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Elimination Reactions. Part II.¹ Pyrolytic and Base-promoted Decompositions of Thujyl Compounds

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Dehydrations of (-)-thujol, (-)-neothujol, (+)-isothujol, and (+)-neoisothujol by pyridine-phosphorus oxychloride, and also pyrolyses of the derived dimethylamine oxides and S-methyl xanthates, gave, singly or in mixture, (-)- α -thujene, (+)- β -thujene, and the hitherto uncharactised (+)- β -isothujene. In view of the known stereospecificity of these reactions, the results con.rm recently assigned configurations for the alcohols. Hofmann degradation of the four thujyltrimethylammonium hydroxides gave products attributable to concurrent anti- and syn-eliminations, and tracer studies showed that part of the latter process from the isothujyl 'onium compound involved the α'-β mechanism. Pyrolysis of thujyl acetates and borates, or treatment of the alcohols with iodine or zinc chloride, resulted exclusively in ring-opened products. A brief study of additions to (+)-sabinene and $(-)-\alpha$ thujene suggests that generation of the 4-thujyl carbonium ion is favoured over that of the 3-thujyl ion, despite the potentialities of the latter for formation of a non-classical species.

THE thujols have recently been assigned the configurations (I)—(IV) on chemical and physical evidence.^{2,3} Analysis of products from eliminations of known stereospecificity should enable the relative configurations to be checked, but studies of such reactions have been fragmentary. Pyrolyses of the S-methyl xanthates of

¹ Part I, M. A. Baldwin, D. V. Banthorpe, A. Louden, and F. D. Waller, J. Chem. Soc. (B), 1967, 509.

- D. V. Banthorpe and H. ff. S. Davies, preceding paper.
 T. Norin and M. S. Bergquist, Arkiv. Kemi., 1964, 22, 137.

(+)-isothujol and (-)-thujol were claimed to give pure $(-)-\alpha$ -thujene (V) and a mixture of this and $(+)-\beta$ thujene (VI), respectively, whereas the xanthate from (-)-neothujol yielded mainly (+)- β -thujene.⁴⁻⁶ Taking into account the syn-periplanar arrangement of leaving groups necessary for these reactions, configurations for the alcohols were proposed, but these are now known to be incorrect.³ These substrates were almost certainly mixtures of isomers, and the methods for productanalyses are suspect. Hofmann degradation of mixtures of thujyl 'onium hydroxides was claimed to give either negligible elimination 7 or a mixture of α - and β -thujenes predominating in the former; ⁸ pyrolysis of the amine oxide (VIII) was briefly reported 9 to give β -thujene, bicyclohexenes of rearranged skeleton, and monocyclic products.



RESULTS

Four isomeric thujylamines with the same prefix nomenclature as the thujols have been described 7,10 but no structural correlations between the classes were carried out. Comparison of the stereochemistry of reduction of ketones with that of oximes (see Experimental section) suggests that similarly named isomers do have similar configurations, and this has been confirmed by chemical and n.m.r. correlations.^{11,12} The thujylamines were converted into oxides and 'onium salts without change of configuration.

Products from several series of eliminations are in Tables 1 and 2. The dehydrations gave much ring-opened material in addition to thujenes, and the balance of the Hofmann degradations was entirely substitution at the N-methyl groups, but the non-thujene products from the

⁴ L. Tschugaev and W. Fomin, Ber., 1912, 45, 1293; Compt. rend., 1910, 151, 1058.

⁵ I. L. Kondakov and W. Skworzov, J. prakt. Chem., 1903,
 67, 574; 1904, **69**, 176; J. Russ. Phys. Chem. Soc., 1910, **42**, 497.
 ⁶ W. von E. Doering and J. B. Lambert, Tetrahedron, 1963,

19, 1989. ⁷ A. G. Short and J. Read, J. Chem. Soc., 1938, 2016.
⁸ L. Tschugaev, Ber., 1901, 34, 2276.

TABLE 1

Pyrolytic eliminations

	Yield (%)	Tł	Thujene (%)	
Substrate	of olefin	α-	β-iso-	β-
Amine oxide $ex(+)$ -neoisothujol	ca. 100	0	>99	<1
Amine oxide $ex(+)$ -isothujol	ca. 100	33	67	0
Amine oxide $ex(-)$ -neothujol	ca. 100	20	0	80
Amine oxide ex (-)-thujol	ca. 100	0	< 1	> 99
Methyl xanthate ex (+)-neoiso-	•			
thujol	ca. 15	0	100	0
Methyl xanthate $ex(+)$ -isothujol	ca. 15	87	13	0
Methyl xanthate $ex(-)$ -neothujol	ca. 15	41	0	59
Methyl xanthate $ex(-)$ -thujol	ca. 15	0	0	100

TABLE 2

Base-promoted eliminations

	Con-	Vield		Thuje)	
Substrate	ditions	(%)	α-	β-iso-	β-	Rate *
(+)-Neoisothujol	Α	63	99	1	0	
(+)-Isothujol	Α	3	0 ‡	100 ‡	0	
(-)-Neothujol	Α	4	0 ‡	0 ‡	100 ‡	
(—)-Thujol	Α	18	96	0 .	4 .	
'Onium salt $ex (+)$ -						
neoisothujol †	в	39	93	7	0	16
'Onium salt $ex (+)$ -						
isothujol	в	78	48	52	0	89
'Onium salt $ex (-)$ -						
neothujol	в	80	4	0	96	100
'Onium salt $ex (-)$ -						
thujol	\mathbf{B}	4	80	0	20	1
'Onium salt $ex (+)$ -						
neoisothujol	С	70	78	22	0	8
'Onium salt $ex (+)$ -						
isothujol	С	95	46	54	0	68
'Onium salt $ex (-)$ -						
neothujol	С	95	3	0	97	68
'Onium salt $ex (-)$ -						
thuiol	С	22	58	0	42	1

A, Phosphorus oxychloride-pyridine at 0°; B, classical conditions of Hofmann degradation; C, Hofmann degradation at low pressures and temperatures.

Relative rates for E2 (total) (within series). † Trimethylammonium salt. \ddagger Error $\pm 5\%$ (actual value) owing to low yield.

xanthate pyrolyses were not characterised. No epimerisation of substrate or products was caused by the basic conditions used in the preparation of xanthates. Controls showed that negligible interconversion or decomposition of thujenes occurred during the eliminations.

A few additional pyolyses were made. Heating of a mixture of thujyl acetates at 370° to 500° with low contact times (ca. 6 sec.) gave results similar to those reported 13 for longer contact times and higher temperatures. Menthadienes and p-cymene, but no thujenes, were formed. The decomposition of thujyl borates at ca. 140° was similar. Acetates and borates of 2-methylcyclopentanol reacted smoothly under these conditions to give methylcyclopentenes in 50-70% yields. Various ancillary experiments relating to E1 mechanisms are described more conveniently in the next section.

⁹ J. N. Lowe, *Diss. Abs.*, 1964, **25**, 840. ¹⁰ H. L. Dickison and A. W. Ingersoll, *J. Amer. Chem. Soc.*, 1939, 61, 2477.

¹¹ E. H. Massey, H. E. Smith, and A. W. Gordon, J. Org. Chem., 1966, **31**, 684.

¹² H. E. Smith, J. C. D. Brand, E. H. Massey, and L. J. Durham, J. Org. Chem., 1966, **31**, 690.
 ¹³ J. W. Daly, F. C. Green, and R. H. Eastman, J. Amer. Chem. Soc., 1958, **80**, 6330.

DISCUSSION

Pyrolyses.—The decompositions of the amine oxides provide good probes of structure as the reactions are clean and utilise an Ei mechanism with a five-membered cyclic transition state having a syn-periplanar arrangement of the leaving groups.14 This transition state is planar and could only be achieved for thujyl compounds when the molecule adopted an L-shaped conformation (IX). On the basis of the recently proposed configurations, the thujyl compound (IX; $A = Me, B = NMe_2O$, C = D = H) and its neoiso-isomer (IX; C = Me, D = NMe_2O , A = B = H) should give (+)- β -thujene and (+)- β -isothujene, respectively, but no (-)- α -thujene, whereas the neo-compound (IX; Z = Me, $D = NMe_2O$, B = C = H) and the iso-compound (IX; C = Me, B = NMe_2O , A = D = H) should give mixtures of $(-)-\alpha$ thujene and the appropriate (+)- β -isomer. Table 1 shows agreement with these expectations, and the results, taken in conjunction with the conclusion from reduction experiments 2,3 that the ring-linked methyl and the methylene bridge are trans in (-)-thujol, confirm the configuration of thujols and thujylamines.



Polar effects are generally unimportant in influencing the orientation of elimination from cyclic amine oxides,¹⁴ but formation of β -olefin is significantly preferred to that of α -olefin for both the neo- and iso-compounds. Either Hofmann-like control is here being exerted by the ring methyl group, or steric interactions, probably involving the bulky N-substituted group, are playing a role. (+)- β -Isothujene (VII) has not been previously characterised or distinguished from its isomer (VI), although impure 'β-thujene' isolated from pyrolysis of 'thujyl xanthate '4 may have contained this compound.

The xanthate pyrolyses are almost certainly Ei reactions with six-membered planar (or very near so) transition states, and although poorer yields of olefins are obtained, similar conclusions as to structure can be drawn from the product-proportions. In contrast to the previous situation, the α -olefin is now preferentially formed from the isothujyl compound, although not from its neothujol isomer. These reactions probably possess

¹⁴ D. V. Banthorpe, 'Elimination Reactions,' Elsevier, Amsterdam, 1963, p. 192.

15 Ref. 14, p. 154.

transition states with greater double-bond character than those of amine oxides,¹⁴ and for the isothujyl compound (IX; C = Me, B = Xanthate, A = D = H) considerable alleviation of steric strain between the ring methyl group and the methylene bridge attends the formation of the transition state leading to $(-)-\alpha$ -thujene, but not that leading to (+)- β -thujene. No such relief attends the route to either α - or β -thujene from the neothujyl isomer, and here orientation is governed by the factors that control the products in amine oxides.

Pyrolyses of thujyl acetates and borates do not give detectable amounts of unrearranged olefins. $(-)-\alpha$ -Thujene, and possibly its β -isomers, are unstable at the temperatures necessary to promote decomposition of acetates, and the low-temperature pyrolyses of borates may involve E1 routes.

Base-promoted Eliminations .- Dehydration with phosphorus oxychloride-pyridine has been used to assign configurations to many steroid and terpene alcohols, as the presumed E2 decomposition of the pre-formed phosphoryl oxychloride ester leads to a strict requirement for an anti-periplanar orientation of the leaving groups.¹⁵ The formation of both $(-)-\alpha$ - and $(+)-\beta$ -olefins from (-)-thujol and (+)-neoisothujol, but the probable sole formation of the corresponding (+)- β -olefin from (+)-isothujol and (-)-neothujol (Table 2), indicates a cisrelationship between the neighbouring methyl and hydroxy-groups in the former pair and a trans-relationship for the latter pair; this is consistent with structures (I)—(IV). The results for (+)-isothujol and (-)-neothujol are approximate, as the low olefin yield has to be corrected for contamination of each isomer by a few per cent of (+)-neoisothujol.

E1 routes proceeding from ground-state conformations of the esters may account for the balance of rearranged olefins in products, but are unlikely to contribute greatly to the formation of thujenes. If such mechanisms occurred, (-)-thujol and (-)-neothujol would yield a formally similar ion, and (+)-isothujol and (+)-neoisothujol would yield another. Consequently, each pair should give the same products, and this is not observed. Also, α -thujene from (+)-neoisothujol is of very high optical purity, $[\alpha]_p - 61.2^\circ$, whereas a racemic product would result from a tris-cyclopropenyl non-classical ion (XI) or an equilibrated system of classical ions.¹⁶

The 'super'-Saytzeff pattern of products from (-)-thujol and (+)-neoisothujol is not typical for this type of dehydration.¹⁵ Two explanations based on the E2 mechanism can be advanced. The bulky ester group must be quasi-axial in the transition state for antielimination, and steric interactions could lengthen and polarise the carbon-oxygen bond and confer E1-like character on the reaction. Such character is known to invoke powerfully the Satyzeff pattern of influences, and a well documented analogy exists.¹⁷ Alternatively or additionally, abstraction of the proton to yield a β -olefin

S. Winstein, E. C. Friedrich, R. Baker, and Y. I. Lin, *Tetrahedron*, 1966, Suppl. 8, pt. II, 621.
 ¹⁷ E. D. Hughes and J. Wilby, J. Chem. Soc., 1960, 4094.

could be more hindered by the rigidly positioned isopropyl group than the alternative abstraction leading to the α -olefin.

Pyrolysis of the four thujvltrimethylammonium hydroxides are also recorded in Table 2. The classical method for Hofmann degradation (heating of a syrup of the 'onium hydroxide at high temperature) gave a lower olefin yield and a more extreme product distribution than when the solvent was removed and the decomposition was conducted at lower temperature and pressure. Both consequences can be attributed to the increased basicity of hydroxide ion in the latter conditions.¹⁸ On the basis of the accepted configurations, only β -olefin would be expected from *anti-E2* reactions of the neo- and iso-thujyl 'onium ions, whereas β : α ratios of 96:4 and 52:48 are found in reactions whose rates (Table 2) are entirely normal. (The rates were calculated with the very reasonable assumption that the rate of $S_N 2$ attack at the N-methyl groups was the same for each isomer.) Clear-cut stereochemical conclusions are thus not possible, and syn-elimination is suspected, such as has been recently characterised in other Hofmann degradations.1,19,20

The contribution of the α' - β mechanism to the decomposition of isothujyl 'onium hydroxide was proved by the recovery of trimethylamine containing some 20% of the monodeuterio-compound from reaction of the trideuterio-'onium salt. ElcB and carbene-producing mechanisms were largely * ruled out by the lack of tracer in olefin product when the reaction was conducted in deuterium oxide. The occurrence of $\alpha'-\beta$ and presumably syn-E2 routes * for the iso- and neo-thujyl 'onium ions is not surprising, as anti-E2 mechanisms would require the bulky ring-methyl and 'onium groups both to be quasi-axial. The neo-isomer can attain this strained situation in the favoured (for the thujane skeleton) 3,12 boat conformation, whereas the other isomer has to go into the less favoured chair form, but both compounds can undergo syn-elimination to form both α - and β -olefins from conformations with both methyl and 'onium groups quasi-equatorial.

The neoisothujyl and thujyl 'onium ions are expected on the basis of *anti-E2* mechanisms to give both α - and β-olefins. This was indeed found, and both decompositions gave a predominance of the product of Saytzefftype orientation. This anti-Hofmann behaviour, a similar example of which occurs in the pinocamphyl series,²¹ may be due to the factors outlined as occurring in dehydration, or may indicate the predominance of syn-elimination. The intrusion of E1 reactions in all these decompositions was ruled out by control experiments.

J. Chem. Soc. (B), 1968

El Reactions and the Generation of 3- and 4-Thujyl Carbonium Ions (work carried out with D. Baxendale and C. Gatford).—Attempts to promote E1 reactions of (+)-neoisothujol and (-)-thujol by treatment with iodine or with zinc chloride in benzene gave epimeric alcohols, p-cymene, and (presumed) cyclopentane derivatives, but no thujenes or menthadienes. The thujvl ion (X) or non-classical species (XI) are apparently unstable with respect to rearrangement under these conditions, as they are in concentrated mineral acid.²² Treatment of the thujols with acetic or formic acids caused only ring-opening, in contrast to the unrearranged olefins obtained from similar treatment of bicyclo-[3,1,0]hexan-3-ol.^{16,23}

Generation of carbonium ions by additions to $(-)-\alpha$ thujene and (+)-sabinene was also attempted. Protonation of sabinene (XII), as the first step in hydration. should occur in Markownikoff manner to give (XIII), which could react by several routes including ringscission. Markownikoff addition to α -thujene (XIV) would also give (XIII), whereas the anti-Markownikoff orientation, that could be enhanced by the possibility of formation of a non-classical ion (XI), would initially give (XV). Reaction of (XV) or (XI) might lead to thujols. In the event, hydration of (+)-sabinene and $(-)-\alpha$ -thujene with 1% aqueous sulphuric acid under identical conditions gave (in addition to ca. 5% of minor products) the ring-opened products α -terpinene, γ terpinene, and 4-terpinenol in respective proportions 10, 21, and 64% and 11, 22, and 62%. These products were stable under the reaction conditions, and no thujols (which would also have been stable), β -thujenes, or unreacted substrates could be detected. This suggests that (XIII) is formed from each substrate, and that a non-classical ion is not favoured.[†]

Products from the addition of hydrochloric acid to $(-)-\alpha$ -thujene in ether at -78° were not fully analysed, but autoxidation of the Grignard reagent prepared from the reaction mixture gave no thujols as would have been formed from any thujyl chloride resulting from anti-Markownikoff addition, or β -thujene that would have resulted from dehydration of thujols during work-up.

The possibility of formation of 3-thujyl carbonium ion in the hydrolysis of (+)-sabinyl acetate (XVI) was also investigated. The potentialities for generation of a non-classical or allylic ion could encourage alkyl-oxy fission of the ester link, although the acyl-oxy mode has been implicitly assumed³ in that configurations for thujols have been based on reductions of sabinyl acetate followed by hydrolysis with supposed retention of configuration at the carbon-oxygen centre. However, alkyl-oxy fission was ruled out by the observations that (a) no sabinyl ethyl ether was formed when the saponifi-

¹⁸ Ref. 14, p. 36. ¹⁹ J. Sicher and J. Zavada, Coll. Czech. Chem. Comm., 1967,

23 T. Norin, Tetrahedron Letters, 1964, 37.

^{*} For a detailed discussion of these points, and a description of the experimental procedure necessary to characterise the α' - β mechanism in an unambiguous manner, see ref. 1.

[†] This non-classical ion could be formed by addition of a proton from the more hindered side of $(-)-\alpha$ -thujene to form a quasi-chair conformation with the ring-methyl quasi-equatorial and overlap between the vacant p-orbital at C-3 and the 'banana orbital of the cyclopropyl ring.

^{32, 2122.} ²⁰ J. Zavada and J. Sicher, Coll. Czech. Chem. Comm., 1967,

L. Tschugaev, J. Russ. Phys. Chem. Soc., 1907, 39, 1324.
 S. Forsen and T. Norin, Tetrahedron Letters, 1966, 4183.

cation was conducted in ethanol, and (b) no tracer was incorporated into (+)-sabinol when the reaction was carried out in 60% aqueous dioxan containing ¹⁸Olabelled water.

No evidence was thus obtained for non-classical ions, and formation of the 4-thujyl carbonium ion is preferred in our systems to that of the 3-thujyl ion. This is in accord with conclusions based on the addition of hydrogen chloride to bicyclo[3,1,0]hex-2-ene^{24,25} and the rates of solvolysis of bicyclo[3,1,0]hexyl toluene-psulphonates.¹⁶ * However, some 10% of the products of hydroboronation of $(-)-\alpha$ -thujene is probably sabinene hydrate which results from anti-Markownikoff addition.²

EXPERIMENTAL

of Materials .- Thujones, thujols, (1) Preparation (+)-sabinene, and (-)- α -thujene had been previously prepared.² G.l.c. techniques have also been described.²

(a) (+)- β -Thujene and (+)- β -isothujene. These were obtained by the pyrolysis of the mixed xanthates (20 g.) of (+)-neoisothujol and (-)-neothujol. Fractional distillation of the products using a Büchi spinning-band column (3 ft. $\times \frac{1}{4}$ in.) gave a mixture, b.p. 31-38°/9 mm., containing five olefins that could be separated by preparative g.l.c. The first and the fourth eluted olefins were not identified, but the second and the third were (+)- β -thujene, $[\alpha]_{D}^{25} + 172 \cdot 8^{\circ}$ (c 2.7 in MeOH) [lit.,⁶ + 185.8° (neat)], and (+)- β -isothujene, $[\alpha]_{D}^{25} + 13.5^{\circ}$ (c 5.7 in MeOH), and the fifth to be eluted was (-)- α -thujene. (-)- α - and (+)- β -Thujene were identified by comparison of their i.r. spectra with authentic traces.⁶ (+)- β -Isothujene had an i.r. spectrum with strong bands at 3.6, 3.7, 7.1, 7.45, 7.55, 8.3, 9.7, 9.9, 11.2, 12.8, and 13.8 μ . The mass spectra of these olefins and of (+)-sabinene were measured at 70 ev on a Metrovick MS.9 instrument with inlet temperature 100°. All showed distinct patterns (Table 3) with meta-

TABLE 3

Mass spectra of thujenes

			Base,	Important				
Compound	Parent	Σ_{27} (%)	peaks					
$(+)$ - β -Isothujene	Mass no. Abundance	$136 \\ 18.5$	93 100, 11·1	121 54	$4\overline{3}$ $3\overline{5}$	77 30	91 30	79 28
(+)- β -Thujene	Mass no. Abundance (%)	$\begin{array}{c} 136\\ 30 \end{array}$	93 100, 26·8	121 46	91 27	77 25	92 23	43 19
(—)-α-Thujene	Mass no. Abundance (%)	$\begin{array}{c} 136\\9\end{array}$	93 100, 30·5	$\begin{array}{c} 77\\ 30 \end{array}$	92 27	91 22	41 10	79 8
(+)-Sabinene	Mass no. Abundance (%)	136 16	93 100, 30·8	77 30	91 23	79 20	41 16	69 12

stable peaks at m/e 53.8 and 89.2, corresponding to transitions $(136^+ \rightarrow 93^+ + 43)$, and $93^+ \rightarrow 91^+ + 2)$ that are also found in the mass spectra of menthadienes.27,28

(b) (+)-Neoisothujylamine. $(-) \alpha$ Thujone [a mixture

* Nitryl chloride and bromide are reported to add to α-thujene with Markownikoff orientation,26 but no proof of the structure of the products was given.

24 P. K. Freeman, M. F. Grostic, and F. A. Raynard, J. Org. *Chem.*, 1965, **30**, 771. ²⁵ P. K. Freeman, F. A. Raynard, and M. F. Grostic, *J. Org.*

Chem., 1967, 32, 24.

obtained from distillation of oil of Thuja occidentalis L. containing (-)-thujone (77%), fenchone (14%), (+)-isothujone (8%), and camphor (1%)]² was condensed with formamide,¹⁰ and the benzene extract was refluxed for 10 hr. with ethanolic sodium hydroxide. The residue after acidification with sulphuric acid and steam-distillation contained all four thujvlamine sulphates. These (175 g.) were boiled with water (80 ml.), and the solution was cooled to to 60° and filtered. The crystals were thrice thus retreated, and the product (2 g.) was basified, in a atmosphere of nitrogen, to liberate the amines. Analytical g.l.c. showed the product to be 98% (+)-neoisothujylamine, $\alpha_{\rm D}^{20}$ +22.7° (neat) [lit.,¹⁰ +28.7° (neat)]. G.l.c. analyses were made on Carbowax 20M columns with conditions and apparatus as previously reported ² except that the supporting medium was pre-coated with potassium hydroxide (20% w/w) before application of the stationary phase. This was necessary to prevent tailing of amine peaks. Relative retention times (column temperature 105-125°, detector and injector temperatures 20° higher) were: (-)-neothujylamine and (+)-isothujylamine 1.00 (unresolved, 16.2 min.); (+)-neoisothujylamine 1.12; (-)-thujylamine, 1.35.

(c) (+)-Isothujylamine. (+)- β -Thujone [obtained from distillation of oil of Tanacetum vulgare L., containing (+)-isothujone (87%), (-)-thujone (4%), and camphor (9%)]² was converted into the oxime (24 hr., 25°), and the extracted product was fractionally distilled to give an oil, 104-106°/4 mm. This deposited (+)-isothujoxime, m.p. 57°, $[\alpha]_{D}^{20} + 104 \cdot 2^{\circ} (c \ 4 \cdot 2 \text{ in MeOH}) \{\text{lit.}, 10^{10} [\alpha]_{D}^{25} + 105 \cdot 3^{\circ}$ (c 5.0 in MeOH), on leaving overnight. The oxime (10 g.) was reduced with sodium in ethanol under reflux, and the steam-distillate was adjusted to pH 5.7 with hydrochloric acid before evaporating to dryness at $30^{\circ}/2$ mm., to give a mixture of (+)-isothujylamine (89%), (+)-neoisothujylamine (6%), and (-)-thujylamine (5%) as the hydrochlorides. Recrystallisation from acetone-ethanol (2:1) gave impure (+)-isothujylamine hydrochloride (4.6 g.), $[\alpha]_{D}^{19} + 74.5^{\circ} (c \ 4.3 \ in \ H_{2}O) \{ lit., 7 \ [\alpha]_{D}^{20} + 79.0^{\circ} (c \ 5 \ in \ H_{2}O) \}.$ Conversion into amine and g.l.c. analysis indicated (+)-isothujylamine (94%) and (+)-neoisothujylamine (6%).

(d) (-)-Thujylamine. (-)- α -Thujone (25 g.) was converted into the oxime after 4 days at 20° in the dark when only fenchone remained unreacted. After dilution and extraction the product was distilled through a helixpacked column (1 ft.), to give (i) fenchone, b.p. 73-75°/ 11.5 mm., and (ii) (-)-thujoxime (18 g.), b.p. 125°/11.5 mm., as a colourless liquid, $[\alpha]_{D}^{22} - 34.6^{\circ}$ (c 13 in MeOH) (lit., $\left[\alpha\right]_{D}^{22}$ -33.8 to -28.3°), which rapidly turned yellow on exposure to light and air. The oxime decomposed on attempted preparative g.l.c. It could not be reduced catalytically over platinum oxide in ether at 6 atm./25°, but treatment with sodium in ethanol under reflux gave a product containing (-)-thujylamine (39%) and (-)-neothujylamine (61%). After conversion into the hydrochlorides and two recrystallisations from acetone-ethanol (2:1), (-)-thujylamine hydrochloride (0.76 g., 99% pure)was obtained, $[\alpha]_{D}^{20} - 10 \cdot 2^{\circ}$ (c 4·3 in H₂O), $[\alpha]_{D}^{16} - 15 \cdot 7^{\circ}$ (c 2 in MeOH). The free amine had $\alpha_{D}^{25} - 22 \cdot 2^{\circ}$ (lit.,¹⁰ $\alpha_{\rm d}^{25} - 22.07^{\circ}$).

26 R. D. Shrivasta and S. S. Deshapande, Proc. Nat. Acad. Sci., India, 1965, **31**, A, 180. ²⁷ R. Ryhage and E. von Sydow, Acta Chem. Scand., 1963, **17**,

2025.

28 A. F. Thomas and B. Willhalm, Helv. Chim. Acta, 1964, 47, 471.

(e) (-)-Neothujylamine. The mother-liquors from the previous experiment were basified, and the extracted mixture of amines was separated by preparative g.l.c. Heart-cutting of the appropriate asymmetric peak with automatic injection (39 cycles, sample 50 μ L.) gave a product (0.7 g.) containing (-)-neothujylamine (94%) and (+)-isothujylamine (6%) with $\alpha_D^{23} - 6.8^\circ$ (neat) [lit.,¹³ $\alpha_{D}^{25} - 14 \cdot 2^{\circ} \text{ (neat)}].$

Although these amines were not chromatographically pure, the recorded optical rotations are close to those reported for samples obtained by laborious techniques of fractional recrystallisation,¹⁰ and they were adequate for use in synthesis of amine oxides and 'onium compounds. N.m.r. studies have shown that the amines as named here have similar configurations to the thujols bearing the same prefixes.12 A similar conclusion was reached from conformational analyses of the reductions used in the preparations. The stereochemistry of both of these reactions should be similar in yielding mainly the more stable product: 29 consequently, the prefix neo was assigned to the main product from reduction of (-)-thujoxime with sodium in ethanol, and the prefix iso was given to the major product from (-)-isothujoxime by analogy with the known² predominant formation of (-)-neothujol and (+)-isothujol from thermodynamically controlled reductions of (-)-thujone and (+)-isothujone. Earlier workers 7 had isolated only the minor product from the reduction of (-)-thujoxime, and were unaware of the existence of the main product. Fortunately they named their product (-)-thujylamine and so adopted the correct nomenclature.

(f) 'Onium Compounds. These were prepared from the corresponding amines (1 g.) by batchwise addition of methyl iodide and sodium methoxide as described for the methylation of piperitylamines.³⁰ The crude 'onium iodide was extracted with chloroform (5 ml./g.), and the product obtained by evaporation of solvent was recrystallised twice from water to give the pure salt in ca. 30% yield. Purity was checked by conversion into the dimethylthujylamine by treatment with lithium aluminium hydride ³¹ and g.l.c. analysis of the product. The 'onium hydroxide was prepared by reaction of the 'onium iodide with moist silver oxide, and the concentrated solution was stored at 0° under nitrogen. Properties of the 'onium iodides are in Table 4;

TABLE 4

Properties of thujvltrimethylammonium iodides

Com-	Fou	nd (S	%)	Mol.		Solu-	
pound	С	н	Ν	wt.*	Purity	bility †	Crystal form
Neoiso	47.5	8.0	$4 \cdot 3$	320	96 + 4%	34	Yellow plates
					neo-		
Iso	48 ·1	$8 \cdot 2$	4.4	329	99%	9	White needles
Neo	48 ·1	8.1	$4 \cdot 2$	323	98 + 2%	16	Pale yellow
					iso-		needles
Thujyl	48.2	8.3	$4 \cdot 2$	323	99%	7	Pale yellow
							plates
Calculated	48·3	8.1	4 ·4	323			

* By titration of the corresponding hydroxide. † G./100 ml. water at 80°.

all decomposed in the range 250-265° (sealed tube). The presence of contaminating isomers in two of the compounds is allowed for in Table 2.

29 H. O. House, 'Modern Synthetic Reactions,' Benjamin, New York, 1965, ch. 1.

 J. Read and R. A. Storey, J. Chem. Soc., 1930, 2777.
 A. C. Cope, E. Ciganek, L. J. Fleckenstein, and M. A. P. Meisinger, J. Amer. Chem. Soc., 1960, 82, 4651.

J. Chem. Soc. (B), 1968

(g) $[{}^{2}H_{3}]$ Isothujyltrimethylammonium iodide. (-)- β -Thujone was deuteriated as described for menthone ¹ but with a three-fold increase in reaction time, and was converted into the 'onium salt as above. Mass spectrometric analysis, using techniques previously developed,¹ showed the product to contain $[{}^{2}H_{3}]$ - (70%), $[{}^{2}H_{2}]$ - (20%), $[{}^{2}H_{1}]$ - (6%), and undeuteriated (4%) species. Deuteriation could only have occurred at ring positions 2 and 4.

(h) Amine oxides. Dimethylthujylamines prepared from purified 'onium iodides were converted into oxides by treatment with hydrogen peroxide.³² Excess of the reagent was destroyed with Adams catalyst, and the solution was clarified by filtration through a Millepore membrane (0.45 μ pore size) and stored at 0° under nitrogen. The purity of the dimethylthujylamines was checked by analytical g.l.c. on the columns used for thujylamines. Retention times were: neothujyl compound 1.00 (11 min.); isothujyl compound 1.12; neoisothujyl and thujyl compounds 1.23 (unresolved).

(i) Xanthates. The purified thujols (20 mg.) were converted into S-methyl xanthates using a recently described general method,³³ although one preparation employed the less convenient classical procedure,⁶ and the esters (5-10)mg.) were pyrolysed without further purification. Very basic conditions were used in this preparation but no epimerisation occurred; treatment of the xanthate from (+)-neoisothujol (the isomer most prone to epimerisation) with lithium aluminium hydride regenerated the starting completely uncontaminated with isomers. alcohol Xanthates may contain peroxides that can initiate nonstereospecific radical decompositions at low temperatures.¹⁴ However, treatment of xanthates with solutions of ferrous salts before pyrolysis gave products identical with those from untreated substrates.

(j) Thujyl and 2-methylcyclopentyl acetates. Mixed acetates of (+)-neoiso- and (-)-neothujol resulted from hydrogenation of (+)-sabinyl acetate over Adams catalyst.² A mixture of cis- and trans-2-methylcyclopentanols was prepared by reduction of 2-methylcyclopentanone with lithium aluminium hydride, and was converted into the mixed acetates by treatment with acetyl chloride. A crude fraction, b.p. 80-83°/15 mm., was obtained on distillation in the spinning-band column, and was used without further purification.

(2) Procedure for Eliminations.—'Onium hydroxides (typically 100-500 $\mu l.$ of concentrated solution) were pyrolysed under nitrogen in a microdistillation apparatus. The bath was heated to 140° at 5°/min., then raised to 155° during 10 min., and finally maintained at 170° for the same period. The products were trapped at -78° , extracted with pentane (1 ml.); the organic layer was washed, separated by centrifugation, and injected into the g.l. chromatograph. Smooth decompositions occurred at 135-150°/760 mm., or 90-130°/25 mm. In a typical control experiment, (+)- β -thujene (17 mg.) (the thermodynamically less stable isomer) in methanol (200 µl.) was mixed with aqueous tetramethylammonium hydroxide (25% w/w; 90 µl.), and either injected into the distillation apparatus which was heated at 160°, or subjected to the stepwise pyrolysis procedure. The olefin was unchanged on recovery except for the formation of about 2% of two pro-

32 A. C. Cope and E. M. Trumbull, Org. Reactions, 1960, 11,

317. ³³ E. J. Corey and H. Uda, J. Amer. Chem. Soc., 1963, 85,

ducts, neither of which was a thujene, and neither of which was detected as products of the eliminations.

Amine oxides (ca. 50 µl. concentrated solution) were decomposed at 130-140° in a stream of nitrogen, and the products similarly collected and analysed. No reaction occurred when the concentrated solution was dissolved in tetrahydrofuran, dried with molecular sieve 5A (Union Carbide), and left to stand for 12 hr. at 20° .

Xanthates $(5-10 \mu l.)$ were pyrolysed in the microdistillation apparatus at 180-205° for 10 min.

Thujyl and 2-methylcyclopentyl acetates were pyrolysed by passing in a stream of nitrogen down an 8 in. furnace packed with glass wool such that the contact time was about 6 sec. No thujenes could be detected in the products over the range 370-500° at which decomposition occurred. α - and β -Thujenes are probably unstable at these temperatures. Seasoning of the furnace packing by repeated pyrolysis of pentyl and octyl acetates before carrying out the experiments with thujyl compounds had no effect on the products. The mixture of cis- and trans-2-methylcyclopentyl acetates smoothly decomposed at 410° to give a mixture of 2- and 3-methylcyclopentenes.

A mixture of (+)-neoiso- and (-)-neo-thujol was heated with boric acid at 138-148° under conditions that are believed to lead to decomposition of the borate esters.³⁴ A product distribution similar to that from the acetate pyrolysis was found.

Preliminary studies of dehydrations with the proportions of pyridine, phosphorus oxychloride, and alcohol in the ratio 40: 4: 1 v/v (as in the standard method) ³⁵ showed that any thujene formed was isomerised by the strongly acid medium formed on quencing the reaction. Accordingly, the alcohol (27 mg.) was dissolved in dry redistilled pyridine (135 µl.), and phosphorus oxychloride (44 µl.) was added dropwise to the well stirred solution which was maintained at 0° . After the mixture had been allowed to stand at 25° for 24 hr., it was neutralised by the addition of saturated sodium hydrogen carbonate solution with efficient cooling and stirring. The products were extracted with ether and dried. No residual alcohol was detected in any experiment. Unidentified olefins were isolated in major yield from the reactions of (-)-neothujol and (+)-isothujol, but were not derived from thujenes under the reaction conditions.

(3) Product Analyses.—A Wilkens Aerograph A700 gas chromatograph was used, equipped with copper helical columns (20 ft. \times $\frac{1}{4}$ in. o.d.) containing kieselguhr (80–100 mesh, acid-alkali washed; J. J. Co. Ltd., Kings Lynn) coated with Carbowax 20M (15% w/w). For mixtures containing amines, the supporting medium was pre-coated with potassium hydroxide (20% w/w). The carrier gas was helium (50 lb./in.² inlet pressure, flow rate 50-100 ml. min.⁻¹) and the column temperature was $90-125^{\circ}$ and the injector and detector temperatures some 10° higher. Sample sizes were typically $0.2-0.5 \mu l$, and relative retention times (Carbowax 20M, not pre-coated) were: (+)- β -thujene 1.00 (7.3 min.); (+)- β -isothujene 1.19; (-)- α -thujene 1.40; (+)-sabinene 1.63. Product proportions were calculated using internal standards or by tri-

34 G. L. O'Connor and H. R. Nace, J. Amer. Chem. Soc., 1955, 77, 1578.
³⁵ B. Cross and G. H. Whitham, J. Chem. Soc., 1960, 3892.
³⁶ A. Schriesheim, R. J. Muller, and C. A. Rowe, J. Amer. Chem. Soc., 1962, 84, 3164.
³⁶ Device Austral I Chem., 1964, 17, 212.

N. R. Davies, Austral. J. Chem., 1964, 17, 212.

³⁸ M. S. Kharasch, R. C. Seyler, and F. R. Mayo, J. Amer. Chem. Soc., 1938, 60, 882.

angulation, and for representative eliminations each olefin was isolated by preparative g.l.c. and identified by comparison of its i.r. spectrum with that of an authentic specimen. The results in Tables 1 and 2 are reproducible to $\pm 2\%$ (actual value) of special significence (see Discussion) was the (-)- α -thujene, $[\alpha]_{D}^{24}$ -61-2° (c 4.3 in CHCl₃), isolated by preparative g.l.c. from dehydration of (+)-neoisothujol (500 mg.). It was accompanied by a terpinyl chloride of molecular weight 172 (mass spectrometry) as a major product.

(4) Decomposition of $[{}^{2}H_{3}]$ Isothujyltrimethylammonium Hydroxide.---This substrate was decomposed in a stream of superheated steam, and the tracer content of the liberated trimethylamine was examined mass-spectrometrically using previously developed techniques.¹ [²H₁]Trimethylamine was present in 19.6% of the total, and no higher deuteriated species was detected. When the protium-containing 'onium salt was pyrolysed in deuterium oxide, no tracer could be detected mass-spectrometrically in the mixed thujenes that were isolated by preparative g.l.c.

(5) E1 Reactions.—(a) (+)-Neoisothujol and (-)-neothujol (each 5 g.) were heated with iodine (1 mg.) at 155- 160° for 60 min. under conditions that should promote the Hibbert reaction. The products were mainly (-)-thujol, unchanged substrate, and rearranged olefins. After 4 hr. at 200°, the reaction had gone to conclusion to give a mixture of olefins and p-cymene. No menthadienes, pinenes, fenchenes, or thujenes were present, and probably ring-opening to cyclopentene derivatives almost exclusively occurred. Control experiments showed that negligible decomposition occurred in the absence of iodine, except that thujones were formed at 200°.

(b) (+)-Neoisothujol (1 g.) in benzene $(1\cdot 3 \text{ ml.})$ was refluxed for $4\frac{1}{2}$ hr. with zinc chloride (0.5 g.). No thujenes or sabinenes were formed, and the main product was p-cymene.

(c) (+)-Neoisothujyl 'onium iodide was heated at 205° / 760 mm. for 2 hr. in the melt. No thujenes, but dimethylthujylamine, p-cymene, and terpinenes (total ca. 10%), could be detected. The mixed 'onium salts [resulting from the Leukart reaction on $(-)-\alpha$ -thujone and subsequent methylation] were heated at 215°/10 mm. Considerable sublimation of substrate occurred, but dimethylthujylamines and α -thujene, menthadienes, and p-cymene (ca. 1%) total) were formed.

(6) Equilibration of Sabinene and Thujenes.-Attempts were made to attain the equilibrium mixture of thujenes by treating (+)-sabinene with reagents that have been used successfully in other olefin systems. Potassium t-butoxide in dimethyl sulphoxide, 36 palladous chloride in acetic acid or ethanol,³⁷ palladous chloride bis-benzonitrile complex,³⁸ Raney nickel,³⁹ metatitanic acid,⁴⁰ and various ion-exchange resins ⁴¹ all either gave no isomerisation, intractable tars, or products containing little (-)- α -thujene together with methadienes and cyclopentene derivatives. Best results were achieved by treatment with rhodium trichloride in propan-2-ol at 50° ; ⁴² a large quantity (ca. 30%) of unidentified products resulted but the balance contained $(-)-\alpha$ -thujene (95%), (+)-sabinene (2%), (+)- β -thujene (2%), and

³⁹ G. Widmark, Acta Chem. Scand., 1955, 9, 938.
 ⁴⁰ M. I. Goryaev, V. I. Shabalina, and A. D. Dembitskii, Doklady Akad. Nauk. S.S.S.R., 1964, 158, 155.

⁴¹ V. I. Shabalina, M. I. Goryaev, and A. D. Dembitskii, Khim. prirod. Soedinenii, 1965, 247.

42 J. F. Harrod and A. J. Chalk, J. Amer. Chem. Soc., 1964, 86, 1776.

(+)- β -isothujene (1%). A referee has suggested that lithium in ethylenediamine ⁴³ may effect this equilibration more efficiently.

(7) Additions to (+)-Sabinene and (-)- α -Thujene.--(a) (+)-Sabinene (6.8 g.) was shaken with sulphuric acid (1%) aqueous; 20 ml.) at 20° for 30 hr. The oily layer and the salted-out ethereal extract of the aqueous layer were combined and analysed, to give α -terpinene (10%), γ -terpinene (21%), 4-terpinenol (64%), and unidentified products (5%). Practically no sabinene remained and no thujols were detected.

(b) (-)- α -Thujene (83 mg.) was similarly treated with acid (0·2 ml.). The product was largely unchanged starting material and α -terpinene (11%), γ -terpinene (22%), 4-terpinenol (62%), and unidentified products (5%). Thujols, terpinenes, and 4-terpinenol were shown by control experiments to be stable under these conditions.

(c) $(-)-\alpha$ -Thujene (1 g.) was dissolved in dry ether (20 ml.) at -78° and ethereal hydrogen chloride (1·2M, 5·3 ml.) was added during 1 hr. The products could not be isolated without decomposition, and so the excess of acid was neutralised with solid sodium hydrogen carbonate, magnesium turnings (0·25 g.) were added, and the mixture allowed to warm to room temperature and then heated under reflux for 1 hr. Oxygen was bubbled into the mixture

for $\frac{1}{2}$ hr., and the Grignard complex was broken down with ammonium sulphate in the usual manner. G.l.c. analysis showed five components, those of lowest retention time being α -thujene and sabinene. No thujols or β -thujenes were formed.

(8) Saponification of (+)-Sabinyl Acetate.—The ester (100 µl.) was refluxed (30 min.) with sodium (0.05 g.) in ethanol (5 ml.). G.l.c. analysis of product showed one component having the relative retention time of (+)-sabinol [rel. ret. time with respect to (-)-thujone, 2.24]. Sabinyl ethyl ether was prepared by the Williamson reaction and was characterised by mass spectrometry. Under the same conditions it possessed a relative retention time of 0.72 with respect to (-)-thujone. The saponification was also carried out in 60% aqueous dioxan containing 0.8M-sodium hydroxide and ¹⁸O-labelled water (3% atoms excess). No tracer was found by mass spectrometry in the isolated (+)-sabinol.

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⁴³ G. Ohloff, K. H. Schulte-Elte, and W. Giersch, *Helv. Chim.* Acta, 1965, **48**, 1665.