# 222. Terpenoids Derived from Linalyl Oxide. Part 3. The Isolation, Structure, Absolute Configuration and Synthesis of the Davanafurans, Nor-sesquiterpenes Isolated from *Artemisia Pallens*

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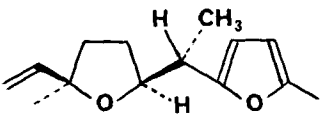
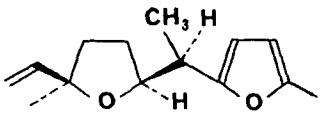
(16. VIII. 74)

*Summary.* The novel nor-sesquiterpenoids, the davanafurans, have been isolated from the oil of *Artemisia pallens*, the principal component being the *cis,threo*-isomer (**1a**). The absolute configuration of this isomer, and the relative stereochemistry of the other isomers, have been established by synthesis from linalool oxides of known configuration.

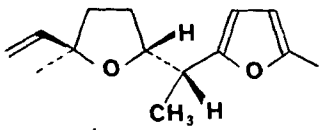
In view of the recent interest in the unusual sesquiterpenes isolated from *Artemisia pallens* (fam. *Compositae*), [1] we wish to report the isolation and synthesis of the 3-methyl-7-(2-methylfur-5-yl)-3,6-oxido-1-octenes (**1**), compounds contributing to the characteristic odor of Davana oil isolated from this plant.



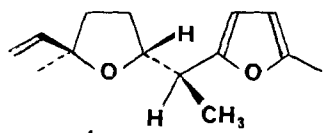

**1a**




**1b**




**1c**




**1d**

The davanafurans were isolated by column chromatography on silica gel, from a fraction of polarity intermediate between that of the hydrocarbons and the davana ethers [1a]. The two oxygen atoms of the compounds, $C_{14}H_{20}O_2$ were thus presumably ether functions. Four isomers were present, but one was predominant, and two others could not be separated on a preparative scale. NMR.-spectra exhibited signals consistent with a 5-substituted 2-methyl-2-vinyl-tetrahydrofuran [1a] [2], and this was supported by the presence of a fragment at *m/e* 111 ($C_7H_{11}O^+$) in the mass-spectrum. A secondary methyl group ($CH_3CH$) and a methyl group attached to an aromatic ring left $C_4H_2O$ unaccounted. The two remaining hydrogen atoms exhibited a singlet at 5.78 ppm in the NMR.-spectra, consistent with the $\beta$-protons on a furan ring, and the main fragment in the mass-spectrum at *m/e* 109 ($C_7H_9O^+$) supported the presence of the $CH_3$-furan-CHMe-structure. The principal isomer had the double doublet signal of the vinyl proton at lower field than the other pure

isomer, and was therefore assigned the *cis* configuration about the tetrahydrofuran ring (**1a** or **1b**)[1]).

The advantage of a synthesis starting from linalyl oxide (**2**) is that the stereochemistry of each isomer is known [2], and, provided the substitution at the tetrahydrofuran ring is undisturbed, it should be possible to prepare davanafurans of the correct absolute configuration[2]). The preparation of 5-isopropenyl-2-methyl-2-vinyltetrahydrofuran (**3**) has been described [1b] [2]; the latter was converted, either by periodic acid treatment of the epoxides (**4**) or by low temperature ozonolysis, to the methyl ketone (**5**). The (−)-*cis*-ketone **5a** was obtained exclusively from (−)-*cis*-linalyl oxide (**2a**), and the (+)-*trans*-ketone **4b** from (+)-*trans*-linalyl oxide (**2b**). Although these ketones undergo a 2,3-sigmatropic rearrangement in presence of *Grignard* reagents [4], lithiated 2-methylfuran reacts normally, yielding two isomers of the alcohols (**6**) from each ketone (**5**). The alcohols (**6**) are not very stable, and initial attempts to purify them led to some decomposition, particularly after chromatography on silica gel. Loss of water occurs; in one direction this leads to dehydrodavanafurans (**7**), but in the other direction the dehydration product (**8**) undergoes a *Cope* rearrangement analogous to the one used in preparing karahanaenone (**9**, R = H) [5], and the substance isolated is 2,5-dimethyl-2-(2-methylfur-5-yl)-cyclohept-4-enone (**9**, R = 5-methyl-2-furyl). Despite this decomposition, a mixture of the two *trans*-alcohols (**6c** and **6d**) could be separated into the components by chromatography on silica gel, as could the mixture of the *cis*-alcohols (**6a** and **6b**). In the event, this separation turned out to be unnecessary, because reduction of either **6a** or **6b** to davanafuran yielded a mixture of the two *cis*-isomers of the latter (**1a** and **1b**), similar epimerization occurring in the case of the *trans*-isomers.

After an abortive attempt to replace the hydroxyl group by hydrogen using sodium in liquid ammonia at low temperature[3]), it was found that lithium aluminum hydride in the presence of aluminum chloride at 0° effected the reduction rapidly and in good yield [6]. Although stereochemistry at the tetrahydrofuran ring was maintained, epimerization occurred at the site of the reduction, and from the mixture of *cis*-alcohols (**6a** and **6b**) a 4:1 mixture of *cis*-davanafurans (**1a** and **1b**) was obtained, while a 3:1 mixture of the *trans*-davanafurans (**1c** and **1d**) was obtained from the *trans*-alcohols. There was little difference in the result if pure *threo* or pure *erythro* alcohols (**6**) were used.

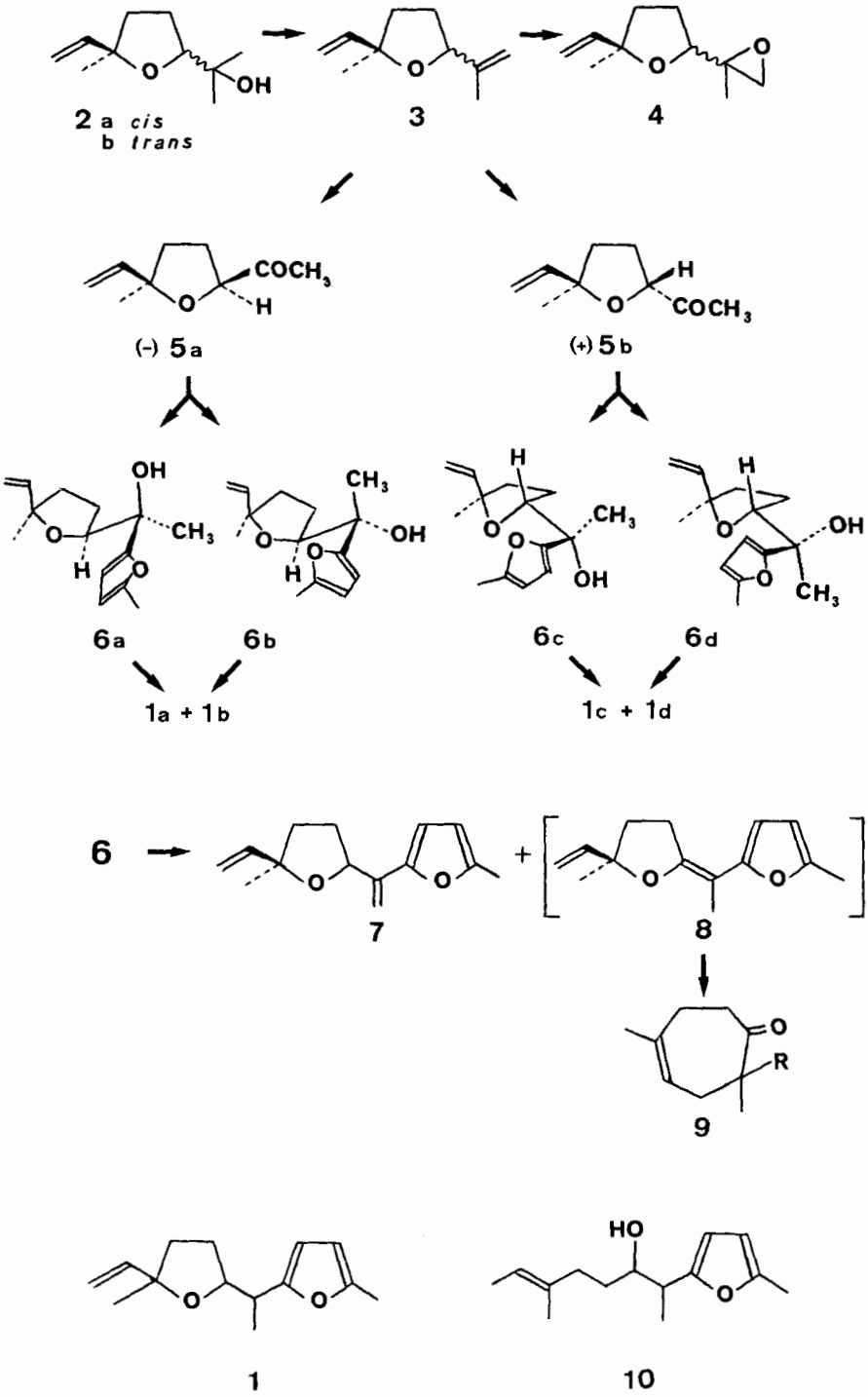
If the reduction was carried out for extended periods, and particularly if the mixture was heated, a heavier substance was obtained, which we identified as a mixture of the alcohols **10** resulting from 1,4-addition of hydrogen to the allyl ether group of davanafuran (**1**).

Consideration of the stereochemistry of epoxidation of the 5-isopropenyl-2-methyl-2-vinyltetrahydrofurans (**3**) serves as introduction to a discussion of the

[1]) In addition to the NMR. spectral assignment for *cis*- and *trans*-substituted 5-substituted 2 methyl-2-vinyltetrahydrofurans [1b] [2], the *trans*-isomers usually have shorter retention times on Carbowax columns, and characteristic changes in the $^{13}C$ resonance have also been observed [3].

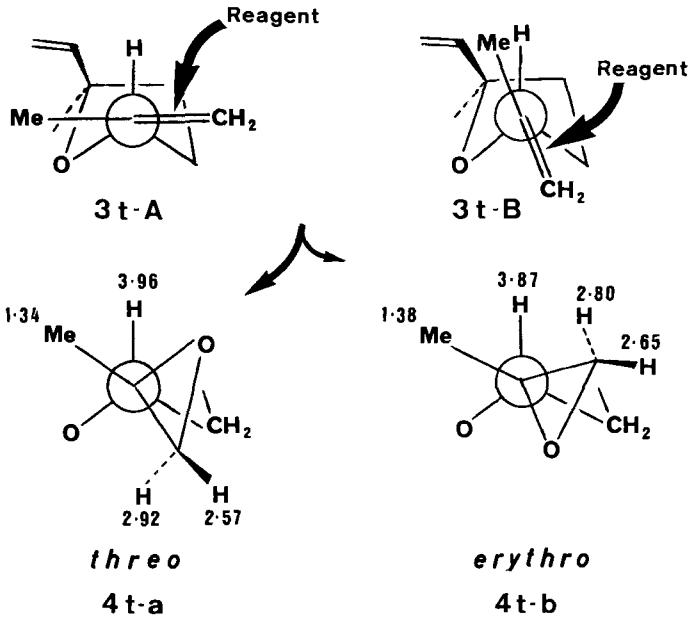
[2]) Initially, the synthesis was carried out with racemic linalyl oxides; for the determination of the absolute stereochemistry, natural (+)-*trans*- and (−)-*cis*-oxides were used.

[3]) This reduction resulted in 1,4-reduction of the vinyl group with opening of the tetrahydrofuran ring, leaving the hydroxyl group next to the furan ring intact.


2 a cis
b trans
3
4
(-) 5a
(+) 5b
6a
6b
6c
6d
1a + 1b
1c + 1d
6
7
8
9
1
10

stereochemistry of this type of system. The *trans*-rotamers 3*t*-A and 3*t*-B appear from models to involve the lowest number of steric interactions, in that they have the less sterically demanding methylene group on the side of the large substituent ($CH_2$) and the methyl group between the medium (oxygen) and small (hydrogen) groups on the adjacent atom (*scheme 1*). Approach of the peracid is in this case

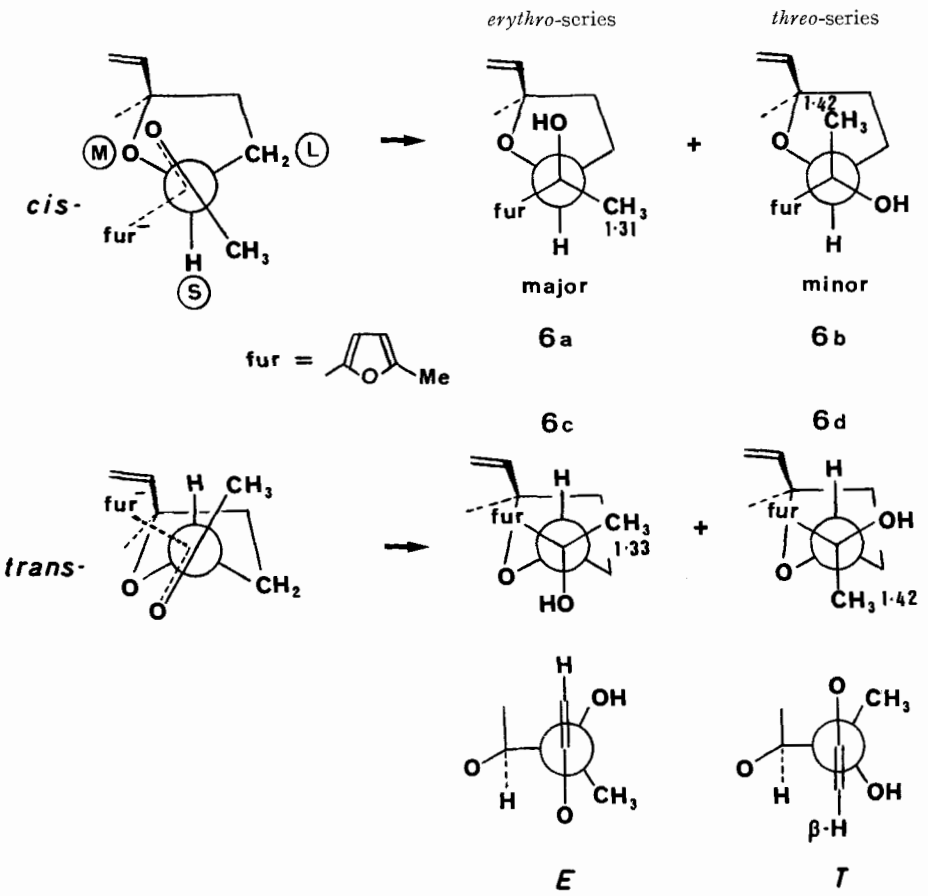
*Scheme 1*




clearly easier from the upper, less hindered side, and it would thus be expected that the *threo*-epoxide (**4***t*-**a**) would be formed in preference to the *erythro*-epoxide (**4***t*-**b**). Of the two *trans*-epoxides acutally isolated, the one with shorter retention time on Carbowax was formed in larger amounts, and this one had a larger difference between the chemical shifts of the epoxide methylene protons than the other epoxide. Furthermore, the proton on the tetrahydrofuran ring was further downfield in this epoxide with the shorter retention time, suggesting that it was in closer proximity to the epoxide oxygen atom. The two structures **4***t*-**a** and **4***t*-**b** illustrate this, and support the hypothesis that the epoxide with shorter retention time is indeed the *threo* isomer (**4***t*-**a**). Although the two isomers in the *cis*-series were not readily separable, NMR. signals for two isomers were clearly discernable (see experimental part) and we again ascribe *cis*,*threo* stereochemistry to the major isomer.

*Felkin*'s modification [7] of the *Cram* rule [8] for the addition of organometallic reagents to carbonyl groups requires approach of the reagent so that it is not eclipsed by the largest substituent on the adjacent carbon atom. The situation is pictured in *scheme 2*, the methylene group (L) being considered bulkier than the oxygen atom (M). Orientation of the $COCH_3$ group is presumed to be such that the methyl group is as near as possible to the small substituent. Approach of the organometallic reagent from an antiparallel direction to the large group (L) would lead preferentially

*Scheme 2*



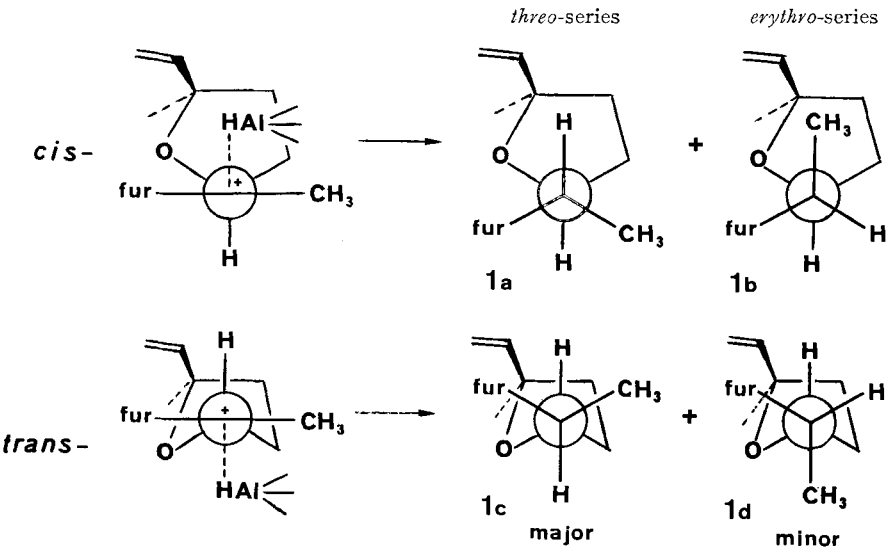

Values indicated are NMR. signals in ppm ($CCl_4$)

to the *erythro* isomers in both the *cis* (**6a**) and *trans* (**6c**) cases. The use of NMR. spectrometry for establishing the configuration of the substances containing the furan ring involves more tenuous reasoning than that of substances of the davanone type [3] [9] because of the uncertainty about the preferred conformation of the furan ring, but we may advance the hypothesis that this will tend to occupy the staggered position between the two smaller groups, namely the oxygen atom of the tetrahydrofuran ring, and the proton adjacent to that oxygen atom. Furthermore, the furan will possibly be oriented in such a way, *i.e.* with its oxygen atom towards the methyl group, that steric interactions with its $\beta$-proton are avoided, as shown in the projection *E* (*erythro*) and *T* (*threo*).

The chemical shift of the carbinol methyl group is thus influenced by the proximity of the oxygen atom of the tetrahydrofuran ring – in the case of the minor isomers (*threo*, **6b** and **6d**) it is at lower field than in the case of the major isomers (*erythro*, **6a** and **6c**) where it is further away from the oxygen atom.

It has been suggested that lithium aluminum hydride reduction in the presence of aluminum chloride proceeds *via* carbonium ions [6] [10], and the fact that similar proportions of davanafurans (**1**) are obtained from both *threo*- and *erythro*-alcohols (**6**) supports this[4]). The most favorable stereochemistry for these ions (*cis* and *trans*) is illustrated in *scheme 3*; an alternative rotamer corresponding to that illustrated in

*Scheme 3*

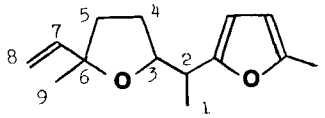



*scheme 2* would seem to be exlcuded on account of the interaction of the bulky furan ring with the substituent on the opposite side of the tetrahydrofuran ring. Reduction will take place by attack from the antiparallel direction to the adjacent proton on the tetrahydrofuran ring. We should thus expect the major *cis*-davanafuran to have the *threo* stereochemistry (**1a**), as should the major product in the *trans* series (**1c**). The table lists the principal signals of the NMR.-spectrum, and the last isomer to be eluted from a polar column (UCON or Carbowax) corresponded in both spectra and retention time with the principal natural isomer. The rotation of this isomer (**1a**) was the same as that of the natural material when the synthetic (+)-davanafuran was prepared from (−)-*cis*-linalyl oxide, so that the principal natural davanafuran corresponds to the absolute stereochemistry of (+)-davanone.

It will be seen that the coupling constants between the protons on C(2) and C(3) are anomalous in both isomers of the *cis*-davanafurans (**1a** and **1b**), and *trans,threo*-davanafuran (**1c**). We ascribe this to rotation about the C(2)–C(3) bond with accompanying change of the dihedral angle between the protons. The chemical shifts of the 1-methyl group and the 2-proton undergo the expected effects from greater or lesser shielding of the oxygen atom of the tetrahydrofuran ring.

4) Note that the designations '*threo*' and '*erythro*' do not refer to the same configurations of furan and methyl groups in the alcohol (**6**) and the davanafurans on account of the change in priorities.

Table. *NMR.-data, and order of elution* (gas chromatography) *of the davanafurans*




| | Order of elution: | 4 | 2 | 3 | 1 |
|---|---|---|---|---|---|
| Attribution | Formula: | **1a** | **1b** | **1c** | **1d** |
| 1-$CH_3$ (*d*) | | 1.25 | 1.36 | 1.26 | 1.32 |
| 2-H (*m*) | | 3.05 | 2.90 | 3.09 | 2.91 |
| 3-H (*m*) | | 4.27 | 4.05 | 4.27 | 4.05 |
| 7-H ($d \times d$) | | 5.96 | 5.95 | 5.91 | 5.89 |
| $J_{2,3}$* (Hz) | | 5.86 | 8.20 | 4.69 | 6.45 |

* Determined by irradiation of the 1-$CH_3$ signal.

## Experimental Part

The spectral measurements were made as described in part 1 [3]. Optical rotations were measured in carbon tetrachloride at about 20% concentration unless otherwise stated. Gas chromatography (GLPC.) was carried out with a *Carlo Erba* model GT. Unless otherwise specified, the column used was Carbowax 20 M, 15% on Chromosorb W 60–80 mesh, acid washed.

*Isolation of the Davanafurans from* Artemisia pallens. Commercial Davana oil[5]) was distilled in a thin-film apparatus (*Leybold Heraeus*, model KDL 1) at 10 mm with the heating oil mantle at 85–90°. From 500 g oil, a distillate of 52.6 g was obtained. Redistillation of this fraction gave 25.1 g of material with b.p. 42–50°/0.08 Torr. Chromatography of 37 g of material thus obtained on 800 g of silica gel yielded the following fractions:

1. 15.3 g eluted with hexane, Rf 0.90[6]), hydrocarbons;
2. 1.9 g of an intermediate fraction, eluted with hexane/ether 95:5;
3. 4.0 g of a fraction with two spots, Rf 0.77 and 0.67 on TLC;
4. The remainder (*ca.* 15 g) was removed from the column by rinsing with ether/methanol, and examined separately.

From fraction 3, davanafuran was isolated by GLPC. (Column OV 17, 190°); the isomeric mixture constituted about 70% of this fraction. The davanafuran mixture collected from the OV 17 column was re-chromatographed on a Carbowax column at 160°, when three fractions were obtained. Comparison of the NMR.-spectra of these fractions with the authentic synthetic isomers (see below) enabled them to be identified as (in order of elution):

A) *trans,erythro*-davanafuran (**1d**) (5% of mixture);
B) A mixture of *trans,threo-* (**1c**) and *cis,erythro*-davanafuran (**1b**) (*ca.* 1:1, 19% of mixture, $[\alpha]_D^{20} - 16.5°$ ($c = 12$, $CCl_4$);
C) *cis,threo*-Davanafuran (**1a**) (76% of mixture), $[\alpha]_D^{20} + 10.0°$ ($c = 16$, $CCl_4$).

The mass-spectra were identical with those of the synthetic samples (see below).

*3,7-Dimethyl-3,6:7,8-diepoxyoct-1-enes.* A solution of peracetic acid (40% in acetic acid, 145 g) was added slowly to a solution of 86 g of 5-isopropenyl-2-methyl-2-vinyltetrahydrofuran (**3**) and 60 g of sodium acetate (anhydrous) in 400 ml of methylene chloride. The temperature was maintained below 30° during the addition with a cold water bath. After the end of the addition (2 h), the mixture was stirred for a further 3 h, then washed once with ice water, sodium hydrogen carbonate solution to neutrality, then with water. After drying and concentrating, the residue was distilled, to obtain 75 g of material, b.p. 77–85°/10 Torr, consisting practically only of the isomers

[5]) Purchased from the *East Indian Sandaloil Distilleries* (Private) Ltd.

[6]) Rf refers to the value measured on *Merck* silica gel plates with hexane/ether 95:5 as developing solvent.

of the title product. If the reaction was carried out with *trans*-5-isopropenyl-2-methyl-2-vinyl-tetrahydrofuran, it was possible to separate the two epoxide isomers by GLPC.[7]). In order of elution, these were the: *trans,threo*-isomer: NMR. ($CDCl_3$): 1.34 (6H, *s*, $CH_3C$—); 1.65 to 2.15 (4H, *m*, $CH_2CH_2$); 2.57 and 2.92 (1H each, *d*, $J = 5$ Hz, C(O)$CH_2$); 3.96 (1H, *m*, $CH_2$—$CH$—O); 5.02 and 5.19 as in *erythro*-isomer, 5.87 ($CH$=$CH_2$). – *trans,erythro*-isomer: NMR. ($CDCl_3$): 1.38 (6H, *s*, $CH_3C$—); 1.65 to 2.15 (4H, *m*, $CH_2CH_2$); 2.65 and 2.80 (1H each, *d*, $J = 5$ Hz, C(O)$CH_2$); 3.87 (1H, *m*, $CH_2$—$CH$—O); 5.02 and 5.19 (2H together, each $d \times d$, CH=$CH_2$); 5.88 (1H, $d \times d$, $J = 10$ and 17 Hz, $CH$=$CH_2$).

The corresponding *cis*-isomers were not separable under the same conditions, but the signals of the two isomers in their NMR.-spectra were readily distinguishable. *cis,threo*-isomer (major product): ($CDCl_3$) 1.31 and 1.33 (6H together, $CH_3$—C); 1.6 to 2.2 ($CH_2$—$CH_2$); 2.57 and 2.90 (each *d*, $J = 5$ Hz, C(O)$CH_2$); 3.93 (*m*, $CH_2$—$CH$—O); 4.98 and 5.17, together with 5.95 ($d \times d$, $J = 10$ and 17 Hz, $CH$=$CH_2$). The most notable difference with the *cis,erythro*-isomer is the presence of a $CH_3$ singlet at 1.36, and the epoxide ring methylene group $d \times d$ at 2.61 and 2.78. – MS. mixture of *trans*-isomers: 43 (100), 55 (67), 111 (40), 41 & 67 (33), 93 (31), 153 (25), 27, 69 & 81 (22), 168 ($M^+ < 1$). Mixture of *cis*-isomers: 43 (100), 55 (98), 111 (58), 93 (48), 67 (44), 41 (41), 153 (37), 81 (32), 27 (30), 39 (23), 168 ($M^+ < 1$).

*5-Methyl-5-vinyltetrahydrofur-2-yl methyl ketone* (**5**). A) A solution of 42.5 g of periodic acid ($HIO_4 \cdot 2H_2O$) in 300 ml of water was added dropwise to 32.2 g of the epoxides described in the previous experiment, dissolved in 300 ml of tetrahydrofuran at 0°. The temperature was allowed to rise to 20°, and the mixture was stirred for a further 3 h, then extracted with pentane. The pentane solution was washed with water, sodium thiosulfate solution, then water to neutrality. The residue from this solution was distilled, b.p. 83°/10 Torr, to give 23 g (90%) of **5**. Pure *cis*- or pure *trans*-epoxides yielded a single isomer of the ketone; the mixture yielded two ketones that could be separated by GLPC., the *trans*-isomer being of shorter retention time on Carbowax.

B) A solution of 7.6 g of 5-isopropenyl-2-methyl-2-vinyl-tetrahydrofuran in 70 ml of ethyl acetate was ozonized at −70° until one equivalent (2.4 g) of ozone had been absorbed (about 45 min). The solution was allowed to warm to −30°, when 6.6 g of zinc powder were added, followed by slow addition of 13 ml of 50% aqueous acetic acid. The mixture was allowed to come to room temperature over 4 h, then filtered, and the products isolated in ether. Distillation gave 7.2 g of material, b.p. 50–83°/10 Torr, which was redistilled, b.p. 72–78°/10 Torr yielding 2.7 g of the title ketones.

cis-*5-Methyl-5-vinyltetrahydrofur-2-yl methyl ketone* (**5a**). NMR. ($CDCl_3$): 1.32 (3H, *s*, $CH_3$—C); 2.21 (3H, *s*, $CH_3CO$); 4.39 (1H, *t*, $J = 7$ Hz, $CH_2CH$(O)—CO); 5.02 (1H, $d \times d$, $J = 10.5$ and 1.5 Hz) and 5.23 (1H, $d \times d$, $J = 18$ and 1.5 Hz); 5.94 (1H, $d \times d$, $J = 10.5$ and 18 Hz) $CH$=$CH_2$. – MS.: 43 (100), 55 (95), 111 (93), 93 (57), 41 (51), 69 (31), 81 (30), 67 (22), 27 (21), 39 (19)... 139 (1), 154 ($M^+$, 1). No fragment at *m/e* 125. – $[\alpha]_D^{20} = -26.8°$ (25% in $CCl_4$), when made from (−)-*cis*-linalool oxide.

trans-*5-Methyl-5-vinyltetrahydrofur-2-yl methyl ketone* (**5b**). NMR. ($CDCl_3$): 1.32; 2.15; 4.29 ($d \times d$, $J = 6$ and 8 Hz); 4.95; 5.10; 5.77, attributions correspond to those of the *cis*-isomer. – MS.: 43 (100), 55 (62), 111 (59), 93 (36), 41 (35), 69 (23), 81 (17), 67 (15), 27 (14), 39 (13)... 125 (6). – When made from (+)-*trans*-linalool oxide, $[\alpha]_D^{20} = +34.1°$ (17% in $CCl_4$).

$C_9H_{14}O_2$ (154.2) Calc. C 70.10 H 9.15% Found (on isomeric mixture) C 70.04 H 9.16%

From all preparations of the ketones (**5**) the major impurity, eluted after the title products on a Carbowax column, was identified by comparison with an authentic sample [11] as the lactone of 4-hydroxy-4-methylhex-5-enoic acid.

*6-Methyl-2-(5-methylfur-2-yl)-3,6-epoxyoct-7-en-ol* (**6**). A solution of 25.5 g of methylfuran in 250 ml of dry ether is stirred at −35° in a current of dry nitrogen while 230 ml of a solution of butyllithium (14%) in hexane are added. The solution is stirred for 3 h at room temperature, then cooled again to −65°, when 53 g of 5-methyl-5-vinyltetrahydrofur-2-yl methyl ketone are in-

[7]) We are indebted to Mr. *J.-C. Egger* for assistance in separating these substances.

introduced fairly rapidly. The mixture is stirred for 15 min at −65° then for 1 h 15 min in an bath. The products are isolated by pouring the reaction mixture onto 200 ml of conc. hydrochloric acid and 400 g of ice, then isolated in ether, to give 34 g of crude material. This has b.p. 95–100°/0.01 Torr, with polymerization. The crude alcohols (33 g) were chromatographed in hexane/ether 95:5, when the first substance to be eluted was 3.1 g of *6-methyl-2-(5-methylfur-2-yl)-3,6-epoxy-octa-1,7-diene* (**7**): NMR.: 1.34 (3 H, *s*, $CH_3$—C(—)(—)—); 1.5–2.1 (4 H, *m*, $CH_2$—$CH_2$); 4.62 (1 H, *d* × *d*, *J* = 11 and 5 Hz, O—C*H*(—)—$CH_2$) partly obscured by 4.8–5.5 (4 H, *m*, C=$CH_2$); 5,85 (*d* × *d*, $CH$=$CH_2$); 5.85 and 6.05 (*β*-furyl *H*)[8]. – MS.: 107 (100), 43 (77), 55 (45), 218 ($M^+$, 39), 108 (37), 41 (27), 95 (25), 93 (24), 77 & 109 (21). – There was no OH absorption in the IR.-spectrum.

$C_{14}H_{18}O_2$ (218.3) Calc. C 77.03 H 8.31% Found C 77.08 H 8.22%

The next substance eluted was 1.5 g of *5-methyl-2-(5-methylfur-2-yl)-cyclohept-4-enone* (**9**, R=5-methylfuryl): NMR.: 1.33 (3 H, *s*, $CH_3$—C(—)(—)—); 1.66 (3 H, *d*, *J* = 1 Hz, $CH_3$—C(—)=CH); 2.20 (3 H, *s*, $CH_3$-furyl) superimposed on 1.8–2.5 (4 H, *m*, $CH_2CH_2$); 2.9–3.7 (2 H, *m*, C=CH—$CH_2$); 5.7–5.9 (2 H, *m*, *β*-furyl *H*). – MS.: 43 (100), 122 (96), 218 ($M^+$, 82), 55 (58), 41 (53), 175 (45), 109 (42), 39 (37), 53 (30), 125 (26).

$C_{14}H_{18}O_2$ (218.3) Calc. C 77.03 H 8.31% Found C 76.58 H 8.34%

Subsequent fractions, containing the title product, were not obtained as single isomers unless the reaction was carried out using pure *cis*-, or pure *trans*-5-methyl-5-vinyltetrahydrofur-2-yl methyl ketone. From the *cis*-ketone (**5a**), the *cis*-6-methyl-2-(5-methylfur-2-yl)-3,6-epoxyoct-7-en-2-ols were separated by chromatography on silica gel in hexane/ether 5:1 into the less polar *cis,threo*-isomer (**6b**) (*ca.* 40% of the mixture by GLPC. on Carbowax, shorter retention time). – NMR.: 1.23 and 1.42 (3 H each, *s*, $CH_3$—C); 1.6–2.1 (4 H, *m*, $CH_2$—$CH_2$); 2.22 (3 H, *s*, $CH_3$-furyl); 4.14 (1 H, *d* × *t*, *J* = 2 and 7 Hz, $CH_2$—C*H*—O); 4.94 (1 H, *d* × *q*, *J* = 2 and 10 Hz); 5.09 (1 H, *d* × *q*, *J* = 2 and 17 Hz); 5.93 (1 H, *d* × *d*, *J* = 10 and 17 Hz), $CH$=$CH_2$; 5.80 and 6.02 (1 H each, *β*-furyl *H*). – The *cis-erythro* (**6a**) isomer eluted next constitutes *ca.* 60% of the mixture by GLPC.; NMR.: 1.22; 1.32; 1.6–2.1; 2.22; 4.21 (*d* × *t*, *J* = 2 and 7 Hz); 4.91; 5.09; 5.92; 5.78; 6.03; same attributions as before.

From the *trans*-ketone (**5b**), the *trans,threo*-isomer (**6d**) (*ca.* 34% of the mixture by GLPC., shorter retention time) is less polar, and is purified by chromatography on silica gel in hexane/ether 5:1. NMR.: 1.21 and 1.42 (3 H each, *s*, $CH_3$—C—); 1.5–2.1 (4 H, *m*, $CH_2$—$CH_2$); 2.24 (3 H, *s*, $CH_3$-furyl); 4.07 (1 H, *d* × *t*, *J* = 1 and 7 Hz, $CH_2$—C*H*—O); 4.95 (1 H, *d* × *q*, *J* = 2 and 10.5 Hz); 5.15 (1 H, *d* × *q*, *J* = 2 and 17 Hz); 5.83 (1 H, *d* × *d*, *J* = 10.5 and 17), $CH$=$CH_2$; 5.80 and 6.01 (1 H each, *β*-furyl *H*). – The *trans, erythro*-isomer (**6c**) (*ca.* 70% of the mixture, longer retention time) was eluted next. NMR.: 1.22 and 1.33; 1.5–2.0; 2.23; 4.16 (*t*, *J* = 6.5 Hz); 4.92; 5.15; 5.83 (*q*), 5.80 and 6.04, attributions as for the *threo*-isomer.

The MS. of all isomers was very similar, and the following was recorded on a mixture of all four isomers: 125 (100), 43 (52), 107 (18), 55 (15), 41, 93 and 109 (13), 218 (8) ... 236 ($M^+$, < 1).

$C_{14}H_{20}O_3$ (236.3) Calc. C 71.16 H 8.53% Found C 70.98 H 8.65%

*Davanafuran* (**1**). Fresh aluminum chloride (2.1 g) is carefully added to 7.5 ml of dry ether while the temperature is maintained below 20°, then 0.3 g of lithium aluminum hydride are added all at once. The mixture was cooled to 0° and 1.4 g of 6-methyl-2-(5-methylfur-2-yl)-3,6-epoxyoct-7-en-2-ol (**6**) was added very slowly. The reaction was very vigorous, and after 10 min, no further starting material was detected by GLPC. After 30 min, the mixture was poured slowly onto 100 g of ice and the product was extracted with ether. The emulsions sometimes encountered during this extraction could be cleared by the addition of a small amount of tartaric acid. The residue after concentration is distilled to give 1.0 g of davanafuran, b.p. 65°/0.01 Torr. For analysis, the products were purified by GLPC. on Carbowax, FFAP or UCON.

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[8] The high field of the double doublet of the vinyl proton corresponds to *trans* rather than *cis* isomerism about the tetrahydrofuran ring. We did not observe the other isomer.

Experiments were run with all four alcohol isomers (**6a–6d**) separately; and the proportion of products was about 1:4 of the less polar : more polar davanafurans in the *cis*-series, and about 1:3 in the *trans* series. Collected separately, the isomers were, in order of elution:

*trans, erythro*-Davanafuran (**1d**): $[\alpha]_D^{20} = +1.3°$

*cis, erythro*-Davanafuran (**1b**): $[\alpha]_D^{20} = -22.8°$

*trans, threo*-Davanafuran (**1c**): $[\alpha]_D^{20} = -17.5°$

*cis, threo*-Davanafuran (**1a**): $[\alpha]_D^{20} = +9.8°$

The NMR.-spectra are described in the theoretical part. The MS. are very similar, the following figures were taken from the *cis, threo*-isomer: 109 (100), 43 (47), 111 (25), 55 (20), 41 and 93 (15), 69 (12), 67 and 85 (9)... 220 ($M^+$, 2).

$C_{14}H_{20}O_2$ (220.3) Calc. C 76.32 H 9.15% Found (on mixture of isomers) C 76.72 H 9.17%

*6-Methyl-2-(5-methylfur-2-yl)-oct-6-en-3-ol.* When the preceding experiment for davanafuran was carried out for longer periods, or with heating at reflux, a product with longer retention time than davanafuran was observed. This product could be purified from the residues of the distillation of davanafuran. For example, chromatography on silica gel of 16 g of these residues in hexane/ether 9:1 gave a substance that had b.p. 73°/0.002 Torr, with a single peak on GLPC. (silicone oil), although the NMR.-spectrum showed the presence of at least two isomers (based on the first signals listed below).

NMR.: 1.24 and 1.25, in ratio of 1:4 (3 H, *d*, $J$ = 7 Hz, $CH_3$—CH, two isomers); 1.60 (3 H, *d*, $J$ = 1 Hz, $CH_3$—C=) superimposed on 1.59 (3 H, *d*, $J$ = 6.5 Hz, $CH_3$—CH=); 2.27 (3 H, *s*, $CH_3$-furyl); 2.90 (1 H, *m*, $CH_3$—C*H*-furyl); 3.66 (1 H, *m*, CH—C*H*(OH)—$CH_2$); 5.28 (1 H, *m*, C=C*H*—$CH_3$); 5.93 (2 H, *m*, $\beta$-furyl *H*). – MS.: 109 (100), 110 (78), 95 (70), 43 (28), 41 (20), 69 (14), 55 (9)... 222 ($M^+$, 4).

$C_{14}H_{22}O_2$ (222.3) Calc. C 75.63 H 9.97% Found C 75.44 H 9.97%

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