*Tetrahedron* Vol. 48, No. 7, pp. 1317-1326, 1992
Printed in Great Britain

0040-4020/92 $3.00+.00


# Pyrrolidines and Allylic Amines from Radical-Induced Cleavage of Aziridines

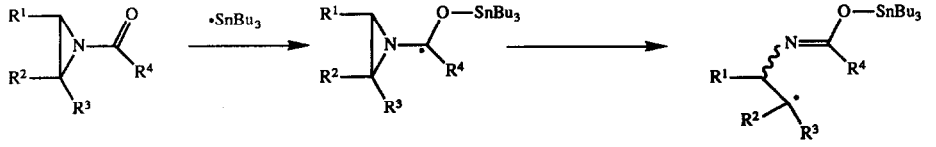
**Julia M. Dickinson and John A. Murphy***

Department of Chemistry, University of Nottingham,
University Park, Nottingham NG7 2RD.

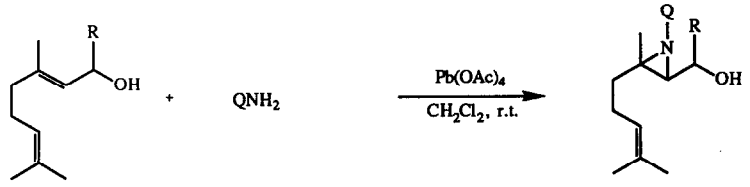
(*Received in UK* 6 *December* 1991)

*Abstract. Cleavage of α-aziridinylalkyl radicals has been observed; the resulting aminyl radicals react with tributyltin hydride to form amines or cyclise onto appropriately sited alkenes to give pyrrolidines.*

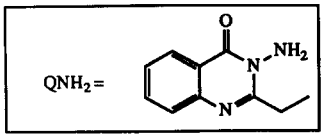
Radical-induced cleavage of epoxides[1] and cyclopropanes[2] has been well explored. In the case of epoxides, cleavage normally occurs to give an alkoxyl radical from which the ultimate products derive. The reaction in which an aminyl radical is generated *via* radical-induced cleavage of an aziridine has not previously been investigated[3] , although acyl aziridines have been subjected to cleavage by Stamm[4] and coworkers as shown below.

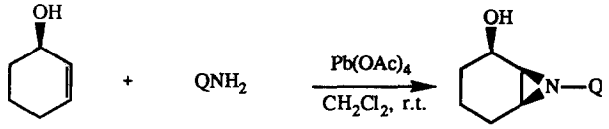



Aminyl radicals have highly interesting properties and have been the subject of a number of recent studies[5], and so we sought a new route to them from opening of aziridines.

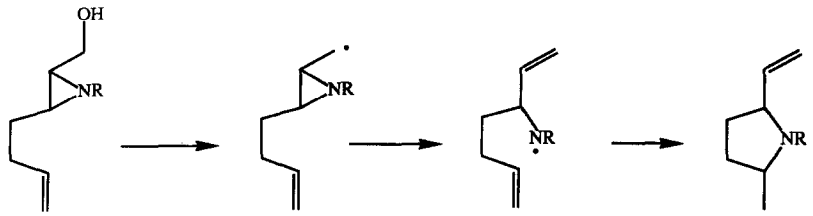



(1) (2) (3)






There has been a lack of general procedures for the synthesis of aziridines which are substituted on the carbon α to the ring with a group suitable for radical formation. Recently, however, Atkinson and coworkers[6a] have discussed the aziridination of geraniol (1, R=H) on reaction with 3-amino-2-ethyl-4(3H)-quinazolinone (2), in the presence of lead tetraacetate, to give (3, R=H) in good yield (76%). The reaction was regioselective. It has also been shown[6b] that, in the reaction of the quinazolinone (2) with allylic alcohols, aziridination is stereoselective. Thus, the hydroxyl group of cyclohex-2-enol appears to act as a "handle" to direct aziridination onto the same face of the molecule as the hydroxyl, and so give high *cis* stereoselectivity. We wished to investigate whether radical-induced C-N bond cleavage of aziridines (5), synthesised by these methods, occurs selectively to give aminyl radicals (6), and whether appropriately substituted cases would lead to cyclization to give pyrrolidines (7).This is by no means certain, since recently a number of cyclisations featuring C-N bond formations have been shown unexpectedly to be reversible[7].

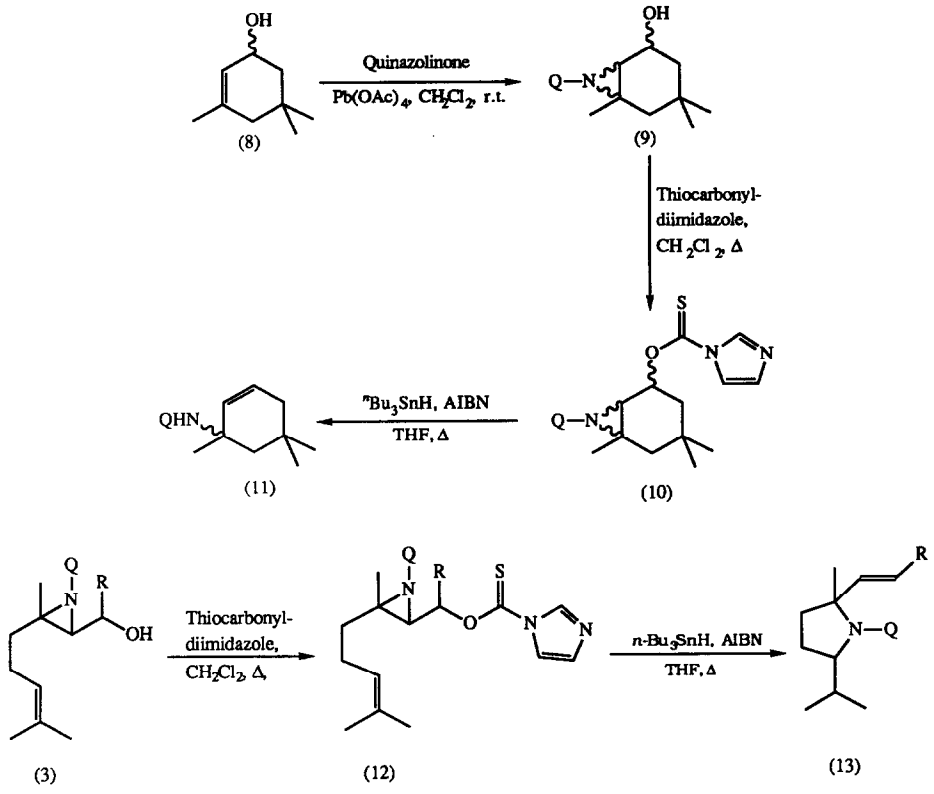



(4) (5) (6) (7)

Isophorol (8) was formed *via* the lithium aluminium hydride reduction of isophorone and was converted to the aziridine (9). Treatment of the thiocarbonylimidazole derivative[1c] (10) with tri-n-butyltin radicals gave the allylic amine (11) in 98% yield confirming that regiospecific formation of allylic amines from allylic alcohols was indeed feasible using this method.

In order to test the cyclisation of aminyl radicals onto alkenes, the aziridine (3, R=H) was synthesised[6a]. The use of trifluoroacetic acid has been reported[8] to improve the yields of aziridine formation in some cases, but this was found not to be so here. In fact, no aziridine was formed at all from geraniol in our hands under such conditions. The thiocarbonylimidazole derivative (12, R = H) was treated with tri-*n*-butyltin radicals to give the required pyrrolidine in 30% yield. The reaction sequence was repeated with the butyl derivative (12, R = Bu). Here, the required pyrrolidine, (13, R = Bu), was afforded in 26% yield.

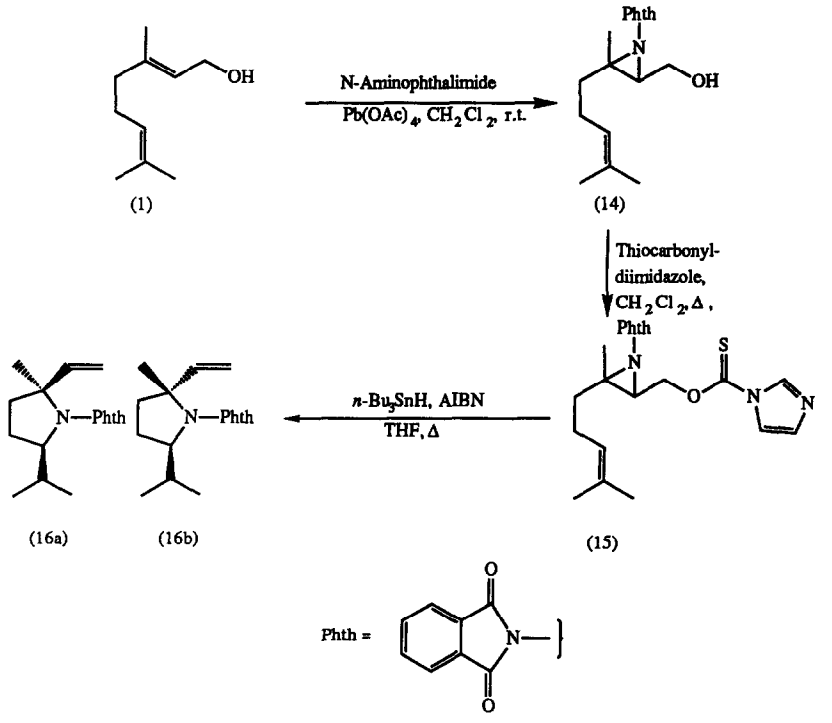
To make these reactions synthetically viable, the yields had to be substantially increased. Surzur[9] has reported that aminyl radical cations (i.e. aminyl radicals complexed with a proton or with a Lewis acid) cyclize much more efficiently onto alkenes than the corresponding neutral aminyl radicals. Hence the thiocarbonylimidazole derivatives (12) of both the geraniol-aziridine (3, R = H) and the butyl analogue (3, R = Bu) were treated with either a protic acid, or a Lewis acid prior to treatment with tri-*n*-butyltin radicals.




Protic acids (sulphuric acid, acetic acid, or trifluoroacetic acid) were found to be unsuitable, as they led to decomposition of the aziridine, giving only base-line products on t.l.c. However, when magnesium bromide etherate, a mild Lewis acid, was used, the yield of the cyclizations improved to 70% for R=H and 83% for R=Bu. In both cases, the Lewis acid was added to the refluxing tetrahydrofuran solution of the aziridine-thiocarbonylimidazolide intermediate, immediately prior to adding the tri-n-butyltin hydride and AIBN. The use of such a mild Lewis acid as magnesium bromide thus transforms the pyrrolidine-forming reaction into a very synthetically efficient process[5].

We have also investigated the comparative efficiency of the phthalimido-aziridine[10] (14) analogous to (3, R=H). The thiocarbonylimidazolide derivative (15) was treated with tri-*n*-butyltin hydride to give pyrrolidine (16) . Purification of the aziridine was not as straightforward as in the quinazolinone cases. Column chromatography on basic alumina gave a mixture of aziridine and geraniol, which could only be separated by preparative t.l.c. The pyrrolidine-forming reaction was performed, both with and without the addition of the Lewis acid, magnesium bromide; strangely, this reaction proceeded better in the *absence* of Lewis acid. In this case, the pyrrolidine (16) was isolated, once again, as a 1:1 mixture of two isomers (16a) and (16b).

These results demonstrate that the radical-induced cleavage of substituted aziridines proceeds well to form the aminyl radicals selectively. These aminyl radicals cyclise to give pyrrolidines. With quinazolinyl aziridines the reaction proceeds efficiently in the presence of the mild Lewis acid, magnesium bromide etherate.




*Experimental Section*

Melting points were carried out on a Kofler hot stage apparatus and are uncorrected. Microanalyses were determined using a Perkin-Elmer 240B elemental analyser. Infrared spectra were obtained on a Perkin Elmer 1720-X FTIR or a Pye-Unicam SP3-100 spectrometer. Ultraviolet spectra were recorded on a Philips PU8700 series instrument. $^1$H n.m.r. spectra were recorded at 90MHz on a Perkin-Elmer R32, at 250MHz on a Bruker WM250 or at 400MHz on a Bruker AM400 spectrometer. $^{13}$C n.m.r. spectra were recorded at 23MHz on a Jeol FX90Q, or at 100MHz on a Bruker AM400 spectrometer. N.m.r. experiments were carried out in deuterochloroform, with tetramethylsilane as internal reference and chemical shifts are quoted in parts per million (δ p.p.m.). The following abbreviations are used for multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br., broad. Coupling constants (*J*) are reported in Hertz (Hz). In the case of ring systems, assignments are made according to the designated numbering system. Mass spectra were recorded on a VG Micromass 70E or an AEI MS902 instrument.

Where necessary, solvents were dried and/or distilled before use. Tetrahydrofuran was distilled from sodium-benzophenone. Chromatography was performed using Sorbsil C60 (May and Baker), Fluka ACT, Kieselgel HF254 or Kieselgel 60 (Art 9385) silica gels.

Preparation of Isophorol (8)

Lithium aluminium hydride (950 mg, 25 mmol) and tetrahydrofuran (50 ml) were stirred under nitrogen, and cooled in ice. Isophorone (3.45 g, 3.75 ml, 25 mmol) in tetrahydrofuran (50 ml) was added slowly dropwise. On completing the addition, the mixture was allowed to warm to room

temperature, and was then heated at reflux overnight. Ethyl acetate (50 ml) was added, followed by 50% aqueous tetrahydrofuran (50 ml). The mixture was concentrated *in vacuo*. The aqueous solution was diluted with 10% hydrochloric acid solution (100 ml), and extracted with ethyl acetate (3 x 100 ml). The combined extracts were washed with water (3 x 100 ml), dried over anhydrous sodium sulphate, and concentrated *in vacuo* to give isophorol (8) as a colourless oil (3.22 g, 92%). (Found: 140.1193. Calc. for $C_9H_{16}O$, 140.1202) $\nu_{max}$ (film): 3 349, 1 708 $cm^{-1}$; $\delta^1H$ ($CDCl_3$): 0.89 and 0.99 (3H, 2 x s, -$C(CH_3)_2$), 1.68 (3H, s, =$CCH_3$), 2.50 (1H, s, -OH), 4.25 (1H, m., -C<u>H</u>OH), 5.43 (1H, m., =CH-); $\delta^{13}C$ ($CDCl_3$): 23.67 ($CH_3$), 26.48 ($CH_3$), 31.25 (C), 31.41 ($CH_3$), 44.47 ($CH_2$), 45.44 ($CH_2$), 66.95 (CH), 124.00 (CH), 135.97 (C). *m/z* (EI): 140 ($[M]^+$, 15%), 125 (67), 122 (35), 107 (100).

<u>Reaction of Isophorol (8) with 3-Amino-2-ethyl-4(3H)-quinazolinone (2) and Lead Tetraacetate</u>

Isophorol (8) (1.40 g, 10 mmol) and 3-amino-2-ethyl-4(3H)-quinazolinone (2) (1.89 g, 10 mmol) were dissolved in dichloromethane (50 ml). Lead tetraacetate (5.2 g, 12 mmol) was added in portions over a period of 10 minutes. The mixture was allowed to stir at room temperature for a further 30 minutes, and was then filtered to remove insoluble lead salts. The filtrate was concentrated *in vacuo* to give a solid which was adsorbed onto basic alumina (1 g), and chromatographed on the same (50 g).

Elution with 10% ethyl acetate in petroleum ether gave the major product as a white solid. Recrystallisation from methanol gave the aziridine (10) as white needles (750 mg, 23%), m.p. 169 - 170 °C. [Found: $(M+H)^+$ 328.2025; $C_{19}H_{26}N_3O_2$ *(M+H)* requires 328.2025]; $\nu_{max}$ (KBr): 3 458, 1 667, 1 595 $cm^{-1}$; $\delta^1H$ ($CDCl_3$): 0.88 (3H, s, -$CH_3$), 0.97 (3H, s, -$CH_3$), 1.21 (3H, s, -$CH_3$), 1.29 (1H, t, *J* = 12 Hz, C<u>H</u>H), 1.31 (3H, t, *J* = 7.3 Hz, -$CH_2C\underline{H}_3$), 1.57 (1H, dd, *J* = 1.8, 14 Hz, C<u>H</u>H-), 1.65 (1H, dd, *J* = 6.3, 12 Hz, C<u>H</u>H-) , 1.85 (1H, d, *J* = 14 Hz, C<u>H</u>H-), 2.81 (1H, dq, *J* = 14, 7.3 Hz, $C\underline{H}_2CH_3$-), 3.04 (1H, dq, *J* = 14, 7.3 Hz, $C\underline{H}_2CH_3$-), 3.12 (1H, d, *J* = 4 Hz, NCH), 4.3(1H, m., -CHOH), 5.02 (1H, d, *J* = 3 Hz, -CHO<u>H</u>), 7.41 (1H, dt, *J* = 8, 1 Hz, Ar-H), 7.64 (1H, d, *J* = , 8 Hz, Ar-H), 7.70 (1H, dt, *J* = 1.2, 7 Hz, Ar-H), 8.15 (1H, dd, *J* = 1, 8 Hz, Ar-H); $\delta^{13}C$ ($CDCl_3$): 10.56 ($CH_3$), 20.96 ($CH_3$), 26.16 ($CH_3$), 28.16 ($CH_2$), 31.25 (C), 31.47 ($CH_3$), 40.46 ($CH_2$), 42.96 ($CH_2$), 53.30 (CH), 53.73 (C), 63.70 (CH), 121.02 (C), 126.17 (CH), 126.27 (CH), 126.98 (CH), 133.80 (CH), 145.99 (C), 158.18 (C), 161.00 (C); *m/z* (FAB): 328 ($[M+H]^+$, 100%), 327 (20), 175 (93).

<u>Reaction of Aziridine (10) with Thiocarbonyldiimidazole Followed by Tri-*n*-butyltin Hydride</u>

Aziridine (10) (250 mg, 0.75 mmol) and thiocarbonyldiimidazole (270 mg, 1.5 mmol, 2 mol. equiv.) in dichloromethane (10 ml) were heated together at reflux with stirring under nitrogen for 4 hours. The mixture was allowed to cool, and the dichloromethane was removed *in vacuo*, to give a yellow solid. This solid was dissolved in tetrahydrofuran (125 ml), and heated at reflux with stirring under nitrogen. Tri-*n*-butyltin hydride (0.58 g, 0.54 ml, 2 mmol) and azobisisobutyronitrile (50 mg) in tetrahydrofuran (30 ml) were added slowly dropwise over a period of 1 hour. On completing the addition, the mixture was heated at reflux overnight.

The reaction mixture was allowed to cool, and then concentrated *in vacuo* to give a brown oil, which was chromatographed on silica (50 g). Elution with 100% petroleum ether removed tin residues. Elution with 10% ethyl acetate in petroleum ether gave the amine (11) as a yellow oil (230 mg, 98%). [Found: $(M+H)^+$ 312.2076; $C_{19}H_{26}N_3O$ *(M+H)* requires 312.2076]; $\nu_{max}$ ($CHCl_3$): 3 286, 1 685, 1 610, 1590 $cm^{-1}$; $\delta^1H$ ($CDCl_3$): 0.99 (3H, s, -$CH_3$), 1.12 (6H, s, $C(CH_3)_2$), 1.31-1.9 (7H, m), 2.90 (1H, m, -CH<u>H</u>$CH_3$), 3.34 (1H, m, -CH<u>H</u>$CH_3$), 5.68 (3H, br.sig., -CH=CH- and -NH-), 7.25 - 7.85 (3H, m, aromatic protons), 8.21 (1H, d, *J* = 7.8 Hz, quinazolinone H-5); $\delta^{13}C$ ($CDCl_3$): 11.54 ($CH_3$), 13.76

($CH_3$), 28.06, 28.44 ($CH_2$), 29.90, 30.33 ($CH_3$), 38.95 ($CH_2$), 48.86 ($CH_2$), 59.75 (C), 120.86 (C), 126.06 (CH), 126.82 (CH), 127.19 (CH), 134.13 (CH), 147.13 (C), 161.43 (C), 163.44 (C); *m/z* (FAB): 312 ($[M+H]^+$, 35%), 175 (16), 123 (100).

Reaction of Geraniol-Aziridine (3, R = H) with Thiocarbonyldiimidazole followed by Tri-*n*-butyltin Hydride

Aziridine (3, R = H) (400 mg, 1.17 mmol) and 1,1'-thiocarbonyldiimidazole (270 mg, 1.5 mmol) were dissolved in dry dichloromethane (50 ml) and were heated at reflux with stirring under nitrogen for 4 hours. The mixture was allowed to cool, and then concentrated *in vacuo* to give a yellow oil. This oil was dissolved in tetrahydrofuran (150 ml) and heated at reflux with stirring under nitrogen. Tri-*n*-butyltin hydride (0.5 ml, 1.5 mmol) and azobisisobutyronitrile (100 mg) in tetrahydrofuran (50 ml) were added slowly dropwise over a period of 1 hour. On completing the addition, the reaction mixture was heated at reflux overnight.

The mixture was allowed to cool, and then concentrated *in vacuo* to give an oil, which was chromatographed on activated basic alumina. Elution with 1% ethyl acetate in petroleum ether gave the required pyrrolidine (13, R = H) , which was contaminated with tin residues. [Further elution with 1% ethyl acetate in petroleum ether gave the starting aziridine (3) (190 mg) as a solid]. The pyrrolidine was rechromatographed on silica. Elution with petroleum ether gave the pyrrolidine (13, R=H), as an oil (83 mg, 21%). [Found: $(M+H)^+$ 326.2241; $(M+H)^+$ $C_{20}H_{28}N_3O$ requires 326.2232]; $\nu_{max}$: 1685, 1595 $cm^{-1}$; $\delta^1H$ ($CDCl_3$): 0.83 (6H, 2 x dd, $-CH(CH_3)_2$), 1.16 (3H, s, $-CH_3$), 1.35 (3H, 2 x t, $-CH_2\underline{CH_3}$), 1.55 - 2.15 (4H, m, pyrrolidine 3-$CH_2$ and 4-$CH_2$), 2.40 - 2.70 (1H, m, $-CH(CH_3)_2$), 3.07 (2H, m, quinazolinone $-CH_2CH_3$), 4.08 (1H, m, pyrrolidine 2-H), 5.01 (2H,m, vinyl-$CH_2$), 6.00 (1H, 2 x dd, vinyl-CH), 7.39 (1H, m, Ar-H), 7.68 (2H, m, Ar-H), 8.20 (1H, m, Ar-H); $\delta^{13}C$ ($CDCl_3$): 11.37 ($CH_3$), 18.09 ($CH_3$), 18.58 ($CH_3$), 20.53 ($CH_3$), 20.63 ($CH_3$), 20.80 ($CH_3$), 25.73 ($CH_2$), 25.83 ($CH_2$), 26.92 ($CH_3$), 27.30 ($CH_2$), 27.78 ($CH_2$), 32.13 (CH), 32.66 (CH), 38.89 ($CH_2$), 68.69 (CH), 69.28(CH), 69.66 (C), 110.78 ($CH_2$), 115.82 ($CH_2$), 122.48 (C), 122.59 (C), 126.06 (CH), 126.17 (CH), 126.82 (CH), 127.19 (CH), 134.13 (CH), 141.06 (CH), 146.54 (CH), 146.91 (C), 162.62, 162.90, 163.11, 163.33 (C); *m/z* (FAB): 326 ($[M+H]^+$, 29%), 173 (20), 152 (79).

Reaction of Geraniol-Aziridine (3, R = H) with Thiocarbonyldiimidazole followed by Magnesium Bromide Etherate and Tri-n-butyltin Hydride

Aziridine (3, R = H) (250 mg, 0.73 mmol) and 1,1'-thiocarbonyldiimidazole (250 mg, 1.4 mmol) were dissolved in dry dichloromethane (10 ml) and were heated at reflux with stirring under nitrogen for 4 hours. The mixture was allowed to cool, and then concentrated *in vacuo* to give a yellow solid. This solid was dissolved in tetrahydrofuran (100 ml) and heated at reflux with stirring under nitrogen. Magnesium bromide etherate (200 mg, 0.77 mmol) was added to the refluxing solution. Tri-n-butyltin hydride (425 mg, 0.4 ml, 1.5 mmol) and azobisisobutyronitrile (50 mg) in tetrahydrofuran (30 ml) were added slowly dropwise over a period of 1 hour. On completing the addition, the reaction mixture was heated at reflux overnight. The mixture was allowed to cool, and then concentrated *in vacuo* to give a yellow oil, which was chromatographed on silica (50 g). Elution with 5% ethyl acetate in petroleum ether gave the pyrrolidine (13, R = H), as an oil (211 mg), which was rechromatographed on silica (10 g). Elution with 2% ethyl acetate in petroleum ether gave the pyrrolidine (13, R = H) as a colourless oil (166 mg, 70%), free from tin residues. Spectral data were identical to those previously obtained.

Reaction of Citral with *n*-Butyllithium

Citral (5.0 g, 33 mmol) was dissolved in tetrahydrofuran (100 ml) and the mixture was cooled to

-78 °C, and stirred under nitrogen. *n*-Butyllithium (25 ml, 1.6 M solution in hexane, excess) was added slowly dropwise. On completing the addition, the mixture was stirred at -78 °C for 15 minutes, and was then allowed to warm to room temperature and stirred for a further 1 hour.

Saturated ammonium chloride solution was added to destroy excess butyllithium, and the mixture was concentrated *in vacuo* to remove tetrahydrofuran. The aqueous solution was diluted with water (100 ml) and extracted with ethyl acetate. The extracts were washed with water, dried over anhydrous sodium sulphate, and concentrated *in vacuo* to give a red oil which was distilled at reduced pressure. 7,11-Dimethyldodeca-6,10-dien-5-ol (1, R = Bu) was collected as a yellow oil at 110 - 112 °C/4 mmHg (4.40 g, 63%). [Found: $(M)^+$ 210.1973; $(M)$ $C_{14}H_{26}O$ requires 210.1984]; $\nu_{max}$ (film): 3 345 (br.), 1 669 $cm^{-1}$; $\delta^1H$ ($CDCl_3$): 0.65 - 1.10 (3H, br t, -$(CH_2)_3\underline{CH_3}$), 1.15 - 1.5 (6H, m, -$(\underline{CH_2})_3CH_3$), 1.6 (3H, s, $CH_3$), 1.65 (6H, s, 2 x Me), 1.90 - 2.20 (4H, m, $CH_2$, $CH_2$), 4.20 - 4.40 (1H, br s, -$\underline{CH}$(OH)-), 5.00 - 5.25 (2H, br. m., =CH); $\delta^{13}C$ ($CDCl_3$): 14.08 ($CH_3$), 16.57, 17.65 ($CH_3$), 22.86, 23.34 ($CH_3$), 25.67 ($CH_3$), 26.59, 26.76 ($CH_2$), 27.73, 27.89 ($CH_2$), 32.45 ($CH_2$), 37.65 ($CH_2$), 39.76 ($CH_2$), 68.20, 68.63 (CH), 124.22 (CH), 128.66, 129.63 (CH), 131.47, 132.12 (C), 137.87, 138.19 (C); *m/z* (EI): 210 (*M*, 1%), 192 (4), 69(100).

Reaction of 7,11-Dimethyldodeca-6,10-dien-5-ol (1, R = Bu) with 3-Amino-2-ethyl-4(3H)-quinazolinone (2) and Lead Tetraacetate

7,11-Dimethyldodeca-6,10-dien-5-ol (1, R = Bu) (4.40 g, 21 mmol) and 3-amino-2-ethyl-4(3H)-quinazolinone (2) (4.0 g, 21 mmol) were dissolved in dichloromethane (100 ml), and the mixture was stirred at room temperature. Lead tetraacetate (11.1 g, 25 mmol) was added in portions over a period of 10 minutes. On completing the addition, the mixture was stirred for a further 1 hour.

The mixture was filtered to remove insoluble lead salts, and the filtrate was concentrated *in vacuo* to give a solid which was chromatographed on activated basic alumina.

Elution with 2% ethyl acetate in petroleum ether gave a mixture of starting material, the desired product (3, R=Bu), and the deaminated quinazolinone. This mixture was dissolved in hot methanol to give, on cooling, 2-ethyl-4(3H)-quinazolinone as white crystals, which were collected by filtration.

The filtrate was concentrated *in vacuo* to give an oil, which was chromatographed on activated basic alumina. Elution with 2% ethyl acetate in petroleum ether gave a mixture of starting material and the major product. This mixture was rechromatographed on activated basic alumina. Elution with 1% ethyl acetate in petroleum ether gave the aziridine (3, R = Bu) as an oil (4.34 g, 51%). [Found: $(M+H)^+$ 398.2808. $(M+H)C_{24}H_{36}N_3O_2$ requires 398.2808]; $\nu_{max}$: 3 446, 1 662, 1 596 $cm^{-1}$; $\delta^1H$ ($CDCl_3$): 0.90 (3H, t, $J$ = 6 Hz, butyl-$CH_3$), 1.00 - 2.20 ( 22H, m), 2.60 - 3.20 (3H, m, aziridine proton and quinazolinone - $C\underline{H_2}CH_3$), 3.50 (1H, m, -$\underline{CH}$OH), 4.35 (1H, br, -CHO$\underline{H}$), 5.13 (1H, br.t., =$\underline{CH}CH_2$-), 7.25 - 7.70 (3H, m, quinazolinone aromatic protons), 8.19 (1H, d, $J$ = 7.5 Hz, quinazolinone H-5); $\delta^{13}C$ ($CDCl_3$): 10.67 ($CH_3$), 14.08 ($CH_3$), 17.33 ($CH_3$), 17.65 ($CH_3$), 22.86 ($CH_2$), 25.62 ($CH_3$), 27.35 ($CH_2$), 27.84 ($CH_2$), 34.77 ($CH_2$), 35.15 ($CH_2$), 54.93, 56.01 (C), 57.91, 58.77 (CH), 70.31, 70.47 (CH), 121.07 (C), 122.54 (CH), 123.08 (CH), 124.11 (CH), 126.33 (CH), 126.92 (CH), 132.94 (C), 133.86 (CH), 145.94 (C), 157.86 (C), 161.38 (C); *m/z* (FAB): 398 ($[M+H]^+$, 20%), 175 (100).

Reaction of aziridine (3, R = Bu) with 1,1-Thiocarbonyldiimidazole followed by Tri-*n*-butyltin Hydride

Aziridine (3, R = Bu) (2.00 g, 5.1 mmol) was dissolved in dichloromethane (100 ml), and thiocarbonyldiimidazole (3 g, 17 mmol) was added. The mixture was heated at reflux with stirring under nitrogen for 2 hours, then allowed to cool, and concentrated *in vacuo* to give a yellow solid. This solid was dissolved in tetrahydrofuran (100 ml), and the mixture was heated at reflux with stirring under

nitrogen. Tri-*n*-butyltin hydride (2.67g, 2.5 ml, 9.34 mmol ) and azobisisobutyronitrile (200 mg) in tetrahydrofuran (50 ml) were added slowly over a period of one hour. On completing the addition, the mixture was heated at reflux for a further 40 hours. At this stage the reaction did not appear to have initiated, and so azobisisobutyronitrile (100 mg) and tri-*n*-butyltin hydride (1 ml) were added, and the mixture was heated at reflux for a further 10 hours. The mixture was allowed to cool, and concentrated *in vacuo* to give an orange oil, which was chromatographed on silica. Elution with 100% petroleum ether gave the major product, contaminated with tin residues. These tin residues were removed by rechromatographing on silica, and eluting with petroleum ether. The pyrrolidine (13, R = Bu) was obtained as an oil (510 mg, 26%). [Found: $(M+H)^+$ 382.2858; $(M+H)^+$ $C_{24}H_{36}N_3O$ requires 382.2858]; $\nu_{max}$: 1 685, 1 596 $cm^{-1}$; $\delta^1H$ ($CDCl_3$): 0.90 - 1.75 ( 26H, m), 3.00 - 3.20 (2H, m, $\underline{CH_2}CH_3$), 4.08 (1H, m, N-CH-), 5.49 (2H, m, olefinic protons), 7.25 - 7.70 (3H, m, Ar-H), 8.10 - 8.25 (1H, m, Ar-H); $\delta^{13}C$ ($CDCl_3$): 11.16, 11.26 ($CH_3$), 13.59, 13.92 ($CH_3$), 17.65, 17.93 ($CH_3$), 20.36, 20.47 ($CH_3$), 21.34, 21.77 ($CH_2$), 22.26, 22.69 ($CH_2$), 25.51, 25.67 ($CH_2$), 27.19, 27.73 ($CH_2$), 27.46 ($CH_3$), 31.25, 31.85 ($CH_2$), 32.07, 32.23 (CH), 39.16, 39.27 ($CH_2$), 68.09, 68.36 (CH), 68.69, 69.34 (C), 122.43, 122.54 (C), 125.68, 125.84 (CH), 126.71 (CH), 127.03, 127.14 (CH), 132.23 (CH), 133.05 (CH), 133.64, 133.86 (CH), 138.35 (CH), 146.86 (C), 162.57, 162.68, 162.84, 163.22 (C); *m/z* (FAB): 382 ($[M+H]^+$, 41%), 208 (100), 175 (31).

Reaction of Aziridine (3, R = Bu) with Thiocarbonyldiimidazole followed by Magnesium Bromide Etherate and Tri-*n*-butyltin Hydride

Aziridine (3, R = Bu) (290 mg, 0.73 mmol) and 1,1'-thiocarbonyldiimidazole (250 mg, 1.4 mmol) were dissolved in dry dichloromethane (10 ml) and were heated at reflux with stirring under nitrogen for 4 hours. The mixture was allowed to cool, and then concentrated *in vacuo* to give a yellow solid. This solid was dissolved in tetrahydrofuran (100 ml) and heated at reflux with stirring under nitrogen. Magnesium bromide etherate (200 mg, 0.77 mmol) was added to the refluxing solution. Tri-*n*-butyltin hydride (425 mg, 0.4 ml, 1.5 mmol) and azobisisobutyronitrile (50 mg) in tetrahydrofuran (30 ml) were added slowly dropwise over a period of 1 hour. On completing the addition, the reaction mixture was heated at reflux overnight. The mixture was allowed to cool, and then concentrated *in vacuo* to give a yellow oil, which was chromatographed on silica (50 g).with 5% ethyl acetate in petroleum ether gave the pyrrolidine (13, R = Bu) , as an oil, which was rechromatographed on silica (20 g). Elution with 2% ethyl acetate in petroleum ether gave the pyrrolidine (13, R=Bu) as a colourless oil (230 mg, 83%), free from tin residues. Spectral data were identical to those previously obtained.

Reaction of Geraniol (1, R = H) with N-Aminophthalimide and Lead Tetraacetate

N-Aminophthalimide (2.11 g, 13 mmol) and geraniol (1, R = H) (2.03 g, 13 mmol) in dichloromethane (25 ml) were stirred together at room temperature. Lead tetraacetate (6.50 g, 15 mmol) was added in portions over a period of 10 minutes. The mixture was stirred at room temperature for a further 15 minutes. The mixture was filtered to remove insoluble lead salts, and the filtrate was concentrated *in vacuo* to give a which was adsorbed onto basic alumina (5 g), and chromatographed on the same (100 g). Elution with 10% ethyl acetate in petroleum ether removed unreacted geraniol. Elution with 20% ethyl acetate in petroleum ether gave the required product, as a mixture with some unreacted geraniol. Attempts at crystallization of the product were unsuccessful, and so the mixture was separated by preparative layer chromatography (50% ethyl acetate in petroleum ether) to give the required product (15), as a yellow oil, (800mg, 20%). (Found: $[M + H]^+$ 315.1702, $C_{18}H_{22}N_2O_3$ requires $[M + H]^+$ 315.1709). $\nu_{max}$ (neat): 3 473 (br), 1 714, 1 611 $cm^{-1}$; $\delta^1H$ ($CDCl_3$): 1.42 (3H, s, $-CH_3$), 1.58, 1.65

(6H, 2 x s, $=C(CH_3)_2$), 1.95 - 2.25 (4H, m, $-CH_2CH_2-$), 2.74 (1H, dd, $J$ = 8.7 Hz, 3.4 Hz, aziridine-H), 3.45 (1H, br s, $CH_2-O\underline{H}$), 3.69 (1H, dd, $J$ = 11.6 Hz, 8.7 Hz, $-C\underline{H}OH$), 3.96 (1H, dd, $J$ = 11.6 Hz, 3.4 Hz, $-C\underline{H}OH$), 5.02 (1H, br.t., $J$ = 5.5 Hz, $=CH-CH_2-$), 7.65 - 7.80 (4H, m, Ar-H); $\delta^{13}C$ ($CDCl_3$): 17.82 ($CH_3$), 25.56 ($CH_2$), 25.83 (2 x $CH_3$), 35.21 ($CH_2$), 51.46 (C), 54.55 (CH), 61.64 ($CH_2$), 123.29 (2 x CH), 130.99 (C), 132.72 (C), 134.35 (CH), 166.42 (C); *m/z* (FAB) (MNBA): 315 $[M + H]^+$(19%), 215 (43), 163 (62), 148 (30), 83 (50), 81 (75), 69 (99), 57 (100).

Reaction of Geraniol/Aziridine-Phthalimide (15) with Thiocarbonyldiimidazole Followed by Tri-*n*-butyltin Hydride

The aziridine (15) (600 mg, 1.9 mmol) and thiocarbonyldiimidazole (750 mg, 4.2 mmol) in dichloromethane (10 ml) were heated together at reflux with stirring under nitrogen for 2 hours. The mixture was allowed to cool, and then concentrated *in vacuo* to remove all traces of dichloromethane. The yellow solid thus obtained was dissolved in tetrahydrofuran (200 ml), and the mixture was heated at reflux with stirring under nitrogen. Tri-*n*-butyltin hydride (1.5 ml, 5.7 mmol) and azobisisobutyronitrile (100 mg) in tetrahydrofuran (50 ml) were added slowly over a period of 2 hours. On completing the addition, heating was continued overnight.

The mixture was allowed to cool, and was concentrated *in vacuo* to give a dark brown oil. The oil was dissolved in ethyl acetate (100 ml), and washed with 10% ammonia solution (3 x 50 ml), and water (2 x 50 ml). The organic phase was dried over anhydrous sodium sulphate, and concentrated *in vacuo* to give a brown oil, which was chromatographed on silica (50 g).

Elution with 2% ethyl acetate in petroleum ether gave the major product as a yellow oil, which was contaminated with some tin residues. Rechromatographing on silica (10 g), and eluting with 100% petroleum ether gave the required pyrrolidine (16) as a pale yellow solid (93 mg, 16%), m.p., 84-85 °C. (Found: $[M]^+$ 299.1760. $C_{18}H_{22}N_2O_2$ requires $[M]^+$ 299.1760); $\delta^1H$ ($CDCl_3$): 0.84 (3H, d, $J$ = 6.8 Hz, isopropyl $-CH_3$), 0.90 (3H, 2 x d, $J$ = 6.8, 2.1 Hz, isopropyl $-CH_3$), 1.23, 1.34 (3H, 2 x s, $-CH_3$), 1.40 - 2.00 (5H, m, pyrrolidine $-CH_2CH_2-$ and isopropyl -CH), 4.05 (1H, m, pyrrolidine -CH), 5.00 (2H, m, $-CH=CH_2$), 6.10 (1H, 2 x dd, $-CH=CH_2$), 7.70 - 7.85 (4H, m, phthalimide aromatic protons); $\delta^{13}C$ ($CDCl_3$): 16.36, 16.66 ($CH_3$), 19.29, 19.40 ($CH_3$), 20.57, 24.64 ($CH_3$), 23.13, 23.40 ($CH_2$), 30.51, 30.90 (CH), 37.10, 37.30 ($CH_2$), 64.56, 64.60 (CH), 67.74, 68.01 (C), 112.99, 113. 63 ($CH_2$), 122.71, 122.78 (CH), 123.29, 123.33 (CH), 129.87, 130.01 (C), 130.12, 130.31 (C), 134.01 (CH), 134.06 (CH), 141.83 (CH), 145.85 (CH), 168.19, 168.27 (C), 168.90, 169.12 (C); *m/z* (FAB) (MNBA): 299 $[M]^+$(61%), 255 (100), 163 (40), 130 (21), 93 (88), 81 (93).

*Acknowledgements*. We thank the SERC for support, and the SERC Mass Spectrometry Service, Swansea for high resolution FAB spectra.

References.

1. (a) E. C. Sabbatino and R. J. Gritter, *J. Org. Chem.*, **1963**, *28*, 3437; (b) R. G. Carlson, J. H. A. Huber and D.E. Henton, *J. Chem. Soc., Chem. Comm.*, **1973**, 223; (c) D. H. R. Barton, R. S. H. Motherwell and W. B. Motherwell, *J. Chem.Soc., Perkin Trans. I*, **1981**, 2363; (d) A. Johns and J. A. Murphy, *Tetrahedron Letters*, **1988**, *29*, 837; (e) A. Johns, J. A. Murphy, C. W. Patterson and N. F. Wooster, *J. Chem. Soc., Chem. Comm.*, **1987**, 1238; (f) J. A. Murphy and C. W. Patterson and N. F. Wooster, *J. Chem. Soc., Chem. Comm.*, **1988**, 294;
2. A. L. J. Beckwith and K. U. Ingold, in Free Radical Rearrangements, Ed. P. de Mayo, Academic Press, New York, 1980, vol. 1, pp. 161-310; for recent applications, seeK. S. Feldman, R. E.

Ruckle, Jr., and A. L. Romanelli, *Tetrahedron Lett.*, **1989**, *30*, 5845; D. L. J. Clive and S. Daigneault, *J. Chem. Soc., Chem. Comm.*, **1989**, 332;

3. For a preliminary account of this work, see J. M. Dickinson and J. A. Murphy, *J. Chem. Soc., Chem. Comm.*, **1990**, 434;
4. J. Werry, H. Stamm, P.-Y. Lin, R. Falkenstein, S. Gries and H. Irngartinger, *Tetrahedron*, **1989**, *45*, 5015; H. Stamm, P. Assithianakis, B. Buchholz and R. Weiss, *Tetrahedron Lett.*, **1982**, *23*, 5021; H. Stamm, P. Assithianakis, R. Weiss, G. Bentz and B. Buchholz, *J. Chem. Soc., Chem. Comm.*, **1984**, 753; D. Archier-Jay, N. Besbes, A. Laurent, E. Laurent, H. Stamm and R. Tardivel, *Tetrahedron Lett.*, **1989**, *30*, 2271;
5. M. Newcomb, T. M. Deeb and D. J. Marquardt, *Tetrahedron*, **1990**, *46*, 2317; M. Newcomb, D. J. Marquardt and T. M. Deeb, *Tetrahedron*, **1990**, *46*, 2329; M. Newcomb, D. J.Marquardt and M. U. Kumar, *Tetrahedron*, **1990**, *46*, 2345; M. Newcomb and M. U. Kumar, *Tetrahedron Letters*, **1990**, *31*, 1675;
6. (a) R. S. Atkinson and B. J. Kelly, *J. Chem.Soc., Chem. Comm.*, **1988**, 624; (b) R. S. Atkinson, B.J. Kelly and C. McNicolas, *J. Chem.Soc., Chem. Comm.*, **1989**, 563;
7. M. Newcomb and T. M. Deeb, *J. Amer. Chem. Soc.*, **1987**, *109*, 3163;
8. R. S. Atkinson, C. M. Darrah and B. J. Kelly, *Tetrahedron Letters*, **1987**, *28*, 1711;
9. J.-M. Surzur in 'Reactive Intermediates', vol. 2, ed., R. A. Abramovitch, Plenum Press, New York, 1982, p.168;
10. R. K. Müller, R. Joos, D. Felix, J. Schreiber, C. Wintner and A. Eschenmoser, *Org. Synth.*, **1976**, *55*, 114;