

Reactions of Terpenoids in Strong Acids. Part I. Novel Rearrangements of Geraniol and Nerol to form 3 β ,6 α ,6 $\alpha\alpha$ -trimethyl-*cis*-perhydrocyclopenta[*b*]furan

By Derek V. Banthorpe* and Paul A. Boullier, Christopher Ingold Laboratories, University College, London WC1

William D. Fordham, Research Laboratories, Bush Boake Allen and Co. Ltd., Blackhorse Lane, Walthamstowe, London E17

Treatment of geraniol or nerol with fluorosulphonic acid at low temperatures gave good (78 and 57%) yields of a novel iridoid ether identified as 3 β ,6 α ,6 $\alpha\alpha$ -trimethyl-*cis*-perhydrocyclopenta[*b*]furan. α -Cyclogeraniol (2,6,6-trimethylcyclohex-2-enylmethanol) and 9-hydroxyirid-1-ene [2-(2,3-dimethylcyclopentyl)propan-1-ol] were converted into the same product (87 and 98% yield, respectively) under the same conditions or (for irid-1-en-9-ol) by treatment with toluene-*p*-sulphonic acid at 70° (44% yield).

¹H N.m.r. spectra of solutions of all four substrates in fluorosulphonic acid at -78° revealed the almost exclusive formation of the oxonium ion of the iridoid which was cleaved above 20° to form a carbonium-oxonium dication derived from irid-1-en-9-ol. These two ions were formed on treatment of geraniol or the iridoid with fluorosulphonic acid-antimony pentafluoride at ca. -70°, but in this medium further rearrangement occurred at higher temperatures to give (exclusively at 27°) a carbonium ion tentatively assigned a bicyclo[2.2.1]heptane skeleton.

NUMEROUS investigations of the reactions of mono-terpenes with aqueous or organic acids have shown that cyclisations and rearrangements generally occur¹ in processes that are believed to involve both classical and non-classical carbonium ions as intermediates.^{2,3} The use of 'super' acids,⁴ however, might be expected to yield different products, for in this case carbonium and oxonium ions might have lifetimes sufficient to sustain unusual reactions, novel carbonium ions might be generated by abstraction of hydride ion from the substrate, and the influence of ion pairing could become decisive. The only recorded studies of this type are the fluorosulphonic acid-catalysed conversions of methyl geranate into methyl α -cyclogeranate⁵ and of longifolene and isolongifolene into several novel sesquiterpenes.⁶

We now report that treatment of geraniol (3,7-dimethylocta-*trans*-2,6-dien-1-ol) or nerol (3,7-dimethylocta-*cis*-2,6-dien-1-ol) with fluorosulphonic acid in sulphur dioxide-carbon disulphide at -78° followed by quenching under carefully defined conditions gave good (78 and 57%) yields of a novel iridoid ether of a class not previously formed^{4,7} in acid-catalysed rearrangements of these or related substrates.

This iridoid behaved as a single compound on two g.l.c. capillary columns and three t.l.c. systems over a range of conditions, and ¹H and ¹³C n.m.r. spectra and degradation to characterised products (Scheme 1; lettering refers to ¹H n.m.r. assignments; see Experimental section) indicated that it possessed either a furan (I) or a pyran (II) ring system. Formation of three isomeric cleavage products (III)—(V) had no structural signifi-

cance as all methods for breaking the ether linkage led to isomerisation of the initial products: moreover product analysis at short reaction times suggested that (IV) was formed in a secondary reaction.

In theory, the splitting of the n.m.r. signals of protons *c*, *d*, and *f* should allow a decision between structures (I) and (II), but the multiplicities could not be established unambiguously for spectra measured either at 220 MHz or in the presence of lanthanoid shift reagents. The following four sets of observations do, however, favour the assignment of structure (I). (a) The *gem*-coupling constant ($J_{AB} - 8.1$ Hz) of the nonequivalent protons *i* which appear in the ¹H n.m.r. spectrum as the AB portion of an ABX system (*i* + *g*) corresponds to a furan rather than a pyran ring.^{8,9} (b) The other parameters for this system ($J_{AX} 0.0$, $J_{BX} 4.5$ Hz; at 100 and at 220 MHz, with or without addition of shift reagents) are also only consistent (Dreiding models) with this structure. (c) The pattern of i.r. bands at 1250—800 cm⁻¹ suggests the presence of a furan, rather than a pyran ring.¹⁰⁻¹³ (d) The mass spectrum ($M^+ 154$; base peak *m/e* 97) closely corresponds to the fragmentation pattern expected of a compound possessing the skeleton (I) (see later) and differs markedly from that of a known compound having the skeleton of (II).¹³

Compound (I) is probably *cis*-fused. Construction of a *trans*-fused molecule with Dreiding stereomodels is impossible, and although the existence of cyclopenta[*c*]furans with *trans* ring junctions has been claimed,¹⁴ such compounds (if correctly identified) must be much less stable than their *cis*-linked counterparts.^{15,16} Four

¹ J. L. Simonsen and L. N. Owen 'The Terpenes,' Cambridge University Press, Cambridge, vol. I, 2nd edn., 1947.

² D. Whittaker in 'Chemistry of Terpenes and Terpenoids,' ed. A. A. Newman, Academic Press, London, 1972, 11.

³ J. A. Berson in 'Molecular Rearrangements,' ed. P. de Mayo, Interscience, New York, 1963, p. 111.

⁴ R. J. Gillespie, *Accounts Chem. Res.*, 1968, **1**, 202.

⁵ M. Kurbanov, A. V. Semenovskii, V. A. Smit, and V. F. Kucherov, *Izvest. Akad. Nauk S.S.S.R., Ser. Khim.*, 1971, 2541.

⁶ D. Farnham and G. Mehta, *Chem. Comm.*, 1968, 1643.

⁷ K. L. Stevens, L. Jurd, and G. Manners, *Tetrahedron*, 1972, **28**, 1939.

⁸ R. C. Cookson, T. A. Crabb, J. J. Frankel, and J. Hudec, *Tetrahedron*, 1966, Suppl. 7, 355.

⁹ A. A. Bothner-By, 'Advances in Magnetic Resonance,' ed. J. S. Waugh, Academic Press, New York, 1965, p. 103.

¹⁰ G. M. Barrow and S. Searles, *J. Amer. Chem. Soc.*, 1953, **75**, 1175.

¹¹ M. L. Maheshwari, T. C. Jain, R. B. Bates, and S. C. Bhat-tachryya, *Tetrahedron*, 1963, **19**, 1079.

¹² H. Stickler, G. Ohloff, and E. Sz. Kovats, *Helv. Chim. Acta*, 1967, **50**, 783.

¹³ S. Isoe, T. Oro, S. B. Hyeen, and T. Sakan, *Tetrahedron Letters*, 1968, 5319.

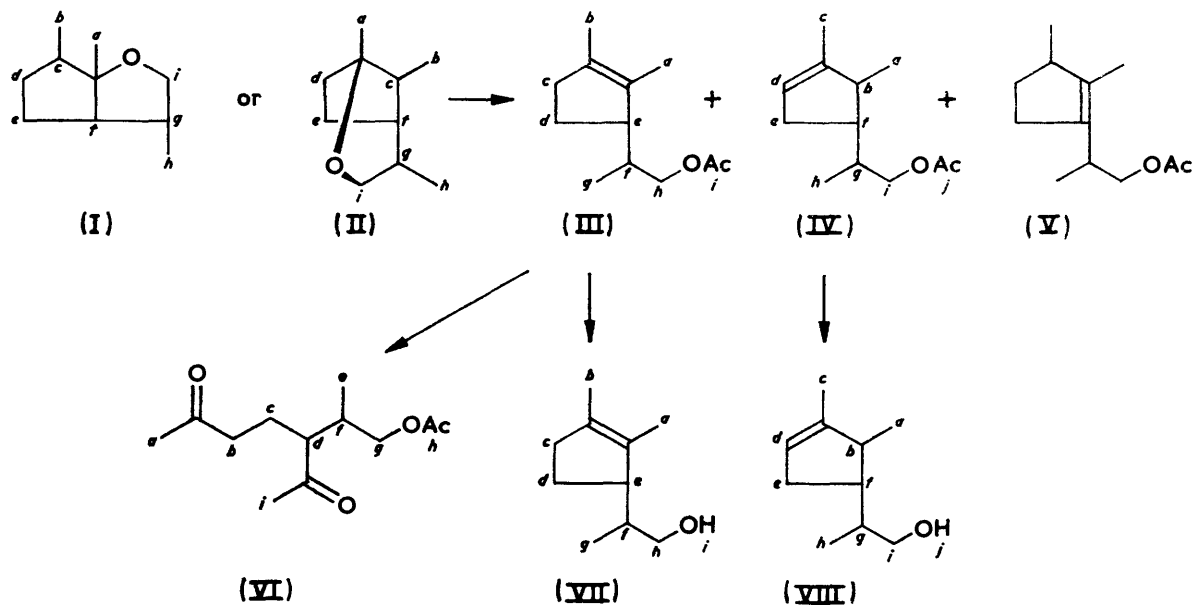
¹⁴ L. N. Owen and A. G. Peto, *J. Chem. Soc.*, 1955, 2383.

¹⁵ J. W. Barrett and R. P. Linstead, *J. Chem. Soc.*, 1936, 611.

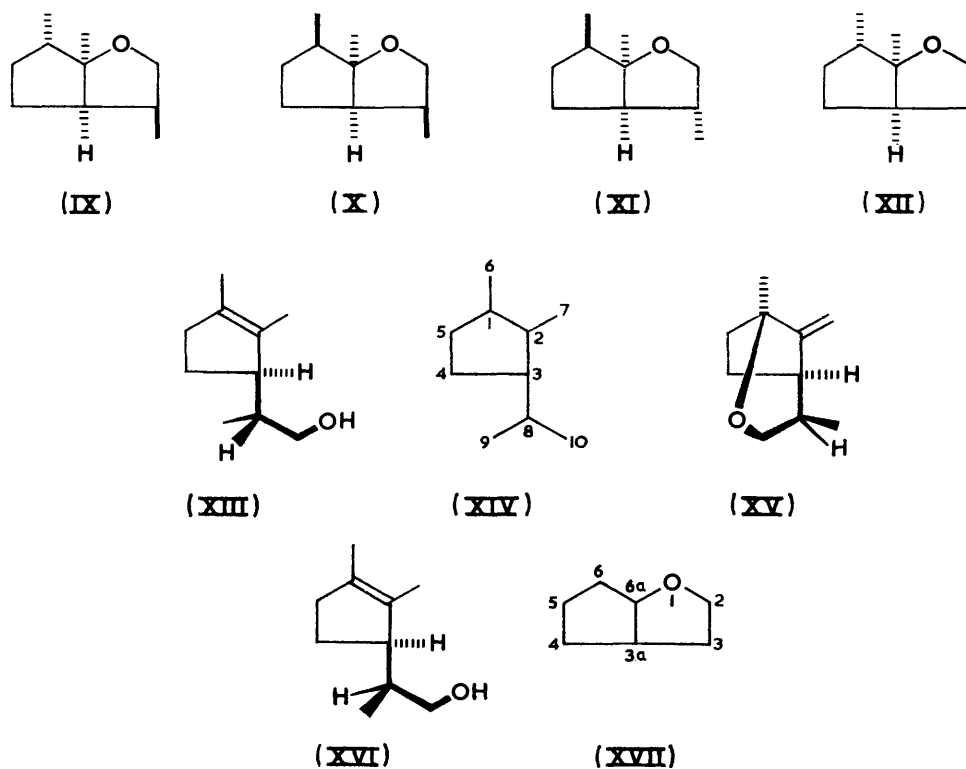
¹⁶ E. L. Eliel, 'Stereochemistry of Carbon Compounds,' McGraw-Hill, New York, 1962, p. 248.

enantiomeric pairs of *cis*-fused cyclopenta[*b*]furans can exist [(IX)—(XII) and their mirror images] and two such compounds [(XI) and (XII)] have been prepared^{13,17}

conclusively established by both spectroscopic¹³ and synthetic¹⁸ studies: the *cis*-fused cyclopenta[*b*]furan skeleton in (XI) and (XII) was inferred from data similar



SCHEME 1



SCHEME 2

by reaction of chiral irid-1-en-9-ol (XIII) [numbering of skeleton in (XIV)] with toluene-*p*-sulphonic acid. Compound (XIII) was derived from the natural product metatabiether (XV), the stereochemistry of which was

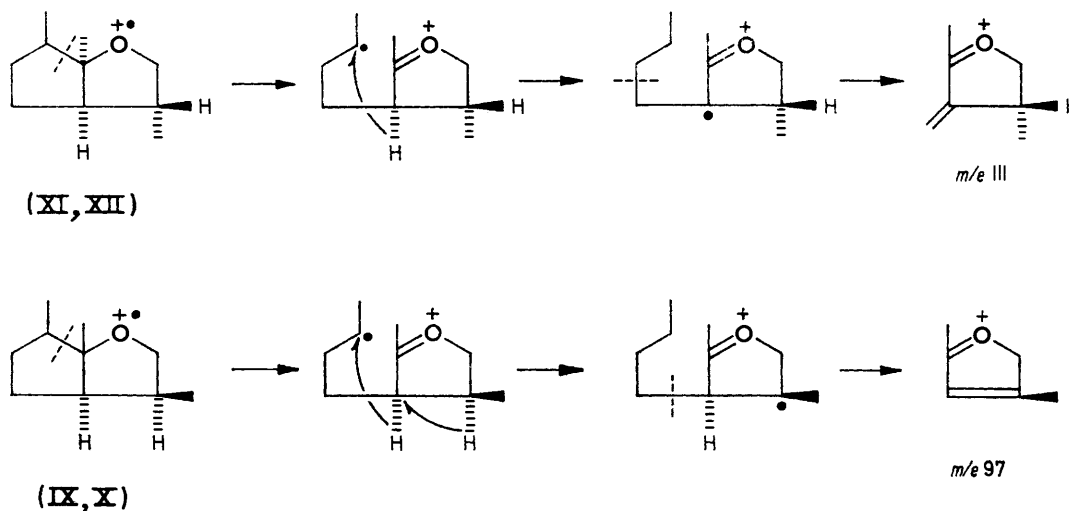
to those obtained for our compound. Treatment of racemic irid-1-en-9-ol prepared from our iridoid (see

¹⁷ Professor S. Isoe (Osaka Univ.), personal communication.

¹⁸ J. Wolinsky and D. Nelson, *Tetrahedron*, 1969, **25**, 3767.

Scheme 1) with toluene-*p*-sulphonic acid under the same conditions as used by the Japanese workers regenerated the iridoid (44% yield) as the only isolable heterocyclic product, and this was shown to differ from both compounds (XI) and (XII) (samples generously provided by Professor Isoe). Thus we conclude that: (a) our

expanded spectrum together with those calculated from a stereomodel of the molecule (IX) in which the latter was assumed to exist predominantly in the stereochemically reasonable conformation (XVIII). Good agreement was noted between the two sets despite the approximate nature of the Karplus equation and comparable



SCHEME 3

sample of irid-1-en-9-ol [one enantiomer of which is (XVI)] is diastereoisomeric with (XIII); and (b), our iridoid is either (IX) or (X). The assignment of a β -methyl group at C-3 [orientation and numbering as in (XVII)] is consistent with the fragmentation of our compound under electron impact. Compounds (XI) and (XII) give a base peak at m/e 111 arising from cleavage of a species formed by a hydrogen shift¹³ (Scheme 3), whereas our iridoid has the corresponding peak at m/e 97, formation of which can be rationalised by the occurrence of two stereoelectronically allowed shifts preceding an analogous cleavage.

Analysis of the ¹H n.m.r. spectrum of the iridoid measured at 100 MHz in the presence of the shift reagent Eu(fod)₃ provided additional assignments. When the optimum mole fraction (*ca.* 0.28) of Eu(fod)₃ was used (to ensure maximum shift consistent with acceptable line-broadening) the spectrum was essentially first-order and vicinal and geminal coupling constants (where directly comparable) were identical with those in the conventional 100 MHz spectrum (*cf.* ref. 19). Although the lanthanoid reagent also removed virtual couplings²⁰ present in the latter spectrum, a complete analysis was precluded owing to superimposition of certain multiplets together with appreciable line-broadening (up to 12 Hz at half peak height). Nevertheless, systematic spin-decoupling allowed assignment of τ values for every proton.

Table 1 lists coupling constants obtained from the

¹⁹ B. L. Shapiro, M. D. Johnson, and R. L. R. Towns, *J. Amer. Chem. Soc.*, 1972, **94**, 4381.

²⁰ R. M. Silverstein and G. C. Bassler, 'Spectrometric Identification of Organic Compounds,' Wiley, New York, 2nd edn., 1967, p. 130.

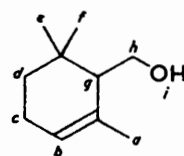
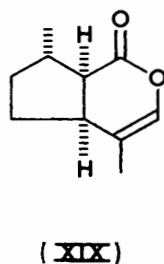
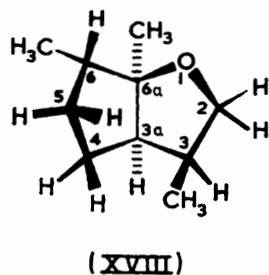
agreement was not obtained for other conformations of (IX), for those of its epimer (X), or for the pyran structure (II). In particular, although detailed analysis of the spectrum in the section 3a-H to 6-H was not feasible,

TABLE 1
Coupling constants for structure (XVIII) *

Hydrogen			J_{obs} †	ϕ_{calc} ‡	J_{calc} §	
2 α -H	a	} AMX	J_{ab}	-8.1	-8.0	
2 β -H	b		J_{bc}	0.0	0.0	
3 α -H	c		J_{ac}	4.5	45°	4.0
3 α -H	c		m		m	
3 $\alpha\alpha$ -H	d		br, m ¶		br, m	
4 α -H	e		J_{fd}	<1 **	90°	0.0
			J_{ef}	-13.0		-13.0
4 β -H	f		J_{eg}	5.5	40°	5.0
			J_{fg}	<1 **	90°	0.0
5 α -H	g		J_{eh}	<i>ca.</i> 13 **	162°	9.0
			J_{fh}	5.5	40	5.0
5 β -H	h		J_{gh}	-13.0		-13.0
			J_{gi}	<1	90°	0.0
			J_{hi}	5-7 **	30°	6.0
			J_{cd}	5-7 **	28°	6.0
6 β -H	i		br, q		qd ††	

* ¹H n.m.r. spectrum at 100 MHz; mole fraction of Eu(fod)₃ = 0.41. † Observed coupling constant (Hz) or multiplicity (where pattern unresolved). ‡ Torsion angle (ϕ , $\pm 5^\circ$) measured from a Dreiding model of (XVIII) incorporating a modified furan ring (parameters from A. D. Mighell and R. A. Jacobson, *Acta Cryst.*, 1964, **17**, 1554). Mean of six independent measurements. § Coupling constants (J , to nearest 0.5 Hz) calculated from measured torsion angles (ϕ) of (XVIII) using $J = 8.5 \cos^2\phi - 0.28$ ($0^\circ < \phi < 90^\circ$) and $J = 9.5 \cos^2\phi - 0.28$ ($90^\circ < \phi < 180^\circ$) or predicted multiplicity. Geminal coupling constants (J_{ab} , J_{ef} , and J_{gh}) are values expected for cyclopentane and furan derivatives. ¶ Multiplet unresolved owing to line broadening. ** J Value inaccurate owing to line broadening and/or overlap of signals. †† Quartet of doublets predicted: i is coupled to 6 β -CH₃ and h (ϕ_{th} 40°) but not to g (ϕ_{g} 90°). In practice, doublets may appear as broad singlets owing to line-broadening.

the symmetry of the line patterns (see Experimental section) reflected the local C_2 symmetry of (XVIII)



(XX)

SCHEME 4

about the mid-point of the 4,5-bond. No conformation of, for example, (X) can exhibit such symmetry.

the lanthanoid (at either of its presumed binding sites) were unconvincing for (XVIII) and for the other possible configurations and conformations of the iridoid. Others have had similar experiences with molecules of comparable complexity,²³ and sophisticated computations^{24,25} may be necessary to evaluate this type of information. Nevertheless, the shifts qualitatively correlate with the vector distances of the protons in (XVIII) from a lanthanoid atom complexed at reasonable contact distances on the (less shielded) α -face: in particular, the fact that the shifts of signals due to the C-6 proton are greater than those of the protons of the methyl group attached to the same carbon atom indicates the β -orientation of the former.*

On the basis of these arguments we conclude the iridoid to be 3 β ,6 α ,6 $\alpha\alpha$ -trimethyl-*cis*-perhydrocyclopenta[b]furan (IX). We hope to confirm this assignment by correlation with nepetalactone (XIX).

Ions formed at Low Temperatures in Super Acids.—Detailed n.m.r. studies on solutions of many classes of compound in super acids have conclusively proved the existence of oxonium and carbonium ions that are stable under these conditions.^{26,27} We have found similar species to be formed from our substrates.

Geraniol, nerol, irid-1-en-9-ol, α -cyclogeraniol (2,6,6-trimethylcyclohex-2-enylmethanol) (XX), and the irid-

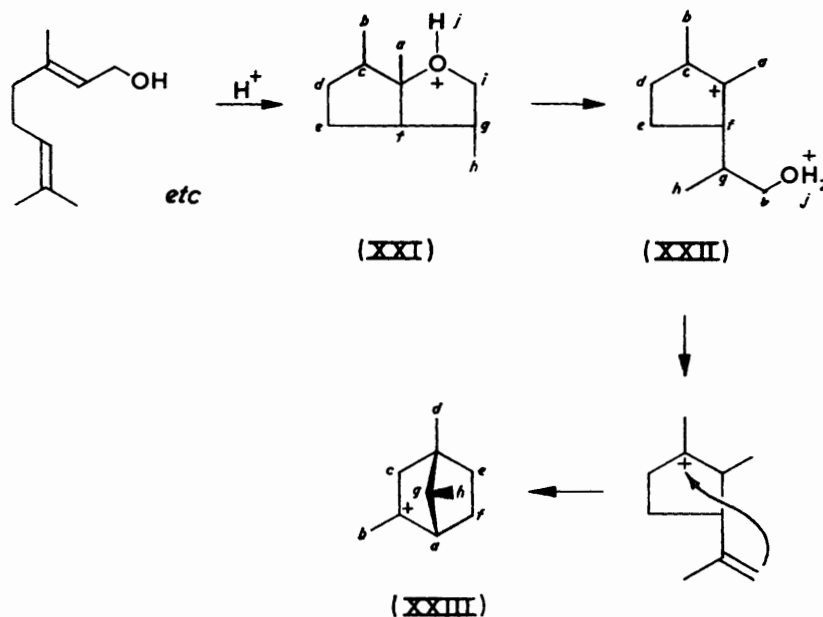


Table 2 records the lanthanoid-induced shifts at various mole fractions of the complexing agent. Attempts by using theoretical equations^{21,22} to correlate these shifts with the vector distances of the protons from

* The 6 β -proton is closer to the metal than are the protons of the methyl group, irrespective of whether complexing occurs at the α - or at the β -face.

²¹ H. M. McConnell and R. E. Robertson, *J. Chem. Phys.*, 1958, **29**, 1361.

²² E. Chong Sen and R. A. Jones, *Tetrahedron*, 1972, **28**, 2871.

oid ether (IX) all formed oxonium ions in fluorosulphonic acid at -78° that could be assigned structure (XXI) on

²³ J. Goodesman and R. S. Matthews, *J.C.S. Chem. Comm.*, 1972, 127.

²⁴ P. H. Mazzocchi, H. L. Ammon, and C. W. Jameson, *Tetrahedron Letters*, 1973, 573.

²⁵ J. W. ApSimon and H. Beierbeck, *Tetrahedron Letters*, 1973, 581.

²⁶ G. A. Olah, A. M. White, and D. H. O'Brien, *Chem. Rev.*, 1970, **70**, 561.

²⁷ G. A. Olah, *Angew. Chem. Internat. Edn.*, 1973, **12**, 173.

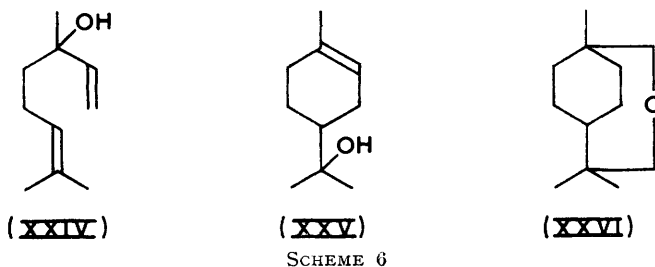
TABLE 2
Lanthanoid-induced shifts of n.m.r. signals of structure (XVIII) *

	τ_1 †	τ_2 ‡	τ_3 §	$\Delta\tau$ ¶
2 β -H	6.33	0.28	-4.97	11.30
2 α -H	6.01	0.44	-4.38	10.39
6 α -CH ₃	8.87	4.13	-0.02	8.89
4 β -H	8.51	4.43	0.78	7.73
5 β -H	8.12	4.87	2.07	6.05
4 α -H	8.51	5.58	3.16	5.35
6 β -H	8.12	5.61	3.07	5.05
3 α -H	8.12	5.88	3.90	4.22
3 α -H	8.12	6.25	4.62	3.50
6 α -CH ₃	9.11	6.75	4.62	4.49
5 α -H	8.81	7.23	5.83	2.98
3 β -CH ₃	9.01	7.67	6.44	2.57

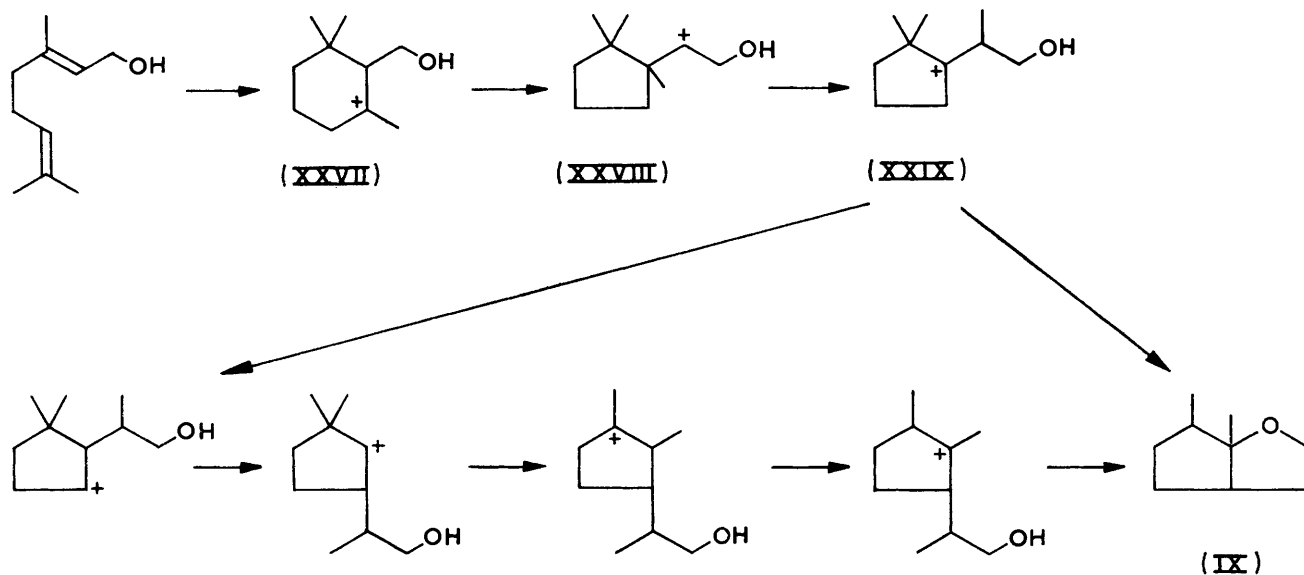
* ¹H N.m.r. spectra at 100 MHz in the presence of various amounts of Eu(fod)₃. Assignments were made by spin-decoupling on the approximately first-order spectrum obtained in the presence of Eu(fod)₃ (mole fraction 0.28). Use of Pr(fod)₃ resulted in extensive line-broadening and uninterpretable spectra. † τ Value in absence of shift reagent. Values were determined in some cases (where components of unresolved multiplets were involved) by linear extrapolation from plots of τ versus mole fraction of Eu(fod)₃ for values 0.17, 0.23, 0.28, and 0.38 of the latter quantity. ‡ τ Value at mole fraction 0.28. § τ Value at mole fraction 0.50. ¶ Change in τ (from position in absence of lanthanoid) caused by addition of Eu(fod)₃ (mole fraction 0.50).

the basis both of n.m.r. evidence (from correlations established for protonated alicyclic ethers²⁸) and of the

dications have been reported previously.³¹ When geraniol or the iridoid was treated with fluorosulphonic acid-antimony pentafluoride at -78°, the oxonium ion (XXI) was again formed, but this was rapidly cleaved to the dication (XXII) above ca. -70°. At -70°, small



amounts (ca. 10%) of another cationic species were present: this became predominant as the temperature was increased and comprised the sole product at 27°. Formation of this second species entailed cleavage of water from (XXII) and the n.m.r. spectrum suggested the structure (XXIII) although the assignments did not all tally (deviations up to 1.5 p.p.m. for certain protons) with those postulated for the related 2-methylnorbornyl cation.³² The cation (XXIII) may be formed by a ring closure (Scheme 5) analogous to known processes in other



recoveries (78, 57, 98, 87, and ca. 100% respectively) of (IX) obtained on quenching. As previously found in the n.m.r. spectra of protonated ethers and alcohols,²⁹ protons showed 1,3-coupling through an oxonium centre in the same way as through a carbonium ion centre.³⁰ Cleavage of the oxonium ion (XXI) to a dication spectrally identified as (XXII) occurred above 20°: analogous

²⁸ G. A. Olah and D. H. O'Brien, *J. Amer. Chem. Soc.*, 1967, **89**, 1725.

²⁹ G. A. Olah, J. Somner, and E. Namanworth, *J. Amer. Chem. Soc.*, 1967, **89**, 3576.

³⁰ G. A. Olah and J. Lukas, *J. Amer. Chem. Soc.*, 1967, **89**, 4739.

super acids.³³ Quenching the acid medium containing (XXIII) under a variety of conditions gave a complex mixture of products which is under investigation.

Mechanism of Formation of the Iridoid.—Linalol (XXIV), α -terpineol (XXV), 1,8-terpin (XXVI), and species derived therefrom are common products of acid-treatment of geraniol and nerol in aqueous media, but

³¹ D. M. Brouwer and J. A. van Dorn, *J. Roy. Netherlands Chem. Soc.*, 1972, **91**, 895.

³² G. A. Olah, J. R. de Member, C. Y. Lui, and A. M. White, *J. Amer. Chem. Soc.*, 1969, **91**, 3958.

³³ G. A. Olah, A. M. White, J. R. de Member, A. Commegras, and C. Y. Lui, *J. Amer. Chem. Soc.*, 1970, **92**, 4627.

these compounds (or their structural equivalents) could not have been intermediates in the super-acid-catalysed rearrangements as they did not yield the iridoid (IX) but gave only tars and high boiling products under these conditions. Moreover, the cyclisation of irid-1-en-9-ol and α -cyclogeraniol in fluorosulphonic acid to give excellent (98 and 87%) yields of (IX) suggests the intermediacy of these compounds or their structural equivalents in the super acids.

A possible reaction scheme is shown (Scheme 7). There are known analogies for the ring-contraction (XXVII) \longrightarrow (XXVIII),^{34,35} and the formation of secondary carbonium ions from tertiary ions has many precedents in reactions catalysed by super or Lewis acids, e.g. in syntheses of adamantane.³⁶ A variant is a short-cut from (XXIX) to (IX) involving a 1,3-hydride shift, but the stereochemistry of the product requires that this must be stepwise rather than a concerted rearrangement-cyclisation.

The conversion of irid-1-en-9-ol into the iridoid ether (IX) on treatment with toluene-*p*-sulphonic acid implies *cis*-addition to the double bond: this is feasible as the addition need not be concerted and inspection of models does not allow a decision as to the relative stabilities of (IX) and its 6 β -methyl epimer. A similar overall *cis*-addition occurred when the 3 α -methyl epimer (XII) of (IX) was formed from a diastereoisomeric form of irid-1-en-9-ol under the same reaction conditions.^{13,17}

EXPERIMENTAL AND RESULTS

Techniques.—¹H N.m.r. spectra of isolated products (10% v/v in deuteriochloroform) were measured with a Varian HA100 (100 MHz) spectrometer, with tetramethylsilane as internal standard: for measurements on solutions in strongly acidic media the same compound was used as an external standard. ¹H N.m.r. (220 MHz) and ¹³C Fourier transform n.m.r. (22.63 MHz) spectra were obtained from the P.C.M.U. (Aldermaston, Berks.). The lanthanoid shift reagents Pr(fod)₃ and Eu(fod)₃ (Aldrich) were added in portions to solutions (10% v/v) in deuteriochloroform up to 1:1 molar proportions. Reference letters for protons are shown in the formulae.

Mass spectra were obtained with a Metrovick MS9 instrument operating at 70 eV ionising potential with the injection chamber at 70°.

Preparative g.l.c. was carried out on a 2.5 m \times 1 cm (o.d.) column of 15% (w/w) Carbowax 20M on 60–80 mesh Supasorb at 120–150° with argon carrier gas (7.2–9.0 l h⁻¹) (column A). Analytical determinations were made on either a 16 m \times 0.5 mm capillary column of Carbowax 20M (Perkin-Elmer) at 100° with nitrogen carrier gas (0.25 l h⁻¹) (column B); or a similar SE30 capillary column (Perkin-Elmer) under the same conditions (column C). Purities of substrates and products were estimated by using the last two columns, and relative retention times with respect to geraniol (*t*_R 100) were measured on column B.

T.l.c., used to check purity of reaction products, was

³⁴ G. A. Olah, J. M. Bollinger, J. Lukas, and C. Cupas, *J. Amer. Chem. Soc.*, 1967, **89**, 2692.

³⁵ N. C. Deno and J. J. Hauser, *J. Amer. Chem. Soc.*, 1964, **86**, 1741.

³⁶ I. Fleming, 'Selected Organic Syntheses,' Wiley, London, 1973, p. 161.

carried out on silica gel H (Merck; 0.25 mm; activated at 100° for 1 h) with (A) ethyl acetate-hexane (15:85 v/v); (B) ethyl acetate-benzene (20:80 v/v); and (C) ethyl acetate-toluene (20:80 v/v) as solvents. The chromatograms were heated (100°; 2 min) after spraying with methanolic 5% phosphomolybdic acid or were treated with iodine vapour for development.

Samples for n.m.r. and i.r. spectroscopy were collected in capillary tubes at the exit port of the gas chromatograph: a micro technique³⁷ (ca. 1 mg sample) was used for the latter measurements.

Materials.—Geraniol (ca. 99.5%) was purified from commercial material through its complex with calcium chloride.³⁸ Nerol (ca. 99%; Fluka A.G.) and linalol, α -terpineol, and 1,8-terpin (all ca. 96%; Bush Boake Allen) were used without further purification. Fluorosulphonic acid (B.D.H.) was redistilled. Fluorosulphonic acid-antimony pentafluoride (1:1 w/w; 'Magic Acid') was purchased from Ozark-Mahonimy Co, inc., Tulsa, Oklahoma.

(i) 3 β ,6 α ,6 $\alpha\alpha$ -Trimethyl-cis-perhydrocyclopenta[b]furan (IX) from Geraniol.—Geraniol (29.7 g) in carbon disulphide (200 ml) cooled at -78° was added (30 min) to a rapidly stirred mixture of fluorosulphonic acid (125 g) and sulphur dioxide (125 g) at -78° under a dry atmosphere. After being stirred for a further 30–40 min, the acid layer (at -78°) was trickled down the wall (over 0.5 h) of a vessel containing a rapidly stirred slurry of potassium carbonate (350 g; added in 50 g portions), methanol (700 ml), and water (100 g) cooled at -78°. Water (2 l) was added and extraction of the resulting solid and liquid phases [hexane (3 \times 80 ml); ether (3 \times 50 ml)] and work-up yielded a yellow oil (26.5 g; b.p. 44–48° at 2.5 mmHg) that predominantly (88%) contained the iridoid (IX). This was purified by g.l.c.; the *product* (>99% pure on g.l.c. columns B and C; *R*_F values on t.l.c. systems A, B, and C: 0.35, 0.38, and 0.41) had b.p. 62–63° at 8 mmHg (Found: C, 78.2; H, 11.9%; *M*⁺, 154.1366. C₁₀H₁₈O requires C, 77.9; H, 11.7%; *M*, 154.1358); relative *t*_R 20.0; *m/e* 154 (*M*⁺, 7%), 98(9), 97(100), 96(5), 69(7), 55(11), 43(20), and 41(12); ν 2958s, 2920s, 2870s, 1492w, 1454m, 1376m, 1257w, 1190w, 1158m, 1148m, 1117m, 1106m, 1068m, 1035m, 1022m, 1008s, 1001s, 964m, 853s, and 819w cm⁻¹; τ (220 Hz) 9.11 (3H, d, *J* 7 Hz, *b*), 9.01 (3H, d, *J* 7 Hz, *h*), 8.87 (3H, s, *a*), 8.81 (1H, m, *1d*), 8.51 (2H, m, *e*), 8.12 (4H, m, *1d* + *f* + *c* + *g*), 6.31 (1H, d, *J* 8 Hz, *1i*), and 5.98 (1H, dd, *J* 8.1 and 4.5 Hz, *1i*); τ [100 MHz; solution containing 0.28 mole fraction of Eu(fod)₃; *J* values in Table 1] 7.23 (1H, dd, 5 α -H), 7.67 (3H, d, 3 β -Me), 6.75 (3H, d, 6 α -Me), 6.25 (1H, m, 3 α -H), 5.88br (1H, s, 3 $\alpha\alpha$ -H), 5.61 (1H, 7-line m, 4 α -H), 5.58br (1H, q, 6 β -H), 4.87 (1H, 7-line m, 5 β -H), 4.43 (1H, dd, 4 β -H), 4.13 (3H, s, 6 $\alpha\alpha$ -Me), 0.44 (1H, dd, 2 α -H), and 0.28 (1H, d, 2 β -H); ¹³C n.m.r. [22.63 MHz; Fourier transform; δ in p.p.m. downfield from Me₄Si (intensity, assignment³⁹): δ 82.73 (104, C-6a), 72.14 (1000, C-2), 50.04 (552, C-3a), 39.19 (554, C-6), 36.13 (725, C-3), 33.47 (828, C-5), 25.67 (796, 6 α -CH₃), 21.77 (679, C-4), 18.52 (756, 6-CH₃), and 14.56 (781, 3-CH₃).

(ii) *Other Preparations of the Iridoid (IX).*—The method of quenching the reaction mixture in the previous section minimised formation of polymer and water-soluble products

³⁷ W. J. de Klein, *Analyt. Chem.*, 1969, **41**, 667.

³⁸ O. Jacobson, *Annalen*, 1871, **157**, 234.

³⁹ L. F. Johnson and W. C. Jankowski, 'Carbon-13 N.M.R. Spectra,' Wiley-Interscience, New York, 1972, pp. 73, 123, 125, 393, 406.

(polyols?). These products, however, predominated if the biphasic reaction system was replaced by a homogeneous medium (by omission of carbon disulphide).

Treatment of nerol as for geraniol gave a product containing much polymer which was removed by passage through silica gel H (column 20 cm \times 1 cm o.d.) before work-up to isolate (IX) (57% yield). Treatment of geraniol (0.5 g) in carbon disulphide (5 ml) with a slurry of either concentrated sulphuric or formic acid (5 ml) in sulphur dioxide (10 ml) at -78° and quenching as above; or treatment of the same substrate (0.2 g) in methyl cyanide (10 ml) with aluminium trichloride (freshly sublimed; 1.3 g) dissolved in methyl cyanide (5 ml) at 0° and quenching at 0° yielded complex mixtures containing much polymer and little (<1%), if any, iridoid (IX). Similar products resulted from treatment of linalol, α -terpineol, and 1,8-terpin with fluorosulphonic acid under the conditions successfully used for the formation of the iridoid (IX) from geraniol.

Geraniol (0.25 g) in sulphur dioxide (1 ml) at -78° was added with stirring to fluorosulphonic acid-antimony pentafluoride (1 : 1 w/w; 1 ml) in sulphur dioxide (2 ml) at -78° . After quenching a complex mixture of products containing little (<5%) of the iridoid (IX) was obtained.

Treatment of irid-1-en-9-ol [(VII); obtained from cleavage of the iridoid (IX); see later] under conditions outlined in the preceding section yielded (IX) (98%). The same product (44%) resulted when the same substrate (0.4 g) was refluxed (40 h) with toluene-*p*-sulphonic acid (10 mg) in benzene (15 ml): two unidentified dienes (n.m.r.; i.r.) were also formed (26 and 16%) and the balance was high-boiling material: no starting material or other iridoid derivative (<1%, if any) was detected.

(iii) *Rearrangements of α -Cyclogeraniol (XX)*.—Geranyl acetate (ca. 99%) was formed when geraniol (17 g), acetic anhydride (300 ml), and pyridine (300 ml) were stirred at 20° for 3 days. This product (6.0 g) was stirred with aqueous phosphoric acid (86%; 6.6 ml) at 25° for 10 min; the mixture was neutralised below 30° , and the organic layer was treated with sodium dihydridobis-(2-methoxyethoxy)aluminate (20% in ether; 8 ml) to give α -cyclogeraniol,⁴⁰ which was purified by preparative g.l.c. (>96% pure; yield 36%); ν_{\max} 3350s, 3020m, 1390s, 1369s, and 809w cm^{-1} ; τ 9.11 and 9.00 (both 3H, s, *e* + *f*), 8.3—8.7 (4H, ms, *d* + *c*), 8.26 (3H, s, *a*), 8.03 (2H, m, *i* + *g*), 6.29 (2H, d, *J* 3.5 Hz, *h*), and 4.45 (1H, m, *b*). No i.r. or n.m.r. bands attributable to $\text{C}=\text{CH}_2$ were found.

α -Cyclogeraniol (45 mg) in carbon disulphide (2 ml) at -78° was added to a stirred, similarly cooled solution of fluorosulphonic acid (0.5 ml) in sulphur dioxide (0.5 g); the mixture was quenched [see section (i)] after 0.5 h to give the iridoid (IX) (39 mg, 87%).

(iv) *Degradation of the Iridoid (IX)*.—The iridoid ether was cleaved by an adaption of a previous method.^{41,42} Compound (IX) (4.1 g) in ether-acetic anhydride (30 ml; 1 : 2 v/v) at 0° was added to a similarly cooled solution of boron trifluoride-ether complex (20 ml; freshly-distilled from calcium hydride; b.p. 46° at 10 mmHg) in ether (10 ml) and the mixture was stirred while it warmed to room temperature (ca. 1 h). After work-up, the product in hexane was passed down a column of silica gel H (25 \times 1.5 cm o.d.) to yield an oil (3.1 g) containing three acetate esters

(90 : 7.8 : 2.2 w/w). Preparative g.l.c. (column A) yielded the main component, *irid-1-en-9-yl acetate* (III) (>98% pure); t_R 56.0 (Found: C, 72.8; H, 10.1. $\text{C}_{12}\text{H}_{20}\text{O}_2$ requires C, 72.3; H, 10.2%); *m/e* 196 (M^+ , 0.1%), 136(80), 123(57), 121(53), 107(38), 93(24), 81(42), 43(100), 41(38), and 39(26); ν_{\max} 2950—2800br,s, 1738s, 1430m, 1361m, 1229s, 1029m, and 600m cm^{-1} ; τ 9.08 (3H, d, *J* 6.5 Hz, *g*), 8.70 (1H, m, *f*); 8.41 and 8.36 (both 3H, s, *a* + *b*), 8.31—8.05 (5H, m, *c* + *d* + *e*), 8.02 (3H, s, *i*), and 6.07 (1H, dd, *J* 11.5 and 3.5 Hz) and 5.84 (1H, dd, *J* 11.5 and 7.8 Hz) [AB portion (*h*) of ABX (*h* + *f*) system].

The second component, *irid-5-en-9-yl acetate* (IV), was obtained 68% pure, contaminated with (III) (17%) and a third acetate (15%). The three compounds had t_R 70.6, 56.0, and 80.0. The mixture showed n.m.r. and i.r. spectra very similar to those of pure (III) and its mass spectrum showed M^+ 196. N.m.r. signals due to (IV), identified by 'subtraction' of those due to (III), appeared at τ 9.09 and 9.07 (both 3H, d, *J* 6.5 Hz, *a* + *h*), 8.33 (3H, s, *c*), 7.97 (3H, s, *j*), 8.5—7.7 (5H, ms, *b* + *e* + *f* + *g*), 6.0—5.6 (2H, m, *i*), and 4.77 (1H, m, *d*). No i.r. or n.m.r. signals compatible with the presence of $\text{C}=\text{CH}_2$ were present and hence the third acetate was inferred to be *irid-2-en-9-yl acetate* (V).

Treatment of the original mixture of acetates [(III) : (IV) : (V), 90 : 7.8 : 2.2] with boron trifluoride under the conditions of the original cleavage altered the proportions to 26 : 58 : 16.

Attempts to cleave the ether (IX) by dropwise addition to refluxing aqueous 5% phosphoric acid followed by immediate collection of steam-volatile material (an effective method for cleaving many ethers to give kinetically controlled products⁴³) was ineffective, but analysis of products from boron trifluoride cleavage after short reaction times suggested that (IV) was not a primary product.

The acetate mixture (90 : 7.8 : 2.2; 1.1 g) in ether (15 ml) was treated (20° ; 1 h) with sodium dihydridobis-(2-methoxyethoxy)aluminate (8 g) in ether (30 ml). The product was worked up at high (>5) pH to give a mixture (0.75 g) of two alcohols (91 and 9%: the third alcohol was presumably lost). These were purified by t.l.c. (systems A and B, R_F 0.55, 0.65 and 0.41, 0.72, respectively) and by preparative g.l.c. (t_R 80.0 and 111). The major component was *irid-1-en-9-ol* (VII) (Found: C, 77.4; H, 11.5. $\text{C}_{10}\text{H}_{18}\text{O}$ requires C, 77.9; H, 11.7%); *m/e* 154 (M^+ , 16%), 123(100), 95(30), 91(33), 81(88), 67(38), 55(39), 43(34), 41(60), and 39(38), m^* 121.4 (154 \rightarrow 136); ν_{\max} 3320s, 2910s, 2860s, 2824m, 1451m, 1382m, 1060m, 1040s, and 1050sh cm^{-1} ; τ 9.05 (3H, d, *J* 6.5 Hz, *g*), 8.8—8.4 (3H, m, *d* + *f*), 8.36 (6H, s, *a* + *b*), 8.3—7.8 (3H, m, *c* + *e*), 8.00 (1H, s, removed by D_2O treatment, *i*), and 6.36 (2H, d, *J* 4.1 Hz, *h*). The minor component was *irid-5-en-9-ol* (VIII) (Found: C, 78.0; H, 11.7%); *m/e* 154 (M^+ , 28%), 123(100), 122(27), 121(50), 107(33), 93(23), 84(22), 82(28), 81(49), and 67(42); ν_{\max} 3330s, 3020s, 2920—2888br,s, 1680w, 1506s, 1382s, 1080m, 1067s, 1016s, 918m, and 910m cm^{-1} ; τ 9.10 and 9.06 (6H, overlapping ds, *J* 6 Hz, *a* + *h*), 8.33 (3H, s, *c*), 8.5—7.6 (6H, ms + s removed by D_2O treatment, *b* + *e* + *f* + *g* + *j*), 6.46 (1H, dd, *J* 10.5 and 8.1 Hz) and 6.16 (1H, dd, *J* 10.5 and 5.0 Hz) [AB portion (*i*) of ABX system (*g* + *i*), and 4.72 (1H, m, *d*).

Irid-1-en-9-yl acetate (III) (114 mg) in purified methanol

⁴⁰ Haarman and Keiner A.G., G. P. 138,141; quoted in ref. 1, p. 49.

⁴¹ C. R. Narayanan and K. N. Iyer, *J. Org. Chem.*, 1965, **30**, 1734.

⁴² Y. Kitahara, T. Kato, N. Ototani, A. Inaue, and H. Izumi, *J. Chem. Soc. (C)*, 1968, 2508.

⁴³ Dr. H. R. Ansari, Bush Boake Allen and Co. Ltd., personal communication.

(1 ml) at -78° was ozonised (Nuair Mk. II ozoniser; flow rate 60 ml min^{-1} ; $1\frac{1}{4}$ h). The product was refluxed (40 min) with water (12 ml) and zinc dust (2 g) and worked up to give, as an oil (52 mg), 3-acetyl-2-methyl-6-oxoheptyl acetate (VI) (64%); t_R 244 (Found: C, 63.9; H, 9.0. $C_{12}H_{20}O_4$ requires C, 63.2; H, 9.0%); m/e 228 (M^+ , 0.2%), 111(18), 98(21), 85(25), 72(47), 71(21), 69(25), 55(25), 43(100), and 41(19); ν_{\max} 2960—2920br,s, 1739s, 1715s, 1455m, 1365s, 1236s, 1170m, and 1035m cm^{-1} ; τ 9.11 (3H, d, J 6.5 Hz, e), 8.5—8.0 (3H, m, $c + f$), 8.00 (3H, s, h), 7.86 (6H, s, $i + a$), 7.50 (2H, t, J 7.5 Hz, b), 7.24 (1H, q, J 6.5 Hz, d), and 5.75 (2H, d, J 6.5 Hz, g). On irradiation of the overlapping multiplet at τ 8.45 (assigned to c) the quartet at τ 7.24 collapsed to a doublet (J 6.5 Hz) and the triplet at τ 7.50 became a singlet. The protons responsible for the quartet at τ 7.24 and the doublet at τ 9.11 were similarly shown not to be coupled.

(v) ^1H N.m.r. Spectra obtained in the Presence of Lanthanoid Shift Reagents.—Shifts induced by addition of $\text{Eu}(\text{fod})_3$ in various amounts to solutions of the iridoid (IX) are in Table 2; assignments were made by systematic spin-decoupling around the periphery of the skeleton. Shifts upfield induced by $\text{Pr}(\text{fod})_3$ were larger but extensive line-broadening occurred at low (*ca.* 0.2) mole fractions of the additive and most of the shifted signals could not be assigned, nor could the coupling constants be elucidated.

(vi) ^1H N.m.r. Spectra at Low Temperatures.—The substrate (250 mg) in carbon disulphide (5 ml) was added slowly (20 min) to the super acid (2.5 ml) and sulphur dioxide (2.5 ml) and the two-phase system was stirred (25 min). Part (1 ml) of the acid layer was then sealed in an n.m.r. tube together with a capillary tube containing tetramethylsilane. The foregoing operations were carried out in a dry-box and solutions were kept near -78° . After equilibration (10 min) in the variable-temperature probe of the spectrometer at the desired temperature, very sharp spectra were obtained and τ values were almost independent of substrate concentration. Signals occurring near that of fluorosulphonic acid (τ -1.07) were shown not to be spinning side-bands.

Such solutions of geraniol, nerol, α -cyclogeraniol, irid-1-

en-9-ol, and the iridoid (IX) with fluorosulphonic acid all gave identical spectra at -78° corresponding to an oxonium ion (XXI): τ 8.92 (6H, d, J 7 Hz, $h + b$), 8.44 (1H, m, $1d$), 8.32 (3H, s, a), 8.06—7.87 (4H, m, $1d + e + g$), 7.48 (2H, m, $f + c$), 5.28 (2H, m, i), and 0.26br (1H, m, j). Irradiation at τ 0.26 simplified the multiplet at τ 5.28 to the AB (i) part of an ABX spectrum: τ 5.20 (1H, dd, J_{AB} 8.8, J_{AX} 4.5 Hz, H_A) and 5.35 (1H, d, J_{AB} 8.8, J_{BX} 0.0, H_B). At above *ca.* -20° , the ion (XXI) was converted into a new species (XXII): τ 8.57 (6H, d, J 2 Hz, $h + b$), 7.50 (4H, m, $d + e$), 6.18br (3H, s, a), 6.15—6.10 (1H, m, g), 5.39 and 5.21 (2H, ms, $c + f$), 4.77 (2H, m, i), and 0.10 (2H, t, J 3.5 Hz, j), and at 27° conversion was complete within 3 min.

When geraniol or the iridoid (IX) was treated with fluorosulphonic acid-antimony pentafluoride (1:1 w/w) at -78° the dication (XXII) was formed predominantly (90%), accompanied by a species tentatively identified as (XXIII) (10%): τ 8.29 (3H, d, J 7 Hz, h), 7.62 (3H, s, d), 7.41—6.96 (5H, ms, $c + e + f_{\text{exo}}$), 6.89br (3H, t, J 3 Hz, b), 6.62br (1H, m, f_{endo}), 6.31 (1H, m, g), and 4.72 (1H, d, J 3.5 Hz, a). Spin-decoupling showed that the protons responsible for the signals at τ 8.29 and 6.31 and at τ 6.31 and 4.72 were coupled. A signal at τ *ca.* 0.0 always accompanied formation of (XXIII) and was probably derived from protonated water or hydrolysis products of the acid system. The cation (XXIII) became the only detectable species when the reaction mixture was maintained at -15° for 1 h, and similarly was the only product when (IX) was treated with fluorosulphonic acid-antimony pentafluoride at 27° .

Quenching [technique as in section (i)] of acid solutions containing the oxonium ion (XXI) or the dication (XXII) resulted in almost quantitative recovery of the iridoid (IX), but similar treatment of a solution containing essentially only (XXIII) led to a complex mixture of products which awaits analysis.

We thank the S.R.C. for a C.A.P.S. Studentship and Messrs. K. Ufton, A. Curtis, R. Duprey, and J. Janes (Bush Boake Allen and Co. Ltd.) for discussions.

[3/1674 Received, 7th August, 1973]