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Synthesis of substituted piperidines, decahydroquinolines and octahydroindolizines by radical rearrangement reactions of 2-alkylideneaziridines

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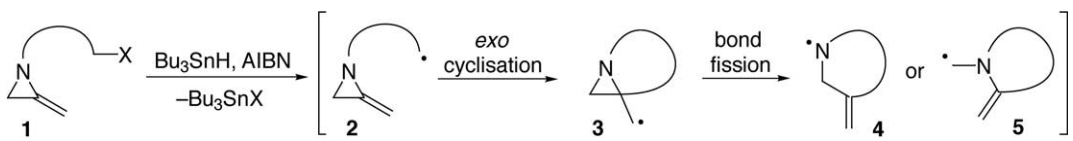
Abstract—Rearrangement of a variety of 3-(2-methyleneaziridin-1-yl)propyl radicals, generated using Bu_3SnH/AIBN by homolytic cleavage of phenylselenide substituted 2-methyleneaziridines, produces 3-methylenepiperidines in yields ranging from 58 to 68%. By combining this radical rearrangement with an additional 5-*exo*-trig cyclisation, this method provides an octahydroindolizine with moderate levels of diastereocontrol (d.r.=4:1). This rearrangement works with related 2-isopropylideneaziridines, but cannot be successfully extended to 4-(2-methyleneaziridin-1-yl)butyl radicals.

1. Introduction

It is well established that relief of ring strain can provide a powerful thermodynamic driving force for novel chemical reactions. Our interest in developing new methods for synthesis based upon this principle has led us to explore the reactivity of 2-methyleneaziridines. This densely functionalised heterocyclic system is calculated to possess 12–13 kcal mol^{-1} (HF/6-31G* level) more ring strain energy than aziridine itself.[1] It transpires that whilst first prepared over 50 years ago,[2] the chemistry of 2-methyleneaziridines has not been extensively explored. Alper and Hamel have shown that this heterocyclic system can be ring expanded to the corresponding α-methylene-β-lactam by palladium catalysed carbonylation.[3] A variety of [2π+2π] and [3π+2π] cycloaddition reactions of the exocyclic double bond have been reported.[4] Furthermore, several reports concerning simple ring opening reactions of the aziridine have been described.[5] Recently, in our own laboratories, we have developed multi-component reactions of 2-methyleneaziridines involving aziridine ring opening as the first step.[6] This methodology has been used to make a wide variety of ketones[6c] and amines, including the hemlock alkaloid (*S*)-coniine in a very concise fashion.[6b]

In seeking to devise new synthetic methods using 2-methyleneaziridines, we became interested in exploring their radical rearrangement chemistry. By analogy with the work of Kilburn et al., who have demonstrated that radical rearrangements of methylenecyclopropanes can be used to construct a variety of carbocyclic ring systems,[7] we wondered whether heterocyclic systems might be accessible by similar reactions involving 2-methyleneaziridines. The basic strategy is outlined in Scheme 1. After generation from a suitable precursor such as 2-methyleneaziridine **1**, the resulting alkyl radical within **2** might be expected to cyclise onto the double bond via an *exo* manifold to generate aziridinylcarbinyl radical **3**. Further relief of ring strain from this system by either C–N or C–C bond fission would lead to aminyl radical **4** or carbon centred radical **5**, respectively. Earlier work by Stamm,[8] Murphy,[9] DeKimpe[10] among others[11] has established that opening of simple aziridinylcarbinyl radicals is facile and usually results in the formation of the aminyl radical by preferential opening of the C–N bond. Thus, we anticipated that aminyl radical **4** would be produced, by an overall process which formally can be considered as a ring expansion. Importantly, we anticipated that by the incorporation of additional radical acceptors into the substrates, further cyclisation reactions of



Scheme 1.

Keywords: aziridines; radicals and radical reactions; strained compounds.

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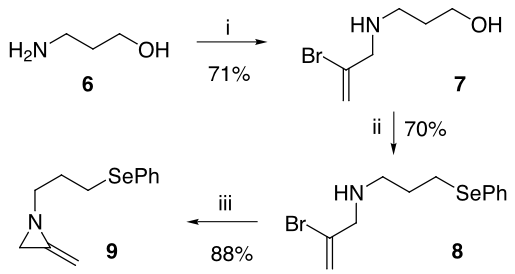


Scheme 2. *Reagents and conditions*: (i) 2,3-dibromopropene, K_2CO_3, THF, reflux; (ii) NPSP, Bu_3P, THF, 0°C; (iii) $NaNH_2$ (15 equiv.), NH_3, 25 min.

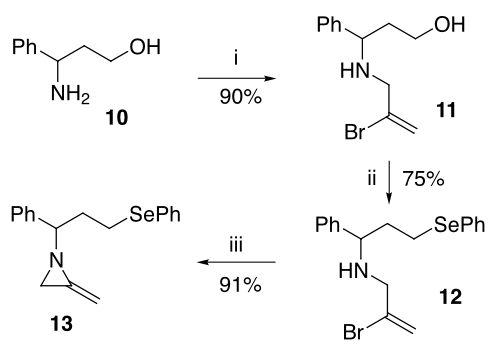
aminyl radical **4** could be realised allowing more complex heterocyclic systems to be assembled by this process.[12] In this paper, we describe in detail our work on such radical rearrangement reactions.[13]

2. Results and discussion

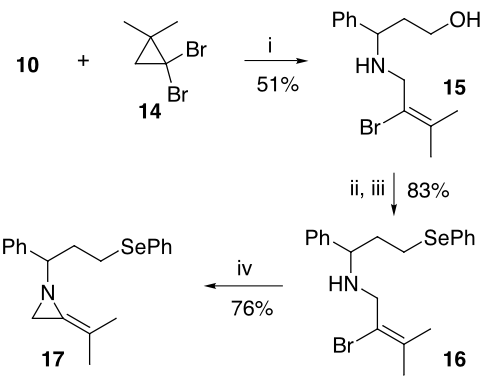
2.1. Precursor synthesis

Whilst a wide variety of C–X bonds can be homolytically cleaved to alkyl centred radicals,[14] we felt that the selection of the X grouping within **1** needed careful consideration (Scheme 1). Since 2-methyleneaziridines are often made under forcing reaction conditions {$NaNH_2$/liq. NH_3},[2,15] traditional radical precursors such as alkyl bromides and iodides could not be used. To circumvent these problems, we chose the more heterolytically robust phenylselenide group (X=PhSe), which has been shown by Clive to be an excellent precursor of carbon centred radicals.[16] An additional advantage of this group in synthetic terms, is that it can be directly introduced from the corresponding alcohol.[17]

With the selection of the radical progenitor made, the synthesis of appropriate radical precursors was relatively straightforward. The synthesis of 2-methyleneaziridine **9** was achieved in three steps from commercially available 3-aminopropanol **6** in good overall yield (Scheme 2). Alkylation of 2,3-dibromopropene with a two-fold excess of this inexpensive amino alcohol yielded **7** in 71% yield. We have found that it is advantageous to use the electrophile as the limiting reagent to suppress the formation of the corresponding tertiary amine. Direct selenation of the hydroxyl group of **7** using *N*-phenylselenophthalimide



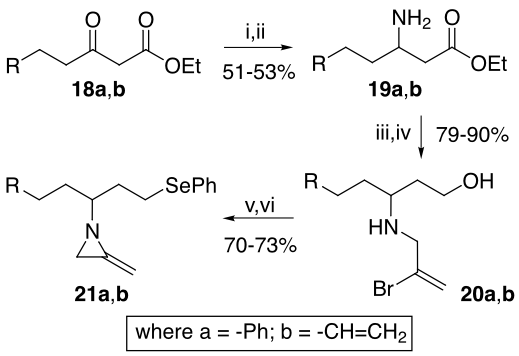
Scheme 3. *Reagents and conditions*: (i) 2,3-dibromopropene, K_2CO_3, THF, reflux; (ii) NPSP, Bu_3P, THF, 0°C; (iii) $NaNH_2$ (15 equiv.), NH_3, 10 min.



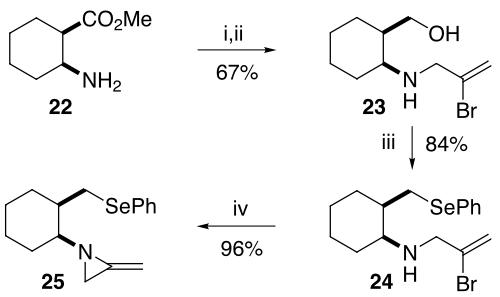
Scheme 4. *Reagents and conditions*: (i) K_2CO_3, 1,2-dichlorobenzene, 160°C; (ii) MsCl, Et_3N, toluene, 0°C→room temperature; (iii) $(PhSe)_2$, $NaBH_4$, EtOH, reflux; (iv) $NaNH_2$ (30 equiv.), NH_3, 90 min.

(*N*-PSP) and tri-*n*-butylphosphine[17] provided selenide **8**, which was transformed into 2-methyleneaziridine **9** by treatment with excess sodium amide in liquid ammonia according to the method originally described by Pollard and Parcell.[2] Attempts to purify **9** and the other 2-methyleneaziridines used in this study by column chromatography or distillation led to extensive degradation. In contrast, related isopropylideneaziridine **17** (Scheme 4) could readily be purified by silica gel chromatography. Fortuitously, **9** (and the other 2-methyleneaziridines) were sufficiently pure that they could be fully characterised and used in the subsequent radical rearrangements without purification beyond a simple aqueous work-up.

Using the same three-step sequence of alkylation, selenation and ring closure, 3-amino-3-phenylpropan-1-ol **10**[18] was converted into 2-methyleneaziridine **13** via **11** and **12** in good overall yield (Scheme 3). An additional substrate for the radical chemistry, namely 2-isopropylideneaziridine **17**, was also made from amino alcohol **10**. Alkenyl bromide **15**, bearing *gem*-dimethyl substitution, was made by ring opening of 1,1-dibromo-2,2-dimethylcyclopropane **14**[19] with **10** in 1,2-dichlorobenzene at 160°C.[20] Mesylation of the hydroxyl group of **15** followed by displacement with phenylselenide anion gave **16**, which after further ring closure gave 2-isopropylideneaziridine **17** (Scheme 4). The two-step sequence used for the introduction of the phenyl selenide group in this example appears to be as effective as the direct *N*-PSP method which was not examined in this



Scheme 5. *Reagents and conditions*: (i) NH_4OAc, AcOH, PhH, Dean–Stark; (ii) $NaBH(OAc)_3$, AcOH; (iii) $LiAlH_4$, THF, 0°C→reflux; (iv) 2,3-dibromopropene, K_2CO_3, THF, reflux; (v) NPSP, Bu_3P, THF, 0°C; (vi) $NaNH_2$ (15 equiv.), NH_3, 20 min.



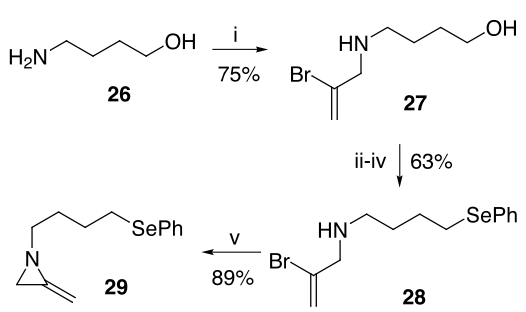
Scheme 6. *Reagents and conditions*: (i) 2,3-dibromopropene, K_2CO_3, THF, reflux; (ii) $LiAlH_4$, THF, 0°C→reflux; (iii) NPSP, Bu_3P, THF, 0°C; (iv) $NaNH_2$ (15 equiv.), NH_3, 55 min.

instance. Interestingly, more forcing conditions were required for this ring closure than were needed to prepare the analogous 2-methyleneaziridine **13** {$NaNH_2$ (30 equiv.), 90 min cf. $NaNH_2$ (15 equiv.), 10 min}.

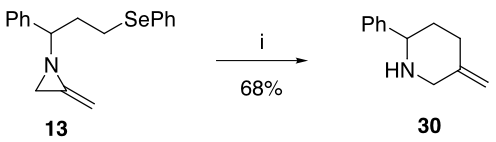
β-Amino esters **19a** and **19b** were made from the corresponding β-keto esters **18a**[21] and **18b**[21] by enamine formation and subsequent reduction using sodium triacetoxyborohydride according to a known method.[22] Reduction with lithium aluminium hydride followed by *N*-alkylation with 2,3-dibromopropene gave amino alcohols **20a** and **20b**, respectively. Selenation and final ring closure yielded 2-methyleneaziridines **21a** and **21b** (Scheme 5).

β-Amino ester **22**, made from 1,2-cyclohexanedicarboxylic anhydride in three steps,[23] was transformed into methyleneaziridine **25** via **23** and **24** in good overall yield using similar chemistry to that described above (Scheme 6).

Finally, to explore the corresponding 6-*exo* radical cyclisation, we prepared homologous methyleneaziridine **29**. To our surprise, the synthesis of this compound was more problematic than initially anticipated. Attempted selenation of alcohol **27**, made by alkylation of 2,3-dibromopropene with 4-aminobutanol **26**, led to complex mixtures from which selenide **28** could not be isolated (cf. **7**→**8**, Scheme 2). Speculating that intramolecular ring closure leading to pyrrolidine formation might be competing with the desired intermolecular substitution reaction, we decided to render the NH non-nucleophilic prior to selenation. After Boc protection of **27**, selenation using *N*-PSP and tri-*n*-butylphosphine proceeded uneventfully, yielding **28** after removal of the Boc group using trifluoroacetic acid (Scheme 7). Subsequent ring closure of **28** using sodium



Scheme 7. *Reagents and conditions*: (i) 2,3-dibromopropene, K_2CO_3, THF, reflux; (ii) $(Boc)_2O$, Et_3N, DMAP, CH_2Cl_2; (iii) NPSP, Bu_3P, THF, 0°C; (iv) TFA, CH_2Cl_2; (v) $NaNH_2$ (15 equiv.), NH_3, 45 min.



Scheme 8. *Reagents and conditions*: (i) Bu_3SnH (slow addition), AIBN, PhH (0.015 M), reflux.

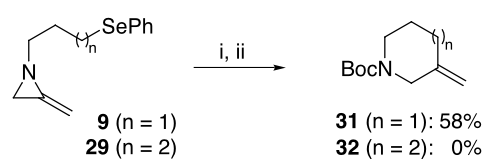
amide gave 2-methyleneaziridine **29** which was again used without further purification.

2.2. Radical rearrangements

Initial efforts to optimise the radical rearrangement chemistry were undertaken using phenyl substituted 2-methyleneaziridine **13** because we anticipated that the products derived from this substrate would be substantially less volatile and water soluble than those derived from the unsubstituted 2-methyleneaziridine **9**. Slow addition over 4.5 h of tri-*n*-butyltin hydride and AIBN in benzene via a syringe pump to a refluxing solution of **13** in benzene provided piperidine **30** in an optimised 68% yield (Scheme 8). We have established that dilute reaction conditions (final [**13**]=0.015 M) and slow addition of the Bu_3SnH/AIBN mixture are necessary to obtain this yield. From a practical standpoint, it is notable that whilst removal of tin residues is often problematic in radical reactions, the use of an acid/base extraction protocol in the work-up of **30** made the removal of the tin byproducts very straightforward in this instance (see Section 3).

The structure of piperidine **30** was unambiguously established using standard spectroscopic techniques. Key structural elements were identified as indicated below. The molecular formula ($C_{12}H_{15}N$) was established by high-resolution mass spectrometry. The exocyclic double bond bearing two hydrogens was identified by ^1H NMR spectroscopy (δ 4.81 and 4.77). The presence of an NH group was established by IR spectroscopy (3288 cm^{-1}) and ^1H NMR spectroscopy (δ 1.85, bs). The presence of CH and CH_2 groups adjacent to nitrogen was apparent by ^{13}C NMR spectroscopy (δ 61.5 and 53.6, respectively). ^1H NMR spectroscopy revealed that this methylene CH_2 was isolated from other hydrogens as it possessed only geminal coupling (J=12.6 Hz). Finally, the presence of two additional methylene carbons (δ 36.2, 33.5) and the connectivity between all the ring carbons was established using correlation spectroscopy.

These optimised reaction conditions were used to study the radical rearrangements of the other 2-alkylideneaziridines (**9**, **17**, **21a**, **21b**, **25**, **29**). Reaction of 2-methyleneaziridine **9** with Bu_3SnH/AIBN under these conditions provided 3-methylenepiperidine **31** in 58% yield after in situ Boc

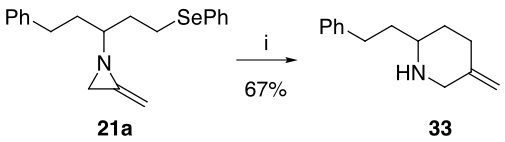


Scheme 9. *Reagents and conditions*: (i) Bu_3SnH (slow addition), AIBN, PhH (0.015 M), reflux; (ii) $(Boc)_2O$, Et_3N.

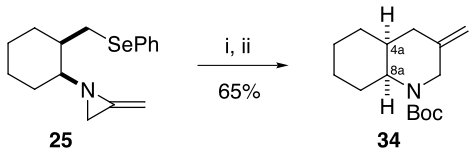
protection to reduce the volatility and water solubility of the product (Scheme 9). However, attempts to extend this chemistry to a larger ring size proved entirely unsuccessful. Under identical conditions, **29** produced no trace of azepane **32**. Analysis of the crude reaction mixture by ^{1}H NMR spectroscopy indicated that the methyleneaziridine ring was largely intact, and that the integration for one methylene triplet (δ 2.88, ascribed to $-CH_2SePh$ in **29**) was significantly reduced relative the methyleneaziridine signals. Direct observation of the anticipated new methyl triplet was not possible because of the presence of Bu_3Sn- signals in this region of the spectrum. On the basis of this evidence, we tentatively suggest that the major product from this reaction is the reduction product, *N*-butyl-2-methyleneaziridine. Unfortunately, repeated attempts to isolate and fully characterise this compound by chromatography were unsuccessful.

Greater success was achieved in the rearrangement of 2-methyleneaziridine **21a**. This substrate was transformed into 6-alkylpiperidine **33** in 67% yield using the same Bu_3SnH/AIBN method (Scheme 10). Furthermore, 2-methyleneaziridine **25** was rearranged to the decahydroquinoline skeleton which was again conveniently isolated after in situ *N*-Boc protection (Scheme 11). The ring junction stereochemistry within **34** was assigned as *cis* on the basis of strong nOe enhancements observed between H-4a and H-8a {H-8a (5.8%) from H-4a; and of H-4a (9.2%) from H-8a}. Furthermore, reaction of isopropylideneaziridine **17** with Bu_3SnH/AIBN then Boc_2O gave piperidine **35** in 62% yield (Scheme 12).

We have examined whether the presumed aminyl radical generated in this rearrangement chemistry will participate in additional radical cyclisations.[12] Treatment of **21b** with Bu_3SnH/AIBN resulted in the isolation of octahydroindolizine **37** in 39% yield as a single diastereomer after careful

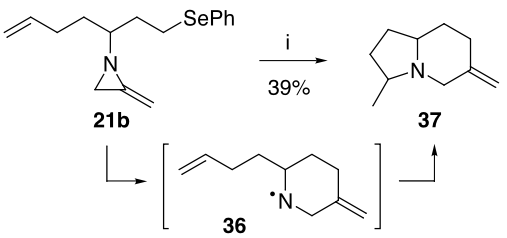


Scheme 10. *Reagents and conditions*: (i) Bu_3SnH (slow addition), AIBN, PhH (0.015 M), reflux.



Scheme 11. *Reagents and conditions*: (i) Bu_3SnH (slow addition), AIBN, PhH (0.015 M), reflux; (ii) $(Boc)_2O$, Et_3N.

Scheme 12. *Reagents and conditions*: (i) Bu_3SnH (slow addition), AIBN, PhH (0.015 M), reflux; (ii) $(Boc)_2O$, Et_3N.



Scheme 13. *Reagents and conditions*: (i) Bu_3SnH (slow addition), AIBN, PhH (0.015 M), reflux.

chromatography on neutral alumina (Scheme 13). More careful analysis by ^{1}H NMR and GC–MS suggests that both of the possible diastereoisomers were produced in the reaction. A diastereomeric ratio (d.r.=4:1) was obtained by integration of the two resolved methyl doublets {δ 1.02 (major) and 1.15 (minor)} in the ^{1}H NMR spectrum ($CDCl_3$) prior to chromatography. We believe the modest isolated yield of octahydroindolizine **37** is largely a reflection of its polarity and volatility, and not the efficiency of this reaction sequence. We were unable to isolate and separately characterise the minor diastereomer from this reaction.

The assignment of the bicyclic structure of **37** was relatively straightforward by NMR spectroscopy (in C_6D_6). In addition to the expected signals for the 3-methylenepiperidine system, it was apparent that the monosubstituted olefin present in **21b** was no longer present, and had been replaced by an additional methine carbon adjacent to nitrogen (δ 53.5) whose hydrogen was coupled to a methyl doublet (δ 1.00) in the ^{1}H NMR spectrum. All other data including ^{1}H–^{13}C and ^{1}H–^{1}H correlation spectra were consistent with the octahydroindolizine skeleton. Unfortunately, we have been unable to unambiguously establish the relative stereochemistry within **37**. ^{1}H NMR experiments (nOe and NOESY) failed to provide any useful information concerning the relative stereochemistry. Furthermore, attempts to grow single crystals of the corresponding hydrochloride salt for X-ray diffraction studies were unsuccessful.

The chemical yields of these radical rearrangements are generally good, especially bearing in mind that the 2-methylenaziridine precursors were not purified (vide supra). We speculate that the reactions proceed via aziridinylcarbinyl radical **3**, formed by 5-*exo*-trig cyclisation of the initially formed alkyl radical, which then undergoes C–N bond cleavage to **4** to relieve the ring strain associated with the 1-azabicyclo[3.1.0]hexane ring system (Scheme 1). We have been unable to detect enamine products derived from the alternative ring fission (i.e. **5**). However, we cannot discount the formation of trace amounts of these materials as they might be expected to be chemically rather labile. The observation that 2-isopropylideneaziridine **17** undergoes rearrangement to **35** indicates that the C–N bond fission step (i.e. **3**→**4**) is facile and occurs even when the intermediate is a more stable, tertiary centred radical.

Indirect evidence for the production of the aminyl radical in these rearrangements is provided by the fact that

2-methyleneaziridine **21b** undergoes a tandem cyclisation to octahydroindolizine **37** presumably via aminyl radical **36** (Scheme 13). Whilst the relative stereochemistry within **37** is unknown, the level of diastereocontrol observed in this reaction (d.r.=4:1) is appreciably higher than that observed by Bowman, who observed essentially no stereocontrol in a related 5-*exo* radical cyclisation of a piperidinyl radical.[24] By analogy with work on 5-*exo* ring closures of cyclohexyl radicals,[25] it is tempting to speculate that the methyl group within the major diastereomer is located *trans* to the ring junction hydrogen.

The failure of homologue **29** to rearrange to azepane **32** via a 6-*exo*-trig cyclisation is perhaps unsurprising. In studying the rearrangement of the related (methylenecyclopropyl)-butyl radicals, Kilburn observed only small amounts of products derived from 6-*exo* cyclisations. The major products they observed were simple reduction of the (methylenecyclopropyl)butyl radical, and competitive 7-*endo*-trig cyclisation of this radical.[26]

In conclusion, our studies have demonstrated for the first time that 2-methyleneaziridines and related structures can participate in radical rearrangements. This chemistry provides a novel entry into a variety of functionalised heterocyclic systems incorporating a piperidine nucleus. Efforts to use these and related rearrangements in synthesis are ongoing in our laboratories.

3. Experimental

3.1. General

All experiments were performed under an inert atmosphere in oven-dried glassware. Tetrahydrofuran (THF) was distilled from sodium/benzophenone immediately prior to use. All other solvents and reagents were purified by standard protocols. Petroleum ether refers to that boiling in the 40–60°C. Chromatography was performed on Fisher Matrex 60 silica gel unless otherwise stated. Other general details have been reported previously.[5c]

3.2. General method A: synthesis of β-amino esters (19a,b)[22]

The β-keto ester (1 M equiv.) and ammonium acetate (10 M equiv.) in benzene and acetic acid were heated under reflux for 3–5 days using a Dean–Stark apparatus to collect water. On cooling, the benzene was removed under reduced pressure. The residue was diluted with EtOAc, washed with saturated $NaHCO_3$ solution to neutralise the acetic acid (CAUTION), then the organic layer dried ($MgSO_4$). The resulting β-enamino ester, contaminated with unreacted β-keto ester, was used without further purification. To a stirred solution of glacial acetic acid was added $NaBH_4$ (2.4–2.5 M equiv.) portionwise whilst the temperature was maintained between 15 and 20°C. After 30 min, hydrogen evolution had ceased. The β-enamino ester prepared above was added in one portion and the mixture stirred for 3 h at room temperature. The acetic acid was removed in vacuo at 50°C, then the residue dissolved in EtOAc and washed several times with water. The pH of the combined aqueous layers was adjusted to pH 12 (CAUTION) using saturated K_2CO_3 solution, then extracted with EtOAc (4×20–40 mL). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure to give the β-amino ester which were characterised and used without further purification.

3.2.1. 3-Amino-5-phenyl-pentanoic acid ethyl ester (19a). 3-Oxo-5-phenyl-pentanoic acid ethyl ester **18a**[21] (6.32 g, 28.7 mmol) and NH_4OAc (22.1 g, 287 mmol) in benzene (287 mL) and AcOH (58 mL) were refluxed for 5 days, then worked up according to General method A. The resulting β-enamino ester was reduced with $NaBH_4$ (2.64 g, 69.8 mmol) in glacial AcOH (80 mL), to give after work-up, **19a** (3.38 g, 53% over two steps) as a colourless oil. IR (film) 3365, 2924, 1731, 1618, 1444, 1163 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.10 (5H, m), 4.15 (2H, q, J=7.1 Hz), 3.26–3.18 (1H, m), 2.80–2.58 (2H, m), 2.49 (1H, dd, J=15.6, 4.0 Hz), 2.30 (1H, dd, J=15.6, 8.7 Hz), 1.88–1.48 (4H, m), 1.26 (3H, t, J=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4 (s), 141.8 (s), 128.5 (d), 128.3 (d), 125.9 (d), 60.3 (t), 48.0 (d), 42.8 (t), 39.3 (t), 32.4 (t), 14.2 (q); MS (EI) m/z 221 (M^+), 204, 91.

3.2.2. 3-Amino-hept-6-enoic acid ethyl ester (19b). 3-Oxo-hept-6-enoic acid ethyl ester **18b**[21] (2.00 g, 11.8 mmol) and NH_4OAc (9.04 g, 117 mmol) in benzene (117 mL) and AcOH (23 mL) were refluxed for 3 days, then worked up according to General method A. The resulting β-enamino ester was reduced with $NaBH_4$ (1.10 g, 29.1 mmol) in glacial AcOH (32 mL), to give after work-up, **19b** (1.03 g, 51% over two steps) as a colourless oil. IR (film) 3370, 2980, 1721, 1639, 1178 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.83–5.70 (1H, m), 5.05–4.90 (2H, m), 4.14 (2H, q, J=7.2 Hz), 3.21–3.15 (1H, m), 2.43 (1H, dd, J=15.7, 4.1 Hz), 2.29 (1H, dd, J=15.7, 8.8 Hz), 2.20–1.98 (4H, m), 1.55–1.38 (2H, m), 1.28 (3H, t, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4 (s), 138.0 (d), 114.9 (t), 60.3 (t), 47.8 (d), 42.5 (t), 36.6 (t), 30.3 (t), 14.2 (q); MS (CI) m/z 172 (MH^+), 158; HRMS (ES^+): calcd for $C_9H_{18}NO_2$ 172.1337; found 172.1336.

3.3. General method B: two step reduction/alkylation sequence for the preparation of 20a,b

To a stirred slurry of lithium aluminium hydride (2.8 M equiv.) in dry THF at 0°C was added **19a**,**b** (1.0 M equiv.) in THF dropwise. The solution was heated to reflux for 3 h, then cooled to 0°C and water (2–4 mL) added (CAUTION). The precipitated salts were filtered off and washed with THF. The filtrate was dried ($MgSO_4$) then the solvent removed in vacuo. To the resulting γ-amino alcohol in THF was added 2,3-dibromopropene (0.4 M equiv.) and K_2CO_3 (0.8–0.9 M equiv.) and the mixture heated at reflux for 2 days. On cooling to room temperature, the mixture was filtered and the precipitate washed with diethyl ether. The filtrate was washed with 10% sodium hydroxide (2×10 mL) and the aqueous layer re-extracted with diethyl ether (3×20 mL). The combined organic extracts were washed with water (2×10 mL), dried ($MgSO_4$) and the solvent removed under reduced pressure. Purification by column chromatography gave **20a**,**b** as detailed below.

3.3.1. 3-[*N*-(2-Bromo-2-propenyl)-amino]-5-phenylpentan-1-ol (20a). Using General method B, **19a** (3.09 g, 14.0 mmol) in THF (20 mL) was reacted with $LiAlH_4$ (1.50 g, 39.5 mmol) in THF (45 mL) to give after work-up, the corresponding alcohol which was further reacted with 2,3-dibromopropene (0.59 mL, 5.71 mmol), K_2CO_3 (1.71 g, 12.4 mmol) in THF (25 mL). Final work-up and purification by column chromatography (40→50% EtOAc in petroleum ether containing 1% Et_3N) gave **20a** (1.34 g, 79%) as a yellow oil. IR (film) 3318, 2924, 2847, 1623, 1444, 1060 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31–7.25 (2H, m), 7.21–7.15 (3H, m), 5.72 (1H, s), 5.53 (1H, s), 3.95–3.88 (1H, m), 3.80–3.74 (1H, m), 3.53 (1H, d, J=14.6 Hz), 3.43 (1H, d, J=14.6 Hz), 3.10–2.70 (2H, bs), 2.88–2.81 (1H, m), 2.73–2.58 (2H, m), 1.95–1.71 (3H, m), 1.63–1.53 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6 (s), 132.5 (s), 128.5 (d), 128.2 (d), 126.0 (d), 118.3 (t), 61.7 (t), 56.0 (d), 54.6 (t), 35.4 (t), 33.8 (t), 32.2 (t); MS (CI) m/z 300 (MH^+: ^{81}Br), 298 (MH^+: ^{79}Br), 220; HRMS (ES^+): calcd for $C_{14}H_{21}BrNO$ 298.0806; found 298.0808.

3.3.2. 3-[*N*-(2-Bromo-2-propenyl)-amino]-hept-6-en-1-ol (20b). Using General method B, **19b** (0.50 g, 2.92 mmol) in THF (5 mL) was reacted with $LiAlH_4$ (313 mg, 8.25 mmol) in THF (10 mL) to give after work-up the corresponding alcohol which was further reacted with 2,3-dibromopropene (0.121 mL, 1.17 mmol), K_2CO_3 (335 mg, 2.42 mmol) in THF (15 mL). Final work-up and purification by column chromatography (30→40% EtOAc in petroleum ether containing 1% Et_3N) gave **20b** (262 mg, 90%) as a yellow oil. IR (film) 3329, 3073, 2929, 1634, 1454, 1070, 906 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.84–5.75 (2H, m), 5.53 (1H, s), 5.05–4.95 (2H, m), 3.85 (1H, ddd, J=10.7, 7.3, 3.3 Hz), 3.75 (1H, ddd, J=10.7, 7.2, 3.5 Hz), 3.56 (1H, d, J=14.7 Hz), 3.44 (1H, d, J=14.7 Hz), 3.20–2.80 (2H, bs), 2.86–2.78 (1H, m), 2.18–2.02 (2H, m), 1.82–1.75 (1H, m), 1.72–1.62 (1H, m), 1.60–1.48 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9 (d), 132.6 (s), 118.1 (t), 115.1 (t), 61.6 (t), 55.9 (d), 54.6 (t), 33.7 (t), 32.8 (t), 30.1 (t); MS (CI) m/z 250 (MH^+: ^{81}Br), 248 (MH^+: ^{79}Br) 168; HRMS (ES^+): calcd for $C_{10}H_{19}BrNO$ 248.0650; found 248.0648.

3.4. General method C: *N*-alkylation of amino alcohol

To a stirred solution of the amino alcohol (2–2.2 M equiv.) in THF was added potassium carbonate (2–2.2 M equiv.) and 2,3-dibromopropene (1.0 M equiv.) dropwise. The resultant mixture was heated under reflux for 2–3 days. On cooling, the solution was filtered and the precipitate washed with diethyl ether. The filtrate was washed with 10% sodium hydroxide (2×10 mL) then the aqueous layer re-extracted with diethyl ether (3×20 mL). The combined organic extracts were washed with water (2×10 mL), dried ($MgSO_4$), the solvent removed in vacuo to give the crude product which was purified by column chromatography.

3.4.1. 3-[*N*-(2-Bromo-2-propenyl)amino]-propan-1-ol (7). Compound **6** (4.0 g, 53.3 mmol) was treated with K_2CO_3 (7.36 g, 53.3 mmol) and 2,3-dibromopropene (4.82 g, 24.1 mmol) in THF (50 mL) for 2 days according to General method C. Work-up and chromatography (30% EtOAc in petroleum ether containing 0.5% triethylamine) gave **7** (3.30 g, 71%) as a pale yellow oil. IR (film) 3298, 2929, 2858, 1623, 1065 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.75 (1H, s), 5.53 (1H, s), 3.74 (2H, t, J=5.5 Hz), 3.42 (2H, s), 3.00 (2H, bs), 2.75 (2H, t, J=5.7 Hz), 1.68 (2H, pentet, J=5.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.7 (s), 118.2 (t), 63.3 (t), 57.2 (t), 47.1 (t), 31.0 (t); MS (CI) m/z 196 (MH^+: ^{81}Br), 194 (MH^+: ^{79}Br), 116; HRMS (CI): calcd for $C_6H_{13}NBrO$ 194.0180; found 194.0181. Anal. calcd for $C_6H_{12}NBrO$: C, 37.13; H, 6.23; N, 7.22%. Found C, 37.37; H, 6.63; N, 7.07%.

3.4.2. 3-[*N*-(2-Bromo-2-propenyl)amino]-3-phenylpropan-1-ol (11). Compound **10**[18] (1.50 g, 9.93 mmol) was treated with K_2CO_3 (1.35 g, 9.77 mmol) and 2,3-dibromopropene (0.91 g, 4.55 mmol) in THF (20 mL) for 3 days according to General method C. Work-up and chromatography (60→70% EtOAc in petroleum ether containing 0.5% triethylamine) gave **11** (1.11 g, 90%) as a pale yellow oil. IR (film) 3324, 2929, 1623, 1449, 1070 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.25 (5H, m), 5.67 (1H, s), 5.54 (1H, s), 3.85 (1H, dd, J=8.6, 4.6 Hz), 3.80–3.75 (2H, m), 3.35 (1H, d, J=14.7 Hz), 3.22 (1H, d, J=14.7 Hz), 2.93 (2H, m), 2.03–1.91 (1H, m), 1.90–1.82 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4 (s), 132.5 (s), 128.7 (d), 127.5 (d), 126.8 (d), 118.4 (t), 61.8 (t), 61.1 (d), 54.9 (t), 39.2 (t); MS (CI) m/z 272 (MH^+: ^{81}Br), 270 (MH^+: ^{79}Br), 192; HRMS (ES^+): calcd for $C_{12}H_{17}BrNO$ 270.0493; found 270.0491.

3.4.3. 4-[*N*-(2-Bromo-2-propenyl)-amino]-butan-1-ol (27). Compound **26** (2.00 g, 22.4 mmol) was treated with K_2CO_3 (3.05 g, 22.1 mmol) and 2,3-dibromopropene (2.24 g, 11.2 mmol) in THF (45 mL) for 2 days according to General method C. Work-up and chromatography (160:40:1; EtOAc–petroleum ether–Et_3N→190:10:1; EtOAc:MeOH:Et_3N) gave **27** (1.76 g, 75%) as a yellow oil. IR (film) 3339, 2934, 2842, 1618, 1444, 1060 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.75 (1H, s), 5.55 (1H, s), 3.58 (2H, t, J=5.3 Hz), 3.43 (2H, s), 3.00 (2H, bs), 2.58 (2H, t, J=6.1 Hz), 1.68–1.55 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.6 (s), 118.3 (t), 62.5 (t), 57.0 (t), 47.4 (t), 31.8 (t), 27.7 (t); MS (CI) m/z 210 (MH^+: ^{81}Br), 208 (MH^+: ^{79}Br), 130; HRMS (ES^+): calcd for $C_7H_{15}BrNO$ 208.0337; found 208.0338.

3.4.4. (1*R,2*S**)-2-[*N*-(2-Bromo-2-propenyl)-amino]-cyclohexane-1-carboxylic acid methyl ester (38).** Compound **22**[23] (0.45 g, 2.86 mmol) was treated with K_2CO_3 (0.39 g, 2.82 mmol) and 2,3-dibromopropene (0.28 g, 1.43 mmol) in THF (15 mL) for 2 days according to General method C. Work-up and chromatography (10→20% EtOAc in petroleum ether) gave **38** (0.40 g, 100%) as a pale yellow oil. IR (film) 3344, 2934, 2858, 1726, 1173 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.80 (1H, s), 5.52 (1H, s), 3.68 (3H, s), 3.47 (1H, d, J=15.5 Hz), 3.41 (1H, d, J=15.5 Hz), 3.00–2.96 (1H, m), 2.67–2.63 (1H, m), 1.97–1.85 (1H, m), 1.84–1.55 (5H, m), 1.55–1.45 (1H, m), 1.40–1.28 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8 (s), 133.9 (s), 116.9 (t), 55.0 (t), 53.5 (d), 51.3 (q), 45.9 (d), 28.7 (t), 24.8 (t), 23.8 (t), 21.6 (t); MS (FAB) m/z 278 (MH^+: ^{81}Br), 276 (MH^+: ^{79}Br), 196; HRMS (ES^+): calcd for $C_{11}H_{19}BrNO_2$ 276.0599; found 276.0599.

3.4.5. 3-[*N*-(2-Bromo-3-methyl-2-butenyl)amino]-3-phenylpropan-1-ol (15). To 1,1-dibromo-2,2-dimethylcyclopropane **14**[19] (1.37 g, 6.01 mmol) in 1,2-dichlorobenzene (10 mL) was added **10**[18] (2.00 g, 13.2 mmol) dropwise then potassium carbonate (0.83 g, 6.01 mmol). The mixture was heated for 72 h at 160°C then allowed to cool to room temperature. Aqueous 2 M NaOH solution (10 mL) was added followed by diethyl ether (15 mL). The organic layer was separated, washed with brine (2×10 mL) then dried ($MgSO_4$). After removal of the diethyl ether on a rotary evaporator, the 1,2-dichlorobenzene was removed by distillation (60°C/15 mm Hg). Purification by column chromatography (30% EtOAc in petroleum ether using silica pretreated with Et_3N) gave **15** (906 mg, 51%) as a colourless oil. IR (film) 3344, 2914, 1736, 1449, 1050 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.20 (5H, m), 3.82 (1H, dd, J=8.0, 4.8 Hz), 3.78–3.71 (2H, m), 3.44 (1H, d, J=13.9 Hz), 3.40–2.80 (2H, bs), 3.34 (1H, d, J=13.9 Hz), 1.93–1.81 (2H, m), 1.84 (3H, s), 1.54 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.8 (s), 134.0 (s), 128.6 (d), 127.3 (d), 126.8 (d), 120.3 (s), 61.7 (t), 61.3 (d), 51.1 (t), 39.5 (t), 25.4 (q), 20.4 (q); MS (EI) m/z 299 (M^+: ^{81}Br), 297 (M^+: ^{79}Br), 254, 252; HRMS (EI): calcd for $C_{14}H_{20}NOBr$ 297.0728; found 297.0723. Anal. calcd for $C_{14}H_{20}BrNO$: C, 56.38; H, 6.76; N, 4.69%. Found C, 56.94; H, 6.84; N, 4.50%.

3.4.6. (1*R* *,2*S* *)-*N*-(2-Bromo-2-propenyl)-2-hydroxymethyl-cyclohexylamine (23). To a slurry of lithium aluminium hydride (0.27 g, 7.11 mmol) in THF (9 mL) at 0°C was added **38** (0.70 g, 2.53 mmol) in THF (2 mL) dropwise. The solution was refluxed for 1 h, recooled to 0°C then water (1 mL) added dropwise (CAUTION). The precipitated salts were filtered off and washed with THF. The filtrate was dried ($MgSO_4$) and the solvent removed under reduced pressure. Column chromatography (90% EtOAc in petroleum ether) gave **23** (0.42 g, 67%) as a pale yellow oil. IR (film) 3329, 2919, 2847, 1629, 1449, 1091, 881 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.78 (1H, s), 5.55 (1H, s), 3.93 (1H, dd, J=11.1, 8.0 Hz), 3.63 (1H, dd, J=11.1, 3.5 Hz), 3.54 (1H, d, J=14.8 Hz), 3.44 (1H, d, J=14.8 Hz), 3.05 (1H, bs), 2.92–2.87 (1H, m), 1.95–1.85 (1H, m), 1.83–1.72 (1H, m), 1.65–1.53 (2H, m), 1.52–1.30 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.8 (s), 118.2 (t), 65.6 (t), 57.0 (d), 55.1 (t), 38.9 (d), 28.0 (t), 26.1 (t), 23.1 (t), 22.9 (t); MS (FAB) m/z 250 (MH^+: ^{81}Br), 248 (MH^+: ^{79}Br); HRMS (ES^+): calcd for $C_{10}H_{19}BrNO$ 248.0650; found 248.0650.

3.4.7. (2-Bromo-2-propenyl)-(4-hydroxybutyl)-carbamic acid *tert*-butyl ester (39). To a stirred solution of **27** (0.50 g, 2.40 mmol) in dichloromethane was added triethylamine (335 μL, 2.40 mmol), di-*tert*-butyl dicarbonate (524 mg, 2.40 mmol) and a catalytic amount of DMAP. After stirring overnight, the solvent was removed in vacuo. Purification by column chromatography (80% EtOAc in petroleum ether) gave **39** (678 mg, 92%) as a colourless oil. IR (film) 3436, 2970, 2929, 2858, 1680, 1403, 1152 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.67 (1H, s), 5.53 (1H, s), 4.01 (2H, bs), 3.64 (2H, t, J=6.2 Hz), 3.24 (2H, bs), 2.20–1.75 (1H, bm), 1.63–1.50 (4H, m), 1.44 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3 (s), 129.8 (s), 116.5 (t), 80.2 (s), 62.3 (t), 54.7 (t), 46.5 (t), 29.6 (t), 28.3 (q), 24.5 (t); MS (CI) m/z 310 (MH^+: ^{81}Br), 308 (MH^+: ^{79}Br), 271, 269; HRMS (ES^+): calcd for $C_{12}H_{23}BrNO_3$ 308.0861; found 308.0859.

3.5. General method D: synthesis of phenylselenides (8, 12, 24, 40, 41a, 41b)

To a stirred solution of the corresponding alcohol (1 M equiv.) in THF at 0°C were added freshly prepared *N*-phenylselenophthalimide (*N*-PSP) (1.7–2.0 M equiv.) and tri-*n*-butylphosphine (1.7–2.0 M equiv.). After 4 h, the solvent was removed under reduced pressure and the residue purified by column chromatography.

3.5.1. (2-Bromo-2-propenyl)-(3-phenylseleno-propyl)-amine (8). Compound **7** (0.50 g, 2.57 mmol) was reacted with *N*-PSP (1.55 g, 5.16 mmol) and PBu_3 (1.04 g, 5.14 mmol) in THF (15 mL) according to General method D. Column chromatography (10% EtOAc in petroleum ether) gave **8** (0.60 g, 70%) as a colourless oil. IR (film) 3324, 3062, 2929, 2822, 1629, 1572, 1470 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56–7.48 (2H, m), 7.32–7.20 (3H, m), 5.76 (1H, s), 5.55 (1H, s), 3.42 (2H, s), 2.99 (2H, t, J=7.3 Hz), 2.67 (2H, t, J=6.8 Hz), 1.90 (2H, m), 1.53 (1H, bs); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.5 (s), 132.6 (d), 130.3 (s), 129.0 (d), 126.8 (d), 117.6 (t), 57.3 (t), 47.3 (t), 30.3 (t), 25.5 (t); MS (CI) m/z 336 (MH^+: ^{80}Se, ^{81}Br), 334 (MH^+: ^{80}Se, ^{79}Br), 332 (MH^+: ^{78}Se, ^{79}Br); HRMS (ES^+): calcd for $C_{12}H_{17}BrNSe$ 333.9709; found 333.9706.

3.5.2. (2-Bromo-2-propenyl)-(1-phenyl-3-phenylseleno-propyl)-amine (12). Compound **11** (1.11 g, 4.11 mmol) was reacted with *N*-PSP (2.11 g, 6.98 mmol) and PBu_3 (1.72 mL, 6.90 mmol) in THF (40 mL) according to General method D. Column chromatography (0→5% EtOAc in petroleum ether) gave **12** (1.26 g, 75%) as a colourless oil. IR (film) 3335, 3060, 2927, 1622, 1468 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46–7.40 (2H, m), 7.35–7.30 (2H, m), 7.30–7.20 (6H, m), 5.64 (1H, s), 5.54 (1H, d, J=1.6 Hz), 3.76 (1H, t, J=6.9 Hz), 3.32 (1H, d, J=15.2 Hz), 3.19 (1H, d, J=15.2 Hz), 2.87–2.75 (2H, m), 2.12–1.97 (2H, m), 1.72 (1H, bs); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4 (s), 133.6 (s), 132.5 (d), 130.1 (s), 129.0 (d), 128.5 (d), 127.5 (d), 127.4 (d), 126.8 (d), 117.9 (t), 60.5 (d), 54.9 (t), 38.2 (t), 24.1 (t); MS (CI) m/z 412 (MH^+: ^{80}Se, ^{81}Br), 410 (MH^+: ^{80}Se, ^{79}Br), 408 (MH^+: ^{78}Se, ^{79}Br); HRMS (CI): calcd for $C_{18}H_{21}BrNSe$ 410.0022; found 410.0016. Anal. calcd for $C_{18}H_{20}BrNSe$: C, 52.83; H, 4.93; N, 3.42%. Found C, 53.07; H, 5.02; N, 3.37%.

3.5.3. (1*R* *,2*S* *)-*N*-(2-Bromo-2-propenyl)-2-phenylselenomethyl-cyclohexylamine (24). Compound **23** (0.42 g, 1.69 mmol) was reacted with *N*-PSP (1.03 g, 3.41 mmol) and PBu_3 (0.84 mL, 3.37 mmol) in THF (20 mL) according to General method D. Column chromatography (0→10% EtOAc in petroleum ether) gave **24** (0.55 g, 84%) as a colourless oil. IR (film) 3344, 3052, 2919, 2847, 1629, 1470 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53–7.50 (2H, m), 7.26–7.19 (3H, m), 5.75 (1H, s), 5.51 (1H, s), 3.39 (1H, d, J=15.1 Hz), 3.32 (1H, d, J=15.1 Hz), 3.20 (1H, dd, J=12.0, 5.9 Hz), 2.85 (1H, dd, J=12.0, 8.5 Hz), 2.84–2.80 (1H, m), 1.90–1.80 (1H, m), 1.68–1.45 (5H, m), 1.45–1.25 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.2 (s), 132.5 (d), 131.1 (s), 129.0 (d), 126.6 (d), 117.2

(t), 55.24 (t), 55.21 (d), 40.1 (d), 29.4 (t), 28.8 (t), 27.8 (t), 23.3 (t), 22.2 (t); MS (CI) *m/z* 390 (MH^+: ^{80}Se, ^{81}Br), 388 (MH^+: ^{80}Se, ^{79}Br), 386 (MH^+: ^{78}Se, ^{79}Br), 232, 230; HRMS (ES^+): calcd for $C_{16}H_{23}BrSeN$ 388.0179; found 388.0179.

3.5.4. (2-Bromo-2-propenyl)-(4-phenylseleno-butyl)-carbamic acid *tert*-butyl ester (40). Compound **39** (0.20 g, 0.65 mmol) was reacted with *N*-PSP (0.39 g, 1.29 mmol) and PBu_3 (0.32 mL, 1.28 mmol) in THF (5 mL) according to General method D. Column chromatography (0⟶5% EtOAc in petroleum ether) gave **40** (0.219 g, 75%) as a yellow oil. IR (film) 3062, 2970, 2924, 1690, 1403 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.47 (2H, m), 7.26–7.21 (3H, m), 5.66 (1H, m), 5.53 (1H, bs), 4.04 and 3.97 (2H, 2×bs), 3.21 (2H, m), 2.91 (2H, t, J=6.7 Hz), 1.70–1.60 (4H, m), 1.44 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4 (s), 155.1 (s), 132.6 (d), 130.2 (s), 130.1 (s), 129.9 (s), 129.7 (s), 129.1 (d), 126.8 (d), 117.0 (t), 116.4 (t), 80.1 (s), 54.7 (t), 54.2 (t), 46.3 (t), 46.1 (t), 28.3 (q), 28.1 (t), 27.5 (t), 27.4 (t); MS (CI) *m/z* 450 (MH^+: ^{80}Se, ^{81}Br), 448 (MH^+: ^{80}Se, ^{79}Br), 446 (MH^+: ^{78}Se, ^{79}Br); HRMS (ES^+): calcd for $C_{18}H_{27}BrSeNO_2$ 448.0390; found 448.0387.

3.5.5. (2-Bromo-2-propenyl)-(3-phenylseleno-1-phenylethyl-propyl)-amine (41a). Compound **20a** (0.20 g, 0.67 mmol) was reacted with *N*-PSP (0.405 g, 1.34 mmol) and PBu_3 (0.33 mL, 1.32 mmol) in THF (8 mL) according to General method D. Column chromatography (2% EtOAc in petroleum ether) gave **41a** (0.23 g, 78%) as a yellow oil. IR (film) 3339, 3047, 2924, 2842, 1634, 1470, 1065 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52–7.50 (2H, m), 7.29–7.26 (5H, m), 7.21–7.16 (3H, m), 5.71 (1H, s), 5.51 (1H, s), 3.40 (2H, s), 3.05–2.93 (2H, m), 2.71 (1H, m), 2.63 (2H, m), 1.93–1.80 (2H, m), 1.79–1.68 (2H, m), 1.50 (1H, bs); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1 (s), 133.6 (s), 132.6 (d), 130.3 (s), 129.1 (d), 128.4 (d), 128.3 (d), 126.8 (d), 125.8 (d), 117.6 (t), 55.1 (d), 54.7 (t), 35.6 (t), 34.3 (t), 32.0 (t), 23.9 (t); MS (CI) *m/z* 440 (MH^+: ^{80}Se, ^{81}Br), 438 (MH^+: ^{80}Se, ^{79}Br), 436 (MH^+: ^{78}Se, ^{79}Br); HRMS (ES^+): calcd for $C_{20}H_{25}BrSeN$ 438.0335; found 438.0337.

3.5.6. (2-Bromo-2-propenyl)-[1-(2-phenylseleno-ethyl)-pent-4-enyl]-amine (41b). Compound **20b** (0.222 g, 0.89 mmol) was reacted with *N*-PSP (0.54 g, 1.79 mmol) and PBu_3 (0.44 mL, 1.77 mmol) in THF (10 mL) according to General method D. Column chromatography (0⟶10% EtOAc in petroleum ether) gave **41b** (0.278 g, 81%) as a yellow oil. IR (film) 3334, 3067, 2924, 1634, 1429 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51–7.42 (2H, m), 7.27–7.21 (3H, m), 5.84–5.75 (1H, m), 5.75 (1H, s), 5.52 (1H, s), 5.04–4.94 (2H, m), 3.39 (2H, s), 3.02–2.90 (2H, m), 2.67 (1H, pentet, J=5.9 Hz), 2.08–2.03 (2H, m), 1.85–1.72 (2H, m), 1.55–1.45 (2H, m), 1.40 (1H, bs); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4 (d), 133.8 (s), 132.5 (d), 130.3 (s), 129.1 (d), 126.8 (d), 117.6 (t), 114.8 (t), 54.9 (d), 54.7 (t), 34.1 (t), 32.9 (t), 29.9 (t), 23.8 (t); MS (CI) *m/z* 390 (MH^+: ^{80}Se, ^{81}Br), 388 (MH^+: ^{80}Se, ^{79}Br), 386 (MH^+: ^{78}Se, ^{79}Br); HRMS (ES^+): calcd for $C_{16}H_{23}BrSeN$ 388.0179; found 388.0178.

3.5.7. (2-Bromo-3-methyl-2-butenyl)-(1-phenyl-3-phenylseleno-propyl)-amine (16). To a stirred solution of **15** (2.03 g, 6.81 mmol) in toluene (60 mL) at 0°C was added triethylamine (0.94 mL, 6.74 mmol) then methanesulphonyl chloride (527 μL, 6.81 mmol) dropwise over 20 min. The mixture was allowed to warm to room temperature and stirred for a further 3 h. The mixture was extracted with ether (130 mL), washed with water (2×60 mL) then brine (60 mL), dried ($MgSO_4$) and the solvent removed in vacuo. To a stirred solution of diphenyl diselenide (2.12 g, 6.79 mmol) in ethanol (40 mL) at 0°C was added sodium borohydride (517 mg, 13.7 mmol) portionwise. The mesylate (2.56 g) in ethanol (3 mL) prepared above was added and the solution heated to reflux for 3 h. On cooling to room temperature, water (10 mL) was added dropwise. The layers were separated and the aqueous layer extracted with EtOAc (3×40 mL). The combined organic extracts were washed with brine (40 mL), dried ($MgSO_4$) and the solvent removed in vacuo. Subsequent column chromatography (5% EtOAc in petroleum ether) gave **16** (2.48 g, 83% over two steps) as a colourless oil. IR (film) 3324, 2909, 1577, 1475, 1019 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45–7.40 (2H, m), 7.35–7.20 (8H, m), 3.71 (1H, t, J=6.7 Hz), 3.40 (1H, d, J=14.4 Hz), 3.29 (1H, d, J=14.4 Hz), 2.84–2.73 (2H, m), 2.15–1.97 (2H, m), 1.88 (3H, s), 1.50 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7 (s), 133.6 (s), 132.5 (d), 130.1 (s), 129.0 (d), 128.4 (d), 127.6 (d), 127.3 (d), 126.7 (d), 121.6 (s), 60.5 (d), 50.9 (t), 38.6 (t), 25.5 (q), 24.1 (t), 20.5 (q); MS (EI) *m/z* 437 (M^+: ^{80}Se, ^{79}Br), 254; HRMS (EI): calcd for $C_{20}H_{24}NSeBr$ 437.0257; found 437.0257. Anal. calcd for $C_{20}H_{24}NSeBr$: C, 54.93; H, 5.53; N, 3.20%. Found C, 54.96; H, 5.71; N, 3.10%.

3.5.8. (2-Bromo-2-propenyl)-(3-phenylseleno-butyl)-amine (28). To a stirred solution of **40** (735 mg, 1.65 mmol) in dichloromethane (20 mL) was added trifluoroacetic acid (1.27 mL, 16.5 mmol). After stirring overnight, the solvent and excess trifluoroacetic acid were removed in vacuo. The residue was dissolved in brine (20 mL), the pH adjusted to pH 10 with 1 M aqueous K_2CO_3 solution, then the mixture extracted with dichloromethane (3×30 mL). The combined organic extracts were dried ($MgSO_4$) and the solvent removed in vacuo. Purification by column chromatography (30% EtOAc in petroleum ether) gave **28** (529 mg, 92%) as a yellow oil. IR (film) 3324, 3057, 2924, 1623, 1470 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.50–7.47 (2H, m), 7.27–7.23 (3H, m), 5.75 (1H, s), 5.54 (1H, s), 3.42 (2H, s), 2.92 (2H, t, J=7.3 Hz), 2.54 (2H, t, J=7.1 Hz), 1.76 (2H, pentet, J=7.4 Hz), 1.60 (2H, pentet, J=7.3 Hz), 1.51 (1H, bs, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.6 (s), 132.5 (d), 130.4 (s), 129.0 (d), 126.7 (d), 117.6 (t), 57.4 (t), 47.1 (t), 30.0 (t), 27.8 (t), 27.7 (t); MS (CI) *m/z* 350 (MH^+: ^{80}Se, ^{81}Br), 348 (MH^+: ^{80}Se, ^{79}Br), 270; HRMS (ES^+): calcd for $C_{13}H_{19}BrSeN$ 347.9866; found 347.9856.

3.6. General method E: preparation of 2-alkylideneaziridines (9, 13, 17, 21a, 21b, 25, 29)

To a three necked flask fitted with a dry ice condenser, calcium chloride drying flask and gas inlet was added sodium amide (15–30 M equiv.). The system was flushed with ammonia then a dry/acetone mixture was added to the condenser and ammonia condensed into the flask. The appropriate vinyl bromide was added and the reaction mixture stirred for 10–90 min. Diethyl ether (2–10 mL) was added followed by the dropwise addition of water (CAUTION) and the ammonia was allowed to evaporate.

Water (2–8 mL) was added followed by diethyl ether (2–10 mL) and the mixture stirred for 2 min. The organic phase was separated and the aqueous phase extracted with diethyl ether (2×10 mL). The combined organic extracts were washed with 10% sodium hydroxide (2×5 mL), then water (2×5 mL), dried ($MgSO_4$) and the solvent removed under reduced pressure to give the 2-alkylideneaziridine.

3.6.1. *N*-(3-Phenylseleno-propyl)-2-methyleneaziridine (9). Treatment of **8** (0.60 g, 1.80 mmol) with sodium amide (1.05 g, 26.9 mmol) in ammonia (20 mL) for 25 min, according to General method E followed by work-up gave **9** (0.40 g, 88%) as a brown oil which was characterised and used without further purification. IR (film) 3047, 2919, 1762, 1465 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55–7.45 (2H, m), 7.30–7.20 (3H, m), 4.70–4.67 (2H, m), 3.04 (2H, t, J=7.4 Hz), 2.60 (2H, t, J=6.8 Hz), 2.04 (2H, s), 2.03–1.96 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.2 (s), 132.6 (d), 130.1 (s), 129.0 (d), 126.8 (d), 82.9 (t), 59.0 (t), 30.8 (t), 30.3 (t), 25.2 (t); MS (CI) m/z 254 (MH^+: ^{80}Se), 98; HRMS (CI): calcd for $C_{12}H_{16}NSe$ 254.0448; found 254.0446.

3.6.2. *N*-(1-Phenyl-3-phenylseleno-propyl)-2-methyleneaziridine (13). Treatment of **12** (1.00 g, 2.44 mmol) with sodium amide (1.43 g, 36.7 mmol) in ammonia (25 mL) for 10 min, according to General method E followed by work-up gave **13** (729 mg, 91%) as a brown oil which was characterised and used without further purification. IR (film) 3060, 2930, 1772, 1574, 1473 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45–7.20 (10H, m), 4.62 (1H, s), 4.47 (1H, s), 2.99 (1H, t, J=6.5 Hz), 2.96–2.80 (1H, m), 2.77–2.68 (1H, m), 2.35–2.25 (2H, m), 2.08 (1H, s), 2.03 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1 (s), 136.6 (s), 132.6 (d), 129.9 (s), 129.1 (d), 128.6 (d), 127.7 (d), 127.5 (d), 83.4 (t), 72.6 (d), 37.6 (t), 30.0 (t), 23.3 (t); MS (CI) m/z 330 (MH^+: ^{80}Se), 174; HRMS (CI): calcd for $C_{18}H_{20}NSe$ 330.0761; found 330.0757.

3.6.3. *N*-(3-Phenylseleno-propyl)-2-isopropylideneaziridine (17). Treatment of **16** (1.0 g, 2.29 mmol) with sodium amide (2.66 g, 68.2 mmol) in ammonia (15 mL) for 90 min, according to General method E followed by work-up and column chromatography (5% ethyl acetate in petroleum ether) gave **17** (617 mg, 76%) as a yellow oil. IR (film) 3062, 2924, 2847, 1798, 1434 cm^{-1}; ^1H NMR (400 MHz, 60°C, $CDCl_3$) δ 7.41 (2H, m), 7.34–7.19 (8H, m), 2.96 (1H, dd, J=7.4, 5.9 Hz), 2.92–2.83 (1H, m), 2.72–2.63 (1H, m), 2.35–2.28 (2H, m), 2.07 (1H, bs), 1.90 (1H, s), 1.70 (3H, s), 1.30 (3H, bs); ^{13}C NMR (100 MHz, 60°C, $CDCl_3$) δ 141.9 (s), 132.6 (d), 130.2 (s), 128.9 (d), 128.3 (d), 128.0 (d), 127.4 (d), 126.7 (d), 123.8 (s), 104.1 (s), 72.6 (d), 37.6 (t), 30.3 (t), 23.7 (t), 20.7 (q), 18.9 (q); MS (CI) m/z 358 (MH^+: ^{80}Se), 275, 200; HRMS (CI) calcd for $C_{20}H_{24}NSe$ 358.1074; found 358.1073. Anal. calcd for $C_{20}H_{23}NSe$: C, 67.41; H, 6.50; N, 3.93%. Found C, 67.79; H, 6.85; N, 3.86%.

3.6.4. *N*-[1-(2-Phenylseleno-ethyl)-3-phenylpropyl]-2-methyleneaziridine (21a). Treatment of **41a** (0.30 g, 0.69 mmol) with sodium amide (0.39 g, 10.0 mmol) in ammonia (8 mL) for 20 min, according to General method E followed by work-up gave **21a** (227 mg, 93%) as a yellow oil which was characterised and used without further purification. IR (film) 3062, 3021, 2934, 1767, 1480 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54–7.52 (2H, m), 7.29–7.26 (5H, m), 7.18–7.16 (3H, m), 4.66 (2H, s), 3.12–2.94 (2H, m), 2.75–2.59 (2H, m), 2.06 (1H, s), 2.04 (1H, s), 2.10–1.98 (3H, m), 1.95–1.88 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9 (s), 135.8 (s), 132.8 (d), 130.0 (s), 129.0 (d), 128.4 (d), 128.3 (d), 126.9 (d), 125.8 (d), 83.0 (t), 66.8 (d), 34.9 (t), 34.1 (t), 31.7 (t), 29.8 (t), 23.4 (t); MS (FAB) m/z 358 (MH^+: ^{80}Se), 200, 172, 145; HRMS (ES^+): calcd for $C_{20}H_{24}SeN$ 358.1074; found 358.1072.

3.6.5. *N*-[1-(2-Phenylseleno-ethyl)-4-pentenyl]-2-methyleneaziridine (21b). Treatment of **41b** (0.45 g, 1.16 mmol) with sodium amide (675 mg, 17.3 mmol) in ammonia (10 mL) for 20 min, according to General method E followed by work-up gave **21b** (306 mg, 86%) as a dark yellow oil which was characterised and used without further purification. IR (film) 3068, 2922, 2845, 1763, 1433, 1166 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52–7.49 (2H, m), 7.27–7.25 (3H, m), 5.85–5.73 (1H, m), 5.04–4.94 (2H, m), 4.63 (2H, s), 3.12–3.03 (1H, m), 3.00–2.97 (1H, m), 2.20–1.93 (5H, m), 2.05 (1H, s), 2.04 (1H, s), 1.71–1.65 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2 (d), 135.8 (s), 132.7 (d), 130.0 (s), 129.1 (d), 126.9 (d), 114.9 (t), 83.1 (t), 66.7 (d), 34.0 (t), 32.3 (t), 29.9 (t), 29.6 (t), 23.3 (t); MS (CI) m/z 308 (MH^+: ^{80}Se); HRMS (ES^+): calcd for $C_{16}H_{22}SeN$ 308.0917; found 308.0922.

3.6.6. (1*R,2*S**)-*N*-(2-Phenylselenomethyl-cyclohexyl]-2-methyleneaziridine (25).** Treatment of **24** (0.55 g, 1.42 mmol) with sodium amide (0.83 g, 21.3 mmol) in ammonia (15 mL) for 55 min, according to General method E followed by work-up gave **25** (416 mg, 96%) as a yellow oil which was characterised and used without further purification. IR (film) 3057, 2929, 2852, 1757, 1429, 1168 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53–7.50 (2H, m), 7.26–7.23 (3H, m), 4.62 (1H, s), 4.59 (1H, s), 3.35 (1H, dd, J=12.3, 5.3 Hz), 2.97 (1H, dd, J=12.1, 8.9 Hz), 2.08 (1H, s), 2.07–2.03 (1H, m), 1.99 (1H, s), 2.00–1.85 (2H, m), 1.85–1.70 (2H, m), 1.60–1.45 (3H, m), 1.42–1.30 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.0 (s), 132.4 (d), 130.9 (s), 129.0 (d), 126.6 (d), 82.4 (t), 68.1 (d), 40.6 (d), 29.8 (t), 29.4 (t), 28.0 (t), 22.8 (t); MS (FAB) m/z 308 (MH^+: ^{80}Se); HRMS (ES^+): calcd for $C_{16}H_{22}SeN$ 308.0917; found 308.0919.

3.6.7. *N*-(4-Phenylseleno-butyl)-2-methyleneaziridine (29). Treatment of **28** (0.45 g, 1.30 mmol) with sodium amide (0.78 g, 20.0 mmol) in ammonia (13 mL) for 45 min, according to General method E followed by work-up gave **29** (307 mg, 89%) as a dark yellow oil which was characterised and used without further purification. IR (film) 3062, 2934, 2837, 1772, 1572, 1475 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51–7.48 (2H, m), 7.26–7.23 (3H, m), 4.70 (1H, s), 4.66 (1H, s), 2.95 (2H, t, J=7.2 Hz), 2.50 (2H, t, J=6.9 Hz), 2.01 (2H, s), 1.90–1.70 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3 (s), 132.6 (d), 130.4 (s), 129.0 (d), 126.7 (d), 82.7 (t), 58.9 (t), 30.7 (t), 29.8 (t), 27.8 (t), 27.7 (t); MS (CI) m/z 268 (MH^+: ^{80}Se), 114; HRMS (ES^+): calcd for $C_{13}H_{18}SeN$ 268.0604; found 268.0603.

3.6.8. 3-Methylene-6-phenylpiperidine (30). To a degased solution of **13** (100 mg, 0.305 mmol) in benzene (15 mL)

under reflux was added a degased solution of AIBN (15 mg, 0.09 mmol) and tri-*n*-butyltin hydride (96 μL, 0.357 mmol) in benzene (5 mL) via a syringe pump over 4.5 h. After the addition was complete, heating was continued for a further 1.5 h. On cooling to room temperature, aqueous 2 M HCl (3 mL) was added, the aqueous layer separated and neutralised with 2 M NaOH solution (CAUTION). The aqueous phase was then extracted with diethyl ether (5×5 mL), the combined organic extracts dried ($MgSO_4$) and the solvent removed in vacuo. Purification by chromatography (2% MeOH in CH_2Cl_2) gave **30** (36 mg, 68%) as a yellow oil. IR (film) 3288, 3057, 2924, 1644, 1439 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.24 (5H, m), 4.81 (1H, d, J=1.5 Hz), 4.77 (1H, s), 3.76 (1H, dd, J=11.3, 2.6 Hz) 3.58 (1H, d, J=12.6 Hz), 3.44 (1H, d, J=12.6 Hz), 2.54–2.47 (1H, m), 2.37–2.27 (1H, m), 2.02–1.95 (1H, m), 1.85 (1H, bs), 1.70–1.58 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0 (s), 144.3 (s), 128.4 (d), 127.1 (d), 126.6 (d), 108.5 (t), 61.5 (d), 53.6 (t), 36.2 (t), 33.5 (t); MS (CI) *m/z* 174 (MH^+); HRMS (ES^+): calcd for 174.1282 $C_{12}H_{16}N$: found 174.1282.

3.6.9. 1-*tert*-Butoxycarbonyl-3-methylenepiperidine (31). To a degased solution of **9** (100 mg, 0.40 mmol) in benzene (21 mL) under reflux was added a degased solution of AIBN (27 mg, 0.16 mmol) and tri-*n*-butyltin hydride (147 μL, 0.55 mmol) in benzene (5 mL) via a syringe pump over 5 h. After the addition was complete, heating was continued for a further 1 h. On cooling to room temperature, di-*tert*-butyl dicarbonate (173 mg, 0.79 mmol) and triethylamine (0.11 mL, 0.79 mmol) were added and the mixture stirred overnight. Removal of the solvent under reduced pressure and subsequent column chromatography (5% EtOAc in petroleum ether) gave **31** (45 mg, 58%) as a colourless oil. IR (film) 3073, 2975, 1685, 1413 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.81 (1H, s), 4.71 (1H, s), 3.86 (2H, s), 3.43 (2H, t, J=5.6 Hz), 2.25 (2H, t, J=6.2 Hz), 1.64–1.58 (2H, m), 1.45 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7 (s), 143.0 (s), 109.7 (t), 79.4 (s), 50.4 (t), 44.1 (t), 32.7 (t), 28.4 (q), 26.6 (t); MS (CI) *m/z* 198 (MH^+), 159, 98; HRMS (CI): calcd for $C_{11}H_{20}NO_2$ 198.1494: found 198.1493.

3.6.10. 3-Methylene-6-(2-phenylethyl)-piperidine (33). To a degased solution of **21a** (108 mg, 0.30 mmol) in benzene (15 mL) under reflux was added a degased solution of AIBN (25 mg, 0.15 mmol) and tri-*n*-butyltin hydride (96 μL, 0.36 mmol) in benzene (5 mL) via a syringe pump over 5 h. After the addition was complete, heating was continued for a further 1 h. On cooling to room temperature, aqueous 2 M HCl (3 mL) was added, the aqueous layer separated and neutralised with 2 M NaOH solution (CAUTION). The aqueous phase was then extracted with EtOAc (5×5 mL), the combined organic extracts dried ($MgSO_4$) and the solvent removed in vacuo. Purification by chromatography (0.5% Et_3N in EtOAc) gave **33** (38 mg, 67%) as a yellow oil. IR (film) 3288, 3062, 2924, 2847, 1649, 1444 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30–7.26 (2H, m), 7.20–7.16 (3H, m), 4.73 (1H, s), 4.69 (1H, s), 3.45 (1H, d, J=13.1 Hz), 3.25 (1H, d, J=13.1 Hz), 2.78–2.62 (3H, m), 2.44–2.37 (1H, m), 2.23–2.10 (2H, m), 1.93–1.88 (1H, m), 1.78–1.68 (2H, m), 1.30–1.19 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0 (s), 142.2 (s), 128.4 (d), 128.3 (d), 125.8 (d), 108.0 (t), 55.8 (d), 52.9 (t), 38.3 (t), 34.8 (t), 32.9 (t), 32.5 (t); MS (CI) *m/z* 202 (MH^+), 96; HRMS (ES^+): calcd for $C_{14}H_{20}N$ 202.1595: found 202.1596.

3.6.11. 1-*tert*-Butoxycarbonyl-3-methylene-decahydroquinoline (34). To a degased solution of **25** (100 mg, 0.33 mmol) in benzene (16 mL) under reflux was added a degased solution of AIBN (25 mg, 0.15 mmol) and tri-*n*-butyltin hydride (103 μL, 0.38 mmol) in benzene (5 mL) via a syringe pump over 5 h. After the addition was complete, heating was continued for a further 1 h. On cooling to room temperature, di-*tert*-butyl dicarbonate (142 mg, 0.65 mmol) and triethylamine (91 μL, 0.65 mmol) were added and the mixture stirred overnight. Removal of the solvent under reduced pressure and subsequent column chromatography (0⟶1% EtOAc in petroleum ether) gave **34** (53 mg, 65%) as a colourless oil. IR (film) 3067, 2929, 2852, 1690, 1403, 1163 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.80 (1H, s), 4.73 (1H, s), 4.28 (1H, bd, J=13.9 Hz), 4.08 (1H, bs), 3.41 (1H, d, J=14.3 Hz), 2.47 (1H, t, J=13.3 Hz), 2.03–1.88 (2H, m), 1.82–1.68 (2H, m), 1.67–1.55 (2H, m), 1.55–1.25 (4H, m), 1.45 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7 (s), 143.6 (s), 109.4 (t), 79.3 (s), 52.4 (d), 45.2 (t), 35.9 (d), 32.7 (t), 30.8 (t), 28.4 (q), 25.6 (t), 23.7 (t), 19.9 (t); MS (CI) *m/z* 252 (MH^+), 152; HRMS (ES^+): calcd for $C_{15}H_{26}NO_2$ 252.1963: found 252.1965.

3.6.12. 1-*tert*-Butoxycarbonyl-3-isopropylidene-6-phenylpiperidine (35). To a degased solution of **17** (0.11 g, 0.31 mmol) in benzene (15 mL) under reflux was added a degased solution of AIBN (28 mg, 0.17 mmol) and tri-*n*-butyltin hydride (0.11 mL, 0.41 mmol) in benzene (5 mL) via a syringe pump over 5 h. After the addition was complete, heating was continued for a further 1 h. On cooling to room temperature, di-*tert*-butyl dicarbonate (134 mg, 0.61 mmol) and triethylamine (86 μL, 0.62 mmol) were added and the mixture stirred overnight. Removal of the solvent under reduced pressure and subsequent column chromatography (4% EtOAc in petroleum ether) gave **35** (0.058 g, 62%) as a colourless oil. IR (film) 2973, 2920, 1693, 1319, 1161 cm^{-1}; ^1H NMR (400 MHz, C_6D_6 at 77°C) δ 7.31–7.15 (5H, m), 5.17–5.13 (1H, m), 4.99 (1H, d, J=15.4 Hz), 3.76 (1H, d, J=15.4 Hz), 2.25–2.05 (2H, m), 1.98–1.88 (1H, m), 1.83–1.75 (1H, m), 1.74 (3H, s), 1.54 (3H, s), 1.43 (9H, s); ^{13}C NMR (100 MHz, C_6D_6 at 77°C) δ 155.1 (s), 144.3 (s), 128.2 (d), 126.6 (s), 126.3 (d), 125.8 (d), 123.4 (s), 78.7 (s), 56.4 (d), 41.9 (t), 30.0 (t), 28.1 (q), 24.6 (t), 19.30 (q), 19.28 (q); MS (EI) *m/z* 301 (M^+), 244, 186; HRMS (EI): calcd for $C_{19}H_{27}NO_2$ 301.2042: found 301.2048. Anal. calcd for $C_{19}H_{27}NO_2$: C, 75.71; H, 9.03; N, 4.65%. Found C, 75.37; H, 9.34; N, 4.44%.

3.6.13. 3-Methyl-6-methylene-octahydro-indolizine (37). To a degased solution of **21b** (145 mg, 0.47 mmol) in benzene (23 mL) under reflux was added a degased solution of AIBN (32 mg, 0.19 mmol) and tri-*n*-butyltin hydride (149 μL, 0.55 mmol) in benzene (8 mL) via a syringe pump over 5 h. After the addition was complete, heating was continued for a further 1 h. On cooling to room temperature, aqueous 2 M HCl (5 mL) was added, the aqueous layer separated, washed with petroleum ether (6×5 mL),

neutralised with 2 M NaOH solution (CAUTION), then extracted with diethyl ether (5×5 mL). The ethereal extracts were combined, dried ($MgSO_4$) and the solvent carefully removed on a rotary evaporator using a partial vacuum with the water bath temperature maintained at ca. 5°C. Purification by chromatography on neutral alumina (2.5% MeOH in CH_2Cl_2) gave **37** (28 mg, 39%) as a single diastereomer (see Section 2) and as a yellow oil. IR (film) 3058, 2955, 2924, 1647, 1441, 1369, 890 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 4.87 (1H, s), 4.82 (1H, s), 3.34 (2H, s), 3.25–3.15 (1H, m), 2.90–2.83 (1H, m), 2.35–2.28 (1H, m), 2.12–1.86 (3H, m), 1.54–1.25 (4H, m), 1.00 (3H, d, J=6.2 Hz); ^{13}C NMR (100 MHz, C_6D_6) δ 144.7 (s), 108.3 (t), 58.6 (d), 53.5 (d), 53.0 (t), 33.2 (t), 31.3 (t), 31.1 (t), 29.3 (t), 17.0 (q); MS (EI) m/z 151 (M^+), 150 ($M-H^+$) 136 ($M-CH_3^+$); HRMS (EI): calcd for $C_{10}H_{17}N$ 151.1361; found 151.1364.

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