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DEUTERIUM ISOTOPE EFFECTS IN CYCLIZATION OF MONOTERPENOIDS

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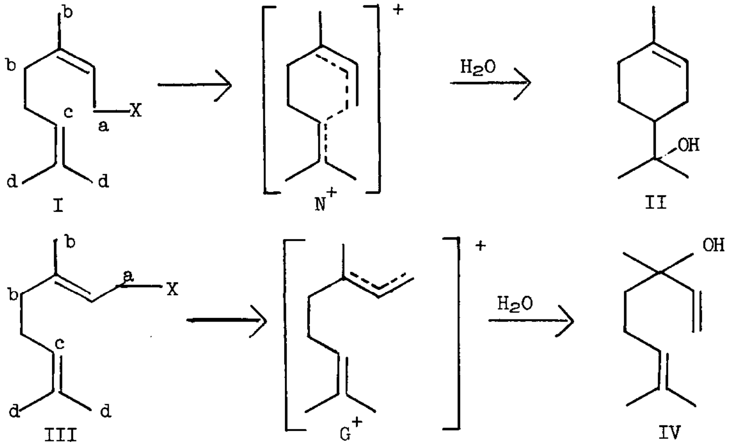
Neryl compounds (I) readily cyclize to terpinyl derivatives (e.g., II) via cationic intermediates, whereas the corresponding geranyl compounds (III) give open chain products (e.g. IV).[1-4]



I N^+ II

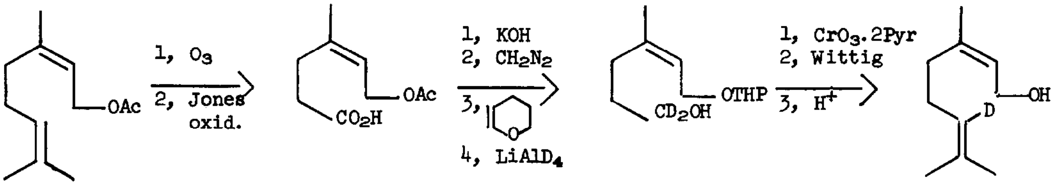
III G^+ IV

X = $-\overset{+}{O}H_2$, $-OPO_3H_2$, -Cl

The cations N^+ and G^+ do not interconvert rapidly and an important question is their nature and the mechanism of their formation, especially with regard to π-participation by the double bond in the initial ionization of (I).[3,5] The formation of terpinyl from neryl derivatives has been explained in terms of π-participation in the transition state, but the rates of solvolysis of the geranyl and neryl phosphates and their dihydro derivatives are similar.[2,3] Ionization of both isomers can be assisted by allylic participation, but from the geometry of N^+ this participation is at the expense of π-participation from the isopropylidene double bond. Also the acid dissociation constants of phosphate monoesters of (I) and (III) may differ, and at pH ≈ 1.2 (a value close to pK_1) the reactants could be mixtures of acids and anions.

The π-participation could occur during formation of the transition state for ionization or during the subsequent collapse of a carbonium ion to products and then affect products not rates, but deuteration can provide evidence for π-participation which involves rehybridization of C-c from sp^2 towards sp^3 in the transition state, as shown in the scheme. (For discussion of deuterium kinetic isotope effects see ref. 6.)

To avoid complications due to acid dissociation we used the chlorides prepared by Stork's method,[7] or mesyl chloride in pyridine-pentane at -5°. Both methods gave samples with identical NMR spectra and the same rate constants. The deuteroalcohols were prepared by the following methods: a-d_2, reduction of methyl nerylate or geranylate with $LiAlD_4$; b-d_5, from methyl nerylate and geranylate prepared from d_5-methylheptenone by a Wittig reaction; d-d_6 by a method similar to that of Thomas and coworkers;[8] and c-d by the reactions (shown below for neryl chloride):



All the rate constants were measured conductimetrically in acetone: water 70:30 v/v at 25.0° and the first order rate constants were calculated using a linear least-squares program with correlation coefficients > 0.999. The kinetic isotope effects (K.I.E.) per deuterium atom are in Table I, based on 2-4 runs per compound.

Table I

Kinetic Isotope Effects in Chloride Hydrolyses[a]

Deuterium Substituent	K.I.E. %[b] Geranyl	Neryl
a $-d_2$	11.4	10.4
b $-d_5$	6.2	5.9
c -d	0.3	-7.5
d $-d_6$	1.1	2.2

(a) At 25.0° in acetone: water 70:30 v/v. For neryl chloride $k = 3.449 \times 10^{-4}$ and for geranyl chloride $k = 1.280 \times 10^{-4}\ sec^{-1}$. (b) per deuterium atom.

Deuteration at positions a and b of neryl and geranyl chlorides gives K.I.E. values similar respectively to those found for S_N1 solvolyses of α-methyl allyl compounds,[9] and suggest that there is allylic delocalization and rehybridization at the reaction center. (For sp^3 to sp^2 rehybridization K.I.E. ≈ 18%). The K.I.E. values for geranyl chloride deuterated in the isopropylidene group (positions c and d) are small and consistent with the assumption that the conformation of this isomer does not allow π-participation,[2-4] but the negative K.I.E. for neryl chloride on position c shows that here ionization is concerted with partial rehybridization from sp^2 to sp^3 and this build up of partial positive charge leads to a small K.I.E. for deuteration at position d. These K.I.E. suggest that delocalization of the forming positive charge over the conjugated allylic system is important in both chlorides and that there is π-participation in the ionization of neryl chloride, but less than that corresponding to complete rehybridization in the transition state.

The products (Table II) are similar to those found for phosphate ester solvolysis,[2-4] but either there is partial interconversion of N^+ and G^+ or I and III can react in different conformations giving noninterconvertible carbonium ions of different conformations. The products change markedly when 3.5 M $LiClO_4$ is added (values in parentheses, Table II). Elimination increases and geranyl chloride gives a large amount of cyclic products. Perchlorate ion probably forms an ion pair with G^+ and increases its lifetime so that it can be converted into N^+.

Table II

Major Solvolysis Products of the Chlorides[a]

	Neryl	Geranyl
open chain olefins	1 (10)	3 (50)
cyclic olefins	1 (29)	4 (29)
linalol	17 (1)	70
nerol	3	--
geraniol	--	16
α-terpineol	78 (58)	6 (19)

(a) Mole % products at 25° in acetone: water 70:30 v/v. The cyclic olefins were limonene and terpinolene and the major open chain olefin was myrcene.

The chlorides give more elimination and rearranged products than the phosphates, pyrophosphates and alcohols,[2,3] possibly because ion pair intermediates are more important in solvolyses of the chlorides in aqueous acetone than in reactions of the other compounds in water.

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