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Cascade Radical Cyclisations of Imines

W. Russell Bowman,*[a] Peter T. Stephenson,[b] and Adrian R. Young[a]

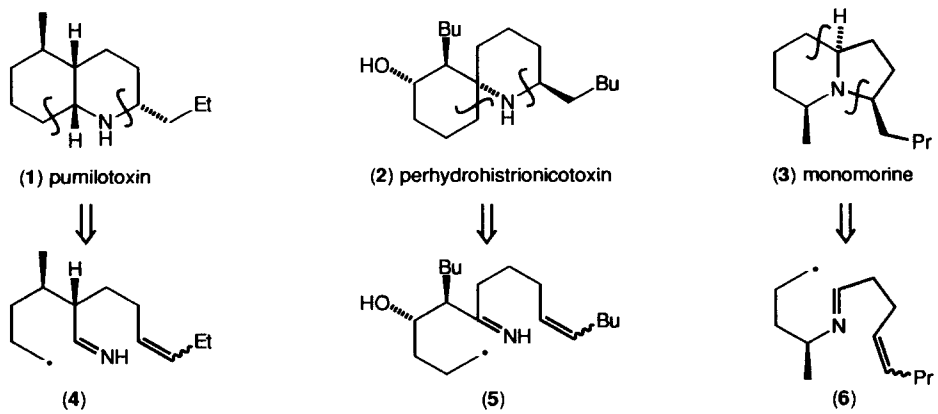
[a] Department of Chemistry, Loughborough University, Loughborough, Leics. LE11 3TU, Great Britain

[b] Department of Discovery Chemistry, Pfizer Central Research, Sandwich, Kent CT13 9NJ, Great Britain

Abstract: *Cascade radical reactions, initiated by cyclisation of* sp^3 *carbon-centred radicals onto the C-atom of imines, have been used to develop a new protocol for the synthesis of a range of nitrogen heterocycles. The C-centred radical intermediates were generated from benzeneselenyl precursors using* Bu_3SnH. *The aminyl radicals generated by cyclisation onto imines undergo further 5- or 6-exo cyclisation with suitably placed alkenes.*

In continuation of our studies of the synthesis of nitrogen heterocycles of pharmaceutical interest using radical methodology, we have developed the use of radical cyclisation onto imines in cascade reactions. Three important target molecules were chosen initially: pumilotoxin **1**, perhydrohistrionicotoxin **2** and monomorine **3**. The putative retrosyntheses to initial radical intermediates, **4**, **5** and **6**, respectively, are shown in Scheme 1. Each route involves two key steps using radicals: (a) cyclisation of a *C*-centred radical onto an imine, and (b) cyclisation of an intermediate aminyl radical onto an alkene. In the overall protocol it was envisaged that the synthesis of the imines from the respective aldehydes or ketones and amines and the cascade radical reactions could be carried out in a 'one-pot' reaction, *e.g.* formation of the imine in refluxing toluene using a Dean-Stark water separator followed by addition of Bu_3SnH and AIBN using a syringe pump. This general methodology would provide an advance in the drive towards 'clean technology' in modern organic chemistry, *i.e.* a large number of synthetic manipulations carried out with only one purification of products, thereby cutting down waste. Our preliminary studies of the radical cyclisation of imines[1] and syntheses using tandem cyclisations[2] have been published. In this paper we report the full details of our studies of model cascade radical reactions towards to syntheses of pumilotoxin **1**, perhydrohistrionicotoxin **2** and monomorine **3**.

Scheme 1



At the time of commencing our studies, there were only a few individual examples of radical reactions involving imines.[3] Shortly after our start, the first major study of the addition of radicals onto imines reported that aryl radical additions proceeded predominantly by 6-*endo* cyclisation.[4] These studies clearly indicated that radical cyclisation onto imines was synthetically useful which has been further elucidated by our studies. Further examples of the use of the cyclisation of aryl radicals onto imines have since been reported.[5]

As modern free radical chemistry develops, the range of unsaturated groups that undergo radical addition[6] continues to grow suggesting that radical addition to unsaturated functional groups can be expected as the norm. The application of the addition of radicals onto thiocarbonyl bonds in the development of synthetic methods has been exploited by several groups, notably by Barton and co-workers.[7] Similarly, the addition of radicals to aldehydes and ketones is now commonly used in synthetic methods.[8] Recent reports indicate that most C=N functional groups undergo radical addition, *e.g.* hydrazones,[1,9] pyridinium and related azahetero-arene salts,[10] nitronates ($R_2C{=}NO_2^-$),[11] and oxime-ethers ($R_2C{=}NOR$).[12] Radical additions to other multiple bonds containing nitrogen include azides,[13] diazirines,[14] diazenes (N=N)[15] and nitriles.[16]

Our earlier studies have indicated that 5- and 6-*exo* cyclisations of weakly nucleophilic sp^3-*C* centred radicals onto the electrophilic *C*-atom of the imine moiety are facile. Although rates of cyclisation have not been measured, the rates of the equivalent cyclisations onto *N,N*-diphenyl hydrazones[9c] are considerably faster (5-*exo*: *ca.* 10^8 and 6-*exo*: *ca.* 10^6) than the cyclisation onto alkenes, *i.e.* 5-hexenyl and 6-heptenyl radicals. With the same polarity as hydrazones, similar fast rates are expected for imines. Substitution on the *C*-atom of the imine (ketimines) is not unfavourable for cyclisation as is observed for equivalent substitution in alkene cyclisations, probably due to the faster rates of cyclisation.

The second cyclisation in the cascade sequence entails aminyl radicals. The cyclisation of aminyl radicals has been extensively studied in recent years by our group[17] and Newcomb and co-workers[18] and they have been generated from several precursors; sulfenamides,[17] *N*-hydroxypyridine-2-thione carbamates,[18] *O*-acylhydroxamic acids[19] and azides.[20]

Radical precursors and general methodology

ω-Benzeneselenyl groups were selected as the precursors for generating the initial *C*-centred radicals because they are inert to most synthetic transformations and unlike the more commonly used halogenoalkanes do not give unwanted reactions with the amino or imino groups.[9a] Benzeneselenyl groups are rapidly abstracted by $Bu_3Sn^\bullet$ radicals to generate alkyl radicals, *e.g.* the rate of abstraction of PhSe by $Bu_3Sn^\bullet$ radicals from $PhSeCH_2CO_2Et$ is 1.0×10^5 M^{-1} s^{-1} at 50 °C.[21]

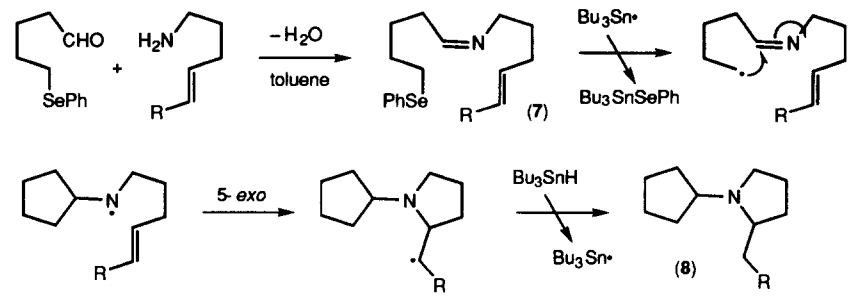
The synthetic building blocks developed in our monocyclisation studies with imines[1] (ω-benzeneselenylalkyl-aldehydes and -alkylamines) were used as far as possible. Certain synthetic schemes (*e.g.* **4** to **1** and **5** to **2**, Scheme 1) requiring primary aminyl intermediates necessitate use of primary imines which are generally unstable. The problem was avoided by using imines of phenylethyl- and benzyl-amine. The phenylethyl and benzyl groups could be easily removed from potential product amines. The formation of imines was carried out as the penultimate step prior to radical cyclisation in order to facilitate 'one-pot' reactions. Imines were formed in quantitative yields and once characterised were used without isolation. The radical reactions were carried out by slow addition of Bu_3SnH and catalytic AIBN to a solution of the imine in toluene at 80-110 °C using a syringe pump. The imine formation - radical cyclisation reactions were not optimised. In cases where the yields of cascade cyclisations were unsatisfactory, a Lewis acid, $MgBr_2.Et_2O$, was added.

***N*-Cycloalkylpyrrolidines**

The simple system shown in Scheme 2 was initially studied in order to determine the feasibility of the cascade radical cyclisation methodology. The cascade reactions of imines **7a** and **7b** gave 2-benzyl-*N*-cyclopentylpyrrolidine **8a** (62%) and 2-methyl *N*-cyclopentylpyrrolidine **8b** (32%) in reasonable yield. Imine **7b** also yielded small amounts of monocyclised product indicating that the aminyl radical cyclisation is less efficient when R = H instead of phenyl in imine **7**. The radical monocyclisations[1] of *N*-(5-benzeneselenylpent-1-ylidine)amines analogous to **7** proceed in good yields (40-75%) with no uncyclised products, therefore the first cyclisation step is expected. Likewise, the cyclisation of 5-phenylpent-4-enylaminyl radicals undergo

Scheme 2

a, R = Ph
b, R = H



high yielding cyclisation[17] and therefore the tandem cyclisation of **7a** is predicted. However, the 5-*exo* cyclisation of 4-pentenylaminyl radicals is reversible with the same rate of cyclisation and ring opening,[18] and low yields of cyclisation are observed.[17,18] Therefore, for imine **7b** the first cyclisation is predicted but the second is not. The reason for the more efficient cyclisation of the aminyl radical in the tandem reaction compared to the equivalent monocyclisation is not clear. Electrophilic aminyl radicals (amidyls, aminium radicals) cyclise in high yield[18] suggesting that some Lewis acid may be present which confers electrophilic behaviour to the intermediate aminyl radical. Evidence has been presented indicating that impurities in commercial Bu_3SnH are able to act as Lewis acids in the cyclisations of aminyl radicals.[22]

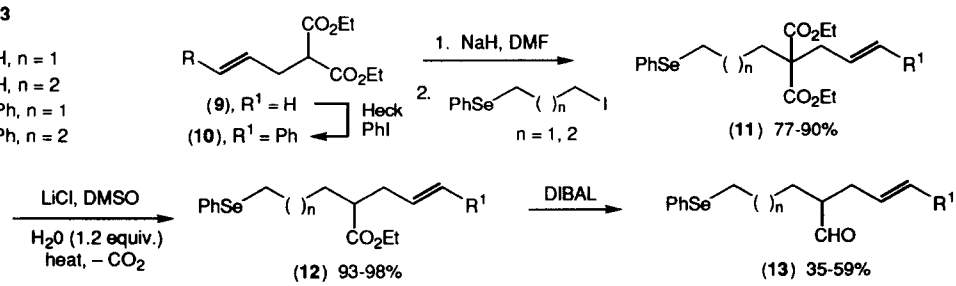
The cyclisation onto the *C*-atom of imines as shown in Scheme 2 provides a further method for the generation of aminyl radicals. In order to generate an intermediate aminyl, a primary amine can be reacted with 5-benzeneselenylpentanal to form the imine, and reacted with Bu_3SnH, *i.e.* the whole procedure from amine to cyclisation carried out in 'one pot'. The procedure is facile but leaves a cyclopentyl moiety attached to the amine. Methods for improvement and exploitation of this protocol for generating aminyls are underway.

2-Azabicyclo[3.3.0]octanes and perhydroindolines

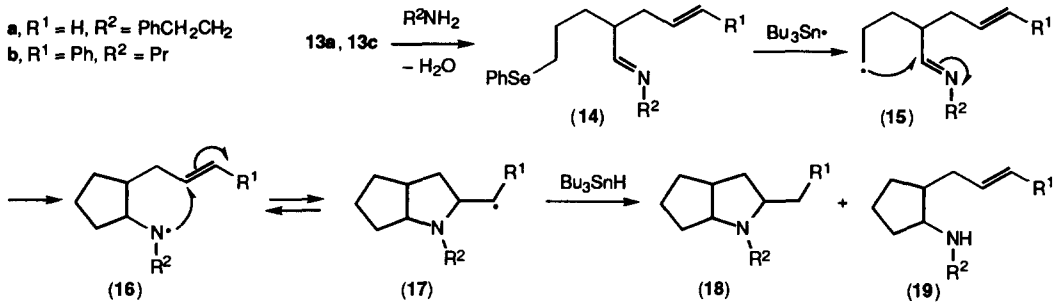
In the investigation of the protocol required for the cascade reactions in the synthesis of pumilotoxin **1** (Scheme 1, **4** to **1**), a range of imine radical precursors were prepared in order to study the following cascade reactions: 5-*exo*, 5-*exo* (2-azabicyclo[3.3.0]octanes), 6-*exo*, 5-*exo* (perhydroindolines), 5-*exo*, 6-*exo* (2-azabicyclo[4.3.0]nonanes), and 6-*exo*, 6-*exo* (2-azabicyclo[4.4.0]decanes). The required aldehydes were prepared as shown in Scheme 3. In the malonate alkylations (**9** and **10** to **11**), alkyl iodides had to be used in order to get satisfactory yields. The malonate esters **11** were ethoxy-decarboxylated in high yield using LiCl in hot DMSO, and the resulting monoesters **12** reduced with DIBAL in reasonable yields to the required aldehydes **13**. The syntheses of the required precursors for the 5-*exo*, 6-*exo* and 6-*exo*, 6-*exo* cyclisations (3-butenyl and 4-phenyl-3-butenyl side chains) were also attempted but the DIBAL reduction step could not be satisfactorily carried out and the corresponding alcohol was the main product in each case. It appears that the position of the double bond is the problem in the DIBAL reduction. Re-oxidation of the alcohols back to the required aldehydes also proved unsatisfactory. Alternative routes of synthesis are underway. The imines were formed *in situ* from the aldehydes by stirring with 4 Å molecular sieves in toluene for 24 h.

Scheme 3

a, R^1 = H, n = 1
b, R^1 = H, n = 2
c, R^1 = Ph, n = 1
b, R^1 = Ph, n = 2



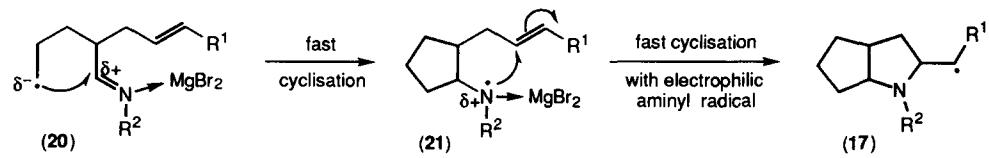
Scheme 4



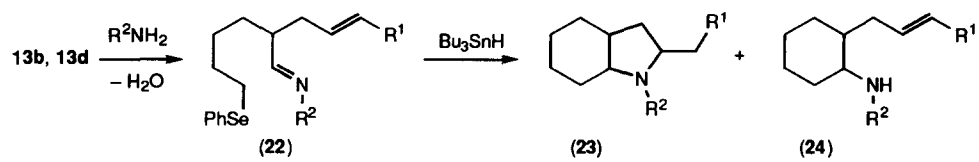
The radical cyclisation reaction of the imine **14a** gave both monocyclised **19a** (23%) and bicyclised **18a** (27%) products indicating that the first cyclisation of **15a** to **16a** takes place efficiently but that equilibration between the aminyl radical **16a** and bicyclised radical **17a** is a problem. In contrast, the imine **14b** yields only the bicyclised product **18b** (40%). This observation is in keeping with our studies of the cyclisation of aminyl radicals.[17] When a phenyl group is present on the alkene the intermediate bicyclised radical **17b** is benzylic and therefore stabilised thus facilitating efficient cyclisation of the intermediate aminyl radical **16b**. 5-*exo* Cyclisation is favoured as predicted with the initial weakly nucleophilic *C*-centred radical in **15** adding to the electrophilic *C*-atom of the imine. 5-*exo* Cyclisation of the aminyl was also as predicted. The stereochemistry of products was not determined but only one diastereoisomer was observed in both reactions.

In order to overcome the problem of reversibility, a Lewis acid ($MgBr_2.Et_2O$) was added prior to the addition of Bu_3SnH. The use of $MgBr_2.Et_2O$ has proved successful in the cyclisation of intermediate aminyl radicals generated by ring-opening of aziridinylcarbinyl radicals by imparting electrophilic behaviour to the aminyl radical.[23] When $MgBr_2.Et_2O$ was added to the reaction of imine **14a**, the yield of bicyclised product **18a** was 35% and no monocyclised material **19a** was detected. We propose, as shown in Scheme 5, that the Lewis acid initially complexes with the imine *N*-atom imparting enhanced electrophilic character to the imine **20** thereby facilitating faster cyclisation. The Lewis acid remains bonded to the *N*-centre thereby imparting the required electrophilic character to the intermediate aminyl radical **21** to facilitate faster cyclisation which over-rides the equilibrium between neutral aminyl **16** (**21**) and cyclised *C*-centred radical **17**.

Scheme 5. Use of the Lewis acid $MgBr_2.Et_2O$ to impart electrophilic behaviour to the intermediate aminyl radical



Scheme 6. **a**, R^1 = H, R^2 = $PhCH_2CH_2$ **b**, R^1 = Ph, R^2 = Pr

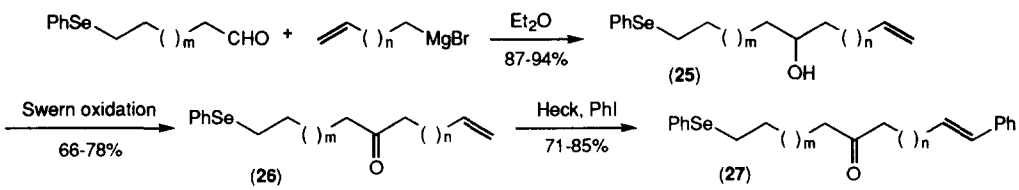


Cyclisation of imine **22a** gave a mixture of the bicyclised product **23a** (33%) and monocyclised product **24a** (18%) indicating similar behaviour between 5-*exo*, 5-*exo* and 6-*exo*, 5-*exo* cyclisations. As expected, the imine **22b** gave only the bicyclised product **23b** (57%). Interestingly, the 6-*exo* cyclisation required for the synthesis of pumilotoxin proceeds without difficulty. Two diastereomers were formed in both reactions.

Spirocyclic amines

The cascade radical methodology to spiroamines required for the synthesis of perhydrohistrionicotoxin **2** was also elaborated, *e.g.* Scheme 1, **5** to **2**. A series of ketones were synthesized in high yields using Grignard reactions and Swern oxidations, as shown in Scheme 7. Heck reactions were used to add on the phenyl moiety to ketones **26a** and **26b**. The 5-benzeneselenylpentanal and 6-benzeneselenylhexanal are building blocks developed in our earlier study of the radical monocyclisation of imines.[1] The ketones were converted *in situ* into imines using 2-phenylethylamine, benzylamine or propylamine (Scheme 8); the 2-phenylethyl and benzyl groups can readily be removed from the spirocyclic amine products to yield the required primary amines.

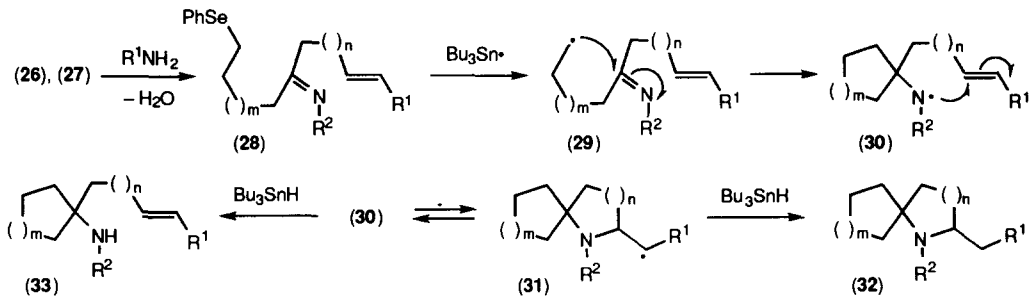
Scheme 7. **a**, m = 1, n = 1; **b**, m = 2, n = 1; **c**, m = 1, n = 2; **d**, m = 2, n = 2



The radical cyclisation of imines **28a** and **28b** with Bu_3SnH gave only monocyclisation to **33a** (34%) and **33b** (35%) via 5- and 6-*exo* cyclisation, respectively. None of the bicyclic amines were observed, unlike cyclisation of **14a** which gave both mono- and bi-cyclisation. Cyclisation of the intermediate aminyl radicals **30a** and **30b** is clearly unfavourable and the reasons are not clear. In contrast, when $MgBr_2.Et_2O$ was added prior to Bu_3SnH, only bicyclisation to **32a** (30%) and **32b** (33%) was observed. We suggest that the same explanation as shown in Scheme 5 also applies to this route, *i.e.* the Lewis acid imparts electrophilic behaviour to the intermediate aminyl radical, thereby facilitating efficient cyclisation. As observed for the cyclisation of imines leading to 2-azabicyclo[3.3.0]octanes, when a phenyl group is attached to the alkene, stabilisation of the intermediate bicyclised *C*-centred radicals (**31c** and **31d** in these reactions) facilitates exclusive bicyclisation. Imines **28c** and **28d** yielded **32c** (27%) and **32d** (39%) via 5-*exo*, 5-*exo* and 6-*exo*, 5-*exo*, respectively. These studies show that the problem of reversibility of the aminyl cyclisation can be readily overcome with phenyl substitution or addition of $MgBr_2.Et_2O$.

Scheme 8.

a, R^1 = H, R^2 = $PhCH_2CH_2$, m = 1, n = 1; **b**, R^1 = H, R^2 = $PhCH_2CH_2$, m = 2, n = 1; **c**, R^1 = Ph, R^2 = Pr, m = 1, n = 1; **d**, R^1 =Ph, R^2 = Pr, m = 2, n = 1; **e**, R^1 = H, R^2 = Bn, m = 1, n = 2; **f**, R^1 = H, R^2 = Bn, m = 2, n = 2



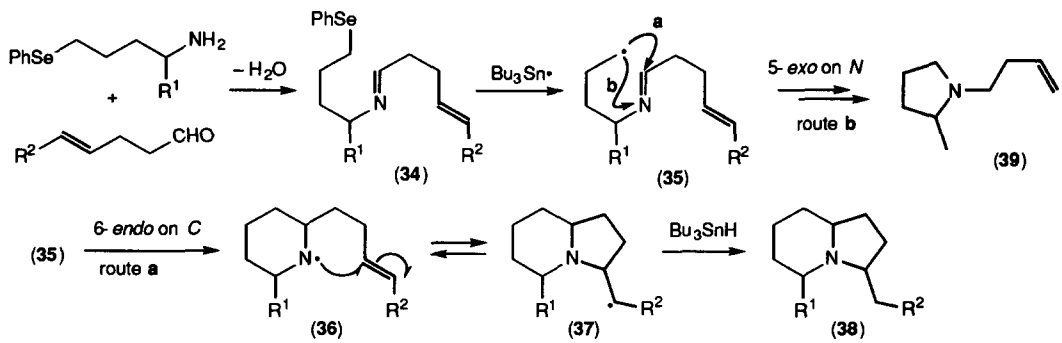
Radical cyclisation of imines **28e** and **28f**, in the presence of $MgBr_2.Et_2O$, gave exclusive bicyclisation to the bicyclic spiroamines **32e** (27%) and **32f** (29%) showing that 6-*exo* cyclisation of the intermediate aminyl radicals proceeds efficiently. In summary, when a Lewis acid is used, the methodology gives selective bicyclisation, with no observable monocyclisation, to spirocyclic amines with 5/5-, 5/6-, 6/5-, and 6/6-membered ring systems. The latter cyclisation should enable the synthesis of perhydrohistrionicotoxin **2**.

This protocol requires initial 5- or 6-*exo* cyclisation of the intermediate *C*-centred radicals in **29** onto a ketimine which was expected from earlier studies of monocyclisation onto ketimines.[1] In the presence of a Lewis acid, the intermediate aminyl radicals **30** cyclise to bicyclic amines by 5- or 6-*exo* cyclisation.

Indolizidines

Studies towards the synthesis of monomorine **3** (Scheme 1, **6** to **3**) require an initial 6-*endo* which is normally unfavourable in intramolecular radical additions. Our early studies[1] of the monocyclisation of imines showed that 6-*endo* cyclisation onto the electrophilic *C*-atom of the imine competes successfully with 5-*exo* cyclisation onto the electronegative *N*-atom (5-*exo*:6-*endo* = 42:18%), *i.e.* polarity and stereoelectronic effects are balanced. As expected, a tandem reaction requiring 5-*endo*, 5-*exo* cyclisation was unfavourable and only reduction of the imine by Bu_3SnH was observed. In order to test the tandem reaction required for the synthesis of monomorine, an aryl group was substituted onto the alkene group of the imine, *i.e.* **34a**, to facilitate the second cyclisation by stabilising the intermediate radical **37a**. Radical cyclisation of imine **34a** yielded the indolizidine **38a** (26%) with no other isolable product (Scheme 9, route **a**). A mixture of two diastereomers (*ca.* 1:1) was obtained. The large amount of intractable material suggested that polymerisation resulted from the intermediate radical formed from **35a** via 5-*exo* cyclisation (route **b**).

Scheme 9. **a**, R^1 = H, R^2 = *p*-tolyl; **b**, R^1 = Me, R^2 = *p*-tolyl; **c**, R^1 = Me, R^2 = H



Monomorine is a 5-methylindolizidine, therefore, the imine **34b** was synthesized and cyclised to yield the indolizidine **38b** (19%). Again a large amount of polymerised material was obtained. However, both of these reactions are facilitated by aryl group stabilisation. Therefore, a simple alkenylaldehyde was condensed to yield imine **34c** which cyclised in low yield to a mixture of the indolizidine **38c** and the monocyclised pyrrolidine **39**. In this case the stereolectronically favoured 5-*exo* cyclisation onto the *N*-atom of the imine does not lead to polymerisation, probably because no styrene moiety is present. Cyclisation of imine **34** with R^1 = Me and R^2 = Pr, required for the synthesis of monomorine, is yet to be undertaken. The yields of these tandem cyclisations need to be optimised in order to provide a satisfactory synthetic route to indolizidines. Use of $MgBr_2.Et_2O$ to increase the yields of 6-*endo* initiated tandem cyclisation failed and non-radical reactions took place. The rate of 6-*endo* cyclisation is possibly too slow and competing non-radical reactions dominate.

Conclusions

Our results indicate that the protocol using initial cyclisation onto imines followed by cyclisation of the aminyl radicals thus formed onto alkenes is as facile as tandem cyclisations of alkenes and provides a useful extension of radical cyclisation. In particular, the methodology provides novel routes to a range of bicyclic nitrogen heterocycles. The stereochemistry of the cyclisations has not yet been determined but would be crucial in carrying out natural product syntheses. Studies of the synthesis of nitrogen heterocycles using cascade cyclisations via intramolecular addition onto imines are continuing.

Acknowledgements
We gratefully thank Pfizer Central Research, Sandwich, and Loughborough University for a Postgraduate Research Studentship (A.R.Y), the EPSRC for a 400 MHz NMR spectrometer and the EPSRC MS Service at University College, Swansea, Wales.

EXPERIMENTAL

General Procedures

IR spectra were run as neat samples using a Nicolet 205 FT-IR spectrometer. Elemental analyses were carried using a Perkin Elmer 2400 CHN Elemental Analyser. Mass spectra were run on a Kratos MS80 spectrometer and also carried out by the EPSRC Mass Spectrometry Service at University College, Swansea. All mass spectra are electron impact (E.I.) spectra unless otherwise stated. ^{1}H NMR spectra were run at 250 MHz and ^{13}C NMR spectra were 62.9 MHz using a Bruker AC 250 spectrometer unless otherwise stated. $CDCl_3$ was used as the NMR solvent with TMS as internal standard. Light petroleum refers to the b.p. 40-60 °C fraction. TLC was performed on aluminium plates coated with Merck silica gel 60F254 or neutral alumina, and compounds were visualised by UV light, iodine vapour, or Dragendorff's reagent. Flash chromatography was carried out using silica gel as absorbent and light petroleum and ethyl acetate mixtures as eluant.

N-Cyclopentylpyrrolidines

General procedure for the formation and radical cyclisation of imines.

(a) 2-Benzyl-N-cyclopentyl-pyrrolidine **8a**. A solution of 5-benzeneselenylpentanal[1] (188 mg, 0.78 mmol) and 5-phenyl-4-penten-1-ylamine[17] (126 mg, 0.78 mmol) in dry toluene (100 cm^3) was refluxed under an atmosphere of nitrogen for 4 h, and the water removed using a Dean-Stark water separator. The imine **7a** was not isolated but reacted directly with Bu_3SnH. Bu_3SnH (0.3 cm^3, 0.86 mmol, 1.1 equiv.) and AIBN (48 mg, 0.29 mmol) were dissolved in toluene (25 cm^3) and nitrogen was bubbled through for 30 min. The solution of Bu_3SnH and AIBN was transferred under nitrogen to a 50 cm^3 syringe and was added to the refluxing imine solution at a rate of 5.0 cm^3/h using a syringe pump. After the addition of the tin hydride was completed, the reaction mixture was refluxed for a further 30 min before cooling to room temperature. The mixture was extracted with 2 M hydrochloric acid and the extracts washed with light petroleum. Solid sodium carbonate was added to neutralise the acid and once all effervescence had ceased the solution was made strongly basic with sodium hydroxide solution and the products extracted into diethyl ether. The extracts were dried and evaporated to dryness at low temperature. The residues were further purified by TLC on alumina plates or by flash chromatography. In this reaction flash chromatography yielded *2-benzyl-N-cyclopentylpyrrolidine* **8a** as a yellow-orange oil (111 mg, 62%); ν_{max} 3025, 2930, 2858, 1656, and 1444 cm^{-1}; δ_H 7.16-7.32 (5 H, m, Ph), 3.28-3.46 (4 H, m, cyclopentyl 1-H, pyrrolidine 2,5-H), 2.87-2.95 (2 H, m, benzylic-H), and 1.56-1.81, (12 H, m); δ_C 129.09 (Ar-CH), 128.95 (Ar-C), 128.17, 125.79 (Ar-CH), 64.62 and 64.05 (CHN), 51.50 (CH_2N), 40.85 (CH_2Ph), 32.14, 28.94, 23.67, and 22.68 (4 x CH_2); *m/z* (C.I.) 230.1909 [MH^+, (49%) $C_{16}H_{24}N$ requires 230.1909], 225 (13), 180 (8), and 138 (100).

(b) N-Cyclopentyl-2-methylpyrrolidine **8b**. *4-Penten-1-ylamine hydrochloride.* Potassium phthalimide (1.852 g, 10 mmol) and 5-bromo-1-pentene (1.49 g, 10 mmol) were stirred in DMF (20 cm^3) for 3 h at 100 °C. The crude mixture was diluted with water and the product extracted into diethyl ether. The extracts were washed with water, dried and evaporated to dryness. *N*-(4-Pentenyl)-phthalimide was isolated as a light yellow viscous oil which was not further purified (1.964 g, 91%); ν_{max} 3078, 2938, 1774 and 1713, 1641, 1616, 1467, 1438, 1397, 1188, 1073, 994, 885, and 720 cm^{-1}; δ_H 7.79-7.85 (2 H m), 7.67-7.73 (2 H, m, Ar-H), 5.74-5.86 (1 H, m, 4-H), 4.95-5.09 (2 H, m, 5-H), 3.70 (2 H, t, *J* 7.1 Hz, 1-H), 1.82-1.88 (2 H, m), and 1.41-1.52 (2 H, m); δ_C 168.25 (C=O), 137.20 (4-C), 133.73 (Ar-CH), 132.10 (Ar-C), 123.04 (Ar-CH), 115.17 (5-C), 37.47, 30.87, and 27.55 (1,2,3-C); *m/z* 215.0948 [M^+, (9.0%) $C_{13}H_{13}NO_2$ requires 215.0946], 173 (15), 160 (100), 148 (27), 130 (16), 104 (17), and 76 (24).

A solution of hydrazine hydrate (400 mg, 8 mmol) and *N*-(4-pentenyl)phthalimide (225) (860 mg, 4 mmol) in ethanol (20 cm^3) was refluxed for 10 h. The white precipitate of phthalhydrazide was filtered and dry HCl bubbled through the filtrate. 4-Penten-1-ylamine hydrochloride was precipitated as a colourless oil which was

dried in a vacuum desiccator for 48 h (376 mg, 39%); δ_H 7.87 (3 H, br s, NH_3), 5.40-5.52 (1 H, m, 4-H), 4.68-4.76 (2 H, m, 5-H), 2.56-2.60 (2 H, m), 1.82-1.88 (2 H, m), and 1.41-1.52 (2 H, m); δ_C 136.38 (4-C), 115.92 (5-C), 39.88, 26.33 and 21.91 (1,2,3-C).

Cyclisation of imine **7b**. A solution of 5-benzeneselenylpentanal (323 mg, 1.34 mmol) and 4-penten-1-ylamine hydrochloride (360 mg, 2.96 mmol) in toluene was refluxed for 4 h with sodium acetate (240 mg, 3 mmol). The water was removed using a Dean-Stark water separator. The imine was not isolated but was cyclised using the general procedure. A solution of Bu_3SnH (0.56 cm^3, 1.6 mmol) and AIBN (75 mg, 0.5 mmol) were added using a syringe pump. Careful work-up using diethyl ether as solvent which was distilled at atmospheric pressure yielded a crude product (90 mg). ^1H NMR spectroscopy indicated that the residue was the largely the bicyclic product with traces of the monocyclised *N*-(4-pentenyl)cyclopentylamine. The bicyclic product **8b** was further purified by precipitation as the hydrochloride salt. *N-Cyclopentyl-2-methylpyrrolidine hydrochloride* (**8b**.HCl) was isolated as a yellow-orange oil (81 mg, 32%); ν_{max} (amine) 3054, 2960, 2871, 1671 1641, 1434, 896, 739 and 704 cm^{-1}; δ_H (2 diastereomeric salts) 5.90 (1 H, t, *J* 3.1 Hz, NH), 3.98-4.04 (1 H, m), 3.45-3.51 (1 H, m), 2.47-2.49 (1 H, m) and 2.39-2.41 (1 H, m, CHN), 2.12-2.19 (4 H, m), 1.80-1.98 (4 H, m), and 1.40-1.75 (4 H, m); δ_C 50.90 and 48.72 (CNH), 38.19 (CH_2N), 32.75, 24.01, 23.37 and 23.09 (CH_2), and 19.66 (Me); *m/z* 154.1596 [MH^+, (100 %, $C_{10}H_{20}N$ requires 154.1596], 150 (22), and 128 (25).

2-Azabicyclo[3.3.0]octanes and perhydroindolines

1-Benzeneselenyl-4-iodobutane. Using the literature procedure,[1] diphenyl diselenide (1.96g, 6.3 mmol), sodium borohydride (600 mg, 15.8 mmol) and 1-chloro-4-iodobutane (2.80 g, 12.8 mmol), gave 1-benzeneselenyl-4-chlorobutane as a yellow-orange oil (3.04 g, 96%); ν_{max} 3072, 2938, 2866, 1579, 1478, 1437, 1073, 1022, 734, and 691 cm^{-1}; δ_H 7.44-7.49 (2 H, m, *o*-H), 7.20-7.26 (3 H, m, Ar-H), 3.49 (2 H, t, *J* 6.2 Hz, 4-H), 2.89 (2 H, t, *J* 6.8 Hz, 1-H), and 2.76-1.90 (4 H, m, 2,3-H); δ_C 132.62 and 129.01 (Ar-CH), 128.19 (Ar-C), 126.86 (Ar-CH), 44.30 (4-C), 32.37, 27.29, and 26.95; *m/z* 247.9871 [M^+ (9.7%), $C_{10}H_{13}ClSe$ requires 247.9871], 234 (6), 213 (47), 157 (39), 91 (65), and 78 (62).

Sodium iodide (6.0 g, 40 mmol), dissolved in dry acetone (10 cm^3) was added to a solution of 1-benzeneselenyl-4-chlorobutane (2.50 g, 10.1 mmol) in acetone and the mixture refluxed for 4 h. The precipitated sodium chloride was removed by filtration and the filtrate evaporated to dryness. The solid residue was triturated with diethyl ether and the solution filtered a second time. The ether solution was evaporated to dryness yielding the product which was purified by quick filtration through silica gel. 1-Benzeneselenyl-4-iodobutane was isolated as a viscous orange oil which gradually darkened (3.39 g, 99%); ν_{max} 3071, 2934, 1579, 1478, 1437, 1299, 1073, 1023, 735, 691, and 670 cm^{-1}; δ_H 7.46-7.50 (2 H, m, *o*-H), 7.23-7.27 (3 H, m, Ar-H), 3.15 (2H, t, *J* 6.8 Hz, 4-H), 2.91 (2 H, t, *J* 6.8 Hz, 1-H), and 1.80-1.91 (4 H, m, 2,3-H); δ_C 132.67 (Ar-CH), 130.05 (Ar-C), 129.07, 126.88 (Ar-CH), 33.23, 30.79, 28.28 (1,2,3-C), and 5.80 (4-C); *m/z* 339.9227 [M^+ (5.6%), $C_{10}H_{13}ISe$ requires 339.9227], 213 (26), 158 (28), 91 (100), 78 (39), and 55 (99).

General procedure for Heck reactions.

Diethyl (3-phenyl-2-propen-1-yl)propanedioate **10**. Diethyl (2-propen-1-yl)propanedioate (4.0 g, 20 mmol), iodobenzene (4.08 g, 20 mmol) and tri-*n*-butylamine (3.7 g, 20 mmol) were dissolved in acetonitrile. Palladium acetate (77 mg, 0.35 mmol) was added to the solution and the mixture refluxed for 3 h. The solvent was removed by evaporation and the brown residue treated with 1.0 M hydrochloric acid. The product was extracted into diethyl ether and the combined extracts washed with water, dried and evaporated to dryness. The product was purified by flash chromatography to yield *diethyl (3-phenyl-2-propen-1-yl)propanedioate* **10** as a yellow viscous oil (4.96 g, 90%); (Found: C, 69.1; H, 7.39. $C_{16}H_{26}O_4$ requires C, 69.5; H, 7.30%); ν_{max} 2983, 1737, 1655, 1599, 1448, 1370, 1227, 1153, 1096, 1033, 747, and 695 cm^{-1}; δ_H (300 MHz) 7.30-7.34 (5 H, m, Ph), 6.50 (1 H, d, *J* 15.6 Hz, 3-H), 6.18 (1 H, dt, *J* 15.6, 7.8 Hz, cinnamyl 2-H), 4.25 (4 H, q, *J* 7.4 Hz, CH_2O), 3.54 (1 H, t, *J* 7.8 Hz, malonate 2-H), 2.85 (2 H, dd, *J* 7.8, 7.8 Hz, 1-H), and 1.32 (6 H, t, *J* 7.4 Hz, Me); δ_C (75 MHz) 168.80 (C=O), 132.69, 128.40, 127.28, 126.08, 125.49 (alkene and Ar-CH), 131.41 (Ar-

C), 61.36 (CH_2O), 51.91 (C), 32.13 (1'-C), and 14.01 (Me); *m/z* (C.I.) 277.1440 [MH^+, (100%), $C_{16}H_{21}O_4$ requires 277.1440], 202 (6), and 178 (7). In some reactions 5 mol% of tri-*o*-tolylphosphine was also added.

General procedure for the 2-alkylation of propanedioate esters.

(a) Diethyl (3-benzeneselenylpropyl)(2-propen-1-yl)propanedioate **11a**. Sodium hydride (160 mg of 60% suspension in mineral oil) was placed in a dried flask under nitrogen and washed with dry light petroleum. Dry and distilled DMF (20 cm^3), followed by a solution of diethyl (2-propen-1-yl)propanedioate (605 mg, 3 mmol) in DMF (5 cm^3), was added to the suspension. After stirring at 50 °C for 30 min, 1-benzeneselenyl-3-iodopropane[1] (975 mg, 3 mmol) in DMF (5 cm^3) was added dropwise over 10 min. The mixture was stirred at 50 °C for 8 h and on cooling, water and 2 M hydrochloric acid were added, and the organic products extracted into diethyl ether. The extracts were washed with water, dried, evaporated to dryness, and the crude product purified using flash chromatography to yield *diethyl (3-benzeneselenylpropyl)-(2-propen-1-yl)propanedioate* **11a** as an orange oil (952 mg, 77%); ν_{max} 3075, 2979, 2935, 2871, 1731, 1642, 1580, 1478, 1438, 1299, 1229, 1154, 1023, 921, 736, and 691 cm^{-1}; δ_H 7.44-7.48 (2 H, m, *o*-H), 7.22-7.26 (3 H, m, Ar-H), 5.55-5.69 (1 H, m, allyl 2-H), 5.00-5.08 (2 H, m, allyl 3-H), 4.13 (4 H, q, *J* 7.0 Hz, CH_2O), 2.87 (2 H, t, *J* 7.1 Hz, CH_2Se), 2.59 (2 H, d, *J* 7.5 Hz, allyl 1-H), 1.94-2.01 (2 H, m), 1.56-1.63 (2 H, m), and 1.20 (6 H, t, *J* 7.0 Hz, Me); δ_C 171.03 (C=O), 132.57, 132.32, 129.02, 126.81 (alkene and Ar-CH), 130.10 (Ar-C), 119.02 (alkene CH_2), 61.25 (CH_2O), 57.10 (quat. C), 37.01, 32.45, 27.68, 24.70 (CH_2), and 14.09 (Me); *m/z* 398.0998 [M^+, (14%), $C_{19}H_{26}O_4Se$ requires 398.0996], 322 (13), 241 (100), 157 (40), 121 (32), 93 (46), 78 (61), and 41 (77).

(b) Diethyl (4-benzeneselenylbutyl)(2-propen-1-yl)propanedioate **11b**. Diethyl (2-propen-1-yl)propanedioate (605 mg, 3 mmol), sodium hydride (160 mg, 4 mmol) and 1-benzeneselenyl-4-iodobutane (1.071 g, 3 mmol) yielded *diethyl (4-benzeneselenylbutyl)(2-propen-1-yl)propanedioate* **11b** as an orange oil (1.01 g, 79%); ν_{max} 3074, 2934, 2866, 1729, 1642, 1579, 1478, 1438, 1367, 1221, 1096, 1023, 922, 736, and 692 cm^{-1}; δ_H 7.45-7.48 (2 H, m, *o*-H), 7.22-7.26 (3 H, m, Ar-H), 5.50-5.67 (1 H, m, allyl 2-H), 5.05-5.12 (2 H, m, allyl 3-H), 4.17 (4 H, q, *J* 7.0 Hz, CH_2O), 2.89 (2 H, t, *J* 6.8 Hz, CH_2Se), 2.64 (2 H, d, *J* 7.5 Hz, allyl 1-H), 1.82-1.89 (2 H, m), 1.69 (2 H, t, *J* 7.5 Hz, $Se(CH_2)_3CH_2$), 1.31-1.34 (2 H, m), and 1.23 (6 H, t, *J* 7.0 Hz, Me); δ_C 171.10 (C=O), 132.56, 132.40, 128.91, 126.67 (alkene and Ar-CH), 130.15 (Ar-C), 118.82 (alkene CH_2), 61.09 (CH_2O), 57.19 (C), 36.80, 31.48, 30.07, 27.37, 23.69 (CH_2), and 14.04 (Me); *m/z* 412.1152 [M^+, (5.3%), $C_{20}H_{28}O_4Se$ requires 412.1152], 242 (15), 157 (40), 139 (100), 91 (28), 81 (52), and 55 (87).

(c) Diethyl (3-benzeneselenylpropyl)(3-phenyl-2-propen-1-yl)propanedioate **11c**. Diethyl (3-phenyl-2-propen-1-yl)propanedioate **10** (825 mg, 3 mmol), sodium hydride (160 mg, 4 mmol) and 1-benzeneselenyl-3-iodopropane (962 g, 3 mmol) yielded *diethyl (3-benzeneselenyl-propyl)(3-phenyl-2-propen-1-yl)propanedioate* **11c** as a red oil (1.276 g, 90%); ν_{max} 3075, 2934, 1737, 1655, 1603, 1579, 1478, 1438, 1158, 1095, 1023, 968, 737, and 692 cm^{-1}; δ_H (300 MHz) 7.44-7.52 (2 H, m, *o*-H), 7.25-7.32 (8 H, m, Ar-H), 6.44 (1 H, d, *J* 15.6 Hz, cinnamyl 3-H), 6.07 (1 H, dt, J15.6, 7.8 Hz, cinnamyl 2-H), 4.21 (4 H, q, *J* 7.2 Hz, CH_2O), 2.93 (2 H, t, *J* 7.3 Hz, CH_2Se), 2.80 (2 H, d, *J* 7.8 Hz, 1-H), 2.05-2.09 (2 H, m), 1.70-1.74 (2 H, m), and 1.25 (6 H, t, *J* 7.2 Hz, Me); δ_C (75 MHz) 171.59 (C=O), 133.75, 132.45, 128.95, 128.40, 127.32, 126.73, 126.14, 123.82 (alkene and Ar-CH), 131.41, 130.15 (Ar-C), 61.25 (CH_2O), 57.63 (C), 36.28, 32.66, 27.58, 24.75 (CH_2), and 14.04 (Me); *m/z* 474.1307 [M^+, (3.4%), $C_{25}H_{30}O_4Se$ requires 474.1309], 404 (2), 317 (13), 245 (11), 169 (12), 157 (17), 129 (38), 117 (100), and 77 (22).

(d) Diethyl (4-benzeneselenylbutyl)(3-phenyl-2-propen-1-yl)propanedioate **11d**. Diethyl (3-phenyl-2-propen-1-yl)propanedioate (825 mg, 3 mmol), sodium hydride (160 mg, 4 mmol) and 1-benzeneselenyl-4-iodobutane (1.02 g, 3 mmol) yielded *diethyl (4-benzeneselenylbutyl)(3-phenyl-2-propen-1-yl)propanedioate* **11d** as a red viscous oil (1.195 g, 82%); ν_{max} 3072, 2935, 2862, 1737, 1651, 1603, 1579, 1478, 1438, 1156, 1095, 1023, 968, 738, and 692 cm^{-1}; δ_H (300 MHz) 7.46-7.52 (2 H, m, *o*-H), 7.25-7.31 (8 H, m, Ar-H), 6.43 (1 H, d, *J* 15.6 Hz, cinnamyl 3-H), 6.04 (1 H, dt, *J* 15.6, 7.8 Hz, cinnamyl 2-H), 4.18 (4 H, q, *J* 7.2 Hz, CH_2O), 2.93 (2 H, t, *J* 7.3 Hz, CH_2Se), 2.81 (2 H, d, *J* 7.8 Hz, 1-H), 1.89-1.93 (2 H, m), 1.71-1.75 (2 H, m), 1.41-1.45 (2 H, m), and 1.26 (6 H, t, *J* 7.2 Hz, Me); δ_C (75 MHz) 171.32 (C=O), 133.70, 132.55,

128.95, 128.42, 127.30, 126.69, 126.13, 124.13 (alkene and Ar-CH), 131.41, 130.15 (Ar-C), 61.19 (CH_2O), 57.74 (C), 36.16, 31.78, 29.96, 27.39, 23.99 (CH_2), and 14.08 (Me); *m/z* 488.1466 [M^+, (6.7%), $C_{26}H_{32}O_4Se$ requires 488.1465], 416 (3), 213 (26), 183 (19), 158 (25), 129 (26), 117 (100), and 91 (84).

General procedure for hydrolytic decarboxylation using lithium chloride in DMSO.

(a) Ethyl 5-benzeneselenyl-2-(2-propen-1-yl)pentanoate **12a**. Lithium chloride (2 equiv.) dissolved in freshly dried and distilled DMSO (2 cm^3) and containing water (1.2 equiv.) was added to the diester **11a** (717 mg, 1.7 mmol) in DMSO (1 cm^3). The mixture was heated at 170 °C for 24 h, cooled to room temperature, and water and dilute hydrochloric acid added. The product was extracted into diethyl ether, the extracts were washed with water, dried, and evaporated to dryness. The residue was purified by flash sinter chromatography to yield *ethyl 5-benzeneselenyl-2-(2-propen-1-yl)pentanoate* **12a** as a red oil (534 mg, 93%); ν_{max} 2983, 2931, 1737, 1655, 1578, 1478, 1438, 1299, 1232, 1158, 1023, 909, and 691 cm^{-1}; δ_H 7.44-7.49 (2 H, m, *o*-H), 7.22-7.26 (3 H, m, Ar-H), 5.60-5.76 (1 H, m, allyl 2-H), 4.98-5.06 (2 H, m, allyl 3-H), 4.09 (2 H, q, *J* 7.0 Hz, CH_2O), 2.87 (2 H, t, *J* 6.8 Hz, CH_2Se), 2.30-2.39 (2 H, m), 2.16-2.21 (1 H, m, 2-H), 1.60-1.74 (4 H, m), and 1.20 (3 H, t, *J* 7.0 Hz, Me); δ_C 175.18 (C=O), 135.18 (alkene CH), 132.54 (Ar-CH), 130.31 (Ar-C), 128.94, 126.71 (Ar-CH), 116.78 (alkene CH_2), 60.18 (CH_2O), 44.70 (CH), 36.35, 31.70, 27.75, 27.41 (CH_2), and 14.23 (Me); *m/z* 326.0787 [M^+, (7.7%), $C_{16}H_{22}O_2Se$ requires 326.0785], 258 (6), 169 (57), 157 (25), 109 (77), 77 (52), 67 (74), 55 (97), and 41 (100).

(b) Ethyl 6-benzeneselenyl-2-(2-propen-1-yl)hexanoate **12b**. The diester **11b** (742 mg) yielded *ethyl 6-benzeneselenyl-2-(2-propen-1-yl)hexanoate* **12b** as a red oil (543 mg, 88%); ν_{max} 3071, 2936, 2834, 1731, 1641, 1579, 1478, 1438, 1367, 1299, 1222, 1154, 1023, 922, 737, and 692 cm^{-1}; δ_H 7.44-7.50 (2 H, m, *o*-H), 7.21-7.26 (3 H, m, Ar-H), 5.66-5.76 (1 H, m, allyl 2-H), 4.98-5.07 (2 H, m, allyl 3-H), 4.12 (2 H, q, *J* 7.1 Hz, CH_2O), 2.88 (2 H, t, *J* 7.2 Hz, CH_2Se), 2.31-2.39 (2 H, m), 2.18-2.26 (1 H, m, 2-H), 1.61-1.73 (4 H, m), 1.39-1.48 (2 H, m), and 1.23 (3 H, t, *J* 7.1 Hz, Me); δ_C 175.43 (C=O), 135.34 (alkene CH), 132.43 (Ar-CH), 130.15 (Ar-C), 128.93, 126.82 (Ar-CH), 116.66 (alkene CH_2), 60.13 (CH_2O), 45.08 (CH), 36.38, 31.10, 29.91, 27.53, 27.28 (CH_2), and 14.28 (Me); *m/z* 340.0941 [M^+, (0.5%), $C_{17}H_{24}O_2Se$ requires 340.0941], 296 (5), 157 (13), 139 (15), 115 (11), 83 (29), and 55 (100).

(c) Ethyl 5-benzeneselenyl-2-(3-phenyl-2-propen-1-yl)pentanoate **12c**. The diester **11c** (1.02 g) yielded *ethyl 5-benzeneselenyl-2-(3-phenyl-2-propen-1-yl)pentanoate* **12c** as a red oil (834 mg, 96%); ν_{max} 3070, 2932, 1731, 1652, 1603, 1579, 1478, 1438, 1160, 1073, 1023, 966, 739, and 692 cm^{-1}; δ_H (300 MHz) 7.46-7.50 (2 H, m, *o*-H), 7.23-7.30 (8 H, m, Ar-H), 6.42 (1 H, d, *J* 14.6 Hz, alkene H), 6.07 (1 H, dt, *J* 14.6, 7.3 Hz, alkene H), 4.16 (2 H, q, *J* 7.2 Hz, CH_2O), 2.92 (2 H, t, *J* 7.2 Hz, CH_2Se), 2.52 (2 H, dd, *J* 7.3,7.2 Hz, allylic H), 1.98-2.05 (1 H, m, 2-H), 1.61-1.82 (4 H, m), and 1.23 (3 H, t, *J* 7.2 Hz, Me); δ_C (75 MHz) 175.20 (C=O), 132.53, 132.00, 128.96, 128.42, 127.11, 126.86, 126.73, 126.02 (alkene and Ar-CH), 131.41, 130.15 (Ar-C), 60.27 (CH_2O), 44.08 (CH), 35.64, 31.77, 27.80, 27.39 (CH_2), and 14.26 (Me); *m/z* 402.1097 [M^+, (4.0%), $C_{22}H_{26}O_2Se$ requires 402.1098], 157 (28), 155 (46), 129 (33), 127 (80), 91 (83), 77 (47), and 51 (100).

(d) Ethyl 6-benzeneselenyl-2-(3-phenyl-2-propen-1-yl)hexanoate **12d**. The diester **11d** (1.08 g) yielded *ethyl 6-benzeneselenyl-2-(3-phenyl-2-propen-1-yl)hexanoate* **12d** as a red oil (895 mg, 98%); ν_{max} 3057, 2933, 2860, 1737, 1652, 1599, 1579, 1478, 1438, 1177, 1073, 1023, 967, 737, and 692 cm^{-1}; δ_H (300 MHz) 7.48-7.52 (2 H, m, *o*-H), 7.26-7.32 (8 H, m, Ar-H), 6.43 (1 H, d, *J* 14.6 Hz, alkene H), 6.15 (1 H, dt, *J* 14.6, 7.3 Hz, alkene H), 4.16 (2 H, q, *J* 7.2 Hz, CH_2O), 2.92 (2 H, t, *J* 7.2 Hz, CH_2Se), 2.45-2.49 (2 H, m, allylic H), 1.84-1.86 (1 H, m, 2-H), 1.67-1.73 (2 H, m), 1.44-1.56 (4 H, m), and 1.25 (6 H, t, *J* 7.2 Hz, Me); δ_C (75 MHz) 175.51 (C=O), 132.40, 131.96, 128.93, 128.41, 127.06, 126.62, 126.12, 125.99 (alkene and Ar-CH), 131.41, 130.15 (Ar-C), 60.20 (CH_2O), 45.66 (CH), 35.64, 31.17, 29.89, 27.52, 27.39 (CH_2), and 14.29 (Me); *m/z* 416.1347 [M^+, (4.0%), $C_{23}H_{28}O_2Se$ requires 416.1254], 204 (17), 157 (26), 130 (53), 117 (97), 91 (100), 83 (64), and 77 (62).

DIBAL reductions of esters. The esters **12** were reduced to aldehydes **13** with DIBAL using the literature procedure for 4-benzeneselenylbutanal.[24]

(a) 5-Benzeneselenyl-2-(2-propen-1-yl)pentanal **13a**. The ester **12a** (321 mg, 1.0 mmol) and DIBAL (498 mg, 3.5 mmol) were reacted over 2 h yielding **13a** as a colourless oil (163 mg, 58%) and *5-benzeneselenyl-2-(2-propen-1-yl)pentan-1-ol* as a yellow oil (62 mg, 22%). Aldehyde **13a**: ν_{max} 3073, 2925, 2854, 2721, 1725, 1640, 1579, 1478, 1438, 1232, 1073, 1023, 736, and 691 cm^{-1}; δ_H (300 MHz) 9.59 (1 H, s, CHO), 7.46-7.49 (2 H, m, *o*-H), 7.26-7.29 (3 H, m, Ar-H), 5.72-5.76 (1 H, m, allyl 2-H), 5.01-5.05 (2 H, m, allyl 3-H), 2.91 (2 H, t, *J* 7.0 Hz, CH_2Se), 2.21-2.37 (2 H, m, allylic H), 2.08-2.12 (1 H, m, 2-H), and 1.52-1.80 (4 H, m); δ_C (75 MHz) 204.19 (C=O), 134.50 (alkene CH), 132.59 (Ar-CH), 130.15 (Ar-C), 128.99, 126.83 (Ar-CH), 113.23 (alkene CH_2), 50.60 (2-C), 32.88, 28.10, 27.51, and 27.31 (CH_2); *m/z* 282.0509 [M^+, (7.9%), $C_{14}H_{18}OSe$ requires 282.0523], 198 (13), 157 (34), 117 (16), 91 (32), 77 (55), 55 (75), and 41 (100).

(b) 6-benzeneselenyl-2-(2-propen-1-yl)hexanal **13b**. The ester **12b** (513 mg) yielded **13b** as a colourless oil (261 mg, 59%) and *6-benzeneselenyl-2-(2-propen-1-yl)hexan-1-ol* as a yellow oil (111 mg, 25%). Aldehyde **13b**: ν_{max} 3073, 29288, 2858, 2712, 1725, 1638, 1579, 1477, 1438, 1265, 1073, 1023, 738, and 691 cm^{-1}; δ_H (300 MHz) 9.59 (1 H, s, CHO), 7.46-7.49 (2 H, m, o-H), 7.25-7.27 (3 H, m, Ar-H), 5.72-5.76 (1 H, m, allyl 2-H), 5.03-5.07 (2 H, m, allyl 3-H), 2.91 (2 H, t, *J* 7.0 Hz, CH_2Se), 2.32-2.40 (2 H, m, allylic H), 2.09-2.13 (1 H, m, 2-H), and 1.42-1.86 (6 H, m); δ_C (75 MHz) 204.42 (C=O), 134.73 (alkene CH), 132.56 (Ar-CH), 130.15 (Ar-C), 128.97, 126.74 (Ar-CH), 113.24 (alkene CH_2), 51.00 (2-C), 35.64, 32.94, 30.05, 27.45, and 27.11 (CH_2); *m/z* 296.0697 [M^+, (9.4%), $C_{15}H_{20}OSe$ requires 296.0679], 212 (21), 171 (15), 158 (47), 91 (40), 78 (52), and 55 (100).

(c) 5-benzeneselenyl-2-(3-phenyl-2-propen-1-yl)pentanal **13c**. The ester **12c** (300 mg) was reacted over 1.25 h and yielded **13c** as an orange oil (147 mg, 55%) and *5-benzeneselenyl-2-(3-phenyl-2-propen-1-yl)-pentan-1-ol* as a yellow oil (59 mg, 22%). Aldehyde **13c**: ν_{max} 3070, 2928, 2856, 2725, 1723, 1640, 1579, 1478, 1438, 1073, 1023, 968, 737, and 692 cm^{-1}; δ_H (300 MHz) 9.68 (1 H, s, CHO), 7.48-7.52 (2 H, m, *o*-H), 7.26-7.32 (8 H, m, Ar-H), 6.45 (1 H, d, *J* 15.6 Hz, cinnamyl 3-H), 6.16 (1 H, dt, *J* 15.6, 7.8 Hz, cinnamyl 2-H), 2.94 (2 H, t, *J* 7.4 Hz, CH_2Se), 2.44-2.54 (2 H, m, allylic H), 2.25-2.29 (1 H, m, 2-H), and 1.50-1.90 (4 H, m); δ_C (75 MHz) 203.26 (C=O), 132.62, 132.40, 128.96, 128.45, 128.15, 126.84, 126.04, 125.22 (alkene and Ar-CH), 131.41, 130.20 (Ar-C), 51.26 (2-C), 32.11, 28.18, 27.50, and 27.29 (CH_2); *m/z* 358.0826[M^+, (2.3%), $C_{20}H_{22}OSe$ requires 358.0836], 199 (19), 171 (14), 157 (38), 129 (13), and 91 (100).

(d) 6-Benzeneselenyl-2-(3-phenyl-2-propen-1-yl)hexanal **13d**. The ester **12d** (300 mg) was reacted over 1.25 h and yielded **13d** as an orange oil (93 mg, 35%) and *6-benzeneselenyl-2-(3-phenyl-2-propen-1-yl)hexan-1-ol* as a yellow oil (87 mg, 33%). Aldehyde **13d**: ν_{max} 3057, 2929, 2857, 2721, 1723, 1640, 1578, 1478, 1438, 1073, 1023, 967, 737, and 692 cm^{-1}; δ_H (300 MHz) 9.68 (1 H, s, CHO), 7.47-7.51 (2 H, m, *o*-H), 7.26-7.32 (8 H, m, Ar-H), 6.45 (1 H, d, *J* 15.4 Hz, (cinnamyl 3-H), 6.18 (1 H, dt, *J* 15.4, 7.7 Hz, cinnamyl 2-H), 2.91 (2 H, t, *J* 7.3 Hz, CH_2Se), 2.36-2.47 (2 H, m, allylic H), 2.01-2.05 (1 H, m, 2-H), and 1.33-1.82 (6 H, m); δ_C (75 MHz) 204.19 (C=O), 132.22, 131.47, 128.94, 128.44, 128.15, 126.70, 126.01, 125.89 (alkene and Ar-CH), 131.23, 130.10 (Ar-C), 51.35 (2-C), 34.63, 32.14, 29.97, 27.73, and 26.96 (CH_2); *m/z* 372.0985 [M^+, (3.0%), $C_{21}H_{24}OSe$ requires 372.0992], 213 (3), 157 (21), 129 (17), 117 (90), and 91 (100).

Cyclisation of imines **14 and 22**. The general procedure for the formation of imines and cyclisation using Bu_3SnH were used in each case.

(a) Imine **14a**. The aldehyde **13a** (189 mg, 0.67 mmol) and 2-phenylethylamine (81 mg, 0.67 mmol) were dissolved in toluene (20 cm^3) and stirred at room temperature over 4 Å molecular sieves for 24 h. Injection by syringe pump of Bu_3SnH (0.3 cm^3, 0.9 mmol) and AIBN (56 mg, 0.34 mmol) in toluene to the refluxing solution of the imine in toluene (100 cm^3) gave 130 mg of the crude amine products, which were dissolved in diethyl ether (10 cm^3) and treated with acetyl chloride and triethylamine. The *N*-acetyl derivative of the monocyclic amine **19a** was separated from bicyclic amine **18a** by acid extraction. Both compounds were purified by column chromatography using alumina as absorbent and light petroleum / ethyl acetate mixtures as eluent. *N-Acetyl-N-(2-phenylethyl)-2-(2-propen-1-yl)cyclopentylamine* **19a**-Ac was isolated as a light yellow oil (42 mg, 23%) and *3-methyl-2-(2-phenylethyl)-2-azabicyclo[3.3.0]octane* **18a** as an orange oil (41 mg, 27%).

Amide **19a**-Ac: ν_{max} 3054, 2958, 2873, 1668, 1637, 1603, 1453, 1422, and 916 cm^{-1}; δ_H (300 MHz) 7.18-7.32 (5 H, m, phenyl-H), 5.74-5.78 (1 H, m, allyl 2-H), 5.02-5.06 (2 H, m, allyl 3-H), 3.71-3.73 (1 H, m,

CHN), 3.41-3.44 (2 H, m, CH_2N), 2.90 (2 H, t, *J* 7.5 Hz, CH_2Ph), 2.36-2.40 (1 H, m, cyclopentyl 2-H), 2.27-2.31 (2 H, m, allylic H), 2.09 (3 H, s, Ac), and 1.33-1.96 (6 H, m); δ_C (75 MHz) 176.85 (C=O), 138.80 (Ar-C), 135.85 (alkene CH), 128.66, 128.52, 126.45 (Ar-CH), 116.46 (alkene CH_2), 65.08 (cyclopentyl 1-C), 44.50 (CH_2N), 41.95 (CH), 37.29, 34.64, 29.37, 29.13, 21.56 (CH_2), and 21.30 and 20.71 (MeCO); *m/z* 271.1938 [M^+ (2.7%), $C_{18}H_{25}NO$ requires 271.1936], 180 (46), 138 (100), 105 (21), 77 (10), and 67 (29). Amine **18a**: ν_{max} 2936, 1670, 1603, 1455, 1373, 749, and 699 cm^{-1}; δ_H (300 MHz) 7.17-7.32 (5 H, m, phenyl-H), 3.49-3.52 (1 H, m, 1-H), 2.81-2.85 (2 H, m, CH_2N), 2.60-2.64 (2 H, m, CH_2Ph), 2.39-2.46 (1 H, m, 5-H), 1.41-1.77 (8 H, m, 4,6,7,8-H), and 1.01 (3 H, d, *J* 6.8 Hz, Me); δ_C (75 MHz) 140.80 (Ar-C), 128.56, 128.23, 125.87 (Ar-CH), 66.64 (1-C), 56.31 (3-C), 51.22 (CH_2N), 40.45 (CH_2Ph), 39.77 (5-C), 35.57, 33.52, 29.01, 25.21 (CH_2), and 15.47 (Me); *m/z* (C.I.) 230.1909 [MH^+ (11%), $C_{16}H_{24}N$ requires 230.1910], 164 (12), 138 (11), 122 (19), 108 (18), 98 (29), 78 (35), 58 (77), and 44 (100).

Cyclisation of imine **14a** *in the presence of magnesium dibromide.* The procedure for the cyclisation of imine **14a** (174 mg, 0.45 mmol) was repeated with the addition of $MgBr_2.OEt_2$ (129 mg, 0.5 mmol) prior to the addition of Bu_3SnH. Injection of Bu_3SnH (0.16 cm^3, 0.6 mmol) and AIBN (25 mg, 0.15 mmol) yielded only the amine **18a** (36 mg, 35%).

(b) Imine **14b**. The aldehyde **13c** (246 mg, 0.69 mmol) and *n*-propylamine (80 mg, 1.35 mmol) yielded *3-benzyl-2-propyl-2-azabicyclo[3.3.0]octane* **18b** as a yellow oil (67 mg, 40%); ν_{max} 2957, 2930, 2872, 1639, 1603, 1453, 1125, 1074, 1023, 747, and 700 cm^{-1}; δ_H (300 MHz) 7.22-7.32 (5 H, m, phenyl-H), 2.96-3.04 (1 H, m, 1-H), 2.73-2.77 (1 H, m, 3-H), 2.55-2.60 (2 H, m, CH_2N), 2.33-2.43 (2 H, m, CH_2Ph), 1.34-1.99 (11 H, m,), 0.91 (3 H, t, *J* 7.6 Hz, Me); δ_C (75 MHz) 137.76 (Ar-C), 129.05, 128.39, 125.84 (Ar-CH), 64.35 (1-C), 50.44 (CH_2N), 46.02 (3-C), 38.02 (CH_2), 32.37 (5-C), 30.76, 29.46, 25.45, 23.01, 22.78 (CH_2), and 11.73 (Me); *m/z* 243.1987 [M^+ (3.1%), $C_{16}H_{23}N$ requires 243.1987], 242 (3), 229 (24), 214 (36), 152 (88), 105 (26), 91 (51), and 41 (100).

(c) Imine **22a**. The imine, formed by condensing aldehyde **13b** (197, 0.67 mmol) and 2-phenylethylamine (81 mg, 0.67 mmol), was cyclised using the standard procedure. *N-Acetyl-N-(2-phenylethyl)-2-(2-propen-1-yl)cyclohexylamine* **24a**-Ac was isolated as a yellow oil (34 mg, 18%) and *2-methyl-1-(2-phenylethyl)-perhydroindoline* **23a** as an orange oil which slowly darkened (54 mg, 33%). Amide **24a**-Ac: ν_{max} 3054, 2932, 2860, 1663, 1639, 1605, 1455, 1429, 1125, 1028, and 803 cm^{-1}; δ_H (300 MHz) 7.18-7.28 (5 H, m, phenyl-H), 5.70-5.74 (1 H, m, allyl 2-H), 5.00-5.05 (2 H, m, allyl 3-H), 3.54 (2 H, m, CH_2N), 3.18-3.23 (1 H, m, CHN), 2.84 (2 H, t, *J* 7.5 Hz, CH_2Ph), 2.38-2.42 (1 H, m, cyclohexyl 2-H), 2.30-2.36 (2 H, m, allylic H), 2.11 (3 H, s, Ac), and 1.29-1.70 (8 H, m); δ_C (75 MHz) 176.93 (C=O), 137.54 (Ar-C), 133.23 (alkene CH), 128.64, 127.43, 126.50 (Ar-CH), 113.09 (alkene CH_2), 51.03 (cyclopentyl 1-C), 40.94 (CH_2N), 32.63 (CH), 35.22, 34.14, 33.24,27.91, 26.75, 26.55 (CH_2), and 22.65 and 20.75 (MeCO); *m/z* 285.2072 [M^+ (1.2%), $C_{19}H_{27}NO$ requires 285.2072], 245 (13), 197 (39), 152 (36), 135 (74), 105 (62), 97 (52), 81 (48), 55 (60), and 43 (100). Amine **23a**: ν_{max} 2928, 2857, 1653, 1605, 1542, 1456, 749, and 699 cm^{-1}; δ_H (300 MHz), 2 stereoisomers: 7.18-7.32 (5 H, m, phenyl H), 3.66.3.70 (1 H, m, 7a-H), 3.26-3.30 (1 H, m, 2-H), 2.85-2.88 (2 H, m, CH_2N), 2.70-2.74 (2 H, m, CH_2Ph), 2.45-2.48 (1 H, m, 3a-H), 2.27-2.30 (2 H, m), 1.45-1.75 (8 H, m), and 1.01 and 1.06 (3 H, 2 x d, *J* 6.8 Hz, Me); δ_C (75 MHz) 140.46 (Ar-C), 128.57, 128.44, 128.32 (Ar-CH), 66.46 (7a-C), 59.96 (2-C), 50.01 (CH_2N), 38.74 (CH_2Ph), 35.28 (3a-C), 34.54, 28.82, 26.25, 24.73, 21.02 (CH_2), and 18.13 (Me); *m/z* 243.1981 [M^+ (0.5%), $C_{17}H_{25}N$ requires 243.1987], 242 (1), 152 (100), 105 (15), 91 (21), 77 (13), and 41 (46).

(d) Imine **22b**. The aldehyde **13d** (130 mg, 0.35 mmol) and *n*-propylamine (50 mg, 0.85 mmol) yielded *2-benzyl-1-propylperhydroindoline* **23b** as a yellow oil (52 mg, 57%); ν_{max} 2954, 2925, 2857, 1644, 1603, 1455, 1065, 1031, 740, and 700 cm^{-1}; δ_H (300 MHz), 2 stereoisomers: 7.21-7.29 (5 H, m, phenyl-H), 3.01-3.11 and 3.41-3.45 (1 H, 2 x m, 7a-H), 2.92-2.97 (1 H, m, 2-H), 2.56-2.67 (2 H, m, CH_2Ph), 2.29-2.33 (1 H, m, 3a-H), 1.45-1.75 (12 H, m), and 0.92 (3 H, t, *J* 7.6 Hz, Me); δ_C (75 MHz) 140.46 (Ar-C), 128.57, 128.44, 128.32 (Ar-CH), 66.46 (7a-C), 59.96 (2-C), 50.01 (CH_2N), 38.74 (CH_2Ph), 35.28 (3a-C), 34.54, 28.82, 26.25, 24.73, 21.02 (CH_2), and 18.13 (Me); *m/z* 257.2131 [M^+ (1.7%), $C_{17}H_{25}N$ requires 257.2143], 256 (1), 228 (8), 214 (7), 166 (100), 122 (5), 91 (21), and 43 (20).

Spirocyclic amines

General procedure for Grignard reactions.

(a) 9-Benzeneselenylnon-1-en-5-ol **25a**. Magnesium turnings (300 mg, 12.5 mmol) and 4-bromo-1-butene (1.35 g, 10 mmol), in a flame-dried 3-necked flask, were reacted in anhydrous diethyl ether (20 cm^3) under nitrogen until the Grignard reagent formed. A solution of 5-benzene-selenylpentanal[1,25] (1.184 g, 4.6 mmol) in diethyl ether (20 cm^3) was added dropwise at 0 °C over 30 min. The mixture was stirred for 24 h, after which water was added followed by hydrochloric acid (1.0 M). The products were extracted into diethyl ether and washed with water, dried and the solution evaporated to dryness. The product was purified by flash chromatography to yield *9-benzeneselenylnon-1-en-5-ol* **25a** as a pale yellow oil (1.197 g, 87%); ν_{max} 3442, 3075, 2977, 2931, 2838, 1641, 1578, 1478, 1438, 1390, 1151, 1119, 1092, 1042, 999, 737, and 692 cm^{-1}; δ_H 7.46-7.49 (2 H, m, *o*-H), 7.22-7.25 (3 H, m, Ar-H), 5.74-5.88 (1 H, m, 2-H), 4.99-5.05 (2 H, m, 1-H), 3.60-3.66 (1 H, m, 5-H), 2.91 (2 H, t, *J* 7.0 Hz, 9-H), 2.16-2.24 (2 H, m, 3-H), 1.88 (1 H, s, OH), 1.68-1.73 (2 H, m), and 1.46-1.55 (6 H, m); δ_C 138.46 (2-C), 132.40 (Ar-CH), 130.80 (Ar-C), 128.93, 126.62 (Ar-CH), 114.75 (1-C), 71.16 (5-C), 36.73, 36.37, 30.07, 29.83, 27.72, and 25.74 (CH_2); *m/z* 298.0883 [M^+, (7.1%), $C_{15}H_{22}OSe$ requires 298.0836], 227 (21), 158 (29), 139 (52), 84 (32), 78 (45), 69 (72), 61 (88), 55 (85), 41 (100).

(b) 10-Benzeneselenyldec-1-en-5-ol **25b**. 6-Benzeneselenylhexanal[1,26] (1.12 g, 4.4 mmol) and 4-bromo-1-butene (810 mg, 6 mmol) yielded **25b** as a pale yellow oil (1.294g, 94%); ν_{max} 3545, 3072, 2931, 2857, 1639, 1579, 1478, 1438, 1374, 1292, 1243, 1073, 1023, 736, and 691 cm^{-1}; δ_H 7.44-7.48 (2 H, m, *o*-H), 7.20-7.26 (3 H, m, Ar-H), 6.70 (1 H, br s, OH), 5.71-5.79 (1 H, m, 2-H), 4.96-5.04 (2 H, m, 1-H), 3.58-3.62 (1 H, m, 5-H), 2.88 (2 H, t, *J* 7.1 Hz, 10-H), 2.10-2.29 (2 H, m, 3-H), 1.64-1.73 (4 H, m), 1.50-1.59 (2 H, m), and 1.33-1.47 (4 H, m); δ_C 138.58 (2-C), 132.41 (Ar-CH), 130.50 (Ar-C), 128.99, 126.64 (Ar-CH), 114.79 (1-C), 71.35 (5-C), 37.27, 36.47, 32.57, 30.07, 29.77, 27.81, and 25.05 (CH_2); *m/z* (C.I.) 330.1336 [MH^+, (100%), $C_{16}H_{25}OSe$ requires 330.1336].

(c) 10-Benzeneselenyldec-1-en-6-ol **25c**. 5-Benzeneselenylpentanal (402 mg, 1.7 mmol) and 5-bromo-1-pentene (742 mg, 5.5 mmol) yielded **25c** as a pale yellow oil (486 mg, 94%); ν_{max} 3344, 3074, 2931, 2857, 1640, 1579, 1478, 1438, 1374, 1292, 1243, 1073, 1023, 912, 736, and 691 cm^{-1}; δ_H 7.44-7.49 (2 H, m, *o*-H), 7.20-7.27 (3 H, m, Ar-H), 5.75-5.84 (1 H, m, 2-H), 4.94-5.08 (2 H, m, 1-H), 3.58-3.64 (1 H, m, 6-H), 2.90 (2 H, t, *J* 7.1 Hz, 10-H), 2.02-2.14 (2 H, m, 3-H), 1.90 (1 H, s, OH), 1.62-1.72 (4 H, m), 1.40-1.53 (6 H, m); δ_C 138.18 (2-C), 132.38 (Ar-CH), 130.30 (Ar-C), 128.93, 126.61 (Ar-CH), 114.81 (1-C), 71.47 (6-C), 36.76, 33.62, 29.83, 28.78, 27.72, 25.89, and 24.81 (CH_2); *m/z* (C.I.) 330.1336 [MH^+, (100%), $C_{16}H_{25}OSe$ requires 330.1336].

(d) 11-Benzeneselenylundec-1-en-6-ol **25d**. 6-Benzeneselenylhexanal (730 mg, 2.9 mmol) and 5-bromo-1-pentene (1.31 g, 9.7 mmol) yielded **25d** as a pale yellow oil (895 mg, 95%); ν_{max} 3361, 3072, 2930, 2855, 1640, 1579, 1478, 1438, 1292, 1073, 1023, 911, 735, and 691 cm^{-1}; δ_H 7.46-7.49 (2 H, m, *o*-H), 7.21-7.25 (3 H, m, Ar-H), 5.71-5.79 (1 H, m, 2-H), 4.95-5.05 (2 H, m, 1-H), 3.57-3.67 (1 H, m, 6-H), 2.91 (2 H, t, *J* 7.1 Hz, 11-H), 2.04-2.12 (2 H, m, 3-H), 1.90 (1 H, s, OH), 1.63-1.71 (4 H, m), 1.37-1.46 (8 H, m); δ_C 138.58 (2-C), 132.43 (Ar-CH), 130.25 (Ar-C), 128.86, 126.54 (Ar-CH), 114.47 (1-C), 71.58 (6-C), 37.22, 36.83, 33.59, 30.00, 29.69, 27.77, 24.97, and 24.82 (CH_2); *m/z* (C.I.) 344.1493 [MH^+, (100%), $C_{17}H_{27}OSe$ requires 344.1492].

General procedure for Swern oxidations.

(a) 9-Benzeneselenylnon-1-en-5-one **26a**. DMSO (200 mg, 2.5 mmol) in CH_2Cl_2 (10 cm^3) was added dropwise over 5 min to a solution of oxalyl chloride (291 mg, 2.3 mmol) in CH_2Cl_2 (10 cm^3) at -78 °C. The mixture was stirred for 10 min before a solution of the alcohol **25a** (618 mg, 2.1 mmol) in CH_2Cl_2 (10 cm^3) was added dropwise over 5 min. The mixture was stirred for a further 10 min and triethylamine (500 mg, 5 mmol) was added. After 15 min stirring, the mixture was warmed to 0 °C and water and dilute hydrochloric acid were added. The product was extracted into the CH_2Cl_2 layer which was washed with water, dried and the solution evaporated to dryness. The product was purified by flash chromatography using silica as absorbent and light petroleum / ethyl acetate mixtures as eluent. **26a** was isolated as a pale orange oil (405 mg, 66%); ν_{max}

3078, 2929, 2858, 1708, 1641, 1579, 1478, 1438, 1381, 1326, 1162, 1073, 1022, 1000, 914, 734, and 691 cm^{-1}; δ_H 7.46-7.49 (2 H, m, *o*-H), 7.22-7.26 (3 H, m, Ar-H), 5.74-5.84 (1 H, m, 2-H), 4.94-5.10 (2 H, m, 1-H), 2.91 (2 H, t, *J* 7.0 Hz, 9-H), 2.28-2.36 (2 H, m, 3-H), 2.05-2.12 (2 H, m, 4-H), and 1.44-1.72 (6 H, m); δ_C 210.30 (C=O), 137.07 (2-C), 132.40 (Ar-CH), 129.30 (Ar-C), 129.01, 126.61 (Ar-CH), 115.23 (1-C), 33.70, 32.10, 29.97, 29.57, 27.44, and 26.50 (CH_2); *m/z* 296.0650 [M^+, (0.9%), $C_{15}H_{20}OSe$ requires 296.0679], 234 (9), 158 (16), 91 (31), 77 (32), 55 (100), 51 (34), and 41 (92).

(b) 10-Benzeneselenyldec-1-en-5-one **26b**. The alcohol **25b** (1.28 g) yielded **26b** as a pale orange oil (892 mg, 71%); ν_{max} 3072, 2931, 2856, 1714, 1641, 1579, 1478, 1438, 1366, 1246, 1190, 1073, 1023, 914, 737, and 692 cm^{-1}; δ_H 7.45-7.49 (2 H, m, *o*-H), 7.22-7.26 (3 H, m, Ar-H), 5.71-5.79 (1 H, m, 2-H), 4.97-5.09 (2 H, m, 1-H), 2.89 (2 H, t, *J* 7.1 Hz, 10-H), 2.31-2.44 (4 H, m, 3,4-H), 1.67-1.70 (2 H, m), 1.57-1.60 (2 H, m), and 1.33-1.44 (4 H, m); δ_C 210.20 (C=O), 137.14 (2-C), 132.50 (Ar-CH), 129.20 (Ar-C), 129.00, 128.70 (Ar-CH), 115.21 (1-C), 42.59, 41.81, 29.90, 29.30, 28.11, 27.63, and 23.13 (CH_2); *m/z* (C.I.) 328.1180 [MNH_4^+, (0.3%), $C_{16}H_{22}OSe$ requires 328.1179], 157 (3), 139 (6), 91 (6), 83 (42), and 55 (100).

(c) 10-Benzeneselenyldec-1-en-6-one **26c**. The alcohol **25c** (366 mg) yielded **26c** as a pale orange oil (244 mg, 67%); ν_{max} 3073, 2932, 2860, 1714, 1640, 1579, 1478, 1438, 1181, 1073, 1023, 913, and 692 cm^{-1}; δ_H (300 MHz) 7.51-7.55 (2 H, m, *o*-H), 7.25-7.30 (3 H, m, Ar-H), 5.77-5.82 (1 H, m, 2-H), 4.98-5.02 (2 H, m, 1-H), 2.93 (2 H, t, *J* 6.8 Hz, 10-H), 2.41-2.47 (4 H, m, 5,7-H), 2.16-2.21 (4 H, m), and 1.67-1.74 (4 H, m); δ_C (100 MHz), 192.02 (C=O), 132.95 (2-C), 132.13 (Ar-CH), 130.15 (Ar-C), 129.15, 128.87 (Ar-CH), 113.17 (1-C), 37.04, 36.80, 32.66, 29.53, 27.63, 25.80, and 22.61 (CH_2); *m/z* 310.0830 [M^+, (0.7%), $C_{16}H_{22}OSe$ requires 310.0836], 241 (9), 157 (19), 125 (32), 91 (40), 81 (57), and 55 (100).

(d) 11-Benzeneselenylundec-1-en-6-one **26d**. The alcohol **25d** (951 mg) yielded **26d** as a pale orange oil (735 mg, 78%); ν_{max} 3073, 2935, 2860, 1717, 1643, 1579, 1478, 1438, 1372, 1073, 1023, and 692 cm^{-1}; δ_H (300 MHz) 7.53-7.57 (2 H, m, *o*-H), 7.26-7.29 (3 H, m, Ar-H), 5.79-5.85 (1 H, m, 2-H), 4.99-5.02 (2 H, m, 1-H), 2.93 (2 H, t, *J* 6.8 Hz, 11-H), 2.40-2.46 (4 H, m, 5,7-H), 2.09-2.14 (4 H, m), and 1.50-1.74 (6 H, m); δ_C (100 MHz) 192.26 (C=O), 133.05 (2-C), 132.37 (Ar-CH), 130.15 (Ar-C), 129.22, 127.45 (Ar-CH), 112.95 (1-C), 37.01, 36.80, 33.54, 32.39, 31.37, 26.75, 24.78, and 22.75 (CH_2); *m/z* 324.0995 [M^+, (4%), $C_{17}H_{24}OSe$ requires 324.0992], 242 (9), 189 (22), 171 (31), 157 (22), 135 (27), 81 (38), and 41 (100).

Heck reactions. The general procedure for Heck reactions was used. *(a) 9-Benzeneselenyl-1-phenylnon-1-en-5-one* **27a**. The ketone **26a** (204 mg, 0.69 mmol), iodobenzene (141 mg, 0.69 mmol) and triethylamine (100 mg, 1 mmol) in the presence of palladium acetate (5 mg, 0.02 mmol) yielded **27a** as a red oil (182 mg, 71%); ν_{max} 3057, 2929, 2856, 1717, 1671, 1598, 1579, 1478, 1438, 1120, 1073, 1023, 737, and 693 cm^{-1}; δ_H 7.44-7.48 (2 H, m, *o*-H), 7.26-7.29 (8 H, m, Ar-H), 6.42 (1 H, d, *J* 15.8 Hz, 1-H), 6.22 (1 H, dt, *J* 15.8, 7.7 Hz, 2-H), 2.90 (2 H, t, *J* 7.2 Hz, 9-H), 2.41-2.54 (4 H, m), 2.05-2.08 (2 H, m), and 1.62-1.75 (4 H, m); δ_C 209.11 (C=O), 132.42, 132.34, 130.68, 129.26, 128.94, 127.03, 126.67, 125.70 (alkene and Ar-CH), 131.40, 130.15 (Ar-C), 32.04, 29.81, 29.64, 27.54, 25.42, and 23.09 (CH_2); *m/z* 372.0983 [M^+, (0.3%), $C_{21}H_{24}OSe$ requires 372.0992], 264 (5), 158 (12), 133 (28), 117 (30), 91 (46), 69 (81), and 41 (100).

(b) 10-Benzeneselenyl-1-phenyldec-1-en-5-one **27b**. The ketone **26b** (220 mg) yielded **27b** as a red oil (187 mg, 85%); ν_{max} 3056, 2931, 2859, 1714, 1655, 1603, 1579, 1478, 1438, 1072, 1023, 966, 737, and 692 cm^{-1}; δ_H 7.46-7.49 (2 H, m, *o*-H), 7.22-7.31 (8 H, m, Ar-H), 6.41 (1 H, d, *J* 15.7 Hz, 1-H), 6.20 (1 H, dt, *J* 15.7, 7.8 Hz, 2-H), 2.90 (2 H, t, *J* 7.5 Hz, 10-H), 2.39-2.50 (4 H, m), 2.03-2.07 (2 H, m), and 1.45-1.73 (6 H, m); δ_C 209.00 (C=O), 133.03, 132.96, 129.30, 128.99, 128.72, 128.46, 127.12, 126.13 (alkene and Ar-CH), 131.40, 130.08 (Ar-C), 32.10, 30.42, 29.64, 27.53, 27.22, 26.58, and 24.09 (CH_2); *m/z* 386.1129 [M^+, (0.3%), $C_{22}H_{26}OSe$ requires 386.1149], 242 (13), 182 (18), 157 (17), 154 (37), 117 (39), 105 (48), 91 (63), 77 (77), and 71 (100).

Cyclisation of Imines . The general procedure for imine formation and radical reactions were used.

(a) Imine **28a**. A solution of the ketone **26a** (225 mg, 0.76 mmol) and 2-phenylethylamine (92 mg, 0.76 mmol) in toluene was refluxed for 8 h, and the water removed using a Dean-Stark water separator. The imine was not isolated and was cyclised using the general procedure. Injection of Bu_3SnH (0.35 cm^3, 1.0 mmol) and

AIBN (42 mg, 0.26 mmol) in toluene using a syringe pump yielded *1-(3-buten-1-yl)-N-(2-phenylethyl)cyclopentylamine* **33a** as the only isolable product, a yellow oil (138 mg, 34%); ν_{max} 3054, 2959, 2869, 1668, 1603, 1497, 1455, and 1031 cm^{-1}; δ_H 7.25-7.32 (5 H, m, phenyl-H), 5.78-5.84 (1 H, m, butenyl 3-H), 5.00-5.04 (2 H, m, butenyl 4-H), 3.50 (1 H, br s, NH), 2.98 (2 H, t, *J* 6.3 Hz, CH_2N), 2.77 (2 H, t, *J* 6.3 Hz, CH_2Ph), 2.52-2.54 (2 H, m, butenyl 2-H), 2.31-2.34 (2 H, m, butenyl 1-H), 2.11-2.21 (2 H, m), and 1.52-1.75 (6 H, m, cyclopentyl H); δ_C (75 MHz) 139.88 (Ar-C), 137.09 (alkene CH), 128.77, 128.38, 126.09 (Ar-CH), 115.16 (alkene CH_2), 65.90 (cyclopentyl 1-C), 43.49, 41.77, 40.01, 36.74, 30.45, and 27.64 (CH_2); *m/z* 243.1987 [M^+ (1.0%), $C_{17}H_{25}N$ requires 243.1987], 182 (34), 149 (17), 105 (100), and 77 (79).

Cyclisation of Imine **28a** *in the presence of magnesium dibromide.* The procedure for the cyclisation of imine **26a** (274 mg, 0.69 mmol) was repeated with the addition of $MgBr_2.OEt_2$ (206 mg, 0.8 mmol) prior to the addition of Bu_3SnH to yield *2-methyl-1-(2-phenylethyl)-1-azaspiro[4.4]nonane* **32a** as a pale yellow oil (50 mg, 30%); ν_{max} 3029, 2930, 2858, 1658, 1604, 1496, 1455, 1367, 1082, and 1031 cm^{-1}; δ_H 7.25-7.32 (5 H, m, phenyl-H), 3.49-3.56 (2 H, m, CH_2N), 3.35-3.30 (1 H, m, 2-H), 2.83 (2 H, t, *J* 7.0 Hz, CH_2Ph), 2.06-2.15 (2 H, m), 1.39-1.80 (10 H, m), and 0.89 (3 H, d, *J* 6.3 Hz, Me); δ_C (100 MHz) 138.89 (Ar-C), 128.84, 128.47, 126.32 (Ar-CH), 57.80 (5-C), 52.12 (2-C), 40.65 (CH_2N), 35.65, 35.12, 30.93, 29.71, 23.35 (CH_2), and 14.02 (Me); *m/z* 243.1986 [M^+ (0.4%), $C_{17}H_{25}N$ requires 243.1987], 212 (13), 188 (9), 167 (100), 152 (15), 105 (25), 91 (23), and 77 (12).

(b) Imine **28b**. A solution of the ketone **26b** (153 mg) yielded 70 mg of crude products which were treated with acetyl chloride and triethylamine. The only isolable product from the reaction was *N-acetyl-1-(3-buten-1-yl)-N-(2-phenylethyl)cyclohexylamine* **33b**-Ac, an orange oil (52 mg, 35%); ν_{max} 3055, 2931, 2859, 1671, 1638, 1604, 1455, 1084, 1031, and 896 cm^{-1}; δ_H (300 MHz) 7.20-7.25 (5 H, m, phenyl-H), 5.79-5.83 (1 H, m, butenyl 3-H), 4.97-5.02 (2 H, m, butenyl 4-H), 3.56-3.60 (2 H, m, CH_2N), 2.84-2.87 (4 H, m), 2.31-2.47 (2 H, m, butenyl 1-H), 2.11 (3 H, s, Ac), and 1.25-1.69 (10 H, m, cyclohexyl H); δ_C (75 MHz), 176.62 (C=O), 140.20 (Ar-C), 137.11 (alkene CH), 128.74, 128.36, 126.06 (Ar-CH), 112.87 (alkene CH_2), 60.93 (cyclo-pentyl 1-C), 43.47, 41.68, 42.02, 40.00, 32.85, 32.52, 27.44 (CH_2), and 23.34 (MeCO); *m/z* 299.2237 [M^+ (0.4%), $C_{20}H_{29}NO$ requires 299.2249] 225 (15), 165 (9), 149 (27), 105 (100), 104 (95), 91 (60), 77 (68), 55 (37), and 41 (49).

Cyclisation of Imine **28b** *in the presence of magnesium dibromide. 2-Methyl-1(-2-phenylethyl)-1-azaspiro-[4.5]decane* **32b**, a pale yellow oil (63 mg, 33%); ν_{max} 3027, 2926, 2856, 1654, 1603, 1497, 1453, 1364, and 1126 cm^{-1}; δ_H 7.22-7.32 (5 H, m, phenyl-H), 3.47-3.55 (2 H, m, CH_2N), 3.27-3.33 (1 H, m, 2-C), 2.83 (2 H, t, *J* 7.0 Hz, CH_2Ph), 2.05-2.12 (2 H, m), 1.28-1.80 (10 H, m), and 0.88 (3 H, d, *J* 6.0 Hz, Me); δ_C (100 MHz) 137.60 (Ar-C), 128.73, 128.57, 126.44 (Ar-CH), 57.75 (5-C), 51.88 (2-C), 40.57 (CH_2N), 35.56, 35.04, 32.85, 30.72, 30.31, 27.76 (CH_2), and 19.71 (Me); *m/z* 257.2157 [M^+ (0.2%), $C_{18}H_{27}N$ requires 257.2143], 212 (13), 188 (9), 167 (100), 152 (15), 105 (25), 91 (23), and 77 (12).

(c) Imine **28c**. A solution of the ketone **27a** (171 mg, 0.46 mmol) and *n*-propylamine (136 mg, 2.3 mmol) in toluene was refluxed for 8 h, and the water removed using a Dean-Stark water separator. Injection of Bu_3SnH (0.23 cm^3, 0.66 mmol) and AIBN (27 mg, 0.16 mmol) in toluene using a syringe pump yielded *2-benzyl-1-propyl-1-azaspiro[4.4]nonane* **32c** as a yellow oil (32 mg, 27%); ν_{max} 3055, 2930, 2858, 1658, 1604, 1438, 1185, 1120, and 896 cm^{-1}; δ_H 7.22-7.34 (5 H, m, phenyl-H), 3.51-3.54 (1 H, m, CHN), 3.16-3.20 (1 H, m, PhCH), 2.80-2.84 (1 H, m, PhCH), 2.43-2.57 (2 H, m, CH_2N), 2.10-2.16 (2 H, m), 1.26-1.66 (12 H, m), and 0.91 (3 H, t, *J* 7.5 Hz, Me); *m/z* 257.2131 [M^+ (1.9%), $C_{17}H_{25}N$ requires 257.2143], 201 (9), 155 (17), 91 (19), and 77 (33), 69 (39), 55 (64), 41 (100).

(d) Imine **28d**. *2-Benzyl-1-propyl-1-azaspiro[4.5]decane* **32d**, a yellow oil (44 mg, 39%); ν_{max} 3057, 2932, 2859, 1658, 1604, 1455, 1073, 1023, and 737 cm^{-1}; δ_H 7.26-7.30 (5 H, m, phenyl-H), 3.61-3.68 (1 H, m, CHN), 2.99 (2 H, m, $PhCH_2$), 2.47-2.50 (2 H, m, CH_2N), 2.24-2.30 (1 H, m), 2.00-2.07 (1 H, m), 1.45-1.90 (16 H, m), and 0.89 (3 H, t, *J* 6.8 Hz, Me).

(e) Imine **28e**. A solution of the ketone **26c** (154 mg, 0.5 mmol) and benzylamine (53 mg, 0.5 mmol) in toluene was refluxed for 6 h, and the water removed using a Dean-Stark water separator. The imine was cyclised using the general procedure, with the addition of $MgBr_2.OEt_2$ (258 mg, 1 mmol) prior to the addition of Bu_3SnH to yield *6-benzyl-7-methyl-6-azaspiro[4.5]decane* **32e** as a pale yellow oil (32 mg, 27%); ν_{max}

3030, 2925, 2854, 1655, 1603, 1459, 1376, 1155, 1074, and 1029 cm^{-1}; δ_H 7.27-7.35 (5 H, m, phenyl-H), 3.83 (2 H, s, CH_2Ph), 3.71-3.75 (1 H, m, 7-H), 1.95-2.09 (2 H, m), 1.20-1.72 (12 H, m), and 0.88 (3 H, d, *J* 6.5 Hz, Me); *m/z* 243.1996 [M^+ (0.3%), $C_{17}H_{25}N$ requires 243.1987], 149 (7), 97 (13), 91 (100), 83 (17), 71 (26), 57 (52), and 43 (59).

(f) Imine **28f**. *1-Benzyl-2-methyl-1-azaspiro[5.5]undecane* **32f**, a pale yellow oil (60 mg, 29%); ν_{max} 3059, 2930, 2855, 1668, 1603, 1496, 1454, 1076, and 1029 cm^{-1}; δ_H 7.27-7.35 (5 H, m, phenyl-H), 3.82 (2 H, 3, CH_2Ph), 3.59-3.63 (1 H, m, 2-H), 1.38-1.80 (16 H, m), and 0.87 (3 H, d, *J* 6.5 Hz, Me); δ_C (100 MHz) 140.67 (Ar-C), 128.93, 128.53, 127.32 (Ar-CH), 60.02 (6-C), 53.54 (CH_2Ph), 48.22 (3-C), 30.53, 30.06, 28.23, 29.90, 27.27, 25.97 (CH_2), and 18.22 (Me); *m/z* 257.2134 [M^+ (0.3%), $C_{18}H_{27}N$ requires 257.2143], 188 (5), 149 (5), 134 (6), 106 (29), 91 (100), 77 (9), and 65 (14).

Indolizidines

Ethyl 5-(4-methylphenyl)-4-pentenoate. Using the general procedure for the Heck reaction, ethyl 4-pentenoate (2.56 g, 20 mmol) and 4-iodotoluene (4.36 g, 20 mmol) yielded *ethyl 5-(4-methylphenyl)-4-pentenoate* as a colourless oil (3.635 g, 83%); (Found: C, 77.0; H, 8.16. $C_{14}H_{18}O_2$ requires C, 77.0; H, 8.31%); ν_{max} 2962, 2936, 2875, 1735, 1654, 1603, 1514, 1464, 1371, 1252, 1181, 1037, 969, and 803 cm^{-1}; δ_H 7.23 and 7.09 (4 H, 2 x d, *J* 8.0 Hz, Ar-H), 6.39 (1 H, d, *J* 16 Hz, 5-H), 6.14 (1 H, dt, *J* 16, 6.5 Hz, 4-H), 4.13 (2 H, q, *J* 7.0 Hz, CH_2O), 2.46-2.53 (4 H, m, 2,3-H), 2.31 (3 H, s, MeAr), and 1.25 (3 H, t, *J* 7.0 Hz, Me); δ_C 177.96 (C=O), 138.13 and 136.77 (Ar-C), 130.71, 129.11, 127.36 and 125.88 (alkene and Ar-CH), 60.29 (CH_2O), 34.08 and 28.25 (2,3-C), 21.05 (MeAr), and 14.19 (Me).

5-(4-Methylphenyl)-4-pentenal. The general procedure for the synthesis of aldehydes using ethyl 5-(4-methylphenyl)-4-pentenoate (1.53 g, 7 mmol) gave *5-(4-methylphenyl)-4-pentenal* as a yellow oil (947 mg, 78%); ν_{max} 3023, 2922, 2861, 2714, 1724, 1675, 1605, 1514, 1446, 1118, 1042, 814, and 698 cm^{-1}; δ_H 9.78 (1 H, s, 1-H), 7.20 and 7.09 (4 H, 2 x d, *J* 8.0 Hz, Ar-H), 6.38 (1 H, d, *J* 16 Hz, 5-H), 6.12 (1 H, dt, *J* 16, 6.5 Hz, 4-H), 2.60 (2 H, m, 3-H), 2.52 (2 H, t, *J* 6.8 Hz, 2-H), and 2.30 (3 H, s, MeAr); δ_C 201.86 (C=O), 130.92 and 130.12 (Ar-C), 129.50, 129.18, 127.03 and 125.90 (alkene and Ar-CH), 43.31, 25.47 (2,3-C), and 21.08 (MeAr); *m/z* 174.1033 [M^+, (35%), $C_{12}H_{14}O$ requires 174.1045], 158 (11), 143 (14), 131 (39), 118 (62), 105 (100), and 91 (35).

5-Benzeneselenyl-2-pentylamine. 4-Benzeneselenylbutanonitrile[1,28] (896 mg, 4.0 mmol) was dissolved in anhydrous diethyl ether and a solution of methylmagnesium bromide in diethyl ether (1.3 cm^3 of 3 M solution) added dropwise over 10 min. The mixture was stirred at room temperature for 4 h. The intermediate imine was not isolated but was treated with sodium borohydride (60 mg, 1.6 mmol) in dry methanol and stirred for 18 h. Water was added to the mixture followed by careful addition of 1.0 M HCl until the aqueous layer was pH 1. The acidic layers were washed with dichloromethane, basified and extracted with dichloromethane. The organic phase was dried and evaporated to dryness yielding the amine as a light orange oil which was not purified further (436 mg, 45%); ν_{max} 3053, 2958, 2927, 2865, 1650, 1577, 1475, 1436, 1375, 737 and 691 cm^{-1}; δ_H 7.46-7.50 (2 H, m, *o*-H), 7.23-7.25 (3 H, m, Ar-H), 2.91 (2 H, t, *J* 7.3 Hz, 5-H), 2.84-2.87 (1 H, m, 2-H), 1.66-1.78 (2 H, m, 3-H), 1.63 (2 H, brs, NH_2), 1.40-1.48 (2 H, m, 4-H), and 1.04 (3 H, d, *J* 7.5 Hz, 1-H); *m/z* 243.0526 [M^+ (1.1%), $C_{11}H_{17}NSe$ requires 243.0526], 157 (5), 86 (59), 77 (11), 69 (25), and 44 (100).

Cyclisation of imines. The imines were formed by refluxing in toluene for 4 h using a Dean-Stark water separator and cyclised using the general procedure.

(a) Attempted 5-endo cyclisation. The imine from 5-(4-methylphenyl)-4-pentenal (261 mg, 1.5 mmol) and 3-benzeneselenyl-1-propylamine[1,27] (321 mg, 1.5 mmol) was cyclised using the general procedure to yield *5-(4-methylphenyl)-N-propyl-4-penten-1-ylamine* as the only isolable product, a yellow oil (88 mg, 27%); ν_{max} 3380, 2955, 2925, 2854, 1656, 1605, 1465, 1136, and 739 cm^{-1}; δ_H 7.22 (2 H, d, *J* 8.1 Hz), 7.07 (2 H, d, *J* 8.1 Hz, Ar-H), 6.35 (1 H, d, *J* 16 Hz, 5-H), 6.15 (1 H, dt, *J* 16, 6.8 Hz, 4-H), 2.55-2.66 (4 H, m, 2 x CH_2N), 2.31 (3 H, s, MeAr), 2.24-2.29 (2 H, m, 3-H), 1.47-1.68 (4 H, m), and 0.91 (3 H, t, *J* 7.5 Hz, propyl 3-H); δ_C 136.57, 134.96 (Ar-C), 130.00, 129.17, 128.27, 125.84, (alkene and aromatic Ar-CH),

51.82, 49.39 (CH_2N), 30.83, 29.62, 23.04 (CH_2), 21.12 (MeAr), and 11.78 (propyl 3-C); *m/z* 217.1830 [M^+, (15%), $C_{15}H_{23}N$ requires 217.1830], 188 (10), 129 (11), 115 (9), 105 (25), 98 (36), and 72 (100).

(b) Imine **34a**. 5-(4-Methylphenyl)-4-pentenal (160 mg, 0.92 mmol) and 4-benzeneselenyl-1-butylamine (210 mg, 0.92 mmol) yielded *3-(4-methylbenzyl)indolizidine* **38a** as the only isolable product, a yellow oil (55 mg, 26%); ν_{max} 3052, 2934, 2859, 1667, 1615, 1445, 1115, 740 and 704 cm^{-1}; δ_H (300 MHz), 2 diastereomers: 7.07-7.11 (4 H, m, phenyl H), 3.59-3.63 and 2.21-2.29 (2 H, 2 x m, CH_2Ph), 3.22-3.26 (1 H, m, 8a-H), 3.01-3.05 and 2.71-2.74 (2 H, 2 x m, 5-H), 2.88-2.90 (1 H, m, 3-H), 2.33 (3 H, m, MeAr), 2.10-2.11 (2 H, m), and 1.30-1.89 (8 H, m); δ_C (100 MHz), 132.40, 132.25 (Ar-C), 128.94, 128.13 (Ar-CH), 46.35 (8a-C), 40.65 (CH_2Ph), 35.64 (5-C), 39.46 (3-C), 30.52, 29.71, 27.96, 27.14, 23.36 (CH_2), and 21.02 (Me); *m/z* 229.1825 [M^+ (3.4%), $C_{16}H_{23}N$ requires 229.1830], 228 (4), 124 (69), 104 (42), 91 (18), 72 (21), 43 (46), and 30 (100).

(d) Imine **34b**. 5-(4-Methylphenyl)-4-pentenal (226 mg, 1.3 mmol) and 5-benzeneselenyl-2-pentylamine (315 mg, 1.3 mmol) yielded *5-methyl-3-(4-methylbenzyl)indolizidine* **38b** as the only isolable product, a red oil (60 mg, 19%); ν_{max} 2924, 1669, 1609, 1515, 1438, 1038, 812, and 737 cm^{-1}; δ_H 6.98-7.05 (4 H, m, Ar-H), 3.64-3.67 and 2.33-2.38 (2 H, 2 x m, CH_2Ph), 3.43-3.46 (1 H, m, 8a-H), 2.77-2.83 (1 H, m, 5-H), 2.59-2.66 (1 H, m, 3-H), 2.34 (3 H, s, MeAr), 1.95-2.08 (2 H, m), 1.45-1.76 (8 H, m), and 0.95 (3 H, d, *J* 6.8 Hz, 5-Me); δ_C (100 MHz) 132.36, 132.15 (Ar-C), 128.94, 127.99 (Ar-CH), 49.62 (5-C), 47.73 (8a-C), 39.46 (3-C), 35.11, 34.06, 32.37, 31.91, 29.71, 29.32 (CH_2), 21.15, and 21.02 (Me); *m/z* 243.1978 [M^+ (0.2%), $C_{17}H_{25}N$ requires 243.1987], 195 (6), 143 (11), 128 (8), 119 (13), 105 (100), and 77 (19).

(e) Imine **34c**. 4-Pentenal (210 mg, 2.5 mmol) and 5-benzeneselenyl-2-pentylamine (124 mg, 0.51 mmol) yielded amine products which were precipitated by bubbling dry HCl through the solution to yield a colourless oil (94 mg, 63%, after drying under vacuum). ^1H NMR and COSY spectroscopy indicated that there were two main products, the monocyclic amine **39** and the indolizidine **38c** in the ratio of 1.60:1. Separation of the two compounds could not be not achieved; ν_{max} 2960, 1671 1641, 1434, and 896 cm^{-1}; δ_C (100 MHz), 136.75, 114.37 (alkene-C), 76.12, 62.99, 55.54, 54.02 (4 x CH), 38.46, 32.74, 31.99, 31.01, 29.49, 28.78, 28.49, 25.92, 25.55, 22.12, 21.77 (11 x CH_2), 16.20, 13.19, and 12.39 (3 x CH_3); *m/z* 154.1531 [MH^+ (4.0%), $C_{10}H_{20}N$ requires 154.1598], 131 (19), 98 (45), 91 (38), 79 (33), 69 (95), 55 (73), and 41 (100).
2-Methyl-N-(4-pentenyl)pyrrolidine hydrochloride **39**.HCl; δ_H (400 MHz) 5.60-5.67 (1 H, m, 4'-H), 4.88-4.98 (5'-H), 3.35-3.44 and 3.16-3.19 (2 H, 2 x m, 5-H), 3.00-3.09 (2 H, m, 1'-H), 2.10-2.35 (8 H, m, 3,4-H, 2'-3'-H), and 1.25 (3 H, d, *J* 6.5 Hz, Me). *3,5-Dimethylindolizidine hydrochloride* **38c**.HCl; δ_H (400 MHz) 4.28-4.32 (1 H, m, 8a-H), 4.02-4.08 and 3.89-3.95 (2 H, 2 x m, 3,5-H), 1.66-1.92 (8 H, m, 1,2,6,7-H) and 1.53 (3 H, d, *J* 6.5 Hz), and 1.30 (6 H, d, 3,5-Me).

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