Opening of the Cyclopropane Ring of the Thujan-3-ols in Fluorosulphuric Acid

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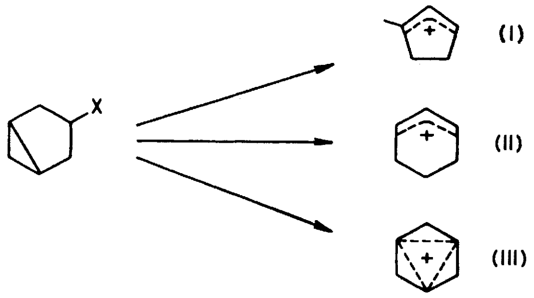
The reactions of the isomeric thujan-3-ols with fluorosulphuric acid to give the 2,3-dimethyl-4-isopropylcyclopentenium ion have been investigated. The initial ring opening involves at least two mechanisms yielding a carbocation and an olefin. Subsequent reaction, possibly by elimination and olefin shift, gives the 2,3-dimethyl-4-isopropylcyclopent-2-enol, which rapidly ionises to the observed ion. The reaction has been studied by means of deuterium tracers, in the solvent and in the substrate, and by comparison of the reaction with those of related substrates.

IN the preceding paper,[1] we discussed the mechanism of opening of the cyclopropane ring in the bicyclo[3.1.0]hexan-3-ols. The reaction is initiated at the cyclopropane ring, rather than at the hydroxy-group, though the latter is subsequently lost during formation of the 1-methylcyclopentenium ion. However, reaction in deuteriated acid [1,2] shows no sign of incorporation of deuterium onto a specific carbon atom; all the carbon atoms are easily detectable by ^{13}C n.m.r. spectroscopy, and the deuterium is not sufficiently incorporated into any position to be visible by ^{1}H n.m.r. spectroscopy. Two possible mechanisms for the ring opening have been suggested. First, the initial protonation may give a protonated cyclopropane intermediate of sufficient stability to permit scrambling of an incorporated deuterium atom before ring opening takes place. Secondly, reaction may involve an edge or face protonated cyclopropane species, which then opens to a mixture of isomeric olefins by a process which does not involve incorporation of the deuterium atoms. Subsequent reaction of the olefins in deuteriated acid would incorporate deuterium onto three different atoms. Our research on the bicyclo[3.1.0]hexan-3-ols was handicapped by the plane of symmetry which these molecules possess; we have therefore investigated ring opening of the thujols, a reaction which the work of Norin,[3] Sorensen,[4] and ourselves [5] have shown to be similar to reactions of the parent system, but in which the substrate lacks the plane of symmetry which the former possesses. We now report in full the labelling experiments which have been outlined previously.[6]

RESULTS AND DISCUSSION

Work on the bicyclo[3.1.0]hexanols showed that reaction at the cyclopropane ring gave rise to the 1-methylcyclopentenium ion (1); reaction involving formation of a carbocation at C-2 gave only the cyclohexenium ion (II), while formation of a carbocation at C-3 leads to either the cyclohexenium ion (II) or the trishomocyclopropenium ion (III), depending on the orientation of the leaving group to the cyclopropane ring.[7]

In the thujane system, it is known that 4β*H*-thujan-3β-ol (isothujol) (IV) or 4β*H*-thujan-3α-ol (neoisothujol) (V) react with superacids to give the 2,3-dimethyl-4-isopropyclyclopentenium ion (VI).†[4] However, the alkenes, α-thujene (VII) and sabinene (VIII) undergo protonation at the double bond, giving rise to the 1-methyl-4-isopropylcyclohexenium ion (IX).[4] We have found that reaction of 4β*H*-thujan-3β-ol (IV), and the isomeric chlorides 4α*H*-thujan-3β-yl chloride (X) and 4β*H*-thujan-3α-yl chloride (XI), with SbF_5 in SO_2ClF all give rise to (IX) as the sole product.



In the reaction of (XI) with SbF_5–SO_2ClF we observed no trace of the trishomocyclopropenium ion, even though reaction of the unsubstituted alcohol gave this ion as the sole product.[7] However, reaction of the 1-methyl-*cis*-bicyclo[3.1.0]hexan-3-ol similarly gave only a cyclohexenium ion, with no trace of the trishomocyclopropenium ion,[7] suggesting that the 1-substituent can inhibit this reaction.

A possible route to (VI) from (IV) and (V) is ionisation of the hydroxy-group to give the carbocation (XII), followed by migration of the positive charge to C-2. The substituent on C-1 may then influence the reaction to give a cyclopentenium ion, though in the unsubstituted case [8] gives a cyclohexenium ion. To check this, we prepared 4β*H*-thujan-2β-ol (XIII) and reacted it with FSO_3H in SO_2 at −78°. The reaction yielded only the 1-isopropyl-4-methylcyclohexenium ion (XIV), which we have not observed in any of the main reactions.

We conclude that, apart from its failure to yield a trishomocyclopropenium ion, the thujyl system behaves

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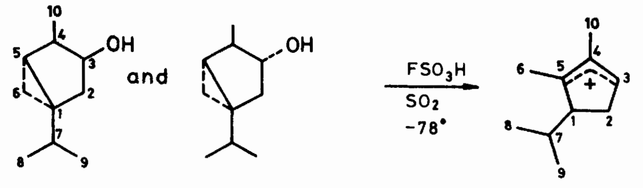
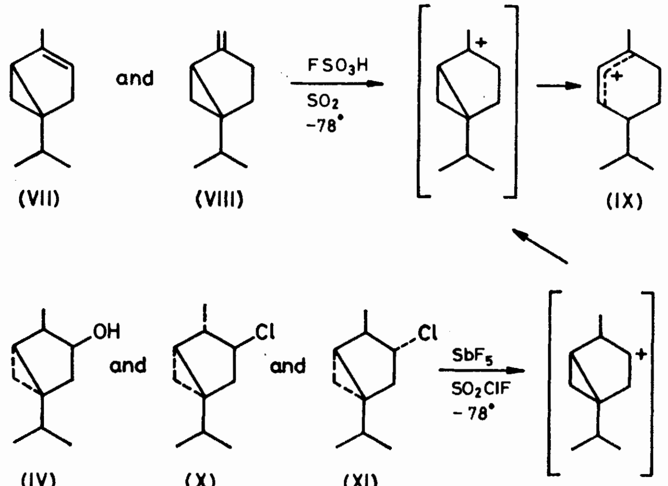
† Throughout this paper, we have numbered (VI) so that the carbon atoms have the same number as the corresponding carbon atoms of (IV) to avoid causing confusion in discussion of labelling experiments. On this numbering, the 2,3-dimethyl-4-isopropylcyclopentenium ion would become the 1-isopropyl-4,5-dimethylcyclopent-3-enium ion.



(IV) (V) (VI)

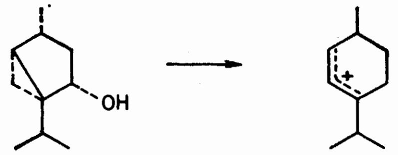


(VII) (VIII) (IX)

(IV) (X) (XI) (XII)

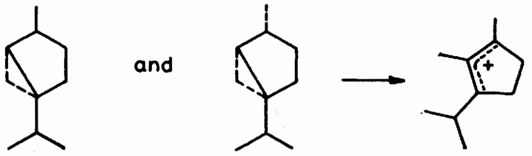
very similarly to the bicyclo[3.1.0]hexyl systems, and that comparison of the two is valid.

Since our main interest is opening of the cyclopropane ring, we first took the simplest possible systems, the two



(XIII) (XIV)

isomeric thujanes, 4αH- (XV) and 4βH-thujane (XVI) and reacted them with FSO$_3$H, with and without SbF$_5$, in SO$_2$ and in SO$_2$ClF. In all cases, we obtained only the 1-isopropyl-2,3-dimethylcyclopentenyl cation (XVII).

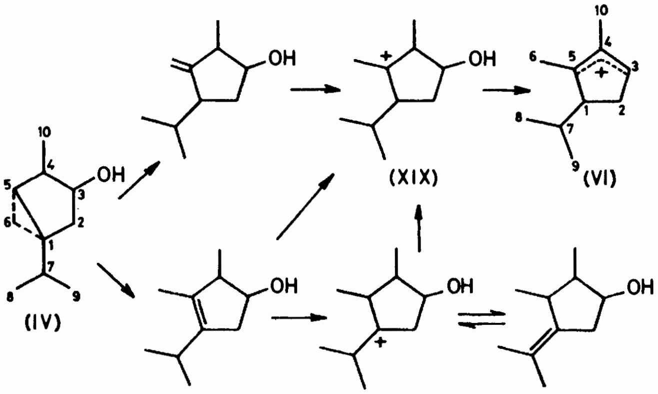


(XV) (XVI) (XVII)

The ion (XVII) is also formed from (VI) on warming; its formation from the alkane indicates that reaction of the latter involves an oxidation step, which is uncommon but not unprecedented.[9]

By analogy with earlier work,[1] we reacted the two chlorides (X) and (XI) with fluorosulphuric acid at −90°; a similar reaction of *cis*-bicyclo[3.1.0]hexyl chloride gave the 3-chloro-1-methylcyclopentyl cation, but in this case a chlorocation was not observed, and we obtained only the cyclopentenium ion (VI).

When we reacted 4βH-thujan-3β-ol (IV) with FSO$_3$D–SbF$_5$–SO$_2$ at −78°, we obtained the ion (VI). The ^{13}C n.m.r. spectrum showed some diminution of the peaks due to C-1, -6, and -7, but was otherwise unchanged, suggesting that the deuterium incorporated from the solvent was spread over these three carbon atoms. This observation of only partial deuteriation of C-6 rules out protonation of the cyclopropane ring to give the species (XVIII) as the sole reaction, since this would fully deuteriate C-6, but requires reaction *via* two mechanisms, since reaction *via* a single olefin would fully deuteriate C-1. However, some reaction must proceed *via* (XVIII), since it is presumably *via* this species that label is incorporated onto C-7.



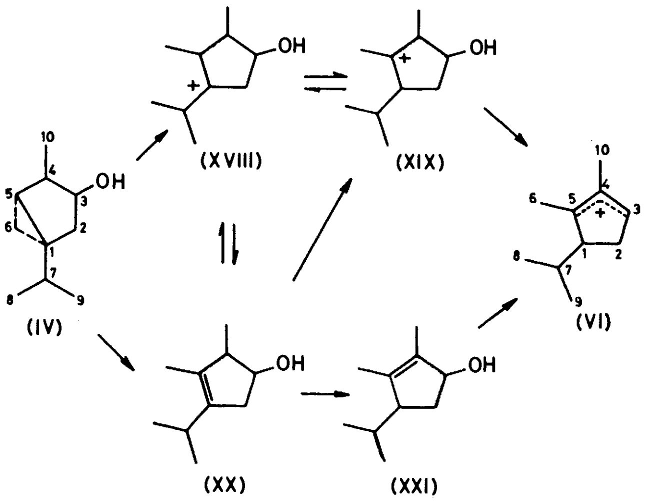
(IV) (XIX) (VI) (XVIII)

Scheme 1

To try to disentangle this system, we labelled (IV) at C-3 and -4, and prepared a mixture of all four isomeric thujols labelled with deuterium at C-2 and -4. In all cases the single ion (VI) was obtained, and in all cases the labels on C-2 and -3 were retained intact, and that on C-4 was lost completely. This did not, however, cause a significant reduction in any other peak of the ^{13}C n.m.r. spectrum of the carbocation. We therefore reacted a sample of (IV) labelled with deuterium on C-2 and -4 with FSO$_3$D at −78°, and obtained two significant results. First, C-7 was now completely deuteriated, and secondly, C-1 was largely (*ca.* 80%) but not entirely deuteriated. Since deuteriation of C-7 occurs *via* the ion (XVIII), it follows that this ion must occupy a key position in the reaction scheme, in that all the reaction must at some stage proceed through this ion. However, since C-1 is not completely deuteriated, in (VI) then the hydride transfer giving (XIX) from (XVIII) must be taking place; and since (XVIII) must have a hydrogen atom on C-5, then (XVIII) cannot arise solely from the olefins shown in Scheme 1, since either would lead to (XIX) with a deuterium atom on C-5. Clearly, this result shows that the olefin mechanism cannot, on its own, explain the labelling observed in the reaction.

On these results, the overall reaction is consistent with Scheme 2.

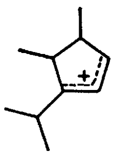
Since the ion, (XIX) reacts to form the ion (VI), it seems somewhat surprising that the ion (XVIII) does not form an ion such as (XXII), which has not been observed by us. Since (XVIII) is formed before (XIX), we sought to expedite the formation of an ion such as (XXII) by making the alcohol group tertiary. We, therefore, prepared the isomeric methyl thujols, 3β-methyl-4α*H*-thujan-3α-ol (XXIII) and 3β-methyl-4β*H*-thujan-3α-ol (XXIV).



Scheme 2

In FSO_3H–SbF_5, (XXIII) gave only the 1,2,3-trimethyl-4-isopropylcyclopentenium ion (XXV), and with SbF_5–SO_2ClF gave only the 1,6-dimethyl-4-isopropylcyclohexenium ion (XXVI).

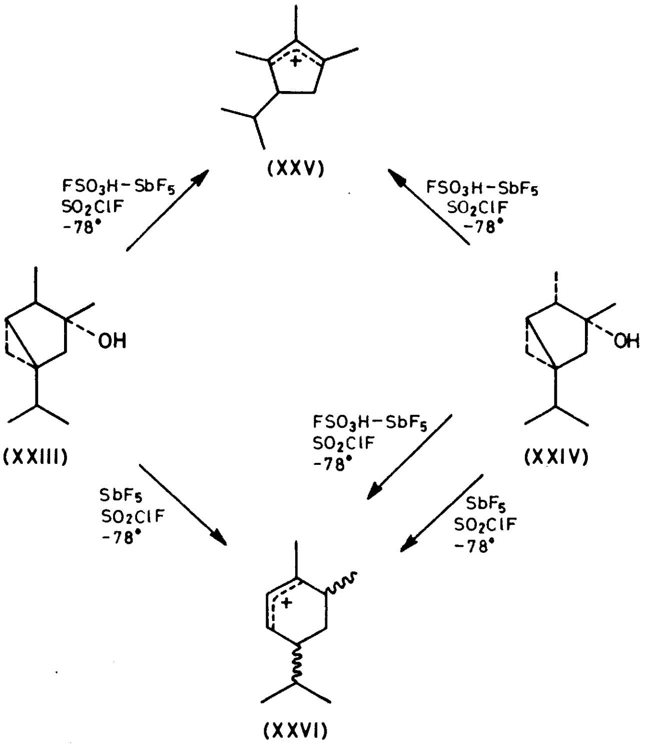
However, in FSO_3H, reaction of (XXIV) proceeded competitively at the hydroxy-group and at the cyclopropane ring, the former reaction giving the cyclohexenium ion and the latter reaction the cyclopentenium ion. With SbF_5, reaction at the hydroxy-group only gave the cyclohexenium ion (XXVI).



(XXII)

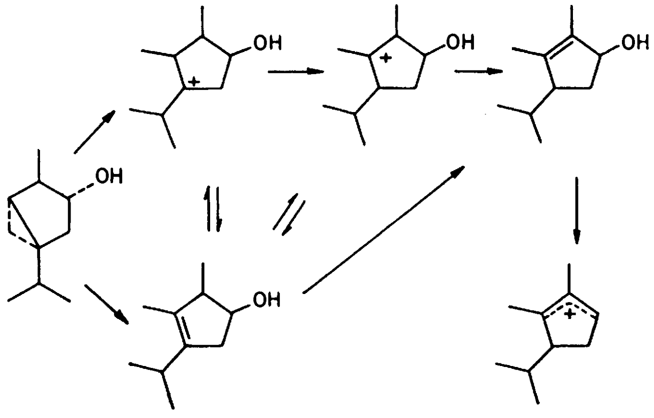
These reactions appear to follow exactly the pattern of the unsubstituted thujols. Thus, both alcohols, when labelled with deuterium at positions 2 and 4 lost the label pentenium ion. Also, (XXIV), labelled on C-2 and -4, gave the cyclohexenium ion labelled on the atoms corresponding to C-2 and -3 [these being C-5 and -6 in (XXVI)], thus providing clear evidence for the 1,2-hydride shift postulated in the path to the formation of the cyclohexenium ion. We suggest that the incursion of this process into the reaction of (XXIV) results from orientation of the C-4 hydrogen to undergo a 1,2-shift concerted with ionisation of the hydroxy-group.

The methylthujols thus parallel closely the reactions of the thujols, and do not give an ion corresponding to (XXII). This suggests that a hydroxy-carbocation probably forms the allylic ion *via* the allylic alcohol, rather than by direct elimination of the hydroxy-group. This process would enable (XIX) to yield (VI), but (XVII) would yield (XX), rather than eliminate to give the less substituted olefin, and thence (XXII). Such a process would not be influenced by substitution at C-3, as we have observed.



We suggest that the overall process fitting the evidence must be that outlined in Scheme 3.

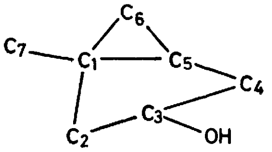
It is impossible to quantify the contribution from each pathway, since these will be affected by the use of deuteriated acids and deuteriated substrates. It seems likely that this is the basic scheme for reaction of all the bicyclo[3.1.0]hexan-3-ols, with structural factors in-



Scheme 3

fluencing the relative importance of the possible pathways.

An unsolved problem which remains is the failure of 4β*H*-thujan-3α-yl chloride (XI) to form a substituted trishomocyclopropenium ion on reaction with SbF_5. Substitution of one ring junction appears to inhibit formation of this ion. The reason for this may well be steric, rather than electronic. We have recently [10] found evidence that the 1-methyl group of 1-methyl-*cis*-bicyclo[3.1.0]hexan-3-ol (XXVII) has the effect of twisting the boat, as shown in (XXVII).



(XXVII)

Consequently, the orbitals of the developing carbocation centre at C-3 when a group *cis* to the cyclopropane ring is departing will no longer be suitably oriented for interaction with the orbitals of the cyclopropane rings; reaction will thus proceed *via* a hydride shift instead. In the 4β*H*-thujanes, this effect is to some extent opposed by the methyl group on C-4 being forced onto an axial position close to the protons on C-2, but it appears from our results that the twist is still sufficient to prevent interaction during formation of the ion.

EXPERIMENTAL

Materials.—α-Thujene was distilled from *Eucalyptus Dives* oil at 86° and 86 mmHg using a spinning band column; sabinene was similarly distilled from Oil of Savin at 95° and 86 mmHg, and 4α*H*-thujan-3-one (thujone) from oil of *Tanaceteum vulgare* L. at 116° and 65 mmHg. We are grateful to Dr. D. V. Banthorpe of University College, London for a gift of Oil of Savin.

^{13}C N.m.r. chemical shifts of carbocations from thujanes (p.p.m. relative to Me_4Si)

	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11
2,3-Dimethyl-4-isopropylcyclopentenium ion (VI)	221.3	159.3	262.7	69.2	45.6	25.9	34.2	16.2	22.7	12.2	
1-Isopropyl-2,3-dimethylcyclopentenium ion (XVII)	250.6	153.9	243.6	42.2	46.9	10.1	37.6	20.6	20.6	24.5	
1,2,3-Trimethyl-4-isopropylcyclopentenium ion (XXV)	243.5	155.9	246.1	64.2	48.0	24.9	32.4	16.3	22.8	10.5	23.8
1-Methyl-4-isopropylcyclohexenium ion (IX)	250.0	141.2	210.7	51.3	22.3	42.3	33.3	20.2	20.2	35.3	
1-Isopropyl-4-methylcyclohexenium ion (XIV)	272.1	145.6	226.8	60.8	25.6	53.5	43.0	21.5	21.2	13.7	
1,6-Dimethyl-4-isopropylcyclohexenium ion (XXVI)	254.8	141.6	208.8	52.8	31.3	48.2	33.1	20.4	20.4	34.3	18.1

4β*H*-*Thujan*-3β-*ol* (*Isothujol*).—This was obtained from α-thujene by hydroboration.[11] The 4-deuterio-compound was obtained by using sodium borodeuteride instead of sodium borohydride.

4βH-*Thujan*-3α-*ol* (*Neoisothujol*).—This was obtained by hydrogenation of sabinyl acetate [12] (from Oil of Savin).

4αH-*Thujan*-3α-*ol* (*Neothujol*).—This was obtained by reduction of 4α*H*-thujan-3-one with $LiAlH_4$ at −78°, giving 87% yield of the required alcohol.[11]

4βH-*Thujan*-3α-*yl Chloride*.—4β*H*-Thujan-3β-ol (18 g) and triphenylphosphine (47 g) were refluxed together in dry carbon tetrachloride for 8 h. The solvent was removed under reduced pressure, then the residue extracted with pentane. Pentane extracts were combined, filtered through Celite, the solvent removed, and the product distilled at 80° at water pump pressure. ^1H and ^{13}C n.m.r. spectra are given elsewhere.[10]

4αH-*Thujan*-3β-*yl Chloride*.—To a stirred solution of *N*-chlorosuccinimide (8.17 g) in dry tetrahydrofuran (200 ml) a solution of triphenylphosphine (16.03 g) in dry tetrahydrofuran was added slowly; a mild exothermic reaction occurred, with separation of a solid.[13] To this suspension a solution of 4α*H*-thujan-3α-ol (10 g) in dry tetrahydrofuran (50 ml) was added, and the mixture stirred for 4 h. The solvent was then removed under reduced pressure and the residue extracted with pentane. Solvent was removed from the combined pentane extracts, and the chloride distilled at water pump pressure.

4βH-*Thujan*-3-*one*.—This was prepared by chromic acid oxidation [14] of 4β*H*-thujan-3β-ol.

2,2,4-*Trideuteriothujan*-3-*one*.—To a flask containing 4β*H*-thujan-3-one (30 g) and deuterium oxide (40 g) was added dry dioxan until the mixture became homogeneous. Sodium methoxide (0.66 g) was then added and the mixture refluxed for 20 h. Extraction of the ketone with pentane was followed by a repeat of the exchange procedure, giving a mixture of 75% of the 4β*H*-ketone and 25% of the 4α*H*-ketone, deuteriated at C-2 and -4 to >90%.

4β*H*-*Thujane*.—This was prepared by hydrogenating sabinene at −20°, as described by Brown.[15]

4αH-*Thujane*.—This was prepared by hydrogenating α-thujene at −20°, as described by Brown.[15]

4βH-*Thujan*-2β-*ol*.—This was prepared by reduction of umbellulone with sodium borohydride.[16]

3β-*Methyl*-4αH-*thujan*-3α-*ol*.—Reaction of methylmagnesium iodide with 4α*H*-thujan-3-one gave the required alcohol as a crystalline *solid*, m.p. 85° (Found: C, 78.65; H, 11.85. $C_{11}H_{20}O$ requires C, 78.5, H, 12.0%). The n.m.r. spectra are described elsewhere.[10]

3β-*Methyl*-4βH-*thujan*-3α-*ol*.—Reaction of methylmagnesium iodide with 4β*H*-thujan-3-one gave the required alcohol as a liquid, b.p. 53° at 0.7 mmHg (Found: C, 78.35; H, 11.95. $C_{11}H_{20}O$ requires C, 78.5; H, 12.0%). The n.m.r. spectra are described elsewhere.[10]

Preparation of Carbonium Ion Solutions.—These were prepared as described in the preceding paper.[1] Spectra were recorded on a Varian XL-100-15 spectrometer, using a deuterium signal of [$^2H_6$]acetone as lock, and chemical shifts are given relative to internal Me_4Si. The ^{13}C chemical shifts of the ions studied are given in the Table.

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