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196. The Synthesis and Reactions of Yomogi Alcohol. Conversion of the Artemisyl Skeleton to the Santolinyl Skeleton by a 1,2-Shift of a Vinyl Group. Synthesis of Santolinatriene

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dedicated to Dr. *Roger Firmenich* on the occasion of his 65th birthday

(3. VIII. 71)

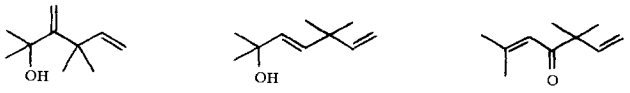
Summary. The synthesis of yomogi alcohol (2,5,5-trimethylhepta-3,6-dien-2-ol, **2**) is described, and experiments directed towards its allylic rearrangement to artemisia alcohol derivatives have been carried out. Acidic reagents open the ring of yomogi alcohol epoxide (**16**) and with participation of the 6,7-double-bond, a shift of the vinyl group results to yield a compound with the santolinyl skeleton. The same reagents are without effect when this double bond is reduced. Action of butyllithium on the benzaldehyde acetal (**41**) of 2,5-dimethyl-4-vinyl-2,3-dihydroxy-hex-5-ene (**28**), obtained by acid-catalyzed ring opening of yomogi alcohol epoxide in the presence of benzaldehyde, leads to santolinatriene (**42**).

This vinyl shift is not observed in the case of O-acetyl yomogi alcohol epoxide (**46**), from which a compound believed to be an oxetan **48** (R = $COCH_3$) is formed with concomitent shift of the acetate group. Further unusual reactions of the oxetan are described, and some observations about the epoxidation of sterically hindered allyl alcohols and their acetates are made.

Introduction

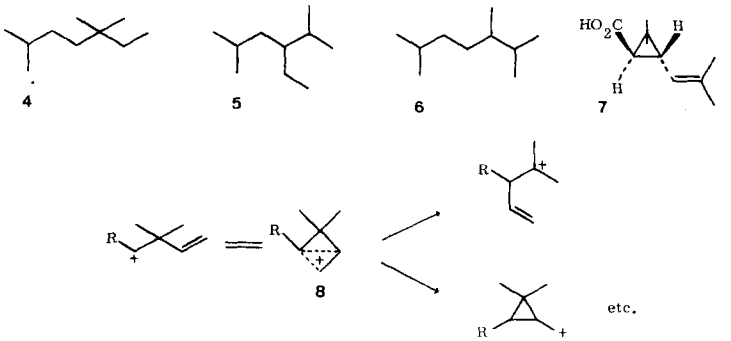
The initial impetus for this work came from a report of the isolation of an alcohol ("yomogi alcohol") of a new structural type, **1**, from *Artemisia feddei, Lév. et Van.* [1], for which we believed the allylically rearranged artemisia alcohol structure (2,5,5-trimethylhepta-3,6-dien-2-ol, **2**) would be better [2]. The correct structure (**2**) was also given by the authors of the original publication [3], and by *Sucrow* [4], who synthesized both yomogi alcohol (by a completely different method from ours) and the compound **1** with the structure originally suggested for **2**. A simple synthesis

of yomogi alcohol (**2**) might, furthermore, provide ready access to artemisia ketone (**3**) by allyl rearrangement and oxidation.



1 **2** **3**

At the same time we were interested in the relationship between the "odd" monoterpenes (*i.e.* those that cannot be formed by a simple head-to-tail linking of two isoprene units) comprising substances having the artemisyl (**4**), santolinyl (**5**) or lavandulyl (**6**) skeletons, all formally derivable by fission of one of the bonds of the cyclopropane ring in a substance of the chrysanthemic acid (**7**) series [5]. Speculations about the biogenesis of substances related to artemisia alcohol (**15**) [6] *via* a [2,3]-sigmatropic rearrangement of di-isoprenyl ether [7] made us question whether chrysanthemic acid or related compounds were actually necessary intermediates for the biogenesis of the "odd" monoterpenes[1]). Homoallyl carbonium ions are well known [9] and, in principle, one derived from the artemisyl skeleton (e.g. **8**) can

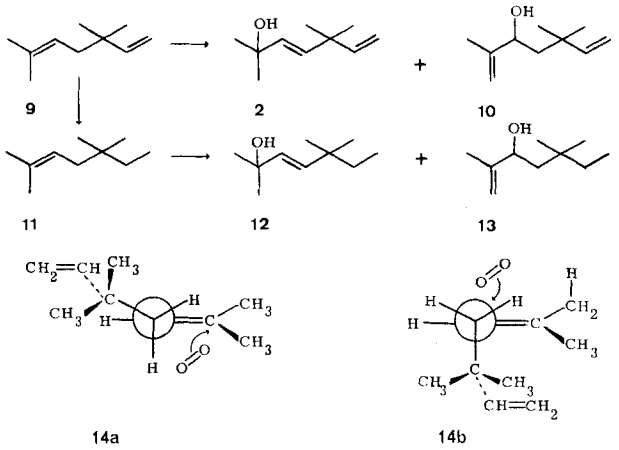


4 **5** **6** **7** **8**

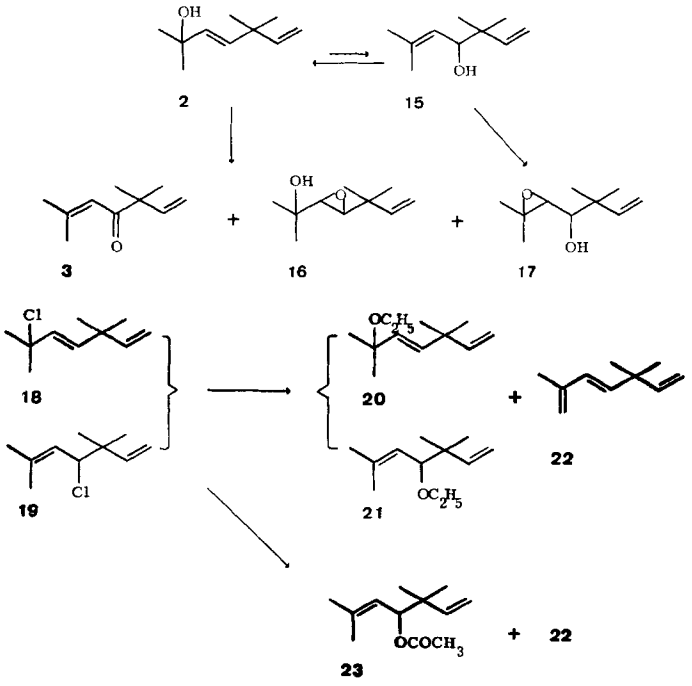
give rise to any of the "odd" structures, as well as to chrysanthemic acid derivatives [10]. This paper describes how one such ion, namely **8** with R = $(CH_3)_2C(OH)CHOH$–, is converted entirely and exclusively into compounds with the santolinyl skeleton.

Synthesis and reactions of yomogi alcohol. The starting material for the preparation of yomogi alcohol (**2**), 2,5,5-trimethylhepta-2,6-diene (**9**), was prepared by coupling two molecules of 3-methylbut-2-enyl chloride with magnesium [11]. Sensitized oxygenation of **9** in the presence of light gave, after reduction of the hydroperoxides with sodium sulfite, a 4:1 mixture of yomogi alcohol (**2**) and 2,5,5-trimethylhepta-1,6-dien-3-ol (**10**). In open-chain systems, the addition of oxygen to the double bond generally yields a secondary-tertiary alcohol mixture 6:4 (see, *e.g.* the photooxidation of citronellol [12]), and it was shown in our case that the difference was not due to the presence of a second double bond, since 2,5,5-trimethylhept-2-ene (**11**) gave, under these conditions, the same proportion of tertiary **12** and secondary **13** alcohols. One explanation for this is furnished by consideration of the conformations of the

[1]) The recent feeding experiments of *Banthorpe & Charlwood* [8] imply that in *Artemisia annua*, biosynthesis of artemisia ketone occurs by the chrysanthemyl route rather than by any of the other pathways proposed.



olefin shown in **14a**, **14b**, which will lead to the tertiary and the secondary hydroperoxide[2]) respectively. Models show that conformation **14b** involves some interaction between the methyls attached to the double bond and the geminal methyl group on C-5, thus favouring conformation **14a**; this has the C-H bond that is to be broken arranged nearly perpendicularly to the double bond attacked by oxygen.



[2]) For a review of the reasoning concerning stereochemical effects in photooxygenation see *Gollnick* [13]. The oxygen approaches from the less hindered side and the hydrogen transferred is perpendicular to the plane of the double bond.

Several attempts were made to convert yomogi alcohol to artemisia ketone (**3**), under acidic conditions, and although some ketone was nearly always detected, yields were very poor; the main product from chromium trioxide oxidations under various conditions was yomogi alcohol epoxide[3]) (**16**), together with a trace of artemisia alcohol epoxide (**17**) and, under vigorous conditions, breakdown (C_5) products. Treatment of yomogi alcohol (**2**) with acid led to an equilibrium mixture containing not more than 20% of artemisia alcohol (**15**). In another experiment, yomogi alcohol (**2**) was converted to a mixture of the corresponding chlorides with thionyl chloride in dry ether; estimation of the composition from the NMR. spectrum by integration of the doublet at 4.39 ppm (the signal arising from the –C*H*–Cl group in **19**) showed that there was about 50% each of secondary **19** and tertiary **18** chloride present. Treatment of this mixture with sodium acetate in ethanol led to about equal amounts of the two ethyl ethers **20** and **21**, at the same time as a substantial amount of artemisia triene (**22**). When the ethanol was replaced by acetic acid, the only acetate detected was O-acetyl artemisia alcohol (**23**) but the yield was less than 10%, the major product being again artemisia triene (**22**). It seems likely that steric compression about the hydroxyl group in artemisia alcohol (**15**) militates against the formation of this isomer and its derivatives.

Rearrangement of yomogi alcohol epoxide (**16**) *to compounds with the santolinyl skeleton.* Treatment of **16** with acid (*p*-toluenesulfonic acid or Dowex 50 exchange resin, H^+ form) in benzene results in different products according to the duration[4]). After 30 min boiling with toluenesulfonic acid in benzene, 85% of the epoxide had disappeared with almost exclusive formation of a single new compound having a much shorter retention time on Carbowax GLPC. columns. This substance was considered to be an oxetan on the grounds of its NMR. spectrum[5]). There is a signal at 4.03 ppm, highly characteristic of the ring proton adjacent to the oxygen of the ring, and coupled ($J = 7.5$ Hz) with the proton at C-3, which is at 3.14 ppm and is in turn coupled with two other protons. The proton next to the ring, on the vinyl group, gives a multiplet with 5 main maxima centered about 5.75 ppm, showing that there is indeed a hydrogen on the neighbouring saturated carbon atom, so that rearrangement must have occurred. We have no chemical or spectral evidence to offer for the stereochemistry of the ring substituents, but in view of what follows we are confident that they are *trans*, and, in any case, only one isomer is formed. The oxetan **24** is itself unstable to acid conditions, and if the reaction is allowed to continue, a mixture of two further substances is formed. One of these has a retention time somewhat longer than the starting material, crystallizes readily, and on spectral grounds it was attributed the structure of the hydroxy-tetrahydrofuran **25**. Acetylation gave the corresponding acetate **26**, whose stability at 500° implies a *cis*-orientation for the substituents, for had there been a hydrogen atom *cis*- to the acetyl group, acetic acid would have been lost at this temperature. A chemical correlation was also carried out (see below). The third product obtained after somewhat longer reaction time was

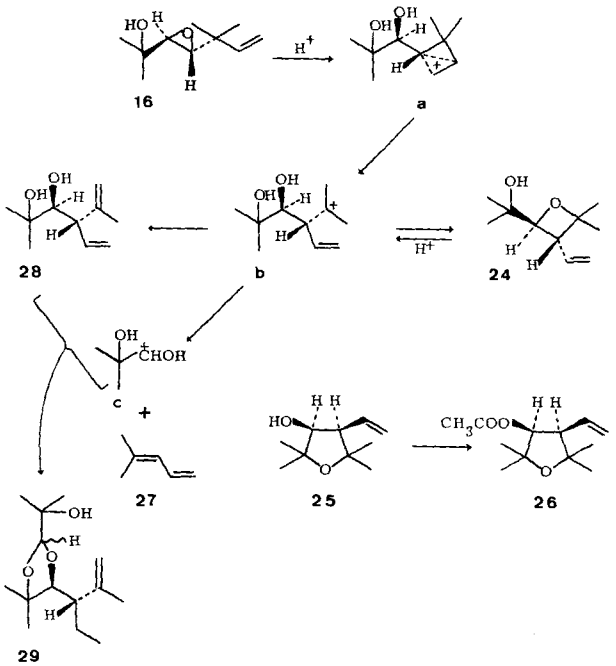
[3]) Chromic acid epoxidation of double bonds has been reported in several cases, *e.g.* [14] and *Marshall & Cohen* discuss a case of a stereochemically hindered secondary allyl alcohol that could not be oxidized [15].

[4]) Dihydroyomogi alcohol epoxide (**12**) is unaffected by any treatment described in this section.

[5]) For NMR. spectra typical of oxetans, see *Schroeter & Orlando* [16], and below.

more polar than either of the others, but had the same molecular formula, and was assigned the *threo*-glycol[6]) structure, **28**. It was somewhat difficult to purify, since it was nearly always contaminated with varying amounts of substances with higher molecular weight, which turned out to be acetals **29**, and was converted very easily to the tetrahydrofuran **25** during purification. Only one isomer of each of the substances **24**, **25**, and **28** was obtained, but two acetals **29** of the glycol **28** were isolated, because of the additional asymmetric centre introduced by ketalization.

The structures assigned to **25** and **28** were confirmed by chemical evidence. Reduction of **25** over palladium gave a tetramethyl-ethyl-tetrahydrofuranol, **35**, the acetate

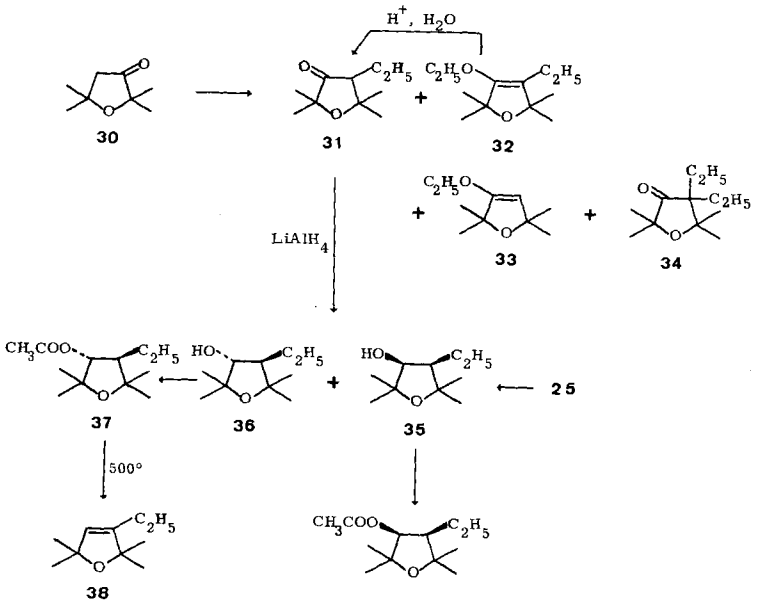


of which was also stable at 450°. This compound **35** was identical with an alcohol made as follows from 2,2,5,5-tetramethyl-tetrahydrofuran-3-one (**30**) [17]. Ethylation of **30** with ethyl bromide and potassium *t*-butoxide in *t*-butanol led to a mixture of C-ethyl, **31**, **32**, **34**, and O-ethyl, **32**, **33**, products. Distillation easily separated the required 2,2,5,5-tetramethyl-4-ethyl-tetrahydrofuran-3-one (**31**), the yield of which could be augmented by acid treatment of its enol ether (**32**), also a major ethylation product[7]). This ketone **31** was reduced with lithium aluminium hydride to give a mixture (13:87) of *cis*- (**35**) and *trans*- (**36**) 2,2,5,5-tetramethyl-4-ethyl-tetrahydrofuran-3-ols. For only one of these compounds (the major product) the derived acetate **37** could be thermolyzed to the dihydrofuran **38** at 450°, and to this one, therefore, the structure **36** with *trans*-configuration was attributed.

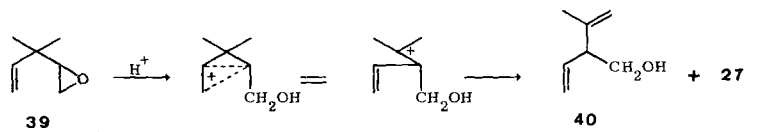
[6]) In this publication "*threo*"-refers to a racemate having adjacent carbon atoms of the same chirality (*R*-*R* and *S*-*S*); "*erythro*-" means the carbon atoms are of *R*-*S* and *S*-*R* chirality.

[7]) Acid-catalyzed hydrolysis of the enol ether **32** was unusually slow, presumably because of the steric hindrance about the ether group.

Before continuing with the chemical verification of the structure of the glycol **28**, it is convenient to discuss the mechanism of the epoxide ring opening on the basis of results described so far. Since for **24**, **25** and **28** only one isomer is observed, the double bond must participate in the ring-opening of the epoxide **16**, leading to the Homoallyl carbonium ion, **a**, which is equivalent to the rearranged carbonium ion, **b**. The latter can now cyclize to the oxetan **24** or to the tetrahydrofuran **25**, or it can lose a proton to give the glycol **28**. Since the stereochemistry is already determined when the ion **a** is formed, only one isomer of each of these products is observed, namely that illustrated in the formulae. There remains the question of the formation of the acetals **29**.

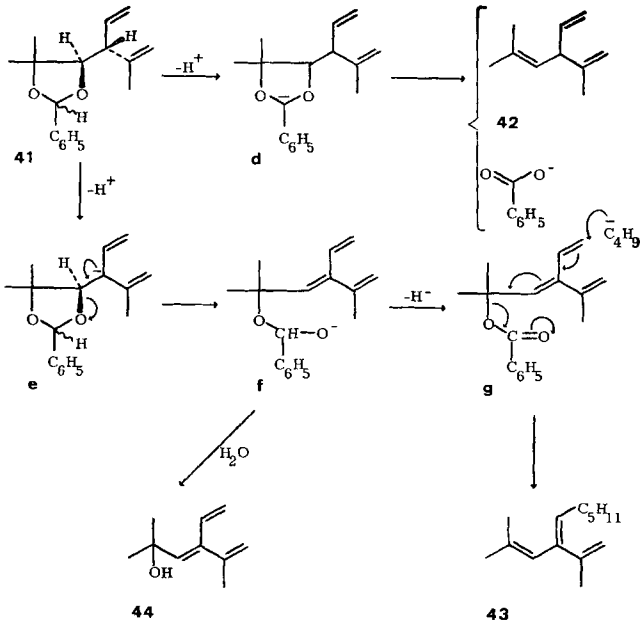


One way for stabilization of carbonium ion **b** might be by carbon-carbon bond fission leading to the hydrocarbon **27** and the protonated form **c** of 2-methyl-2-hydroxy-butanal, which would be ideal for reacting with the glycol **28** to yield the two acetals **29**. Decomposition of the acetals by acid would, of course, inevitably lead to protonation of the glycol **28** product, leading again to carbonium ion **b**. While we did not identify the hydrocarbon **27** from this particular reaction (presumably because of its volatility under the conditions used), in a similar case we did find it, *i.e.* when the model epoxide, 3,3-dimethyl-1,2-epoxy-pent-4-ene (**39**), was treated with Dowex 50 resin (H^+ form). From this reaction the main products characterized were the hydrocarbon **27** and the rearranged alcohol **40**, which corresponds to the production



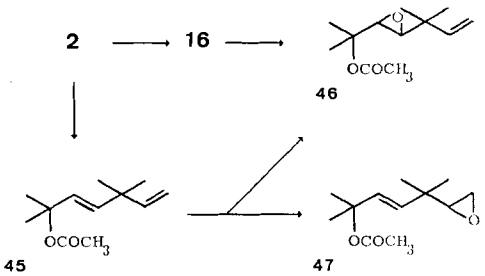
of glycol **28** from yomogi alcohol epoxide (**16**). In the case of the model **39**, no oxetan was found—possibly its formation requires a certain amount of steric constriction.

The structure of the glycol **28** was confirmed by converting it to the natural product, santolinatriene (**42**), the first discovered compound of the santolinyl series isolated by us some time ago from *Santolina chamaecyparissus* [18], and later synthesized by *Sucrow* [19]. If our mechanistic reasoning were correct, the acid-catalyzed rearrangement, when carried out in the presence of excess benzaldehyde, should lead to a mixture of the two benzalacetals **41**; in fact these were the only products found. This mixture of acetals was treated with butyllithium in hexane, a reaction that *Whitham et al.* have shown to give stereospecifically the olefin corresponding to removal of the two oxygen atoms and C-2 of the dioxalane system [20]. One of the compounds thus obtained was santolinatriene (**42**), but the major product was another hydrocarbon containing C_4H_8 more than santolinatriene, isolated together with an alcohol, $C_{10}H_{16}O$. The mechanism suggested [20] for the butyllithium reaction of acetals is the reverse of a [2,3]-cycloaddition, for the operation of which, removal of a proton from C-2 of the dioxalan (to anion **d**) is a prerequisite. In our case, removal of this proton competed with removal of another proton, namely that on the carbon atom between the two double bonds, leading to the anion **e**. Ring-opening of this anion would lead to another anion **f** with the charge centred on one of the oxygen atoms, from which a hydride ion must be lost in order to give the benzoate, **g**. The anion **f** is similar to certain intermediate ions commonly supposed to arise in the course of the *Canizzaro* reaction. Attack by butyllithium on **g** then leads to the observed product **43**, the attack being assisted by the presence of the leaving group (benzoate) at the other end of the molecule. The hydride ion possibly reduces the benzoate, produced at the same time as santolinatriene (**42**), as well as from **g** itself,

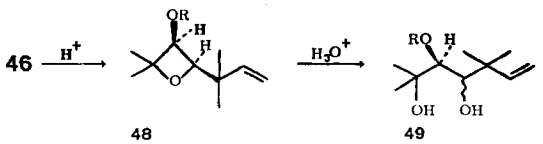


and indeed a large amount of 1-phenylpentan-1-ol (by addition of butyllithium to benzaldehyde) was also found. Pentanophenone (from benzoate and butyllithium) was found in smaller amounts. The alcohol **44** must result from quenching of the anion **f** with water.

Reaction of O-acetyl-yomogi-alcohol epoxide with acid. By protecting the hydroxyl group of yomogi alcohol epoxide (**16**), we hoped to inhibit formation of the tetrahydrofuran **25**, therefore acetylation of the epoxyalcohol (**16**) as well as epoxidation of O-acetyl yomogi alcohol (**45**) were examined. The first method, apart from requiring slightly more vigorous conditions than usual (a tertiary hydroxyl group was to be acetylated), caused no difficulty, but epoxidation of the acetate **45** gave large amounts of the epoxide **47** by reaction at the terminal bond after treatment for a long period which nevertheless left a certain amount of starting material unchanged. This is again undoubtedly a manifestation of the steric hindrance about the double bond in the 3,4-position of the artemisyl skeleton.



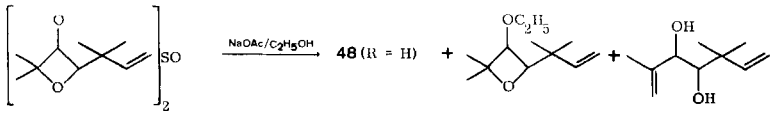
Treatment of the epoxyacetate **46** with Dowex 50 resin (H^+ form) in ether gave a fairly rapid reaction, and the NMR. spectrum of the main product after 1 h implied that there was indeed an acetoxyoxetan present, with the vinyl group intact and still attached to a quaternary carbon atom. Reduction of this acetate with lithium aluminium hydride gave the corresponding alcohol **48** (R = H) which had spectra characteristic of a 3-hydroxyoxetan [16]. It resisted oxidation by chromium trioxide under a variety of conditions, but confirmation of the oxetan structure was obtained when the acetate **48** ($R = COCH_3$) was treated with Dowex 50 in moist ether for a longer time, when it was slowly replaced by a compound containing one molecule of water more than the oxetan. The evidence favours a 1,3-glycol structure **49** for this substance, the acetyl group remaining fixed, since there is no reaction with sodium periodate, and the IR. spectrum of a dilute solution showed a difference in frequency between the free and bonded hydroxyl groups of more than 85 cm^{-1}, consistent with the formulation as a 1,3-glycol, but not as a 1,2-glycol [21].



The formation of an oxetan from a vicinal acetoxy-epoxide is reminiscent of the recent report that solvolysis of certain 2,3-epoxy-propan-1-yl esters leads to esters

of 3-oxetanols, a reaction in which an oxabicyclobutonium cation was invoked [22]. In our case, however, the reaction is acid-catalyzed, and is possibly unrelated.

Only one oxetan **48** (R = H) is formed, and a discussion of the mechanism would be facilitated if we had incontrovertible evidence for its stereochemistry. We consider the determination of the stereochemistry of oxetans by using coupling constants in the NMR. spectra to be dangerous; even when both isomers are available the differences are small[8]) and certainly depend on the distorsion of the ring by the size of the substituents. Nevertheless, we attempted to invert the configuration at the 3-position of the oxetan ring by converting the alcohol to its *p*-toluenesulfonate **48** (R = CH_3–C_6H_4–SO_2) which we tried to solvolyze. In fact we recovered only toluenesulfonate, after treatment either with sodium acetate in ethanol at 120°, or with tetramethylammonium acetate. Consistent with the stability of this toluenesulfonate is the fact that lithium aluminium hydride reduction gave only the original oxetan alcohol **48** (R = H), sulfur-oxygen bond fission predominating over carbon-oxygen fission [26]. Another attempt to invert the 3-configuration was made by treating the alcohol **48** (R = H) with thionyl chloride in pyridine. The resulting mixture of sulfites (**50**) was then heated with sodium acetate in ethanol when, again in analogy with *Gassman*'s observations [26], the major product arose by S–O bond cleavage, and proved to be once more the unchanged oxetan alcohol **48** (R = H), although small amounts of one of the possible 3-ethoxyoxetans **48** (R = C_2H_5), probably of the same stereochemistry as the starting material, were observed, together with some 2,5,5-trimethyl-3,4-dihydroxy-hepta-3,4-diene (**51**) of unknown stereochemistry[9]).



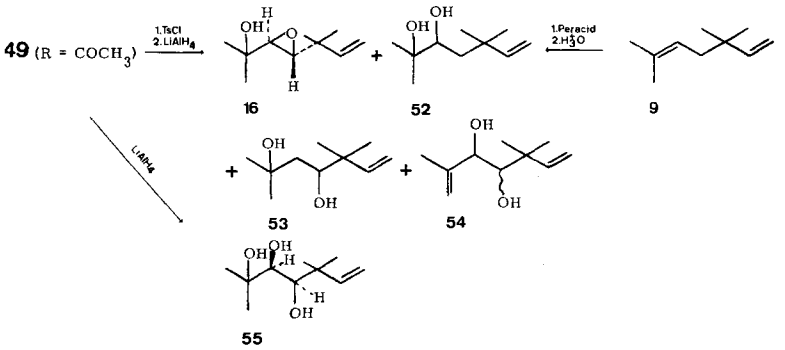
50 **51**

The pure, crystalline acetoxy-diol **49** (R = $COCH_3$), obtained from the acetoxyoxetan **48** (R = $COCH_3$) by acid-catalyzed reaction with water, was allowed to react with a trace of sulfuric acid in ether, when a very complex mixture of products was obtained, among which was the original acetoxyoxetan **48** (R = $COCH_3$) as well as the acetoxy-epoxide **46** from which it had been derived, thus showing that reactions **46** → **48** → **49** were all reversible. Before the position of the acetoxyl group had been clearly established, an attempt was made to remove the secondary hydroxyl group by conversion to the *p*-toluenesulfonate and reducing this with lithium aluminium hydride. A mixture of substances was obtained, consisting of the 1,2-glycol **52** (14%, confirmed by preparing it from 2,5,5-trimethyl-hepta-2,6-diene (**9**)), and the 1,3-glycol **53** (46%), together with yomogi alcohol epoxide (**16**, 12%) and a compound

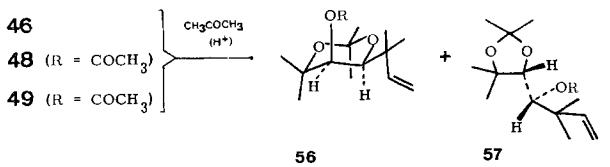
[8]) *Yang & Eisenhardt* [23] quote 6.7 Hz for coupling constants of *cis* protons in a methyl substituted oxetan, with 6.1 Hz for corresponding *trans* protons. In another case, the figures they give are somewhat different from those given for the same substance by *Pihlaja et al.* [24]. It is generally accepted (albeit on the strength of a fairly small number of examples) that $J_{cis} > J_{trans}$ [25].

[9]) The NMR. spectrum (see experimental part) of substance **51** suggested that this glycol was stereochemically homogeneous, unlike **54** (below), that appeared to be a mixture.

identified as 2,5,5-trimethyl-hepta-1,6-diene-3,4-diol (**54**, 27%, probably a mixture of isomers). There was also a certain amount of 2,5,5-trimethyl-hept-6-ene-2,3,4-triol (**55**), – no doubt arising from unreacted acetoxy-diol **49** (R = $COCH_3$) as it is easily prepared from the latter by reaction with lithium aluminium hydride. Reduction of tosylates with lithium aluminium hydride *via* intermediate carbonium is well known) (for some exemples see [27][10])), and our products **52** + **55** may be accounted for by invoking a carbonium ion.



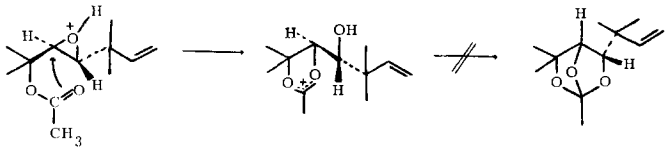
Further information about the stereochemistry of the systems was obtained by reaction of either the acetoxy-epoxide **46**, the acetoxy-oxetan (**48**, R = $COCH_3$), or the acetoxy-triol (**49**, R = $COCH_3$) with acetone, all of which gave, in the presence of a trace of acid or of Dowex 50 resin, a mixture of two acetonides that are not just stereoisomers, but were identified by their NMR. and mass spectra as a 1,3-dioxan (**56**, R = $COCH_3$) and a 1,3-dioxalan (**57**, R = $COCH_3$). The stereochemistry of the former must be as illustrated for **56**, because the NMR. coupling constant of the two protons on the ring is only 7 Hz, which is too low for *trans-diaxal* protons. Reduction of the acetates **56** (R = $COCH_3$) and **57** (R = $COCH_3$) with lithium aluminium hydride led to the corresponding alcohols **56** (R = H) and **57** (R = H), and treatment of the pure triol **55** with acetone and Dowex 50 resin H^+ form gave only the acetonide **57** (R = H), so that the presence of the acetoxy group in **49** evidently does not influence the stereochemistry of the reaction with acetone.



The obvious mechanism to examine in the first place involves participation of the acetoxy group during the epoxide ring opening, for many years recognized to occur in vicinal acetoxy-epoxides [28] and solvolysis reactions of 1,2-diol mono-O-acetyl derivatives [29]. Nearly all the work on this type of reaction has been carried out on necessarily *cis*-cyclic-epoxides. In these cases, rear-side attack leads to an

[10]) Many other publications on related reactions exist.

acetoxonium ion [30] which can be converted to various products *via* ortho-esters formed with hydroxylated compounds [31]. *Buchanan* once suggested formation of an internal ortho-ester by reaction of an acetoxonium ion with a hydroxyl group elsewhere in the molecule [28] and although he subsequently modified this idea [32], it is not unreasonable, and we might follow the same reasoning by allowing the acetoxonium ion **i** arising from the protonated epoxide **h** to react with the remaining hydroxyl group. The ortho-ester formed in this case, **j**, is, however, very unlikely because of the steric compression of the methyl and dimethylallyl groups in *endo* positions on either side of the trioxanorbornane ring.



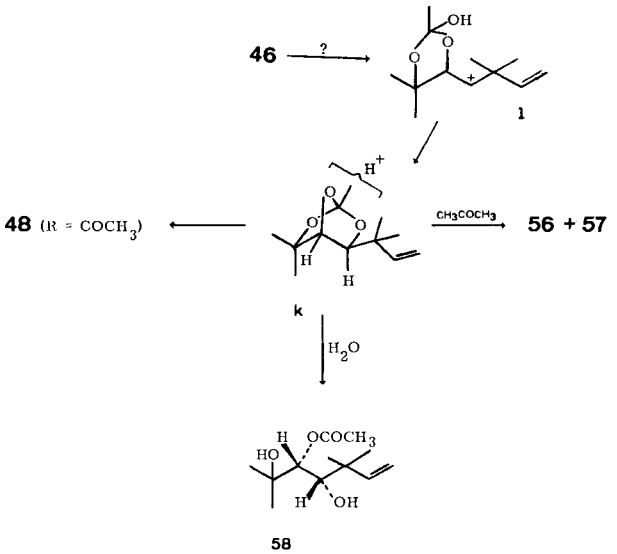
h **i** **j**

One suggestion is that the stereochemistry of all the products we find in the various acid-catalyzed reactions is governed by that of the stereoisomer **k** of ortho-ester **j**, *i.e.* one having a favourable *exo-orientation* of the large group. This ortho-ester might be formed by a front-side reaction of the acetoxy group with the protonated epoxide[11]), or from a carbonium ion such as **l**, but in any case, such compounds once formed, are known to react with acetone with retention of the stereochemistry [28], and closely related compounds undergo reaction with water, also with retention of stereochemistry [30]. This implies the *threo* configuration **58** for the 2-acetoxy-triol, as well as *cis*-substitution for the oxetan **48**, and the structures we have already described for the acetonides **56** and **57**.

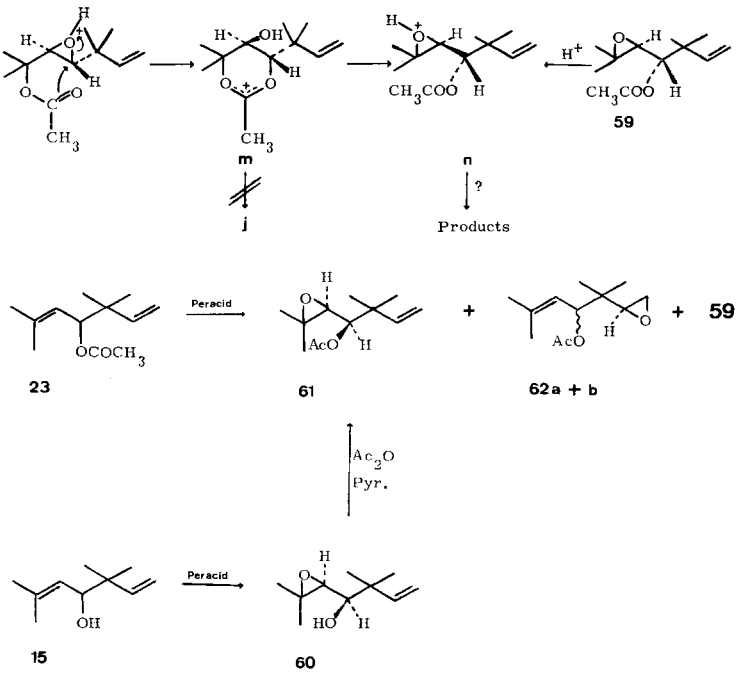
An alternative for the onset of the reaction is by way of anchimeric assistance by the acetate group, not on the adjacent position of the epoxide ring, but at one carbon atom further away, necessitating a shift back again to achieve the final structures. This would imply the presence of a protonated O-acetyl artemisia alcohol epoxide **n** in the reaction pathway, the initially formed ion **m** being unable to cyclize to the orthoester **j** for the steric reasons already mentioned. We therefore examined the preparation of artemisyl acetate epoxide (**59**).

Peroxyacid treatment of artemisia alcohol (**15**) yielded a single substance **60**, to which we ascribed the *threo* configuration from the numerous examples of peroxy-acid attack from the same side of the double bond as the hydroxyl group in allyl

[11]) *Eschenmoser et al.* [33] have expressed doubts about the validity of "endocyclic" *SN*-type reactions, but these doubts were attenuated in so far as epoxides are concerned. As we are talking of an acid-catalyzed reaction, our *ad hoc* suggestion is not necessarily related to those concerned with *SN*-reactions. Actually, we do not even know whether the acetate group might be protonated before that of the epoxide, which would lead to a different sequence of events. Prof. *Buchanan* (private communication) has suggested a modification of the scheme described here; initial opening of the epoxide (**46**) might involve formation of a homoallylic ion (such as **a**) which then undergoes attack by the acetoxy group. The terminal double bond would thus be necessary for the reaction to occur. Experiments are being undertaken to verify this point.



alcohols [34]. Acetylation of this compound in pyridine yielded the *threo* acetoxy-epoxide **61**. Actually the ion **n** is derived from the *erythro* acetoxy-epoxide **59**, and we thought that epoxidation of artemisyl acetate (**23**) would lead to it. Peroxyacid treatment of **23** led to the same major product as we had obtained from the alcohol (after acetylation), with only a minor amount of the *erythro* acetoxy-epoxide **59**,



together with small amounts of the two epoxides **62a** and **b**, resulting from attack on the terminal double bond .This is because the dimethylallyl group is bulkier than the acetate group, so the peroxyacid is constrained to attack the acetate **23** from the opposite side of the molecule, *i.e.* from the same side as the acetate group. A certain reluctance of the doubly substituted double bond to react is indicated by the isolation of the terminal epoxides **62**.

As the *threo* acetoxy-epoxide **61** was the only one available in reasonable amounts, and this was unreactive towards Dowex 50 resin, even at reflux temperatures, we cannot comment about the likelihood of a reaction path going through **n**.

Experimental Part

M.p.s were taken in capillaries and corrected. IR. spectra were measured with a *Perkin-Elmer* type 125 spectrophotometer. NMR. spectra were obtained with a *Varian* type A-60 instrument, and chemical shifts are given in ppm with tetramethylsilane as 0.00 ppm. Mass spectra were measured on the *Atlas* CH 4 mass spectrometer, using an inlet temperature of about 150° and electrons of 70 eV energy. Gas chromatography (GLPC.) was carried out on a *Carlo Erba* Fractovap type P (preparative) or a *Carlo Erba* type GT (analytical and semi-preparative), using Carbowax 20 M 15% on Chromosorb W 60–80 mesh, acid-washed.

2,5,5-Trimethyl-hepta-2,6-diene (**9**) [11]. To a stirred suspension of 45 g magnesium turnings (activated with a little methyl iodide) in 1.5 l of dry ether were added slowly 370 g of 3-methyl-but-2-enyl chloride, maintaining the temperature below 15° throughout. After addition the mixture was stirred for 1 h at room temperature, then decomposed with ice-cold water. The organic phase was separated, the aqueous phase washed with pentane, and the combined organic phases dried and concentrated to give 162 g of a mixture b.p. 31–44°/10 Torr. Redistillation yielded 92 g of pure trimethylheptadiene **9**, b.p. 34°/10 Torr. NMR. spectrum: 0.94 (6H, *s*, CH_3–C<), 1.55 and 1.67 (3H each, *s*, $(CH_3)_2C$=), 1.89 (2H, *d*, J = 7.5 Hz, $-CH_2-CH$=), 4.6 and 4.85 (mult., =CH_2) overlapping with 5.01 (*t*, J = 7.5 Hz, C=$CH-CH_2$), 5.69 (*d* of *d*, J = 9.5 and 17.5 Hz, $-CH$=CH_2). Mass spectrum: *m/e* (% relative abundance): 69 (100), 41 (60), 70 (19), 95 (4), 123 (2.5), 138 (M^+, <1).

$C_{10}H_{18}$ Calc. C 86.88 H 12.12% Found C 86.82 H 13.08%

From the end fractions of the distillation, 2,7-dimethyl-octa-2,6-diene was isolated by GLPC. NMR. spectrum: 1.58 and 1.65 (6H, *s*, $(CH_3)C$=), 1.9 to 2.1 (4H, mult., $-CH_2CH_2-$), 4.9 to 5.2 (2H, broad, >C=$CH-CH_2$). Mass spectrum: 69 (100), 41 (63), 70 (16), 82 (10), 95 (4), 138 (M^+, 3).

$C_{10}H_{18}$ Calc. C 86.88 H 13.12% Found C 87.12 H 12.25%

2,5,5-Trimethyl-hepta-3,6-dien-2-ol (*Yomogi alcohol*, **2**) *and 2,5,5-Trimethyl-hepta-1,6-dien-3-ol* (**10**). Oxygen was passed through a solution of 11 g of 2,5,5-trimethyl-hepta-2,6-diene and 0.1 g of bengal red in 120 ml of methanol. After 2.5 h, 1.77 l of oxygen (corrected to 0° and 760 Torr) had been absorbed (theor. 1.79 l). The solution of hydroperoxides was decomposed with 125 g of sodium sulfite in 700 ml of water. Extraction with pentane, washing with sodium hydrogencarbonate solution, drying, and concentration yielded 7 g of a mixture of 80% yomogi alcohol (**2**) and 20% 2,5,5-trimethyl-hepta-1,6-dien-3-ol (**10**). The yield of this mixture was practically quantitative when larger amounts were used. Distillation gave, first, yomogi alcohol, b.p. 71–72°/10 Torr, $d_4^{20} = 0.8446$; $n_D^{20} = 1.4527$. NMR. spectrum identical with that described [1] [2]. Mass spectrum: 43 (100), 59 (53), 85 (27), 81 (25), 41 and 139 (24), 55 (17), 96 (16), 67 and 95 (15), 97 (14), 41, 69, 93 and 121 (10), also 39, 53, 57, 72, 77, 79, 82, 83, 91, 105.

$C_{10}H_{18}O$ Calc. C 77.86 H 11.76% Found C 77.69 H 11.46%

The alcohol **10** had b.p. 79–80°/10 Torr. NMR. spectrum: 1.04 (6H, *s*, CH_3C<), 1.4 to 1.5 (mult., 2H, CH_2), 1.65 (3H, *d*, J = 1 Hz, CH_3-C=), 3.9 to 4.0 (broad signal, 1H, $-CH-OH$), 4.5 to 5.0 (4H, mult., >C=CH_2), 5.78 (*d* of *d*, J = 9.5 and 17.5 Hz, $-CH$=CH_2). Mass spectrum:

69 (100), 71 (99), 41 (95), 55 (55), 43 (53), 84 (30), 70 (23), 39 (22), 27 (19), 67 and 83 (16), 29, 72 and 139 (13), 53 and 85 (12), 68 and 111 (10).

$C_{10}H_{18}O$ Calc. C 77.86 H 11.76% Found C 77.76 H 11.70%

Chromium trioxide oxidation of yomogi alcohol (**2**). A solution of 10 g of **2** dissolved in 150 ml of acetone was treated at $-5°$ to 0° with 25 ml of a solution of 53.4 g of chromium trioxide in 46 ml of conc. sulfuric acid made up to 200 ml with water. After 2 h, the mixture was neutralized with sodium hydrogencarbonate solution, somewhat concentrated and the products extracted with ether. The complex mixture was not examined in detail, but collection of the peaks from GLPC. showed: 5% of artemisia ketone (**3**), identical with authentic material, 16% of unchanged **2**, 45% of 2,5,5-trimethyl-3,4-epoxy-hept-7-en-2-ol (**16**), identical with that prepared in the next experiment, and finally traces of fission products (3-methyl-but-2-enal and the corresponding acid), together with about 4% of 2,5,5-trimethyl-2,3-*trans*-epoxy-hept-6-en-4-ol (artemisia alcohol epoxide, see below).

*2,5,5-*Trimethyl-*3,4-epoxy-hept-6-en-2-ol* (**16**). A suspension of 10 g of anhydrous sodium acetate in 200 ml of methylene chloride and 11.5 g of yomogi alcohol was stirred at 0° to 5° while 17 g of peroxyacetic acid (40%) was added dropwise, after which the mixture was stirred for a further 2 h at room temperature, then poured into water, and the organic phase washed with sodium hydrogencarbonate, then water, and dried. After concentration, 9 g of practically pure epoxide was obtained, b.p. 95°/17 Torr; $d_4^{20} = 0.9230$; $n_D^{20} = 1.4460$. NMR. spectrum: 1.01, 1.03, 1.12, 1.21 (3H each, *s*, CH_3—C<), 2.60 and 2.76 (1H each, *d*, J = 2 Hz, —CH—CH—, O), 4.85 and 5.10 (1H each, mult., —CH=CH_2), 5.76 (1H, *d* of *d*, J = 9.5 and 17.5 Hz, —CH=CH_2). Mass spectrum: 43 (100), 41 (61), 69 (56), 59 (48), 97 (36), 67 (32), 55 (30), 72 (29), 39 (17), 83 (16), 27, 29, 57 (15), 70 (12), 137 (1.5).

$C_{10}H_{18}O_2$ Calc. C 70.54 H 10.66% Found C 70.65 H 10.55%

Reaction of yomogi alcohol with acid in dioxan. A mixture of 3 g of yomogi alcohol and 8 ml of 10% sulfuric acid in 24 ml of dioxane was stirred for 5 h, then neutralized with 3 g of solid potassium carbonate, filtered, and concentrated. The residue consisted (GLPC.) of 80% of starting material and 20% of artemisia alcohol. The same result was obtained with perchloric acid in place of sulfuric acid. When 3 g of yomogi alcohol and 1.5 g of concentrated sulfuric acid were stirred in 30 ml dioxan, the yomogi alcohol disappeared slowly, but no formation of artemisia alcohol was observed.

2,5,5-Trimethyl-2-ethoxy-hepta-3,6-diene (**20**) *and 2,5,5-trimethyl-4-ethoxy-hepta-2,6-diene* (**21**). To a solution of 3 g of yomogi alcohol in 50 ml of dry ether cooled to $-10°$, 3 g of thionyl chloride was added dropwise and the mixture stirred at 0° for 1.5 h, then concentrated. The NMR. spectrum of the crude mixture was identical with that of the distilled chlorides (b.p. 60°/10 Torr). A mixture of chlorides thus prepared (30 g) was heated under reflux with 60 g of anhydrous sodium acetate in 200 ml ethanol for 9 h, the mixture filtered, concentrated, and distilled rapidly, when 22 g of a mixture of three substances was obtained. By GLPC. they were identified as 2,5,5-trimethyl-hepta-1,3,6-triene (28%) (artemisia triene, **22**), identical with an authentic sample[12]), and the compounds **20** (32%) and **21** (36%). Distillation separated artemisia triene (b.p. 46°/10 Torr) from the other compounds. 2,5,5-Trimethyl-4-ethoxy-hepta-2,6-diene (**21**), contaminated with about 25% of the isomer **20**, distilled at b.p. 64–66°/10 Torr, and was purified by GLPC. NMR. spectrum: 0.93, 0.95 (3H each, *s*, CH_3—C<), 1.09 (3H, *t*, J = 6.5 Hz, CH_3—CH_2), 1.62 and 1.74 (3H each, *d*, J = 1 Hz, CH_3—C(=)—CH—), 3.18 (2H, *q*, J = 6.5 Hz, O—CH_2—CH_3), 3.52 (1H, *d*, J = 9.5 Hz, CH—CH—O), 4.65 to 5.1 (3H, mult., =CH— and =CH_2), 5.92 (1H, *d* of *d*, J = 10 and 18 Hz, —CH=CH_2). Mass spectrum: 113 (100), 85 (91), 41 (25), 43 (14), 29 (12), 55, 67, 114 (7), 167 (2).

$C_{12}H_{22}O$ Calc. C 79.06 H 12.16% Found C 78.68 H 11.83%

Finally, pure 2,5,5-trimethyl-2-ethoxy-hepta-3,6-diene (**20**) distilled at 67°/10 Torr. NMR. spectrum: 1.09, 1.18 (*s*, each CH_3—C<), superimposed on 1.23 (*t*, J = 7 Hz, CH_3—CH_2), (9H together in these signals), 3.23 (2H, *q*, J = 7 Hz, CH_2—CH_3), 4.65 to 5.1 (2H, CH=CH_2), 5.6 (2 signals, 2H, —CH=CH—), 5.80 (1H, *d* of *d*, J = 9.5 and 17.5 Hz, —CH=CH_2). Mass spectrum:

[12]) Prepared from chrysanthemyl alcohol [35].

43 (100), 167 (62), 113 (58), 85 (52), 41 and 95 (42), 59 (40), 55 (24), 29, 81 and 121 (22), 57, 67, 69, 87 and 123 (17), 73 and 83 (16), 137 (14), also above 10%: 27, 39, 53, 79, 93, 97, 139.

$C_{12}H_{22}O$ Calc. C 79.06 H 12.16% Found C 78.93 H 11.81%

2,5,5-Trimethyl-hept-2-ene (**11**). A solution of 30 g of 2,5,5-trimethyl-hepta-2,6-diene in 300 ml ethanol was hydrogenated over 0.5 g palladium on charcoal (10%). In 30 min, 5.0 l of hydrogen (corrected to 0° and 760 Torr, theor. 4.87 l) was absorbed and cooling was necessary. Filtration and concentration gave a product which distilled at 152°/735 Torr; yield 21 g (82%). NMR. spectrum: 0.80 (6H, *s*, $2CH_3$–C<), overlapping with m of CH_3CH_2, 1.55 and 1.67 (3H each, *s*, (borad), CH_3–C=), 1.78 (2H, *d*, J = 7 Hz, –CH_2–CH=), 5.01 (1H, *t*, J = 7 Hz, =CH–CH_2). Mass spectrum: 43 (100), 71 (87), 70 (65), 41 (39), 69 (35), 55 (27), 27 and 29 (14), 39 (12), 111 and 140 (7).

2,5,5-Trimethyl-hept-3-en-2-ol (**12**) *and 2,5,5-trimethyl-hept-1-en-3-ol* (**13**). Photo-oxygenation of 2,5,5-trimethyl-hept-2-ene (**11**) was carried out exactly as described in the preparation of yomogi alcohol (above); 21 g of hydrocarbon gave a practically quantitative yield of **12** with **13**, which were separately obtained pure by distillation.

2,5,5-Trimethyl-hept-3-en-2-ol: b.p. 74°/10 Torr; d_4^{20} = 0.8313; n_D^{20} = 1.4424. NMR. spectrum: 0.76 (3H, *t*, J = 7 Hz, CH_3–CH_2), 0.95 and 1.24 (6H each, *s*, CH_3–C<), hidden mult. about 1.25 (2H), 5.43 (2H, *s*, –CH=CH–). Mass spectrum: 43 (100), 85 (37), 141 (20), 109 (17), 41 and 69 (16), 71 (15), 59 (14), 55 (12).

$C_{10}H_{20}O$ Calc. C 76.86 H 12.90% Found C 76.37 H 12.80%

2,5,5-Trimethyl-hept-1-en-3-ol: b.p. 82°/10 Torr; d_4^{20} = 0.8546; n_D^{20} = 1.4501. NMR. spectrum: 0.82 (*t*, J = 7 Hz, CH_3–CH_2), 0.91 (*s*, CH_3–C<), these two signals integrating for 9H, 1.1 to 1.5 (4H, mult.) 1.70 (3H, *d*, J = 1 Hz), 4.08 (1H, *t*, J = 6 Hz, CH_2–CH–O), 4.68 and 4.9 (1H each, mult., CH=CH_2). Mass spectrum: 71 (100), 43 (56), 41 (15), 57 (13), 86 (12), 70 (11).

$C_{10}H_{20}O$ Calc. C 76.86 H 12.90% Found C 76.47 H 12.60%

2,5,5-Trimethyl-3,4-epoxy-heptan-2-ol. The oxidation of 3.8 g of 2,5,5-trimethyl-hept-3-en-2-ol with chromic oxide was carried out as described for the oxidation of yomogi alcohol (above), to give 2.5 g of a mixture, b.p. 74–95°/10 Torr, which consisted mainly of starting material (by GLPC.), the remainder being 93% 2,5,5-trimethyl-3,4-epoxy-heptan-2-ol. NMR. spectrum: 0.80, 0.85, 1.13, 1.22 (3H each, *s*, CH–C<), superimposed on 0.88 (3H, *t*, J = 7 Hz, CH_3–CH_2), 2H more hidden under signals at 1.1 to 1.5, 2.6 to 2.75 (2H, mult., –CH(O)–CH–). Mass spectrum: 85 (100), 43 (85), 72 (57), 59 (46), 69 (39), 41 (34), 55 (26), 71 (25), 29 and 57 (20), 45 (17), 27 and 83 (13), 99 and 101 (6), 139 (3).

$C_{10}H_{20}O_2$ Calc. C 69.72 H 11.70% Found C 69.52 H 11.59%

In addition, 5% of 2,5,5-trimethyl-2,3-epoxy-heptan-4-ol was isolated by GLPC., with a slightly longer retention time on the Carbowax column. NMR. spectrum: 0.83, 0.90 superimposed on the CH_3–CH_2 triplet (3H each, *s*, CH_3–C<), 1.27 (6H, *s*, CH_3–C<), 2.67 (1H, *d*, J = 8 Hz, C(O)–CH–CH), 3.04 (1H, *d*, J = 8 Hz, HO–CH–CH–O). Mass spectrum: 43 (100), 55 (63), 85 (56), 71 (52), 87 (35), 41 (30), 59 (25), 57 (22), 29, 70, 72, 84 (20), 27, 45, 101 (14), 39 (12), 73 (10).

Reaction of 2,5,5-trimethyl-3,4-epoxy-hept-6-en-2-ol (**16**) *with acid.* A mixture of 1,5 g of **16** and 50 mg of *p*-toluenesulfonic acid was heated in benzene under reflux. After 30 min, more than 70% of the product was a single compound of shorter retention time on Carbowax columns, and after distillation (b.p. 80–81°/10 Torr), the *2,2-dimethyl-3-vinyl-4-[1-methyl-1-hydroxy-ethyl]-oxetan* (**24**) was purified by GLPC. d_4^{20} = 0.9261; n_D^{20} = 1.4475. NMR. spectrum: 0.96, 1.07, 1.28, 1.30 (3H each, *s*, CH_3–C<), 3.14 (1H, *t*, J = 7.5 Hz, CH–CH–CH=), 4.03 (1H, *d*, J = 7.5 Hz, O–CH–CH), 4.82 and 5.06 (1H each, mult., –CH=CH_2), 5.75 (1H, mult., –CH–CH=CH_2) Mass spectrum: 43 (100), 97 (47), 69 (46), 59 (41), 82 (32), 41 (30), 67 (26), 55 (14), 39 (10), 112 (6).

$C_{10}H_{18}O_2$ Calc. C 70.54 H 10.66% Found C 70.31 H 10.78%

After heating the acid mixture for a further 2 h, about 50% of the product consisted of a substance having slightly longer retention time on GLPC. than the starting material, and was

identified as *2,2,5,5-tetramethyl-4-vinyl-3*-cis-*hydroxy-tetrahydrofuran* (**25**). Sometimes, on concentrating the neutralized reaction mixture, this substance crystallized directly and was purified by recrystallization from hexane, m.p. 126–127°. NMR. spectrum (in perdeuterio-dimethylsulfoxide): 1.10 (9H, *s*, CH_3—C<), 1.17 (3H, *s*, CH_3—C<), 2.59 (1H, *d* of *d*, J = 5 and 9 Hz, CH—CH—CH=), 3.71 (1H, *d*, J = 5 Hz), 4.95 and 5.18 (1H each, mult., —CH=CH_2), 6.03 (1H, mult., —CH—CH=CH_2). Mass spectrum: 69 (100), 43 (82), 97 (50), 112 (40), 41 (34), 59 (28), 71 (13), 55, 79 (12), 39, 83 and 94 (11), 155 (1.8).

$C_{10}H_{18}O_2$ Calc. C 70.54 H 10.66% Found C 70.37 H 10.41%

From the same mixture, the more polar threo-*2,5-dimethyl-4-vinyl-hex-5-en-2,3-diol* (**28**) was isolated. NMR. spectrum: 1.13 and 1.16 (3H each, *s*, CH_3—C<), 1.72 (3H, broad *s*, CH_3—C=), 2.78 (1H, *t*, J = 8.5 Hz), C=CH—CH—C=C), 3.40 (1H, *d*, J = 8.5 Hz, CH—CH—O), 4.8 (3H, CH mult.) and 5.1 (1H, mult., —CH=CH_2), 5.86 (1H, mult., CH—CH=CH_2). Mass spectrum: 59 (100), 82 (91), 43 (64), 67 (56), 41 (38), 81 (33), 71 (26), 69 (21), 39, 55, 79 (17), 31, 83 and 97 (13), 27 and 53 (10), 137 (1.6).

$C_{10}H_{18}O_2$ Calc. C 70.54 H 10.66% Found C 69.90 H 10.75%

Immediately after this compound, on polar columns two further compounds were eluted which were difficult to separate, namely the two 2-methyl-2-hydroxy-propional acetals (**29**) of the above diol **28**. The less polar of the two, after purification by GLPC., had NMR. spectrum: 1.08 (6H), 1.15, 1.25 (3H each, *s*, CH_3—C<), 1.72 (3H, *s*, CH_3—C=), 2.87 (1H, broad *t*, J = 9.5 Hz, C=CH—CH—CH—C=C), 3.65 (1H, *d*, J = 9.5 Hz, O—CH—CH—), 4.54 (1H, *s*, ), 4.6 to 5.8 (5H). Mass spectrum: 81 (100), 71 (37), 43 (31), 181 (26), 59 (22), 41 (16), 72, 89 and 135 (13), 79 (11), 159 (4). The more polar of the two acetals had an identical NMR. spectrum, except for the following difference: 4.63 (1H, *s*, ). The mass spectrum was also the same, except that the most important fragment (*m/e* 81) constituted a greater amount of the total ionization. $C_{14}H_{24}O_3$ Calc. C 69.96 H 10.07% Found C 69.82 H 10.14%

2,2,5,5-Tetramethy -4-vinyl-3-cis-*acetoxy-tetrahydrofuran* (**26**). 0.75 g 2,2,5,5-tetramethyl-4-vinyl-tetrahydrofuran-3-*cis*-ol was acetylated in 2 ml of dry pyridine with 2 g of acetic anhydride at 40° for 24 h, the mixture decomposed with ice water, the product extracted with ether, and the organic phase washed with dilute sulfuric acid, water, sodium hydrogencarbonate solution and finally water. Concentration and distillation (b.p. 60° (bath temp.)/10 Torr) gave the acetoxy product, purified by GLPC. NMR. spectrum: 1.12, 1.13, 1.17, 1.22 (12H in all, *s*, CH_3—C<), 2.05 (3H, *s*, CH_3COO), 2.80 (1H, *d* of *d*, J = 5.5 and 8.5 Hz, =CH—CH—CH<), 5.0 (*d*, J = 5.5 Hz, CH—CH—OCO) superimposed on 4.9 to 5.3 (mult., —C=CH_2), 5.80 (1H, mult., CH=CH=CH_2). Mass spectrum: 43 (100), 112 (43), 69 (28), 79 (18), 154 (16), 94 (13), 41, 59 and 97 (10), 197 (1).

$C_{12}H_{20}O_3$ Calc. C 67.89 H 9.50% Found C 67.70 H 9.43%

This compound was recovered unchanged after passage through a tube (30 cm × 2 cm) filled with glass helices and heated to 500°.

2,2,5,5-Tetramethyl-4-ethyl-3-cis-*hydroxy-tetrahydrofuran* (**35**). A solution of 0.8 g of 2,2,5,5-tetramethyl-4-vinyl-3-*cis*-hydroxy-tetrahydrofuran in 20 ml ethanol was shaken in hydrogen with about 0.05 g of palladium on charcoal (10% Pd). In one h the theoretical volume (106 ml) of hydrogen was absorbed, and after filtration and concentration of the solution, the product crystallized. Recristallized from pentane, m.p. 62°. NMR. spectrum: mult. 1.0 to 1.25 with max. at 1.09, 1.13, 1.17 and 1.23 (15H, CH_3—C< and CH_3—CH_2—), 1.5 to 1.9 (3H, mult., CH—CH—CH_2—CH_3), 3.0 (1H, *d*, J = 4.5 Hz, >CH—OH)[13]), 3.78 (1H, *t*, J = 4.5 Hz, HO—CH—CH—).

[13]) The doublet observed for the hydroxyl bond implies there is only slow exchange with the traces of HCl in the CCl_4 used in the NMR. determination. The reason for this is not yet clear, but the same was also observed with some artemisia alcohol derivatives.

Mass spectrum: 85 (100), 43 (88), 71 (53), 99 (40), 114 (30), 41 (21), 59 (13), 157 (11). IR. spectrum (in CCl_4): 3440 cm^{-1} (bonded OH), 3620 cm^{-1} (free OH).

$C_{10}H_{20}O_2$ Calc. C 69.72 H 11.70% Found C 69.77 H 11.66%

Ethy ation of 2,2,5,5-tetramethyl-tetrahydrofuran-3-one (**30**). To a solution of 9.6 g of potassium in 120 ml of dry *t*-butanol under nitrogen 20 g of the furanone [16] were added at room temperature, followed by 49.6 g of ethyl iodide with stirring and the mixture was heated 5 min at reflux. It was then filtered, concentrated, and the residue taken up in ether, the ether solution washed with water, dilute HCl, sodium hydrogencarbonate and water. Rapid distillation of the residue, after concentration of the solution, yielded 18 g of material that was distilled on the spinning band column to yield the following products in order of b.p. (yields are from GLPC., of the rapidly distilled material): starting material (8%).

2,2,5,5-Tetramethyl-3-ethoxy-2,5-dihydrofuran (**33**, 25%), b.p. 51°/14 Torr. Retention time on GLPC. (Carbowax) longer than that of starting material. NMR. spectrum: 1.22 (12H, *s*, CH_3—C<), 1.28 (3H, *t*, J = 7 Hz, CH_3—CH_2), 3.72 (2H, *q*, J = 7 Hz, CH_3—CH_2—O), 4.34 (1H, *s*, —CH=C—). Mass spectrum: 155 (100), 43 and 127 (72), 109 (31), 41 and 89 (15), 55 (11), 83 (10).

$C_{10}H_{18}O_2$ Calc. C 70.54 H 10.66% Found C 70.83 H 10.82%

2,2,5,5-Tetramethyl-4-ethyl-tetrahydrofuran-3-one (**31**, 36%), b.p. 65°/14 Torr. Retention time on GLPC. longer than that of compound **32**. NMR. spectrum: 1.05, 1.17, 1.37 (*s*, hiding other signals, at least 15H), 1.4 to 1.75 (<2H, mult., >CH—CH_2—CH_3), 2.11 (1H, *d*, J = 7 Hz, CO—CH—CH_2). Mass spectrum: 69 (100), 84 (86), 41 and 43 (30), 70 (15), 59 (10), 142 (3), 155 (2.5), 170 (M^+, 1).

$C_{10}H_{18}O_2$ Calc. C 70.54 H 10.66% Found C 70.68 H 10.76%

2,2,5,5-Tetramethyl-4-ethyl-3-ethoxy-2,5-dihydrofuran (**32**, 24%), b.p. 70°/14 Torr. NMR. spectrum: 1.07 (3H, *t*, part hidden, J = 7.5 Hz, CH_3—CH_2), 1.18 (12H, *s*, CH_3—C<), 1.26 (3H, *t*, J = 6 Hz, O—CH_2—CH_3), 2.03 (2H, *q*, J = 7.5 Hz, CH_3—CH_2—C), 3.96 (2H, *q*, J = 7 Hz, O—CH_2—CH_3). Mass spectrum: 183 (100), 155 (78), (68), 41 and 137 (23), 109 (20), 55 (16), 29 and 67 (12), 69 (10), 198 (M^+, 1).

$C_{12}H_{22}O_2$ Calc. C 72.68 H 11.18% Found C 72.49 H 11.25%

After refluxing 2.5 g of this compound with 10 ml of 5% sulfuric acid and 2.5 ml of tetrahydrofuran for at least 30 h, conversion to 2,2,5,5-tetramethyl-4-ethyl-tetrahydrofuran-3-one was complete.

2,2,5,5-Tetramethyl-4,4-diethyl-tetrahydrofuran-3-one (**34**, 6%), b.p. 90°/14 Torr. NMR. spectrum: 0.76 (6H, *t*, J = 7.5 Hz, CH_3—CH_2), 1.18 and 1.22 (6H together, *s*, CH_3—C<), 1.3 to 1.9 (4H, mult., —CH_2—CH_3). Mass spectrum: 70 (100), 84 (68), 55 (34), 41, 43 and 97 (31), 69 and 112 (25), 140 (19), 198 (M^+, 13).

$C_{12}H_{22}O_2$ Calc. C 72.68 H 11.18% Found C 72.68 H 10.78%

Lithium aluminium hydride reduction of 2,2,5,5-tetramethyl-4-ethyl-tetrahydrofuran-3-one (**31**). A solution of 1.7 g **31** in 10 ml dry ether was added dropwise to 0.3 g of lithium aluminium hydride in 20 ml of dry ether. After stirring 1 h at room temperature, the excess hydride was decomposed with water, the mixture filtered, and the filtrate concentrated to give 1.8 g of a mixture that was separated by GLPC. into 7% of 2,2,5,5-tetramethyl-*cis*-4-ethyl-tetrahydrofuran 3-ol (**35**), identical with the product obtained from yomogi alcohol epoxide (above), and 93% of the *trans*-isomer (**36**), with a slightly longer retention time on GLPC. d_4^{20} = 0.9470; n_D^{20} = 1.4517. NMR. spectrum: mult. 1.0 to 1.3 with max. at 1.03, 1.07, 1.09 and 1.24 (15H, CH_3—C< and CH_3—CH_2), 1.5 to 1.9 (3H, mult., CH_3—CH_2—CH—), 3.52 (1H, *d* of *d*, J = 6.5 and 6 Hz, HO—CH—CH), 3.9 (1H, *d*, J = 6 Hz, HO—CH)[12]. Mass spectrum: 85 (100), 43 (69), 99 (40), 114 (28), 71 (23), 41 (29), 59 (13), 157 (5.9). IR. spectrum: 3440 cm^{-1} (bonded OH), 3610, 3620 cm^{-1} (free OH).

$C_{10}H_{20}O_2$ Calc. C 69.72 H 11.70% Found C 69.74 H 11.47%

*2,2,5,5-Tetramethyl-4-e hyl-3-*trans*-acetoxy-tetrahydrofuran.* The alcohol **36** above was acetylated with acetic anhydride in pyridine, and the acetate purified for analysis by GLPC. NMR. spectrum: 0.8 to 1.25 mult. with max. at 0.93, 1.0, 1.07 and 1.22 (15H), 1.99 (3H, *s*, CH_3COO—),

4.88 (1H, *d*, J = 10 Hz, CO—O—CH—CH). Mass spectrum: 43 (100), 85 (61), 96 (37), 139 (33), 114 (29), 127 (18), 41 and 81 (14), 59 and 99 (11), 55 and 97 (10), 199 (7).

$C_{12}H_{22}O_3$ Calc. C 67.25 H 10.35% Found C 67.02 H 10.14%

*2,2,5,5-Tetramethyl-4-ethyl-3-*cis*-acetoxy-tetrahydrofuran* was made in the same way from the *cis*-alcohol **35**. d_4^{20} = 0.9500; n_D^{20} = 1.4325. NMR. spectrum 1.00 (*t*, partly visible, J = 7 Hz, CH_3—CH_2), 1.06 (6H, *s*), 1.19 (6H, *s*), 2.01 (3H, *s*, CH_3COO), 5.07 (1H, *d*, J = 5 Hz, CO—C—CH—CH). Mass spectrum: 43 (100), 85 (37), 114 (33), 96 (28), 71 (20), 41, 81, 97 and 199 (13), 99, 127 and 139 (10).

$C_{12}H_{22}O_3$ Calc. C 67.25 H 10.35% Found C 67.59 H 10.47%

This substance was recovered unchanged after passage through a gas chromatograph where the evaporator was heated to 450–470°.

2,2,5,5-Tetramethyl-3-ethyl-2,5-dihydrofuran (**38**). 2,2,5,5-Tetramethyl-4-ethyl-3-*trans*-acetoxy-tetrahydrofuran, injected into a gas chromatograph in which the evaporator was heated to 450–470°, was quantitatively converted to acetic acid and **38**. Larger amounts of **38** were made by passing 3 g of the *trans*-acetate in 5 ml of toluene through a column filled with quartz chips and heated to 480°, and were purified by preparative GLCP. NMR. spectrum: 1.10 (3H, *t*, J = 7 Hz, CH_2—CH_2), 1.19 (12H, *s*, CH_3—C<), 1.92 (2H, *q* + further coupling, J = 7 Hz, C=C—CH_2—CH_3), 5.17 (1H, *t*, J = 1.5 Hz, CH=C—CH_2). Mass spectrum: 139 (100), 43 (70), 81 (14), 41 (13), 140 (10).

$C_{10}H_{18}O$ Calc. C 77.86 H 11.76% Found C 77.76 H 11.73%

1,2-Epoxy-3,3-dimethyl-pent-4-ene (**39**). (This and the next experiment were carried out by *M. Ozainne*). A solution of 9.6 g of 3,3-dimethyl-penta-1,4-diene [36] and 10 g of sodium acetate in 200 ml of methylene chloride was treated at 0° with 20 g of peroxyacetic acid (39.4% in acetic acid). The reaction, followed by thin-layer chromatography, was finished after 40 h. Filtering and washing the organic phase, followed by careful evaporation left a residue (6 g) still containing solvent which by preparative GLPC. gave **39** which distilled at 118°/730 Torr. NMR. spectrum: 0.97 and 1.02 (3H each, *s*, CH_3—C<), 2.35 to 2.50 (2H, mult., CH_2—CH), 2.5 to 2.75 (1H, mult., CH_2—CH—C), 4.75 to 4.9 and 4.95 to 5.15 (2H, mult., HC=CH_2), 5.75 (1H, *d* of *d*, J = 10 and 17.5 Hz, —CH=CH_2). Mass spectrum: 41 (100), 67 (59), 69 (46), 39 (30), 97 (19), 43 and 55 (16), 53, 54 and 82 (13), 112 (M^+, 1).

$C_7H_{12}O$ Calc. C 74.95 H 10.78% Found C 75.02 H 10.98%

Reaction of 1,2-epoxy-3,3-dimethylpent-4-ene (**39**) *with cation exchange resin.* A suspension of 0,1 g of Dowex 50 (acid form) ion exchange resin in 50 ml of dry ether was stirred with 1.0 g of the epoxide **39**. After 24 h at room temperature, the mixture, analysed by GLCP., consisted of 25.8% of 4-methyl-penta-1,3-diene, 49.9% of starting material, and 12.3% of 3-methyl-2-vinyl-but-3-en-1-ol, together with a total of about 10% of three other products having retention times close to that of the alcohol. The 4-methyl-penta-1,3-diene was collected by GLCP.: NMR. spectrum: 1.73 (6H, *s*, CH_3—C=), 4.77, 4.88, 5.06 (2H together, C=CH_2), 5.73 (1H, *d*, J = 10.5 Hz), 6.1 to 6.8 (1H, mult., CH—CH=CH_2). Mass spectrum: 67 (100), 82 (M^+, 59), 41 (54), 39 (45), 27 (20), 31 (18), 54 (16), 63 (15), 81 (13), 65 (12). 3-Methyl-2-vinyl-but-3-en-1-ol was also purified by GLCP. for analysis: NMR. spectrum: 1.71 (3H, *d*, J = 1 Hz, CH_3—C=), 2.80 (1H, *q*, J = 7 Hz, C=C—CH(CH=)—CH_2—), 3.52 (2H, *d*, J = 7 Hz, CH—CH_2OH), 4.7 to 5.2 (3H, mult., >C=CH_2 and CH=CH_2), 5.4 to 6.05 (1H, mult., CH—CH=CH_2). Mass spectrum: 82 (100), 67 (96), 41 (80), 81 (71), 39 (56), 79 (52), 53 (50), 27 (28), 31 (21), 55 (18), 29, 54, 77 (15), 97 (6). IR. spectrum: 1732, 890, 913 cm^{-1} (C=CH_2).

$C_7H_{12}O$ Calc. C 74.95 H 10.78% Found C 74.39 H 10.81%

Threo-*2ξ-phenyl-4-(2-methyl-penta-1,4-dien-3-yl)-5,5-dimethyl-1,3-dioxalan* (**41**). To a solution of 0.5 g of *p*-toluenesulfonic acid in 250 ml toluene (dried by heating under reflux for 1 h) at 100°, 17 g of yomogi alcohol epoxide and 15 g of benzaldehyde were added. After stirring for 3 h at 100°, the solution was cooled, washed with sodium hydrogencarbonate solution and water,

dried, and concentrated to give 13 g of a product which was distilled, b.p. 105–110°/0.01 Torr, yielding 12 g of a mixture showing two incompletely resolved peaks on GLPC. (nearly 50% of each). The analyses refer to the 1:1 mixture. NMR. spectrum: 1.17, 1.23 and 1.29 (6H, CH_3—C—, two isomers), 1.73 (3H, broad, CH_3—C=), 2.6 to 3.2 (1H, mult., C=CH—CH—CH—, 3.60 (*d*, J = 7.5 Hz) and 3.78 (*d*, J = 7.5 Hz) ,(together 1H, O—CH—CH—, two isomers), 4.65 to 5.9 (6H, mult., CH=CH_2 and C=CH_2, and O—CH—O), 7.15 to 7.45 (5H, mult., C_6H_5—). Mass spectrum: 107 (100), 177 (56), 79 (38), 81 and 105 (31), 43 and 77 (16), 41, 71 and 91 (11), 257 (M-1$^+$, 2.2).

$C_{17}H_{22}O_2$ Calc. C 79.03 H 8.58% Found C 79.16 H 8.71%

Treatment of dioxalan **41** *with butyllithium.* To a solution of 2.2 g of **41** in 10 ml of tetrahydrofuran, cooled to −80° under nitrogen in strictly anhydrous conditions, 12 ml of butyllithium (1.65) in hexane was added dropwise. The solution turned yellow, and was allowed to warm to −10°, then maintained at −10° to −6° overnight. After pouring into water and isolating the products with pentane, 1.8 g of material was obtained. By GLPC. the following substances were identified (yields are only very approximate, because of evaporation of the lighter components during concentration of the solvent): (a) *Santolinatriene* (**42**, 8%), identical (NMR., IR. and mass spectra) with that previously described [7]. (b) *2-Methyl-4-isopropenyl-deca-2,4-diene* (**43**, 9%). NMR. spectrum: 0.89 (3H, *t*, CH_3—CH_2), 1.2 to 1.4 (6H, —CH_2—), 1.72 (9H, *s*, CH_3—C=), 1.8 to 2.2 (2H, mult., =CHCH_2), 4.6 to 4.7 and 4.85 to 4.95 (2H, C=CH_2), 5.15 (1H, *t*, J = 7.5 Hz, CH_2—CH=C), 5.58 (1H, broad *s*, C=CH—C=). Mass spectrum: 107 (100), 135 (80), 121 (75), 93 (60), 41 and 43 (46), 91 (39), 122 (35), 192 (M^+, 31), 79 and 177 (27), 55 and 105 (25), 77 (24), 29 (20), 108 (19), 41 (15), 27 (13), 53, 69, 81, 94 and 119 (11).

$C_{14}H_{24}$ Calc. C 87.42 H 12.58% Found C 87.62 H 12.69%

c) *2,5-Dimethyl-3-vinyl-hexa-1,3-dien-5-ol* (**44**, 14%). NMR. spectrum: 1.35 (6H, *s*, $(CH_3)_2$C), 1.83 (3H, broad *s*, CH_3—C=), 4.75 to 5.6 (4H, C=CH_2 and C—CH—C=), 7.04 (1H, *d* of *d*, J = 12 and 16.5 Hz, H_2C=CH—C=). Mass spectrum: 43 (100), 67 (38), 109 (36), 41 and 134 (25), 119 (23), 55 (22), 39, 79, 91 (19), 81 and 137 (17), 77 (16), 93 and 95 (12), 27 (10).

$C_{10}H_{16}O$ Calc. C 78.89 H 10.59% Found C 78.91 H 10.18%

d) *Pentanophenone* (13%) and e) *1-phenylpenten-1-ol* (31%), identical with authentic material.

O-Acetylyomogi alcohol (**45**). To 15 g of yomogi alcohol in 15 g of dimethylaniline cooled to 0°, a mixture of 10 g of acetyl chloride and 5 g of acetic anhydride was added dropwise with stirring. The mixture was then heated to 40° for 5 h, and poured into ice and 5% sulfuric acid. The product was extracted with ether, and after the usual washings and concentration, distilled: b.p. 75°/10 Torr. NMR. spectrum: 1.08 (6H, *s*, $(CH_3)_2$C), 1.45 (6H, *s*, $(CH_3)_2$C), 4.7 and 4.95 (2H, mult., C=CH_2), 5.47 (2H, *s*, —CH=CH—), 5.69 (1H, *d* of *d*, J = 10 and 17 Hz, H_2C=CH—C—). Mass spectrum: 85 (100), 43 (83), 127 (39), 41 and 95 (15), 121 (14), 72 and 93 (10), 196 (M^+, <1).

$C_{12}H_{20}O_2$ Calc. C 73.43 H 10.27% Found C 73.33 H 10.50%

Reaction of O-acetylyomogi alcohol (**45**) *with peroxyacetic acid.* O-Acetylyomogi alcohol (**45**) was treated with peroxyacetic acid in methylene chloride solution containing sodium acetate exactly as described above for the preparation of **16**. After 10 h at room temperature, GLPC. showed that the three principal components were (1) unchanged O-acetylyomogi alcohol (13%); (2) 2,5,5-trimethyl-3,4-epoxy-hept-6-en-2-yl acetate (**46**, identical with that described below, (36%); (3) 2,5,5-trimethyl-6,7-epoxy-hept-3-en-2-yl acetate (**47**, 40%). (The yields refer only to the lighter fractions; there were two other substances with much longer retention times, but these were not examined.) For **47**: NMR. spectrum: 0.97, 1.01 (3H each, CH_3—C<, O), 1.43 (6H, *s*, CH_3—C<), 1.89 (3H, *s*, CH_3COO), 2.4 to 2.7 (3H, mult., CH—CH_2), 5.55 (2H, *d*, J = 4.5 Hz, —CH=CH—). Mass spectrum: 43 (100), 85 (72), 127 (25), 41 and 109 (20), 67 (18), 55, 68, 69 and 107 (13), 91 (10), 197 (M-15$^+$, <1).

$C_{12}H_{20}O_3$ Calc. C 67.89 H 9.50% Found C 67.50 H 9.51%

2,5,5-Trimethyl-3,4-epoxy-hept-6-en-2-yl acetate (**46**). The acetylation of 2,5,5-trimethyl-3,4-epoxy-hept-6-en-2-ol (**16**) was carried out in exactly the same way as that of yomogi alcohol, described above. The product had b.p. 94°/10 Torr; d_4^{20} = 0.9622; n_D^{20} = 1.4420. NMR. spectrum:

1.17 (6H, *s*, CH_3—C<), 1.29 and 1.37 (3H each, *s*, CH_3—C<), 1.91 (3H, *s*, CH_3COO), 2.63 and 2.95 (1H each, *d*, J = 2.5 Hz, —CH—CH—), 4.8 to 5.2 (2H, mult., $=CH_2$), 5.75 (1H, *d* of *d*, J = 10 and 17.5 Hz, $—CH=CH_2$). Mass spectrum: 43 (100), 82 (17), 72 (16), 41 and 69 (15), 67 (13).

$C_{12}H_{20}O_3$ Calc. C 67.89 H 9.50% Found C 67.98 H 9.56%

Reaction of artemisia alcohol (**15**) *with peroxyacetic acid.* Treatment of 11.5 g of **15** [7] with 17 g of peroxyacetic acid (40%) as for other epoxidations, with a reaction time of 2 h at room temperature, gave after distillation (b.p. 88°/10 Torr) 9 g of practically pure threo-*2,5,5-trimethyl-2,3-epoxy-hept-6-en-4-ol* (**60**). NMR. spectrum: 1.42, 1.07 (3H each, *s*, CH_3—C—), 1.25 (6H, *s*, CH_3—C—), 2.64 and 3.10 (1H each, *d*, J = 8 Hz, C—CH—CH—OH), 4.75 to 5.15 (2H, mult., $=CH_2$), 5.97 (1H, *d* of *d*, J = 9.5 and 18 Hz, $CH=CH_2$). Mass spectrum: 55 (100), 70 (62), 41 (43), 43 (40), 69 (28), 39 and 73 (13), 101 (12).

$C_{10}H_{18}O_2$ Calc. C 70.54 H 10.66% Found C 70.92 H 10.93%

Reaction of O-acetylartemisia alcohol (**23**) *with peracetic acid.* A mixture of 1 g of **23**[14]) and 0.5 g of sodium acetate in 10 ml of methylene chloride was epoxidized with 1 g of 40% peracetic acid in the usual way. The products were separated by GLPC., and were, in order of elution: (1) Unchanged **23** (20%); (2) Erythro-*2,4,5-trimethyl-2,3-epoxy-hept-6-en-3-yl acetate* (**59**, 7%), NMR. spectrum: 1.03 (6H, *s*, CH_3—C<), 1.22 and 1.29 (3H each, *s*, CH_3-C<), 2.00 (3H, *s*, CH_3COO), 2.62 (1H, *d*, J = 9.5 Hz, CH—CH—C<), 4.62 (1H, *d*, J = 9.5 Hz, CH—CH—$OCOCH_3$), 4.8 to 5.2 (2H, mult., $=CH_2$), 5.88 (1H, *d* of *d*, J = 9.5 and 18 Hz, $CH=CH_2$). Mass spectrum: 43 (100), 85 (19), 41 and 69 (14), 143 (6); (3) Threo-*2,5,5-trimethyl-2,3-epoxy-hept-6-en-3-yl acetate* (**61**, 67%), NMR. spectrum: practically the same as that of the *erythro*-isomer, but with the following differences: 1.02 and 1.08 (3H each), 1.23 (6H), 4.42 (1H, *d*, J = 8.5 Hz, CH—CH—$OCOCH_3$), the coupling constant of the proton CH—C was 8.5 Hz. The mass spectrum was practically identical with that of the *erythro*-compound.

$C_{12}H_{20}O_3$ Calc. C 67.89 H 9.50% Found C 67.64 H 9.56%

The same compound was obtained (identical by NMR., IR. spectra and GLPC. retention time) by acetylation of the alcohol (**60**) described above with acetic anhydride in pyridine; (4) A mixture of threo *and* erythro-*2,5,5-trimethyl-6,7-epoxy-hept-2-en-4-yl acetate* (**62**, 6%), NMR. spectrum: 1.7 to 1.95 (6H, three signals corresponding to various *s* of CH_3—C—), 1.75 (6H, *s*, CH_3—C=), 2.35 to 2.85 (3H, mult., CH—CH_2), 5.1 to 5.3 (1H, —CH—$OCOCH_3$), partially superimposed on a signal with two maxima, 5.3 and 5.47 (1H, C=CH—CH—O). Mass spectrum: 85 (100), 43 (62), 127 (18), 41 and 68 (14), 55 (10), 197 (<1).

Reaction of O-acetylyomogi alcohol epoxide (**46**) *with Dowex 50 resin.* A suspension of 5 g of Dowex 50 resin (acid form) was stirred with 5 g of **46**, and from time to time samples were analysed by GLPC. After about 24 h, about 90% of the starting material had been replaced by a substance having a shorter retention time. This was isolated by concentrating the solution and distilling, b.p. 33–39°/1 Torr. Purification by GLPC. yielded *2-(α,α-dimethylallyl)-3-cis-acetoxy 4,4-dimethyl-oxetan* (**48**, R = $COCH_3$). NMR. spectrum: 0.96, 1.00, 1.23, 1.31 (3H each, *s*, CH_3—C<). 1.99 (3H, *s*, CH_3COO—), 4.08 (1H, *d*, J = 6.5 Hz, O—CH—CH), 4.72 (1H, *d*, J = 6.5 Hz, CH_3COO—CH—CH), 4.8 to 5.2 (2H, mult., C=CH_2), 5.87 (1H, *d* of *d*, J = 9.5 and 18.5 Hz, $—CH=CH_2$). Mass spectrum: 43 (100), 72 (22), 41 and 97 (12), 69 (11), 143 (6).

$C_{12}H_{20}O_3$ Calc. C 67.89 H 9.50% Found C 68.19 H 9.67%

The reaction was continued for a further two days (less time was needed if a few drops of water were added to the mixture), when concentration yielded crystals identified as threo-*2,4-dihydroxy-2,5,5-trimethyl-hept-6-en-3-yl acetate* (**58**), m.p. 81–82° (from hexane). NMR. spectrum:

[14]) A sample of **23** was supplied by Dr. *V. Rautenstrauch.*

1.03 (6H), 1.13 (3H), 1.28 (3H), (all *s*, CH_3—C—), 1.92 (3H, *s*, CH_3COO), 3.62 (1H, *d*, J = 9.5 Hz, CH—C*H*—O), 4.7 to 5.1 (3H, mult., C*H*—O and C=CH_2), 5.81 (1H, *d* of *d*, J = 10 and 17.5 Hz, —C*H*=CH_2). Mass spectrum: 43 (100), 72 (17), 41, 59, 70 and 97 (14), 69 (12), 55 (10), 161 (2). IR. spectrum (0.1% in CCl_4): 3530 cm^{-1} (bonded OH), 3615 cm^{-1} (free OH).

$C_{12}H_{22}O_4$ Calc. C 62.58 H 9.63% Found C 62.55 H 9.63%

*2-(α,α-Dimethylallyl)-3-*cis*-hydroxy-4,4-dimethyl-oxetan* (**48**, R = H). The acetate **48** (R = $COCH_3$) from the previous experiment was added to an excess of lithium aluminium hydride in ether at room temperature, the excess of the reagent decomposed with water, and the product isolated from the filtered ether solution and purified by GLPC. NMR. spectrum: 0.97 (6H, *s*), 1.21, 1.28 (3H each, *s*), 3.93 (2H, broad *s*, O—C*H*—C*H*—O), 4.85 and 5.08 (2H, mult., CH=CH_2), 5.85 (1H, *d* of *d*, J = 9.5 and 18.5 Hz, C*H*=CH_2). Mass spectrum: 72 (100), 55 (58), 97 (51), 41 43 and 57 (49), 69 and 70 (33), 27, 29, 39 and 73 (14), 112 (5).

$C_{10}H_{18}O_2$ Calc. C 70.54 H 10.66% Found C 70.53 H 10.86%

The p-*toluenesulfonate* was prepared from 0.5 g alcohol **48**, 0.57 g of *p*-toluenesulfonyl chloride and 0.34 g of dry potassium hydroxide in 30 ml of dry ether. After 3 h at 0°, the mixture was filtered, concentrated at room temperature and purified by chromatography on silica gel. The pure *p*-toluenesulfonate was eluted with hexane-ether (9:1), but did not crystallize. NMR. spectrum: 0.78, 0.89, 1.20, 1.33 (3H each, *s*, CH_3—C⩤), 2.42 (3H, *s*, CH_3-phenyl), 4.08 (1H, *d*, J = 6.5 Hz, O—C*H*—CH), 4.40 (1H, *d*, J = 6.5 Hz, Ts—O—C*H*—CH), 4.75 to 5.0 (2H, mult., CH=CH_2), 5.71 (1H, *d* of *d*, J = 10.5 and 17 Hz, C*H*=CH_2), 7.3 and 7.7 (4H, two *d*, J = 8 Hz, phenyl).

$C_{17}H_{24}O_4S$ Calc. C 62.95 H 7.46 S 9.88% Found C 62.96 H 7.32 S 9.76%

The *p*-toluenesulfonate was recovered unchanged after heating for one week under reflux with sodium acetate in acetic acid or for eight days with excess tetraethylammonium acetate in acetone at 110° in a sealed tube. After 2 h with excess lithium aluminium hydride in dry tetrahydrofuran, 2-(α,α-dimethylallyl)-3-*cis*-hydroxy-4,4-dimethyl-oxetan, identical with that described above, was recovered as the sole product.

The *sulfite* **50**, prepared from **48** with excess thionyl chloride in dry pyridine, was purified by GLPC. Two incompletely resolved peaks in a ratio of about 4:1 were observed, but separation into pure products was not achieved. NMR. spectrum: ca. 4.1 (1H, two *d* superimposed, J = 6.5 Hz, CH—C*H*—O), ca. 4.55 (1H, two *d*, J = 6.5 Hz, CH—C*H*—O). Mass spectrum: 43 (100), 84 (69), 41 (54), 64 (52), 71 and 85 (46), 55 (45), 29 and 69 (44), 57 (42), 56 (37), 72 (30), 153 (20).

$C_{20}H_{34}O_5S$ Calc. C 62.14 H 8.86 S 8.29% Found C 62.19 H 9.06 S 8.01%

*Reaction of the sulfite of 2-(α,α-dimethylallyl)-3-*cis*-hydroxy-4,4-dimethyl-oxetan with sodium acetate.* A solution of 0.5 g of the sulfite **50** and 3 g of sodium acetate in 30 ml of ethanol was heated for 36 h under reflux. Concentration of the solution showed that about half the sulfite had been transformed into a mixture of products, 90% of which was identical with the original 2-(α,α-dimethylallyl)-3-hydroxy-4,4-dimethyl-oxetan. The following were also identified: (1) One isomer of 2,5,5-trimethyl-hepta-1,6-diene-3,4-diol (**51**), identical in retention time and mass spectrum with the product obtained in the lithium aluminium hydride reduction of the acetoxy-p-tosyl-diol (see below), but with an NMR. spectrum lacking some of the signals, in particular, 3.28 (1H, *d*, J = 6.5 Hz, —CH—C*H*—O), 3.96 (1H, *d*, J = 6.5 Hz, C=C—C*H*—O); for the remaining signals, see below. (2) 2-(α,α-Dimethylallyl)-3-ethoxy-4,4-dimethyloxyetan (**48**, R = C_2H_5), NMR. spectrum: 0.97, 1.00, 1.28, 1.31 (3H each, *s*, CH_3—C—), 1.33 (3H, *t*, J = 5 Hz, CH_3—CH_2—), 3.91 (broad *q*, CH_3—CH_2—O), superimposed on 4.10 (*d* with further coupling, J = 6.5 Hz, O—C*H*—CH), 4.50 (1H, *d* with further coupling, CH—C*H*—O), 4.8 to 5.2 (2H, mult., CH=CH_2), 5.90 (1H, *d* of *d*, J = 9.5 and 18 Hz, —C*H*=CH_2). Mass spectrum: 43 (100), 41 (72), 55 (66), 29 and 69 (62), 72 (50), 83 (40), 97 (38), 71 (31), 100 and 73 (28), 59 (25), 111 (15), 125 (6).

Threo-*2,3,4-trihydroxy-2,5,5-trimethyl-hept-6-ene*, was prepared by reduction of *threo*-2,4-dihydroxy-2,5,5-trimethyl-hept-6-en-3-yl acetate with excess lithium aluminium hydride in ether. Mp. 122–123° (hexane). Mass spectrum: 43 (100), 59 (96), 70 (87), 72 (82), 55 (71), 97 (68), 41 (55), 69 (40), 71 (36), 57 (29), 31 (20), 39, 42, 83 and 112 (14).

$C_{10}H_{20}O_3$ Calc. C 63.79 H 10.71% Found C 63.95 H 10.68%

Reduction of the toluenesulfonate of threo-*2,4-dihydroxy-2,5,5-trimethylhept-6-en-3-yl acetate with lithium aluminium hydride.* To a solution of 1.1 g of acetoxy-diol **58** and 1.9 g *p*-toluenesulfonyl chloride in dry ether were added in small portions 1.1 g of powdered potassium hydroxide (dry) at 0°. The mixture was then stirred for 2 h, filtered, and concentrated to dryness at room temperature. The residue, taken up in 5 ml dry ether, was added to 1.5 g of lithium aluminium hydride in 50 ml dry ether and after 30 min, the excess hydride was decomposed with water, the solution filtered and the solvent removed. On adding a little pentane to the residue, 80 mg of crystals were obtained which had the same m.p. and mixed m.p. as the triol described above. The remainder of the product, soluble in pentane, was purified by GLPC., giving in order of elution: (1) Yomogi alcohol epoxide, 12%, identical with authentic material; (2) *2,3-Dihydroxy-2,5,5-trimethyl-hept-6-ene* (**52**, 14%), identical with material prepared by a different route (see below); (3) *2,4-Dihydroxy-2,5,5-trimethyl-hept-6-ene* (**53**, 46%), NMR. spectrum: 0.98 (6H, *s*, CH_3—C<), 1.20 (6H, broad *s*, CH_3—C<), 4.4 to 4.7 (2H, mult., >CH—O and O*H*), 4.7 to 5.1 (2H, mult., CH=CH_2), 5.78 (1H, *d* of *d*, J = 9.5 and 18 Hz, CH=CH_2). Mass spectrum: 70 (100), 59 (96), 43 (83), 85 (67), 41 (53), 55 (48), 57 (40), 69 (27), 29 (18), 31, 39, 42, 71 and 103 (12), 139 (4).

$C_{10}H_{20}O_2$ Calc. C 69.72 H 11.70% Found C 69.50 H 11.62%

(4) *3,4-Dihydroxy-2,5,5-trimethyl-hepta-1,6-diene* (**54**, 27%), NMR. spectrum: 1.07 (6H, *s*, CH_3—C<), 1.73 (3H, *s*, CH—C=), 2.40 (1H, *d*, O*H*), 3.0 to 3.4 (2H, mult. consisting of three *d*, >CH—O and O*H*), 3.90 (*d*, J = 6.0 Hz) and 3.96 (*d*, J = 6.5 Hz), (together 1H, O—CH—CH, 2 isomers), 4.8 to 5.2 (4H, mult., C=CH_2), 5.93 (1H, *d* of *d*, J = 9.5 and 17.5 Hz, CH=CH_2). Mass spectrum: 43 (100), 72 (88), 70 (43), 55 (42), 41 (39), 57 (33), 71 (16), 39 and 69 (14), 83 (7), 99 and 100 (1).

$C_{10}H_{18}O_2$ Calc. C 70.54 H 10.66% Found C 70.15 H 10.62%

2,3-Epoxy-2,5,5-trimethyl-hept-6-ene. A solution of 40 g of 2,5,5-trimethyl-hepta-2,6-diene (**9**) in 500 ml of methylene chloride was treated with 36 g of sodium acetate and 70 g of peroxyacetic acid for 5 h at 0° to 15°. After the usual working up, 40 g of crude product were purified by distillation, b.p. 52°/10 Torr.

$C_{10}H_{18}O$ Calc. C 77.86 H 11.76% Found C 77.56 H 11.80%

2,3-Dihydroxy-2,5,5-trimethyl-hept-6-ene (**52**). A solution of 10 g of the above epoxide was added dropwise to 20 ml of 10% aqueous sulfuric acid and 10 ml of dioxan. After 15 m n the product was extracted as usual, and distilled, b.p. 108–110°/10 Torr. The spectra were identical with the sample obtained from the lithium aluminium hydride reduction of the *p*-toluenesulfonate described above. NMR. spectrum: 1.05 (12H, *s*, CH_3—C<), 1.31 (2H, *d*, J = 4 Hz, —CH_2—CH), 3.2 to 3.5 (1H, mult., superimposed on O*H*, —CH_2—C*H*OH), 4.65 to 5.1 (2H, mult., CH=CH_2), 5.83 (1H, *q*, J = 10 and 17.5 Hz, CH=CH_2). Mass spectrum: 59 (100), 41, 43 and 69 (32), 70 (30), 55 and 72 (21), 71 (16), 97 (9).

$C_{10}H_{20}O_2$ Calc. C 69.72 H 11.70% Found C 69.65 H 11.84%

Reaction of threo-*2,4-dihydroxy-2,5,5-trimethyl-hept-6-en-3-yl acetate* (**49**, R = $COCH_3$) *with acetone.* One drop of concentrated sulfuric acid was added to a solution of 0.5 g of **49** (R = $COCH_3$) in 5 ml of acetone. The reaction was followed by testing small amounts with thin layer chromatography; when no more starting material was present (24 h), dry potassium carbonate was added, the mixture filtered, and concentrated. The product was purified by chromatography on silica gel in hexane. Concentration of the first fractions gave a substance which was submitted to molecular distillation.

$C_{15}H_{26}O_4$ Calc. C 66.63 H 9.69% Found C 66.62 H 9.20%

GLPC. of this product gave two peaks, and although they were not completely separated, concentration of each was achieved sufficiently to be able to distinguish their NMR. spectra. That of compound a, *4-[1'-acetoxy-2',2'-dimethyl-but-3'-en-1'-yl]-2,2,5,5-tetramethyl-1,3-dioxolan:* 1.0 to 1.4 (18H, many signals, CH_3—C<), 1.93 (3H, *s*, CH_3COO), 3.65 (1H, *d*, J = 10 Hz, CH—CH—O), 4.68 (*d*, J = 10 Hz, CH—C*H*—$OCOCH_3$), superimposed on signals from 4.75 to 5.1 (3H together, CH=CH_2), 5.86 (1H, *d* of *d*, J = 9.5 and 18 Hz, CH=CH_2). NMR. spectrum of compound b, *4-(α,α-dimethylallyl)-5-*cis*-acetoxy-2,2,6,6-tetramethyl-1,3-dioxan:* 0.97 (6H), 1.02

(3H), 1.33 (9H), (CH_3—C<), 1.94 (3H, *s*, CH_3COO), 3.39 (1H, *d*, J = 7 Hz, CH—C*H*—O), 4.64 (1H, *d*, J = 7 Hz, CH—C*H*—$OCOCH_3$), 4.7 to 5.1 (2H, mult., C=CH_2), 5.80 (1H, *d* of *d*, J = 10 and 18 Hz, —C*H*=CH_2).

The mixture of the two acetates just described was reduced with excess lithium aluminium hydride in dry ether, and after working up as usual, the products were separated by GLPC. That, m.p. 50°, with shorter retention time[15]) was ascribed the structure of *4-[1'-hydroxy-2',2'-dimethyl-but-3'-en-1'-yl]-2,2,5,5-tetramethyl-1,3-dioxolan* (**57**, R = H), largely on account of the fission in the mass spectrum to a fragment at *m/e* 129[16]), which would be unlikely in the other isomer. Isomer, mp. 50°: NMR. spectrum: 1.07 (6H), 1.16 (3H), 1.25 (6H), 1.30 (3H), (all CH_3—C<), 3.1 to 3.6 (2H, mult., O—C*H*—C*H*—O), 4.8 to 5.2 and 5.5 to 6.1 (C*H*=CH_2). Mass spectrum 43 (100), 59 (96), 70 (65), 55 (51), 101 (33), 41 (29), 71 (26), 69 (22), 129 and 213 (18). The isomer, m.p. 36°, with longer retention time was ascribed the structure of *4-(α,α-dimethylallyl)-5-cis-hydroxy-2,2,6,6-tetramethyl-1,3-dioxan* (**56**, R = H). NMR. spectrum: 1.06 (6H), 1.13 (3H), 1.25 (3H), 1.33 (6H), (all CH_3—C<), 3.2 to 3.4 (2H, appears as signal of 5 Hz width at half height, and two maxima, O—C*H*—C*H*—O), 4.8 to 5.2 (2H, mult., CH=CH_2), 6.0 (1H, *d* of *d*, J = 10 and 18 Hz, C*H*=CH_2). Mass spectrum: 59 (100), 43 (84), 97 (80), 72 (65), 112 (37), 41 (33), 69 (30), 55 (21), 57, 71 and 83 (18), 213 (2.5), 129 (0).

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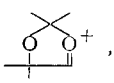
[15]) It was established that the retention times of the two alcohols correspond to those of the acetates, the acetate with shorter retention time giving the alcohol also with shorter retention time.

[16]) This fragment corresponds to loss of the side chain from the dioxalan ring:  , and is also present in the mass spectrum of the corresponding acetate, but not in that of the dioxane acetate.

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197. Applications synthétiques de la cyclisation d'alcools tertiaires γ-éthyléniques en α-bromotétrahydrofurannes sous l'action du N-bromosuccinimide. II.

Cyclisation du (±)-nérolidol en diméthyl-2,5-(méthyl-4-pentène-3-yl)-2-cycloheptène-4-one, tétraméthyl-3,3,7,10-oxa-2-tricyclo[5.5.0.0^{1,4}]-dodécène-9, β-acoratriène, cédradiène-2,8, *épi*-2-α-cédrène et α-cédrène[1)2)]

par **E. Demole, P. Enggist** et (en partie) **Mlle C. Borer**

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Dédié au Dr *Roger Firmenich* à l'occasion de son 65e anniversaire

(24 VIII 71)

Summary. The ionic reaction of (±)-nerolidol (*cis/trans* mixture) with N-bromosuccinimide in CCl_4 at room temperature afforded 2-methyl-2-vinyl-5-(2-bromo-6-methyl-hept-5-en-2-yl)-tetrahydrofuran (**4**) in high yield. This compound was readily dehydrobrominated by refluxing collidine to the intermediate allyl vinyl ether **8**, which immediately undergoes [3,3]-sigmatropic rearrangement to 2,5-dimethyl-2-(4-methylpent-3-enyl)-cyclohept-4-enone (**11**). By treatment with $SnCl_4$ in nitromethane at room temperature **11** was in turn cyclised to *cis*-3,3,7,10-tetramethyl-2-oxa-tricyclo[5.5.0.0^{1,4}]dodec-9-ene (**12**), an oxetane closely related to the sesquiterpene *carotol.* This oxetane (**12**) underwent a stereospecific ring contraction when treated by *Lewis*

[1)] Ce travail a fait l'objet d'une Communication préliminaire [1].
[2)] Pour la première publication de cette série voir [2].