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PAPER

Lewis acid promoted intramolecular (3 + 2) 'cycloadditions' of methyleneaziridines with alkene and alkyne acceptors†

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2-Methyleneaziridines can be tethered to a variety of alkene or alkyne acceptors through the saturated carbon of the heterocyclic ring by application of a simple lithiation/alkylation sequence (8 examples, 31–59%). Treatment of the resultant alkene bearing substrates with $BF_3{\cdot}OEt_2$ leads to *cis*-octahydrocyclopenta[c]pyrroles in which up to four contiguous stereocentres are created in a diastereocontrolled manner after reductive work-up. Using an alkyne based substrate, a 2,4,5,6-tetrahydrocyclopenta[c]pyrrole is produced by rapid tautomerisation of the initially formed *bis*enamine. Evidence that these (3 + 2) 'cycloadditions' proceed in a stepwise manner *via* a 2-aminoallyl cation is presented.

Introduction

Five membered nitrogen heterocycles are found in many natural products and pharmaceuticals, and there is much interest in the development of efficient methods for their synthesis.[1] Aziridines often serve as excellent starting materials because of the high reactivity associated with their ring strain.[2] Indeed, aziridines have been extensively used for the synthesis of five membered nitrogen heterocycles through application of (3 + 2) cycloaddition processes.‡[3,4] Classically, they have been used as precursors to azomethine ylides through conrotatory C–C bond cleavage,[5] and also reactions involving zwitterion formation through C–N bond cleavage have been reported.[6] Intramolecular variants of these reactions offer opportunities to assemble more complex heterocycles. Whilst intramolecular cycloadditions involving azomethine ylids generated from aziridines have been used extensively in the synthesis of alkaloids,[7] intramolecular (3 + 2) cycloadditions involving aziridine C–N bond cleavage are much less common.[8]

In this article, the first examples of intramolecular (3 + 2) 'cycloadditions' of 2-methyleneaziridines with alkene and alkyne acceptors are described through controlled C–N cleavage. The basic idea behind this investigation is illustrated for generalised alkene containing substrate **2** in Scheme 1. Using this approach, it was imagined that readily available methyleneaziridines such as **1** could be easily transformed into complex nitrogen heterocycles with the creation of up to three contiguous stereocentres in just two synthetic operations. At the outset, it was felt that the introduction of an exocyclic double bond on the three membered ring could have a number of advantages. Firstly, it was expected that the cycloaddition substrates would be more reactive as a result of the additional 12–13 kcal mol^{-1} of ring strain energy.[9] Secondly, it is known that 2-methyleneaziridines undergo facile lithiation/substitution at C–3 with carbon-based electrophiles,[10] which was expected to make the synthesis of the requisite cycloaddition precursors straightforward. Finally, the exocyclic double bond of the methyleneaziridine increases the amount of functionality incorporated in the resultant cycloadduct.

Based upon earlier work on the (4 + 3) cycloadditions of methyleneaziridines with 1,3-dienes,[11] treatment of **2** with Lewis acids such as $BF_3{\cdot}OEt_2$ was expected to generate highly strained and reactive aziridinium ion **3**, which might undergo facile ring opening by the appended nucleophilic π-bond producing carbenium ion **4**. Subsequent ring closure to yield enamine **5** as the initially formed cycloadduct was anticipated.§ If good levels of stereocontrol could be achieved in this process, then this highly asynchronous 'cycloaddition' process might serve as a very direct and attractive route to octahydrocyclopenta[c]pyrroles and related scaffolds. Here, we report the first examples of this new cycloaddition, and highlight the scope of this approach to a variety of nitrogen heterocycles.

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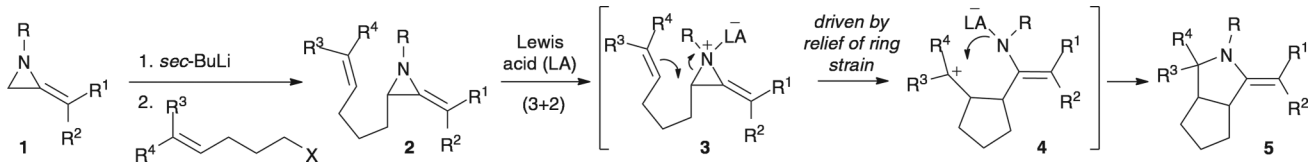
† Electronic supplementary information (ESI) available: ^1H and ^{13}C NMR spectra for **6–12**, **19–24**, **26**, **27** and **31**. CCDC reference number 842811. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob06578e

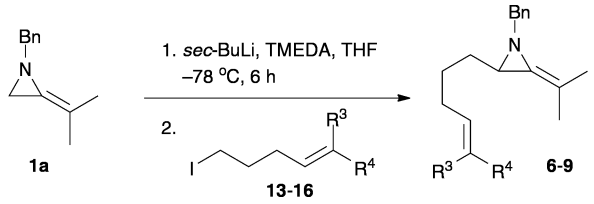
‡ According to the IUPAC system for the classification of cycloaddition reactions, square and round brackets denote the number of electrons and atoms, respectively, involved in the transformation. P. Muller, *Pure Appl. Chem.*, 1994, **66**, 1077.

§ It is conceivable that ring closure might also proceed through the β-carbon atom of the complexed enamine **4**, producing the corresponding cyclopentanone imine. No products of this type were observed during this investigation.



Scheme 1 Generalised depiction of intramolecular Lewis acid promoted (3 + 2) cycloaddition of 2-methyleneaziridines.

Table 1 Preparation of methyleneaziridines **6–9** by lithiation/alkylation



Entry	R^3	R^4	Iodide	Product	Yield[a] (%)
1	H	Ph	(*E*)-**13**	(*E*)-**6**[b]	54
2	Ph	H	(*Z*)-**13**	(*Z*)-**6**	57
3	Ph	Ph	**14**	**7**	41
4	H	4-C_6H_4OMe	(*E*)-**15**	(*E*)-**8**	57
5	H	4-$C_6H_4CF_3$	(*E*)-**16**	(*E*)-**9**	59

[a] Isolated yield after column chromatography. [b] See ref. 10.

Results and Discussion

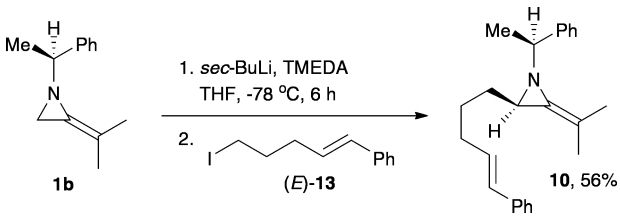
Design and synthesis of cycloaddition precursors

Methyleneaziridines possessing at least one substituent on the exocyclic double bond were used (*i.e.* R^1 and/or $R^2 \neq H$) throughout this study. This was because: (i) substitution on the exocyclic double bond was expected to make enamine **5** less reactive and hence easier to isolate/manipulate; (ii) substituents on the exocyclic double bond might encourage ring opening of aziridinium ion **3** if the chemistry proceeds *via* a 2-aminoallyl cation (*vide infra*); (iii) alkylideneaziridines are relatively stable[9a] making the purification of the requisite cycloaddition precursors straightforward.

A total of eight (3 + 2) cycloaddition precursors were made for this study. In order to encourage the proposed cycloaddition, substrates **6–12** capable of stabilising the proposed carbenium ion **4** through use of an aryl group were selected (Scheme 1). Both the (*Z*)- and (*E*)-diastereoisomer of styrene **6** were made to ascertain if the alkene geometry would impact the propensity and/or stereochemical course of the cycloaddition. To gain insight into the reaction mechanism, **10** possessing a stereocentre of defined absolute stereochemistry on the aziridine ring was made. Finally, to establish if the chemistry could be extended to other π-systems, two alkyne bearing substrates **11** and **12** were used.

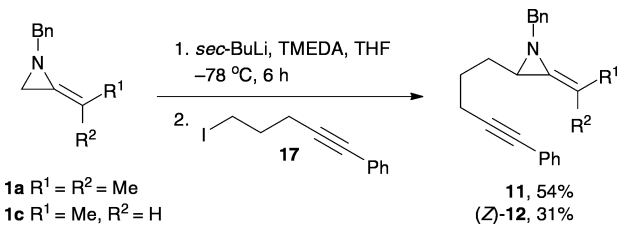
All the substrates used in this study were made in a very direct manner by reaction of known methyleneaziridines **1a–c**[12] with iodides **13–17** containing the requisite alkene or alkyne acceptors. The synthesis of all these iodides has been described previously. Lithiation of *N*-benzyl-2-isopropylidineaziridine (**1a**) with *sec*-butyllithium and tetramethylethylenediamine (TMEDA) followed by addition of 1-[(*E*)-5-iodopent-1-enyl)]benzene (**13**) provided aziridine (*E*)-**6** in 54% yield after column chromatography (Table 1, entry 1).[10] Using electrophiles bearing different alkene substitution patterns, it was possible to produce related substrates (*Z*)-**6**, **7**, (*E*)-**8** and (*E*)-**9** in an identical manner (Table 1, entries 2–5).

Lithiation and alkylation of (*S*)-*N*-(1-phenylethyl)-2-isopropylidineaziridine (**1b**) with (*E*)-**13** produced the alkylated aziridine as a 91 : 9 mixture of diastereomers (Scheme 2). The major isomer **10** was isolated in 56% yield and tentatively assigned as having the (*S*,*R*)-stereochemistry by analogy with related alkylations.[10]



Scheme 2 Stereocontrolled synthesis of methyleneaziridine **10**.

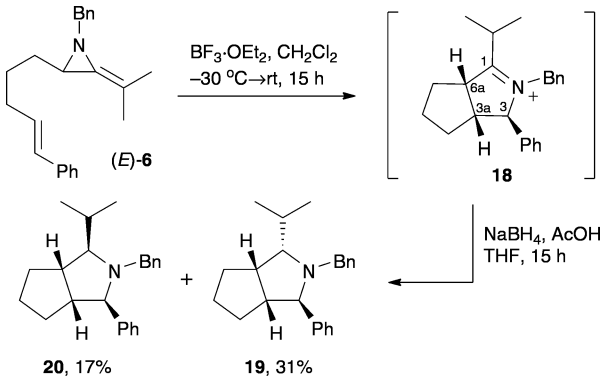
Finally, to introduce alkyne acceptors, 1-(5-iodopent-1-ynyl)benzene (**17**) was used as the electrophile. Thus, deprotonation of **1a**, or (*Z*)-*N*-benzyl-2-ethylideneaziridine (**1c**), and further treatment with **17** gave **11** (54%) and (*Z*)-**12** (31%) respectively (Scheme 3).



Scheme 3 Preparation of alkyne based substrates **11** and **12**.

Lewis acid promoted (3 + 2) cycloadditions involving alkenes

As stoichiometric quantities of $BF_3{\cdot}OEt_2$ are known to effect intramolecular (4 + 3) cycloadditions of methyleneaziridines with 1,3-dienes,[11b] this Lewis acid was selected for the initial study, using (*E*)-**6** bearing a disubstituted alkene. Upon addition of excess $BF_3{\cdot}OEt_2$ (150 mol%) in CH_2Cl_2 at –30 °C, followed by slow warming to room temperature over 15 h, (*E*)-**6** was converted to the iminium ion **18** as essentially a single diastereomer (Scheme 4). Further treatment of **18** with $NaBH_4$/AcOH in THF provided separated diastereomers **19** and **20** in a combined yield of 48%. The stereochemistry of **18** is inferred from that of **19** and **20**, whose assignments were deduced by NOE experiments. These revealed the same stereochemical relationship at C–3, C–3a and C–6a in

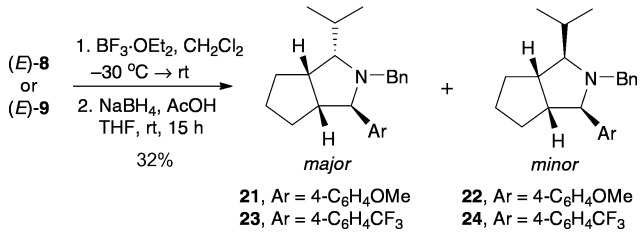


Scheme 4 Lewis acid promoted (3 + 2) cycloaddition/reduction sequence to *cis*-octahydrocyclopenta[c]pyrroles **19** and **20**.

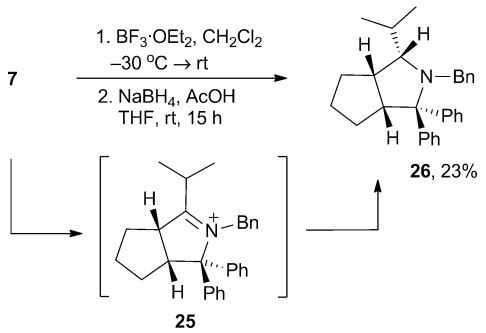
each compound, as well as the relative configurations at C–1.¶ These assignments were reinforced by an X-ray crystal structure of a related cycloadduct (*vide infra*). Gratifyingly, this (3 + 2) cycloaddition proceeds with good levels of diastereocontrol although the facial selectivity in the final reduction is modest (crude dr: 41 : 59). Evidently, hydride delivery from the *Re* face of iminium ion **18** is favoured leading to **19**, as approach from the concave *Si* face is sterically hindered. Preliminary attempts to improve the diastereoselectivity of this step using other hydride sources (Et_3SiH/TFA, $NaBH_3CN$/AcOH and L-Selectride®) led to lower yields with little improvement in selectivity. The cyclisation of the corresponding (*Z*)-isomer of **6** is discussed later.

To determine the impact of electronic effects on the efficiency of this (3 + 2) cycloaddition/reduction sequence, the reactivity of aziridines (*E*)-**8** and (*E*)-**9** bearing electron donating –OMe and withdrawing $–CF_3$ groups respectively on the phenyl ring were explored (Scheme 5). Both substrates behaved very similarly to (*E*)-**6**, yielding *cis*-octahydrocyclopenta[c]pyrroles **21** and **23** possessing the (1*S**,3*R**,3a*R**,6a*S**)-configuration as the major product. In both cases, the products were produced as an epimeric mixture at C–1 in a combined 32% yield (crude dr: **21**/**22** = 60 : 40; **23**/**24** = 58 : 42). These findings suggest that the electronic nature of the aromatic substituent exerts little influence on the ease of the cycloaddition. In the case of (*E*)-**8**, crystallisation of the major diastereomer **21** provided a single crystal suitable for X-ray diffraction, allowing its gross structure and relative stereochemistry to be confirmed.‖

Treatment of trisubstituted alkene **7** with $BF_3·OEt_2$ under the same conditions followed by reduction with $NaBH_4$/AcOH provided pyrrolidine **26** in 23% yield (Scheme 6). Only one diastereomer was observed in this reaction, presumably because hydride delivery to the concave *Si* face of the iminium ion



Scheme 5 Synthesis of *cis*-octahydrocyclopenta[c]pyrroles **21**–**24**.



Scheme 6 *cis*-Octahydrocyclopenta[c]pyrrole **26** from aziridine **7**.

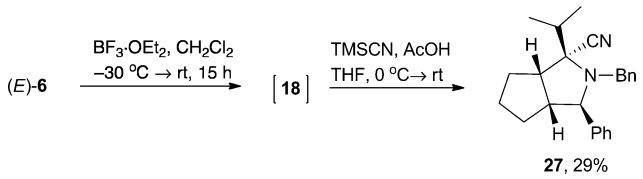
25 is hindered by the additional *endo* phenyl ring (*cf.* Scheme 4).** Efforts to improve the yield of this cycloaddition/reduction sequence by screening alternative Lewis acids ($Sc(OTf)_3$, $SnCl_4$, $AgSbF_6$), Brønsted acids [*p*-TsOH, $(PhO)_2P(O)OH$)] and solvents (CH_2Cl_2, DCE, PhH, CH_3CN, Et_2O) was largely unsuccessful. However, a modest improvement to 27% was realised using stoichiometric amounts of $Sc(OTf)_3$ (150 mol%) in place of $BF_3·OEt_2$. In all the cyclisations studied, the integral for the aromatic region in the ^1H NMR spectrum immediately after work-up was higher than expected. One can speculate that this might indicate competitive debenzylation under the reaction conditions although further proof in support of this hypothesis has yet to be obtained.

To determine if difficulties with hydride delivery to iminium ions **18** and **25** might be responsible in part for the low yields, and to extend the usefulness of this chemistry, capture of the intermediate iminium ion **18** with cyanide was investigated. Using HCN, generated *in situ* from trimethylsilyl cyanide and glacial AcOH, α-aminonitrile **27** was produced as a single stereoisomer from (*E*)-**6** in 29% yield (Scheme 7). Based upon this and other evidence, we conclude that it is the (3 + 2) reaction and not the iminium ion capture that is the low-yielding step. Unexpectedly, in **27** strong NOE enhancements were seen between all the hydrogens of the ^{i}Pr group and H–6a revealing a *syn*-relationship between the isopropyl group and the hydrogens of the ring junction. This implies that cyanide delivery occurs to the more hindered *Si* face of the iminium ion **18**. To account for this observation, we suggest that because cyanide is a good leaving group, the formation of **27** is under thermodynamic control, and at equilibrium the smaller cyano group (*A*-values: C≡N = 0.17; ^{i}Pr = 2.15)[13] prefers to reside in the sterically congested *endo* position. In contrast, the formation

¶ In major diastereomer **19**, reciprocal NOEs were observed between H–1, H–3a, H–6a and the *ortho*-hydrogens of the Ph group located at C–3. These data led us to conclude that H–1, H–3a, H–6a and the C–3 phenyl group reside on the same face of **19**. For minor diastereomer **20**, irradiation of H–6a led to NOE enhancements of H–3a and the isopropyl methyl groups. Moreover, reciprocal NOEs were seen between H–1 and H–3 in this compound but not **19**. These findings led us to deduce that **20** is epimeric at C–1. All other NOEs were consistent with these assignments.

‖ **Crystal Data for 21**. CCDC 842811. $C_{24}H_{31}NO$, M = 349.50, monoclinic, a = 11.4815(14) Å, b = 17.5731(15) Å, c = 10.4720(10) Å, β = 105.993(11)°, U = 2031.1(4) Å^3, T = 100(2), space group $P2_1/c$ (no. 14), Z = 4, μ(CuKα) = 0.523, 10496 reflections measured, 3819 unique (R_{int} = 0.0901) which were used in all calculations. The final $wR(F_2)$ was 0.2554 (all data).

** Reciprocal NOEs in **26** between the ring junction hydrogens (H–3a and H–6a) and between H–3 and H–3a indicated that the three hydrogens of the pyrrolidine ring reside on the same face. *Note*: ring numbering priorities changed relative to **19**/**20** due to an additional Ph group.

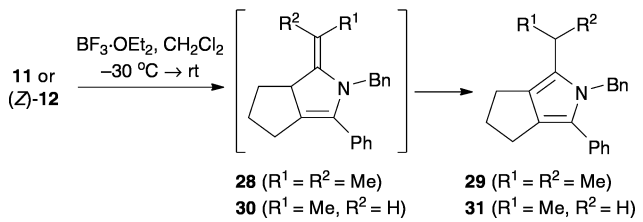


Scheme 7 (3 + 2) Cycloaddition/cyanide capture sequence.

of **19**/**20** is under kinetic control with preferential attack of hydride from the less hindered *Re* face.

Lewis acid promoted (3 + 2) cycloadditions involving alkynes

Based upon the work with alkene acceptors, it seemed likely that reactions involving alkynes might generate *bis*enamines as the initial (3 + 2) products. Such molecules might be expected to be rather unstable, and undergo isomerisation to aromatic pyrroles under the reaction conditions. To test this concept, aziridine **11** was treated with $BF_3{\cdot}OEt_2$ without recourse to $NaBH_4$ work-up. Analysis of the mixture by NMR suggested that dienamine **28** had been formed although the exocyclic tetrasubstituted double bond proved reluctant to isomerise to pyrrole **29**. Attempts to reduce **28** ($NaBH_4$/AcOH or H_2, Pd/C), or catalyse its isomerisation to pyrrole **29** (AcOH, reflux) were undertaken without success. Reasoning that a less substituted *bis*enamine such as **30** might more readily tautomerise to the pyrrole, the chemistry was repeated with aziridine (*Z*)-**12** bearing a single methyl group on the exocyclic double bond of the methyleneaziridine. Gratifyingly, treatment of (*Z*)-**12** with $BF_3{\cdot}OEt_2$ afforded pyrrole **31** in 38% yield after chromatography (Scheme 8). In this case, isomerisation of exocyclic olefin occurs spontaneously with no trace of *bis*enamine **30** seen in the mixture.

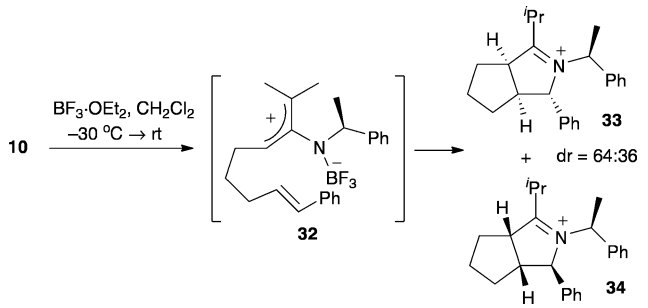


Scheme 8 Synthesis of 2,4,5,6-tetrahydrocyclopenta[c]pyrroles.

Mechanism of the (3 + 2) 'cycloaddition'

At first glance, the observation that **18** is formed from (*E*)-**6** implies a stereospecific (3 + 2) process in which the geometry of the alkene is relayed into the stereochemistry at C–3 of the cycloadduct. If this is the case, (*Z*)-**6** should produce the iminium ion with the opposite stereochemistry at this centre. However, treatment of (*Z*)-**6** under identical conditions to those used for (*E*)-**6** proceeded very poorly, with the only detectable iminium ion **18** being formed in trace amounts. As such, no significant conclusions can be drawn from these experiments other than that cyclisation to **18** is more facile than that to its C–3 epimer. The fact that (*E*)-**8** and (*E*)-**9** cyclise with equal propensity (based upon product yields) suggests that the reaction is not especially sensitive to electronic effects.

As a further mechanistic probe, cyclisation of homochiral isopropylideneaziridine **10** was examined (Scheme 9). If the



Scheme 9 Evidence for the involvement of a 2-aminoallyl cation.

(3 + 2) proceeds in a concerted manner, or involves S_N2 attack of the appended alkene onto aziridinium ion **3** as depicted in Scheme 1, the resultant iminium ion would be expected to be formed as a single stereoisomer. Alternatively, if cyclisation proceeds through a planar 2-aminoallyl cation, such as **32**, then partial or complete loss of the stereochemical information at C–3 of the starting aziridine would be expected (Scheme 9). Such intermediates have been suggested in the related (4 + 3) cycloadditions of methyleneaziridines with 1,3-dienes.[11] Treatment of **10** with $BF_3{\cdot}OEt_2$ provided two diastereomeric iminium ions in a 64 : 36 mixture, assigned as **33** and **34**. This finding supports the hypothesis that the major reaction pathway involves a planar 2-aminoallyl cation.[14]

Conclusions

The first examples of Lewis acid promoted (3 + 2) cycloadditions of methyleneaziridines are reported which provide new insights into the reactivity of this highly strained ring system. The reaction is used in an intramolecular manifold to produce *cis*-octahydrocyclopenta[c]pyrroles and 2,4,5,6-tetrahydrocyclopenta[c]pyrroles through reaction with tethered alkenes and alkynes respectively. Evidence is obtained that suggests this (3 + 2) most likely proceeds in an asynchronous manner through the involvement of a planar 2-aminoallyl cation. In combination with a reductive work-up, this new 'cycloaddition' is used to provide a very direct route to highly functionalised, stereodefined *cis*-octahydrocyclopenta[c]pyrroles. The intermediate iminium ions can also be captured with cyanide to generate heterocycles containing fully substituted stereocentres. Using alkyne acceptors, tautomerisation of the initially formed *bis*enamines to 2,4,5,6-tetrahydrocyclopenta[c]pyrroles is possible. The modest yields from the (3 + 2) cycloaddition (yields up to 48%) are offset, in part, by the fact that the substrates can be assembled in a very direct manner, and that the (3 + 2) creates considerable molecular complexity. Ongoing work is focused on identifying improved reaction conditions and applying this new methodology in target synthesis.

Experimental

General

Anhydrous solvents were purchased in Sure/Seal™ bottles from Sigma-Aldrich. 1-Benzyl-2-(1-methylethylidene)aziridine (**1a**), 1-[(*S*)-1-phenylethyl]-2-(propan-2-ylidene)aziridine (**1b**), and (*Z*)-1-benzyl-2-ethylideneaziridine (**1c**) were prepared according to

published procedures.[12] Similarly, all the iodide electrophiles used in this study are known: 1-[(*E*)-5-iodopent-1-enyl]benzene [(*E*)-**13**],[10] 1-[(*Z*)-5-iodopent-1-enyl]-benzene [(*Z*)-**13**],[15] 5-iodo-1,1-diphenylpent-1-ene (**14**),[16] 1-[(*E*)-5-iodopent-1-enyl]-4-methoxybenzene [(*E*)-**15**],[17] 1-[(*E*)-5-iodopent-1-enyl]-4-trifluorotoluene [(*E*)-**16**],[17] and 1-(5-iodopent-1-ynyl)benzene (**17**).[18] All other solvents and reagents were used as received or purified by standard protocols. Petroleum ether refers to the fraction of petroleum ether having a boiling point between 40–60 °C. All experiments were performed under an inert atmosphere (N_2) and moisture sensitive reactions were conducted in oven- or flame-dried glassware. Flash chromatography was carried out using Matrex silica 60. Thin layer chromatography was performed on pre-coated aluminium-backed plates and developed using UV fluorescence (254 nm) and/or potassium permanganate, followed by heating. Infrared spectra were recorded neat or as thin films on NaCl plates using a PerkinElmer Spectrum One FT-IR spectrometer with internal calibration. ^{1}H and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz respectively on a Bruker DPX-300; at 400 MHz and 100 MHz respectively on a Bruker DPX-400; and at 600 MHz and 150 MHz respectively on a Bruker AV-600 spectrometer. High resolution mass spectra were obtained on a Bruker MicroTOF instrument. Melting points were recorded on a Gallenkamp MPD350 apparatus.

General procedure for the synthesis of (3 + 2) cycloaddition precursors 6–12

To a stirred solution of the methyleneaziridine (1.0 equiv.) in THF at −78 °C, was added TMEDA (1.2 equiv.) and *sec*-BuLi (1.4 M in hexane, 1.9 equiv.) dropwise. The reaction was stirred at −78 °C for 6 h, then quenched with a solution of the electrophile (1.2–2.0 equiv.) in THF and allowed to warm to room temperature overnight. Water was added, the layers separated, and the aqueous phase extracted with Et_2O (3×). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by column chromatography afforded the title compounds.

1-Benzyl-2-((*E*)-5-phenylpent-4-enyl)-3-(propan-2-ylidene)aziridine [(*E*)-6]

(*E*)-**6** was prepared from **1a** (198 mg, 1.14 mmol), TMEDA (0.21 mL, 1.37 mmol), *sec*-BuLi (1.55 mL, 2.17 mmol) in THF (10 mL) and a solution of 1-((*E*)-5-iodopent-1-enyl)benzene [(*E*)-**13**] (373 mg, 1.37 mmol) in THF (1 mL) in accordance with the general procedure. Work-up followed by purification on silica (0.5% Et_3N and 2% EtOAc in petroleum ether) afforded (*E*)-**6** (197 mg, 0.62 mmol, 54%) as a yellow oil. δ_H (400 MHz, $CDCl_3$) 7.37–7.24 (9H, m), 7.20–7.15 (1H, m), 6.28 (1H, d, J = 15.8 Hz), 6.11 (1H, dt, J = 15.8, 6.8 Hz), 4.17 (1H, d, J = 13.3 Hz), 3.18 (1H, d, J = 13.3 Hz), 2.14–2.10 (2H, m), 2.02 (1H, t, J = 5.8 Hz), 1.77 (3H, s), 1.74 (3H, s), 1.66–1.38 (4H, m); δ_C (100 MHz, $CDCl_3$) 139.1 (C), 137.9 (C), 130.7 (CH), 130.0 (C), 129.9 (CH), 128.5 (2 × CH), 128.4 (2 × CH), 128.3 (2 × CH), 127.1 (CH), 126.8 (CH), 125.9 (2 × CH), 104.0 (C), 62.1 (CH_2), 44.1 (CH), 32.7 (CH_2), 31.9 (CH_2), 27.2 (CH_2), 20.7 (CH_3), 19.1 (CH_3). Spectral data were in accordance with literature data.[10]

1-Benzyl-2-((*Z*)-5-phenylpent-4-enyl)-3-(propan-2-ylidene)aziridine [(*Z*)-6]

(*Z*)-**6** was prepared from **1a** (148 mg, 0.85 mmol), TMEDA (0.16 mL, 1.03 mmol), *sec*-BuLi (1.16 mL, 1.63 mmol) in THF (8 mL) and a solution of 1-((*Z*)-5-iodopent-1-enyl)benzene [(*Z*)-**13**] (280 mg, 1.03 mmol) in THF (1 mL) in accordance with the general procedure. Work-up followed by purification on silica (0.5% Et_3N and 2% EtOAc in petroleum ether) afforded (*Z*)-**6** (154 mg, 0.49 mmol, 57%) as a pale yellow oil, as an inseparable 91 : 9 (*Z* : *E*) mixture of geometrical isomers. ν_{max} (neat) 2923, 1798, 1601, 1494, 1447, 1128, 731, 696 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.35–7.18 (10H, m), 6.37 (1H, d, J = 11.7 Hz), 5.55 (1H, dt, J = 11.7, 6.7 Hz), 4.13 (1H, d, J = 13.3 Hz), 3.17 (1H, d, J = 13.3 Hz), 2.25 (2H, q, J = 7.4 Hz, 1.97 (1H, t, J = 5.8 Hz), 1.74 (3H, s), 1.72 (3H, s), 1.63–1.47 (2H, m), 1.44–1.36 (2H, m); δ_C (100 MHz, $CDCl_3$) 139.1 (C), 137.7 (C), 132.7 (CH), 129.9 (C), 129.0 (CH), 128.8 (2 × CH), 128.5 (2 × CH), 128.3 (2 × CH), 128.1 (2 × CH), 127.1 (CH), 126.5 (CH), 104.0 (C), 62.0 (CH_2), 44.0 (CH), 31.9 (CH_2), 28.3 (CH_2), 27.8 (CH_2), 20.6 (CH_3), 19.1 (CH_3); HRMS (ESI) calculated for $C_{23}H_{28}N$ [M + H]: 318.2216, found 318.2218.

1-Benzyl-2-(5,5-diphenylpent-4-enyl)-3-(propan-2-ylidene)aziridine (7)

7 was prepared from **1a** (201 mg, 1.16 mmol), TMEDA (0.21 mL, 1.39 mmol), *sec*-BuLi (1.58 mL, 2.21 mmol) in THF (10 mL) and a solution of 5-iodo-1,1-diphenylpent-1-ene (**14**) (486 mg, 1.39 mmol) in THF (1 mL) in accordance with the general procedure. Work-up followed by purification on silica (1% Et_3N in petroleum ether) afforded **7** (188 mg, 0.48 mmol, 41%) as a yellow oil. ν_{max} (neat) 2919, 1796, 1596, 1493, 1442, 1129, 1028, 760, 698 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.35–7.10 (15H, m), 5.97 (1H, t, J = 7.5 Hz), 4.10 (1H, d, J = 13.4 Hz), 3.15 (1H, d, J = 13.4 Hz), 2.04 (2H, q, J = 7.4 Hz), 1.93 (1H, t, J = 5.8 Hz), 1.73 (3H, s), 1.71 (3H, s), 1.58–1.35 (4H, m); δ_C (100 MHz, $CDCl_3$) 142.8 (C), 141.7 (C), 140.2 (C), 139.1 (C), 130.0 (C), 129.9 (2 × CH), 129.8 (CH), 128.5 (2 × CH), 128.3 (2 × CH), 128.2 (2 × CH), 128.1 (2 × CH), 127.2 (2 × CH), 127.1 (CH), 126.9 (CH), 126.8 (CH), 104.0 (C), 62.0 (CH_2), 44.0 (CH), 31.9 (CH_2), 29.4 (CH_2), 27.8 (CH_2), 20.6 (CH_3), 19.1 (CH_3); HRMS (ESI) calculated for $C_{29}H_{32}N$ [M + H]: 394.2529, found 394.2539.

1-Benzyl-2-((*E*)-5-(4-methoxyphenyl)pent-4-enyl)-3-(propan-2-ylidene)aziridine [(*E*)-8]

(*E*)-**8** was prepared from **1a** (149 mg, 0.86 mmol), TMEDA (0.16 mL, 1.03 mmol), *sec*-BuLi (1.17 mL, 1.64 mmol) in THF (8 mL) and a solution of 1-((*E*)-5-iodopent-1-enyl)-4-methoxybenzene [(*E*)-**15**] (312 mg, 1.03 mmol) in THF (1 mL) in accordance with the general procedure. Work-up followed by purification on silica (0.5% Et_3N and 2% EtOAc in petroleum ether) afforded (*E*)-**8** (170 mg, 0.49 mmol, 57%) as a pale yellow oil. ν_{max} (neat) 2924, 1797, 1607, 1509, 1453, 1244, 1174, 1034, 964, 698 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.36–7.21 (7H, m), 6.82 (2H, d, J = 8.6 Hz), 6.23 (1H, d, J = 15.8 Hz), 5.96 (1H, dt, J = 15.8, 6.9 Hz), 4.16 (1H, d, J = 13.3 Hz), 3.77 (3H, s), 3.18 (1H, d, J = 13.3), 2.10 (2H, q, J = 7.1 Hz), 2.02 (1H, t, J = 5.7 Hz), 1.76 (3H, s), 1.73 (3H, s), 1.65–1.35 (4H, m); δ_C (100 MHz, $CDCl_3$) 158.7 (C), 139.2 (C), 130.7 (C), 130.0 (C), 129.3 (CH), 128.5 (2 × CH) 128.5 (CH), 128.3 (2 × CH),

127.1 (CH), 127.0 (2 × CH), 113.9 (2 × CH), 104.0 (C), 62.1 (CH_2), 55.3 (CH_3), 44.1 (CH), 32.7 (CH_2), 31.9 (CH_2), 27.3 (CH_2), 20.6 (CH_3), 19.1 (CH_3); HRMS (ESI) calculated for $C_{24}H_{30}NO$ [M + H]: 348.2322, found 348.2324.

1-Benzyl-2-((*E*)-5-(4-trifluoromethylphenyl)pent-4-enyl)-3-(propan-2-ylidene)aziridine [(*E*)-9]

(*E*)-**9** was prepared from **1a** (186 mg, 1.08 mmol), TMEDA (0.19 mL, 1.29 mmol), *sec*-BuLi (1.46 mL, 2.04 mmol) in THF (8 mL) and a solution of 1-((*E*)-5-iodopent-1-enyl)-4-trifluorotoluene [(*E*)-**16**] (439 mg, 1.29 mmol) in THF (1 mL) in accordance with general procedure. Work-up followed by purification on silica (0.5% Et_3N and 2% EtOAc in petroleum ether) afforded (*E*)-**9** (244 mg, 0.63 mmol, 59%) as a pale yellow oil. ν_{max} (neat) 2924, 1652, 1615, 1495, 1453, 1323, 1162, 1118, 1066, 967, 699 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.45 (2H, d, *J* = 8.1 Hz), 7.36–7.17 (7H, m), 6.22 (1H, d, *J* = 16.0 Hz), 6.13 (1H, dt, *J* = 16.0, 6.6 Hz), 4.11 (1H, d, *J* = 13.3 Hz), 3.09 (1H, d, *J* = 13.3 Hz), 2.06 (2H, q, *J* = 7.1 Hz), 1.95 (1H, t, *J* = 6.0 Hz), 1.69 (3H, s), 1.67 (3H, s), 1.60–1.29 (4H, m); δ_C (125 MHz, $CDCl_3$) 141.3 (C), 139.1 (C), 133.5 (2 × CH), 129.8 (2 × C), 128.8 (CH), 128.5 (CH), 128.3 (CH), 127.1 (CH), 126.0 (CH), 125.5 (CH), 125.4 (3 × CH), 122.2 (CF_3, J_{C-F} = 273.3 Hz), 104.1 (C), 62.1 (CH_2), 43.9 (CH), 32.7 (CH_2), 31.8 (CH_2), 26.9 (CH_2), 20.6 (CH_3), 19.1 (CH_3); HRMS (ESI) calculated for $C_{24}H_{27}F_3N$ [M + H]: 386.2090, found 386.2087.

1-((*S*)-1-Phenylethyl)-2-((*E*)-5-phenylpent-4-enyl)-3-(propan-2-ylidene)aziridine (10)

10 was prepared from **1b** (202 mg, 1.08 mmol), TMEDA (0.20 mL, 1.29 mmol), *sec*-BuLi (1.46 mL, 2.05 mmol) in THF (10 mL) and a solution of 1-((*E*)-5-iodopent-1-enyl)benzene [(*E*)-**13**] (587 mg, 2.16 mmol) in THF (1 mL) in accordance with the general method. Work-up followed by purification on silica (0.25% Et_3N and 1% EtOAc in petroleum ether) afforded **10** (202 mg, 0.61 mmol, 56%) as a yellow oil. ν_{max} (neat) 2926, 1718, 1448, 1132, 964, 745, 697 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.40–7.16 (10H, m), 6.40 (1H, d, *J* = 15.8 Hz), 6.24 (1H, dt, *J* = 15.8, 6.8 Hz), 2.91 (1H, q, *J* = 6.6 Hz), 2.32–2.26 (2H, m), 2.04–1.93 (1H, m), 1.78–1.51 (4H, m), 1.66 (3H, s), 1.46 (3H, d, *J* = 6.6 Hz), 1.03 (3H, s); δ_C (100 MHz, $CDCl_3$) 145.2 (C), 137.8 (C), 130.7 (CH), 130.1 (CH), 129.6 (CH), 128.5 (2 × CH), 128.3 (2 × CH), 127.6 (2 × CH), 127.1 (CH), 126.9 (CH), 126.0 (2 × CH), 104.1 (C), 68.3 (CH), 43.1 (CH), 33.1 (CH_2), 32.3 (CH_2), 27.7 (CH_2), 23.6 (CH_3), 21.1 (CH_3), 19.1 (CH_3); HRMS (ESI) calculated for $C_{24}H_{30}N$ [M + H]: 332.2373, found 332.2376.

1-Benzyl-2-(5-phenylpent-4-ynyl)-3-(propan-2-ylidene)aziridine (11)

11 was prepared from **1a** (202 mg, 1.17 mmol), TMEDA (0.21 mL, 1.40 mmol), *sec*-BuLi (1.57 mL, 2.19 mmol) in THF (9 mL) and a solution of 1-(5-iodopent-1-ynyl)benzene (**17**) (374 mg, 1.39 mmol) in THF (1 mL) in accordance with the general method. Work-up followed by purification on silica (0.5% Et_3N and 5% EtOAc in petroleum ether) afforded **11** (198 mg, 0.63 mmol, 54%) as a pale yellow oil. ν_{max} (neat) 3028, 2923, 2361, 1796, 1598, 1490, 1452, 755, 693 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.38–7.25 (10H, m), 4.18 (1H, d, *J* = 13.3 Hz), 3.19 (1H, d, *J* = 13.3 Hz), 2.31 (2H, t, *J* = 7.0 Hz), 2.06 (1H, t, *J* = 5.7 Hz), 1.78 (3H, s), 1.74 (3H, s), 1.67–1.48 (4H, m); δ_C (100 MHz, $CDCl_3$) 139.1 (C), 131.6 (2 × CH), 129.7 (C), 128.5 (2 × CH), 128.4 (2 × CH), 128.2 (2 × CH), 127.5 (CH), 127.2 (CH), 124.0 (C), 104.2 (C), 89.9 (C), 80.8 (C), 62.1 (CH_2), 43.7 (CH), 31.4 (CH_2), 26.5 (CH_2), 20.7 (CH_3), 19.1 (CH_3), 19.1 (CH_2); HRMS (ESI) calculated for $C_{23}H_{26}N$ [M + H]: 316.2060, found 316.2061.

(*Z*)-1-Benzyl-2-ethylidene-3-(5-phenylpent-4-ynyl)aziridine [(*Z*)-12]

(*Z*)-**12** was prepared from **1c** (212 mg, 1.33 mmol), TMEDA (0.24 mL, 1.60 mmol), *sec*-BuLi (1.80 mL, 2.53 mmol) in THF (11 mL) and a solution of 1-(5-iodopent-1-ynyl)benzene (**17**) (431 mg, 1.60 mmol) in THF (2 mL) in accordance with the general method. Work-up followed by purification on silica (0.5% Et_3N and 0–1% EtOAc in petroleum ether) afforded (*Z*)-**12** (125 mg, 0.41 mmol, 31%) as a yellow oil. ν_{max} (film) 2936, 1780, 1598, 1490, 1454, 1303, 1130, 756, 692 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.39–7.23 (10H, m), 5.12 (1H, q, *J* = 6.7 Hz), 4.20 (1H, d, *J* = 13.4 Hz), 3.29 (1H, d, *J* = 13.4 Hz), 2.32 (2H, t, *J* = 7.0 Hz), 2.03 (1H, t, *J* = 5.9 Hz), 1.78–1.47 (7H, m); δ_C (100 MHz, $CDCl_3$) 138.7 (C), 135.3(C), 131.6 (2 × CH), 128.5 (2 × CH), 128.4 (2 × CH), 128.2 (2 × CH), 127.5 (CH), 127.3 (CH), 124.0 (C), 94.9 (CH), 89.9 (C), 80.9 (C), 61.8 (CH_2), 42.9 (CH), 31.2 (CH_2), 26.3 (CH_2), 19.0 (CH_2), 13.3 (CH_3); HRMS (ESI) calculated for $C_{22}H_{24}N$ [M + H]: 302.1903, found 302.1906.

General procedure for boron trifluoride promoted intramolecular (3 + 2) cycloaddition/hydride reduction

To a stirred solution of aziridine (1.0 equiv.) in CH_2Cl_2 at –30 °C was added $BF_3{\cdot}OEt_2$ (2.2 equiv.). The mixture was allowed to warm slowly to room temperature over 15 h, then quenched by the addition of saturated aq. $NaHCO_3$ solution. The mixture was extracted with EtOAc (3×), and the combined organic extracts dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude iminium ion was taken up in THF and added to a stirred solution of $NaBH_4$ (3 equiv.) in glacial AcOH. The mixture was stirred at room temperature for 12 h, then basified by the addition of 2 M aq. NaOH solution. The mixture was extracted with EtOAc (3×), dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude product. Purification by column chromatography afforded the title compounds.

(1*S**,3*R**,3a*R**,6a*S**)-2-Benzyl-octahydro-1-isopropyl-3-phenylcyclopenta[c]pyrrole (19) and (1*R**,3*R**,3a*R**,6a*S**)-2-benzyl-octahydro-1-isopropyl-3-phenylcyclopenta[c]pyrrole (20)

To a stirred solution of (*E*)-**6** (178 mg, 0.56 mmol) in CH_2Cl_2 (11 mL) at –30 °C was added $BF_3{\cdot}OEt_2$ (0.16 mL, 1.23 mmol) in accordance with the general method, then the crude mixture was dissolved in THF (4 mL) and added to a stirred solution of $NaBH_4$ (65 mg, 1.68 mmol) in glacial AcOH (10 mL). Work-up followed by purification on silica (0.5–1.5% Et_2O in petroleum ether) afforded successively **20** (30.7 mg, 0.10 mmol, 17%) as a colourless oil and **19** (55.4 mg, 0.17 mmol, 31%) as a yellow oil. Compound **19**: ν_{max} (neat) 2952, 1690, 1452, 697 cm^{-1}; δ_H (400 MHz, C_6H_6) 7.33 (2H,

d, J = 7.5 Hz), 7.20 (2H, t, J = 7.5 Hz), 7.15–7.04 (4H, m), 6.98 (2H, d, J = 7.5 Hz), 3.92 (1H, d, J = 3.9 Hz), 3.76 (1H, d, J = 14.5 Hz), 3.19–3.13 (2H, m), 2.57–2.51 (1H, m), 2.47–2.39 (1H, m), 1.90–1.77 (3H, m), 1.68–1.60 (1H, m), 1.52–1.43 (1H, m), 1.40–1.24 (2H, m), 1.06 (3H, d, J = 6.8 Hz), 0.99 (3H, d, J = 7.0 Hz); δ_C (100 MHz, C_6D_6) 141.9 (C), 139.8 (C), 128.0 (2 × CH), 127.0 (2 × CH), 126.9 (2 × CH), 126.6 (2 × CH), 125.4 (CH), 125.3 (CH), 70.8 (CH), 66.7 (CH), 49.6 (CH_2), 48.8 (CH), 46.2 (CH), 33.3 (CH_2), 28.4 (CH_2), 27.1 (CH_2), 27.1 (CH), 19.2 (CH_3), 17.4 (CH_3); HRMS (ESI) calculated for $C_{23}H_{30}N$ [M + H]: 320.2373, found 320.2370. Compound **20**: ν_{max} (neat) 2950, 1718, 1453, 1246, 1166, 699 cm^{-1}; δ_H (600 MHz, DMSO-d_6) 7.42 (2H, d, J = 7.1, Hz), 7.35 (2H, t, J = 7.6 Hz), 7.25–7.22 (3H, m), 7.18–7.15 (1H, m), 7.03 (2H, d, J = 7.1 Hz), 3.62 (1H, d, J = 14.5 Hz), 3.29 (1H, d, J = 14.5 Hz), 3.04 (1H, d, J = 8.7 Hz), 2.31–2.26 (1H, m), 2.23 (1H, dd, J = 3.5, 6.5 Hz), 2.15 (1H, q, J = 8.4 Hz), 1.96–1.89 (1H, m), 1.58–1.25 (6H, m), 0.88 (3H, d, J = 6.7 Hz), 0.85 (3H, d, J = 7.0 Hz); δ_C (150 MHz, DMSO-d_6) 144.3 (C), 137.5 (C), 129.5 (2 × CH), 128.9 (2 × CH), 128.2 (2 × CH), 128.1 (2 × CH), 127.5 (CH), 127.1 (CH), 74.8 (CH), 74.4 (CH), 54.0 (CH_2), 52.8 (CH), 41.3 (CH), 33.9 (CH_2), 29.5 (CH_2), 27.8 (CH), 25.0 (CH_2), 20.6 (CH_3), 15.6 (CH_3); MS (ES^+) m/z 320 [M + H^+]; HRMS (ES^+) calcd. for $C_{23}H_{30}N$ [M + H^+]: 320.2373; found 320.2373.

(1*S**,3*R**,3a*R**,6a*S**)-2-Benzyl-octahydro-1-isopropyl-3-(4-methoxy-phenyl)cyclopenta[c]pyrrole (21) and (1*R**,3*R**,3a*R**,6a*S**)-2-benzyl-octahydro-1-isopropyl-3-(4-methoxy-phenyl)cyclopenta[c]pyrrole (22)

To a stirred solution of (*E*)-**8** (167 mg, 0.48 mmol) in CH_2Cl_2 (10 mL) at −30 °C was added $BF_3{\cdot}OEt_2$ (0.13 mL, 1.05 mmol) in accordance with the general method, then the crude mixture was dissolved in THF (4 mL) and added to a stirred solution of $NaBH_4$ (56 mg, 1.44 mmol) in glacial AcOH (10 mL). Work-up followed by purification on silica (2% Et_2O in petroleum ether) afforded successively **22** (20.6 mg, 0.06 mmol, 12%) as a colourless oil and **21** (33.2 mg, 0.10 mmol, 20%) as a colourless oil. Compound **21**: ν_{max} (film) 2953, 1608, 1510, 1453, 1250, 1038, 822 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.19–7.18 (4H, m), 7.14–7.09 (1H, m), 6.79 (2H, d, J = 8.6 Hz), 6.69 (2H, d, J = 8.6 Hz), 3.74–3.69 (5H, m), 3.03 (1H, t, J = 5.8 Hz), 2.98 (1H, d, J = 14.5 Hz), 2.60–2.50 (2H, m), 1.97–1.86 (2H, m), 1.83–1.64 (3H, m), 1.45–1.31 (2H, m), 1.03 (3H, d, J = 6.8 Hz), 0.93 (3H, d, J = 7.0 Hz); δ_C (75 MHz, $CDCl_3$) 157.1 (C), 140.0 (C), 133.8 (C), 129.1 (2 × CH), 127.0 (4 × CH), 125.1 (CH), 111.9 (2 × CH), 69.6 (CH), 66.3 (CH), 54.2 (CH_3), 49.4 (CH_2), 48.5 (CH), 46.2 (CH), 33.6 (CH_2), 28.6 (CH_2), 27.2 (CH_2), 27.1 (CH), 19.4 (CH_3), 17.5 (CH_3); HRMS (ESI) calculated for $C_{24}H_{32}NO$ [M + H]: 350.2478, found 350.2479. Compound **22**: ν_{max} (film) 2952, 1611, 1511, 1453, 1247, 1038, 826 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.27 (2H, d, J = 8.6 Hz), 7.17–7.06 (3H, m), 6.98–6.96 (2H, m), 6.80 (2H, d, J = 8.6 Hz), 3.73 (3H, s), 3.60 (1H, d, J = 14.4 Hz), 3.27 (1H, d, J = 14.4 Hz), 2.91 (1H, d, J = 8.5 Hz), 2.26–2.10 (3H, m), 1.94–1.86 (1H, m), 1.54–1.22 (6H, m), 0.84 (3H, d, J = 6.7 Hz), 0.82 (3H, d, J = 7.0 Hz); δ_C (75 MHz, $CDCl_3$) 158.0 (C), 137.0 (C), 135.8 (C), 128.9 (2 × CH), 128.4 (2 × CH), 127.0 (2 × CH), 125.8 (CH), 113.1 (2 × CH), 74.0 (CH), 73.2 (CH), 54.6 (CH_3), 53.1 (CH_2), 52.1 (CH), 40.6 (CH), 33.3 (CH_2), 28.9 (CH_2), 27.2 (CH), 24.4 (CH_2), 19.7 (CH_3), 14.6 (CH_3); MS (ES^+) m/z 350 [M + H^+]; HRMS (ES^+) calcd. for $C_{24}H_{32}NO$ [M + H^+]: 350.2478, found 350.2479.

(1*S**,3*R**,3a*R**,6a*S**)-2-Benzyl-octahydro-1-isopropyl-3-(4-trifluoromethylphenyl)cyclopenta[c]pyrrole (23) and (1*R**,3*R**,3a*R**,6a*S**)-2-benzyl-octahydro-1-isopropyl-3-(4-trifluoromethylphenyl)cyclopenta[c]pyrrole (24)

To a stirred solution of (*E*)-**9** (202 mg, 0.53 mmol) in CH_2Cl_2 (10 mL) at −30 °C was added $BF_3{\cdot}OEt_2$ (0.14 mL, 1.15 mmol) in accordance with the general method, then the crude mixture was dissolved in THF (5 mL) and added to a stirred solution of $NaBH_4$ (60 mg, 1.57 mmol) in glacial AcOH (10 mL). Work-up followed by purification on silica (2% Et_2O in petroleum ether) afforded a 58 : 42 diasteromeric mixture of **23** and **24** (74 mg, 0.19 mmol, 32%) as a colourless oil. ν_{max} (film) 2954, 2869, 1692, 1618, 1323, 1162, 1120, 1066, 1017, 827, 804, 740 cm^{-1}; HRMS (ESI) calculated for $C_{24}H_{29}F_3N$ [M + H]: 388.2247, found 388.2247. Compound **23**: δ_H (400 MHz, $CDCl_3$) 7.39 (2H, d, J = 8.0 Hz), 7.22–7.08 (5H, m), 7.01 (2H, d, J = 8.0 Hz), 3.80 (1H, d, J = 14.2 Hz), 3.78 (1H, d, J = 2.7 Hz), 3.15 (1H, d, J = 14.2 Hz), 3.06 (1H, t, J = 6.1 Hz), 2.63–2.48 (2H, m), 2.02–1.89 (2H, m), 1.87–1.67 (3H, m), 1.52–1.32 (2H, m), 1.07 (3H, d, J = 6.8 Hz), 0.95 (3H, d, J = 7.0 Hz); δ_C (100 MHz, $CDCl_3$) 147.9 (C), 139.4 (C), 136.0 (C), 128.5 (2 × CH), 127.1 (2 × CH), 126.9 (CH), 125.6 (CH), 124.5 (CH), 124.2 (2 × CH), 123.4 (CF_3, J_{C-F} = 272.1 Hz), 70.4 (CH), 67.4 (CH), 50.0 (CH_2), 49.5 (CH), 46.7 (CH), 33.5 (CH_2), 28.5 (CH_2), 27.1 (CH_2), 26.9 (CH), 19.5 (CH_3), 17.9 (CH_3). Compound **24**: δ_H (400 MHz, $CDCl_3$) 7.48–7.38 (5H, m), 7.09 (2H, d, J = 7.6 Hz), 6.91 (2H, d, J = 7.6 Hz), 3.54 (1H, d, J = 14.3 Hz), 3.35 (1H, d, J = 14.3 Hz), 3.16 (1H, d, J = 8.6 Hz), 2.32–2.22 (2H, m), 2.13 (1H, q, J = 8.1 Hz), 2.02–1.89 (1H, m), 1.59–1.11 (6H, m), 0.90 (3H, d, J = 6.9 Hz), 0.86 (3H, d, J = 7.1 Hz); δ_C (100 MHz, $CDCl_3$) 146.7 (C), 139.5 (C), 136.0 (C), 127.8 (2 × CH), 127.1 (2 × CH), 126.9 (CH), 126.7 (CH), 125.4 (CH), 123.5 (2 × CH), 123.4 (CF_3, J_{C-F} = 272.1 Hz), 73.6 (CH), 73.2 (CH), 53.1 (CH_2), 52.1 (CH), 40.4 (CH), 32.8 (CH_2), 28.3 (CH_2), 26.8 (CH), 24.0 (CH_2), 19.2 (CH_3), 14.2 (CH_3).

(3*S**,3a*S**,6a*R**)-2-Benzyl-octahydro-3-isopropyl-1,1-diphenylcyclopenta[c]pyrrole (26)

To a stirred solution of **7** (169 mg, 0.43 mmol) in CH_2Cl_2 (9 mL) at −30 °C was added $BF_3{\cdot}OEt_2$ (0.12 mL, 0.94 mmol) in accordance with the general method, then the crude mixture was dissolved in THF (4 mL) and added to a stirred solution of $NaBH_4$ (49 mg, 1.28 mmol) in glacial AcOH (10 mL). Work-up followed by purification on silica (2% Et_2O in petroleum ether) afforded **26** (39 mg, 0.10 mmol, 23%) as a white solid. mp 119–122 °C; ν_{max} (film) 2956, 1601, 1493, 1443, 1262, 1028, 909, 734 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 7.34–7.12 (15H, m), 4.29 (1H, d, J = 16.0 Hz), 3.68 (1H, d, J = 16.0 Hz), 3.28–3.27 (1H, m), 3.22–3.17 (1H, m), 2.75–2.71 (1H, m), 2.01–1.96 (1H, m), 1.74–1.69 (1H, m), 1.58–1.36 (4H, m), 1.12–1.08 (1H, m), 0.57 (3H, d, J = 6.8 Hz), 0.11 (3H, d, J = 6.8 Hz); δ_C (150 MHz, $CDCl_3$) 147.1 (C), 146.8 (C), 141.0 (C), 129.0 (2 × CH), 128.6 (2 × CH), 128.2 (2 × CH), 127.5 (2 × CH), 127.3 (2 × CH), 127.1 (2 × CH), 126.2 (CH), 126.2 (CH), 125.7 (CH), 76.1 (C), 73.0 (CH), 55.4 (CH), 50.0 (CH_2), 41.6 (CH), 34.0 (CH_2), 31.3 (CH_2), 28.2 (CH), 26.2 (CH_2), 20.5 (CH_3), 17.0 (CH_3);

HRMS (ESI) calculated for $C_{29}H_{34}NO$ [M + H]: 396.2686, found 396.2683.

(1*R,3*R**,3a*R**,6a*S**)-2-Benzyl-octahydro-1-isopropyl-3-phenylcyclopenta[c]pyrrole-1-carbonitrile (27)**

To a stirred solution of (*E*)-**6** (152 mg, 0.48 mmol) in CH_2Cl_2 (10 mL) at −30 °C was added $BF_3{\cdot}OEt_2$ (0.13 mL, 1.05 mmol). The resulting mixture was allowed to warm slowly to room temperature over 15 h, and then quenched by the addition of saturated aq. $NaHCO_3$ solution. The mixture was extracted with EtOAc (3×) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was taken up in THF (5 mL) and cooled to 0 °C. In a separate flask, glacial AcOH (0.07 mL, 1.20 mmol) was added to a solution of TMSCN (0.09 mL, 0.72 mmol) in THF (1 mL) at 0 °C (CAUTION: HCN must be handled with extreme caution). After stirring at 0 °C for 2 h, this mixture was added to the stirred solution of the crude iminium ion. The resultant mixture was warmed to room temperature and stirred for 15 h. Water followed by saturated aq. $NaHCO_3$ were added and the mixture extracted with Et_2O (3×). The combined organic layers were washed with saturated aq. $NaHCO_3$ then brine, were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification on silica (2% Et_2O in petroleum ether) afforded **27** (48 mg, 0.14 mmol, 29%) as a white solid. mp 109–110 °C; ν_{max} (film) 2956, 1601, 1493, 1443, 1262, 1028, 909, 734 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 7.39 (2H, d, J = 7.3 Hz), 7.29 (2H, t, J = 7.6 Hz), 7.22 (1H, t, J = 7.3 Hz), 7.15–7.08 (5H, m), 3.66 (2H, s), 3.30 (1H, d, J = 8.9 Hz), 2.64 (1H, dt, J = 2.9, 9.6 Hz), 2.47 (1H, m), 1.98–1.86 (2H, m), 1.76–1.66 (3H, m), 1.57–1.54 (1H, m), 1.47–1.40 (1H, m), 0.98 (3H, d, J = 6.7 Hz), 0.84 (3H, d, J = 6.7 Hz); δ_C (150 MHz, $CDCl_3$) 142.2 (C), 138.9 (C), 129.3 (2 × CH), 128.5 (2 × CH), 128.3 (2 × CH), 127.8 (2 × CH), 127.7 (CH), 126.8 (CH), 118.9 (C), 77.4 (C), 76.6 (CH), 54.5 (CH_2), 52.2 (CH), 44.2 (CH), 33.1 (CH), 32.2 (CH_2), 29.0 (CH_2), 25.7 (CH_2), 19.0 (CH_3), 15.1 (CH_3); HRMS (ESI) calculated for $C_{24}H_{29}N_2$ [M + H]: 345.2325, found 345.2322.

2-Benzyl-1-ethyl-2,4,5,6-tetrahydro-3-phenylcyclopenta-[c]pyrrole (31)

To a stirred solution of (*Z*)-**12** (118 mg, 0.39 mmol) in CH_2Cl_2 (8 mL) at −30 °C was added $BF_3{\cdot}OEt_2$ (0.07 mL, 0.59 mmol). The resulting mixture was allowed to warm slowly to room temperature over 15 h, and was then quenched by the addition of saturated $NaHCO_3$ solution. The resulting mixture was extracted with EtOAc (3×). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude product. Purification on silica (0–2% Et_2O in petroleum ether) afforded **31** (45 mg, 0.15 mmol, 38%) as a yellow oil. ν_{max} (film) 2940, 1596, 1494, 1453, 1352, 701 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 7.30–7.14 (8H, m), 6.98 (2H, d, J = 7.4 Hz), 5.10 (2H, s), 2.76–2.72 (4H, m), 2.44 (2H, q, J = 7.6 Hz), 2.37–2.33 (2H, m), 1.18 (3H, t, J = 7.6 Hz); δ_C (100 MHz, $CDCl_3$) 139.9 (2 × C), 133.8 (C), 129.5 (C), 128.6 (2 × CH), 128.4 (2 × CH), 128.3 (2 × CH), 127.1 (C), 126.8 (CH), 125.8 (3 × CH), 124.7 (C), 48.0 (CH_2), 31.1 (CH_2), 25.8 (CH_2), 25.5 (CH_2), 19.9 (CH_2), 12.9 (CH_3); HRMS (ESI) calculated for $C_{22}H_{24}N$ [M + H]: 302.1903, found 302.1905.

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