The Cyclisation of Geraniol in Superacids

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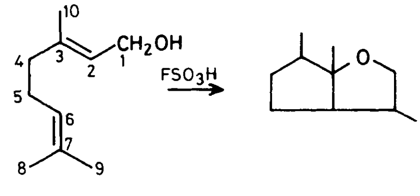
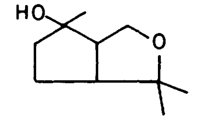
The cyclisation of geraniol (1) [(*E*)-3,7-dimethylocta-2,6-dien-1-ol] in FSO_3H-SO_2 at −78 °C to yield the iridoid ether 3β,4α,6aα-trimethyl-*cis*-perhydrocyclopenta[*b*]furan was investigated. Decomposition of the ether in FSO_3H at room temperature gave the 2-isopropyl-1,3-dimethylcyclopentenium ion, whose structure was confirmed independently. Synthesis of geraniol labelled with deuterium on the *gem*-dimethyl group and on the single methyl group established the positions of these methyls in the iridoid ether. Synthesis of 2-(1-hydroxy-2,2-dimethylcyclopentyl)propan-1-ol established that the ion derived from it did not lie on the reaction pathway.

The cyclisation of geraniol (1) [(*E*)-3,7-dimethylocta-2,6-dien-1-ol] in dilute acids gives complex mixtures of monoterpenoids,[1] but reaction with superacids is reported[2] to give an iridoid ether (2) (3β,6α,6aα-trimethyl-*cis*-perhydrocyclopenta[b]furan). The reaction is believed to involve protonation of the non-allylic double bond as the first step, unlike the reaction in dilute acids, where ionisation of the hydroxy group is the initial reaction. The product, however, differs considerably from the product (3) of cyclisation of geraniol with thallium perchlorate,[3] a reaction which is also believed to involve initial attack of the reagent on the non-allylic double bond. The route from (1) to (2) is clearly complex, and to-date has been the subject of speculation only. We have therefore investigated the reaction by means of deuterium-labelling techniques.

Banthorpe *et al.*,[2] report that (2) is formed from (1) at −78 °C, but on warming to +20°C is converted into an ionic species which they were unable to positively identify by ^1H n.m.r. spectroscopy. We therefore repeated their experiment, warming a solution of the ether (2) in FSO_3H-SO_2 to room temperature for two hours, after which it was cooled, fresh liquid SO_2 added, and the spectrum run at −30 °C. Ring opening and dehydration of (2) was expected to give the known[4] ion (4), but it was not detected. Instead, we observed the spectrum of a symmetrical species, subsequently identified as (5). Proof of the identity of (5) was obtained by synthesis of the diene (6), which had to be stored in solution, since it polymerised rapidly at room temperature, but could be extracted from CS_2 solution at −78 °C into FSO_3H-SO_2 to give the ion (5). Earlier studies[4] of the ion (4) have shown that it is stable at room temperature over a period of hours, and does not rearrange to give (5); we conclude that (5) must have been formed from the iridoid ether. This implies that either a complex rearrangement has taken place on ring opening, or the structure of (2) is incorrect. To check this, we opened the ring of (2) using BF_3 diethyl etherate–acetic anhydride, a method reported[2] to give the iridenyl acetate, which could be reduced to the alcohol, which recyclised[2] to (2) in FSO_3H-SO_2 at −78 °C. We dissolved the acetate in FSO_3H-SO_2 at −78 °C, but the ^{13}C spectrum showed no alkenyl cation, no olefinic carbons, no protonated carbonyl centres, and there was no indication that acetic acid had been eliminated. Instead, the spectrum was consistent with the formation of two similar delocalised oxenium ions, presumably by attack of the carbonyl at either of two possible carbenium ion centres. We suggest that the major ion is due to formation of a six-membered ring (7) and the minor due to formation of a seven-membered ring (8), the ratio being roughly 2:1. We were not able to confirm identifications, as we could not obtain these species from other sources. After warming the mixture to room temperature for 30 min, the spectrum was recorded at −30 °C. Protonated acetic acid was present, indicating opening of the oxenium ions followed by *O*-alkyl cleavage. The symmetrical 2-isopropyl-1,3-dimethylcyclopentenyl cation (5) was formed, but the major ion formed, in the ratio 2:1, was an alkenyl cation with its charge delocalised across three tertiary carbon atoms. This ion was assigned the structure (9). We suggest that these ions can arise from the oxenium ions as shown below.



(1) (2)



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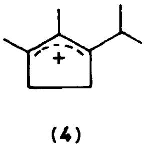

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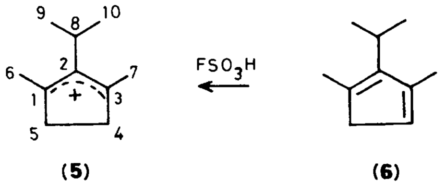
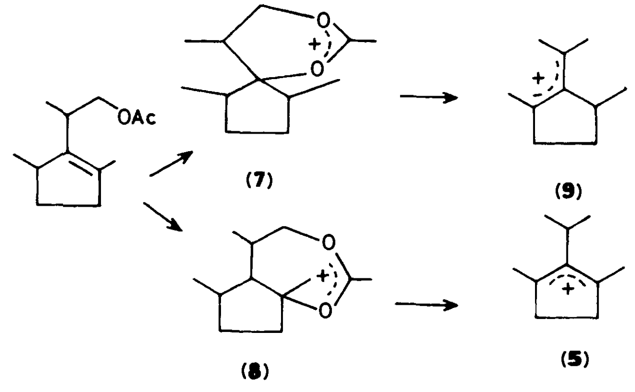
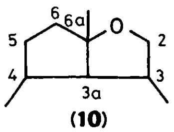


(5) (6)



The ions (5) and (9) showed no sign of equilibration.

We have now formed (5) directly from the iridoid ether, and



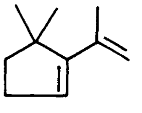
(10)

from an iridenyl acetate made by opening the ring of the iridenyl ether. The iridenol is known to cyclise back to the iridoid ether. We suggest, then, that the actual structure of the iridoid ether is (**10**) rather than (**2**).

The ^{13}C n.m.r. spectrum of the protonated ether was readily assigned, and is given in the Table. The ^{1}H n.m.r. spectrum was recorded at 400 MHz, but we were still unable to evaluate accurately the rather broad couplings of the cyclopentane ring protons.

Mechanism of Formation of the Iridoid Ether.—The initial strategy of the investigation was to attempt the cyclisation of substrates similar to geraniol. To this end, the reactions of geranyl chloride in SbF_5–SO_2ClF, myrcene in FSO_3H–SO_2, and linalol in FSO_3H–SO_2 were studied at −78° C. In all cases, only polymeric materials were observed. However, reaction of geranyl chloride in FSO_3H–SO_2 showed peaks indicative of the presence of an alkenyl cation among extensive polymers, which made assignment of a structure to the cation impossible.

We therefore examined geraniol in FSO_3H–SO_2 as reported,[2] and found the peaks of the protonated iridoid ether (**10**) in addition to the alkenyl cation peaks found using geranyl chloride as substrate. Quenching of the reaction, followed by preparative gas chromatography, yielded (**10**) plus a small amount of material identified from ^{1}H n.m.r. and mass spectrometric data as the diene (**11**).



(11)

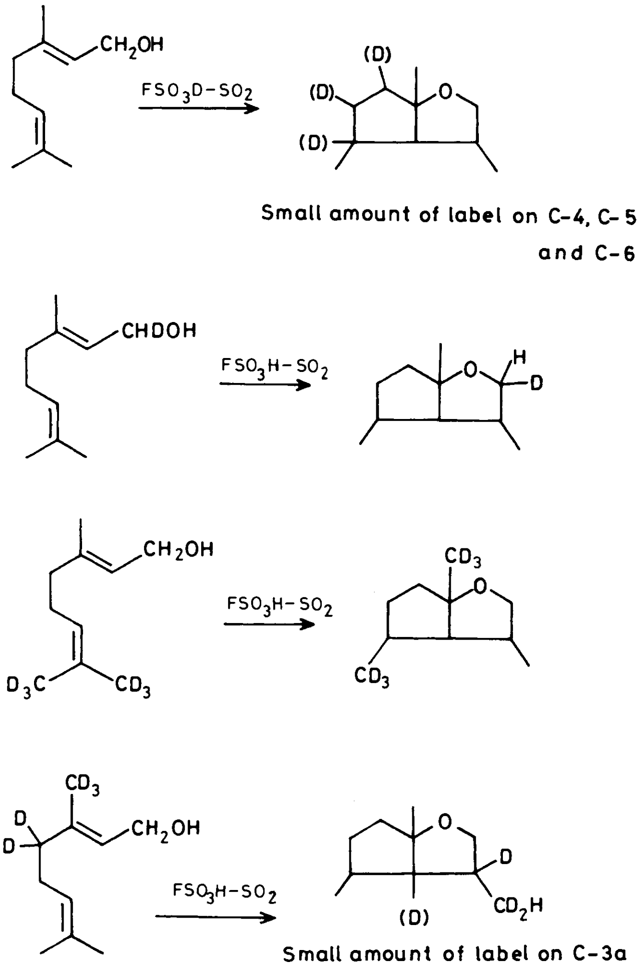
We sought to examine the formation of (**10**) from (**1**) by preparing a series of samples of (**1**) labelled with deuterium, then following the position of the deuterium by using the collapse of the ^{13}C n.m.r. signal of any carbon atom carrying a deuterium atom rather than a proton.

Geraniol was readily labelled at C-1 by oxidation to the aldehyde, followed by reduction with lithium aluminium deuteride.

Labelling of geraniol with deuterium on C-8 and C-9 was accomplished by the method of Bunton, Leresche, and Hachey,[5] in which 5-iodopentan-2-one was converted into the acetal with ethylene glycol, and thence by reaction of the triphenylphosphonium iodide with [$^{2}H_6$]acetone to yield the labelled 6-methylhepten-2-one. Reaction of trimethyl phosphonoacetate with the ketone yielded methyl geranate, with methyl nerylate impurity, from which labelled geraniol containing 19% labelled nerol was obtained. Since both nerol and geraniol are reported to yield (**10**) on reaction in fluorosulphuric acid, the material was used without further purification.

Labelling of geraniol on C-4 and C-10 was accomplished by a similar route; unlabelled 6-methylhepten-2-one was exchanged with D_2O to incorporate the label, then reacted as before to yield geraniol with nerol impurity.

The reactions of the substrates were carried out in FSO_3H–SO_2 at −78 °C. ^{13}C N.m.r. spectra were recorded, then the samples quenched in aqueous potassium carbonate in methanol. The results of these experiments are summarised in the Scheme.



Small amount of label on C-4, C-5 and C-6

Small amount of label on C-3a

Scheme.

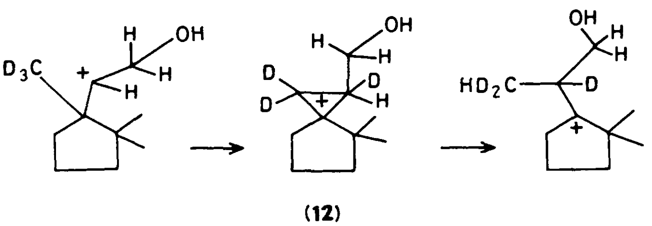
The cyclisation of geraniol in FSO_3D yielded a cleaner product than cyclisation in the protonated acid, the alkenyl cation being absent and the polymer reduced. There was some deuterium incorporation, observed by reduction in size of the C-3, -4, and -5 peaks; this was not due to exchange of the ether in FSO_3D, as no further deuterium was incorporated on standing.

Cyclisation of geraniol labelled on C-1 showed no shift of label; clearly, the hydroxy group is not shifted in the reaction. The shift of the labelled methyl groups, C-8 and C-9 to become the methyl groups on C-4 and C-6a in the iridoid ether appeared to be quantitative. The geraniol labelled on C-4 and C-10 gave a more complicated reaction however. Mass spectrometry of the product showed an average label retention of 3.5 deuterium atoms. The ^{1}H n.m.r. spectrum of the product showed the methyl group on C-3 as a small singlet, its size indicating an average of 0.8 of a proton, and its lack of splitting indicating extensive labelling of C-3 of the iridoid ether. In confirmation of this, the ^{1}H n.m.r. spectrum showed the peak at δ 4.00 had collapsed to a doublet, J 8 Hz. The ^{13}C n.m.r. spectrum showed a small reduction in the peak due to C-3a, suggesting that it contained some label.

The results of the first three labelling experiments are fairly straightforward, the last one more complex. The obvious route to loss of a deuterium from CD_3 is *via* the vinyl group, followed by protonation, but this process would probably be repeated, and result in loss of all three deuterium atoms. A possible explanation of the result is a reaction *via* a cyclopropane intermediate, such as (**12**) shown below.

Table. ^{13}C N.m.r. shifts (p.p.m. from Me_4Si) in FSO_3H–SO_2 at −78 °C

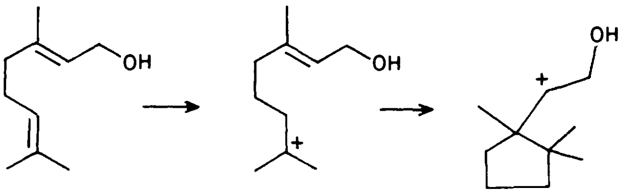
Compd.	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
(4)	239	151	247	44	38	22	7	35	18	18
(5)	244	163	244	48	48	28	28	27	20	20
(9)	230	147	44	30	39	29	15	226	19	17
	C-1	C-2	C-3	C-3a	C-4	C-5	C-6	C-6a		
(10)	—	82	39	50	32	25	34	114	Me on C-3 Me on C-4 Me on C-6a	18 14 20



(12)

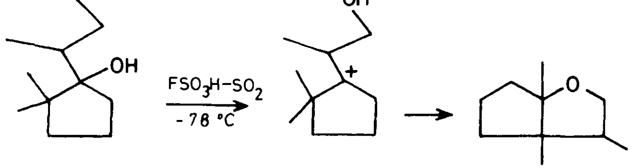
Movement of three deuterium atoms and a proton around the cyclopropane ring would give a labelling pattern close to that observed. It remains unclear, however, why this route should be preferred to a simple methyl shift.

A possible mechanism for geraniol cyclisation starts with protonation of the non-allylic double bond, followed by cyclisation to give the cyclopentane ring.



A number of possible reactions to put the substituents in the correct positions can be drawn; they mostly involve the ion (**13**) at some stage, and as this is a possible precursor of both the ether (**10**) and the diene (**11**) it appears to be a key intermediate in possible schemes. However, it does seem likely that (**13**) could cyclise readily to an ether (**14**) without further rearrangement.

To resolve this problem the probable precursor of ion (**13**), 2-(1-hydroxy-2,2-dimethylcyclopentyl)propan-1-ol (**15**), was prepared by reaction of 2,2-dimethylcyclopentanone with ethyl 2-bromopropionate and zinc.

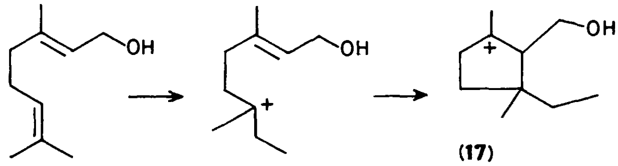


(15) **(13)** **(14)**

Reaction in FSO_3H–SO_2 at −78 °C gave the ether (**14**) in 60% yield, together with 12% of an unidentified ether. The diene was not detected. The ^1H n.m.r. spectrum of (**14**) was very different from that of (**10**). The protons 2e- and 2a-H occur at δ 3.8 (triplet, *J* 7.8 Hz) and δ 3.25 (doublet of doublets, *J* 10.8 Hz, 8 Hz), and 3-CH_3 occurs at δ 1.92. Thus, the proton which is *trans* to 3-H is furthest upfield. If the C-3-Me is α, as are C-6a-Me and C-3a-Me, this proton will be deshielded; if the C-3-Me is β, this proton is no longer affected by the influence of the methyl groups on C-3a and C-6a, and is instead shielded by the oxygen as well as the methyl group on C-3, whereas 2e-H is deshielded. On this basis the methyl group on C-3 has a β-orientation. The ether (**14**) is thus 3β,3aα,6aα-trimethyl-*cis*-perhydrocyclopenta[*b*]furan. It is possible to apply similar arguments to the stereochemistry of the original iridoid ether (**10**), but the position of the methyl on C-4 makes the interpretation less certain.

This result shows that the ion (**13**) does not lie on the path from geraniol to the iridoid ether (**10**). Rearrangement of an ether once formed is unlikely,[6] since even at −78 °C the thermodynamically stable ether is usually formed. We conclude, then, that the methyl shifts involved in this reaction must take place at an earlier stage, before the hydroxy carbocation is capable of cyclisation, otherwise cyclisation will occur prematurely.

Our work on ether formation in superacids[6] shows that a CH_2OH group attached to a ring will not cyclise, whereas a CH_2CH_2OH group cyclises readily, even if a methylene hydrogen is replaced by an alkyl substituent. The mechanism of formation of (**10**) may involve the extensive rearrangements of alkyl groups taking place before the $CH(Me)CH_2OH$ group is formed; this precludes the initial step suggested above. A possible route to a non-cyclisable cyclopentane derivative is shown below.



(16) **(17)**

The first step, formation from geraniol of (**16**), proceeds by a process known to occur in acyclic terpenoids[7] and is followed by cyclisation to (**17**). However, possible routes from (**17**) to (**10**) have so far been excluded by the pattern of methyl shifts shown by our labelling experiments.

The problem of the mechanism of the rearrangement remains unsolved.

Experimental

^1H N.m.r. spectra were recorded on a Perkin-Elmer R34 (220 MHz) spectrometer using $CDCl_3$ as solvent and tetramethylsilane (Me_4Si) as internal standard. Decoupling experiments were carried out on a Bruker WM250 (250 MHz) spectrometer operating in the F.T. mode. ^{13}C N.m.r. spectra were recorded on a Varian XL 100 (25.2 MHz) spectrometer with $CDCl_3$ as solvent and Me_4Si as internal standard for neutral solutions and sulphur dioxide or sulphuryl chloride fluoride as solvent for superacidic solutions with an external deuterium lock of [$^2H_6$]acetone or [$^2H_4$]methanol and external standard of Me_4Si enclosed within a 5 mm n.m.r. tube.

I.r. spectra were recorded on a Perkin-Elmer 1320 i.r. spectrometer using either liquid films or Nujol mulls. Mass spectra were recorded on an A.E.I. MS 12 spectrometer. Accurate mass and g.l.c.–mass spectral analysis were recorded on a VG 707OE mass spectrometer.

Reaction mixtures were analysed by Perkin-Elmer F17 and Dani 3800 gas–liquid chromatographs with flame ionisation detectors using nitrogen as the carrier gas.

The F17 employed a 5 ft stainless steel column of 2 mm internal diameter using 10% OV351 on Celite as support material. The Dani 3800 employed a 25 m capillary column with 0.3 mm internal diameter and coated with OV351.

Preparative separation were carried out on a Perkin-Elmer F21 instrument using a 10 ft glass column of 3 mm internal diameter containing Celite 68–80 mesh as support, and 20% Reoplex 100 as coating.

2-*Methyl*-5-(2-*methylpropanoyl*)*furan*. This was prepared by a modification of Gilman's method.[8] A mixture of 2-methylfuran (41 g, 0.5 mol) and methyl propionic anhydride (80 g, 0.51 mol) was stirred in a vessel equipped with a reflux condenser and cooled to −10 °C in a salt–ice-bath. Boron trifluoride diethyl etherate (6 ml) was added in one aliquot and the cooled solution was stirred for 30 min. To the mixture aqueous sodium hydroxide (200 ml; 2M) was added and the mixture stirred for 2 h. The organic layer was then extracted with dichloromethane, dried ($MgSO_4$), and the solvent removed under reduced pressure. Distillation (60 °C at 1 mmHg) yielded the product (23.5 g); M^+ 152; δ 1.18 (6 H, d, CHMe_2), 2.38 (3 H, s, furyl-Me), 3.29 (1 H, m, CHMe$_2$), 6.18 (1 H, d, furyl), and 7.14 (1 H, d, furyl); $\nu_{max.}$ 3 120, 2 970, 2 930, 1 670, 1 510, and 1 030 cm^{-1}.

2-*Methyl*-5-(2-*methylpropyl*)*furan*.[9] 2-Methyl-5-(2-methylpropanoyl)furan (20 g) was added to a solution of ethylene glycol (100 ml), potassium hydroxide (25 g), water (7 ml), and hydrazine hydrate (15 g). The solution was then refluxed for 2 h and then steam distilled to give the product (12 g); M^+ 138; $\nu_{max.}$ 2 960, 1 570, 1 020, and 780 cm^{-1}.

7-*Methylocta*-2,5-*dione*. 2-Methyl-5-(2-methylpropyl)furan (11 g, 0.08 mol) was added to a solution of water (6 ml) and acetic acid (15 ml). Sulphuric acid (1 ml) was added and the mixture refluxed for 5 h. The product was extracted from the cooled mixture with pentane, dried, and the solvent removed under reduced pressure. Distillation gave the product (6.8 g; 98—99 °C at 6 Torr; lit.,[10] 100 °C at 12 Torr); M^+ 156; δ 0.93 (6 H, d, CHMe_2), 2.18 (3 H, s, Me), 2.2 (1 H, m, CHMe$_2$), 2.3 (2 H, m, CH_2Pr^i), and 2.68 (4 H, s, CH_2CH_2); $\nu_{max.}$ 2 960, 1 715, 1 370, and 1 160 cm^{-1}.

3-*Methyl*-2-(*prop*-1-*enyl*)*cyclopent*-2-*enone*. 7-Methylocta-2,5-dione (6.5 g, 0.04 mol) was added to a 2% aqueous solution of sodium hydroxide (75 ml) and methanol (10 ml) and refluxed for 3 h. On cooling, the solution was extracted into ether, dried, and the ether removed under reduced pressure. The pure product (6.1 g) was obtained on distillation (75—76 °C at 6 mmHg); M^+ 138; δ 1.15 (6 H, d, CHMe_2), 2.05 (3 H, s, Me), 2.37 (4 H, q, CH_2CH_2), and 2.79 (1 H, m, CHMe$_2$); $\nu_{max.}$ 2 960, 1 695, 1 640, and 1 385 cm^{-1}.

2-*Isopropyl*-1,3-*dimethylcyclopenta*-1,3-*diene* (**6**). The Grignard reagent methylmagnesium iodide was prepared by the addition of methyl iodide (5.15 g, 2.5 equiv.) to magnesium (0.7 g, 0.03 mol) in ether (30 ml). This suspension was cooled to −5 °C in an ice–salt-bath and 2-isopropyl-1-methylcyclopent-1-en-3-one (2 g, 0.0145 mol) in ether (20 ml) added slowly keeping the reaction vessel cold. The mixture was then stirred for 30 min and quenched with iced water, keeping the temperature of the reaction mixture below 5 °C. Hydrochloric acid (0.5M) was added to the slurry until pH 4 and the mixture extracted with ether. The ethereal layer was dried ($MgSO_4$), followed by removal of the ether under reduced pressure to give a product 95% pure by g.l.c., which was used immediately since it polymerised readily; M^+ 136; δ 1.17 (6 H, d, CHMe_2), 1.95 (3 H, s, CH$_2$CMe), 1.98 (3 H, m, CH=CMe), 2.7 (2 H, m, CH_2), 2.84 (1 H, m, CHMe$_2$), and 5.8 (1 H, s, CH=); $\nu_{max.}$ 2 940, 1 380, 1 050, and 730 cm^{-1}.

2-(2,5-*Dimethylcyclopent*-1-*enyl*)*propyl acetate*.[2] The bicyclic ether 3β,4α,6aα-trimethyl-*cis*-perhydrocyclopenta[*b*]-furan (1 g) in acetic anhydride (5 ml) and ether (2.5 ml) was added dropwise to boron trifluoride diethyl etherate (5 ml) in ether (2.5 ml) and the temperature kept below 0 °C by a salt–ice-bath. The solution was allowed to reach room temperature over 1 h then quenched by the addition to 50 ml of iced water containing potassium carbonate (10 g). The ethereal layer was separated and the aqueous layer extracted with ether then pentane. The organic extracts were combined, dried ($MgSO_4$), and the solvent removed under reduced pressure. The oil produced was eluted with 5% ether–pentane down a 20 cm Florisil column, collected, and the solvent removed to give a product which was 91% pure by g.l.c. and shown to be the required acetate by its i.r. spectrum; $\nu_{max.}$ 2 900, 1 739, 1 230, and 1 030 cm^{-1}, consistent with that recorded previously.[2]

Geranyl chloride[11] [(*E*)-3,7-*dimethylocta*-2,6-*dienyl chloride*]. A solution of geraniol (50 g, 0.33 mol) and triphenylphosphine (85.1 g, 0.33 mol) in dry tetrachloromethane (200 ml) was refluxed for 2 h. The solvent was then removed under reduced pressure and the residue extracted with pentane and filtered through Celite. Removal of the pentane and distillation of the residue gave geranyl chloride, 49—51 °C at 0.55 mmHg; M^+ 174, 172; δ 1.56 (3 H, s, Me), 1.68 [6 H, s, (Me)$_2$], 2.08 [4 H, m, (CH$_2$)$_2$], 4.00 (2 H, d, J 9 Hz, CH$_2$Cl), 5.08 (1 H, m, vinyl), and 5.43 (1 H, m, vinyl); $\nu_{max.}$ 2 950 and 1 590 cm^{-1}.

Quenching of the Geraniol Carbocation.—A solution of geraniol in FSO_3H–SO_2 at −78 °C was quenched in H_2O–MeOH–K_2CO_3 as described later. Extraction with pentane and solvent removal gave a brown oil, from which volatile components were removed by vacuum transfer, and the polymeric residue discarded. The volatile components were purified by preparative-scale gas chromatography using a Perkin-Elmer F21 chromatograph with a 10 ft × 3 mm glass column, with stationary phase consisting of 10%. Reoplex 100 coated on 60—80 mesh Celite. The volatile products were 3β,4α,6aα-trimethyl-*cis*-perhydrocyclopenta[*b*]furan, and a compound whose mass spectrum showed its mass ion at m/z 136, whose ^{13}C n.m.r. spectrum showed two double bonds, and which had $\nu_{max.}$ at 3 040, 2 950, 2 900, 1 600, 895, and 815 cm^{-1}. This suggested a cyclic diene; the ^{1}H n.m.r. spectrum consisted of δ 5.61 (1 H, br m), 4.95 (1 H, m), 4.90 (1 H, m), 2.12 (2 H, br m), 1.80 (3 H, dd), 1.45 (2 H, t), and 1.05 (6 H, s). The peak at δ 1.80 (3 H, dd) indicates coupling through a double bond with two vinyl protons, consistent with the structure (**11**), 2-isopropenyl-1,1-dimethylcyclopent-2-ene.

Geranial (trans-*citral*). Chromic acid from a mixture of sodium dichromate (10 g), 98% sulphuric acid (7.5 ml), and water (10 ml), was dripped into a rapidly stirring solution of geraniol (10 g) in ether (40 ml) cooled in an ice-bath. The mixture was stirred for 1.5 h at ambient temperature then the ether layer was separated and the aqueous layer washed with ether (2 × 50 ml). The ether extracts were combined and stirred overnight over powdered calcium chloride to remove residual geraniol. The solid was removed by filtration and ether removed under reduced pressure leaving geranial (5.8 g); M^+ 152; δ 5.9

(1 H, d, *J* 8 Hz, $\mathrm{CH{=}O}$), 5.1 (1 H, m, vinyl unconjugated), 4.17 (1 H, m, *J* 8 Hz, vinyl conjugated), 2.16 (3 H, s, $\mathit{Me}\mathrm{C{=}CHCHO}$), 2.0—2.1 [4 H, m, $\mathrm{(CH_2)_2}$], and 1.16 and 1.68 (6 H, both s, *gem*-$\mathrm{Me_2}$).

[1-$^2H_1$]*Geraniol.* Geranial (5.8 g) was dissolved in dry ether (40 ml) and added dropwise to a suspension of $\mathrm{LiAlD_4}$ (1 g) in ether (30 ml) cooled in an ice-bath. The suspension was refluxed for 30 min then worked up in the usual manner. The product (5.5 g) was found to be 98% [1-$^2H_1$]geraniol; M^+ 155; δ 1.63 (3 H, s, $\mathit{Me}\mathrm{CH{=}}$), 1.68 (6 H, s, *gem*-$\mathrm{Me_2}$), 2.1 [4 H, br m, $\mathrm{(CH_2)_2}$], 4.1 (1 H, br d, $\mathrm{C}\mathit{H}\mathrm{DOH}$), 5.1 (1 H, m, $\mathrm{C}\mathit{H}\mathrm{{=}CMe_2}$), and 5.39 (1 H, d, *J* 6 Hz, $\mathrm{{=}C}\mathit{H}\mathrm{CHDOH}$); $\nu_{max.}$ 2 900, 1 675, 1 630, 1 610, 1 195, 1 120 $\mathrm{cm^{-1}}$.

5-*Iodopentan*-2-*one.*[5] To 5-chloropentan-2-one (33 g, 0.27 mol) in dry acetone (180 ml) was added sodium iodide (55 g) and the mixture refluxed for 6 h. The solid was filtered off and the acetone removed from the filtrate. The product was then re-extracted into benzene, filtered, then the solvent removed under reduced pressure. The crude iodoketone was used undistilled for the next stage; δ 3.12 (2 H, t, $\mathrm{CH_2I}$), 2.59 (2 H, t, $\mathrm{CH_2CO}$), 2.17 (3 H, s, Me), and 2.07 (2 H, s, $\mathrm{ICH_2C}\mathit{H}_2$); $\nu_{max.}$ 2 920, 1 700, and 675 $\mathrm{cm^{-1}}$.

5-*Iodopentan*-2-*one ethylene acetal.*[5] The crude iodoketone (55 g) with ethylene glycol (36 g, 0.6 mol) was dissolved in benzene (200 ml) with a trace of methanesulphonic acid. The solution was refluxed and the water removed azeotropically. On cooling, the solvent was removed under reduced pressure then the crude product distilled to give the title compound (32.5 g, 0.127 mol), 75—80 °C at 0.5 mmHg; δ 3.95 (4 H, s, $\mathrm{OCH_2CH_2O}$), 3.56 (2 H, t, *J* 7 Hz, $\mathrm{CH_2I}$), 1.85 (4 H, m, $\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}_2\mathrm{CH_2I}$), and 1.3 (3 H, s, Me); $\nu_{max.}$ 2 960, 2 860, 1 370, 1 040, and 675 $\mathrm{cm^{-1}}$.

4,4-(*Ethylenedioxy*)*pentyltriphenylphosphonium iodide.*[5] 5-Iodopentan-2-one ethylene acetal (27.5 g, 0.1 mol) and triphenylphosphine (30 g, 0.1 mol) were refluxed in benzene (150 ml) under nitrogen. On cooling, the slurry was filtered and the phosphonium salt (33.5 g) washed with benzene and dried *in vacuo*; δ 1.18 (3 H, s, Me), 1.73 (2 H, m, $\mathrm{CH_2C}\mathit{H}_2\mathrm{CH_2}$), 2.03 (2 H, t, $\mathrm{CH_2COR_2}$), 3.79 (2 H, m, $\mathrm{C}\mathit{H}_2\overset{+}{\mathrm{P}}\mathrm{Ph_3}$), 3.85 (4 H, s, $\mathrm{OCH_2CH_2O}$), and 7.7—7.9 (15 H, m, Ar).

[$^2H_6$]-6-*Methylhept*-5-*en*-2-*one ethylene acetal.*[5] 4,4-(Ethylenedioxy)pentyltriphenylphosphonium iodide (33 g, 0.1 mol) was stirred in tetrahydrofuran (THF) (250 ml) cooled to −20 °C while butyl-lithium in hexane (75 ml, 105 mmol) was added dropwise under nitrogen. When all the butyl-lithium had been added and the dark red colour of the ylide developed, the solution was cooled to −78 °C and [$^2H_6$]acetone (10 ml) added dropwise in dry THF (30 ml). After stirring for 15 min the solution was allowed to warm to room temperature; δ 1.29 (3 H, s, Me), 1.9 [4 H, br m, $\mathrm{(CH_2)_2}$], 3.75 (4 H, s, $\mathrm{OCH_2CH_2O}$), and 4.94 (1 H, t, vinyl); $\nu_{max.}$ 2 920, 2 860, 2 210, 2 190, 2 100, and 2 050 $\mathrm{cm^{-1}}$.

[$^2H_6$]-6-*Methylhept*-5-*en*-2-*one.*[5] The parent acetal (8 g) was refluxed for 30 min in 5% aqueous sulphuric acid. The mixture was then extracted with pentane, dried, and the solvent removed under reduced pressure to give the product as a pale yellow oil (4.2 g); δ 2.12 (3 H, s, Me), 2.23 (2 H, q, *J* 7 Hz, $\mathrm{CH_2C{=}C}$), 2.95 (2 H, t, *J* 7 Hz, $\mathrm{CH_2C{=}O}$), and 5.05 (1 H, t, *J* 7 Hz, vinyl); $\nu_{max.}$ 2 900, 2 220, 2 190, 2 100, 2 050, and 1 710 $\mathrm{cm^{-1}}$.

Methyl geranylate and [$^2H_6$]*nerylate.*[5] Trimethyl phosphonoacetate (5.5 g, 32 mmol) in dry ether (20 ml) was added to lithium hydride (5 g) in ether (60 ml) under nitrogen. The mixture was refluxed overnight under nitrogen then [$^2H_6$]methylheptenone (4.2 g, 31.8 mmol) in ether (20 ml) was added and the mixture refluxed for a further 6 h. The reaction was quenched with water and extracted with ether and pentane. The organic extracts were combined, dried, and the solvent removed. Distillation yielded the product (4.0 g) as an oil, 48—50 °C at 0.2 Torr; δ 2.12 (7 H, m, $\mathrm{MeC{=}CCH_2CH_2}$), 3.65 (3 H, s, OMe), 5.0—5.1 (1 H, m, vinyl), and 5.54 (1 H, s, vinyl); $\nu_{max.}$ 2 220, 2 185, 2 105, and 2 060 $\mathrm{cm^{-1}}$.

[$^2H_6$]*Geraniol*–[$^2H_6$]*nerol.*[5] The methyl geranylate–[$^2H_6$]-nerylate mixture (3.5 g) in ether (20 ml) was added dropwise to a suspension of lithium aluminium hydride (0.5 g) in ether (20 ml) and the mixture refluxed for 30 min. The reaction was quenched with water and extracted with ether. Drying of the solution followed by removal of the ether yielded a mixture of 81:19 [$^2H_6$]geraniol:[$^2H_6$]nerol; M^+ 160; δ 1.65 (3 H, s, Me), 2.04 [4 H, m, $\mathrm{(CH_2)_2}$], 4.13 (2 H, d, *J* 8 Hz, $\mathrm{C}\mathit{H}_2\mathrm{OH}$), 5.08 and 5.4 (both 1 H, t, vinyl); $\nu_{max.}$ 3 330, 2 220, 2 190, 2 100, and 2 060 $\mathrm{cm^{-1}}$.

Quenching of [$^2H_6$]*geraniol in* $\mathrm{FSO_3H}$. [$^2H_6$]Geraniol was treated with $\mathrm{FSO_3H}$ and quenched as in the method described below and the product ether purified by preparative g.l.c., *m*/*z* 160, 103, and 43; δ 0.96 (3 H, d, 3-Me), 1.19 (1 H, br d, 3a-H), 1.42—1.50 (2 H, m, 5a-, 6a-H), 1.8—2.0 (4 H, br s, 3-, 4-, 5b-, 6b-H), 3.7 (1 H, d, 2a-H), and 4.00 (1 H, q, 26-H).

[1,3-$^2H_5$]-6-*Methylhept*-5-*en*-2-*one.* 6-*Methylhept*-5-*en*-2-*one* (25.2 g, 0.2 mol) was stirred in a solution of THF (100 ml) containing $\mathrm{D_2O}$ (50 ml, 2.5 mol) which had been treated with sodium (100 mg). The reaction was shaken for 3 days in a sealed flask and then the ketone was isolated and treated with fresh $\mathrm{D_2O}$ (50 ml). The product was extracted into ether, dried thoroughly, and the ether removed before distillation to give the deuterioketone (18 g) shown by n.m.r. spectroscopy to be 92%-[$^2H_5$]; δ 1.62 and 1.68 (both 3 H, s, $\mathrm{{=}CMe_2}$), 2.25 (2 H, d, *J* 7 Hz, $\mathrm{C}\mathit{H}_2\mathrm{CH{=}}$), 5.09 (1 H, t, *J* 7 Hz, $\mathrm{CH_2C}\mathit{H}\mathrm{{=}}$), and 2.1 and 2.43 small multiplets totalling 0.4 H; $\nu_{max.}$ 3 330, 2 900, 2 100 br, and 1 715 $\mathrm{cm^{-1}}$.

[$^2H_5$]*Geraniol*–[$^2H_5$]*nerol.* [$^2H_5$]-6-Methylhept-5-en-2-one was condensed with the anion of trimethyl phosphonoacetate as previously described; δ 1.55 and 1.63 (6 H, both s, $\mathrm{CH{=}}\mathit{Me}_2$), 2.1 (2 H, br d, $\mathrm{CH_2}$), 3.63 (3 H, s, OMe), 5.0—5.1 (1 H, m, $\mathrm{{=}C}\mathit{H}\mathrm{CO_2Me}$), and 5.62 (1 H, m, $\mathrm{{=}CH}$).

The methyl ester was then reduced in $\mathrm{LiAlH_4}$–ether to give [$^2H_5$]geraniol–[$^2H_5$]nerol; δ 1.62 and 1.69 (both 3 H, s, *gem*-$\mathrm{Me_2}$), 2.2 (2 H, d, *J* 7 Hz, $\mathrm{CH_2}$-vinyl), 4.1 (2 H, d, $\mathrm{CH_2OH}$), and 5.1 and 5.6 (each 1 H, t, vinyl).

Quench of [$^2H_5$]*geraniol in* $\mathrm{FSO_3H}$. [$^2H_5$]Geraniol was treated with $\mathrm{FSO_3H}$ and quenched as in the method described below. The product ether was purified by preparative g.l.c., *m*/*z* 158, 157, 98, 97, and 43; δ 0.85 (3 H, d, 4-Me), 0.96 (0.8 H, s, 3-Me), 1.13 (3 H, s, 6a-Me), 1.18 (1 H, m, 3a-H), 1.42—1.48 (2 H, m, 6a-, 5a-H), 1.8—2.00 (3 H, m, 4-, 5b-, 6b-), 3.68 (1 H, d, *J* 8 Hz, 2a-H), and 4.00 (1 H, d, *J* 8 Hz, 2b-H).

2,2-*Dimethylcyclopentanone.*[12] 2-Methylcyclopentanone (10 g) was converted into 2,2-dimethylcyclopentanone by the method of Boatman, Harris, and Hauser.[12] The product (2 g) was used for the next reaction without distillation; *m*/*z* 112; δ 1.03 (6 H, s, Me), 1.7—1.85 (4 H, m, $\mathrm{CH_2}$), and 2.24 (2 H, t, $\mathrm{CH_2CO}$); $\nu_{max.}$ 2 950, 1 740, 1 450, and 1 060 $\mathrm{cm^{-1}}$.

Ethyl 2-(1-*hydroxy*-2,2-*dimethylcyclopentyl*)*propionate.* 2,2-Dimethylcyclopentanone was esterified using ethyl 2-bromopropionate and zinc powder by a modified Reformatsky reaction.[13] A portion (10 ml) of a mixture of 2,2-dimethylcyclopentanone (1.4 g, 0.0125 mol), benzene (12 ml), toluene (10 ml), and ethyl bromopropionate (2.3 g, 0.0127 mol) was added to zinc powder (1.03 g, 0.016 mol) in a 100 ml three-necked round-bottomed flask, equipped with condenser, stirrer, and dropping funnel. The contents were heated to 100 °C whereupon a vigorous reaction set in. The remainder of the solution was run in to maintain reflux. After addition, the solution was refluxed for a further 2 h. After cooling, the solution was acidified with dilute $\mathrm{H_2SO_4}$ and the organic layer separated, dried, and concentrated. The resultant crude oil (1.4 g), which was used for the reduction, showed δ 1.0 and 1.07

[both 3 H, s, Me (*cis*)], 0.82 and 0.89 [both 3 H, s, Me (*trans*)], 1.26 [3 H, t, CH_2*Me* (*cis* and *trans*)], 1.23 [3 H, d, MeC-H (*cis* and *trans*)], 1.5—2.5 [7 H, m, CH_2-ring (*cis* and *trans*) and CHMse], and 4.13 [2 H, q, C*H*$_2$Me (*cis* and *trans*)]; $\nu_{max.}$ 3 250, 2 750, 1 650, 1 450, and 1 200 cm^{-1}.

2-(1-*Hydroxy*-2,2-*dimethylcyclopentyl*)*propan*-1-*ol*. Ethyl 2-(1-hydroxy-2,2-dimethylcyclopentyl)propionate (1.4 g, 0.0065 mol) was reduced by $LiAlH_4$ (0.5 g, 0.013 mol) in ether. Work-up gave 1 g of a viscous oil; $\nu_{max.}$ 3 400, 2 950, 1 450, 1 100, 1 030, and 950 cm^{-1}.

Quenching of 2-(1-*Hydroxy*-2,2-*dimethylcyclopentyl*)*propan*-1-*ol in* FSO_3H.—The diol (1 g) was acidified and quenched as described below. G.l.c. of the resulting oil showed two ethers (60% yield) in the ratio 4:1 with similar R_F values. The major ether, identified as 3β,3aα,6aα-trimethyl-*cis*-perhydrocyclopenta[*b*]furan (**14**), was purified by preparative g.l.c. (85% pure); *m*/*z* 154 (M^+, 0.1%), 139 (8.2), 112 (100), and 97 (70); $\nu_{max.}$ 2 950, 1 450, 1 350, 1 200, and 1 050 cm^{-1}; the ^1H n.m.r. has already been discussed.

Generation of Carbocations with FSO_3H.—Sulphur dioxide (1 ml) was condensed in a 10 ml round-bottomed flask and FSO_3H (2.5 ml) added. The solution was cooled to −78 °C using a solid CO_2–acetone bath. The substrate (250—500 mg) was dissolved in sulphur dioxide (1 ml) and cooled to −78 °C then added dropwise, down the inside of the cooled reaction vessel, to the stirred FSO_3H–SO_2 solution. The reaction mixture was stirred for 10 min and added to a 12 mm bore n.m.r. tube also cooled in a CO_2–acetone bath. The n.m.r. tube was removed from the cooling mixture, quickly cleaned of any residual acetone and placed within the spectrometer. The probe had been previously cooled in a stream of nitrogen passed through a heat-exchanger immersed in liquid nitrogen. The temperature of the probe and sample was then regulated using a heating coil in the nitrogen stream.

With a substrate which polymerised readily, a modification of the above procedure was used. The substrate was first dissolved in carbon disulphide, cooled to −78 °C, and added to the FSO_3H–SO_2 solution as described. The mixture was then stirred for 20 min before transfer to the n.m.r. tube and used as before.

Generation of Carbocations using SbF_5.—Antimony pentafluoride (1 ml) was condensed in a 10 ml round-bottomed flask cooled to −78 °C, after evaporation under reduced pressure from a connected vessel. Sulphuryl chloride fluoride (2 ml) was then added to the condensed solid and the mixture warmed until dissolution. The solution was then recooled to −78 °C and the cooled substrate solution (250—500 mg in 2 ml SO_2) added dropwise down the side of the reaction vessel. The reaction mixture was then treated as with the FSO_3H reaction mixture.

Quenching of Carbocation Solutions.—Carbocation solutions in FSO_3H–SO_2 were prepared as described previously but on a larger scale *i.e.*, 10—50 g substrate. These solutions were then added dropwise from a cooled separating funnel to a rapidly stirring, cooled slurry of potassium carbonate in methanol. On completion of the addition, the slurry was allowed to warm to room temperature then water was added. Further potassium carbonate was added to ensure the solution was basic then sodium chloride was added to saturation. The aqueous solution was then extracted with ether and then pentane, the extracts combined, dried, and the solvent removed under reduced pressure. The oil produced could then be purified by, if necessary, passing down a Florisil column, eluting with pentane to remove most of the polymer present, and distilled.

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