Rearrangement of Linalool, Geraniol, and Nerol and Their Derivatives

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Acid-catalyzed conversion of linalool into geraniol, nerol, and α-terpineol is slower than the corresponding reactions of geraniol and nerol, because the tertiary linalyl carbocation reverts to linalool rather than going forward to rearranged products. The linalyl carbocation does not lose its stereochemical identity, and oxygen exchange of linalool is faster than rearrangement or cyclization. Solvolyses of linalyl esters and chloride are faster than those of the geranyl and neryl derivatives. These solvolyses are different from acid heterolysis of linalool in that there is extensive racemization of linalool, but cyclization to α-terpineol goes with considerable retention of configuration. Participation by the 6,7-double bond controls the stereochemistry of linalool heterolysis and solvolysis of linalyl esters, but it does not markedly affect the reaction rates.

Pyrophosphate esters of the allylic prenols, geraniol (*E*, C_{10}) and farnesol (2*E*,6*E*, C_{15}) are precursors of most isoprenoid natural products.[1,2]

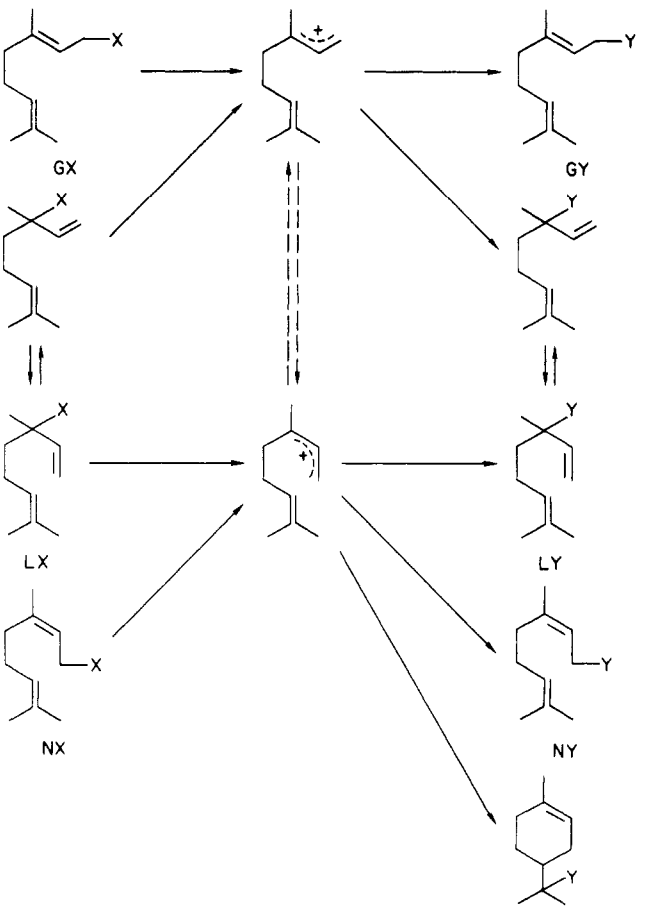
In some cases neryl pyrophosphate (NPP), the *Z* isomer of geranyl pyrophosphate (GPP), is a precursor of plant isoprenoids,[3–6] and tertiary derivatives such as linalyl pyrophosphate (LPP) or nerolidyl pyrophosphates (C_{15}) also have roles in terpenoid biosynthesis.[2,6,7]

The acid-catalyzed rearrangements of nerol (NOH) and geraniol (GOH) and solvolyses of their derivatives have been considered as models for terpenoid biosynthesis.[8,9] In these reactions, nerol or its derivatives give predominantly cyclic products, α-terpineol (TOH), or limonene, whereas geraniol or its derivatives generate largely linalool (LOH) plus acyclic alkenes.[8–14] Linalyl derivatives form acyclic and cyclic products, but under thermodynamic control, i.e., in acidic media, α-terpinyl derivatives are major products.[8,10,11,13,14]

The various reactions are assumed to involve carbocationic intermediates, some of which do not interconvert rapidly. Scheme I illustrates, in a simplified way, the main substitution reactions.

Scheme I is oversimplified because it neglects the possible intermediacy of ion pairs, π-participation of the remote double bond or conformational effects.[8,9,11–15] For example, substrates probably exist largely in extended conformations, and acyclic products could be formed from carbocations which have extended conformations. The cis

Scheme I



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and trans carbocations, generated from neryl and geranyl derivatives, respectively, do not readily interconvert. Only substitution products are shown but elimination predominates in solvents of low nucleophilicity.[16] Formation of cyclic products seems to be favored by factors which increase the lifetime of the carbocations, e.g., low solvent nucleophilicity or the presence of low charge density anions.[12-17] Similar effects are seen in other reactions involving neighboring group participation.[18]

Overall rates of solvolysis of *E* and *Z* isomers (GX and NX) are similar,[8b,9,14,15] but neryl compounds give largely cyclic and geranyl largely acyclic products, regardless of the leaving group. As expected, solvolyses of linalyl derivatives are faster than those of the corresponding neryl and geranyl derivatives.[8b,13] But in acidic media, interconversion of linalool and its isomers is slow enough for it to accumulate in acid-catalyzed rearrangements of geraniol and nerol, and it is converted into α-terpineol but more slowly than is nerol.[11,19]

This apparently low reactivity of a tertiary alcohol, linalool, as compared with primary alcohols, e.g., geraniol or nerol, is unusual, because tertiary alcohols are typically more acid labile than otherwise similar primary or secondary alcohols. One explanation of this behavior is that an intermediate carbocation reverts preferentially to linalool instead of going forward to rearranged products (Scheme I). But then return must occur without racemization, because in acidic media optically active linalool rearranges to optically active α-terpineol.[19,20]

There is ample precedent for return of a linalyl cation to a neutral substrate. Hydrolysis of linalyl *p*-nitrobenzoate[13] gives optically active α-terpineol, as does hydrolysis of linalyl phosphate, but here there is no evidence for return of an ion pair to substrate.[8]

In these reactions interactions between a leaving anion and a linalyl carbocation may be important, but such Coulombic interactions are absent when the leaving group is formally a water molecule, as in acid-promoted reactions of linalool. It is therefore difficult to reconcile the apparent low reactivity of linalool in acid-catalyzed rearrangement with formation of optically active α-terpineol.

Participation by the remote 6,7-double bond[8b,13] explains the stereochemistry of the conversion of linalyl into α-terpinyl derivatives, and subsequent attack of water at Cl would give linalool of retained configuration. In this context cyclization of a (1*S*)-[(1-2H)neryloxy]pyridinium involves inversion of configuration at C1,[21a] with π-participation, or with C1–C6 ring closure being faster than reorientation of the chiral C1.[21] Kinetic evidence is ambiguous; for example, hydrolysis of 6,7-dihydroneryl phosphate is slightly faster than that of neryl phosphate, and for hydrolyses of the geranyl phosphates the 6,7-dihydro derivative is slightly slower.[8b] Secondary deuterium kinetic isotope effects support π-participation in hydrolysis of neryl chloride[15] but not in cyclization of farnesyl phosphate.[22] Replacement of H by F strongly inhibits solvolyses of neryl and geranyl mesylate consistent with strong electron withdrawal by F, but the change in the ratio of cyclic to acyclic products suggests that π-participation is important only when formation of a neryl carbocation is strongly inhibited by electron withdrawal.[21b]

Interpretation of these results is complicated because the beneficial effects of π-participation are offset by loss of rotational entropy and unfavorable syn-butane interactions.[14] In addition reactions may be stepwise or concerted depending upon electronic demands at the reaction center and solvation of the initial and transition states and ion pair return.[13,14]

Our aim was to compare rates of acid-catalyzed rearrangement, racemization and oxygen exchange of linalool with those of rearrangements of primary alcohols geraniol and nerol (Scheme I), because oxygen exchange should measure the rate of carbocation formation. We also examined rates and product formation in spontaneous hydrolyses of the chlorides or esters for comparison with reactions of the alcohols.

Experimental Section

Materials. Nerol and geraniol were from Fluka or Columbia Organics, α-terpinol was from MCB, and (*R*)-(−)-linalool was from Fritzsche and racemic linalool from Aldrich. A sample of racemic linalool showed a small peak on GLC analysis (25-m, 0.2-mm Ultra II capillary column, 5% phenyl methyl silicone in a 25m × 0.3 mm ESOT column with OV-101, 0.5-μm film), with retention time almost identical with that of linalool. We did not find this peak when GLC analysis was performed with a 50-m, 0.25-mm capillary column (Carbowax 4000) nor with a variety of packed columns. The retention time did not correspond to those of the other isomeric terpenoid alcohols, and we did not see this peak with (−)-linalool; a referee suggests that it was due to a dehydro derivative.

The preparation of neryl, geranyl, and α-terpinyl chloride has been described.[12] Linalyl chloride was prepared by treating geraniol (1 g) with a twofold excess of freshly distilled $SOCl_2$ (1.6 g) in Et_2O for 2 days. The solvent was evaporated and the residual oil was washed quickly with cold H_2O and cold saturated $NaHCO_3$. Hydrolysis was followed immediately, and kinetic analysis showed that the sample contained approximately 30% geranyl and 3% terpinyl chloride. The rate constants of hydrolysis of these chlorides are sufficiently different for this analysis.

6,7-Dihydrogeranyl and 6,7-dihydroneryl chlorides were prepared as follows: a mixture of *cis*- and *trans*-ethyl 3,7-dimethyl-2-octenoate[23] was prepared by treating 6-methyl-2-heptanone (0.15 mol) with the sodium salt of ethyl (diethoxyphosphinyl)acetate (0.15 mol) under reflux in dry dimethoxyethane for 6 h. The reaction was quenched (H_2O), and the products were extracted into Et_2O. The extract was washed (saturated aqueous NaCl) and dried ($MgSO_4$). The crude mixture of cis and trans isomers was separated by using a spinning band column, giving one fraction which contained 80% cis ester and another with 99.8% *trans*. The crude cis ester was reduced with $LiAlH_4$ in Et_2O, and 6,7-dihydronerol was purified by preparative GLC ($^3/_8$ in. × 24 ft Carbowax 20 M at 168 °C). Carbowax 20 M at 168 °C). The trans ester was reduced similarly and 6,7-dihydrogeraniol was purified by preparative GLC. The NMR spectrum (60 MHz) showed one vinyl proton at 5.40 ppm and two methylene protons at 4.12 ppm (doublet) for 6,7-dihydronerol and one vinyl proton at 5.45 ppm and two methylene protons at 4.15 ppm (doublet) for the trans isomer. Analytical GLC showed that these samples did not contain the corresponding nerol or geraniol. The purified alcohols were converted into the corresponding chlorides as described.[12] Their hydrolyses followed good first-order kinetics for over 90% reaction.

The trifluoroacetates were prepared by treating the alcohol (32.5 mmol) with $(CF_3CO)_2O$ (35 mmol) in dry pyridine (25 mL) for 4 h at 0 °C. The reaction mixture was poured into cold H_2O, and the products were rapidly extracted with Et_2O. The extract was washed several times with 5% H_2SO_4 and then with saturated $NaHCO_3$ and then dried ($MgSO_4$). The esters were distilled in

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Table I. Solvolyses of the Chlorides[a]

alkyl group	vol % H_2O[b]						
	10	30	40	50	60	30[c]	0[c]
linalyl	1.9	96		1900		1400	
geranyl	0.29	12.7	40.6	413	1380	330	4.20
neryl	0.53	36.1	147	464		430	7.90
α-terpinyl		0.52		7.8		7.1	

[a] Values of 10^5k, s^{-1}, at 25.0 °C. [b] The cosolvent is acetone unless specified. [c] Cosolvent is methanol.

vacuo: NTFA and TTFA, 49–50 °C (0.4 mm); GTFA, 52–53 °C (0.65 mm); LTFA, 40–41 °C (0.4 mm). Linalyl trifluoroacetate has $[\alpha]^{25}$ −3.65°. These esters decomposed in a few days even at 0 °C. The absence of alcohols and rearranged impurities in the esters was demonstrated by NMR and IR spectrometry, and hydrolyses were first order for 90% reaction.

1,2-Dihydrolinalyl trifluoroacetate was prepared by treating 6-methyl-5-heptene-2-one (0.2 mol) with EtMgBr (0.25 mol) in Et_2O. 2-Hydroxy-3,7-dimethyl-6-octene (1,2-dihydrolinalool) was isolated in 66% yield [bp 57–58.5 °C (1.5 mm); lit.[24] bp 94–94.5 °C (14 mm)] and trifluoroacetylated as above in 85% yield. 1,2-Dihydrolinalyl trifluoroacetate had bp 42–43 °C (0.3 mm). The NMR spectrum (60 MHz) had methyl peaks at 1.5, 1.6, and 1.68 (singlets) and 0.95 ppm (triplet) and a single vinyl proton at 5.09 ppm.

Experiments with the trifluoroacetates and chlorides were carried out on freshly prepared samples stored briefly at low temperature over Drierite.

Kinetics. Solvolyses were followed conductimetrically using 10^{-3} M substrates. The mixed solvents were made up by weight to give the specified volume compositions at 25 °C. The first-order rate constants were calculated by using a linear least-squares program, and, except where noted, the reactions were cleanly first order for four half-lives.

Products. Product compositions were determined by GLC by methods already described.

(*R*)-(−)-Linalyl trifluoroacetate, prepared from (−)-linalool ($[\alpha]_D$ −21.6°; c.f. ref 8b) was hydrolyzed in H_2O–MeCN (25:75 v/v) at 25 °C, and linalool and α-terpineol were isolated by preparative GLC. Reactions were carried out both in the absence of added solute and in 3.6 M $LiClO_4$. The isolated linalool was racemic, within experimental error (linalool does not racemize in the conditions of hydrolysis). Isolated (*R*)-α-terpineol had $[\alpha]_D$ 61.8° and 9.7° from reaction in the presence of $LiClO_4$.

Reaction of the Alcohols. Reactions were carried out at 25 °C, typically with 0.05–0.08 M prenyl alcohol in 10 mL of solvent. Aliquots (1 mL) were withdrawn, and the solution was extracted with pentane. In the experiments with $C_{12}H_{25}SO_3H$, the surfactant was first precipitated with $Ba(OH)_2$. The extract was washed (NaOH, H_2O) and dried (K_2CO_3), and the samples were analyzed by GLC generally in a 5% Carbowax/Chromosorb column (6 ft × $^1/_8$ in.) with temperature programming from 80 °C. The first-order rate constants were calculated from the initial part of the reaction, typically less than 10% conversion. The major products were alcohols, and the formation of small amounts of alkene was neglected in calculating the rate constants. Product interconversion became all important in later stages of the reaction[11] (c.f. Figure 1).

Racemization of Linalool. The change of optical rotation of (*R*)-(−)-linalool was followed at 25 °C in Autopol III polarimeter or on a Cary 60 ORD spectrophotometer. Reaction in H_2O–MeCN (2:3 v/v) with 0.12 M H_2SO_4 was followed under the conditions used for examination of the products. Under these conditions the ratio of TOH to total alcohol products (TOH + NOH + GOH) is 0.41. The initial rotation is α_0 −0.286° so that if linalool goes to α-terpineol with no loss of stereochemistry and if it does not itself racemize directly, the calculated final rotation α_∞ will be +(0.286 × 4.65 × 0.41)° based on $[\alpha]_D$ −21.6° and +100.5° for *R*-(−)-linalool and (*R*)-α-terpineol, respectively.[8b] A plot of ln $(\alpha_\infty - \alpha_t)$ against time *t*, over a period of 90 h gave a first-order rate constant of 1.6 × 10^{-6} s^{-1}. The value of α_∞ cannot be estimated by isolating α-terpineol at the end of the reaction, because subsequent conversion of nerol into α-terpineol gives racemic product, just as geraniol gives racemic linalool.

Table II. Hydrolysis of the Trifluoroacetates[a]

alkyl group	10^5k, s^{-1}	alkyl group	10^5k, s^{-1}
linalyl	7.04	α-terpinyl	0.33
geranyl	1.54	1,2-dihydrolinalyl	0.51
neryl	1.52		

[a] At 25.0 °C in H_2O–acetone (30:70 v/v).

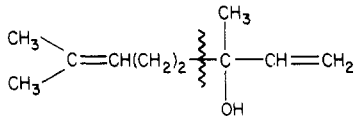
Table III. Temperature Effects on Solvolysis of the Chlorides[a]

alkyl group	*T*, °C		
	25.0	32.5	40.0
geranyl	12.7	28.8	62.5
neryl	36.1	69.0	146
6,7-dihydrogeranyl	15.7	34.4	78.4
6,7-dihydroneryl	10.1	22.7	53.6

[a] Values of 10^5k, s^{-1}, in H_2O–acetone (30:70 v/v).

In qualitative experiments at 25 °C with 0.1 M $C_{12}H_{25}SO_3H$ in H_2O and 0.1 M HCl in H_2O–MeCN (1:1 v/v), the rotation of (*R*)-(−)-linalool gradually decreased with time and finally changed sign, corresponding to formation of (*R*)-(+)-α-terpineol. These systems were not examined quantitatively, but the rate of change of rotation was qualitatively similar to the rate of disappearance of LOH in solutions of $C_{12}H_{25}SO_3H$.

Oxygen Exchange of Linalool. Exchanges were carried out at 25 °C with ca. 0.1 M LOH in 2 mL of $H_2{}^{18}O$–MeCN (2:3 v/v) and 0.12 M H_2SO_4, with $H_{12}{}^{18}O$ of 9.4 atom % excess abundance. The experiments are complicated by a slow rearrangement to geraniol and its return to linalool, so isotopic exchange could not be usefully followed to equilibrium. Oxygen exchange of linalool is sufficiently faster than its rearrangement that this reaction does not seriously affect our estimated rate constants of exchange. After 20 or 46.6 h the individual samples were extracted (pentane), washed (NaOH, H_2O), and dried (K_2CO_3). Linalool was isolated by preparative GLC using a 20% Carbowax 20M/Chromosorb column (10 ft × $^1/_4$ in.) at 105 °C. The molecular ion of linalool was not observed with either electron impact or chemical ionization (CH_4) on a ZAB-2F mass spectrometer; but strong peaks at unit masses 71 and 73 (for the ^{18}O-labeled material) were used to estimate the ^{18}O abundance. These peaks arise from the cleavage as illustrated.



mass 71

The chemical composition of the ion mass 71 was confirmed by precise mass measurement. The samples isolated after 20 and 46.6 h had excess abundance of ^{18}O of 2.87 and 6.17 atom %, respectively, giving first-order rate constants of oxygen exchange, 10^6k = 5.3 and 6.5 s^{-1}.

Results

Tables I and II give rate constants for solvolysis of the chlorides and trifluoroacetones. The 1,2-allylic double bond in linalyl trifluoroacetate speeds hydrolysis by a factor of 14, relative to the 1,2-dihydro compound. The "remote" 6,7-double bond of neryl chloride speeds hy-

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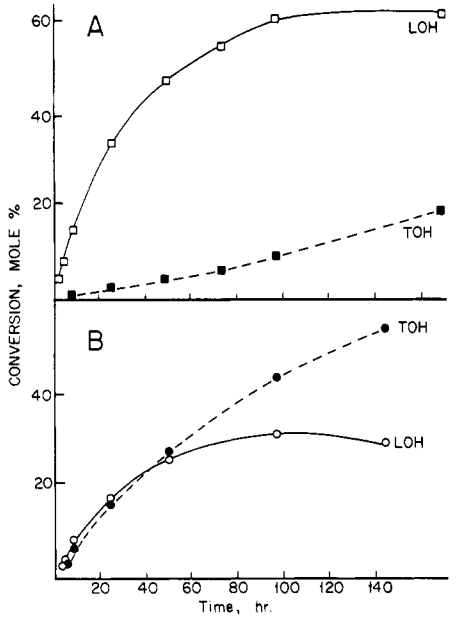

Figure 1. Rearrangements of geraniol (A) and nerol (B) in H_2O–MeCN (2:3 v/v) and 0.118 M H_2SO_4 at 25.0 °C.

Table IV. Solvent and Activation Parameters for Solvolysis of the Chlorides[a]

alkyl group	m	$\Delta H^{\ddagger}$, kcal·mol^{-1}	$\Delta S^{\ddagger}$, eu
linalyl	1.1		
geranyl	0.9	20.1	−12.5
neryl	1.0	19.6	−12.4
6,7-dihydroneryl		22.4	−5.5

[a] Activation parameters are for reactions in water–acetone (30:70 v/v).

Table V. Products of Solvolysis of the Trifluoroacetates[a]

	alkyl groups		
	geranyl	neryl	linalyl
limonene	*b*	3.0	0.8 (1.8)
terpinolene	*b*	0.6	0.2 (3.5)
myrcene	8.3	8.7	12.5 (3.2)
ocimene	0.8	1.5	8.2 (4.9)
linalool	18.9	13.2	30.8 (16.8)
nerol	0.8	37.8	10.0 (1.1)
geraniol	68.3	*b*	21.2 (5.6)
α-terpineol	2.4	34.7	13.8 (60.4)
alkenes, %	9.8	14.3	24.2 (15.1)
cyclic, %	2.4	38.3	14.8 (65.7)
cyclic/acyclic	*c*	0.62	0.17 (1.9)

[a] At 25.0 °C in H_2O–acetone (1:3 v/v); values in parentheses are for solutions containing 3.6 M $LiClO_4$. [b] Trace. [c] Very small.

drolysis by a factor of 3.6 relative to reaction of the dihydro derivative, but there is slight inhibition for the geranyl derivatives (c.f. ref 8b).

Rate constants increase markedly with increasing water content of the solvent. The m values and the activation parameters (Tables III and IV) are typical of S_N1 reactions.[25] The range of solvent compositions is too small to justify use of four-parameter equations which take solvent nucleophilicity into account.[26]

Products of hydrolysis of the trifluoroacetates (Table V) are similar to those of hydrolyses of other derivatives.[8,9,12-15,21] The increase of cyclic alkenes and total cyclic products from reaction of the trifluoroacetates on addition of $LiClO_4$ agrees with results on the chlorides.[12]

Hydrolysis of (*R*)-(−)-linalyl trifluoroacetate gives racemic linalool and (*R*)-(+)-α-terpineol (Table VI). Added $LiClO_4$ increases the proportion of cyclic products (Table V) and loss of optical activity of α-terpineol.

Rearrangements of nerol and geraniol in dilute acid have similar initial rates (Table VII–IX and ref 9), but linalool rearranges much more slowly. In these tables the subscript denotes the substrate and the superscript the product. Geraniol gives largely acyclic products whereas nerol and linalool give both acyclic and cyclic products. The values of k (Table VIII and IX) are for overall rearrangement. In acidic aqueous solvents little alkene is formed, even though the alkenes are not rapidly hydrated under these conditions. With time the acyclic alcohols give α-terpineol with thermodynamic control.[11] The rates of these acid-

Table VI. Solvolysis of Chiral Linalyl Trifluoroacetate[a]

product	$[\alpha]^{25}_D$
α-terpineol[b]	+61.8 (+9.7)
linalool[b]	0.0 (0.0)

[a] At 25.0 °C in water–acetone (1:3 v/v); values in parentheses are in 3.6 M $LiClO_4$. [b] $[\alpha]^{20}_D$ +100.5° and −21.6° for (*R*)-α-terpineol and (*R*)-linalool, respectively.[8b]

Table VII. Reaction of Geraniol

conditions	$10^6 k_G^L$, s^{-1}
0.1 M $C_{12}H_{25}SO_3H$, H_2O, 25 °C	26
0.12 M H_2SO_4, H_2O–MeCN (2:3), 25 °C[a]	6
0.07 M HCl, H_2O–MeCN (2:1), 37 °C	17
0.05 M HCl, H_2O–Me_2CO (1:1), 37 °C[b]	5

[a] After 35% reaction α-terpineol was detected. [b] Reference 9.

Table VIII. Reactions of Nerol

conditions	$10^6 k_N^L$, s^{-1}	$10^6 k_N^T$, s^{-1}	$10^6 k$, s^{-1}
0.1 M $C_{12}H_{25}SO_3H$, H_2O, 25 °C	17	19	36
0.12 M H_2SO_4, H_2O–MeCN (2:3), 25 °C	3.0	2.7	5.7
0.07 M HCl, H_2O–MeCN (2:1), 37 °C[a]	7.5	11.5	19
0.05 M HCl, H_2O–Me_2CO (1:1), 37 °C[b]	3.0	2.2	5.2

[a] After 35% reaction geraniol was detected. [b] Reference 9.

Table IX. Reactions of Linalool

conditions	$10^6 k_L^T$, s^{-1}	$10^6 k_L^G$, s^{-1}	$10^6 k_L^N$, s^{-1}	$10^6 k$, s^{-1}
0.1 M $C_{12}H_{25}SO_3H$, H_2O, 25 °C[a]				5.5
0.12 M H_2SO_4, H_2O–MeCN (2:3), 25 °C	0.57	0.50	0.13	1.2[c]
0.12 M H_2SO_4, H_2O–MeCN (2:3), 25 °C[b]	0.56	0.57	0.13	1.3[c]
0.07 M HCl, H_2O–MeCN (1:2), 37 °C[a]				5.3
0.07 M HCl, H_2O–MeCN (1:1), 37 °C[a]				4.3
0.07 M HCl, H_2O–MeCN (2:1), 37 °C[a]				2.8

[a] Only α-terpineol was detected in the products. [b] (*R*)-(−)-Linalool. [c] Under these conditions the first-order rate constants for loss of optical activity and oxygen exchange are 1.6×10^{-6} and ca. 6×10^{-6} s^{-1}, respectively.

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(26) (a) Bentley, T. W.; Schleyer, P. v. R. *Adv. Phys. Org. Chem.* **1977**, *14*, 1. (b) Bentley, T. W.; Carter, G. E. *J. Am. Chem. Soc.* **1982**, *104*, 5741.

catalyzed rearrangements increase with increasing water content of the solvent.

Generally we followed only the initial part of the reaction to minimize reaction of the first formed products. This is a serious problem for reaction of linalool and for its reaction in $C_{12}H_{25}SO_3H$ and at 37 °C we detected no geraniol or nerol (Table IX). In subsequent experiments, in aqueous MeCN at 25 °C, we took pains to examine the initial products and then observed formation of nerol and geraniol.

Linalool readily exchanges its oxygen with that of water.[27] In H_2O–MeCN (2:3 v/v) at 25.0 °C and 0.12 M H_2SO_4 the first-order rate constant for oxygen exchange is ca. 6×10^{-6} s^{-1} (Experimental Section). The first-order rate constants for loss of optical activity under these conditions is 1.6×10^{-6} s^{-1} (Experimental Section), which is similar to the value of the rate constant of ca. 1.3×10^{-6} s^{-1} for the conversion of linalool into α-terpineol, geraniol, and nerol (Table IX). This similarity suggests that the loss of optical activity is due to formation of achiral nerol and geraniol and of (*R*)-(+)-α-terpineol and not to racemization of linalool. The rate constant for heterolysis of linalool is the sum of its rate constants of oxygen exchange and rearrangements (Table IX), is therefore approximately 7×10^{-6} s^{-1}, and is slightly larger than those for rearrangement of nerol and geraniol.

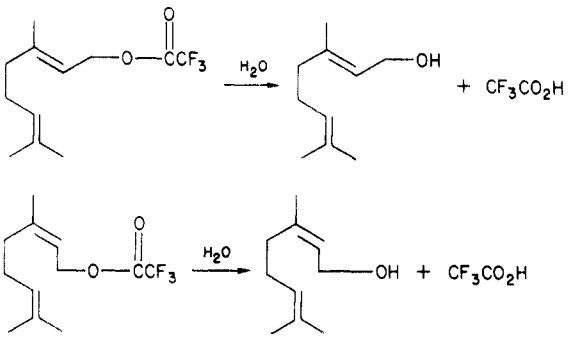
Discussion

The reactivity sequence for solvolyses of the chlorides and trifluoroacetates in aqueous acetone is linalyl > neryl ~ geranyl > α-terpinyl (Table I–III), as observed with other leaving groups, e.g., phosphate, pyrophosphate, *p*-nitrobenzoate, mesylate, and 2,4-dinitrophenoxy, over a wide range of solvent polarity, represented at the extremes by water and acetic acid.[8,9,12-15,21] Electronic delocalization into the allylic double bond is of key importance, but participation by the 6,7-double bond is less important kinetically. The Mn^{2+}-catalyzed hydrolysis of citronellyl pyrophosphate is much slower than that of geranyl pyrophosphate.[17] This effect of the allylic double bond is much larger than that for hydrolyses of the linalyl derivatives and is due, in part, to the different electronic requirements of primary and tertiary carbocations.

The relatively small rate effects of the remote 6,7-double bond are not inconsistent with π-participation in heterolysis because its beneficial effects are offset by loss of entropy and interactions in cisoid transition states. The rotational barrier in butane is ca. 4 kcal·mol^{-1}, which is equivalent to a rate effect of ca. 10^3-fold,[28] and Astin and Whiting estimate the unfavorable entropy effect to be 5.4 eu for neryl 2,4-dinitrophenyl ether.[14] The kinetic role of π-participation in reactions of neryl, or linalyl, derivatives probably depends upon a fine balance of factors, including the number of possible rotational conformers, the nature of the leaving group, and initial- and transition-state solvation. For example, some reactions of neryl derivatives are believed to be assisted by π-participation, whereas with C_{15}, farnesyl derivatives it is believed to occur after the transition state for bond breaking.[21,22]

For reactions in solvents of high water content, product compositions are relatively insensitive to the nature of the leaving group, except that extensive amounts of unrearranged alcohols are formed in hydrolyses of geranyl and neryl trifluoroacetate (Table V), presumably due to attack of water upon the acyl group (mechanism $B_{Ac}2$, Scheme II).

Scheme II



Alkyl trifluoroacetates react readily by the $B_{AC}2$ mechanism,[29] but its contribution is not all important in our reactions because the relative reactivities of linalyl, geranyl, and neryl chlorides and trifluoroacetates are very different (Table I and II), and rearranged products are formed. The tertiary linalyl ester should be less reactive than the primary geranyl and neryl esters by the $B_{AC}2$ mechanism.[30]

Solvolyses of the chlorides and trifluoroacetates were cleanly first order for up to at least three half-lives.[31] This result confirms that substrate rearrangement is unimportant[8b] whereas in water–acetone (30:70 v/v) linalyl *p*-nitrobenzoate is rearranged to less reactive isomeric esters, probably via ion pair return.[13,14] This difference suggests that if linalyl trifluoroacetate generates an ion pair the lower nucleophilicity of trifluoroacetate, as compared with *p*-nitrobenzoate, ion precludes collapse to rearranged ester.[32]

Another marked difference between solvolyses of linalyl *p*-nitrobenzoate and the corresponding trifluoroacetate or phosphate is that the latter reactions give racemic linalool from chiral substrate even though (*R*)-α-terpineol is formed (Table VI and ref 8b). Solvolysis of linalyl *p*-nitrobenzoate gives linalool with approximately 20% retention of configuration.[13]

Rittersdorf and Cramer postulated π-participation in the spontaneous conversion of (*R*)-linalyl phosphate into (*R*)-α-terpineol.[8b] The stereochemical control is not complete because there is some loss of optical activity in α-terpineol formed in hydrolysis of this and other esters, depending upon the leaving group. Retention of optical activity follows decreasing stability of the leaving anion and percentage retentions are 90, 62, and 40 for *p*-nitrobenzoate, phosphate, and trifluoroacetate, respectively, neglecting differences in reaction conditions (Table VI and ref 8b and 13).

Acid-catalyzed oxygen exchange of chiral alcohols is typically accompanied by racemization,[33] and if strongly electon-releasing groups stabilize a carbocation the two processes have the same rate.[33c,34] A tertiary allylic car-

(27) Reversible interconversions of linalool into geraniol[11] leads to loss of optical activity and oxygen exchange, but it is too slow to be a major contributor to oxygen exchange under our initial conditions.

(28) Hannack, M. "Conformation Theory"; Academic Press: New York, 1965; p 31.

(29) Bunton, C. A.; Hadwick, T. *J. Chem. Soc.* **1958**, 3248.

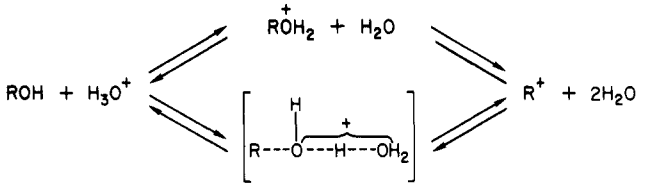
(30) The first-order rate constant for spontaneous hydrolysis of methyl trifluoroacetate in dioxane–water (70:30 v/v) at 25 °C is ca. 10^{-4} s^{-1}.[29] Comparison of this rate constant with those in Table II suggests that there is an appreciable contribution of mechanism $B_{AC}2$ in hydrolyses of geranyl and neryl trifluoroacetate. It is not known whether this mechanism contributes to hydrolysis of geranyl *p*-nitrobenzoate.[13]

(31) Only initial rates of hydrolysis of linalyl chloride were followed because of the presence of less reactive impurities.

(32) Reactions of the *p*-nitrobenzoates[13] were followed at higher temperatures (50–100 °C) than those used here or with the phosphates,[8b] but there is no evidence that high temperatures favor ion pair return.

(33) (a) Grunwald, E.; Heller, A.; Klein, F. S. *J. Chem. Soc.* **1957**, 2604. (b) Bunton, C. A.; Llewellyn, D. R. *Ibid.* **1957**, 3402. (c) Bunton, C. A.; Llewellyn, D. R.; Wilson, I. *Ibid.* **1958**, 4747.

Scheme III



bocation should therefore only maintain its stereochemical identity by virtue of π-participation of the 6,7-double bond in the linalyl carbocation. There is a major difference between reactions of linalool and its esters in that the esters give linalool which is largely or completely, racemic,[8b,13] whereas activity is not lost in oxygen exchange of the alcohol. This difference does not seem to be related to solvent composition because the reaction of linalyl phosphate was in water[8b] and those of linalool on the *p*-nitrobenzoate[13] or trifluoroacetate were in mixed solvents (Tables II and IX). The difference is therefore probably related to differences in the leaving group, which, for the esters is an anion, but for the alcohol is formally a water molecule.

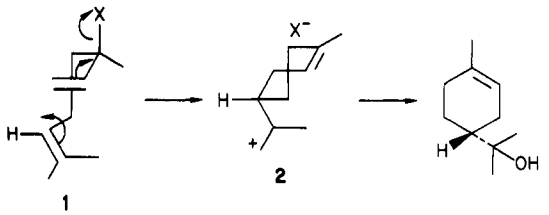
Acid heterolysis of alcohols can be written as involving a preequilibrium proton transfer, followed by spontaneous loss of a carbocation from the oxonium ion,[35] and this second step is akin to the ionization step of an S_N1 solvolysis. But the steps are concerted if the carbocation is relatively stable,[36,37] and Ritchie has postulated this situation for many alcohol heterolyses[36] (Scheme III).

Ionization of a neutral substrate can generate an ion pair directly, but acid-catalyzed alcohol heterolysis cannot, and the latter reaction can be regarded as an S_E2 reaction on oxygen, akin to acid hydrolyses of orthoesters and similarly activated substrates. Therefore there could be mechanistic differences between these reactions and S_N solvolyses.

The loss of optical activity in linalool derived from hydrolyses of the esters suggests that attack of water at the tertiary carbon 3 occurs later than attack at carbon 7, which gives α-terpineol. The leaving, or other, anion could protect carbon 3 from attack by water, and $LiClO_4$ apparently protects carbon 3 in solvolysis of linalyl trifluoroacetate, because it favors formation of α-terpineol, but it also increases its racemization (Table VI). This effect of $LiClO_4$ appears to be due to specific interactions that increase the lifetime of the carbocation.[38] If the salt had a nonspecific effect, e.g., if it merely decreased water reactivity, there is no reason why it should favor formation of α-terpineol over linalool. There is also the possibility that products, and stereochemistry, are controlled by initial state conformations, but it is then hard to explain retention of configuration in reactions of linalool and its *p*-nitrobenzoate or the effect of $LiClO_4$.

Following Arigoni and co-workers[39] we show the transformation of linalool or its esters into α-terpineol as in Scheme IV. Conversion of neryl into α-terpinyl derivatives also occurs via a similar anti conformation.[21a]

Scheme IV



The initial state is written as 1, although it will be an ensemble of conformations. The initial state extended conformations may very well give allylically stabilized, extended, carbocations which could go forward to geraniol, for example.[12,14] Alternatively the lifetime of the carbocation could be long enough to allow conformational interconversion of carbocation 2 with partial loss of stereochemical control or its conversion into an extended carbocation. The carbocation 2 is written as a classical structure, but it is more reasonable to assume that the positive charge will be delocalized; see, however, ref 21 and 22. Winstein, Valkanas, and Wilcox have pointed out that there could be a balance between the contributions of various "terpinyl" carbocations which differ in conformation and configuration, although there is predominant retention of configuration. The observation that neryl substrates give large amounts of cyclic products, whereas geranyl substrates give largely acyclic products,[8-21] shows that rotational interconversion of the delocalized carbocations is slow. There is, however, some rearrangement to cyclic products in reactions of geranyl substrates which seems to be related to the lifetime of the carbocation.

Oxygen exchange of linalool occurs without racemization, and its stereospecific conversion into α-terpineol requires that the "remote" 6,7-double bond controls conformation of the forming carbocation long enough for H_2O to leave C3, exchange with solvent water, and attack C3 with retention of configuration.[39] Protonation of the hydroxyl group is probably concerted with C–O bond breaking and therefore with electronic delocalization from the 6,7-double bond, and microscopic reversibility requires that (base-catalyzed)[40] attack of water upon C3 of the carbocation will be concerted with the electronic motion. As for reactions of the esters, acid-catalyzed conversion of linalool into geraniol (Table IX) may involve reaction in an extended conformation.

Over a wide range of conditions the rate sequence for reactions of esters, chlorides and 2,4-dinitrophenyl ethers, is linalyl > neryl ~ geranyl. The differences in reactivities are larger in the less polar solvents,[8b,9,13-15] e.g., there is a factor of ca. 10^2 for acetolysis of the ethers[14] and less than an order of magnitude for hydrolyses of the chlorides or trifluoroacetates[41] (Tables I and II).

Although oxygen exchange of linalool is faster than its rearrangement the overall heterolysis is only slightly faster than reactions of nerol and geraniol under the same conditions (Table VIII–IX). The difference in behavior of the alcohols and the other derivatives could arise from two factors: (i) Affinity of the hydroxyl group toward H_3O^+ may be greater in nerol or geraniol than in linalool.[42] But bulky alkyl groups do not markedly decrease the basicity of primary amines,[43] so steric effects should also be small

(34) Because of differences in experimental conditions we cannot compare our current results with the earlier data, but qualitatively the reactivities of nerol and geraniol in dilute acid are between those of 1-phenylethanol[33a] and (*p*-methoxyphenyl)phenylmethanol.[33c]

(35) Lowry, T. H.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry", 2nd ed.; Harper and Row: New York, 1981; p 373.

(36) Ritchie, C. D.; Wright, D. J.; Huang, D.-S.; Kamego, A. A. *J. Am. Chem. Soc.* **1975**, *97*, 1163.

(37) Bunton, C. A.; Davoudzadeh, F.; Watts, W. E. *J. Am. Chem. Soc.* **1981**, *103*, 3855.

(38) Ride, P. H.; Wyatt, P. A. H.; Zochowski, Z. M. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1188. Bunton, C. A.; Huang, S. K. *J. Am. Chem. Soc.* **1974**, *96*, 515.

(39) Godtfredsen, S.; Obrecht, J. P.; Arigoni, D. *Chimia* **1977**, *31*, 62.

(40) The base is water in our experiments.

(41) The relative reactivities of the trifluoroacetates (Table II) are affected by probable incursion of mechanism $B_{Ac}2$ in hydrolysis of the primary allylic derivatives.

(42) The appropriate property would be basicity only if the proton is fully transferred in the transition state.

(43) Hall, H. K. *J. Am. Chem. Soc.* **1957**, *79*, 5441.

on alcohol basicity. (ii) If proton transfer is concerted with C–O bond breaking, electron-releasing substituents will be less effective than in spontaneous ionization of nonionic substrates, and this seems to be the situation here. In addition, the effects of electron donation should become less important with increasing solvent polarity and nucleophilicity.

An additional question is that of the timing of departure of the leaving group and attack of water. Nucleophilic solvent participation has been postulated in S_N1 solvolyses of *tert*-butyl compounds.[26b,44] Solvolyses of linalyl esters give linalool which is racemized or of retained configuration, so that water attack on C3 is not concerted with bond-breaking (Table VI and ref 8b and 13). However, attack upon C7, giving α-terpineol, from linalyl or neryl derivatives, does not necessarily have to follow loss of the leaving group.

Although participation of the remote, 6,7-double bond controls conversion of neryl into α-terpinyl derivatives, it is difficult to know whether it is always involved in formation of the transition state.[8,9,11-15,21,22] Overall rate effects are small, probably because of conformational effects on formation of a "folded", cisoid transition state.[14] In addition the kinetic role of π-participation may depend upon the structure of the substrate, for example, on the ease of departure of the leaving group, and it may be easier for a small neryl group than a large farnesyl group to take up a cisoid conformation.[14,21,22] However, the assumption that the initial ionization of neryl derivatives is not assisted by π-participation requires that conformational interconversion of the carbocation must be much faster than its capture by nucleophiles, despite the unfavorable conformational change.[14] The lifetime of the carbocation could be relatively long in apolar solvents, but not in solvents of high water content,[45] and it is hard to explain retention of configuration in oxygen exchange of linalool except in terms of π-participation.

Acknowledgment. This work was supported by the National Science Foundation (Chemical Dynamics Program and International Programs) and by the Departmento de Investigacion y Bibliotecas (Universidad de Chile), the Fondo Nacional de Ciencia y Technologia, and CONICYT.

Registry No. Linalyl chloride, 471-10-3; geranyl chloride, 5389-87-7; neryl chloride, 20536-36-1; α-terpinyl chloride, 39864-10-3; geraniol, 106-24-1; nerol, 106-25-2; linalool, 78-70-6; (−)-linalool, 126-91-0; neryl trifluoroacetate, 101010-61-1; α-terpinyl trifluoroacetate, 28664-18-8; 1,2-dihydrolinalyl trifluoroacetate, 101010-62-2; 6,7-dihydrogeranyl chloride, 101010-63-3; linalyl trifluoroacetate, 28673-26-9; geranyl trifluoroacetate, 74367-67-2; 6,7-dihydroneryl chloride, 101010-64-4; (*R*)-linalyl trifluoroacetate, 101010-65-5.

(44) Kevill, D. N.; Kamil, W. A.; Anderson, S. W. *Tetrahedron Lett.* **1982**, *23*, 4635.

(45) Rappoport, Z. *Tetrahedron Lett.* **1979**, 2559. Richard, W. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1082**, *104*, 4689.

Benzobicyclo[4.1.0]hepta-2,4,6-trienes

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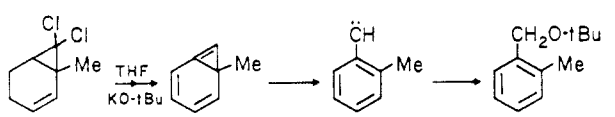
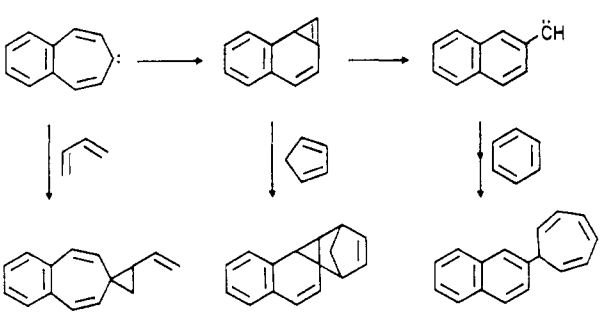
Irradiation of the naphthyldiazomethanes matrix isolated in argon at 15 K gives in each case the benzobicyclo[4.1.0]hepta-2,4,6-triene. The photochemistry of the naphthyldiazomethanes thus contrasts sharply with that of phenyldiazomethane, which gives 1,2,4,6-cycloheptatetraene. Flash vacuum thermolysis of the naphthyldiazomethanes followed by matrix isolation of the pyrolyzate produces a common product, tentatively identified as 4,5-benzocyclohepta-1,2,4,6-tetraene.

Vander Stouw and Shechter postulated a bicyclo[4.1.0]hepta-2,4,6-triene as the first intermediate in the rearrangement of arylmethylenes in 1964.[1,2] The firmly established cyclization of vinylmethylenes to cyclopropenes provided precedence for such a mechanism.[3] Billups generated 1-methylbicyclo[4.1.0]hepta-2,4,6-triene in solution.[4] The triene acts as a source of arylcarbene, but



Scheme I



no role in the interconversion of arylcarbenes was demonstrated. Our thermal and photochemical studies of phenylmethylene failed to provide evidence for the triene intermediate and suggested that ring expansion is a direct process.[5]

(1) Vander Stouw, G. G. Ph.D. Dissertation, The Ohio State University, Columbus, OH, 1964. Vander Stouw, G. G.; Kraska, A. R.; Shechter, H. *J. Am. Chem. Soc.* **1972**, *94*, 1655-1661.

(2) (a) Jones, W. M.; Brinker, U. H. In "Pericyclic Reactions"; Marchand, A. P., Lehr, R. E., Eds.; Academic Press: New York, 1977; Vol. 1, Chapter 3. (b) Jones, W. M. In "Rearrangements in Ground and Excited States"; deMayo, P., Ed.; Academic Press: New York, 1980; Vol. 1, Chapter 3. (c) Wentrup, C. In "Reactive Intermediates"; Abramovitch, R. A., Ed.; Plenum Press: New York, 1980; Vol. 1, Chapter 4.

(3) Closs, G. L.; Closs, L. E. *J. Am. Chem. Soc.* **1963**, *85*, 99-104 and references cited therein.

(4) Billups, W. E.; Reed, L. E.; Casserly, E. W.; Lin, L. P. *J. Org. Chem.* **1981**, *46*, 1326-1333.

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