Synthesis and Resolution of Albicanic Acid. Simple Access to Optically Active Drimane Sesquiterpenes

Valentine Ragoussis* and Maria Liapis
Organic Chemistry Laboratory, University of Athens, 13a Navarinou Street, Athens, Greece
Nikitas Ragoussis
Vioryl S. A. Research Department, Kato Kifissia, Athens, Greece

The synthesis of albicanic acid (±)-(**2**) and the resolution to its enantiomers (+)-(**2**) and (−)-(**2**) are described. Determination of their optical purity was by ^{1}H n.m.r. spectroscopy of the corresponding methyl esters (+)-(**1**) and (−)-(**1**) with Eu(dcm)$_3$. The absolute configuration of the acids (+)-(**2**) and (−)-(**2**) has been determined by transformation to their alcohols (−)-(**5**) and (+)-(**5**) and interrelation with the natural albicanol. An efficient formal total synthesis of both enantiomeric forms of three drimanic sesquiterpenes, drimenin (**7**), isodrimenin (**8**), and drim-7-ene-11,12-diol (**9**), presenting special synthetic interest, is reported, starting from the corresponding enantiomers of albicanic acid (**2**).

Several sesquiterpenes of the drimane class have recently attracted interest because of their important biological activity.[1] However, a convenient method for the total synthesis of such compounds in chiral form is not available. Among the numerous syntheses that have appeared within the last 10 years,[2] very few led to optically active compounds.[3] In all of these cases the starting material is a natural product possessing the suitable absolute configuration. Indeed, as far as we are aware, there has been no enantiomerically specific total synthesis of the drimanic ring skeleton and, furthermore, there is no possibility for adaptation of any step of the described methods for construction of asymmetric centres. Our aim was, therefore, (i) to synthesise drimanic compounds by a method whereby an intermediate in racemic form could be resolved into its enantiomers and (ii) to elaborate each of the resolved enantiomers to optically active products. The recently published[4] simple and high-yield total synthesis of racemic drimenin from commercially available linalool through the methyl ester (**1**) prompted us to explore a flexible entry into the realm of optically active drimane derivatives. In considering an approach that could provide the ester (**1**), the key compound of the above synthesis, in chiral form, we were attracted to the corresponding acid (±)-(**2**), known in the literature as albicanic acid.[5] This acid was a suitable intermediate which could be resolved. Thus, resolution of this acid and subsequent re-esterification of its enantiomers would give us the desired starting esters (+)-(**1**) and (−)-(**1**) for further chemical transformation to optically active drimane sesquiterpenes.

Initially we attempted the preparation of racemic albicanic acid (±)-(**2**) (Scheme 1) by hydrolysis of its methyl ester (±)-(**1**). Several attempts to hydrolyse this ester employing standard conditions, such as by refluxing it in alcoholic KOH or by using specific conditions for highly hindered esters (*e.g.* quinoline-acetic acid,[6] Bu^{t}OK in DMSO[7]), were unsuccessful or they led in low yield to mixtures of acids epimeric at C-1. We were pleased to find that the use of Dean's reagent[8] easily gave the required product. Thus, the racemic acid (±)-(**2**) was obtained, without epimerisation, by demethylation of the ester (±)-(**1**) in the presence of a 8-fold excess of LiI in refluxing dimethylformamide (DMF). After hydrolysis of the reaction mixture in dil. aqueous HCl and recrystallisation of the white crystalline product in diethyl ether, we obtained very pure albicanic acid (±)-(**2**) in 75% yield.

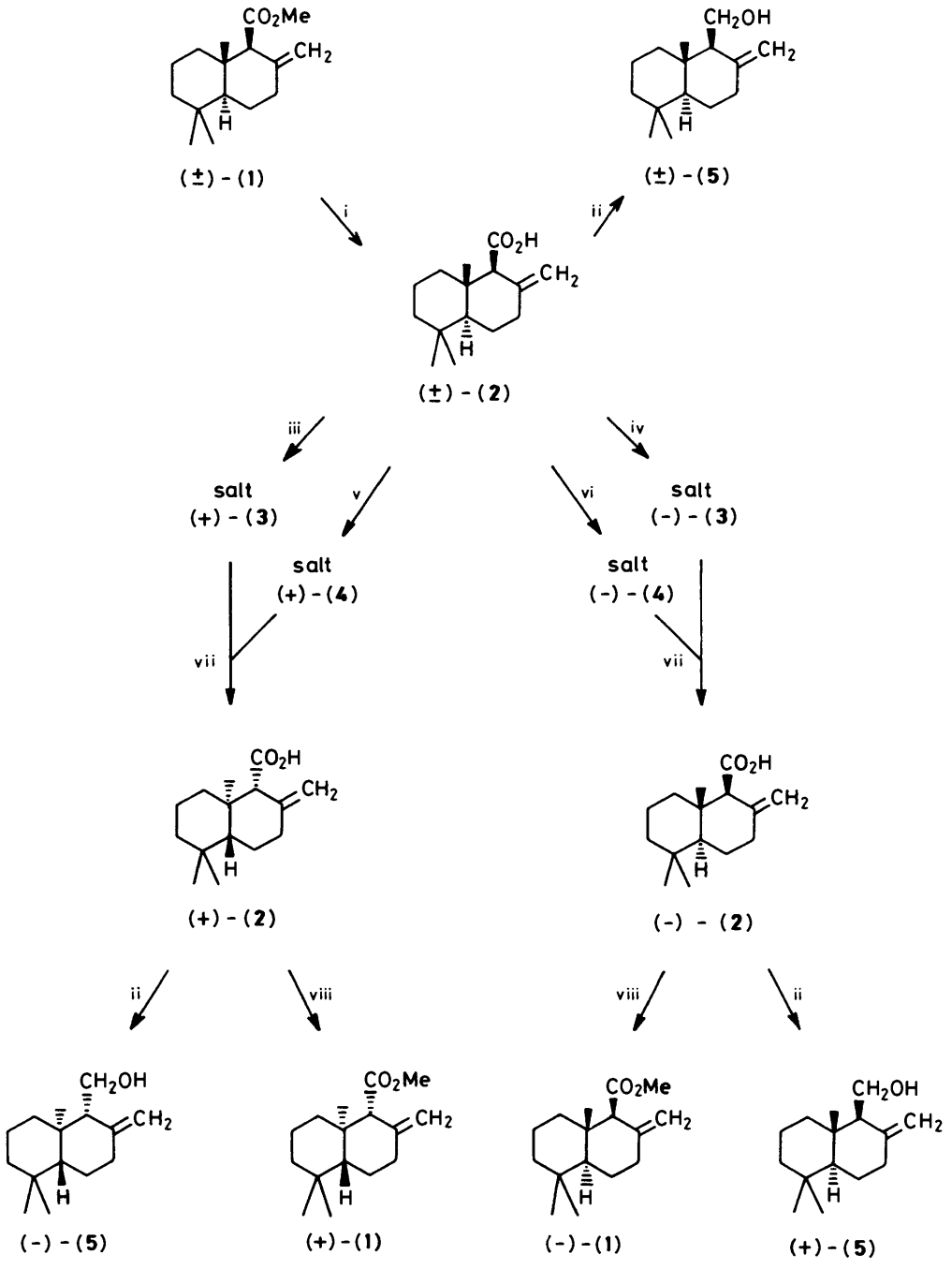
The acid (±)-(**2**) has not as yet been found in nature in either racemic or chiral form. To our knowledge, it has been obtained only by oxidation of the corresponding natural alcohol, albicanol,[5] but it has not been described in full (*e.g.* its m.p. and optical rotation values have not been reported).

For the resolution of albicanic acid (±)-(**2**) we made a series of preliminary tests using various optically active amines in different solvents.[9] We were finally able to achieve an exceptionally efficient resolution *via* the diastereoisomeric salts of the acid (±)-(**2**) with the enantiomers of α-phenylethylamine in absolute ethanol.[10] The progress of the separation was followed by determination of m.p.s and optical rotations of the corresponding salts (+)-(**3**) and (−)-(**3**) (Scheme 1). These salts were decomposed quantitatively by dil. aqueous HCl in MeOH, affording the enantiomers of albicanic acid (+)-(**2**) and (−)-(**2**). Successive resolutions of the remaining unresolved material gave satisfactory yields (66—78%). All the spectra of the acids (+)-(**2**) and (−)-(**2**) were identical with those of the acid (±)-(**2**), described in the Experimental section.

It is of interest to note that the application of the enantiomers of ephedrine for the resolution of the acid (±)-(**2**) gave also the same values for the optical rotations and m.p.s of the two antipodes of (±)-(**2**). However, in this case the recrystallisation of the intermediate salts (+)-(**4**) and (−)-(**4**) was more difficult, and a slightly lower yield was obtained.

The enantiomeric purity of the resolved acids (−)-(**2**) and (+)-(**2**) was determined by ^{1}H n.m.r. spectroscopy of the corresponding methyl esters (−)-(**1**) and (+)-(**1**), using a chiral shift reagent. It was found that the resolved acids were quantitatively esterified by diazomethane. Both enantiomeric esters were liquids, with all their spectroscopic properties similar to those of the ester (±)-(**1**).[4] The methyl-group absorption of the ester (±)-(**1**) in the 60 MHz ^{1}H n.m.r. spectrum was clearly split into two sharp singlets at δ 3.66 and 3.70 in the presence of 0.7 equiv. of tris(dicampholyl-d_2-methanato)europium(III).[11] Pure ester (+)-(**1**) gave only one singlet, at δ 3.66, and pure ester (−)-(**1**) gave a singlet at δ 3.70. In a separate experiment when 5% of ester (−)-(**1**) was added to the pure ester (+)-(**1**), the singlet of the ester (−)-(**1**) at δ 3.70 could clearly be distinguished. Therefore it was evident that the enantiomeric purity of (+)-(**2**) and (−)-(**2**) was >95%.

It then became necessary to investigate the absolute configuration of the chiral forms of albicanic acid. Their absolute configuration was not established, but was assumed by correlation with a substance of known absolute configuration. As point of reference we selected the natural albicanol (+)-(**5**). This enantiomer of albicanol has been isolated from the europian liverwort *Diplophyllum albicans*,[12] from the japanese liverwort *Bazzania species*,[5] and from the Dorid nudibranch

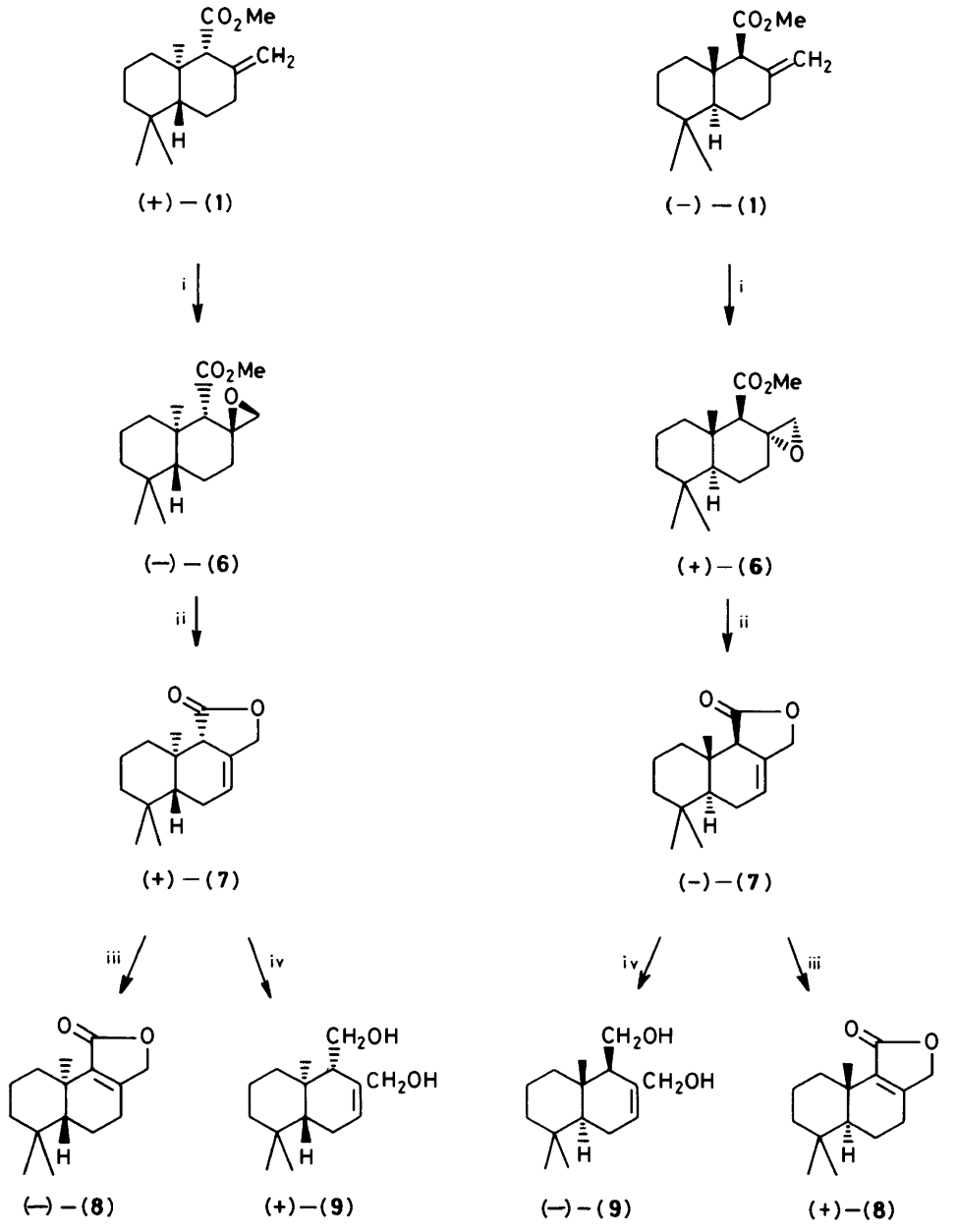


Scheme 1. *Reagents:* i, LiI, DMF; ii, RED-AL, ether; iii, (−)-α-phenylethylamine; iv, (+)-α-phenylethylamine; v, (−)-ephedrine; vi, (+)-ephedrine; vii, aq. HCl, MeOH; viii, CH_2N_2

Cadlina luteomarginata.[13] It can also be obtained by hydrolysis of its natural esters albicanyl acetate[13] and albicanyl 3,4-dihydroxycinnamate.[5] In all of the above cases the stereochemistry of natural albicanol (+)-(**5**) was confirmed to be identical with the stereochemistry of higher terpenoids, having a *trans* (10β-Me) AB ring junction and the β configuration at C-9 as shown in Scheme 1.

Reduction of albicanic acid (−)-(**2**) with a solution of sodium bis-(2-methoxyethoxy)aluminium hydride, 70% in benzene (RED-AL), easily gave the albicanol (+)-(**5**). Comparison of the physical properties of the albicanol (+)-(**5**) obtained from albicanic acid (−)-(**2**) with those of natural (+)-albicanol, described by Hellou *et al.*,[13] showed the two substances to be the same, m.p. 68—69 °C (lit.,[13] 68—69 °C); $[\alpha]_D^{25}$ +11° ($CHCl_3$) {lit.,[13] $[\alpha]_D^{25}$ +13° ($CHCl_3$)}. Since the absolute configuration of (+)-(**5**) has been established,[13] we can attribute the same absolute configuration (1*S*,4a*S*,8a*S*) to the albicanic acid (−)-(**2**) because (i) the reduction of albicanic acid to albicanol does not affect the asymmetric centres of the molecule and (ii) there is no migration of the ethylenic linkage during this reduction with RED-AL. Obviously, the other enantiomer of albicanic acid, (+)-(**2**), has the stereostructure 1*R*,4a*R*,8a*R*.

Albicanic acid, after its resolution, afforded a convenient means of access to a variety of chiral drimane structures, *via* the previously described method.[4] To demonstrate the utility of this



Scheme 2. *Reagents:* i, *m*-Chloroperbenzoic acid, CH_2Cl_2; ii, *p*-$MeC_6H_4SO_3H$, $CHCl_3$; iii, MeONa, MeOH; iv, RED-AL, ether

approach, we successfully completed the synthesis of both enantiomers of drimenin, (+)-(**7**) and (−)-(**7**), isodrimenin, (+)-(**8**) and (−)-(**8**), and drim-7-ene-11,12-diol, (+)-(**9**) and (−)-(**9**).

Thus esterification (diazomethane) of the albicanic acid (−)-(**2**) gave the methyl albicanate (−)-(**1**) (Scheme 1). Epoxidation of (−)-(**1**) gave the epimeric epoxide (+)-(**6**) (Scheme 2). Acid treatment of the latter gave drimenin (−)-(**7**) {m.p. 129—130 °C (lit.,[14] 133 °C); $[\alpha]_D^{20}$ −54.5° (C_6H_6), −43° ($CHCl_3$) [lit.,[14] −42° (C_6H_6)]}. Subsequent isomerisation of (−)-(**7**) in alkaline conditions gave isodrimenin (+)-(**8**), m.p. 129—130 °C (lit.,[3d] 131—132 °C); $[\alpha]_D^{20}$ +98° ($CHCl_3$) [lit.,[3d] +93° ($CHCl_3$)]. The above sequence of reactions from chiral albicanic acid (−)-(**2**) to drimenin (−)-(**7**) and isodrimenin (+)-(**8**) does not affect any asymmetric centre of albicanic acid.

The constitution and absolute configuration of natural drimenin (−)-(**7**) and natural isodrimenin (+)-(**8**) have been elucidated by relating them with (−)-drimenol.[14] Thus, for these epimers of drimenin and isodrimenin, Appel *et al.*[14] gave the same stereochemistry with a *trans* (10β-Me) AB ring junction. Therefore, the transformation of albicanic acid (−)-(**2**) to drimenin (−)-(**7**) and to isodrimenin (+)-(**8**) provides additional confirmation of the absolute configuration of albicanic acid (−)-(**2**). Reduction of drimenin (−)-(**7**) with RED-AL gave the drim-7-ene-11,12-diol (−)-(**9**) with the same absolute stereochemistry as albicanic acid (−)-(**2**).

A similar sequence of reactions was also accomplished starting from albicanic acid (+)-(**2**) and led to the optical antipodes of the above compounds, *i.e.* drimenin (+)-(**7**), isodrimenin (−)-(**8**), and drim-7-ene-11,12-diol (+)-(**9**) (Scheme 2).

Spectral data of the chiral forms of the above sesquiterpenes are the same as that of their racemic form already described.[4,15] Physical constants are given in the Experimental section.

The above synthetic drimane derivatives are of importance because they have often been used as basic building intermediates in the synthesis of biologically active drimane members including waburgranal,[16–18] polygodial,[15,19–21] confertifolin,[22] and cinnamolide.[19,23] The synthesis and resolution of albicanic acid and the transformation of its enantiomers to both enantiomeric forms of drimenin, isodrimenin, and drim-7-ene-9,11-diol, described herein in connection with the previously reported total syntheses of the ester (±)-(**1**),[2d,4] constitute, to our knowledge, the first access by formal total synthesis to chiral drimanic compounds.

In conclusion, it should be emphasised that the foregoing synthesis offers a useful preparative route to a variety of drimanic derivatives in their natural and unnatural forms. Such syntheses will be reported at a later date.

Experimental

M.p.s were measured on a Büchi 510 apparatus and are uncorrected. I.r. spectra were obtained in CCl_4 solution and recorded on a Perkin-Elmer 1750 i.r. Fourier transform spectrometer. ^1H N.m.r. spectra were obtained for solutions in CCl_4 unless otherwise stated, and recorded on a Varian E.M. 360 instrument (60 MHz) at room temperature. Chemical shifts are reported in p.p.m. (δ) relative to internal $SiMe_4$. Mass spectra were taken with a Hewlett Packard 5980 A instrument. Optical rotations were determined at 20—25 °C on a Perkin-Elmer 141 polarimeter. Analytical t.l.c. was carried out on Merck Kieselgel (G and HF_{254}, or G and $AgNO_3$ 3.5%) using mixtures of diethyl ether–light petroleum (b.p. 40—60 °C) as developer, and spots were visualised with aqueous H_2SO_4 or with iodine. Preparative t.l.c. (p.l.c.) was performed with 2 mm Merck precoated silica gel 60 F_{254} plates. All compounds were homogeneous by t.l.c.

Ether refers to diethyl ether. DMF was dried by distillation from 4Å molecular sieves and was stored over 4Å molecular sieves. RED-AL was a 70% in benzene. Organic ethereal extracts were dried over Na_2SO_4. The general methods and materials employed in this work were similar to those described in our previous paper.[4] The i.r., n.m.r., and mass spectra of the optically active compounds are identical with those of the corresponding racemic compounds already reported[4] or described in the present paper.

(±)-(1RS,4aRS,8aRS)-*Decahydro*-5,5,8a-*trimethyl*-2-*methylenenaphthalene*-1-*carboxylic Acid* (*Racemic Albicanic Acid*) (±)-(**2**).—The ester (±)-(**1**) (8 g, 0.032 mol) was dissolved in DMF (150 ml), and dry LiI (25 g, 0.186 mol) was added. The mixture was heated under reflux in an atmosphere of nitrogen for 40 h, when t.l.c. showed that the starting material had disappeared. The reaction mixture was cooled and poured into a solution of 10% HCl. This solution was then extracted with $CHCl_3$. The extract was washed successively with dil. aqueous $NaHSO_3$ and with water, dried over Na_2SO_4, and concentrated to afford the racemic albicanic acid (7.4 g) as a white powder, which was recrystallised from ether to give the pure acid (4.55 g), m.p. 162—163 °C. The remaining mother liquor was purified by column chromatography on silica gel. Elution with a mixture of light petroleum–ether (5:1) produced pure *albicanic acid* (±)-(**2**) (1.20 g, overall yield 76%). Two recrystallisations from ether raised the m.p. to 164—166 °C (Found: C, 76.0; H, 10.35. $C_{15}H_{34}O_2$ requires C, 76.27; H, 10.16%); $\nu_{max.}$ 3 530, 3 084, 2 990, 2 940, 2 870, 2 846, 1 755, 1 712, 1 650, 1 460, 1 445, 1 425, 1 390, 1 365, 1 280, 1 225, 1 210, 1 110, 900, 696, and 643 cm^{-1}; δ ($CDCl_3$) 0.88 (3 H, s), 0.90 (3 H, s), 1.07 (3 H, s), 2.82 (1 H, s), 4.71 (1 H, s), and 4.79 (1 H, s); *m/z* 236 (M^+, 22.7%), 221 (19.1) 176 (17), 137 (100), 123 (50.3), 95 (35), 81 (36.5), and 69 (42.9)

Resolution of Albicanic Acid (±)-(**2**), *using Optically Active Amines*

Resolution with (+)-*and* (−)-*Phenylethylamine.*—(*a*) *Preparation of the enantiomeric salts* (−)-(**3**) *and* (+)-(**3**). A solution of the acid (±)-(**2**) (1.9 g, 8 mmol) in hot absolute ethanol (8 ml) was treated with (+)-α-phenylethylamine (0.5 ml, 4 mmol, 0.5 equiv.). After having cooled slowly to room temperature, the clear solution was placed in the refrigerator overnight. The resulting fine crystals were filtered off and washed with cold ethanol. One recrystallisation from ethanol gave the salt (−)-(**3**) (0.7 g, 50%) as fine white needles, m.p. 163—165 °C; $[\alpha]_D^{25}$ −8.5° (*c* 1 in $CHCl_3$). The m.p. and the optical rotation were unchanged after a second recrystallisation.

The combined supernatant from the above recrystallisations was diluted with water (20 ml) and acidified with 1M-HCl to pH 2. Extraction with ether (3 × 10 ml), and concentration, afforded a white solid enriched in the other enantiomer (1.35 g, 93% recovery). To this material, dissolved in hot absolute ethanol (5 ml), was added (−)-α-phenylethylamine (0.5 ml, 4 mmol, 1 equiv. based on the acid present). The resulting crystals were collected, and recrystallisation from ethanol afforded pure salt (+)-(**3**) (0.65 g, 45%), m.p. 164—165 °C; $[\alpha]_D^{25}$ +8.5° (*c* 1 in $CHCl_3$).

The filtrates from the above recrystallisations were acidified with (1M-HCl to pH 2, and extracted with ether. Concentration of the extract gave unresolved albicanic acid (0.88 g, 96% recovery). The process described above was repeated twice and finally gave the salt (−)-(**3**) (1.10 g, 78.6%), the salt (+)-(**3**) (0.92 g, 65.7%), and unresolved albicanic acid (±)-(**2**) (0.23 g).

(*b*) *Hydrolysis of the salts* (−)-(**3**) *and* (+)-(**3**): *preparation of* (−)-(1S,4aS,8aS)-*decahydro*-5,5,8a-*trimethyl*-2-*methylenenaphthalene*-1-*carboxylic acid* (*albicanic acid*) (−)-(**2**). The salt (−)-(**3**) (1.1 g, 3 mmol) was dissolved in methanol (10 ml), by heating if necessary; the solution was acidified with 1M-HCl to pH 2 and was then diluted with water (10 ml). A white precipitate was separated which, after having cooled for 2 h to 0 °C, was filtered off, washed with cold water, and dried *in vacuo* to give (quantitatively) the corresponding albicanic acid (−)-(**2**) as a white solid, m.p. 130—132 °C; $[\alpha]_D^{25}$ −28.2° (*c* 1 in $CHCl_3$). Attempted purification of acid (−)-(**2**) by recrystallisation was unsuccessful because of its great solubility in the common solvents.

Preparation of (+)-(1R,4aR,8aR)-*decahydro*-5,5,8a-*trimethyl*-2-*methylenenaphthalene*-1-*carboxylic acid* (*albicanic acid*) (+)-(**2**). This compound was similarly obtained in quantitative yield from the salt (+)-(**3**) according the above procedure. Recrystallisation was not effected. The title acid had m.p. 129—130 °C; $[\alpha]_D^{25}$ +29° (*c* 1 in $CHCl_3$) (Found C, 76.0; H, 10.3. $C_{15}H_{34}O_2$ requires C, 76.27; H, 10.16%).

Resolution with (+)- *and* (−)-*Ephedrine.*—(a) *Preparation of the enantiomeric salts* (+)-(**4**) *and* (−)-(**4**). The racemic albicanic acid (±)-(**2**) (1 g, 4.2 mmol) was dissolved in acetone (12 ml), and (−)-ephedrine (0.7 g, 4.2 mmol) was added. A thick white precipitate was formed at once, which was dissolved by heating the mixture in a water-bath. The clear solution was concentrated (to 5—6 ml) and was left to crystallise at 5 °C. Crystallisation was quite difficult, but it afforded fine white needles (0.45 g, 50%). Two recrystallisations from acetone gave an analytical sample, m.p. 160—162 °C; $[\alpha]_D^{25}$ +16.3° (*c* 1.01 in $CHCl_3$).

The combined filtrates from the above crystallisations were acidified with 1M-HCl to pH 2, and the precipitated acid (**2**) (0.7 g, 2.95 mmol), enriched in the other enantiomer, was filtered and then treated, in the same way as above, with (+)-ephedrine (0.5 g, 3 mmol). The obtained crystals (0.35 g, 38%) were

recrystallised twice from acetone to give the (−)-salt (**4**), m.p. 162—164 °C; $[\alpha]_D^{20}$ −17.2° (*c* 1.5 in $CHCl_3$).

(b) *Hydrolysis of the salts* (+)-(**4**) *and* (−)-(**4**). *Preparation of the albicanic acid* (+)-(**2**). This compound was obtained quantitatively from the salt (+)-(**4**) by hydrolysis with 1M-HCl and filtration. Recrystallisation was not effected. The acid had m.p. 129—131 °C; $[\alpha]_D^{20}$ +26° (*c* 1 in $CHCl_3$).

Preparation of the albicanic acid (−)-(**2**). This compound was obtained as above by acidic hydrolysis of the salt (−)-(**4**). The resulting white solid had, without recrystallisation, m.p. 127—129 °C; $[\alpha]_D^{20}$ −27.5° (*c* 1.2 in $CHCl_3$).

(±)-(1RS,4aRS,8aRS)-*Decahydro*-5,5,8a-*trimethyl*-2-*methylene*-1-*naphthylmethanol* (*Albicanol*) (±)-(**5**).—Albicanic acid (±)-(**2**) (0.25 g, 1.05 mmol) was dissolved in ether (15 ml) and the solution was treated dropwise with a solution of RED-AL (excess). The solution was kept overnight at room temperature. Hydrolysis with dilute HCl (10%), followed by extraction with ether and the usual work-up, gave white crystals of racemic (±)-(**5**) (0.2 g, 85%) pure by t.l.c. (light petroleum–ether 2:1). Recrystallisation from hexane gave the *title product*, m.p. 67—68 °C (Found: C, 81.3; H, 11.9. $C_{15}H_{26}O$ requires C, 81.08; H, 11.7%); $\nu_{max.}$ 3 610, 3 080, 2 935, 2 870, 2 845, 1 640, 1 460, 1 390, 1 030, 964 and 895 cm^{-1}; δ($CDCl_3$) 0.75 (3 H, s), 0.83 (3 H, s), 0.90 (3 H, s), 3.75 (1 H, br s), 3.85 (1 H, s), 4.6 (1 H, s), and 4.9 (1 H, s); *m/z* 222 (M^+, 11.1%), 207 (8.3), 204 (7.9), 189 (9.2), 137 (100), 123 (31.8), 109 (30.5), 95 (45.8), 81 (56.4), 69 (49), 55 (52), and 41 (52).

(−)-(1R,4aR,8aR)-*Decahydro*-5,5,8a-*trimethyl*-2-*methylene*-1-*naphthylmethanol* (*Albicanol*) (−)-(**5**).—With albicanic acid (+)-(**2**) as starting material in the procedure described above, the epimer (−)-(**5**) was obtained. Recrystallisation twice from hexane gave crystals, m.p. 69—70 °C; $[\alpha]_D^{20}$ −11.5° (*c* 0.8 in $CHCl_3$).

(+)-(1S,4aS,8aS)-*Decahydro*-5,5,8a-*trimethyl*-2-*methylene*-1-*naphthylmethanol* (*Albicanol*) (−)-(**5**).—With albicanic acid (−)-(**2**) as starting material in the above procedure, the epimer (+)-(**5**) was obtained. Recrystallisation twice from hexane gave crystals, m.p. 68—69 °C (lit.,[13] 68—69 °C); $[\alpha]_D^{20}$ +11° (*c* 1.05 in $CHCl_3$) [lit.,[13] +13° (*c* 0.6 in $CHCl_3$)] (Found: C 81.3; H, 11.95. calc. for $C_{15}H_{26}O$: C, 81.08; H, 11.7%).

(+)-*Methyl* (1R,4aR,8aR)-*Decahydro*-5,5,8a-*trimethyl*-2-*methylenenaphthalene*-1-*carboxylate* (*Methyl Albicanate*) (+)-(1).—Albicanic acid (+)-(2) was quantitatively converted into its methyl ester on treatment with an excess of diazomethane in ether solution. The ester (+)-(**1**) was obtained as an oil (homogeneous by t.l.c.; light petroleum–ether 10:1); $[\alpha]_D^{25}$ +22.8° (*c* 1 in $CHCl_3$).

(−)-*Methyl* (1S,4aS,8aS)-*Decahydro*-5,5,8a-*trimethyl*-2-*methylenenaphthalene*-1-*carboxylate* (*Methyl Albicanate*) (−)-(1).—This compound was obtained quantitatively from the albicanic acid (−)-(**2**), under conditions similar to those described above. The ester (−)-(**1**) was an oil, pure by t.l.c., $[\alpha]_D^{25}$ −23.2° (*c* 1 in $CHCl_3$).

(−)-*Methyl* (1S,2S,4aR,8aR)-*Decahydro*-5,5,8a-*trimethylnaphthalene*-2-*spiro*-2′-*oxirane*-1-*carboxylate* (−)-(**6**).—This compound was prepared, in 90% yield, starting from the ester (+)-(1) according to the procedure described in the literature.[4] Two recrystallisations from light petroleum gave fine white needles, m.p. 112—113 °C; $[\alpha]_D^{25}$ −7° (*c* 1 in $CHCl_3$).

(+)-*Methyl* (1R,2R,4aS,8aS)-*Decahydro*-5,5,8a-*trimethylnaphthalene*-2-*spiro*-2′-*oxirane*-1-*carboxylate* (+)-(**6**).—This compound was obtained in 90% yield from the ester (−)-(**1**) as above. It was recrystallised twice from light petroleum to give fine needles, m.p. 113 °C; $[\alpha]_D^{25}$ +6° (*c* 1 in $CHCl_3$).

(+)-(5aR,9aR,9bS)-5,5a,6,7,8,9,9a,9b-*Octahydro*-6,6,9a-*trimethylnaphtho*[1,2-c]*furan*-1(3H)-*one* (*Drimenin*) (+)-(**7**).—This enantiomer was obtained in 95% yield from the epoxide (−)-(**6**), using the known procedure.[4] Two recrystallisations from methanol gave fine white crystals, m.p. 129—131 °C; $[\alpha]_D^{25}$ +44° (*c* 1 in $CHCl_3$) and $[\alpha]_D^{25}$ +53.5° (*c* 1 in C_6H_6).

(−)-(5aS,9aS,9bR)-5,5a,6,7,8,9,9a,9b-*Octahydro*-6,6,9a-*trimethylnaphtho*[1,2-c]*furan*-1(3H)-*one*(*Drimenin*) (−)-(**7**).—This compound was obtained from the epoxide (+)-(**6**) as in the above case. After two recrystallisations from MeOH, the title product had m.p. 129—130 °C (lit.,[14] 133 °C); $[\alpha]_D^{20}$ −54.5° (*c* 1 in C_6H_6), −43° (*c* 1 in $CHCl_3$) [lit.,[14] −42° (*c* 0.76 in C_6H_6)] (Found: C, 76.7; H, 9.5. Calc. for $C_{15}H_{22}O_2$: C, 76.92; H, 9.40%).

(−)-(5aR,9aR)-4,5,5a,6,7,8,9,9a-*Octahydro*-6,6,9a-*trimethylnaphtho*[1,2-c]*furan*-1(3H)-*one* (*Isodrimenin*) (−)-(**8**).—Isomerisation of drimenin (+)-(**7**) in MeONa–MeOH[13] gave (quantitatively) pure crystalline (−)-(**8**). Recrystallisation from light petroleum gave fine white needles, m.p. 128—129 °C; $[\alpha]_D^{20}$ −96° (*c* 0.4 in $CHCl_3$).

(+)-(5aS,9aS)-4,5,5a,6,7,8,9,9a-*Octahydro*-6,6,9a-*trimethylnaphtho*[1,2-c]*furan*-1(3H)-*one* (*Isodrimenin*) (+)-(**8**).—This enantiomer was obtained from (−)-(**7**) in the same manner as above. Recrystallisation from light petroleum gave crystals, m.p. 129—130 °C (lit.,[3b,3d,14] 131—132 °C); $[\alpha]_D^{20}$ +98° (*c* 0.5 in $CHCl_3$) [lit.,[14] +87° (*c* 2.02 in $CHCl_3$); lit.,[3b] +86° (*c* 2 in $CHCl_3$); lit.,[3d] +93° (*c* 1.1 in $CHCl_3$)] (Found: C, 76.7; H, 9.6. calc. for $C_{15}H_{22}O_2$: C, 76.92; H, 9.40%).

(+)-(1S,4aR,8aR)-1,4,4a,5,6,7,8,8a-*Octahydro*-5,5,8a-*trimethylnaphthalene*-1,2-*diyldimethanol* (*Drim*-7-*ene*-11,12-*diol*) (+)-(**9**).—Drimenin (+)-(**7**) (120 mg, 0.5 mmol) was dissolved in ether (8 ml), and a solution of RED-AL was added dropwise to excess. The mixture was kept overnight at room temperature. Hydrolysis with dil. HCl (10%), followed by extraction with ether, and the usual work-up of the extract gave a crude product (130 mg). Purification was achieved by p.l.c. on silica gel (light petroleum–ether 1:7) to afford the *title product* (+)-(**9**) (105 mg, 90%) as an oil (homogeneous on t.l.c.). This oil crystallised from hexane after several hours. Recrystallisation from hexane gave beautiful white plates, m.p. 70—71 °C; $[\alpha]_D^{20}$ +7° (*c* 1 in $CHCl_3$), +9.3° (*c* 1 in C_6H_6) (Found: C, 75.8; H, 11.3. $C_{15}H_{26}O_2$ requires C, 75.58; H, 10.99%); $\nu_{max.}$ 3 620, 3 305 br, 3 045, 2 920, 2 865, 2 852, 1 665, 1 460, 1 440, 1 388, 1 368, 1 074, 1 040, 990, and 680 cm^{-1}; δ 0.75 (3 H, s), 0.86 (6 H, s), 1.1—1.6 (7 H, m), 1.8—2.15 (3 H, m), 3.62 (1 H, s), 3.83 (1 H, s), 4.05 (1 H, s), 4.25 (1 H, s), and 5.58 (1 H, br s); *m/z* 238 (M^+, 4%), 207 (3.4), 190 (36.2), 124 (17.3), 109 (100), 69 (23), 55 (18), and 41 (24.9).

(−)-(1R,4aS,8aS)-1,4,4a,5,6,7,8,8a-*Octahydro*-5,5,8a-*trimethylnaphthalene*-1,2-*diyldimethanol* (*Drim*-7-*ene*-11,12-*diol*) (−)-(**9**).—Reduction of drimenin (−)-(**7**) with RED-AL was carried out in the same manner as described above for the epimer (+)-(**7**). The obtained *product* was recrystallised from hexane, m.p. 73—74 °C (lit.,[14] 73.5—74.5 °C); $[\alpha]_D^{20}$ −6.7° (*c* 1 in $CHCl_3$), −9° (*c* 1 in C_6H_6) [lit.,[14] −7° (*c* 1.38 is C_6H_6)] (Found: C, 75.8; H, 10.8. $C_{15}H_{26}O_2$ requires C, 75.58; H, 10.99%).

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