165° (0.03 mm) but pyrolized at 220° (0.25 mm) to a tar and a small amount or yellow gummy material that was carbonate-free in the ir.

Stirring a sample of this compound (15) in benzene with either acid ion exchange resin or sodium hydride for 18 hr gave no reaction (tlc and ir).

Addition of 1.00 g (2.47 mmol) of the adduct 15 to a suspension of benzene-washed sodium hydride in benzene (0.5 g), and refluxing the mixture for 6 hr, produced 0.137 g (17%) of a yellow dimeric adduct (28) after chromatography on silica gel plates in dichloromethane: mp 192–193°; uv max (95% C₂H₅OH) 225, 251, 290 (shoulder), 325, and 410 m μ ; ir (KBr) 1700, 1540, 1190, and 1094 cm⁻¹; nmr (CDCl₃) δ 0.97 (t, 6 H), 3.08 (q, 4 H), and 7.17 and 7.52 (two m, total 9.5 H).

Anal. Calcd for (C₂₂H₁₉NO₂)₂: C, 80.22; H, 5.81; N, 4.25. Found: C, 80.43; H, 5.83; N, 4.01.

Registry No.-1, 17691-75-7; 2, 2348-82-5; 3, 36623-54-8; 4, 26391-04-8; 5, 36623-56-0; 6, 36623-57-1; 7, 4231-26-9; 8, 4231-35-0; 9, 1785-65-5; 10, 36623-61-7; 11, 36674-94-9; 12, 36623-62-8; 13, 36623-63-9; 14, 36674-95-0; 15, 36623-64-0; 16, 36674-96-1; 17, 130-15-4; 19, 36623-65-1; 20, 36623-66-2; 21, 36623-67-3; 22, 36623-68-4; 23, 36623-69-5; **24**, 36623-70-8; **25**, 36623-71-9; **26**, 36674-97-2; 27, 36623-72-0; 28, 36674-98-3.

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Deamination of Nerylamine and Geranylamine¹

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The products of deamination of nervlamine and geranylamine in water and acetic acid have been compared with the products of hydrolysis of neryl and geranyl chlorides, phosphates, and pyrophosphates. Deamination of nervlamine gives less cyclic products than hydrolysis of the nervl compounds, and deamination of geranylamine gives a much lower ratio of linalyl to geranyl products than do the corresponding hydrolyses. Alcohols as well as acetates are formed in the deamination in glacial acetic acid, and the product compositions suggest that ion pairs of the diazonium ions with hydroxide or acetate ions are reaction intermediates and that the substitution products can be formed either by ion-pair collapse or attack of an external nucleophile. Differences between the olefinic products of deamination and hydrolysis can also be explained in these terms.

The solvolysis of derivatives of nerol (I, X = OH)and geraniol (II, X = OH) have been studied extensively as models for cyclization and rearrangement in terpene biosynthesis. Neryl derivatives give largely cyclic products, e.g., α -terpineol (III) and olefins



related to it, whereas geranyl derivatives give largely linalool (IV) and olefins related to it. $^{2-5}$ These results



are readily understandable in that the configuration of nerol allows a carbonium ion derived from it or its derivatives to take up a conformation which favors cyclization, whereas a carbonium ion derived from geraniol has to rotate about the 2,3 double bond before it can cyclize to terpineol.⁶ Phosphates,^{3,4} alcohols,⁴ and chlorides,⁹ have been used in these experiments, and the product compositions are relatively insensitive to the solvent composition or the nature of the leaving group.

Carbonium ions are often invoked as intermediates in deaminations by nitrous acid which can be regarded as SN1 reactions of an unstable diazonium ion, but the products of such reactions are often very different from those of solvolyses, and a number of workers have speculated on the nature of the intermediates. $^{10-12}$ Deaminations of neryl and geranylamine (I, II, X = NH₂) were therefore examined, because of the possibility that a major change in the leaving group would markedly change the products.

Experimental Section

Materials .- Nerol and geraniol were obtained from Fluka, Chemical Samples Co. or Columbia Organics. Their purities were tested by glc, and samples having >95% overall purity and <0.1% of the other geometrical isomer were used. Preparation of geranyl chloride by reaction of the alcohol with PCl₂ or SOCl₂ has been reported,¹³ but in our hands these methods gave mix-

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tures of chlorides. We therefore used Stork's method¹⁴ or, more often, a simpler variant of it, described here for neryl chloride. Nerol (65 mmol) was dissolved in dry pentane (250 ml) and freshly distilled mesyl chloride (130 mmol) was added slowly at -5° with stirring. Dried pyridine (130 mmol) in pentane (50 ml) was then added, and the stirred solution was allowed to come slowly to room temperature (4 hr). The pentane layer was washed with cold 5% HCl and then with saturated NaHCO₃ and was dried (MgSO₄). A colorless oil [bp 44–46° (0.5 mm), lit.¹⁴ bp 66–69° (0.4 mm)] was obtained in 40% yield using a shortpath distillation apparatus. A similar preparation of geranyl chloride on a 500-mmol scale gave geranyl chloride in 79% yield [bp 46–48° (0.5 mm), lit.¹⁴ bp 64–65° (0.04 mm)]. The ir spectra of these chlorides showed the absence of OH groups and characteristic broad absorptions at 1750 cm⁻¹ due to carbon–carbon double bond stretch.

The chemical shifts (60 MHz) of the alcohols and chlorides are given in Table I. The nmr spectra were determined using Varian

TABLE I CHEMICAL SHIFTS^a X = OHX = ClGroup $-CH_2X$ 4.08(4.14)4.00(4.02) $= CHCH_2X$ 5.42(5.42)5.41(5.41) $-CH_2CH_2$ 2,10(2,08)2.09(2.08) $Me_2C = CH$ 5.10(5.15)5.08(5.05) $CH_3C=CCH_2X$ 1.60(1.72)1.75(1.56) $(CH_3)_2C==C$ 1.72(1.72)1.58(1.68)

^a In ppm relative to TMS; the values for the geranyl derivatives are in parentheses. The boldface H' sindicate the protons examined.

A 60 or T 60 or Jeolco C-60 H nmr spectrometers. Solvolyses of these chlorides gave clean first-order kinetics for more than 3 half-lives.⁹

Attempts to prepare the amines by treating the chlorides with sodamide or with sodium azide, followed by reduction,15,16 gave mixtures. The amines were therefore prepared from freshly prepared samples of the chlorides via the phthalimides which have already been reported but without full details of their prepara-Geranyl chloride (390 mmol) was heated on a steam bath tion.17 with potassium phthalimide (450 mmol) in dry DMF (250 ml) for The amide product was recrystallized twice (MeOH) and 22 hr. geranylphthalimide, mp 60-61.5°, was obtained in 80% yield. Its nmr spectrum (60 MHz) showed aromatic protons (4) at 7.72 ppm, vinyl protons (2) at 5.25 and 5.02 ppm, and -CH₂NH protons (2) at 4.28 ppm. It was decomposed using 0.85 M hydrazine in refluxing ethanol (3 hr). The amine was extracted into hexane, and the solution was washed with solid NaHCO₈, and dried and distilled in a short-path apparatus [bp 49–52°, (0.25 mm), lit.¹⁶ 105° (19 mm)]. The overall yield was 20% largely because of losses in crystallization of the phthalimide.

The same method was used for nerylamine, starting with 100 mmol of the chloride. Neryl phthalimide had mp $59-60.5^{\circ}$, and the nmr spectrum (60 MHz) showed four aromatic protons at 7.70 ppm and two vinyl protons at 5.20 ppm. Nerylamine, prepared as already described, had bp $48-50^{\circ}$ (0.3 mm).

The phosphates and pyrophosphates of nerol and geraniol were prepared by Cramer's method,⁸ with some modifications. Nerol (30 mmol) was treated with trichloroacetonitrile (62.5 mmol) in dry CH₃CN (100 ml). Di(triethyl)ammonium phosphate (60 mmol) was added over 0.5 hr with stirring; after a further 4 hr the solvent was removed *invacuo* and the residual oil was dissolved in NH₃-EtOH. The white solid was filtered and washed with dry Me₂CO and then treated with cyclohexylamine (5 ml) in 70% aqueous MeOH (50 ml). Crystals of the dicyclohexylammonium phosphate separated on cooling and were washed with acetone and then with ether. The phosphate was recrystallized from water containing cyclohexylamine giving a 12% yield. The filtrate was treated with LiCl (100 mmol) giving the lithium salt of the pyrophosphate, which was purified by solution in water and precipitation with acetone in 12% yield.

Geranyl phosphate and pyrophosphate were prepared by this method. Hydrolysis of these esters using alkaline phosphatase from $E. \ coli$ (Worthington) gave alcohols which were pure by glc.

Deamination.—The amines were deaminated under four sets of conditions, on a 5-mmol scale using 30 mmol of NaNO₂: (i) in 0.1 M HCl (100 ml) with NaNO₂ at 23° with stirring for 1 hr; (ii) in glacial HOAc (50 ml) with NaNO₂ at 23° with stirring for 1.5 hr; (iii) in glacial HOAc (50 ml) and 1 M NaOAc with NaNO₂ added with stirring (the mixture was left for 18 hr at 23°); (iv) in 100 ml of aqueous 1 M HOAc and 1 M NaOAc, pH 4.7 with NaNO₂ at 23° with stirring for 15 hr.

The products were extracted with ether after neutralization of the reaction solution by adding it slowly to aqueous $NaHCO_3$.

Hydrolyses.—The phosphates and pyrophosphates (1 mmol) were allowed to hydrolyze in stirred water (50 ml) for 30 min. The pH was adjusted using dilute HCl. The solution was extracted with pentane, and the pentane solution was washed with a NaHCO₃ and then dried (MgSO₄). The solution was concentrated using a 2-ft Vigreux column. The same general procedure was used for hydrolysis of the chlorides.

Product Analyses.—The products were analyzed by glc using a Varian Aerograph 1200 with a flame ionization detector and a Disc integrator. Tests with synthetic mixtures of the products showed that the products were stable under the reaction conditions and were not lost in the isolation, and the response of the detector was corrected for the various products.

Three columns were used for the glc analyses: (i) $24 \text{ ft} \times {}^{1}/_{16} \text{ in.}$ 1.5% TCEP, 1.5% Carbowax-4000 at 95° for olefins and methyl ethers and 90–150° at 4°/min for alcohols; (ii) 24 ft $\times {}^{1}/_{16}$ in. 2% Carbowax-4000 at 90° for olefins and methyl ethers and 90– 140° at 2°/min for alcohols; (iii) 150 ft \times 0.01 in. Carbowax-4000 and 1.3–2.4 ml min⁻¹ flow rate of N₂. Chromosorb G (100– 120) and a flow rate of 50 ml min⁻¹ was used for the packed columns.

Results

Hydrolysis Products.—The products of hydrolyses of neryl and geranyl chloride in acetone-water are very similar to those for hydrolyses of the phosphates and pyrophosphates in dilute acid (Tables II and III

,	Fable II	
Solvolysis Prod	UCTS OF THE CHI	LORIDES ^a
	Neryl	Geranyl
Limonene	3	la
Terpinolene	$2\int^{(1)}$	∫ ^(⊈)
Myrcene		1
Other olefins	1^{b} (1^{b})	$1^{c} (3^{c})$
Linalool	20 (17)	81 (70)
Nerol	2(3)	
Geraniol		10(16)
α -Terpineol	72 (58)	7(6)
Total evelization	77 (63)	7(10)

° Mol% at 25° in acetone water 5:95 v/v; the values in parentheses are for acetone-water 70:30 v/v. ^b Myrcene and ocimene. ^c Largely ocimene.

	TABLE	III		
Hydrolysis of F	HOSPHATES	S AND PY	ROPHOSPI	HATES ^a
Product	$N P^b$	NPP^b	G₽¢	GPP^b
Acyclic olefins	Trace		1.5	Trace
Limonene	1.9	1.5		
Terpinolene	1.4	1.2		
Linalool	24.9	26.5	88.1	66.7
Nerol	2.9			0.3
Geraniol	Trace		9.8	5.3
α -Terpineol	69.0	70.2	0.6	20.7
Total cyclization	72.3	72.9	0.6	20.7
² At 25° in water. ^b	pH 2. °p	H 1.5.		

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and ref 3 and 4), although we used a higher pH for hydrolyses of the phosphates and pyrophosphates and aqueous organic solvents for hydrolysis of the chlorides. The chlorides give slightly more olefinic products than the phosphates and pyrophosphates, possibly because of differences in the solvents.

Deamination.—Although similar products are obtained in the deaminations as in the solvolyses (Tables II-V and ref 3 and 4), the compositions differ.

TABLE IV Deamination of Nerylamine^a

	Solvent			
Product	H₂O	HOAc ^b	HOAc	OAc HOAc ^d
Limonene	9.6	14.2	10.7	9.6
Linalyl acetate		7.1	6.3	1.7
Nerol	13.7	6.4	9.8	2.9
Neryl acetate		46.2	50.1	17.6
Geraniol	9.4	1.5	1.6	4.6
Geranyl acetate		5.6	4.5	14.9
α -Terpineol	32.5	2.8	2.5	33.9
α -Terpinyl acetate		12.8	10.9	3.2
Total cyclization	32.5	29.8	24.1	46.7

^a At 25.0°. ^b Glacial HOAc. ^c 1 M NaOAc in glacial HOAc. ^d 1 M NaOAc + 1 M HOAc in water at pH 4.7.

TABLE V			
DEAMINATION OF GEBANYLAMINI			

	Solvent			
Product	H_2O	$HOAc^{b}$	HOAc	OAc HOAc ^d
Acyclic olefins	4.0	2,9	7.2	5.1
Linalool	28.7	4.3	3.5	23.5
Linalyl acetate		9.7	8.6	2.8
Nerol	14.8	3.6	1.4	5.9
Neryl acetate	-	19.0	6.7	12.3
Geraniol	51.0	6.4	8.1	11.4
Geranyl acetate		52.9	64.2	37.9
α -Terpineol	0.6	0.3		0.7
α -Terpinyl acetate		0.6	Trace	Trace
Total cyclization	4.6	3.8	7.2	5.8

⁴ At 25.0°. ^b Glacial HOAc. ^c 1 M NaOAc in glacial HOAc. ^d 1 M NaOAc + 1 M HOAc in water at pH 4.7.

One notable difference is that limonene (V) was the only olefin found from nerylamine, whereas only acyclic olefins were obtained from geranylamine (these acyclic olefins were myrcene and ocimene, but the glc conditions used for these particular experiments did not separate them cleanly). In addition, more olefinic products are formed in deamination than in solvolysis. Other marked differences are that cyclization is less important in deamination than in solvolysis, and that nerol and geraniol are much more evident in deaminations than in solvolyses.

Discussion

Variation of Leaving Group.—The formation of cyclic products in SN1 reactions of neryl compounds has long been recognized,²⁻⁴ and kinetic deuterium isotope effects show that there is π participation by the isopropylidene group and allylic stabilization in transition state formation,⁹ as suggested from studies of the alcohol, phosphate, and pyrophosphate reactions. Only



allylic stabilization is important in SN1 reactions of geranyl chloride, and the carbonium ions generated in solvolysis undergo only limited interconversion.



Deamination of aliphatic amines gives products whose composition and stereochemistry are sufficiently different from those of solvolysis products to suggest differences in the carbonium ion intermediates in the two sets of reactions.¹⁰⁻¹² These differences are apparent in the reactions discussed here (Tables II-V). Cyclization is less for deamination than solvolysis, probably because π participation is kinetically important in the formation of the transition state from neryl chloride or phosphate whereas loss of nitrogen from a diazonium ion requires no assistance from a neighboring group, and there is no restriction on the conformation of the reacting nervlamine or the cationic intermediates derived from it. There is much less interconversion of the geometrically isomeric nervl and geranyl compounds in solvolyses (Tables II and III and ref 3 and 4) than in deamination (Tables IV and V). This greater interconversion can be ascribed to the high energy of the cationic intermediates found in deamination.¹⁰

Solvolysis also differs from deamination in that its major products are tertiary alcohols (linalool or α terpineol) or their derivatives, whereas deamination gives considerable amounts of the primary alcohols, suggesting that structural reorganization is relatively unimportant in the conversion of a diazonium ion into a carbonium ion and thence into products.

The formation of the acyclic olefins, myrcene and ocimene, by deamination of geranylamine and in solvolysis is readily understandable.^{2,3} However the differences in the olefins formed by deamination of nerylamine and solvolyses of neryl chloride and phosphates are striking because, whereas deamination gives almost wholly the cyclic olefin limonene (V), solvolysis gives approximately equal amounts of limonene (V) and terpinolene (VI).^{3,9} A rationalization of this behavior is that the counterion (e.g., acetate) selectively deprotonates the methyl group during decomposition of the diazonium ion, as shown in Scheme I for that part of the reaction which gives elimination. Removal of a proton by the counterion also accounts for the greater proportion of elimination in deamination than in solvolysis of the chlorides or phosphates. (similar mechanisms could be written for decomposition of a covalent diazoacetate, although an ion pair is a more probable intermediate). For solvolysis of the chloride we assume that loss of the proton from the

DEAMINATION OF NERVLAMINE AND GERANYLAMINE



methyl group is not assisted by the leaving group, so that the terpinyl cation (VII) can give either limonene (V) or terpinolene (VI).



The substitution products of deamination can be explained by invoking ion-paired intermediates.¹⁰⁻¹² The formation of both alcohols (ca. 15%) and acetates (ca. 85%) even for deamination in glacial acetic acid suggests the following reactions, assuming acetyl nitrite as the most important nitrosating agent (Scheme II).



For deamination in glacial acetic acid the ratio of acetate to alcohol in the products is affected little by addition of acetate ion, as predicted by Scheme II.

Deamination of nerylamine in aqueous acetate buffer (2 M, pH 4.7) gives an acetate to alcohol ratio of 3-6:1 for geranyl and neryl products, but one of *ca*. 0.1:1 for linally and terpinyl products. Both product ratios are greater than the molar ratio of 0.04:1 for acetate ion to water, as expected in view of the greater nucleo-

philicity of acetate ion, and these results suggest that the nitrosation gives largely a diazo compound which collapses internally *via* VIII to geranyl or neryl acetates (IX and X), but which is attacked by water or acetate ion from the bulk of the solvent to give acetate to alcohol ratios for linalool and α -terpineol which are close to the acetate ion to water ratio (Scheme III).



These results can be related to the changes in alcohol to acetate ratio in the deamination of benzyl-, diphenylmethyl-, and tritylamines in nitrous acid-acetic acid, where the acetate to alcohol ratio decreases with increasing carbonium ion stability.¹⁰ The variation of products in the deamination of 1- and 4-aminooctane can also be explained in terms of ion-pair intermediates which can decompose either by collapse of an ion pair or by attack of an external nucleophile, and where the products can be related to carbonium ion stability.¹²

The differences between the products of deamination and solvolysis in neryl and geranyl compounds are understandable in terms of the energetic carbonium ions formed in deamination which decompose with little discrimination to a variety of products, and before the counterion has time to diffuse away.

Within the accuracy of the measurements no bicyclic terpenoids have been detected as products of the solvolysis of neryl and geranyl compounds,^{2-4,18} and we found none in our reactions. Their absence is understandable in terms of the reluctance of an α -terpinyl-like cation to take up a boat conformation which would be required for formation of bicyclic products. However, thermodynamic considerations suggest that such products could be derived from acyclic precursors.¹⁹

Registry No.—Nerylamine, 36615-19-7; geranylamine, 6246-48-6; geranylphthalimide, 36615-20-0; nerylphthalimide, 36615-21-1.

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