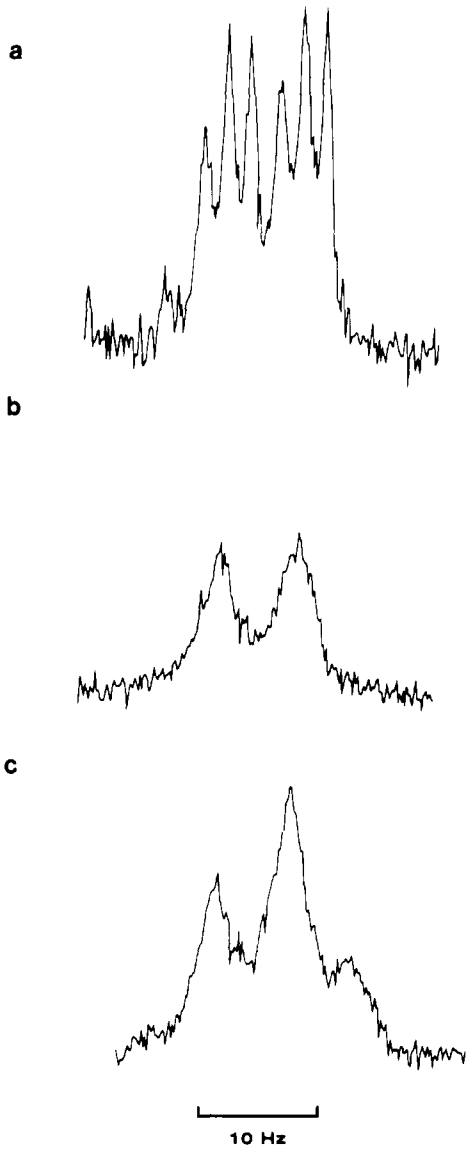
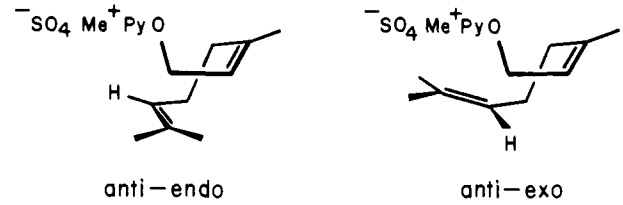


Figure 1. ^1H NMR spectra for H_b in [2-^{2}H]**3**-(3′-oxobutyl)-4,4-dimethylbutyrolactone] ([2-^{2}H]**7**) recorded in benzene-d_6 at 300 MHz. (a) [2-^{2}H]**7** from [3-^{2}H]**4**-OH obtained during solvolysis of (*S*)-[1′-^{2}H]**1**-OPy$^+$MeSO$_4^-$; (b) same as (a) with 7.2 equiv of (*S*)-2,2,2-trifluoro-1-(9′-anthryl)ethanol added; (c) same as (a) with 1.5 equiv of [2-^{2}H]**7** obtained from (*R*,*S*)-[1-^{2}H]**1**-OH and 11.2 equiv of (*S*)-2,2,2-trifluoro-1-(9′-anthryl)ethanol added.

pattern shown in Figure 1c, formed from overlapping doublets (J = 8 Hz) with the low field pattern being more intense. Similar behavior was seen for H_a. According to the assignments presented in Table I, the deuteron in [2-^{2}H]**7** is cis to H_c when C(3) is *S* and trans when C(3) is *R*. These experiments clearly establish that [2-^{2}H]**7** obtained from (*S*)-[1-^{2}H]**1**-OH is a mixture of only the 2*S*,3*R* and 2*S*,3*S* diastereomers.[24] Labeled α-terpineol derived from (*S*)-[1′-^{2}H]**1**-OPy$^+$MeSO$_4^-$ must, therefore, consist of only the 3*R*,4*R* and 3*R*,4*S* stereoisomers. The obvious conclusion is that cyclization is stereospecific at C(1) and proceeds with inversion of configuration.

It follows that the fraction of **1**-OPy$^+$MeSO$_4^-$ which cyclizes to α-terpineol must do so from a conformation where the remote double bond is positioned at the backside of C(1). Two limiting orientations which accomodate this restriction are shown below. Although we cannot distinguish between the anti-endo and anti-exo modes, the topologically related linalyl system is known to cyclize preferentially from an anti-endo conformation,[4] and a similar preference is expected for its allylic isomer. The stereoselectivity



we observed at C(1) for the direct process is measurably higher than the preference reported for the anti-endo mode in the allylic displacement. The difference might indicate that allylic cyclization can also occur by competing anti-exo or syn modes. The former possibility cannot be detected by the technique we employed, and the latter is precluded for a direct displacement. Linalyl *p*-nitrobenzoate was, however, used to study the allylic displacement,[4] and loss of stereocontrol could have resulted from internal return of the anionic leaving group.

As mentioned earlier, a concerted mechanism offers an attractive rationale for the stereochemistry of direct and allylic displacements. It must be emphasized, however, that while a concerted electrophilic cyclization requires stereospecificity, the converse—that stereospecificity establishes concertedness—does not hold. A stepwise process where cyclization is faster than reorientation of the side chain is also consistent with the stereochemistry of the electrophilic cyclizations. This question is addressed in the following communication.

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Registry No. **1**-OPy$^+$MeSO$_4^-$, 80387-02-6; α-terpineol, 98-55-5; (3*R*,4*R*)-[3-^{2}H]-**4**, 80375-27-5; (3*R*,4*S*)-[3-^{2}H]-**4**, 80408-85-1; (2*S*,3*R*)-[2-^{2}H]-**7**, 80375-28-6; (2*S*,3*S*)-[2-^{2}H]-**7**, 80408-86-2; (*R*)-**7**, 38746-47-3; (*S*)-**7**, 80408-87-3; ((*S*)-[1′-^{2}H]**1**-OPy$^+$MeSO$_4^-$), 80387-04-8.

(24) We saw no peaks for the 2*R*,3*R* and 2*R*,3*S* stereoisomers, even at high spectrum amplitudes, and conservatively estimate that they constituted less than 5% of the mixture.

Model Studies of Terpene Biosynthesis. A Stepwise Mechanism for Cyclization of Nerol to α-Terpineol

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Electrophilic alkylations of remote double bonds by allylic moieties are important carbon–carbon bond forming reactions in terpene metabolism and related biomimetic olefin cyclizations.[1-4] The enzymatic and nonenzymatic reactions are both characterized by a high degree of stereoselectivity. Two explanations have evolved for this phenomenon.[5] One is the reactions are concerted. This is attractive since stereospecificity is a logical result of the synchronous changes in bonding that occur in concerted reactions. The other explanation is a nonconcerted process involving a series of conformationally rigid intermediates where topology is maintained between the initiation and termination steps.[2,3,5-10]

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Table I. First-Order Rate Constants for Solvolysis of Neryl and Geranyl Methanesulfonates[a]

reactant	solvent acetone/water (v/v)	T, °C	k, s^{-1}	k_{rel}	k_1/k_2
1a-OMs	9:1	0	$(3.2 \pm 0.05) \times 10^{-3}$		
	9:1	25	$(3.84 \pm 0.08) \times 10^{-2}$		
	9:1	60	0.67[b]	1	
2a-OMs	9:1	0	$(1.46 \pm 0.18) \times 10^{-3}$		2.2
	9:1	25	$(2.57 \pm 0.14) \times 10^{-2}$		1.5
	9:1	60	0.70[c]	1.04	
1b-OMs	9:1	35	$(4.14 \pm 0.06) \times 10^{-4}$		
	9:1	45	$(1.08 \pm 0.02) \times 10^{-3}$		
	9:1	60	4.2×10^{-3}[d]	6.3×10^{-3}	
2b-OMs	9:1	35	$(3.29 \pm 0.09) \times 10^{-4}$		1.3
	9:1	45	$(9.35 \pm 0.25) \times 10^{-4}$		1.2
	9:1	60	4.0×10^{-3}[e]	6.0×10^{-3}	
1c-OMs	2:3	60	$(1.04 \pm 0.04) \times 10^{-2}$		
	1:1	60	$(4.18 \pm 0.31) \times 10^{-3}$		
	9:1	60	2.6×10^{-5}[f]	3.9×10^{-5}	
2c-OMs	2:3	60	$(7.31 \pm 0.39) \times 10^{-4}$		14.2
	1:1	60	$(2.90 \pm 0.07) \times 10^{-4}$		14.4
	9:1	60	1.6×10^{-6}[h]	2.4×10^{-6}	
1d-OMs	2:3	60	$(1.78 \pm 0.05) \times 10^{-3}$		
	1:1	60	$(6.97 \pm 0.19) \times 10^{-4}$		
	9:1	60	3.7×10^{-6}[g]	5.5×10^{-6}	
2d-OMs	2:3	60	$(1.19 \pm 0.32) \times 10^{-4}$		15.0
	1:1	60	$(4.78 \pm 0.45) \times 10^{-5}$		14.6
	9:1	60	3.0×10^{-7}[h]	4.5×10^{-7}	

[a] Measured by the conductance method and analyzed by curve fitting with the nonlinear least-squares procedure of Powell and MacDonald. Powell, D. R.; MacDonald, J. R. *Comput. J.* 1977, *15*, 148–158. [b] Extrapolated from lower temperatures, $\Delta H^{\ddagger} = 15.5 \pm 0.1$ kcal/mol, $\Delta S^{\ddagger} = -13 \pm 1$ eu. [c] Extrapolated from lower temperature, $\Delta H^{\ddagger} = 18.0 \pm 0.5$ kcal/mol, $\Delta S^{\ddagger} = -5 \pm 2$ eu. [d] Extrapolated from lower temperatures, $\Delta H^{\ddagger} = 18.1 \pm 0.5$ kcal/mol, $\Delta S^{\ddagger} = -15 \pm 2$ eu. [e] Extrapolated from lower temperatures, $\Delta H^{\ddagger} = 19.7 \pm 0.6$ kcal/mol, $\Delta S^{\ddagger} = -11 \pm 3$ eu. [f] Extrapolated from 2:3 and 1:1 acetone/water; $m = 0.68$. [g] Extrapolated from 2:3 and 1:1 acetone/water; $m = 0.70$. [h] Reference 6.

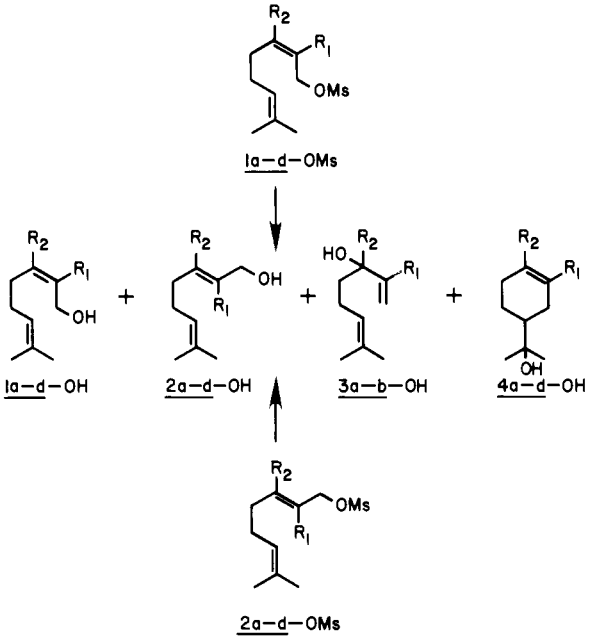
The electrophilic cyclizations of nerol (**1a**-OH) and linalool (**3a**-OH), or appropriate derivatives, to α-terpineol (**4a**-OH) are among the simplest examples of biosynthetic–biomimetic alkylations. These reactions have been studied extensively, and several lines of evidence have been interpreted in favor of a concerted mechanism. These include high stereoselectivity for the cyclization of linalool to α-terpineol,[1,11,12] slightly faster rates for solvolysis of neryl derivatives vs. their geranyl counterparts,[1,12–15] and a small secondary kinetic isotope effect for the olefinic proton at C(6) of nerol.[16] In opposition, Brody and Gutsche[10] reported that the secondary kinetic isotope effect at C(1) during solvolysis of (*Z*,*E*)-farnesyl phosphate indicated the reaction occurred without participation by the remote C(6)–C(7) double bond. Thus, results of kinetic isotope experiments are contradictory, and stereochemical studies or comparisons of solvolytic rates for neryl and geranyl derivatives, while suggestive of participation, are not definitive. It occurred to us that it would be possible to distinguish between concerted and nonconcerted processes by replacing hydrogens around the periphery of the C(2)–C(3) double bond with substituents which destabilize the developing allylic cation. If cyclization is concerted, the neryl–geranyl rate differential and the proportion of α-terpinyl products from the neryl precursors will increase with increasing electron demand, whereas little amplification is expected for nonconcerted processes. In this communication, we present kinetic and product studies for a series of neryl and geranyl derivatives which permit us to evaluate the timing of ionization and cyclization.

Table II. Products from Solvolysis of Neryl and Geranyl Methanesulfonates[a]

reactant	solvent acetone/water (v/v)	T, °C	1,[b] %	2,[b] %	3,[b] %	4,[b] %	4/(1 + 2 + 3)
1a-OMs	9:1	25	16	4	35	45	0.8
2a-OMs	9:1	25	3	27	53	17	
1b-OMs	9:1	35	17	3	35	45	0.8
2b-OMs	9:1	35	2	22	65	11	
1c-OMs	1:1	60	5			95	19
2c-OMs	1:1	60		100			
1d-OMs	1:1	60	5			95	19
2d-OMs	1:1	60		100			

[a] 2,6-Lutidine was added to neutralize acid generated during solvolysis. [b] Determined by GLPC on a 500-ft × 0.03-in. WCOT column; normalized to 100%, material balance >95%.

First-order rate constants for solvolysis of neryl methanesulfonate (**1a**-OMs), geranyl methanesulfonate (**2a**-OMs), and the three sets of fluorinated derivatives[17,18] shown below are presented in Table I. The experimental values were extrapolated



a, $R_1 = H$; $R_2 = CH_3$
b, $R_1 = F$; $R_2 = CH_3$
c, $R_1 = H$; $R_2 = CHF_2$
d, $R_1 = H$; $R_2 = CF_3$

to 60 °C and 9:1 acetone/water for comparisons of the effects of the substituents on the reactivities of the methanesulfonates. As expected, the rates of neryl and geranyl derivatives decreased progressively as peripheral hydrogens on the allylic moiety were replaced by fluorine, with a maximal depression of 10^7 for R_2 = trifluoromethyl. Replacement of the hydrogen at C(2) by fluorine decreased the rates for *both* double bond isomers by 160-fold, whereas substitution of the C(3) methyl by difluoromethyl or trifluoromethyl resulted in *larger* decreases for the geranyl derivatives in comparison with their neryl counterparts. The discontinuity in kinetic behavior is most easily seen by comparing

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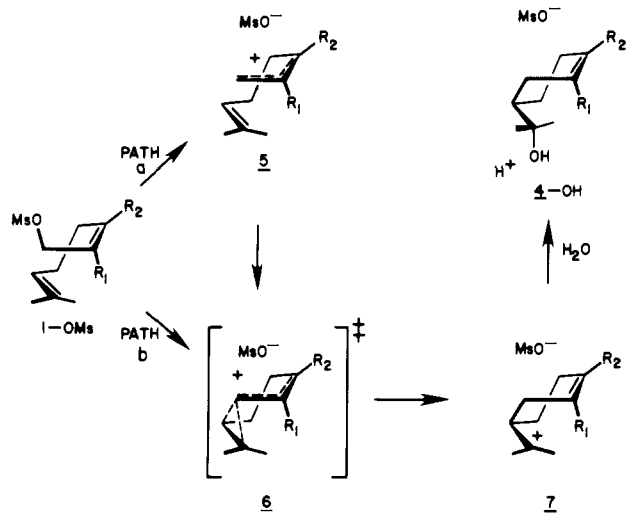
Scheme I. Mechanisms for Cyclization of 1a–d-OMs



neryl/geranyl rate ratios (k_1/k_2), which increased abruptly from 1.2–2.2 for the parent compounds and the 2-fluoro derivatives to 14.2–15.0 for the difluoromethyl and trifluoromethyl compounds.

A similar discontinuity is seen in the product distributions for methanesulfonates **1a–d-OMs** listed in Table II.[19] The parent methanesulfonates and the 2-fluoro derivatives gave very similar distributions of allylic and cyclic isomers. Product distributions for the difluoromethyl and trifluoromethyl compounds were, however, markedly different. The most striking trend is the abrupt increase in the ratio of cyclic (**4**) to noncyclic (**1 + 2 + 3**) alcohols from 0.8 to 19 for the neryl derivatives.

The discontinuities in neryl–geranyl rate ratios and in cyclic–acyclic product ratios for the neryl series between the 2-fluoro and the 3-difluoromethyl derivatives signal a change in mechanism which we interpret as the onset of π participation by the remote double bond. Our observations are similar to those reported in the 7-norbornenyl system where π participation also begins abruptly as a function of increasing electron demand.[20] Since the parent neryl system is rather far removed from the break point ($1.6 \times 10^2 < k_{1a}/k_{break} < 2.6 \times 10^4$), a neryl–geranyl rate ratio (k_{1a}/k_{2a}) of greater than unity in the parent system is not the result of delicately balanced competing assisted and nonassisted pathways but rather is caused by more subtle conformational effects. The assisted pathway does, however, become dominate for the less reactive difluoromethyl and trifluoromethyl derivatives. Stepwise (path a) and concerted (path b) mechanisms are presented in Scheme I. The driving force for both cyclizations is formation of a relatively strain-free cyclohexenyl ring with concomitant loss of the C(6)–C(7) double bond.

Although the conformation of the side chain exerts little influence on the reactivity of the allylic moiety, it is important with regard to which products are obtained. Since the cyclization is stereospecific and neryl cation **5** is an intermediate, that portion of **1**-OMs which cyclizes must adopt a folded conformation (the anti-endo orientation[21] is shown in Scheme I) before ionization. In view of the high proportion of α-terpineol formed during solvolysis, neryl systems must favor a folded conformation in polar solvents. Reaction from an extended conformation is also possible and may, in fact, account for most of the acyclic products.[22] While we cannot determine precisely how **5** partitions among various reaction pathways when in a folded orientation, cyclization is at least 5 times faster than reaction with water during solvolysis of *N*-methyl-4-(neryloxy)pyridinium methyl sulfate[23] in aqueous sodium bicarbonate. Thus, the intramolecular alkylation reaction is considerably faster than conformational reorientation of the side chain and reaction of the allylic cation with water.

Since ionization and cyclization are distinct steps during solvolysis of nerol and its derivatives, it follows that they are also distinct steps during solvolysis of the slightly more reactive linalyl system. Thus, the direct cyclization of nerol and the allylic cyclization of linalool merge into a set of mechanistically related reactions sharing a common allylic cationic intermediate following the initial ionization step.

Alkylations that are stepwise *and* stereospecific require a delicate balance of conformational control in the reactant(s) and reactivity in the initial cationic intermediate. These points are illustrated by three examples. If the 3,3-dialkylallylic cation typical of terpenes is sufficiently destabilized, for example, by fluorinated substituents, the reaction becomes concerted. If, however, the cation is made too stable by additional alkyl substituents at C(1) and C(3), the reaction is stepwise, but stereorandom.[24] Finally, the intermolecular alkylation of dimethylallyl acetate by dimethylallyl cation, a system with no restraints on the orientation of the reactants, is stereorandom.[25] One should, therefore, anticipate a spectrum of mechanisms for biomimetic and enzymatic olefin alkylation reactions which depend on the nature of the electrophile and the double bond.

Acknowledgment. This work was supported by the Institute of General Medical Sciences of the National Institutes of Health, GM 21328.

Registry No. **1a**-OH, 106-25-2; **1a**-OMs, 80359-44-0; **1b**-OH, 80359-45-1; **1b**-OMs, 80359-46-2; **1c**-OH, 80359-47-3; **1c**-OMs, 80359-48-4; **1d**-OH, 80375-23-1; **1d**-OMs, 80359-49-5; **2a**-OH, 106-24-1; **2a**-OMs, 78130-96-8; **2b**-OH, 80359-50-8; **2b**-OMs, 80359-51-9; **2c**-OH, 76480-98-3; **2c**-OMs, 80359-52-0; **2d**-OH, 76481-03-3; **2d**-OMs, 80359-53-1; **3a**-OH, 78-70-6; **3b**-OH, 64031-55-6; **4a**-OH, 98-55-5; **4b**-OH, 80359-54-2; **4c**-OH, 80359-55-3; **4d**-OH, 80359-56-4.

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Silylene Rearrangements in the Reactions of Recoiling Silicon Atoms with Trimethylsilane

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Atoms created in nuclear transformations are usually born as high-energy cations that have broken free from the molecules in which their parent atoms were covalently bonded.[1] Before a recoiling atom can incorporate itself by its reactions in a new molecule, it must lose much of its initial kinetic energy in a series of collisions in which electron exchange and electronic transitions can also occur.[2] Thus the interpretation of the results of hot-atom experiments can be complicated by the simultaneous presence of several different charge and electronic states of the reacting species.

The exploration of atom–molecule reactions above their threshold energies is a major task of hot-atom chemists, and where

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