and 149 (base) (Found: M^+, 198.1608. $C_{12}H_{22}O_2$ requires M, 198.1621).

Preparation of the cis-β-*Methyl Ketone* **22**.—A solution of the diol **21** (5 mg) in dichloromethane (0.5 cm^3) was treated with PCC (20 mg) and powdered molecular sieves (4 Å; 31 mg) at room temperature for 2 h. Dry diethyl ether was added and the mixture was passed through a short column of silica gel to afford the *ketone* **22** (3 mg, 72%), ν_{max}(film)/cm^{-1} 1695; δ_H 0.95 (3 H, d, *J* 6.8), 1.08 (3 H, d, *J* 7.1) and 2.79 (1 H, q, *J* 8.4); δ_H (C_6D_6) 0.75 (3 H, d, *J* 6.8), 1.02 (3 H, d, *J* 7.1), 2.09 (1 H, m) and 2.58 (1 H, q, *J* 8.5); δ_C(C_6D_6) 16.3 (Me), 20.0 (Me), 26.7 (CH_2), 27.0 (CH_2), 32.5 (CH_2), 33.1 (CH_2), 40.3 (CH), 42.7 (CH), 50.5 (CH), 50.6 (CH) and 231.8 (C); *m/z* 166 (M^+), 151, 148, 137, 124, 111, 108, 95, 81 (base) and 67 (Found: M^+, 166.1346. $C_{11}H_{18}O$ requires M, 166.1358).

Preparation of the cis-α-*Methyl Diol* **24**.—The epoxy acetate **20** (113 mg) was treated with Me_2CuLi as above to afford the *diol* **24** (117 mg), ν_{max}(film)/cm^{-1} 3400; δ_H 0.95 (3 H, d, *J* 6.6), 1.02 (3 H, d, *J* 6.8) and 3.59 (2 H, s); δ_C 15.8, 22.2, 24.0, 26.3, 27.8, 32.3, 35.4, 39.1, 44.5, 45.7, 68.0 and 75.5; *m/z* 198 (M^+), 181, 167, 163 and 149 (base) (Found: M^+, 198.1589. $C_{12}H_{22}O_2$ requires M, 198.1620).

Preparation of the cis-α-Methyl Ketone **25**.—The diol **24** (5 mg) was oxidized by PCC as above to afford the *ketone* **25** (3 mg, 72%), ν_{max}(film)/cm^{-1} 1700; δ_H 0.95 (3 H, d, *J* 6.3), 1.01 (3 H, d, *J* 6.6) and 2.70 (1 H, br t, *J* 6.4); $\delta_H(C_6D_6)$ 0.73 (3 H, d, *J* 6.4), 1.04 (3 H, d, *J* 6.6) and 2.26 (1 H, br t, *J* 7.5); $\delta_C(C_6D_6)$ 15.1 (Me), 18.3 (Me), 22.3 (CH_2), 24.5 (CH_2), 32.1 (CH_2), 32.5 (CH_2), 35.1 (CH), 44.8 (CH), 51.4 (CH), 53.3 (CH) and 211.2 (C); *m/z* 166 (M^+), 151, 137, 124, 111 (base), 95, 81, 67, 58, 55 and 41 (Found: M^+, 166.1357. $C_{11}H_{18}O$ requires M, 166.1358).

Preparation of the Epoxy Acetates **27** *and* **28**.—A solution of the allyl alcohol **18** (30 mg) was treated with MCPBA (59 mg) at 0 °C for 4 h. The usual work-up afforded a mixture of epoxides (31 mg), ν_{max}(film)/cm^{-1} 3400; δ_H 0.95 (6 H, d, *J* 5.5), 3.24 (2 H, m), 3.75 (2 H, s), 3.60 (1 H, d, *J* 12.5) and 3.90 (1 H, d, *J* 12.3); δ_C 18.6 (× 2), 22.3, 24.1 (× 2), 24.5, 25.0, 25.8, 31.4, 31.5, 36.6, 38.0, 45.4, 46.0, 46.5, 50.3, 55.9, 56.4, 61.9, 62.5, 63.0 and 63.5; *m/z* 182 (M^+), 165, 151 (base), 147, 95 and 81.

The mixture of epoxides (357 mg) was treated with acetic anhydride (0.5 cm^3) and pyridine (1 cm^3) at room temperature for 6 h. The usual work-up afforded a residue (288 mg), which was separated by column chromatography over silica gel (AcOEt–hexane, gradient) to give the β-*epoxide* **27** (54 mg, 12%) and the α-*epoxide* **28** (26 mg, 6%). For compound **27**: ν_{max}(film)/cm^{-1} 1740; δ_H 0.94 (3 H, d, *J* 5.7), 2.08 (3 H, s) and 3.12 (1 H, br d, *J* 3.2); δ_C 18.5, 20.8, 24.0, 24.5, 24.8, 31.2, 37.9, 45.2, 46.2, 57.1, 60.8, 65.7 and 170.7; *m/z* 224 (M^+), 182, 164 (base) and 149 [Found: $(M - 42)^+$ 182.1306. $C_{11}H_{18}O_2$ requires *m/z* 182.1307]. For compound **28**: ν_{max}(film)/cm^{-1} 1740; δ_H 0.97 (3 H, d, *J* 5.5), 2.08 (3 H, s), 3.89 (1 H, d, *J* 12.1) and 4.41 (1 H, d, *J* 12.3); *m/z* 182 $(M - 42)^+$, 169, 164, 151, 138 and 125 (base) [Found: $(M - 42)^+$, 182.1331].

Preparation of the trans-α-*Methyl Diol* **29**.—The β-epoxide **27** (65.4 mg) was methylated with Me_2CuLi prepared from LiMe (1 mol dm^{-3} in Et_2O; 5.7 cm^3) and CuI (553 mg) as before to afford the trans-α-*methyl diol* **29** (57 mg, 99%), ν_{max}(film)/cm^{-1} 3400; δ_H 0.95 (3 H, d, *J* 7.5), 0.96 (3 H, d, *J* 5.7) and 3.52 (2 H, br s); δ_C 15.5, 18.5, 22.5, 24.5, 28.9, 31.6, 35.2, 39.0, 45.7, 47.5, 67.6 and 75.8; *m/z* 198 (M^+), 167 and 149 (base) (Found: M^+, 198.1618. $C_{12}H_{22}O_2$ requires M, 198.1621).

Preparation of the trans-α-*Methyl Ketone* **30**.—A solution of the diol **29** (6 mg) in dichloromethane (1 cm^3) was treated with PCC (34 mg) and powdered 4 Å molecular sieves (38 mg) at room temperature for 2 h. Work-up as before afforded the trans-α-*methyl ketone* **30** (3.3 mg, 66%), ν_{max}(film)/cm^{-1} 1700; $\delta_H(C_6D_6)$ 0.79 (3 H, d, *J* 6.6), 0.89 (3 H, d, *J* 7.3), 2.13 (1 H, ddd, *J* 7.3, 10.3 and 12.7) and 2.44 (1 H, m); $\delta_C(C_6D_6)$ 17.5 (Me), 18.1 (Me), 21.6 (CH_2), 24.8 (CH_2), 31.7 (CH_2), 33.2 (CH_2), 40.6 (CH), 44.4 (CH), 53.5 (CH), 55.1 (CH) and 212.2 (C); *m/z* 166 (M^+), 151, 148, 138, 137, 124, 111, 109 (base) and 95 (Found: M^+, 166.1348. $C_{11}H_{18}O$ requires M, 166.1358).

Preparation of the Alcohol **31**.—The ketone **30** (3.3 mg) was treated with $LiAlH_4$ (50 mg) in diethyl ether (0.5 cm^3) at room temperature for 2 h. The usual work-up afforded the *alcohol* **31** (0.6 mg), ν_{max}(film)/cm^{-1} 3650; $\delta_H(C_6D_6)$ 0.91 (3 H, d, *J* 6.8), 0.93 (3 H, d, *J* 8.1) and 3.23 (1 H, dd, *J* 10.5 and 4.6); *m/z* 168 (M^+), 150, 137, 135 and 111 (base) (Found: M^+, 168.1511. $C_{11}H_{20}O$ requires M, 168.1514).

2. *Alkylation Route*

Preparation of the Diene **33**.—A solution of the enone **5** (45 mg) in dry THF (1 cm^3) was added to a solution of methylenetriphenylphosphorane prepared from methyltriphenylphosphonium bromide (476 mg) and Bu^{n}Li (1.6 mol dm^{-3}; 0.84 cm^3) in THF (5 cm^3) at room temperature. The mixture was stirred at the same temperature for 18 h. Water was added and the mixture was extracted with hexane (50 cm^3 × 2). The extract was washed successively with water and brine, dried over $MgSO_4$, filtered and evaporated to afford a residue (181 mg), which was purified by column chromatography over silica gel (AcOEt–hexane, gradient) to give the diene **33** (38 mg, 85%), ν_{max}(film)/cm^{-1} 1600 and 870; $\delta_H(C_6D_6)$ 0.91 (3 H, d, *J* 5.1), 4.78 (2 H, br s) and 5.99 (1 H, m); $\delta_C(C_6D_6)$ 18.2 (Me), 28.3 (CH_2), 29.6 (CH_2), 31.2 (CH_2), 33.3 (CH_2), 41.7 (CH), 49.4 (CH), 108.1 (CH_2), 122.3 (CH), 144.3 (C) and 150.3 (CH); *m/z* 148 (M^+), 133, 120, 106, 91 (base) and 79.

Preparation of the Olefin **34**.—Lithium (1 g) was dissolved in liq. NH_3 (100 cm^3) at −78 °C and Bu^{t}OH (2.7 cm^3) and THF (20 cm^3) were added. A solution of the diene **33** (2.1 g) and Bu^{t}OH (5 cm^3) in THF (40 cm^3) was added slowly and the mixture was stirred at the same temperature for 15 min. Bu^{t}OH (5 cm^3) and MeOH (40 cm^3) were added and most of the NH_3 was evaporated off. Water was added and the mixture was extracted with diethyl ether (200 cm^3 × 2). The extract was washed successively with water and brine, dried over $MgSO_4$, filtered and evaporated to afford the *olefin* **34** (1.5 g, 71%), ν_{max}(film)/cm^{-1} 1450 and 1370; $\delta_H(C_6D_6)$ 0.96 (3 H, d, *J* 5.9), 1.63 (3 H, br s) and 5.35 (1 H, m); $\delta_C(C_6D_6)$ 20.3, 24.1, 25.0, 27.7, 32.2, 34.0, 37.3, 39.7, 44.9, 126.3 and 132.4; *m/z* 150 (M^+), 135 (base), 121, 107, 93 and 79 (Found: M^+, 150.1423. $C_{11}H_{18}$ requires M, 150.1409).

Preparation of the Alcohol **35**.—To a stirred solution of the olefin **34** (1.54 g) in dry THF (8.6 cm^3) was added BH_3·THF (1 mol dm^{-3}; 10.3 cm^3) and the mixture was stirred for 1 h. Water (2.6 cm^3), 3 mol dm^{-3} NaOH (3.4 cm^3) and 30% H_2O_2 (3.4 cm^3) were added successively and the mixture was stirred for 1 h. Diethyl ether was added and the ethereal solution was washed successively with water and brine, dried over $MgSO_4$, filtered and evaporated to afford the *alcohol* **35** (1.65 g, 95%), ν_{max}/cm^{-1} 3300; $\delta_H(C_6D_6)$ 0.93 (3 H, d, *J* 6.6), 1.06 (3 H, d, *J* 6.6) and 3.56 (1 H, br t, *J* 8.6); $\delta_C(C_6D_6)$ 19.0 (Me), 19.7 (Me), 24.7 (CH_2), 27.4 (CH_2), 29.6 (CH_2), 32.5 (CH_2), 34.3 (CH), 39.9 (CH), 49.0 (CH), 49.2 (CH) and 77.8 (CH); *m/z* 168 (M^+), 150, 135 (base), 121, 108, 95 and 81 [Found: $(M - H_2O)^+$, 150.1395. $C_{11}H_{18}$ requires *m/z* 150.1409].

Oxidation of the Alcohol **35** *to the Ketone* **25**.—A solution of the alcohol (1.65 g) in dichloromethane (10 cm^3) was treated with PDC (11.6 g) and powdered 4 Å molecular sieves (5 g) at room temperature for 4 h. Work-up as before afforded the ketone **25** (1.50 g, 88%).

Epimerization of the Ketone **25**.—A solution of the ketone **25** (1.50 g) in MeOH (50 cm^3) was treated with K_2CO_3 (100 mg) for 12 h. Water was added and the mixture was extracted with diethyl ether (200 cm^3 × 2). The extract was washed successively with water and brine, dried over $MgSO_4$, filtered, and evaporated to afford a residue (1.15 g). The residue was separated by HPLC (Chemcopak 50-5; 10 × 250 cm^3; 3% EtOAc–hexane) to give the ketones **25** (313 mg recovery), **7** (238 mg), **22** (82 mg) and **30** (15 mg). For *compound* **7**: ν_{max}(film)/cm^{-1} 1710; $\delta_H(C_6D_6)$ 0.80 (3 H, d, *J* 6.6), 1.07 (3 H, d, *J* 6.6), 1.88 (1 H, m) and 2.06 (1 H, m); $\delta_C(C_6D_6)$ 14.6 (Me), 18.2 (Me), 21.4 (CH_2), 29.4 (CH_2), 32.0 (CH_2), 37.3 (CH_2), 40.6 (CH), 44.7 (CH), 56.8

(CH), 58.0 (CH) and 209.6 (C); *m/z* 166 (M^+), 151, 148, 138, 137, 124, 111, 109 (base) and 95 (Found: M^+, 166.1332. $C_{11}H_{18}O$ requires M, 166.1358).

Preparation of the Epoxides **36** *and* **37**.—The ketone **7** (126 mg) was treated with a solution of methylenetriphenylphosphorane prepared from methyltriphenylphosphonium bromide (214 mg) and Bu^{n}Li (1.6 mol dm^{-3}; 2.28 cm^3) in dry THF (18 cm^3) at room temperature for 12 h. Water was added and the mixture was extracted with hexane. The extract was washed successively with water and brine, dried over $MgSO_4$, filtered and evaporated to afford a residue, which was purified by column chromatography over silica gel to give the corresponding olefin (120 mg, 96%), $\delta_H(C_6D_6)$ 0.92 (3 H, d, *J* 6.2), 1.09 (3 H, d, *J* 6.4) and 4.76 (2 H, s).

A solution of the olefin (120 mg) in dichloromethane (5 cm^3) was treated with MCPBA (190 mg) at 0 °C for 4 h. The usual work-up afforded a residue (130 mg), which was purified to give a mixture of epoxides (102 mg). The mixture was further separated by HPLC (Chemcopak 50-5; 3% EtOAc–hexane) to give the β-*epoxide* **36** (33.4 mg, faster moving) and the α-epoxide **37** (51.4 mg, slower moving). For compound **36**: ν_{max}(film)/cm^{-1} 1450, 1370, 1345 and 950; $\delta_H(C_6D_6)$ 0.70 (3 H, d, *J* 5.9), 0.91 (3 H, d, *J* 5.1), 2.23 (1 H, d, *J* 4.6) and 2.49 (1 H, d, *J* 4.6); *m/z* 180 (M^+), 165, 149, 138 (base), 123, 107 and 93 (Found: M^+, 180.1516. $C_{12}H_{20}O$ requires M, 180.1514. For compound **37**: ν_{max}(film)/cm^{-1} 1450, 1360 and 900; $\delta_H(C_6D_6)$ 0.74 (3 H, d, *J* 6.4), 0.89 (3 H, d, *J* 5.9), 2.39 (1 H, d, *J* 4.2) and 2.46 (1 H, d, *J* 4.2); *m/z* 180 (M^+), 165, 149, 138 (base), 123, 107 and 93 (Found: M^+, 180.1520).

Reduction of the β-*Epoxide* **36**.—A solution of the β-epoxide **36** (11.2 mg) in THF (4 cm^3) was treated with $LiAlH_4$ (12 mg) for 5 h. The usual work-up afforded the *alcohol* **38** (9.1 mg, 80.4%), $\nu_{max}(CHCl_3)$/cm^{-1} 3650; $\delta_H(C_6D_6)$ 0.96 (6 H, d, *J* 5.9) and 0.99 (3 H, s); *m/z* 182 (M^+), 167, 149, 135, 125 (base), 107 and 93 (Found: M^+, 182.1682. $C_{12}H_{22}O$ requires *M*, 182.1671).

Reduction of the α-*Epoxide* **37**.—A solution of the α-epoxide **37** (9.0 mg) in THF (4 cm^3) was treated with $LiAlH_4$ (10 mg) for 5 h. The usual work-up afforded the *alcohol* **39** (9.0 mg, 99%), $\nu_{max}(CHCl_3)$/cm^{-1} 3600; $\delta_H(C_6D_6)$ 0.86 (3 H, s), 0.91 (3 H, d, *J* 6.2) and 0.95 (3 H, d, *J* 5.7); *m/z* 182 (M^+), 167, 149, 135, 125 (base), 107 and 95 (Found: M^+, 182.1669. $C_{12}H_{22}O$ requires M, 182.1671).

Methylation of the Ketone (±)-**7**.—A solution of the ketone (±)-**7** (16.6 mg) in THF (0.5 cm^3) at 0 °C was treated with MeLi (1.08 mol dm^{-3} in Et_2O; 1.0 cm^3) for 6 h. The usual work-up afforded the alcohol **38** (7.1 mg, 39%).

Alkylation of the β-*Epoxide* **36** *with Isopropenyllithium*.—To a stirred solution of the β-epoxide **36** (9.2 mg) in diethyl ether (0.5 cm^3) was added isopropenyllithium prepared from 2-bromopropene (0.02 cm^3) and Bu^{t}Li (1.5 mol dm^{-3} in pentane; 0.3 cm^3) in diethyl ether (1 cm^3) at −78 °C. The mixture was stirred for 2 h at the same temperature. Wet diethyl ether and water were added successively and the mixture was extracted with diethyl ether (30 cm^3 × 2). The extract was washed with $MgSO_4$, filtered and evaporated to afford a residue, which was purified by column chromatography over silica gel to give the alcohol **40** (5.2 mg), $\nu_{max}(CHCl_3)$/cm^{-1} 3650, 3550, 1600 and 890; δ_H 0.94 (3 H, d, *J* 5.9), 0.96 (3 H, d, *J* 6.3), 1.73 (3 H, s), 4.85 (1 H, br s) and 4.88 (1 H, br s); *m/z* 222 (M^+), 207, 179, 149 (base), 137, 121, 109 and 93.

Preparation of Tamariscol **1** *and its Isomer* **41**.—Bu^{t}Li (1.5 mol dm^{-3} in pentane; 10 cm^3) was added to a solution of 1-bromo-2-methylprop-1-ene (0.8 cm^3) in diethyl ether (6 cm^3) at −78 °C and the mixture was stirred for 30 min. A solution of ketone (±)-**7** (237 mg) in diethyl ether (5 cm^3) was added and the mixture was stirred for 3 h at the same temperature. Wet diethyl ether was added and the mixture was extracted with diethyl ether (200 cm^3 × 2). The extract was washed successively with water and brine, dried over $MgSO_4$, filtered and evaporated to afford a residue (427 mg), which was separated by column chromatography over silica gel (EtOAc–hexane, gradient) followed by HPLC (Chemcopak 50-5; 3% EtOAc–hexane) to yield compound **41** (304 mg, 96%) and tamariscol (±)-**1** (6 mg, 2%). For compound **41**: ν_{max}(film)/cm^{-1} 3550; $\delta_H(C_6D_6)$ 0.96 (3 H, d, *J* 6.6), 0.98 (3 H, d, *J* 6.6), 1.67 (3 H, s), 1.91 (3 H, s) and 4.91 (1 H, s); $\delta_C(C_6D_6)$ 15.7, 18.9, 19.1, 23.5, 28.0, 30.1, 30.6, 31.9, 39.8, 42.1, 46.4, 56.3, 76.5, 130.9 and 132.1; *m/z* 222 (M^+), 191, 177 and 165 (base). For compound (±)-**1**: the spectral data were identical with those of natural tamariscol (−)-**1**.

3. *On the Absolute Configuration*

Isolation of (−)-*Tamariscol* **1**.—*Frullania tamarisci* collected in Taiwan was purified and pulverized, and extracted with dichloromethane to afford, after evaporation, a residue (2 g). The crude extract was separated by column chromatography over silica gel three times (EtOAc–hexane, gradient; benzene; and chloroform, respectively) to afford pure tamariscol **1** (39 mg). For (−)-**1**: $[\alpha]_D$ −20.5° (*c* 3.46 in $CHCl_3$), $[\alpha]_D$ −22.6° (*c* 1.58 in MeOH); ν_{max}(film)/cm^{-1} 3500; δ_H 0.89 (3 H, d, *J* 6.6), 0.94 (3 H, d, *J* 6.6), 1.76 (3 H, s), 1.90 (3 H, s) and 5.08 (1 H, s); $\delta_H(C_6D_6)$ 0.92 (3 H, d, *J* 6.6), 0.99 (3 H, d, *J* 6.6), 1.72 (3 H, d, *J* 1.5), 1.99 (3 H, d, *J* 1.2) and 5.13 (1 H, br s); δ_C 14.9 (Me), 18.8 (Me), 19.9 (Me), 23.7 (CH_2), 28.1 (Me), 30.0 (CH_2), 31.7 (CH_2), 32.8 (CH_2), 39.5 (CH), 45.4 (CH), 49.9 (CH), 58.3 (CH), 79.0 (C), 121.5 (CH) and 136.3 (C); $\delta_C(C_6D_6)$ 15.3 (Me), 19.0 (Me), 20.1 (Me), 24.1 (CH_2), 28.3 (Me), 30.5 (CH_2), 32.3 (CH_2), 33.2 (CH_2), 40.0 (CH), 46.2 (CH), 50.3 (CH), 59.2 (CH), 79.1 (C), 121.9 (CH) and 136.5 (C); *m/z* 222 (M^+), 204, 189 and 165 (base).

Degradation of Tamariscol (−)-**1** *into the Ketone* (+)-**7**.—A solution of tamariscol **1** (26 mg) in dichloromethane (4 cm^3) was treated with MCPBA (31 mg) at 0 °C for 4 h. The usual work-up afforded a mixture of epoxides **47** (27 mg, 97%), ν_{max}(film)/cm^{-1} 3500; $\delta_H(C_6D_6)$ 0.92 (3 H, d, *J* 5.5), 1.01 (3 H, d, *J* 7.0), 1.10 (3 H, s), 1.13 (3 H, s), 2.68 (1 H, s) and 2.72 (1 H, s).

A solution of the mixed epoxides **47** (7.2 mg) in benzene (2 cm^3) was treated with $LiAlH_4$ (8 mg) under reflux for 3 h. The usual work-up afforded a residue (7 mg), which was separated by column chromatography over silica gel (EtOAc–hexane, gradient) to give the alcohols **48a** (1.1 mg, 16%), **48b** (4 mg, 57%) and **49** (0.5 mg). For compound **48a**: ν_{max}(film)/cm^{-1} 3500; $\delta_H(C_6D_6)$ 0.99 (3 H, d, *J* 6.7), 1.17 (3 H, d, *J* 7.0), 1.90 (3 H, s), 4.14 (1 H, d, *J* 5.5), 4.73 (1 H, m) and 4.82 (1 H, m); *m/z* 238 (M^+), 220, 205, 167 and 149 (base). For compound **48b**: ν_{max}(film)/cm^{-1} 3500; $\delta_H(C_6D_6)$ 0.94 (3 H, d, *J* 6.4), 1.12 (3 H, d, *J* 6.7), 1.90 (3 H, s), 4.13 (1 H, d, *J* 5.5), 4.69 (1 H, m) and 4.76 (1 H, m); *m/z* 238 (M^+), 220, 205, 167 and 149 (base). For compound **49**: $\delta_H(C_6D_6)$ 0.93 (3 H, d, *J* 6.6), 0.97 (3 H, d, *J* 6.4) and 3.43 (1 H, br s, $w_{\frac{1}{2}}$ 7); *m/z* 168 (M^+), 150, 137, 111 (base) and 95.

A solution of the diol mixture **48** (53.5 mg) in a mixture of EtOH (5 cm^3) and water (2 cm^3) was treated with $NaIO_4$ (58 mg) for 4 h. The usual work-up afforded the ketone (+)-**7** (34 mg, 91%), $[\alpha]_D$ +10.1° (*c* 0.76 in $CHCl_3$); $[\theta]_{294}$ −4384 (*c* 2.85 × 10^{-3} in $CHCl_3$), $[\theta]_{288}$ −9912 (*c* 2.85 × 10^{-3} in EtOH); other spectral data were identical with those of racemic ketone.

Preparation of Dihydrocarvone **51**.—To a suspension of Te (6.5 g) in EtOH (200 cm^3) was added $NaBH_4$ (4.5 g) and the

mixture was heated under reflux for 2 h to afford deep wine-red coloured mixture. The mixture was cooled to 0 °C and a solution of *l*-carvone **50** (3 g) in EtOH (20 cm^3) was added in one portion. The mixture was stirred at room temperature overnight before being filtered through Celite and washed with dichloromethane. The filtrate was then passed through a short column of silica gel (elution with dichloromethane) to afford dihydrocarvone **51** (2.6 g, 86%) after evaporation of the solvents; ν_{max}(film)/cm^{-1} 1710; δ_H 1.03 (3 H, d, *J* 6.0), 1.09 (3 H, d, *J* 5), 1.74 (3 H, s) and 4.74 (2 H, s).

Preparation of the THP-Ethers **52**.—Dihydrocarvone **51** (2.6 g) was reduced by $NaBH_4$ (485 mg) in MeOH (80 cm^3) at room temperature for 0.5 h. The usual work-up afforded a residue (2.6 g, 99%), which was further treated with a solution of dihydropyran (3.6 cm^3) and PPTS (425 mg) in dichloromethane (90 cm^3). Work-up as usual afforded a mixture of *THP-ethers* **52** (3 g, 75%), ν_{max}(film)/cm^{-1} 1640 and 880; δ_H 1.03 (3 H, d, *J* 6.0), 1.68 (3 H, s) and 4.57 (2 H, s); *m/z* 238 (M^+), 231, 219, 181 and 169 (base) (Found: M^+, 238.1945. $C_{15}H_{26}O_2$ requires M, 238.1933).

Preparation of the Ketones **53**.—Ozone was passed through a solution of the THP-ethers **52** (6.3 g) in dichloromethane (350 cm^3) at −78 °C for 1 h. Triphenylphosphine (6.3 g) was added and the mixture was kept at room temperature for 1 h. Evaporation of the solvent afforded a residue, which was purified by column chromatography over silica gel (EtOAc–hexane, gradient) to give the *mixed ketones* **53** (4 g, 64%), ν_{max}(film)/cm^{-1} 1700; δ_H 0.95 (3 H, d, *J* 6.0) and 2.12 (3 H, s); *m/z* 240 (M^+), 155, 139, 95 and 85 (base) (Found: M^+, 240.1701. $C_{14}H_{24}O_3$ requires M, 240.1725).

Preparation of the Methyl Esters **54**.—Trimethyl phosphonoacetate (3.9 cm^3) was added to a suspension of NaH (60%; 1.1 g) in dry benzene (150 cm^3) and the mixture was stirred at room temperature for 1 h. A solution of the ketones **53**, (4.1 g) in benzene (10 cm^3) was added and the mixture was heated under reflux for 8 h. Work-up as usual afforded a residue (5.24 g), which was purified by column chromatography over silica gel (EtOAc–hexane, gradient) to give the *methyl esters* **54** (3.0 g, 59%), $[\alpha]_D$ −23.8° (*c* 1.1 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1720 and 1640; δ_H 0.92 (3 H, d, *J* 6.0), 1.04 (3 H, d, *J* 6.0), 2.15 (3 H, s), 3.69 (3 H, s), 4.49 (1 H, br s), 4.83 (1 H, br s) and 5.68 (1 H, br s); *m/z* 296 (M^+), 212, 195, 163, 135 and 85 (base) [Found: $(M - CH_3OH)^+$, 264.1700. $C_{16}H_{24}O_3$ requires *m/z* 264.1725].

Preparation of the Esters **55**.—A solution of the methyl esters **54** (3.0 g) in EtOAc (50 cm^3) was hydrogenated in the presence of 10% Pd–C (300 mg) at room temperature for 10 h. Filtration and evaporation afforded the *dihydro derivative esters* **55** (2.9 g, 95%), $[\alpha]_D$ −21.8° (*c* 1.28 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1740; δ_H 0.80 (6 H, d, *J* 7.0) and 3.55 (3 H, s); *m/z* 298 (M^+), 197, 165, 123, 85 (base), 67 and 55 (Found: M^+, 298.2143. $C_{17}H_{30}O_4$ requires M, 298.2144).

Preparation of the Alcohols **56**.—A solution of the esters **55** (1.7 g) in diethyl ether (80 cm^3) was treated with $LiAlH_4$ (1.1 g) at room temperature for 2 h. Work-up as usual afforded the *alcohols* **56** (1.1 g, 72%), $[\alpha]_D$ −18.5° (*c* 1.30 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3355; δ_H 0.83–1.08 (4 sets of doublets) and 4.83 and 4.55 (THP); *m/z* 270 (M^+), 186, 169, 151, 95, 85 (base), 81 and 55 (Found: M^+, 270.2233. $C_{16}H_{30}O_3$ requires M, 270.2195).

Preparation of the Diols **57**.—A solution of the alcohols **56** (2.8 g) in MeOH (100 cm^3) was treated with PPTS (280 mg) at room temperature for 24 h. The usual work-up afforded the *diols* **57** (1.6 g, 80%), $[\alpha]_D$ −3.3° (*c* 1.64 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3325; δ_H 0.86 (3 H, d, *J* 5.0), 0.99 (3 H, d, *J* 5.0) and 3.65 (2 H, t, *J* 6.0); *m/z* 186 (M^+), 124, 113, 95 (base) and 55 [Found: $(M - H_2O)^+$, 168.1482. $C_{11}H_{20}O$ requires *m/z* 168.1514].

Preparation of the Keto Aldehydes **58**.—Swern oxidation of the diols **57** (2.2 g) afforded the *keto aldehydes* **58** (2.1 g, 99%), $[\alpha]_D$ +11.1° (*c* 1.27 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1705; δ_H 0.96 (3 H, d, *J* 5.0), 1.02 (3 H, d, *J* 6.0) and 9.77 (1 H, t, *J* 2.2); *m/z* 182 (M^+), 138 (base) and 111 [Found: $(M - H_2O)^+$, 164.1164. $C_{11}H_{16}O$ requires *m/z* 164.1201].

Aldol Condensation of the Keto Aldehydes **58**.—A mixture of the keto aldehydes **58** (2.2 g), benzoic acid (1.5 g), Et_3N (1.7 cm^3), and benzene (80 cm^3) was heated under reflux for 22 h. Diethyl ether was added and the solution was washed successively with dil. HCl and brine, dried over $MgSO_4$, filtered and evaporated to afford a residue (1.9 g), which was purified by column chromatography over silica gel (EtOAc–hexane, gradient) to give a residue (304 mg, 15%), which was further purified by HPLC (Chemcopak 50-5; 5% EtOAc–hexane; 8 cm^3 min^{-1}) to yield *enone* **59** (36 mg; t_R 19.5 min) and *enone* **60** (42.4 mg; t_R 20.0 min). For compound **59**: $[\alpha]_D$ −9.20° (*c* 1.85 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1680 and 1610; δ_H 1.14 (3 H, d, *J* 5.0), 1.15 (3 H, d, *J* 4.0) and 6.51 (1 H, d, *J* 2.0); *m/z* 164 (M^+), 136, 121, 107 and 94 (base) (Found: M^+, 164.1208. $C_{11}H_{16}O$ requires M, 164.1201). For compound **60**: $[\alpha]_D$ +26.9° (*c* 1.45 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1680 and 1630; δ_H 0.87 (3 H, d, *J* 7.0), 1.15 (3 H, d, *J* 7.0) and 6.54 (1 H, d, *J* 3.0); *m/z* 164 (M^+), 136, 94 and 69 (base) (Found: M^+, 164.1231).

Preparation of the Ketone (−)-**22**.—A solution of the enone **59** (6 mg) in hexane (1 cm^3) was hydrogenated in the presence of PtO_2 (3 mg) at room temperature for 3 h. Filtration and evaporation afforded the ketone (−)-**22** (5 mg, 81%), $[\alpha]_D$ −58.0° (*c* 1.3 in MeOH); $[\theta]_{296}$ −1785 (*c* 6.33 × 10^{-3} in $CHCl_3$); other spectral data were identical with those of (±)-**22**.

Isomerization of the Ketone (−)-**22**.—The ketone (−)-**22** (20 mg) was isomerized under K_2CO_3–MeOH conditions mentioned above to afford a residue (15 mg), which was separated by HPLC as before to yield the ketones (−)-**25** (4.2 mg); (−)-**7** (2.5 mg); (−)-**22** (1.4 mg recovery); and **30** (0.1 mg). For compound (−)-**25**: $[\alpha]_D$ −10.5° (*c* 0.42 in $CHCl_3$); $[\theta]_{291}$ + 1581 (*c* 0.0253 in $CHCl_3$). For compound (−)-**7**: $[\alpha]_D$ −14.3° (*c* 0.25 in $CHCl_3$); $[\theta]_{294}$ +3638 (*c* 0.0151 in $CHCl_3$). For compound (−)-**22**: $[\alpha]_D$ −52.2° (*c* 0.138 in $CHCl_3$); $[\theta]_{294}$ −3069 (*c* 8.31 × 10^{-3} in $CHCl_3$). The specific rotation of compound **30** was not measured due to the minute quantity obtained. Spectral data for these compounds were identical with those of the racemic compounds.

4. *Synthesis of Hydrindenone* **5** *by an Alternative Route*

Preparation of the Esters **62**.—Trimethyl phosphonoacetate (13 cm^3) was added into a mixture of NaH (3.5 g) and dry PhH (100 cm^3) at room temperature and the mixture was stirred for 1 h under nitrogen. To this mixture was added a solution of *p*-methoxyacetophenone **61** (10 g) in dry PhH (20 cm^3). The mixture was refluxed for 7 h before water was added. Extraction with PhH, washing of the extract with dil. HCl and then with brine, and evaporation of the solvent afforded a mixture of (*E*)- and (*Z*)-methyl 3-(4′-methoxyphenyl)but-2-enoate **62** (12 g), ν_{max}(film)/cm^{-1} 1715, 1600 and 1160; δ_H 2.13 (d, *J* 1.8, *Z* 4-H), 2.56 (d, *J* 1.8, *E* 4-H), 3.72 (s, CO_2Me), 3.78 (s, 4′-OMe), 5.88 (m, *Z* 2-H), 6.12 (m, *E* 2-H) and 6.88 and 7.41 (each d, *J* 8.5, ArH); *m/z* 206 (M^+), 175, 135 (base) and 77 (Found: M^+, 206.0946. $C_{12}H_{14}O_3$ requires M, 206.0943).

Hydrogenation of Methyl Esters **62**.—A solution of the olefin mixture **62** (5 g) in MeOH (50 cm^3) was treated with hydrogen in the presence of 10% Pd–C (250 mg) for 5 h. After the catalyst had been filtered off, the solvent was evaporated off under reduced pressure to afford *methyl* 3-(4′-*methoxyphenyl*)*butanoate* **63** (5 g), ν_{max}(film)/cm^{-1} 1730, 1610, 1510, 1450 and 1430; δ_H 1.25 (3 H, s, *J* 6.8, 4-H_3), 2.57 (2 H, d, *J* 7.0, 2-H_2), 3.22 (1 H, m, 3-H), 3.57 (3 H, s, CO_2Me), 3.73 (3 H, s, 4′-O*Me*) and 6.80 and 7.11 (each 2 H, d, *J* 8.8, ArH); δ_C 21.6 (3-Me), 35.4 (C-3), 42.7 (C-2), 51.0 (CO_2*Me*), 54.8 (4′-OMe), 113.7 (C-3′), 127.3 (C-2′), 137.5 (C-1′), 158.0 (C-4′) and 172.4 (CO); *m*/*z* 208 (M^+), 193, 177, 151, 135 (base), 121, 105 and 91 (Found: M^+, 208.1101. $C_{12}H_{16}O_3$ requires M, 208.1099).

Preparation of the Indanone **65**.—The methyl ester **63** (5 g) was hydrolysed in 5% aq. KOH (30 cm^3) and MeOH (30 cm^3) for 18 h. The mixture was worked up as usual to afford 3-(4′-methoxyphenyl)butanoic acid **64** (4.0 g); δ_H 1.10 (3 H, d, *J* 6.6, 4-H_3), 2.40 (2 H, m, 2-H_2), 2.98 (1 H, m, 3-H), 3.57 (3 H, s, OMe), 6.62 and 6.95 (each 2 H, d, *J* 8, ArH) and 10.45 (1 H, s, CO_2H).

The acid **64** (4.0 g) was treated with PPA (40 g) at 90 °C for 10 min. Water was added and the mixture was stirred for 6 h. Extraction with diethyl ether, washing of the extract with water and then with brine, and drying over $MgSO_4$ gave a residue (5.2 g), which was purified by silica gel (150 g) column chromatography with PhH–AcOEt (95:5) as eluent to afford 6-*methoxy*-3-*methylindan*-1-*one* **65** (1.8 g), ν_{max}(film)/cm^{-1} 1700, 1610 and 1485; δ_H 1.31 (3 H, d, *J* 7.7, 3-Me), 2.17 (1 H, dd, *J* 20.5 and 3.8, 2-H^b), 2.86 (1 H, dd, *J* 20.5 and 7.7, 2-H^a), 3.28 (1 H, m, 3-H), 3.80 (3 H, s, OMe) and 7.07–7.43 (3 H, m, ArH); *m*/*z* 176 (M^+), 161, 148, 133, 118, 105 and 77 (Found: M^+, 176.0834. $C_{11}H_{12}O_2$ requires M, 176.0837).

Reduction of the Indanone **65**.—To a stirred solution of the indanone **65** (500 mg) in MeOH (5 cm^3) was added $NaBH_4$ (110 mg) and the mixture was stirred for 30 min. Usual work-up gave 6-*methoxy*-3-*methylindan*-1-*ol* **66** (400 mg), ν_{max}(film)/cm^{-1} 3350, 1610 and 1485; δ_H 1.34 (3 H, d, *J* 7.7, 3-Me), 2.63–3.09 (3 H, m, 2-H_2 and 3-H), 3.80 (3 H, s, OMe), 5.14 (1 H, t, *J* 7.7, 1-H) and 6.80–7.29 (3 H, m, ArH); *m*/*z* 178 (M^+), 163 (base), 135, 121 and 91 (Found: M^+, 178.0995. $C_{11}H_{14}O_2$ requires M, 178.0994).

Hydrogenolysis of the Indanol **66**.—A solution of the indanol **66** (1.3 g) in MeOH (20 cm^3) was treated with hydrogen in the presence of 10% Pd–C (50 mg) at room temperature overnight. Filtration of the catalyst and evaporation of the solvent afforded 5-*methoxy*-1-*methylindane* **67** (1.1 g), ν_{max}(film)/cm^{-1} 1600 and 1485; δ_H 1.19 (3 H, d, *J* 6.4, 1-Me), 1.3–3.2 (5 H, m, 1-H, and 2- and 3-H_2), 3.61 (3 H, s, OMe), 6.64 (1 H, br d, *J* 7.7, 6-H), 6.88 (1 H, br s, 4-H) and 6.97 (1 H, d, *J* 7.7, 7-H); δ_C 20.0 (Me), 31.3 (CH_2), 35.0 (CH_2), 38.4 (CH), 54.8 (Me), 109.6 (CH), 111.8 (CH), 123.3 (CH), 140.5 (C), 144.9 (C) and 158.6 (C); *m*/*z* 162 (M^+), 147 (base), 134, 115, 103 and 91 (Found: M^+, 162.1060. $C_{11}H_{14}O$ requires M, 162.1045).

Birch Reduction of the Indane **67**.—The indane **67** (9.56 g) was treated with Li (7.39 g) in liq. NH_3 (300 cm^3), THF (200 cm^3), and Bu^{t}OH (150 cm^3) for 4 h. MeOH (50 cm^3) was added and the solvents were evaporated off before extraction with diethyl ether. The extract was washed successively with dil. HCl and brine and evaporated to afford a diene (9.26 g), which was dissolved in 3 mol dm^{-3} HCl in MeOH and refluxed for 6 h. Work-up as usual gave (1R*,7aS*)-1-*methyl*-7,7a-*dihydroindan*-5(6H)-*one* **5** (8.24 g), ν_{max}(film)/cm^{-1} 1680 and 1660; δ_H 1.12 (3 H, d, *J* 5.5, 1-Me) and 5.86 (1 H, m, 4-H); δ_C 17.7 (Me), 27.5 (CH_2), 30.6 (CH_2), 32.7 (CH_2), 37.2 (CH_2), 41.0 (CH), 49.9 (CH), 122.4 (CH), 175.4 (C) and 199.4 (C); *m*/*z* 150 (M^+), 135, 122 and 107 (base) (Found: M^+, 150.1043. $C_{10}H_{14}O$ requires M, 150.1045).

Grignard Reaction of the Indanone **6**.—A solution of the indanone **6** (5.2 g) in dry THF (80 cm^3) was added to a solution of methylmagnesium iodide prepared from Mg (7.5 g) and iodomethane (19.5 cm^3) in diethyl ether (60 cm^3) under reflux. The reaction mixture was refluxed for 6 h. Usual work-up afforded 5-methoxy-1-methylindan-1-ol **68** (5.6 g). When compound **68** was left at room temperature overnight, most of the sample dehydrated to afford the indene **69**.

Hydrogenolysis of the Indanol **68**.—The indanol **68** (3.2 g) was treated with H_2 in the presence of 10% Pd–C (270 mg) in PhH (30 cm^3) for 18 h at room temperature. The usual work-up afforded the indane **67** (2.7 g, 93%).

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