Tetrahedron, 1966, Vol. 22, pp. 309 to 320. Pergamon Press Ltd. Printed in Northern Ireland

THE ABSOLUTE CONFIGURATION OF THUJANE

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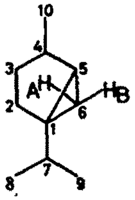
(*Received 5 June* 1965)

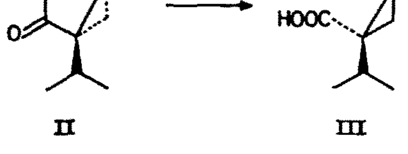
Abstract—(+)-*cis*- and (+)-*trans*-Thujane (XIV and XV) have been correlated with (+)-pulegone (IX) via (+)-pulegene (XIII). Using stereospecific reactions, the hydrocarbons of the thujane series have been linked with their oxygenated members. The absolute configurations found by Norin for these substances are in accord with our findings.

Zusammenfassung—(+)-*cis*- und (+)-*trans*-Thujan (XIV und XV) wird über (+)-Pulegen (XIII) mit dem (+)-Pulegon (IX) verknüpft. Durch Anwendung stereospezifischer Reaktionen können die Kohlenwasserstoffe der Thujanreihe mit ihren sauerstoffhaltigen Vertretern verbunden werden. Die von Norin für diese Verbindungsklasse angegebene absolute Konfiguration stimmt mit unserem Ergebnis überein.

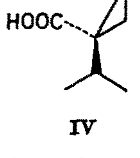
The first successful studies on the absolute configuration of thujane and its derivatives led to the establishment of the spatial environment about C-1[1] in I by means of an asymmetric synthesis of (−)-*cis*- and (−)-*trans*-umbellulic acids (III and IV).[2] From this synthesis the diastereoisometric carboxylic acids were obtained in 6% and 2·7%



I



II III



IV

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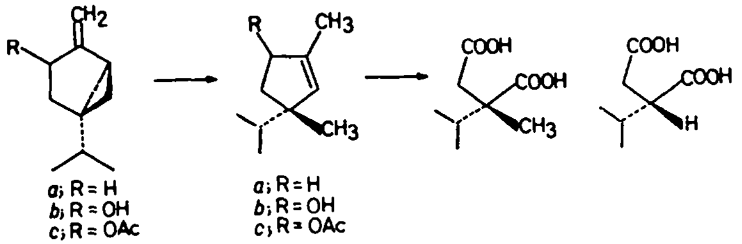
[1] The numbering in the system is taken from *System of Nomenclature for Terpene Hydrocarbons*, *Adv. in Chem.* Ser. 14; p. 8. A.C.S. (1955).

[2] H. M. Walborsky, T. Sugita, M. Ohno and Y. Inouye, *J. Amer. Chem. Soc.* **82**, 5255 (1960).

optical yield. Conversion of (—)-umbellulone (II) to these acids and further degradation,[3] as well as degradation of the three (+)-sabinene derivatives (Va, Vb and Vc)[4] led to the known (S)-(+)-α-methyl-α-isopropylsuccinic acid (VII). Fredga's quasiracemate method[5] in fact established the same configuration for VII[6] as for unsubstituted (+)-isopropylsuccinic acid (VIII).[5]



V VI VII VIII

Thus all the related thujane derivatives were also correlated configuratively.[7] Extensive work in the series led Norin[4,8] to establish the steric relationships between the oxygenated thujanes.

In order to confirm the absolute configuration of this class of monoterpenes, we felt that it would be of interest to establish a third, completely independent method. We therefore undertook a direct correlation of thujane (I) with (+)-pulegone (IX).[11,12]

(+)-*trans*-Pulegenic acid (X), readily available[13] by Favorski rearrangement from IX, was first reduced as its methyl ester with LAH to the corresponding alcohol (XI), which, on pyrolysis (480°/40 mm) gave exclusively (+)-pulegene (XIII) in 90% yield. The formation of XIII selectively from XI is required by the elimination of formaldehyde from the cyclic intermediate (XII), a reaction that has been well established for

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[3] H. E. Smith and A. Waters Gordon, *J. Amer. Chem. Soc.* **84**, 2840 (1962).

[4] T. Norin, *Acta Chem. scand.* **16**, 640 (1962); cf. also J. D. Edwards, jr., and N. Ichikawa, *J. Org. Chem.* **29**, 503 (1964).

[5] A. Fredga and E. Leskinen, *Arkiv f. Kemi, Min. o. Geol.* **19 B**, No 1, S. 1–6 (1944).

[6] J. Porath, *Arkiv f. Kemi* **1**, 385 (1949).

[7] J. L. Simonsen *The Terpenes*, (Second Edition Revised and Reset) Vol. II; pp. 5–60. Cambridge University Press, England (1957).

[8] E. Gildemeister and Fr. Hoffman *Die Aetherischen Oele* (4.Auflg. von W. Treibs and E. Merkel) Bd. IIIa; S. 109–118 Akademie Verlag, Berlin; (1960); Bd. IIIb; S. 131–137 and 209–213 (1962); Bd. IIIc, S. 270–284 and 340–344 (1963).

[9] M. S. Bergquist and T. Norin, *Arkiv för Kemi* **22**, 137 (1963).

[10] T. Norin, *Tetrahedron Letters* 37 (1964).

[11] K. Freudenberg and W. Lwowski, *Liebigs Ann.* **587**, 213 (1954).

[12] Exhaustive attempts have already been made to prepare thujane from menthone with retention of the configuration at C-4. Reduction of 2,4-dibromomenthone by P. C. Guha and B. Nath, *Ber. Dtsch. Chem. Ges.* **70**, 931 (1937), led, however, not to the reported optically active bicyclic hydrocarbon, but to the 4-alkoxymenthone, according to W. G. Dauben, A. C. Albrecht, E. Hoerger and H. Takimoto, *J. Org. Chem.* **23**, 457 (1958).

[13] O. Wallach, *Liebigs Ann.* **289**, 349 (1895); *Ibid.* **300**, 259 (1898); *Ibid.* **327**, 125 (1903); *Ibid.* **392**, 49 (1912); **414**, 233 (1918); L. Bouveault and L. Tetry, *Bull. Soc. Chim. Fr.* [3] **27**, 307 (1902); H. Rupe and J. Burgin, *Ber. Dtsch. Chem. Ges.* **43**, 1228 (1910); H. Rupe and K. Schäfer, *Helv. Chim. Acta* **11**, 463 (1928); J. Wolinsky, H. Wolf and T. Gibson, *J. Org. Chem.* **28**, 274 (1963); S.A. Achmad and G. W. K. Cavill, *Proc. Chem. Soc.* 166 (1963).

other $\beta\gamma$-unsaturated alcohols.[15] Addition of carbene from iodomethyl-zinc iodide[16,17] to (+)-pulegene (XIII) led to a mixture of two thujanes which must belong to both stereochemical series, and whose absolute and relative configurations must be given by formulae XIV and XV. The main component of this reaction ((+)-thujane B, ~85%), after gas chromatographic purification, exhibited a low optical rotation of $[\alpha]_D^{20} = +6{\cdot}7°$, the accompanying product ((+)-thujane A, ~15%) having $[\alpha]_D^{20} = +87°$.

(+)-Thujane A (XV) is also formed as a byproduct (29%; $[\alpha]_D^{20} = +87°$), in addition to (−)-thujane B (XVI; 71%), having a rotation $[\alpha]_D^{20} = -6°$, from a Wolff-Kishner reduction of a naturally occurring mixture of the two thujones (XIX and XX)[17a]. The same thujanes ((+)-thujane A and (−)-thujane B, XV and XVI) resulted from mild hydrolysis[18,19] of trithujylborane (C10), obtained by hydroboration of (+)-sabinene (Va). On the other hand (+)-sabinyl acetate was converted[20] to

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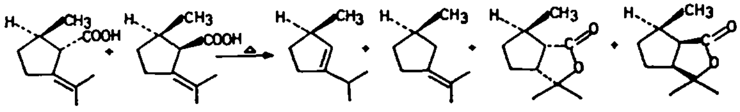
[14] O. Wallach, *Liebigs Ann.* **289**, 353 (1896); **300**, 259 (1898); **327**, 131 140 (1903); **414**, 234 (1917). According to these sources, pyrolysis of (+)-pulegenic acid should lead directly to pulegene (XIII) by elimination of CO_2. Our own study of this reaction showed, however, that X yields more than six reaction products at 450°, among which XIII ($[\alpha]_D^{20} = +58{\cdot}31°$; d_4^{20} 0·7916; n_D^{20} 1·4402) is only formed to a lesser extent (11% yield). The isomer XXVI ($[\alpha]_D^{20} = +31{\cdot}68°$; d_D^{20} 0·8030; n_D^{20} 1·4550) was identified, as well as the two lactones XXVII and XXVIIa[18] (65% yield). According to a thesis


X Xa XIII XXVI XXVII XXVIIa

of Catherine Ouannes of Paris University (we are greatly obliged to Dr. J. Jacques, C.N.R.S., for drawing our attention to this work), pyrolysis of (+)-pulegenic acid in the presence of quinoline at 230° leads in 82% yield to a pulegene with α_D +76·48°. cf. D. Varech, C. Ouannes and J. Jacques, *Bull Soc. Chim.* 1662 (1965).

[15] R. L. Webb and J. P. Bain, *J. Amer. Chem. Soc.* **75**, 4279 (1953); G. Ohloff, *Chem. Ber.* **93**, 2673 (1960); R. T. Arnold and G. Smolinsky, *J. Amer. Chem. Soc.* **81**, 6443 (1959); *J. Org. Chem.* **25**, 129 (1960); *J. Amer. Chem. Soc.* **82**, 4918 (1960); R. T. Arnold and P. Veeravagu, *Ibid.* **82**, 5441 (1960).

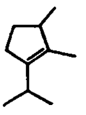
[16] H. E. Simmons and R. D. Smith, *J. Amer. Chem. Soc.* **81**, 4256 (1959).

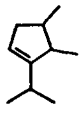
[17] G. Wittig and K. Schwarzenbach, *Liebigs Ann.* **650**, 1 (1962).

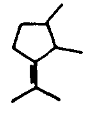
[17a] Kishner, *J. Russ. phys. chem. Ges.* **42**, 1199 (1910); **43**, 586 (1911); cf. F. Richter, W. Wolff and W. Presting, *Ber.* **64**, 871 (1931).

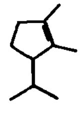
[18] G. Zweifel and H. C. Brown, *J. Amer. Chem. Soc.* **86**, 393 (1964).

[19] The usual hydrolysis conditions[18] gave no thujane, but more than 10 isomerization products belonging either to the iridane series (H. Strickler, G. Ohloff and E. sz. Kovats, *Tetrahedron Letters* 649 (1964) or deriving from *p* menthane. The following compounds were identified after gas chromatographic separation (carbowax column at 100°) by their NMR and mass spectra (see experimental section): Irid-2-ene (XXVIII, 19%), irid-3-ene (XXIX, 6%), irid-3(8)-ene (XXX,


XXVIII

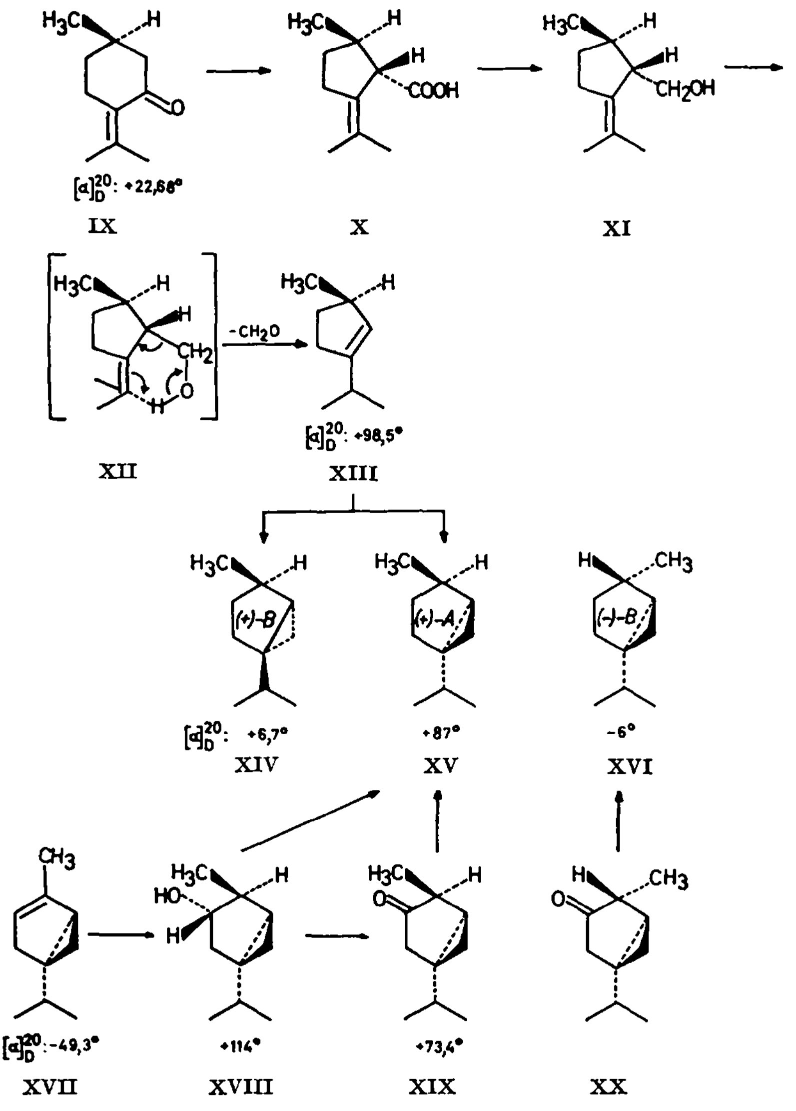

XXIX


XXX


XXXI

7%), irid-1-ene (XXXI, 18%), *p*-menth-3-ene (12%), α terpinene (17%), γ-terpinene (4·5%) and β-mentha-2,4(8)-diene (5%).

[20] A. J. Birch, *J. Chem. Soc.* 811 (1945).



(−)-α-thujene (XVII) which, after hydroboration and oxidation with H_2O_2[21] gave almost exclusively (+)-isothujyl alcohol. The latter was then oxidized under the standard conditions[22] of the Jones oxidation[23] to pure (+)-isothujone (XIX).

DISCUSSION OF RESULTS

Both dextrorotatory thujanes A and B (XV and XIV), the configurations about C-4 of which have been fixed with respect to (+)-pulegone (IX),[11] are stereoisomers in two

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[21] H. C. Brown and P. A. Tierney, *J. Amer. Chem. Soc.* **80**, 1552 (1957).

[22] C. Djerassi, R. R. Engle and A. Bowers, *J. Org. Chem.* **21**, 1547 (1956); G. Ohloff, J. Osiecki and C. Djerassi, *Chem. Ber.* **95**, 1400 (1962).

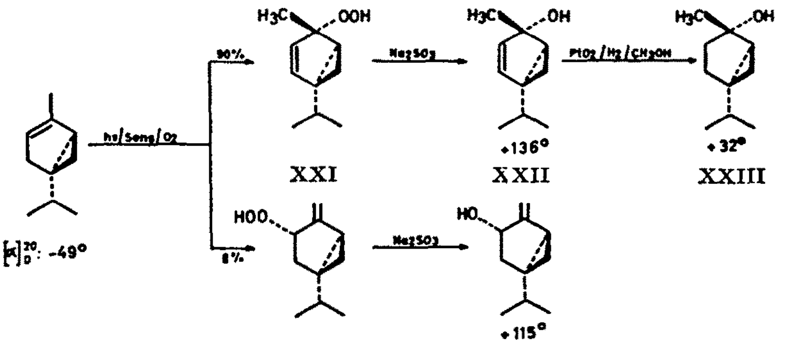
[23] K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.* 39 (1946).

different series. (+)-A and (−)-B (XV and XVI) are, on the other hand, diastereomers, while the two hydrocarbons (+)-B and (−)-B (XIV and XVI) are enantiomers. The conversion of XVII to (+)-thujane (XV),[24] as well as XIX via XVIII (or directly) to XV, fixes the configuration about C-4 of (+)-isothujyl alcohol (XVIII) and (+)-isothujone (XIX). From this, it follows that (−)-thujone (XX) is linked with the previously unknown (+)-thujane (XVI). The relative position of the substituents in XVIII is given by the stereospecific hydroboration of (−)-α-thujene (XVII), i.e. the *cis*-addition occurs preferentially from the less hindered side of the molecule away from the cyclopropane ring. The *cis*-substitution in XIV also devolves from the stereospecific carbene addition to (+)-3-methyl-1-isopropylcyclopentene (XIII) giving (+)-thujane (XIV).

A discussion of the spectral characteristics of the thujanes appears as an appendix to this paper.

A further example of a reaction in this series that takes place highly stereospecifically is the photosensitized oxidation of (−)-α-thujene (XVII). It leads to a sterically homogeneous addition product (XXI) in 90% yield, that, after reduction of the hydroperoxide group, catalytic hydrogenation converted to pure (+)-*trans*-sabinene hydrate (XXIII)[25] (m.p. 61°). The IR and NMR spectrum confirms the structure of the new alcohol (XXII) as (+)-*trans*-thuj-2-en-4-ol.

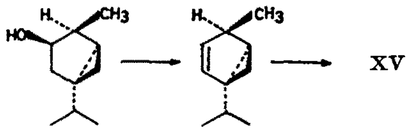
In addition to the latter, 8% of the reduced photo-oxidation product consisted of a secondary alcohol, m.p. 45–46°. The IR spectrum of this compound was very similar



XXI XXII XXIII

XVII XXIV XXV

[24] L. Tchougaeff and W. Formin, *C.R. Acad Sci., Paris* **151**, 1058 (1910) obtained a (+)-thujane of $[\alpha]_D^{20} = +34{\cdot}72°$ by catalytic reduction of (+)-β-thujene (XXXIII), the latter having been obtained by pyrolysis of a (+)-thujylalcohol xanthogenate. In view of our present correlations (cf. footnote 8), the hydrocarbon must have been (+)-*trans*-thujane (XV) and the alcohol leading to (+)-β-thujene (XXXIII) must have been (+)-neoisothujyl alcohol (XXXII).



XXXII XXXIII

[25] J. W. Daly, F. Ch. Green and E. H. Eastman, *J. Amer. Chem. Soc.* **80**, 6330 (1958).

to that of the natural product Vb,[26] and the mass spectrum[27] was virtually identical with Vb, but the physical constants showed big differences. Since the attack of molecular oxygen on XVII can only take place from the side of the molecule away from the cyclopropane ring, the reduced photo-product XXV must be the unknown *cis*-sabinol. The same reasoning leads to further conformation of the *trans*-structure of the sabinene hydrate (XXIII) found in Hinoki oil,[28] American peppermint[25] and spearmint[29] oils and in mandarin oil.[30]

The structural attribution of the secondary (Vb) alcohol was confirmed by its NMR spectrum. The two sabinols show marked differences since the carbinol substituent above the ring is directly in front of the cyclopropane ring, and so heavily shielded by it.[31] Thus in the new *cis*-sabinol, the proton on the carbinol carbon is a multiplet centred on 4·0 ppm, whilst in natural *trans*-sabinol it is a broadened doublet at 4·33 ppm. In natural sabinol, the effect of the oxygen on the 6A proton is to shift it to lower field than the methyl signals, while the 6B proton results in a multiplet at 0·70 ppm. The new alcohol has the oxygen removed from these protons, which accordingly appear at 0·60 and 0·51 ppm.

The formation primarily of the tertiary allyl hydroperoxide (XXI) with only relatively little secondary hydroperoxide (XXIV) is the more surprising, in that attack of photosensitized oxygen on α-pinene,[32] although occurring from the unhindered side of the molecule, goes almost entirely on the unsubstituted end of the double bond,[33] leading to *trans*-pinocarveyl hydroperoxide. The comparable car-3-ene[34] yields tertiary and secondary allyl-hydroperoxides in equal amounts.

EXPERIMENTAL

Mps are uncorrected.

Preparative gas chromatography was carried out either on a Wilkens Aerograph A 700 Autoprep or on a previously described apparatus.[35] The analytical gas chromatography was carried out on an apparatus (type 58c) developed in our analytical laboratory (Dr. E. Palluy) and filled with an integrator, or on the laboratory gas chromatography model 59 T (developed by E. Palluy) made by the Société d électronique et de mécanique Aquitaine, Pau France (under licence from Firmenich et Cie.) using a 3 m 15% carbowax on chromosorb W column at 100–150° carrier gas 40 ml He/min.

IR spectra were measured on a Perkin-Elmer model A-21 using a NaCl prism or on the grating model 125; solids in KBr pellets, liquids between NaCl plates.

NMR spectra were measured on a Varian model A-60 in CCl_4 with tetramethylsilane as internal reference. The following abbreviations are used: s = singlet, d = doublet, t = triplet, m = multiplet, b = broad, av = average value. Mass spectra (M.S.) were measured on an Atlas model

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[26] For Refs see E. Gildemeister and Fr. Hoffmann *Die aetherischen Oele* (4th Edition revised by W. Treibs and D. Merkel) Vol. IIIb, p. 209.

[27] B. Willhalm, A. F. Thomas and M. Stoll, *Acta Chem. Scand.* **18**, 1573 (1964).

[28] A. F. Thomas, *Perf. and Ess. Oil Record* **56**, 301 (1965).

[29] I. C. Nigam and L. Levi, *Agric. Food Chem.* **11** [3], 276 (1963).

[30] E. Kugler and E. sz. Kovats, *Helv. Chim. Acta* **46**, 1480 (1963).

[31] S. Forsén and T. Norin, *Tetrahedron Letters* 2845 (1964).

[32] G. O. Schenck, H. Eggert and W. Denk, *Liebigs Ann.* **584**, 177 (1953).

[33] G. Helms, Thesis, Göttingen (1961). Careful analysis of the photooxidation products of α-pinene shows that 95% *trans*-pinocarveyl hydroperoxide and 0·56% *cis*-pin-3-ene-2-hydroperoxide is formed.

[34] G. O. Schenck, S. Schroeter and G. Ohloff, *Chem. & Ind.* 459 (1962).

[35] E. Heilbronner, E. Kovats and W. Simon, *Helv. Chim. Acta* **40**, 2410 (1957); E. Kovats, W. Simon and E. Heilbronner, *Ibid*, **41**, 275 (1958).

CH-4. Inlet temp 150°, ion source temp approx. 250° at 70 eV energy. The most important fragment in the group is given, with the relative intensity as % base peak in brackets after the mass number.

The UV spectrum was measured on an Optica CF-4.

1. *Preparation of* (+)-*pulegen* (XIII) *from* (+)-*pulegone* (IX)

(a) (+)-*2-Hydroxy-3-isopropylidene-1-methylcyclopentane* (XI). (+)-Pulegone (IX) (d_4^{20} 0·9349; n_D^{20} 1·4876; $[\alpha]_D^{20}$ +22·68°) was converted[36] *via* the corresponding dibromide (yield: 95%) to X (yield: 52%) having b.p. 111–118° (3 mm); d_4^{20} 1·0124; n_D^{20} 1·4840; $[\alpha]_D^{20}$ +40·40°.

(+)-Pulegenic acid (63 g) in 320 ml ether at 0° was esterified with 750 ml 0·5N diazomethane in ether to obtain 59 g (92·3%) methyl (+)-pulegenate b.p. 89–92° (10 mm); d_4^{20} 0·9592; n_D^{20} 1·4677; $[\alpha]_D^{20}$ +41·50°.

Gas chromatography showed the main part (over 65%) to be the *trans*-ester, the secondary product being the *cis*-ester.

Methyl (+)-pulegenate (48 g) in 400 ml dry ether was added dropwise over 1 hr to 5·7 g LAH in 400 ml ether, then refluxed 2 hr. After customary working-up, the product, XI,[37] (35·7 g, 87%) was distilled at 99–102° (10 mm); d_4^{20} 0·9329; n_D^{20} 1·4801; $[\alpha]_D^{20}$ +3·5°. In conformity with the ester mixture used, this alcohol consisted (by gas chromatographic analysis) of 65% *trans*-XI and 35% *cis*-alcohol.

(b) (+)-*Pulegene* (XIII). The alcohol (XI; 30 g) was passed during 2½ hr through a pyrolysis column[38] maintained at 480° and 40 mm press., the pyrolysate being condensed in two traps at − 80° connected in series. The pyrolysate was washed with a little water then distilled at atm. press. (730 mm). The hydrocarbon (XIII) distilled at 135–142° (8·3 g; 34·4%), leaving a residue of unchanged starting material (XI) . Twice repeating this procedure yielded a total of 20·6 g (85·3%) (XIII); b.p. 132–135° (730 mm); $[\alpha]_D^{20}$ +92·7°. Gas chromatographic analysis showed the purity to be better than 95%. Purified on an Apiezon L column, (+)-pulegene (> 99% pure) had d_4^{20} 0·791; n_D^{20} 1·4402; $[\alpha]_D^{20}$ +98·5°.[39]

NMR spectrum 5·16 ppm = $>=<_{H}$; 2·25 ppm (b. av) = 4 allyl protons; 1·3 ppm (av) = 2 methylene protons.

The combined washings of the pyrolysate were heated with a concentrated dimedone solution. A copious white precipitate (m.p. 189°) of formaldehyde-dimedone was obtained.

2. *Preparation of* (+)-cis- *and* (+)-trans-*thujane* (XIV and XV)

(a) *Reaction of* (+)-*pulegene* (XIII) *with carbene*. 20 ml Iodomethyl-zinc iodide complex[17] in ether, containing 0·02 mole active methylene was added at 0° to a vigorously stirred solution of 2·48 g (0·02 mole) XIII in 3 ml ether and protected by an argon atm. After allowing to react for ½ hr at 0° and standing for 18 hr at room temp, the mixture was decomposed with ice. The organic phase was washed with 2N NH_4OH and then with water. After removing the solvent, the cyclopropane product had b.p. 63–65° (10 mm); $[\alpha]_D^{20}$ +30·4°; yield 2·5 g (90·6%).

According to gas chromatographic analysis, the carbene addition product consisted of 32% (XV), 67% (XIV), and 0·8% unidentified material. The reaction mixture was separated by preparative gas chromatography.[35] In addition to unchanged starting material, two fractions were obtained:

Fraction	(+)-Pulegene (XIII)	(+)-Thujane A (XV)	(+)-Thujane B (XIV)	unknown	$[\alpha]_D^{20}$
1	100%	—	—	—	+ 98·5°
2	—	32·2%	67·0%	1·5%	+ 30·4°
3	—	1·9%	97·3%	0·8%	+ 8·2°

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[36] H. Rupe and K. Schäfer, *Helv. Chim. Acta* **11**, 466 (1928).

[37] J. Wolinsky, B. Challar and M. Bairol, *J. Amer. Chem. Soc.* **84**, 2775 (1962).

[38] G. Ohloff, *Chem. Ber.* **93**, 2673 (1960).

[39] see footnote 14. Using our value for *d*, the specific rotation of XIII, calculated from J. Jacques *et al.* is $[\alpha]_D$ +96·69°.

If the byproduct is optically inactive, the optical activity of thujanes A and B may be computed as follows: (+)-thujane-A (XV), $[\alpha]_D^{20}$ +80°; (+)-thujane-B (XIV), $[\alpha]_D^{20}$ +6·7°. The physical data of practically pure (XIV): d_4^{20} 0·821; n_D^{20} 1·4413.

(b) *Wolff-Kishner reduction of thujones* XIX *and* XX. (+)-Thujone (mixture of isomers obtained from *Thuja occidentalis* L[40]; 12 g) was boiled with 6 g hydrazine hydrate and 50 ml EtOH for 2 hr. Most of the solvent was evaporated and the residue heated for 13 hr at 180° in a sealed tube with EtONa (from 4 g Na and 45 ml absolute EtOH). Working up as usual gave 11·9 g crude product, most of which distilled at 63–65° (10 mm). Gas chromatography on a carbowax column showed 29% (+)-thujane A and 71% (−)-thujane B. After separation, (−)-thujane B has the same IR and NMR spectra as (+)-thujane B, and the following constants were observed: (+)-*trans*-thujane A (XV): α_4^{20} 0·815; n_D^{20} 1·4393; $[\alpha]_D^{20}$ +87·0°. $J_{110}^{A} = 943$ (retention index[41] on Apiezon-L at 110°). (−)-*cis*-thujane B (XV): d_D^{20} 0·820; n_D^{20} 1·4417; $[\alpha]_D^{20}$ −6·0°; $J_{110}^{A} = 952$.

The physical data of *trans*-thujane (XV) were measured on a sample containing 11% impurity, *cis*-thujane (XVI) together with 1·5% unknown substances. The *cis*-thujane still contained 2·4% XV. The rotations stated are valid for the pure compounds XV and XVI, and were calculated from the $[\alpha]_D^{20}$ values observed on the samples obtained.

(c) *Hydroboration*[18] *of* (+)-*sabinene*. The following experiments were carried out using (Va) distilled from Formosan Hinoki leaf oil.[28] The pure hydrocarbon had b.p. 69° (30 mm); d_4^{20} 0·8436; n_D^{20} 1·4681; $[\alpha]_D^{22}$ +87°.

Boron trifluoride-etherate (5·7 g; freshly distilled) in 6 ml diglyme were added over 30 min to a solution of 1·134 g $NaBH_4$ and 13·6 g Va in 55 ml diglyme. After 5 min more, 11 ml propionic acid were added and the mixture immediately heated at reflux (about 150°) for 2 hr. Neutralization with 10% NaOH aq and extraction with pentane gave 13·4 g of a mixture b.p. 48–59° (100 mm) consisting of more than ten products. Heating the organoborane at reflux for 2 hr before addition of the acid leads to the same mixture. Neither *cis*- nor *trans*-thujane could be detected in this mixture, which consisted mostly of monocyclic hydrocarbons derived from iridane and menthane. The following (representing 88·5% of the hydrocarbons) were identified spectroscopically after gas chromatographic purification on a carbowax column (in order of elution): Irid-2-ene (XXVIII; 19%); NMR $CH_3—CH<$ 0·95 ppm (*d*, J = 7 c/s, 9 protons) $CH_3—\overset{|}{C}=$ 1·53 ppm M.S.:[42] m/e 138, 3·5% Σ_{25}; m/e 123, 9·0% Σ_{27} (allyl methyl); m/e 95, 32·5% Σ_{27} (isopropyl).

Irid-3-ene (XIX, 6%); NMR 12 protons at 0·8–1·1 ppm (four CH_3 on saturated C), —C═C—H 5·15 ppm (av, b.). Mass spectrum: m/e 138, 4·2% Σ_{27}; m/e 123, 8·3% Σ_{27} (allyl methyl; m/e 95, 25% Σ_{27} (isopropyl).

Irid-3(8)-ene (XXX, 7%); NMR $CH_3—CH<$ 0·77 and 0·95 ppm (*d*, J = 7 c/s, 3 protons each), $CH_3—\overset{|}{C}═$ 1·59 ppm (6 protons). Mass Spectrum: m/e 138, 4·6% Σ_{27}; m/e 123, 10·5% Σ_{27} (allyl methyl), m/e 95, 17% (no isopropyl).

p-Menth-3-ene (12%). Spectra identical with authentic material.

Irid-1-ene (XXXI, 18%); NMR $CH_3—CH<$ 0·64 and 0·90 ppm (*d*, J = 7 c/s, 3 protons each); $CH_3—\overset{|}{C}═C$ approx 1·57 ppm (av, 6 protons). Mass spectrum: m/e 138, 4·4% Σ_{27}; m/e 123, 2·7% Σ_{27} (no allyl methyl); m/e 95, 47·3% Σ_{27} (allyl isopropyl).

α-Terpinene (17%), γ-terpinene (4·5%) and *p*-mentha-2,4 (8)-diene (5%) were identified spectrally with authentic materials.

Irid-1-, -2- and -3(8)-ene (XXXI, XXVIII and XXX) had no sharp strong bands in their IR spectra at 1600–1700 cm^{-1}, in accordance with their having tetrasubstituted double bonds.

(c_2). The organoborane, prepared as described above (c_1), was stirred at 0–20° with the corresponding amount of propionic acid for 2 hr, and only then heated 2 hr at reflux. After workup, 8·2 g (60%) distilled at b.p. 40–42° (10 mm), and consisted, by gas chromatographic analysis on a carbowax

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[40] The commericially available thujone consisted (by gas chromatographic analysis) of about 70% (−)-thujone (XX), 15% (+)-isothujone (XIX) and 15% unidentified material.

[41] E. Kovats, *Helv. Chem. Acta* **41**, 1915 (1958); E. Kovats, *Z. analyt. Chem.* **181** (1960).

[42] The mass spectral deductions were made on the relative importance of the three fragments given (as % total ionization), and compared with the same fragments in the mass spectra of various menthenes (see Ref. 46).

column, of 35% *cis*- (XVI) and 65% *trans*-thujane (XV). Heating the organoborane 2¼ hr at reflux then treating as described with cold propionic acid gave the same yield of thujane mixture, this time having 43% *cis*- (XVI) and 57% *trans*-thujane (XV).

(d) (+)-trans-*Thujane* (XV) *by lithium aluminium hydride reduction of* (+)-*isothujyl*-p-*toluenesulphonate*. Crude XVIII (2 g), prepared according to 3c (below) was dissolved in 2 ml benzene and 4 ml dry pyridine, the calculated amount (+10% excess) *p*-toluenesulphonyl chloride added, and the mixture allowed to stand with occasional shaking for 4 days at room temp. The unreacted *p*-toluenesulphonyl chloride was filtered from the red-brown reaction mixture, the pyridine solution taken up in ether and washed successively with cold 10% H_2SO_4, 5% NaOH aq and water until neutral. Removal of the ether left a solid residue that was precipitated from a petroleum (b.p. 80–100°) solution. Washed with petroleum, the fine needles[10] had m.p. 87–88° $[\alpha]_D^{20}$ +95° ($c = 10$ in $CHCl_3$). (Found: C 66·79; H 7·73, S 10·37%. $C_{17}H_{24}O_3S$ requires: C 66·21; H 7·85; S 10·38%.)

Toluenesulphonate (1 g) was dissolved in 3 ml absolute tetrahydrofuran and slowly added dropwise to a stirred slurry of 0·4 g LAH in 5 ml tetrahydrofuran at room temp. The mixture was then heated 4 hr at reflux, cooled and carefully decomposed with water, the product being isolated by repeated ether extraction. After concentration, the residue (0·8 g) consisted of a liquid, together with crystals of unchanged toluenesulphonate. It was cooled to − 30°, when most of the toluenesulphonate crystallized out, then the liquid (about 350 mg) was removed by means of a fine capillary.

Gas chromatographic analysis showed the liquid to be homogeneous and identical with the *trans*-thujane (XV) obtained from the reaction of XIII with carbene. The *trans*-thujane (XV) thus prepared has $[\alpha]_D^{20}$ +87·7°.

3. *Preparation of* (+)-*isothujone* (XIX) *from* (+)-*isothujyl-alcohol* (XVIII)

(a) (−)-α-*Thujene* (XVII) *by Birch reduction of sabinyl acetate* (cf. Ref. 20). Sabinyl acetate (Vc; 100 g; pure, distilled from Savin oil[43] and having $[\alpha]_D^{20}$ +79·3; d_4^{20} 0·9667; n_D^{20} 1·4707) in 10 ml absolute EtOH was added over 2 hr to a vigorously stirred solution of 56 g Na in about 1·2 l. liquid ammonia. The reaction was allowed to evaporate (about 24 hr) in the open. The product, obtained in the usual way, was a pale oil (58·2 g, 83%) distilling at 151–159° (738·5 mm).

The main fraction consisted, by gas chromatographic analysis, of XVII together with about 15% Va and had α_D^{20} −16·4°; d_4^{20} 0·8357; n_D^{20} 1·4556.

The pure hydrocarbons were separated on a carbowax column and had the following constants:
(−)-α-Thujene (XVII): $[\alpha]_D^{20}$ −49·3°; d_4^{20} 0·8308; n_D^{20} 1·4511.
(+)-Sabinene (Va): $[\alpha]_D^{20}$ +107·2°; d_4^{20} 0·8428; n_D^{20} 1·4672.

(b) (+)-*Isothujyl alcohol* (XVIII) *by hydroboration of* (−)-α-*thujene* (XVII). Excess gaseous diborane, prepared from 1 g $NaBH_4$ in 10 ml diglyme and 4·1 g BF_3–etherate, was passed into a solution of 5 g crude XVII (α_D^{20} − 16·4°, containing Va)] in 20 ml absolute tetrahydrofuran at < 0° over 3 hr. The mixture was stirred for a further hr at 0° and the free diborane decomposed with 5 ml water in 20 ml tetrahydrofuran. Alcoholic KOH (10%; 11 ml) were then dropped in, followed by 4·2 ml H_2O_2 (30%) at 0°. The oxidation mixture was taken up in ether and washed with water until free from alkali and H_2O_2. The viscous residue weighed 5·6 g, and was chromatographed on 250 g alumina (Woelm, activity III), taking 12 petroleum (b.p. 30–50°) fractions of 30 ml. Fractions 2–5 gave an oily liquid (3·95 g, 70%) consisting of a main product together with 15% of a compound with longer retention time on a carbowax column. The main component (XVIII) had the following constants after gas chromatographic purification: $[\alpha]_D^{20}$ +114°; d_4^{20} 0·9154; n_D^{20} 1·4602.

(c) *Jones oxidation of* (+)-*isothujylalcohol* (XVIII). Gas chromatographically pure XVIII (1·95 g) was dissolved in 100 ml oxygen-free acetone and oxidized with standardized chromic acid solution with vigorous stirring. The usual working-up gave 1·8 g (93·5%). The gas chromatographically pure XIX has the following constants: $[\alpha]_D^{20}$ +73·4°[44]; d_4^{20} 0·9185; n_D^{20} 1·4508. UV spectrum:[45] λ_{max}^{EtOH} 291·1 mμ ($\varepsilon = 218$); λ_{max}^{EtOH} 204·8 mμ ($\varepsilon = 519$).

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[43] A. B. Booth, *Amer. Perf.* **69,** 45 (1957).

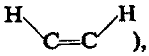
[44] O. Wallach, *Ber. Dtsch. Chem. Ges.* **28,** 1965 (1895) found $[\alpha]_D$ +76·16° for a ketone, "β-thujone", he regenerated from its semicarbazone A. G. Short and J. Read, *J. Chem. Soc.* 2016 (193 8) found α_D^{15} +72·45°.

[45] H. Mohler and H. Lohr, *Helv. Chem. Acta* **20,** 1183 (1937).

4. *Photosensitized oxygenation of* (−)-α-*thujene to* (+)-trans-*thuj-2-en-4-ol* (XXII) *and* (+)-cis-*sabinol* (XXV)

A preliminary experiment showed that 1·66 g pure (−)-α-thujene and 60 mg Bengal red dissolved in 120 ml MeOH absorbed 1 mole (307·7 ml) O_2 in 37 min on irradiation with a Hg-lamp (Philips HPK 125 W). Two further additions of dyestuff had to be made when the colour was bleached.

Accordingly, 10 g (−)-α-thujene in 200 ml MeOH was irradiated until 1 mole O_2 was absorbed, when the irradiation was stopped. The solution gave a positive KI–acetic acid test. About ¾ of the solvent was removed below 20° (rotary evaporator) and the stirred solution at 0° was immediately treated with 25 g Na_2SO_3 in 180 ml water, added dropwise over 2 hr. The product was isolated in ether, and, after routine washing, etc., formed 10·8 g (96%) of a mobile oil consisting, by gas chromatographic analysis, essentially of two substances—peak 1 (90%) and peak 2 (8%)—of very different retention times.

Distillation at 10 mm resulted in incomplete separation, so the products were purified gas chromatographically. Peak 1 had $[\alpha]_D^{20}$ +136°; n_D^{20} 1·4668; d_4^{20} 0·9223. IR spectrum λ_{max} 3400 cm^{-1}, 1900 cm^{-1} (OH); 753 cm^{-1} (*cis*  $\overset{\mathrm{H}\diagdown\quad\diagup\mathrm{H}}{\mathrm{C{=}C}}$), 1600 cm^{-1} (C=C), 3070 cm^{-1} (CH).
MS: Molecular ion m/e 152 (< 1%); m/e 137 (18%); 134 (3%); 119 (16%); 109 (100%); 91 (57%); 67 (19%); 55 (10%); 43 (57%). NMR: 5·90 ppm (d, J = 6 c/s) and 5·29 ppm (d, further splitting, J = 6); $\mathrm{^{H}{>}C{=}C{<}^{H}}$ 1·27 ppm (s), $CH_3{=}C{\leqslant}$.

Peak 2 crystallized on cooling, m.p. 45–46°; $[\alpha]_D^{20}$ +115·0° (c = 10 $CHCl_3$). IR spectrum λ_{max} 3375, 1860 cm^{-1} (OH); 880, 1660, 3080 cm^{-1} (exocyclic >C—CH_2). Only small differences with the IR spectrum of Vb were observed. The mass spectrum was practically identical with that of Vb[38] but with intensity of m/e 109 30% of base instead of 37%, and m/e 81 55% instead of 60%.
NMR: 4·0 ppm (t, further splitting) >CH—OH; 0·60 ppm (s, b) and 0·51 ppm (s), $\rhd CH_2$.

(a) (+)-trans-*Sabinene hydrate* (XXIII). Pure XXII (1·22 g) in 6 ml MeOH was shaken in H_2 with pre-reduced Adams' catalyst (100 mg), when 210 ml was absorbed in 2·5 hr. Removal of catalyst and solvent yielded 1·0 g colourless felted crystals, subliming rapidly at room temp, m.p. 60–61°; $[\alpha]_D^{20}$ +32° (c = 10 EtOH); $[\alpha]_D^{20}$ +14·2° (c = 10 $CHCl_3$).
M.S.: Molecular ion m/e 154 (2·2%); 139 (9%); 136 (15%); 121 (20%); 111 (18%); 93 (100%); 77 (31%); 71 (48%); 55 (19%); 43 (61%).
NMR: 1·22 ppm (s) $CH_3{=}C{\leqslant}$, ~ 0·2 ppm (m, 2 protons) $\rhd CH_2$.

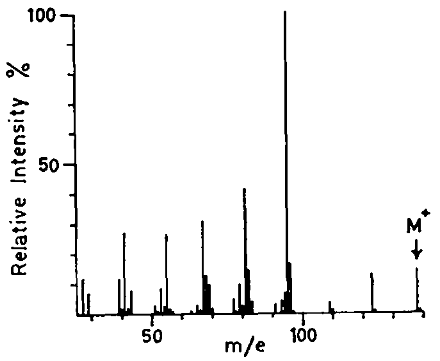
Appendix

The spectral characteristics of the thujanes. The mass spectra of the two thujanes XV and XVI were practically identical. The importance of the molecular ions was 3·46% Σ_{27} (total ionization) for *cis*-XVI and 3·34% Σ_{27} for *trans*-XV, and it was not possible to use the spectra with certainty to confirm the stereochemistry, as has been possible with other stereoisomeric monoterpenes.[46] This thermodynamic similarity of the hydrocarbons is also reflected in the relatively unstereospecific hydroboration of sabinene, the *cis-trans*-composition of the organoborane being only slightly changed on heating, in contrast to the organoborane from β-pinene.[18]

[46] A. F. Thomas and B. Willhalm, *Helv. Chim. Acta* **47**, 475 (1964). The differences in stability of the molecular ion of *trans*- and *cis*-menthanes and menth-8-enes is described herein, as well as exo- and endo-isocamphane. We have recently found that *trans*- and *cis*-pinanes show the molecular ion as 0·5% and 0·55% Σ_{27} (% total ionization) respectively. In these cases, the fragment at m/e 55, formed by the strain-releasing fission of the four carbons not involved in the cyclobutane ring is 9·39% (*trans*-) and 11·38% Σ_{27} (*cis*-), rendering a distinction possible. [The pinene quoted in the paper cited is *cis*-, and the importance of the fragment at m/e 80 should read 6·2% of base peak (not 62%).] See also examples of the variations of stability of stereoisomers in P. Natalis, *Soc. Chim. Belg.* **69**, 519 (1960) and of the menthones in B. Willhalm and A. F. Thomas, *J. Chem. Soc.* in press.

FIG. 1

Mass spectrum of Thujane



The experimental results are much better supported by the NMR spectra of XV and XVI (Figs 2 and 3), the chemical shifts necessary to the structural attribution being given in Table 1.[47]

In the *cis*-thujanes (XIV and XVI), the dihedral angle between the hydrogens on C-4 and C-5, measured on Dreiding models, is only slightly more than 90°, so that no coupling is to be expected between these protons. In fact the C-5, C-6A, C-6B protons

FIG. 2

trans-Thujane

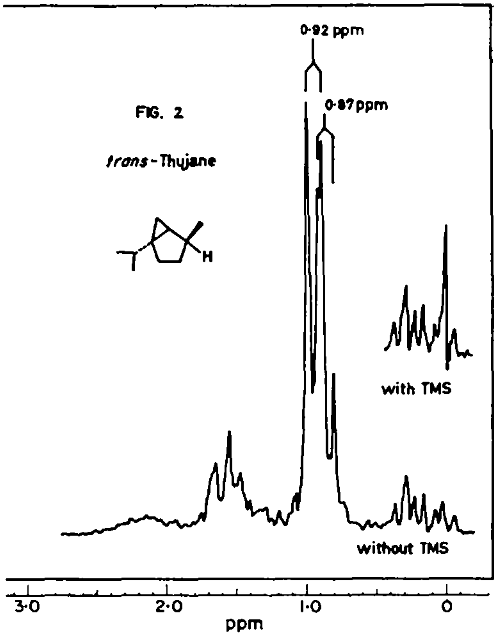
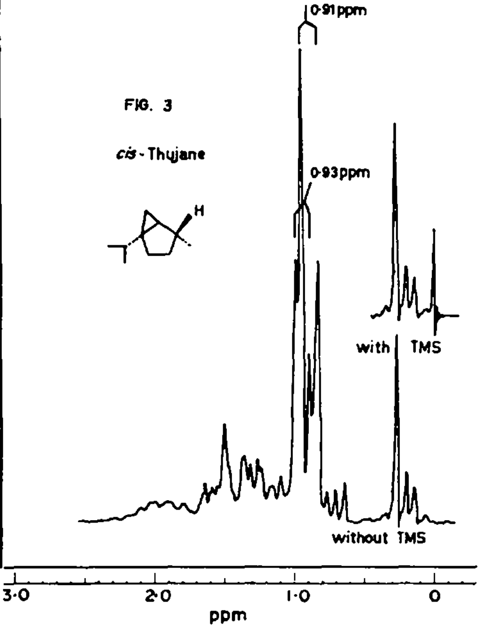


FIG. 3

cis-Thujane



[47] The chemical shifts listed in the Table were taken from the 60 Mc/s spectra, and form the subject of a publication of A. Dieffenbacher and W. V. Philipsborn (Chemistry Laboratory, Zürich University) to appear in *Helv. Chim. Acta*. These authors carried out analyses of the thujane spectra using a Varian 100 Mc/s spectrometer with double and triple resonance.

TABLE 1

Protons on carbons in Formula I	Chemical shift (δ, ppm) in *trans*-thujane (Thujane A)	*cis*-thujane (Thujane B)
4	2·1	1·95
5	~0·9	0·72
6A	0·09	0·23
6B	0·29	~0·23
10	0·87	0·93
8/9[48]	0·92	0·91
$J_{4,5}$	Spin coupled	Not coupled

in the 60 Mc/s spectrum form almost an isolated A_2B system, changing to an ABX system in the 100 Mc/s spectrum. *trans*-Thujane (XV), on the other hand, exhibits coupling between these two protons, a dihedral angle of about 30° being observed on models. Our measurements are in accord with similar observations by Norin[9] on known thujane derivatives. A further argument for this attribution is provided by the comparison of the chemical shifts of the C-6A proton. This should be more shielded in thujane A by the methyl group *cis*- to it; the diamagnetic shift in thujane A (XV) compared with thujane B (XIV and XVI) confirms the configuration. Finally, the additional shielding of the protons on C-10 caused by the cyclopropane ring when the latter is on the same side of the ring is evident in *trans*-thujane as is the shielding on the C-4 proton in *cis*-thujane (cf. Ref. 31).

Acknowledgement—The authors are grateful to Dr. B. Willhalm for valuable discussions.

[48] Average chemical shift of the methyl groups of the isopropyl chain.