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Regio- and Stereoselective Synthesis of N-H Aziridines by N-N Bond Reduction of *N*-Quinazolinyl Aziridines

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Abstract: Hydroxyl-directed aziridination of the isoprenoid alcohols - geraniol, nerol, and (*E,E*)-farnesol - with Atkinson's *N*-acetoxyamino-2-ethyl-4(3*H*)-quinazolone reagent (**4**) afforded *N*-substituted 2,3-epimino alcohols. Reduction of these and related *N*-substituted aziridines with metal-ammonia or lithium-naphthalenide reagents furnished a series of N-H aziridino alcohols (53-74%) including 2,3- and 6,7-epimino geraniols (**10** and **13**), 2,3-epimino nerol (**17**), (*E,E*)-2,3-epimino farnesol (**23**), and *syn*-2,3-epimino isophorol (**20**). A less efficient synthesis of the *trans*-2,3-epimino isoprenoid alcohols **10** and **23** by irradiation of allylic azidoformates and hydrolysis of the oxazolidinone photoproducts is also reported. These approaches complement known methods for synthesis of N-H aziridines of isoprenoid polyenes.

Keywords: aziridines, polyenols, quinazolinones, reduction.

INTRODUCTION

N-H Aziridine derivatives of isoprenoid polyenes and steroids have significant biological activities and applications as selective inhibitors of sterol biosynthesis enzymes. 2,3-Epimino squalene[1,2] is a potent inhibitor of oxidosqualene cyclases from rat liver,[1,3] pea seedlings,[3] and yeast.[3,4] This inhibitor has been used to impede cyclase activity in a study on the substrate selectivity of squalene oxidase[5] and to block *de novo* sterol biosynthesis in yeast[6] and fungi.[7]

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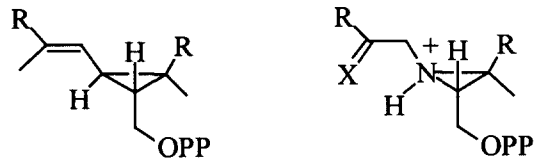
24,25-Epimino lanosterol, a product of 2,3-epimino squalene metabolism in *Gibberella fujikuroi*,[8] and 24,25-epimino zymosterol[9] inhibit essential sterol side chain alkylations catalyzed by *S*-adenosyl-L-methionine:$\Delta^{24(25)}$ sterol transferases from this fungus[10] and from sunflower seeds[9a] and yeast[9b] with K_i = 3-10 nM. 24,28-Imino fucosterol blocked the phytosterol side chain dealkylation essential for growth and development of the silk worm *Bombyx mori* [11] and inhibited the side chain methylation in the biosynthesis of 24-propylidene cholesterol in cell-free extracts from the marine alga *Chrysoderma mucosa*.[12] Imino analogs of Cecropia juvenile hormones (JH)[13] potentiate the intrinsic JH activity of the natural epoxide metamorphosis regulators in assays with silkworm pupa*Antheraea polyphemus* and the bug *Pyrrhocoris apterus*.[13a] 10β-Aziridinyl estranes[14a] and 17β-aziridinyl androstanes[14b] are potent inhibitors of the C-C bond cleaving oxidases, aromatase and 17β-hydroxylase/C17,20-lyase, respectively.

A variety of methods have been used to synthesize these isoprenoid and steroid N-H aziridines. 2,3-Epimino squalene was first obtained by HN_3 addition to 2,3-oxidosqualene, sulfonylation, and hydride reduction.[1] A more direct conversion of squalene to the 2,3-epimino derivative has been accomplished by iodoazide[15] and bromoazide additions[16] and subsequent hydride reduction. The halo azide methods have been utilized for regioselective synthesis of 6,7-epimino geraniol and 10,11-epimino farnesol.[16,17] The imine analogs of JH were synthesized from epoxide[13a] or α-azido ketone precursors.[13b] Aziridinations of 2-cholestene[18] as well as side chain 24(25)[16,18] and 24(28) double bonds[11] of sterols have been effected by iodo isocyanate[11,18,19] and iodoazide[17] additions followed by methanol addition or hydride reduction. The aziridinyl estranes[14a] and androstanes[14b,20] were prepared by $LiAlH_4$ reductions of the 10β- and 17β-acetyl steroid oximes.



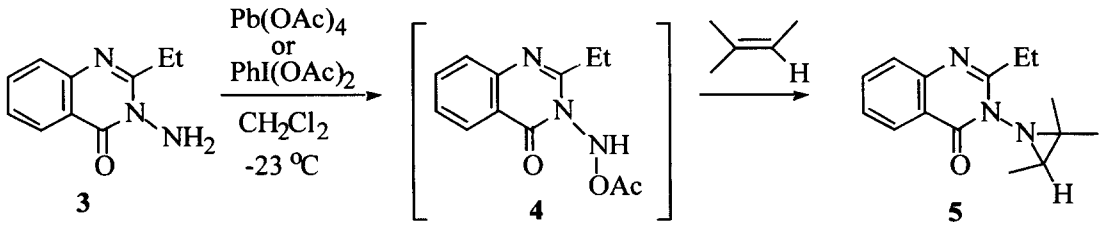
1 **2** (X = H_2, CH_2)

R = (*E*)-4,8-dimethyl-3,7-nonadienyl

In connection with recent investigations in these laboratories on the synthesis of aziridine analogs (**2**) of presqualene diphosphate (**1**) as novel inhibitors of squalene synthase,[21] we required access to 2,3-imino farnesol (**23**). Atkinson and Kelly have reported that regioselective aziridination of geraniol can be effected at the 2,3-double bond by reaction with *N*-amino-4(*3H*)-quinazolone **3** and lead tetraacetate,[22] and similar hydroxyl-directed

aziridination occurs with *N*-aminophthalimide.[23] The active aziridinating agent in the former case has been shown to be the *N*-acetoxyamino quinazolone (**4** = QNHOAc),[24] and this unstable reagent can also be generated by oxidation of **3** with iodosobenzene diacetate.[25] These reagents provide a general one-step procedure for converting olefins to aziridines bearing the heterocyclic substituent (Scheme 1).[26] However, to our knowledge the known methods for removal of *N*-quinazolinyl substituents are limited to hydrazinolysis of an activated trifluoromethyl analog to an *N*-amino aziridine,[27a] SmI_2 or Al·Hg reduction of *N*-quinazolinyl amino esters[27b] or amines[26a], and a de-silylative elimination-cyanation sequence in which an N-H aziridine arises from re-addition of cyanide to an azirine intermediate.[27c]

Scheme 1



We have found that the N-N bond of the *N*-quinazolinyl aziridines (**5**) undergo reductive cleavage with metal-ammonia or lithium-naphthalene to liberate the N-H aziridines, including 2,3-epimino geraniol (**10**) and 2,3-epimino farnesol (**23**).

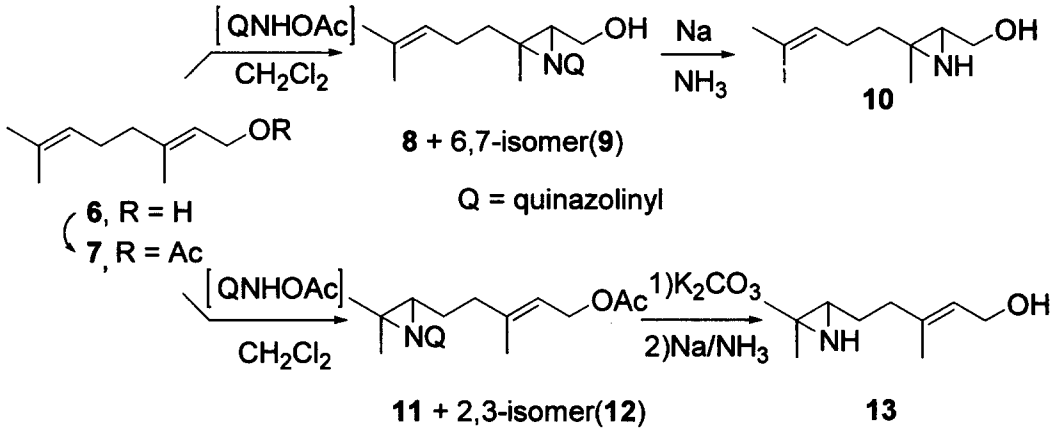
RESULTS AND DISCUSSION

N-Aminoquinazolone **3** was prepared by acylation of methyl anthranilate with propionic anhydride, hydrazinolysis, and cyclodehydration.[28] In most cases the *N*-acetoxyamino quinazolone reagent **4** was generated by oxidation of **3** with an equimolar amount of iodosobenzene diacetate[25] (CH_2Cl_2, -23°C, 30 min), the olefins (0.5 equiv.) were added at -23°C, and after ~2.5 h the reactions were warmed to room temperature. This procedure and stoichiometry with a two-fold excess of the *N*-acetoxy reagent were utilized for aziridinations of geraniol (**6**),[22] geranyl acetate (**7**), nerol (**14**), and isophorol (**18**)[23] (Schemes 2 and 3). The yields of the major and minor *N*-substituted aziridines based on the olefin reactants are presented in Table 1. Since in most cases significant amounts of the starting olefins were recovered during purification, adjusted yields based on unrecovered olefins are also shown. The relatively polar *N*-quinazolinyl and *N*-phthalimido aziridines were easily separated from unreacted olefin if present and from the more polar N-H quinazolone by chromatography on

silica gel. The majority of this heterocyclic by-product arising from competing decomposition of **4** could be removed by extractions with aqueous base.

Aziridination of geraniol (**6**, 4.45g scale) by this modified procedure afforded the known *N*-quinazolinyl 2,3-epimino geraniol (**8**)[22] in good yield (77%). The lower yield and regioselec-

Scheme 2



tivity of aziridination of geraniol with *N*-(acetoxyamino)phthalimide[23] (Table 1, 36%, ~4:1) may reflect alternative hydrogen-bonding arrays in this reagent and/or the transition state. However, it should be borne in mind that the ratios of the major and minor product yields do not precisely reflect the inherent aziridination selectivities at the 2,3 and 6,7 double bonds because the small amounts and instability of the minor isomers together with the difficulty in separating impurities of similiar polarity rendered quantitative recoveries problematic.

The predominant product from geranyl acetate (**7**) was the 6,7-aziridine **11** (50% or 82% based on recovered olefin). The opposite regioselectivity and lower conversion (64%) in this case are consequences of the absence of the allylic OH group to stabilize the transition state by hydrogen bonding and the inductive deactivation caused by the acetoxy substituent. Methanolysis of the acetate afforded *N*-quinazolinyl 6,7-epimino geraniol (**9**, 89%) identical to the minor product isolated from aziridination of geraniol.

The conversion of geraniol and nerol (Scheme 3) to isomeric 2,3-aziridines (**8** and **15**) with no evidence of cross contamination provides further evidence for the suprafacial stereospecificity of these nitrenoid cycloaddition reactions.[26] Aziridination of isophorol with **4** gave the known syn *N*-quinazolinyl epimino alcohol **19**[23] in 75% yield and high syn selectivity

in accord with the literature. Geraniol and (*E,E*)-farnesol were aziridinated with *N*-acetoxyamino reagent **4** generated with $Pb(OAc)_4$ under reversed stoichiometry conditions (1.5:1 olefin/oxidant ratio). The yields of *N*-substituted 2,3-epimino geraniol (**8**) and 2,3-imino farnesol (**22**) after chromatographic purification were 35% and 29%, respectively (63% and 73% based on unrecovered isoprenoid alcohol).

Table 1. Products and Yields from Olefin Aziridinations with *N*-Acetoxyaminoquinazolone (**4**) and N-N Bond Cleavages with Sodium- or Lithium-Ammonia (see Schemes 2 and 3).

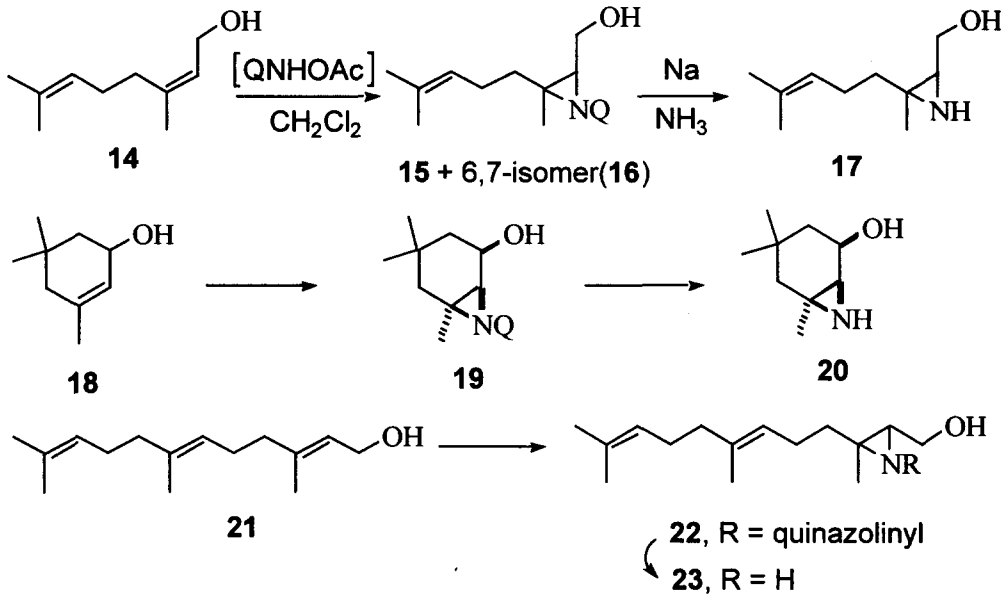
	N-Substituted Aziridines				N-H Aziridines	
	Major		Minor			
Olefin	No.	Yield(%)[a]	No.	Yield(%)[a]	No.	Yield(%)[b]
geraniol (**6**)	**8**	77	**9**	3[c]	**10**	66
	8	_(63)[d]	**9**	_(5)[d]	**10**	72[e]
	8[f]	_(36)[d]	**9**[f]	_(9)[d]	**10**	58[e]
geranyl acetate (**7**)	**11**	50(82)	**12**	11	**13**	53[g]
nerol (**14**)	**15**	49(84)	**16**	5	**17**	68
isophorol (**18**)	**19**	75(86)	_	_	**20**	74
farnesol (**21**)	**22**	_(73)[d]	_	_(12)[d,h]	**23**	67

[a] Yields based on olefin starting material. Those shown in parentheses are based on unrecovered olefin. [b] Na (3 equiv) used unless noted otherwise. [c] Estimate based on ^1H NMR analysis. [d] $Pb(OAc)_4$ was used as oxidant and **3** was limiting reagent. [e] Li (6 equiv) was used. [f] *N*-phthalimido aziridine. [g] Reduction carried out on alcohol **11**. [h] Mixture of 6,7- and 10,11-aziridines.

The structure assignments for the regioisomeric aziridino geraniols, nerols, and farnesols are based on their ^1H NMR spectra as well as literature precedent and independent syntheses of 2,3-epimino geraniol and farnesol (Scheme 4). The spectra of the 2,3-aziridine isomers show vinyl hydrogens at 4.91-5.08 ppm whereas the C2 vinyl protons for the 6,7-aziridines **9** and **12** are found further downfield at 5.37-5.50 ppm owing to the electron-withdrawing influence of the allylic oxygen substituents. Also the hydroxymethyl protons (CH_2OH) appear at δ_H 3.75-4.04 in the former and at δ_H 4.16-4.20 in the latter. The aziridinyl ring protons in all three *N*-quinazolinyl 2,3-epimino alcohols (**8**, **15**, and **22**) appear as doublets of doublets (J = 9 and 3 Hz at δ_H 3.0). A remarkable upfield shift of one C4 methylene proton (δ_H 0.84) is observed in

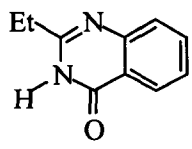
the spectra of 2,3-epimino geraniol and farnesol (**8** and **22**) whereas the same proton in 2,3-epimino nerol (**15**) is located at 1.56 or 1.93 ppm. In contrary fashion the C3 methyl groups on

Scheme 3



the aziridine ring appear downfield (δ_H 1.44 and 1.42) in the former and upfield (δ_H 1.14) in the latter. The anisotropic shielding effect of the quinazolone ring or its proximal carbonyl group on the C4 protons (in **8** and **22**) and the C3 methyl protons (in **15**) in the more stable invertomers is the likely cause of these upfield shifts.

The formation of N-H aziridines by Na/NH_3 reduction of an *N*-methoxy aziridine[29a] and by SmI_2,[29b] arene radical ions,[30a] and Mg/MeOH[30b] reductions of *N*-toluenesulfonyl aziridines provides precedent for the stability of these strained heterocycles to dissolving metal reagents. Procedures for N-N bond cleavage by Li/NH_3 reduction of *N*-pyrrolidine carbamates[31] and cyclic hydrazine derivatives[32] have been reported. Reductions of the five *N*-quinazolinyl aziridines as well as *N*-phthalimido 2,3-epimino geraniol[23] with 3 or 6 equivalents of lithium or 3 equivalents of sodium in liquid ammonia with THF as co-solvent at -33°C for typically 4-7 min followed by addition of solid NH_4Cl afforded the corresponding N-H aziridino alcohols in 53-74% yields (Table 1). The accompanying 2.5:1 mixtures of heterocyclic by-products, 2-ethylquinazolin-4(3*H*)-one (**24**) and its 5,8-dihydro derivative (**25**), were separated from the less polar N-H aziridino alcohols during purifications by flash chromatography on silica gel.



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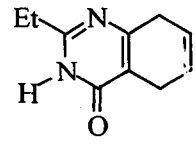

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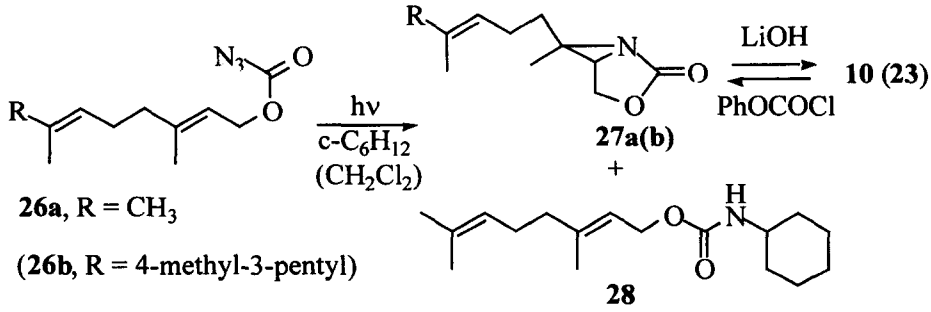
The minimum amount of sodium required for complete consumption of the *N*-quinazolinyl aziridines was estimated to be ca. 3-g.atom equivalents by incremental additions of the metal and TLC analyses. Since 3-g.atom equivalents of sodium would be required to cleave the N-N bond completely and to consume the active OH proton, the further reduction of quinazolone **24** to dihydroquinazolone **25** indicates that the OH proton is actually serving in part as the proton donor necessary for this Birch reduction. Thus, the N-N bond reduction must be somewhat faster than direct reaction of sodium with the OH group to liberate hydrogen. The successful Na/NH_3 reduction of the remote *N*-quinazolinyl aziridine **9** to 6,7-epimino geraniol **13**, albeit in a somewhat low 53% yield, shows clearly that the proximal OH group is not required for survival of the aziridine. This known N-H aziridine[16,17] was independently prepared by the procedure of Krief[16b] and identified by appropriate spectral comparisons. Larger scale reductions of crude **8** (ca. 19.5 mmol) and **15** (ca. 17.0 mmol) gave comparable overall yields (51 and 42%) for the two steps.

Two other reduction procedures were evaluated for the capacity to cleave the N-N bond. Reaction of *N*-quinazolinyl aziridine **8** with 4-g.atom equivalents of lithium-naphthalenide in THF[33] at room temperature gave 2,3-epimino geraniol (**10**) in 98% yield. However, the same *N*-substituted aziridine proved to be stable to SmI_2 in THF.[29b]

2,3-Epimino geraniol and farnesol (**10** and **23**) were independently synthesized in 5 steps by intramolecular nitrene additions (Scheme 4).[34] Geranyl and farnesyl azidoformates (**26a**

Scheme 4



and **26b**) were prepared by carboxylation of the alcohols with phenyl chloroformate, hydrazinolysis (neat NH_2NH_2, rt), and nitrosation of the carbazates ($NaNO_2$, aq. AcOH).[35] Irradiation of azidoformate **26a** in cyclohexane[36] (5 x 10^{-3} M, 2537 Å, rt) afforded the bicyclic aziridine **27a** (20%) and geranyl *N*-cyclohexylcarbamate (**28**, 52%), the latter formed by insertion of the nitrene into a C-H bond of the solvent. Thermal generation of the nitrene in refluxing benzene and *o*-xylene gave similar low yields of oxazolidinone **27a** accompanied by azepines (40-55%) arising from nitrene addition to the aromatic solvent followed by electrocyclic ring opening.[37]

Hydrolysis of **27a** (LiOH, aq. THF) provided 2,3-epimino geraniol **10** (69%), identical to the N-H aziridine obtained by Na/NH_3 reduction of *N*-quinazolinyl aziridine **8**. This aziridino alcohol was converted back to the oxazolidinone (80%) in two steps by formation of the phenyl carbonate (PhOCOCl, Et_3N, ether, -5°C) and base-catalyzed cyclization (neat Et_3N, reflux). Similar irradiation of (*E,E*)-farnesyl azidoformate (**26b**) in CH_2Cl_2 furnished the corresponding homogeranyl oxazolidinone (**27b**, 19%) which was hydrolyzed to 2,3-epimino farnesol **23**.

In conclusion, hydroxyl-directed aziridination of the isoprenoid alcohols - geraniol, nerol, and farnesol - with Atkinson's *N*-acetoxyamino quinazolone reagent **4** followed by Na/NH_3 reduction provides convenient access to the N-H aziridino alcohols **10**, **17**, and **23**. This approach complements known methods for synthesis of the isomeric N-H-aziridines functionalized at the opposite end of the isoprenoid chain.[1,13,16,17]

EXPERIMENTAL

Materials and Methods.[38] Reactions were stirred magnetically unless otherwise indicated. Triethylamine was distilled from P_2O_5 and stored over KOH pellets. Glassware was flame-dried under a slightly positive nitrogen pressure. All reactions were monitored by TLC on Merck glass plates precoated with 0.25 mm of silica gel 60 F-254. The residual peaks for $CHCl_3$ (δ 7.26 ppm for ^1H and δ 77.0 ppm for ^{13}C) were used as internal references in NMR spectra. The abbreviation "app" in ^1H NMR data refers to the appearance or first order analysis of the multiplet which maybe an oversimplification. The purity of all major products was judged to be >90-95% from inspection of ^1H and ^{13}C NMR spectra, unless specified otherwise. Elemental analyses were performed by the Microanalytical Laboratory at the School of Chemical Sciences, University of Illinois.

3-Amino-2-ethylquinazolin-3*H*-4-one (3). A modification of a literature procedure was used.[28] A solution of methyl anthranilate (20.0 g, 132 mmol) in propionic anhydride (24.1 g, 185 mmol) was heated without solvent at 105 °C for 15 min under N_2, cooled to 75 °C, and diluted with absolute EtOH (10 mL). Anhydrous hydrazine (8.48 g, 265 mmol) was added in 2 portions at 5-min intervals. The solution was stirred and heated at reflux for 45 min, cooled to

room temperature, and allowed to crystallize. Recrystallization (ethyl acetate-hexane) afforded 22.3 g (86%) of **3** as a white crystalline solid: mp 121.5-122 °C (lit.[39] mp 126 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (t, *J* = 7.5 Hz, 3H, C*H*$_3$), 2.97 (q, *J* = 7.5 Hz, 2H, C*H*$_2$), 4.90 (s, 2H, N*H*), 7.40 (dt, *J* = 8.0, 1.0 Hz, 1H, Ar H), 7.62 (d, *J* = 8.0 Hz, 1H, Ar H), 7.70 (dt, *J* = 8.0, 1.2 Hz, 1H, Ar H), 8.19 (dd, *J* = 8.0, 1.0 Hz, 1H, Ar H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 10.72, 27.72, 119.88, 126.15, 126.29, 127.05, 134.16, 146.99, 159.09, 161.77; IR ($CHCl_3$) ν_{max} 3329, 3217, 3016, 1673, 1596 cm.$^{-1}$

Aziridinations with *N*-Acetoxyaminoquinazolone 4. Aziridinations were carried out with iodosobenzene diacetate ($PhI(OAc)_2$)[40] as oxidant unless specified otherwise. In most cases, the reactions were carried out at -23 °C for 2-2.5h, warmed to rt, and allowed to stir at rt for 12-48 h. Methods of isolation and purification were analogous to those in the representative procedure. The following abbreviated format is used to present specific information about other aziridinations with $PhI(OAc)_2$: starting olefin; total reaction time; flash chromatography eluent; products and by-products in elution order. In each case the majority of the N-H quinazolone by-product was removed by repeated extractions with 0.5 M KOH. This byproduct, always the most polar component, was still evident by TLC of the crude product, but it was not isolated. A procedure for aziridination of farnesol with $Pb(OAc)_4$ as oxidant is also presented.

***trans*-1-(2-Ethyl-4-oxoquinazolin-3-yl)-3-hydroxymethyl-2-methyl-2-(4-methyl-3-pentenyl)aziridine (8). Representative Aziridination Procedure:** A modification of literature procedures was used.[25,41] A suspension of iodosobenzene diacetate (19.2 g, 57.7 mmol) in CH_2Cl_2 (140 mL) was stirred and cooled at -23 °C as aminoquinazolone **3** (10.9 g, 57.7 mmol) in CH_2Cl_2 (70 mL) was added dropwise over 30 min. After 30 min at -23 °C, geraniol (4.45 g, 28.8 mmol) in CH_2Cl_2 (20 mL) was added dropwise over 10 min. After an additional 2.5 h at -23°C the reaction mixture became homogeneous. The resulting orange solution was allowed to warm to room temperature and diluted with Et_2O (150mL). The ethereal solution was washed with 0.5 M KOH (2 x 75 mL) and H_2O (3 x 75 mL), dried ($MgSO_4$), and concentrated by rotary evaporation to give a dark orange oil. Purification by silica gel chromatography (3:2 hexane/EtOAc as eluent) afforded 7.55 g (77%) of **8** and 0.30 g (3%) of the 6,7-regioisomer **9**. Data for **8**: mp 129-131 °C (lit[22] mp, 128-130 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (ddd, *J* = 12.4, 10.0, 6.9 Hz, 1H, =CCH$_2$C*H*H), 1.39 (t, *J* = 7.5 Hz, 3H, CH$_2$C*H*$_3$), 1.44 (s, 3H, C*H*$_3$), 1.53 (s, 3H, C*H*$_3$), 1.61 (s, 3H, C*H*$_3$), 1.70 (ddd, *J* = 12.9, 9.4, 5.2 Hz, 1H, C*H*$_2$), 2.00 (dq, *J* = 13.0, 7.6 Hz, 1H, C*H*$_2$), 2.15 (m, 1H, C*H*$_2$), 2.78 (dq, *J* = 16.0, 7.3 Hz, 1H, C*H*$_2$CH$_3$), 3.00 (dd, *J* = 9.2, 2.8 Hz, 1H, C*H*N), 3.08 (dq, *J* = 16.0, 7.3 Hz, 1H, C*H*$_2$CH$_3$), 3.70-4.02 (m, 2H, C*H*$_2$OH), 4.52 (br d, *J* = 4.6 Hz, 1H, O*H*, D_2O exch.), 4.91 (t, *J* = 7.1 Hz, 1H, C=C*H*), 7.42 (dt, *J* = 8.0, 1.0 Hz, 1H, H7'), 7.64 (d, *J* = 8.0 Hz, 1H, H8'), 7.70 (dt, *J* = 7.0, 1.2 Hz, 1H, H6'), 8.16 (dd, *J* = 8.0, 1.0 Hz, 1H, H5'); ^{13}C NMR (101 MHz, $CDCl_3$) δ 10.58, 11.94, 17.57, 25.21, 25.51, 27.59, 34.42, 54.33, 66.39, 120.83, 122.11, 126.05, 126.22, 126.76, 132.88, 133.72, 145.74, 157.68, 160.91; IR ($CHCl_3$) ν_{max} 3453, 2962, 1665, 1600 cm^{-1}.

Data for **9**: mp 59.5-60.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$, D_2O exch) δ 1.10 (s, 3H, C*H*$_3$), 1.39 (t, *J* =7.2 Hz, 3H, CH$_2$C*H*$_3$), 1.40 (s, 3H, C*H*$_3$), 1.60 (m, 1H, C*H*$_2$), 1.73 (s, 3H, C*H*$_3$), 2.29 (m, 3H, C*H*$_2$), 2.71 (dq, *J* =15.0, 7.5 Hz, 1H, C*H*$_2$CH$_3$), 2.85 (br s, 1H, C*H*N), 3.05 (dq, *J* =15.0, 7.5 Hz, 1H, C*H*$_2$CH$_3$), 4.12 and 4.17 (dABq, J_{AB}= 12.4, *J* = 7.2 Hz, 2H, C*H*$_2$OH), 5.50 (t, *J* = 7.3 Hz, 1H, C=C*H*), 7.39 (ddd, *J* = 9.0, 7.0, 1.5 Hz, 1H, H7'), 7.52 (dd, *J* = 8.0, 1.0

Hz, 1H, H8'), 7.64 (ddd, J = 9.0, 7.0, 1.5 Hz, 1H, H6'), 8.15 (dd, J = 8.0, 1.0 Hz, 1H, H5'); ^{13}C NMR (126 MHz, $CDCl_3$) δ 10.61, 16.28, 18.71, 20.61, 26.69, 27.75, 36.61, 50.90, 53.94, 59.25, 121.36, 123.95, 126.05, 126.12, 126.73, 133.48, 138.87, 145.92, 158.52, 160.58; IR ($CHCl_3$) ν_{max} 3420, 2972, 1667 cm^{-1}. Anal. Calcd for $C_{20}H_{27}N_3O_2$: C, 70.35; H, 7.97; N, 12.31. Found: C, 70.72; H, 8.32; N, 12.52.

3-((*E*)-5-Acetoxy-3-methyl-3-pentenyl)-2,2-dimethyl-1-(2-ethyl-4-oxo-quinazolin-3-yl)aziridine (11): geranyl acetate[42] (**7**, 2.18 g, 11.23 mmol); overnight; 1% Et_3N in 3:1 hexane/EtOAc; recovered **7** (848 mg, 4.32 mmol); **11**(2.15 g, 82% based on unrecovered **7**); **12** (290 mg, 11%). Data for **11**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (s, 3H, C*H*$_3$), 1.38 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.40 (s, 3H, C*H*$_3$), 1.54 (m, 1H, C*H*$_2$), 1.74 (s, 3H, C*H*$_3$), 2.00 (s, 3H, CH_3CO), 2.24 (m, 1H, C*H*$_2$), 2.34 (m, 2H, C*H*$_2$), 2.73 (dq, J =16.1, 7.3 Hz, 1H, CH_2CH_3), 2.81 (br s, 1H, C*H*N), 3.04 (dq, J =16.2, 7.3 Hz, 1H, CH_2CH_3), 4.53 and 4.60 (dABq, J_{AB}= 13.1, J = 7.3 Hz, 2H, CH_2OAc), 5.37 (tsept, J = 7.1, 1.2 Hz, 1H, C=C*H*), 7.37 (ddd, J= 8.1, 6.9, 1.3 Hz, 1H, H7'), 7.59 (dd, J = 8.2, 1.3 Hz, 1H, H8'), 7.64 (ddd, J = 8.2, 6.9, 1.4 Hz, 1H, H6'), 8.14 (dd, J = 8.1, 1.4 Hz, 1H, H5'); ^{13}C NMR (101 MHz, $CDCl_3$) δ 10.66, 16.49, 18.74, 20.60, 26.73, 27.80, 36.72, 50.98, 54.14, 61.28, 118.81, 121.43, 126.06, 126.17, 126.79, 133.51, 141.67, 145.98, 158.57, 160.57, 171.13; IR ($CHCl_3$) ν_{max} 2956, 1737, 1672 cm^{-1}. Anal. calcd for $C_{22}H_{29}N_3O_3$: C, 68.90; H, 7.62; N, 10.96. Found: C, 68.65; H, 7.82; N, 10.95.

Data for **12:** colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.81 (m, 1H, C*H*$_2$) 1.38 (t, J = 7.3 Hz, 3H, CH_3CH_2), 1.47 (s, 3H, C*H*$_3$), 1.52 (s, 3H, C*H*$_3$), 1.60 (s, 3H, C*H*$_3$), 1.68 (m, 1H, C*H*$_2$), 1.93 (m, 1H, C*H*$_2$), 2.13 (s, 3H, CH_3CO), 2.17 (m, 1H, C*H*$_2$), 2.74 (dq, J = 14.7, 7.3 Hz, 1H, CH_2CH_3), 3.04 (dq, J = 14.7, 7.3 Hz, 1H, CH_2CH_3), 3.24 (br s, 1H, C*H*N), 4.20 (dd, J = 11.7, 7.7 Hz, 1H, CH_2O), 4.69 (dd, J = 11.7, 5.1 Hz, 1H, CH_2O), 4.94 (tsept, J = 7.1, 1.2 Hz, 1H, C=C*H*), 7.40 (ddd, J = 8.1, 7.2, 1.2 Hz, 1H, H7'), 7.61 (dd, J = 8.2, 1.0, Hz, 1H, H8'), 7.67 (ddd, J = 8.2, 7.1, 1.1 Hz, 1H, H6'), 8.16 (dd, J = 8.1, 1.2, Hz, 1H, H5'); ^{13}C NMR (126 MHz, $CDCl_3$) δ 10.62, 16.98, 17.62, 20.90, 25.20, 25.59, 27.71, 34.26, 50.69, 54.24, 62.44, 121.32, 122.37, 126.20, 126.31, 126.81, 132.86, 133.67, 145.93, 157.99, 160.49, 170.86; IR ($CHCl_3$) ν_{max} 3018, 1739, 1673 cm^{-1}. Anal. Calcd for $C_{22}H_{29}N_3O_3$: C, 68.90; H, 7.62; N, 10.96. Found: C, 68.80; H, 7.63; N, 10.98.

Basic Hydrolysis of 11 to the *N*-Quinazolinyl Aziridino Alcohol 9. A solution of the *N*-substituted aziridinyl acetate **11** (2.15 g, 5.60 mmol) in MeOH (40 mL) at 25 °C was stirred as K_2CO_3 (1.52 g, 8.12 mmol) was added. The suspension was stirred for 24 h, H_2O (150mL) was added, and the product was extracted with CH_2Cl_2 (4 x 50mL). The combined organic layers were dried ($MgSO_4$) and concentrated. Purification by flash chromatography on silica gel (3:2 EtOAc/hexane as eluent) gave 1.60 g (84%) of a white solid which had similar mp, and identical spectra to those reported above.

***cis*-1-(2-Ethyl-4-oxoquinazolin-3-yl)-3-hydroxymethyl-2-methyl-2-(4-methyl-3-pentenyl)aziridine (15)**: nerol (1.71 g, 11.08 mmol); 14 h; 5:2 hexane/EtOAc; recovered nerol (715 mg, 2.20 mmol, 20%); 1.86 g (49% or 85% based on recovered nerol) of **15**; 6,7-regioisomer **16** (110 mg, 5%). Data for **15**: mp 67.5-68.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.14 (s, 3H, C*H*$_3$), 1.38 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.56 (ddd, J = 13.4, 10.7, 6.0 Hz, 1H,

CH_2), 1.60 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 1.93 (m, 1H, CH_2), 2.07 (m, 1H, CH_2), 2.13 (m, 1H, CH_2), 2.75 (dq, J = 15.0, 7.5 Hz, 1H, CH_2CH_3), 2.96 (dd, J = 9.5, 3.0 Hz, 1H, CHN), 3.05 (dq, J = 15.0, 7.5 Hz, 1H, CH_2CH_3), 3.69 (ddd, J = 10.2, 9.7, 2.5 Hz, 1H, CH_2OH), 4.10 (ddd, J = 11.5, 6.5, 3.0 Hz, 1H, CH_2OH), 5.08 (tsextets, J = 7.0, 1.0 Hz, 1H, C=CH), 7.40 (ddd, J = 9.0, 7.0, 1.5 Hz, 1H, H7'), 7.63 (d, J = 8.0 Hz, 1H, H8'), 7.68 (ddd, J = 9.0, 7.0, 1.5 Hz, 1H, H6'), 8.13 (dd, J = 8.0, 1.0 Hz, 1H, H5'); ^{13}C NMR (126 MHz, $CDCl_3$) δ 10.58, 17.60, 17.98, 24.60, 25.68, 27.58, 34.14, 54.95, 55.07, 61.40, 120.99, 122.71, 126.19, 126.39, 126.89, 132.93, 133.89, 145.84, 157.93, 161.15; IR ($CHCl_3$) ν_{max} 3441, 3018, 1658 cm^{-1}; HRMS (FAB) *m/z* calcd for $C_{20}H_{27}N_3O_2$ (M+1): 342.2181, found 342.2180.

Data for **16**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.11 (s, 3H, CCH_3), 1.40 (t, J= 7.5 Hz, 3H, CH_2CH_3), 1.43 (s, 3H, CH_3), 1.61 (ddd, J= 13.2, 6.5, 1.5, Hz, 1H, CH_2), 1.81 (s, 3H, CH_3), 2.21 (ddd, 1H, J= 12.5, 6.5, 3.0 Hz, CH_2), 2.35 (m, 1H, CH_2), 2.45 (m, 1H, CHN), 2.76 (dq, J = 16.0, 7.5 Hz, 1H, CH_2CH_3), 2.92 (br s, 1H, OH), 3.07 (dq, J= 16.0, 7.5 Hz, 1H, CH_2CH_3), 4.12-4.22 (symmetric 8 lines, app AB of ABX, 2H, CH_2OH), 5.50 (t, J= 7.5, 1H, C=CH), 7.39 (td, J = 8.0, 1.5 Hz, 1H, H7'), 7.62 (d, J = 8.0 Hz, 1H, H8'), 7.67 (td, J = 8.0, 1.5Hz, 1H, H6'), 8.14 (dd, J =8.0,1.5Hz,1H,H5'); ^{13}C NMR (126 MHz,$CDCl_3$) δ 10.63, 15.25, 18.73, 20.62, 23.41, 27.18, 27.80, 50.74, 53.61, 58.86, 121.34, 125.13, 126.14, 126.18, 126.73, 133.57, 139.07, 145.96, 158.51, 160.70; IR ($CHCl_3$) ν_{max} 3412, 1668, 1594 cm^{-1}.

***cis*-7-(2-Ethyl-4-oxoquinazolin-3-yl)-4,4,6-trimethyl-7-azabicyclo-[4.1.0]heptan-2-ol (19)**: isophorol (750 mg, 5.35 mmol); 48 h; 1:1 hexane/EtOAc; recovered isophorol (100 mg, 13%); 1.31 g (75%, 86% based on unrecovered isophorol). ^{1}H and ^{13}C NMR data matched those reported in the literature.[23] Data for **19**: mp 176-176 °C (lit.[23] mp, 169-170 °C); Anal. calcd for $C_{19}H_{25}N_3O_2$: C, 69.70; H, 7.70; N, 12.83. Found: C, 69.63; H, 7.73; N, 12.67.

***trans*-2-((*E*)-4,8-Dimethyl-3,7-nonadienyl)-1-(2-ethyl-4-oxoquinazolin-3-yl)-3-(hydroxymethyl)-2-methylaziridine (22).** The following procedure is based on those reported by Atkinson.[41] Dry CH_2Cl_2 (10 mL) was stirred and cooled at -23 °C under N_2 in a 100 mL, three-necked, round-bottomed flask equipped with two dropping funnels and a thermometer. Solutions of *N*-aminoquinazolone **3** (1.04 g, 5.51 mmol) in CH_2Cl_2 (10 mL) and $Pb(OAc)_4$ (2.87 g, 6.48 mmol) in CH_2Cl_2 (10 mL) were added simultaneously 5 drops at the time over 20 min. The yellow suspension formed was allowed to stir for 0.5h before neat farnesol (**21**, 1.83 g, 8.26 mmol) was added over 5 min. After 1.5 h at -23°C, the heterogeneous mixture was warmed to rt, $Pb(OAc)_2$ was filtered by gravity, and the solid was washed with 30 mL of CH_2Cl_2. The filtrate was washed with satd. $NaHCO_3$ (3 x 50 mL) and H_2O (3 x 50 mL), dried ($MgSO_4$), and concentrated. Purification by flash chromatography (50 % EtOAc/hexane as eluent) afforded in elution order 1.09 g (60 %) of recovered **21**, 0.99 g (73 %, based on unrecovered **21**) of **22** as a pale yellow oil, 0.17 g (12%) of a mixture of internal and distal aziridines, and 0.15 g of N-H quinazolone. Data for **22**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (ddd, J = 12.8, 10.0, 6.8 Hz, 1H, CH_2), 1.42 (t, J = 7.6 Hz , 3H, CH_2CH_3), 1.45 (s, 3H, CH_3), 1.53 (s, 6H, CH_3), 1.62 (d, J = 1.2 Hz, 3H, CH_3), 1.71 (ddd, J = 13.2, 9.6, 5.2 Hz,1H, CH_2), 1.95 (m, 5H, allylic CH_2), 2.19 (m, 1H, allylic CH_2), 2.78 (dq, J = 15.8, 7.2 Hz, 1H, CH_2CH_3), 3.00 (dd, J = 9.2, 3.2 Hz, 1H, NCH), 3.08 (dq, J = 15.8, 7.2 Hz, 1H, CH_2CH_3), 3.69 (ddd, J = 11.4, 9.4, 2.2 Hz; dd upon D_2O exch, J = 10.8, 9.2 Hz, 1H; CH_2OH), 4.06 (ddd, J = 11.4, 6.8, 3.0 Hz; dd upon D_2O exch, J = 11.2, 3.2 Hz, 1H, CH_2OH), 4.54 (dd, J = 6.6, 2.2 Hz, 1H, OH,

exch with D_2O), 4.93 (t of sextets, J = 7.2, 1.2 Hz, 1H, C=C*H*), 5.00 (t of septets, J = 7.2, 1.2 Hz, 1H, C=C*H*), 7.44 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H, C7'-H), 7.64 (dd, J = 8.2, 0.4 Hz, 1H, C8'-H), 7.72 (ddd, J = 8.5, 6.4, 1.6 Hz, 1H, C6'-H), 8.18 (dd, J = 7.8, 1.2 Hz, 1H, C5'-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.6, 16.0, 17.1, 17.6, 25.3, 25.6, 26.4, 27.7, 34.4, 39.5, 54.5, 61.5, 120.9, 121.9, 123.9, 126.1, 126.3, 126.8, 131.5, 133.8, 136.6, 145.8, 157.7, 161.0; IR (neat)ν_{max} 3447. 2928, 2246, 1663, 1592, 1039, 912, 772, 731, 691 cm^{-1}.MS(+)FAB m/z 410.3; HRMS calcd for $C_{25}H_{35}N_3O_2$ 410.2811, found 410.2807. Anal. Calcd. for $C_{25}H_{35}N_3O_2$: C, 73.31; H, 8.61; N, 10.26. Found: C, 73.52; H, 8.51; N, 10.05. Aziridination of geraniol (1.76 g, 11.39 mmol) by the procedure described for farnesol afforded 67 mg (35%, 63% based on unrecovered geraniol) of **8** and 60 mg (5% based on recovered geraniol) of **9**.

Representative Procedure for Reductive Cleavages of N-N Bonds. Most reductions were performed using sodium and ammonia as described in Method A below. Some reductions with Li/NH_3 affording **10** and **23** are also presented. The presence of N-H quinazolone (**24**) and N-H dihydroquinazolone (**25**) was evident in TLC analyses of the crude products, but they were not isolated unless otherwise stated. The following abbreviated format is used to present specific information for reduction of other *N*-quinazolinyl aziridines with Na/NH_3 (Method A): starting material; flash chromatography eluent; N-H aziridine.

***trans*-3-Hydroxymethyl-2-methyl-2-(4-methyl-3-pentenyl)aziridine(10). Method A. By Na/NH_3 and Li/NH_3 reductions.** This procedure was developed from a literature method.[31] Anhydrous ammonia (7 mL) was condensed into the flask and allowed to reflux at -33°C. A solution of *N*-substituted aziridine **8** (100 mg, 0.29 mmol) in THF (3 mL) was added. The solution was stirred at reflux as sodium metal (20 mg, 0.88 mg-atom) was added in three portions over 1 min. The initial light yellow solution turned red after thefirst portion of Na, then green after the second, and finally dark blue immediately after the final portion of metal was added. After ~5 min solid NH_4Cl (500 mg, 9.37 mmol) was added, and the NH_3 was allowed to evaporate. The solid residue was partitioned between H_2O (30 mL) and EtOAc (20 mL), and the aqueous layer was extracted with EtOAc (2 x 15 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated by rotary evaporation. Purification by flash chromatography (7:2 EtOAc/MeOH as eluent) afforded 33 mg (66%) of **10** as a yellow solid, mp 27-28 °C, the N-H quinazolone **24** (38 mg, 65%), and the N-H dihydroquinazolone **25** (11 mg, 26%). Data for **10**: ^1H NMR (500 MHz, $CDCl_3$) δ 1.18 (s, 3H, C*H*$_3$), 1.34 (m, 1H, C*H*$_2$), 1.57 (m, 1H, C*H*$_2$), 1.61 (s, 3H, C*H*$_3$), 1.68 (s, 3H, C*H*$_3$), 1.97 (br s, 2H, N*H* and O*H*), 2.10 (m, 3H, C*H*$_2$ and C*H*N), 3.54 (m, 1H, C*H*$_2$OH), 3.76 (dd, J = 9.9, 4.8 Hz, 1H, C*H*$_2$OH), 5.08 (t, J = 5.8 Hz, 1H, C=C*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.90, 17.50, 24.55, 25.55, 39.21, 41.27, 43.60, 61.03, 123.22, 131.98; IR ($CHCl_3$)ν_{max} 3293, 2985, cm^{-1}; HRMS (FAB) *m/z* calcd for $C_{10}H_{19}NO$ (M+H): 170.1545, found 170.1545. A large-scale reduction carried out similarly with 6.67 g of crude **8** [prepared from 3.01 g (19.5 mmol) of geraniol] and 2.25 g (97.7 mg-atom) of sodium afforded 1.70 g (51% based on geraniol) of **10**. This aziridine was also prepared by Li/NH_3 reduction as follows: A solution of **8** (300 mg, 0.88 mmol) in 2 mL of THF was added to a solution of lithium (40 mg, 5.28 mg-atom) in liquid NH_3 at -78 °C. The mixture was allowed to warm to -33 °C and after 2 h at reflux, the product was isolated as described above and purified by flash chromatography (15% $MeOH/CH_2Cl_2$ as eluent) to afford 107 mg (72%) of **10** as yellow oil. Li/NH_3 reduction of *N*-phthalimido aziridine[23] (0.81 g, 2.56 mmol) by this Li/NH_3 reduction procedure gave 253 mg (58%) of **10**.

Method B. By Lithium naphthalenide reduction. Lithium naphthalenide (1.0 M) in THF was prepared by the addition of lithium (820 mg, 12.0 g-atom) to naphthalene (16.6 g, 13.0 mmol) in THF (180 mL) with subsequent stirring for 24 h at rt.[33] A solution of **8** (266 mg, 0.78 mmol) in THF (8 mL) was stirred at 25 °C under N_2 while lithium naphthalenide (3.12 mL, 3.12 mmol) was added dropwise over 5 min. After 5 min, H_2O (2 mL) was added and the suspension was evaporated to dryness. The resulting solidwas partitioned between EtOAc (25 mL) and H_2O (5 mL). The aqueous layer was washed with Et_2O (8 x 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. Purification by flash chromatography (7:2 EtOAc/MeOH as eluent) afforded 131 mg (99%) of **10** as a yellow solid, mp 27-28 °C.

Method C. By hydrolysis of oxazolidinone 27a. Pellets of $LiOH{\cdot}H_2O$ (1.41 g, 33.6 mmol) were added slowly to a solution of **27a** (0.41 g, 1.56 mmol) in THF/H_2O (20 mL of 1:1 solution) at rt under N_2. The suspension was stirred for 5 min and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. Purification by flash chromatography (10 % $MeOH/CH_2Cl_2$) afforded 257 mg (69 %) of **10** as pale yellow oil, the spectra of which were identical to those of the product obtained from dissolving metal reductions of **8**.

2-Ethylquinazolin-3*H*-4-one (24): mp >200°C (lit[43] mp, 233°C); ^1H NMR (400 MHz, $CDCl_3$) δ 1.45 (t, *J* = 7.8 Hz, 3H, C*H*$_3$), 2.84 (q, *J* = 7.7 Hz, 2H, C*H*$_2$), 7.46 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H, Ar C*H*), 7.69 (dd, *J* =8.0, 1.0 Hz, 1H, Ar C*H*), 7.73 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H, Ar C*H*), 8.32 (dd, *J* = 8.0, 1.0 Hz, 1H, Ar C*H*), 12.10 (br s, 1H, N*H* (D_2O exch)); ^{13}C NMR (101 MHz, $CDCl_3$) δ 11.42, 29.02, 120.36, 126.09, 126.19, 127.08, 134.64, 149.38, 157.55, 164.33.

2-Ethyl-5,8-dihydroquinazolin-3*H*-4-one (25): mp >200 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 1.30 (t, *J* =7.2 Hz, 3H, C*H*$_3$), 2.69 (q, *J* = 7.2 Hz, 2H, C*H*$_2$CH$_3$), 3.15 (m, 2H, C*H*$_2$), 3.25 (m, 2H, C*H*$_2$), 5.81 (dddt, *J* = 7.7, 5.2, 3.3, 2.0 Hz, 1H, C=C*H*), 5.87 (dddt, *J* = 7.8, 5.2, 3.1, 1.9 Hz, 1H, C=C*H*), 11.80 (br s, 1H, N*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ 11.79, 23.81, 28.69, 32.34, 116.47, 122.94, 123.83, 159.56, 159.96, 164.35; IR ($CHCl_3$) ν_{max} 3020, 1643, cm^{-1}; HRMS (FAB) *m/z* calcd for $C_{10}H_{12}N_2O$ (M+1): 177.1028, found 177.1028.

2,2-Dimethyl-3-((*E*)-5-hydroxy-3-methyl-3-pentenyl)aziridine(13). Method A. By Na/NH_3 reduction of 9: **9** (153 mg, 0.45 mmol); 5:2 EtOAc/MeOH; **13** (50 mg, 69%) as a yellow oil: ^1H NMR (500 MHz, $CDCl_3$) δ 1.13 (s, 3H, C*H*$_3$), 1.22 (s, 3H, C*H*$_3$), 1,52 (m, 2H, C*H*$_2$), 1.63 (s, 3H, C*H*$_3$), 1.74 (t, 1H, *J* = 7.0 Hz, C*H*N), 1.95 (br s, 2H, N*H*,O*H* , exch with D_2O), 2.10 (m, 2H, C*H*$_2$), 4.11 (d, 2H, *J* = 7.2 Hz, C*H*$_2$OH), 5.39 (tsept, *J* = 7.0, 1.5 Hz, C=C*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ 16.24, 19.51, 27.27, 27.90, 35.88, 37.67, 43.22, 58.81, 124.39, 138.05; IR ($CHCl_3$) ν_{max} 3543, 3024 cm^{-1}.

Method B. By bromo azide addition/reduction. A modification of a literature procedure was used.[16] A suspension of NaN_3 (13.7 g, 210 mmol) in a solution of DME (270 mL), H_2O (68 mL) and 7[41] (8.24 g, 42.0 mmol) was stirred and cooled at -5 °C as NBS (10.5 g, 58.8 mmol) was added in portions over 15 min. The suspension was stirred for 2 h at -5°C, water (200 mL) was added, and the product was extracted with hexane (4 x 100 mL). The

hexane extracts were combined, dried ($MgSO_4$), and concentrated. A suspensionof $LiAlH_4$ (7.97g, 210 mmol) in Et_2O (275 mL) was stirred and cooled at 0 °C as the crude 6,7-bromoazide (13.3 g, ca 42.0 mmol) in Et_2O (20 mL) was added dropwise over 55 min. After 30 min, water (8 mL), 15% NaOH (8 mL), and H_2O (21 mL) were slowly added in succession over 55 min with addition of more Et_2O (150 mL). The resulting suspension was filtered, and the salts were washed with Et_2O (4 x 100 mL). The organic filtrates were combined, dried ($MgSO_4$), and concentrated by rotary evaporation. Purification by flash chromatography (7:2EtOAc/MeOH as eluent) afforded 4.65 g (65% from **7**) of **13** as a yellow oil, the NMR spectra of which were identical to those prepared by Method A.

***cis*-3-Hydroxymethyl-2-methyl-2-(4-methyl-3-pentenyl)aziridine (17):** **15** (300 mg, 0.88 mmol); 4:1 EtOAc/acetone; **17** (102 mg, 68%) as a low melting yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 3H, C*H*$_3$), 1.32 (ddd, *J* = 16.0, 10.5, 6.3 Hz, 1H, C*H*$_2$), 1.51 (ddd, *J* = 15.8, 10.3, 5.5 Hz, 1H, C*H*$_2$), 1.55 (s, 3H, C*H*$_3$), 1.63 (s, 3H, C*H*$_3$), 1.98 (m, 2H, C*H*$_2$), 2.08 (dd, *J* = 8.2, 4.3 Hz, 1H, C*H*N), 2.75 (br s, 2H, N*H* and O*H*), 3.39 (dd, *J* = 12.2, 8.2 Hz, 1H, C*H*$_2$OH), 3.72 (dd, *J*= 11.8 4.2 Hz, 1H, C*H*$_2$OH), 5.01 (tsext, *J*= 6.8, 1.4 Hz, 1H, C=C*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.43, 24.49, 24.66, 25.50, 33.81, 39.59, 44.78, 60.59, 123.60, 131.71; IR ($CHCl_3$) ν_{max} 3312, 3018, cm^{-1}; HRMS (FAB) *m/z* calcd for $C_{10}H_{19}NO$ (M+1): 170.1545, found 170.1545. A large-scale reduction carried out similarly with 13.6 gof crude **15** [prepared from 2.63 g (17.0 mmol) of nerol] with 3.66 g (159 mg-atom) of sodium afforded 1.21 g (42% based on nerol) of **17**.

***endo*-4,4,6-Trimethyl-7-azabicyclo[4.1.0]heptan-2-ol (20):** **19** (750 mg, 2.29 mmol); 9:2 EtOAc/MeOH; **20** (267 mg, 75%) as a white crystalline solid: mp 109-109.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.82 (s, 3H, C*H*$_3$), 0.83 (s, 3H, C*H*$_3$), 1.03 (dd, *J* = 12.6, 11.1 Hz, 1H, C*H*$_{ax}$HCHOH), 1.27 (s, 3H, C(N)C*H*$_3$), 1.33 (dd, *J* = 14.2, 2.1 Hz, 1H, CH*H*$_{eq}$), 1.41 (ddd, *J* = 12.7, 6.2, 2.1 Hz, C*H*$_{eq}$HCHOH), 1.46 (d, *J* = 14.2 Hz, 1H, CH*H*$_{ax}$), 2.25 (d, *J* = 3.5 Hz, 1H, C*H*N), 4.04 (ddd, *J* = 11.1, 6.1, 3.6 Hz, 1H, C*H*OH); ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.03, 27.97, 31.22, 31.68, 38.77, 40.42, 42.82, 43.25, 65.83; IR ($CHCl_3$)ν_{max} 3427, 3017, cm^{-1}; HRMS (FAB): *m/z* calc'd for 156.1388, found 156.1389.

***trans*-2-((*E*)-4,8-Dimethyl-3,7-nonadienyl)-3-(hydroxymethyl)-2-methylaziridine (23).** This aziridine was prepared by both Li/NH_3 reduction of *N*-quinazolinyl aziridine **22** (0.99 g, 2.42 mmol) and by hydrolysis of bicyclic aziridine **27b** (0.41 g, 1.56 mmol) as described above for **10**. Purification by flash chromatography (15% MeOH/CH_2Cl_2 as eluent) afforded 383 mg (67%) of **23** from **22** and 257 mg (69 %) of **23** from **27b** as yellow oils: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16, 1.57, 1.58, 1.65 (4s, 3H each, C*H*$_3$), 1.31 (m, 1H, C*H*$_2$), 1.55 (m, 1H, C*H*$_2$), 2.02 (m, 7H, allylic C*H*$_2$ and NC*H*), 2.20 (s, 2H, exch with D_2O, N*H* and O*H*), 3.46 (m, dd upon D_2O exch, *J* = 11.6, 7.2 Hz, 1H, C*H*$_2$OH), 3.73 (dd, *J* = 11.6, 5.2 Hz, 1H, C*H*$_2$OH), 5.06 (m, 2H, C=C*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9. 17.1, 17.6, 24.5, 25.6, 26.5, 39.3, 39.6, 41.4, 43.4, 61.2, 123.1, 124.1, 131.4, 135.7; IR (neat)ν_{max} 3266, 2918, 1450, 1037, 858 cm^{-1}. MS(+)FAB m/z 238.2; HRMS calcd for $C_{15}H_{27}NO$ 238.2172, found 238.2170. Anal. Calcd. for $C_{15}H_{27}NO$: C, 75.89; H, 11.46; N, 5.90. Found: C, 76.03; H, 11.66; N, 6.22.

(*E*)-3,7-Dimethyl-2,6-octadienyl Phenyl Carbonate. The following procedure is based on that reported by Carpino.[35] A solution of PhOCOCl (6.24 g, 5 mL, 40 mmol) in 20 mL of

CH_2Cl_2 was stirred and cooled at 0 °C under N_2 as a 1:1 mixture of geraniol (4.4 g, 5 mL, 28.5 mmol) and freshly distilled $PhNMe_2$ (6.8 g, 7.2 mL, 57 mmol) in anhydrous CH_2Cl_2 (10 mL) was added. After 20 min at rt, the suspension was washed with satd. $NaHCO_3$ (3 x 30 mL), 10% HCl (3 x 30 mL), and brine (3 x 30 mL). The organic layer was dried ($MgSO_4$) and concentrated. Purification by flash chromatography (10% EtOAc/hexanes as eluent) afforded 7.5 g (94%) of the carbonate as an oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.61, 1.68, 1.75 (3s, 3H each, C*H*$_3$), 2.1 (m, 4H, C*H*$_2$C*H*$_2$), 4.77 (d, J = 7.2 Hz, 2H, C*H*$_2$O), 5.09 (m, 1H, C=C*H*), 5.45 (tq, J = 1.6, 6.9 Hz, 1H, C=C*H*), 7.22 (3H, m, Ar*H*), 7.38 (2H, m, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 17.5, 25.5, 26.1, 39.4, 65.2, 117.1, 120.9, 123.5, 125.8, 129.3, 131.7, 143.7, 151.0, 153.6; IR (neat) ν_{max} 1761 (C=O) cm^{-1}. Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.46; H, 8.10.

(*E*)-3,7-Dimethyl-2,6-octadienyl Carbazate. The following procedure is based on that reported by Carpino.[35] The preceding carbonate (2.00 g, 7.3 mmol) was stirred as a neat liquid at rt under N_2 as anhydrous hydrazine (0.25 g, 0.25 mL, 8.0 mmol) was added dropwise. After 5 min the reaction was complete (TLC analysis). Purification by flash chromatography (40 to 50% EtOAc/hexanes as eluent) afforded 1.48 g (96%) of the carbazate as an oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.60, 1.68, 1.71 (3s, 3H each, C*H*$_3$), 2.07 (m, 4H, allylic C*H*$_2$), 3.75 (d, 2H, J = 4.2 Hz, NH_2 exch with D_2O), 4.63 (d, J = 7.0 Hz, 2H, C*H*$_2$O), 5.08 (m, 1H, C=C*H*), 5.34 (t, J = 7.1 Hz, 1H, C=C*H*), 6.04 (s, 1H, NH, exch with D_2O); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1, 17.3, 25.3, 25.9, 39.2, 62.0, 118.1, 123.4, 131.4, 142.0, 158.8; IR (neat) ν_{max} 1713 (C=O) cm^{-1}. Anal. Calcd for $C_{11}H_{20}N_2O_2$: C, 62.23; H, 9.50; N, 13.20. Found: C, 62.27; H, 9.52; N, 13.20.

(*E*)-3,7-Dimethyl-2,6-octadienyl Azidoformate(26a). The following procedure is based on that reported by Carpino.[35] A solution of the preceding carbazate (1.44 g, 6.78 mmol) and acetic acid (0.77 mL, 13.55 mmol) in H_2O (1mL) was stirred and cooled at 0 °C as $NaNO_2$ (0.51g, 7.45 mmol) was added. The solution turned yellow and sodium acetate precipitated. After 5 min, H_2O (1 mL) and ether (3 mL) were added, and the aqueous layer was extracted with ether (3 x 4 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. Purification by flash chromatography (35% EtOAc/hexanes as eluent) afforded 1.06 g (70%) of **21** as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.60, 1.68, 1.72 (3s, 3H each, C*H*$_3$), 2.07 (m, 4H, allylic C*H*$_2$), 4.72 (d, J = 7.4 Hz, 2H, C*H*$_2$O), 5.07 (m, 1H, C=C*H*), 5.39 (tq, J = 1.2, 7.2 Hz, 1H, C=C*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 17.5, 25.5, 26.0, 39.4, 65.1, 116.8, 123.4, 131.8, 144.2, 157.3; IR (neat) ν_{max} 1730 (C=O), 2133 (N_3) cm^{-1}. Anal. Calcd for $C_{11}H_{17}N_3O_2$: C, 59.17; H, 7.68; N, 18.82. Found: C, 59.23; H, 7.70; N, 18.77.

***trans*-6-Methyl-6-(4-methyl-3-pentenyl)-3-oxo-1-azabicyclo[3.1.0]-hexan-2-one (27a). Method A. By irradiation of 26a.** The following procedure is based on that reported by Lwowski.[36] A solution of **26a** (112 mg, 0.50 mmol) in 100 mL of cyclohexane at rt under N_2 was stirred and irradiated at 2537 Å in a quartz flask in aRayonet photochemical reactor. After 30 min (TLC analysis), the solution was concentrated by rotary evaporation. Purification by flash chromatography (35% EtOAc/hexanes as eluent) afforded 17 mg (19%) of **27a** as a pale yellow oil and 73 mg (52 %) of **28** as a colorless oil. Data for **27a**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.39, 1.62, 1.68 (3s, 3H each, C*H*$_3$), 2.1 (m, 4H, C*H*$_2$), 3.05 (dd, J = 2.6, 6.0 Hz, 1H, NC*H*), 4.51 (dd, J = 6.0, 10.1 Hz, 1H, C*H*$_2$O),4.40 (dd, J = 2.2, 10.0 Hz, 1H, C*H*$_2$O), 5.07

(m, 1H, C=C*H*). ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 17.7, 23.7, 25.6, 38.60, 48.9, 51.0, 64.5, 122.7, 132.7, 165.6; IR (neat) ν_{max} 1773 (C=O). Low-resolution EI-MS, *m/z:* 195 (M^+). Data for **28**: ^1H NMR (200 MHz, $CDCl_3$) δ 1.25 (10H, m, 5 CH_2), 1.60, 1.68, 1.70 (3s, 3H each, CH_3), 1.91 (m, 1H, C*H*NH), 2.06 (m, 4H, allylic CH_2), 3.50 (s, 1H, N*H*, exchanges with D_2O), 4.57 (d, J = 7.6 Hz, 2H, CH_2O), 5.09 (m, 1H, C=C*H*), 5.34 (t, J = 8.4 Hz, 1H, C=C*H*).

Method B. By cyclization of the phenyl carbonate. The following procedure is based on that reported by Laurent.[44] A solution of **10** (60 mg, 0.25 mmol) and NEt_3 (77 μL, 56 mg, 0.55 mmol) in ether (5 mL) was stirred and cooled at -5 °C under N_2 as PhOCOCl (35 μL, 43 mg, 0.28 mmol) was added dropwise. The yellow suspension was stirred for 1 h and H_2O (10 mL) was added. The aqueous layer was extracted with EtOAc (3 x 10 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated by rotary evaporation to a yellow oil. A solution of this crude material in dry NEt_3 (10 mL) was stirred and heated at reflux for 1 h under N_2. The brown solution was cooled slowly and partitioned between H_2O (10mL) and EtOAc (20 mL). The aqueous layer was washed with EtOAc (3 x 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. Purification by flash chromatography (50% EtOAc/hexanes as eluent) afforded 45 mg (80% from **10**) of **27a**, the spectra of which were identical to those of the product obtained from method A.

***trans*-6-((*E*)-4,8-Dimethyl-3,7-nonadienyl)-6-methyl-3-oxo-1-azabicyclo[3.1.0]hexan-2-one(27b).** Oxazolidinone **27b** was prepared by both irradiation of azidoformate **26b** (516 mg, 1.77 mmol) in CH_2Cl_2 (200 mL) and by reaction of 2,3-epimino farnesol **23** (60 mg, 0 25 mmol) with PhOCOCl followed by cyclization in NEt_3 as described above for **26a.** Purifications by flash chromatography (40% EtOAc/hexanes as eluent) afforded 72 mg (19%) of **27b** from **26b** and 45 mg (80%) of **27b** from **23** as a yellow oil : ^1H NMR (400 MHz, $CDCl_3$) δ 1.36, 1.57, 1.58, 1.65 (4s, 3H each, CH_3), 1.57 (m, 2H, CH_2) 2.06 (m, 6H, allylic CH_2), 3.04 (dd, J = 6.0, 2.4 Hz, 1H, NC*H*), 4.25 (dd, J = 9.8, 2.4 Hz, 1H, CH_2O),4.48 (dd, J = 9.8, 6.4 Hz, 1H, CH_2O), 5.05 (m, 2H, C=C*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.0,15.9, 17.6, 23.5, 25.6, 26.4, 38.5, 39.5, 48.9, 50.9, 64.5, 122.5, 124.0, 131.3, 136.2, 165.5; IR (neat) ν_{max} 1733 (C=O) cm^{-1}. MS(+)FAB m/z 264.2; HRMS calcd for $C_{16}H_{25}NO_2$ 264.1967, found 264.1963. Azidoformate **26b** (0.618 g, 60%) was prepared in three steps by conversion of farnesol (3.55 g, 15.95 mmol) to the phenyl carbonate and carbazate derivatives followed by nitrosation as described above for **26a.**

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