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Reactivity of allenoates towards aziridines: synthesis of functionalized methylenepyrrolidines and pyrroles

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ABSTRACT

The reactivity of buta-2,3-dienoates towards aziridines is reported. Typically, allenoates react as the 2π-component in the [3+2] cycloaddition with azomethine ylides generated from aziridines, affording 4-methylenepyrrolidines in a site-, regio- and stereoselective fashion. However, *N*-cyclohexyl- or *N*-*tert*-butyl-2-benzoyl-3-phenylaziridines showed a different reactivity in the reaction with buta-2,3-dienoates. Pyrrole derivatives were obtained as single or major products resulting from a formal [3+2] cycloaddition via C–N bond cleavage of the three-membered ring heterocycle leading to functionalized pyrroles. From the reaction with allenoates bearing bulkier C-4 substituents 4-methylenepyrrolidines were also formed as minor products.

1. Introduction

Nitrogen-containing five-membered heterocycles are among the most common structures in biologically active compounds making them important target molecules. In fact, pyrroles represent an important class of heterocycles due to their broad distribution in nature as constituents of the framework of a range of natural products and also of synthetic bioactive molecules.[1] Polypyrroles also find applications in materials science, nonlinear optics and supramolecular chemistry as molecular sensors and devices.[2] Pyrrolidine derivatives are also present in many bioactive compounds. The development of synthetic routes to methylenepyrrolidine derivatives are of particular interest since the presence of an unsaturated bond allows further elaboration.[3]

We have recently described preliminary results on the study of the reactivity of buta-2,3-dienoates towards aziridines.[4] Our aim was to explore the cycloaddition of azomethine ylides generated from aziridines via conrotatory electrocyclic ring opening with buta-2,3-dienoates. Allenes can participate in cycloadditions as dipolarophiles with a variety of 1,3-dipoles namely nitrile oxides, nitrones, carbonyl ylides, nitrile imines, azides and diazomethanes but the 1,3-dipolar cycloaddition with azomethine ylides is an almost unexplored research topic.[5–9] Nevertheless, the enantioselective synthesis of 3-methylenepyrrolidine via catalytic 1,3-dipolar cycloaddition of allenoates and azomethine ylides generated in situ from aldehydes and amino esters has been reported.[10]

Our preliminary results showed that the substitution pattern of the aziridine determines the chemical behaviour of allenoates towards these three-membered heterocycles.[4] Allenoates can react as the 2π-component in the [3+2] cycloaddition with the azomethine ylide generated from aziridines affording 4-methylenepyrrolidines but they can also react via formal [3+2] cycloadditions leading to functionalized pyrroles. In this paper, we describe full details of the study on the reactivity of aziridines in the presence of allenoates.

2. Results and discussion

The reaction of *cis*-1-benzyl-2-benzoyl-3-phenylaziridine (**1**) with allenoates was explored (Scheme 1). Aziridine **1** was prepared following a known synthetic procedure[11a] and its X-ray structure determined in order to unambiguously establish the cis stereochemistry (Fig. 1). Thermolysis of aziridine **1** in the presence of benzyl buta-2,3-dienoate[12] (**3a**) in refluxing toluene for 24 h did not lead to the target cycloadduct. However, 4-methylenepyrrolidine **4a**

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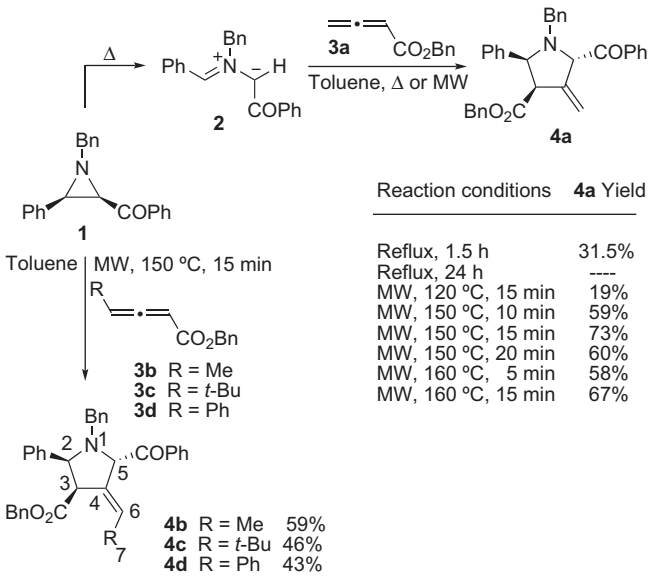


Scheme 1. Synthesis of 4-methylenepyrrolidine **4a**–**d** via [3+2] cycloaddition of azomethine ylide **2** and allenoates **3a**–**d**.

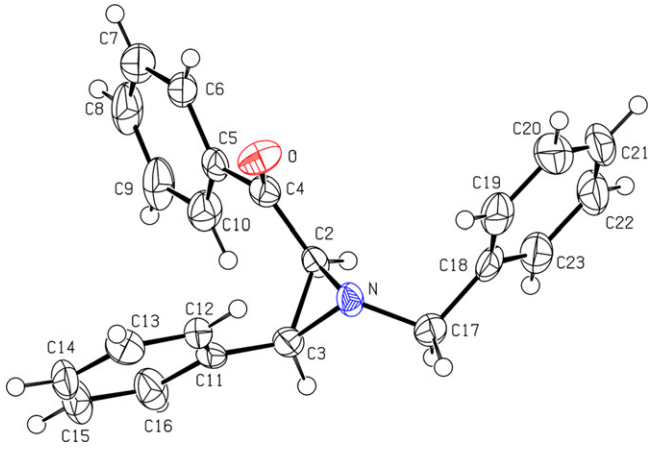


Fig. 1. X-ray structure of 2-benzoyl-1-benzyl-3-phenylaziridine (**1**). Selected bond distances (Å): C2–N1 1.451, C2–C3 1.511, C3–N1 1.459. Selected bond angles (°): N1–C2–C3 59.0; N1–C3–C2 58.5, C2–N1–C3 62.6.

could be obtained as single stereoisomer in moderate yield (31.5%) when a significantly shorter reaction time was used (1.5 h). These results indicate the lack of stability of compound **4a** to prolonged heating. The stuctural assignment of compound **4a** was supported by two-dimensional COSY, NOESY, HMQC, and HMBC spectra (400 MHz).[4] We have previously reported that the microwave methodology for the conrotatory ring opening of an aziridine, leading to the corresponding 1,3-dipole and the subsequent cycloaddition is more efficient than the conventional heating.[13] Thus, the microwave-assisted 1,3-dipolar cycloaddition of azomethine ylide **2** with benzyl buta-2,3-dienoate (**3a**) was carried out under different reaction conditions in order to optimize the synthetic procedure. We observed that the 1,3-dipolar cycloadduct **4a** was obtained in 73% yield in a site-, regio- and stereoselective fashion under microwave irradiation at 150 °C for 15 min.

The work was extended to the microwave induced reaction of aziridine **1** with benzyl penta-2,3-dienoate (**3b**), benzyl 5,5-dimethylhexa-2,3-dienoate (**3c**)[12] and benzyl 4-phenylbuta-2,3-dienoate (**3d**).[12] Using the optimized reaction conditions, the target molecules **4b**–**d** were also selectively obtained (Scheme 1). Under conventional heating (reflux, 1.5 h) the reaction of allene **3d** with 1,3-dipole **2** also afforded 4-methylenepyrrolidine **4d** in 43% yield.

The geometry of the carbon–carbon double bond of compound **4b** was assigned based on the NOESY spectrum. In fact, in this spectrum methyl protons (H-7) show connectivity with H-3 but no connectivity was observed with H-5. On the other hand, H-2 shows connectivity with H-3 and H-5 shows connectivity with H-6. The structure of methylenepyrrolidine **4d** was determined by X-ray crystallography allowing the complete stereochemistry assignment (Fig. 2). In the ^{1}H NMR spectrum of compound **4d** the coupling between H-2 and H-3, which are in a cis configuration, is characterized by a coupling constant of 8.0 Hz.

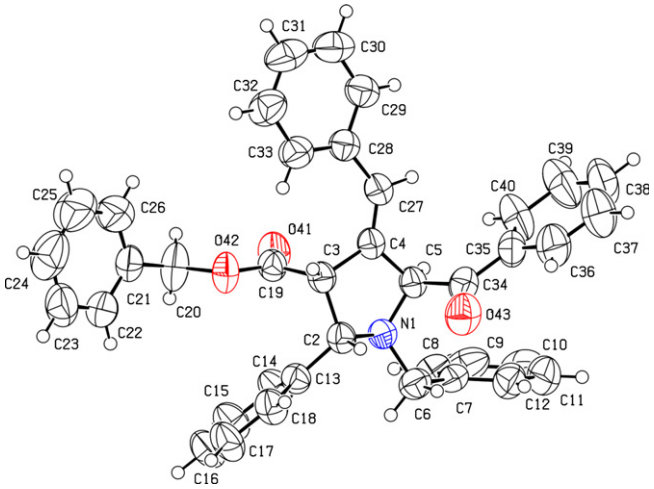
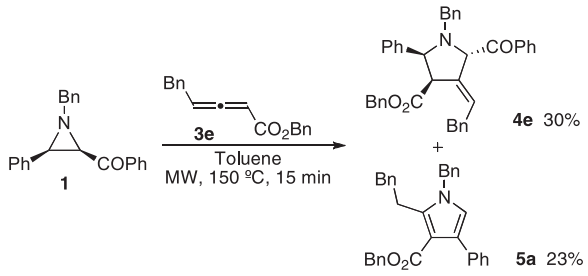


Fig. 2. X-ray structure of 4-methylenepyrrolidine **4d**.

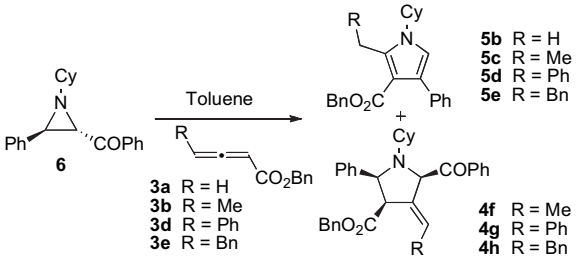
A different outcome was observed from the reaction of aziridine **1** with benzyl 5-phenylpenta-2,3-dienoate (**3e**)[12] (Scheme 2). The expected 4-methylenepyrrolidine **4e** was obtained in 30% yield together with the formation of pyrrole **5a** in 23% yield resulting from a formal [3+2] cycloaddition (see below).



Scheme 2. Reaction of aziridine **1** with allene **3e**.

trans-2-Benzoyl-1-cyclohexyl-3-phenylaziridine **6** was also synthesized by a known procedure[14] and its reactivity towards buta-2,3-dienoates studied (Table 1). Carrying out the reaction with benzyl buta-2,3-dienoate (**3a**) in refluxing toluene, pyrrole **5b** was obtained in 55.5% yield as single product (entry 1). A significantly lower yield was obtained when the reaction was carried out with longer reaction time. From the reaction of aziridine **6** with allene **3b** under conventional heating pyrrole **5c** was the major product (62%) and 4-methylenepyrrolidine **4f** was isolated in 19% yield (entry 2). Similar chemical behaviour was observed when aziridine **6** was reacted with allene **3d** under microwave irradiation giving pyrrole **5d** and pyrrolidine **4g** in 64% yield and 10% yield, respectively (entry 3). The reaction of *N*-cyclohexylaziridine **6** with allene **3e** was also carried out. Heating a solution of these compounds in refluxing toluene pyrrole **5e** (26%) and pyrrolidine **4h** (23%) were obtained, whereas the microwave induced reaction led to the isolation of pyrrole **5e** as the only product (entries 4 and 5). However, no reaction was observed using 5,5-dimethylhexa-2,3-dienoate (**3c**) as dipolarophile.

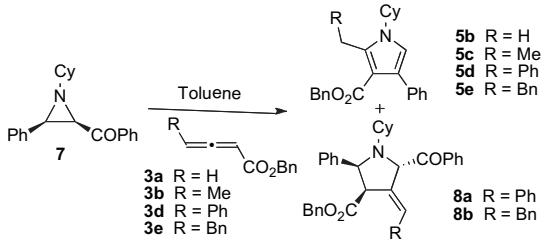
Table 1
Synthesis of pyrroles and pyrrolidines from the reaction of aziridine **6** with allenoates



Entry	Allene	Reaction conditions	Product (Yield %)	
1	**3a**	Reflux, 1.5 h	**5b** (55.5%)	—
2	**3b**	Reflux, 1.5 h	**5c** (62%)	**4f** (19%)
3	**3d**	MW, 150 °C, 15 min	**5d** (64%)	**4g** (10%)
4	**3e**	Reflux, 1.5 h	**5e** (26%)	**4h** (23%)
5	**3e**	MW, 150 °C, 15 min	**5e** (65%)	—

Aiming to find out whether the stereochemistry of the starting aziridine had a role in determining the outcome of the reaction with allenoates the reactivity of *cis*-2-benzoyl-1-cyclohexyl-3-phenylaziridine **7**[11a] was also studied (Table 2). It was observed that aziridine **7** reacted with benzyl buta-2,3-dienoate (**3a**) under conventional thermolysis affording pyrrole **5b** in 54% yield (entry 1). Pyrrole **5c** was isolated in high yield (86%) from the reaction of aziridine **7** with allene **3b** (entry 2). The reaction with allenoate **3d** gave the corresponding pyrrole **5d** as the major product with the simultaneous formation of pyrrolidine **8a**, either under conventional heating or under microwave irradiation (entries 3 and 4). Finally, the reactivity of aziridine **7** towards benzyl 5-phenylpenta-2,3-dienoate (**3e**) was explored. Under conventional heating pyrrole **5e** (43%) and pyrrolidine **8b** (33%) were obtained, whereas the microwave induced reaction gave pyrrole **5e** (75%) as single product (entry 6).

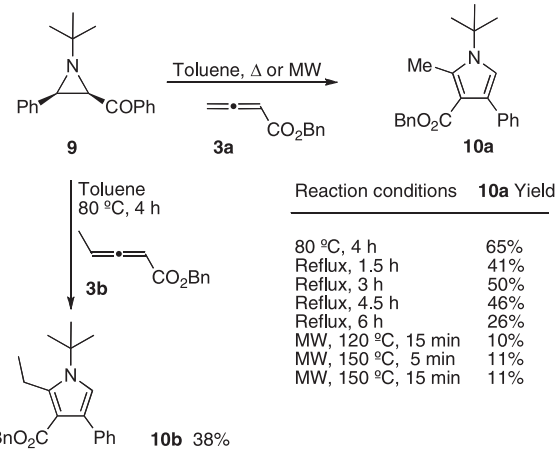
Table 2
Synthesis of pyrroles and pyrrolidines from the reaction of aziridine **7** with allenoates



Entry	Allene	Reaction Conditions	Product (Yield %)	
1	**3a**	Reflux, 1.5 h	**5b** (54%)	—
2	**3b**	Reflux, 1.5 h	**5c** (86%)	—
3	**3d**	Reflux, 1.5 h	**5d** (41%)	**8a** (35%)
4	**3d**	MW, 150 °C, 15 min	**5d** (53%)	**8a** (12%)
5	**3e**	Reflux, 1.5 h	**5e** (43%)	**8b** (33%)
6	**3e**	MW, 150 °C, 15 min	**5e** (75%)	—

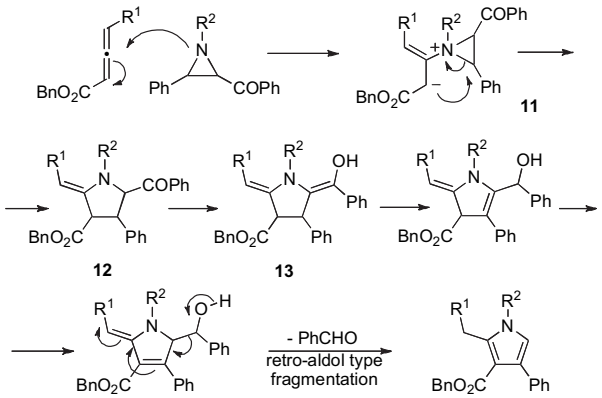
These results allowed us to conclude that the nature of the *N*-substituent of the 2-benzoyl-3-phenylaziridines determines the chemical behaviour of these three-membered heterocycles in the presence of allenoates. The bulkier cyclohexyl *N*-substituent seems to hinder the 1,3-dipolar cycloaddition favouring the formal [3+2] cycloaddition. However, this reaction pathway becomes less favourable with allenoates with a bulkier C-4 substituent. Furthermore, the unsuccessful attempt to promote the reaction of *N*-cyclohexylaziridine **6** with 5,5-dimethylhexa-2,3-dienoate (**3c**) mentioned above is in accordance with these observations.

In order to support this rationalization, *cis*-2-benzoyl-3-phenylaziridine **9**, bearing a bulky *N*-*tert*-butyl substituent, was prepared[11] and its reactivity studied (Scheme 3). As expected, the reaction of aziridine **9** with allene **3a** gave pyrrole **10a**. The optimized reaction conditions for the conventional thermolysis (80 °C, 4 h) allowed the isolation of pyrrole **10a** in 65% yield. Under microwave irradiation compound **10a** was obtained in poor yield (10–11%). The reaction of aziridine **9** with allene **3b** also afforded the corresponding formal [3+2] cycloadduct **10b**. No reaction was observed between allene **3d** and *cis*-2-benzoyl-1-*tert*-butyl 3-phenylaziridine **9**.



Scheme 3. Synthesis of pyrroles **10** via formal [3+2] cycloaddition of aziridine **9** and allenoates.

The formation of pyrroles **5** and **10** can be explained as outlined in Scheme 4. Nucleophilic addition of the aziridine to the activated allene double bond giving intermediate **11** followed by the intramolecular attack of the carbanion center on the aziridine ring, affords the five-membered heterocycles **12** via C–N bond cleavage. Tautomerisms and the subsequent aromatization lead to pyrrole **13** bearing a hydroxybenzyl sidechain, which is converted into the final product and benzaldehyde via retro-aldol type fragmentation.[15]

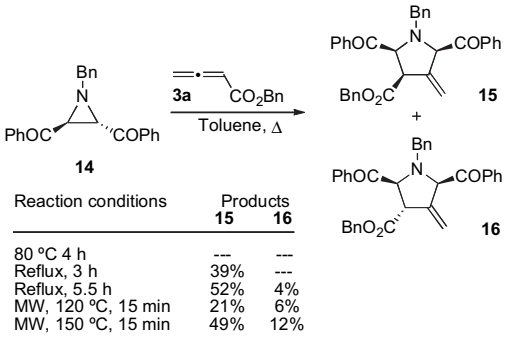


Scheme 4. Mechanism proposal of the formal [3+2] cycloaddition of aziridines and allenoates.

The reactivity of aziridines participating in formal [3+2] cycloadditions via C–N bond cleavage with activated acetylene derivatives has been reported.[16] Mattay and Gaebert demonstrated that the dipolar intermediate formed from *N*-butyl-2-phenylaziridine and diethyl acetylenedicarboxylate could be trapped by carrying out the reaction in methanol.[16a] Therefore, the reaction of aziridine **6** with allene **3a** in methanol was also performed. However, we were unable to trap intermediate **11** since at room

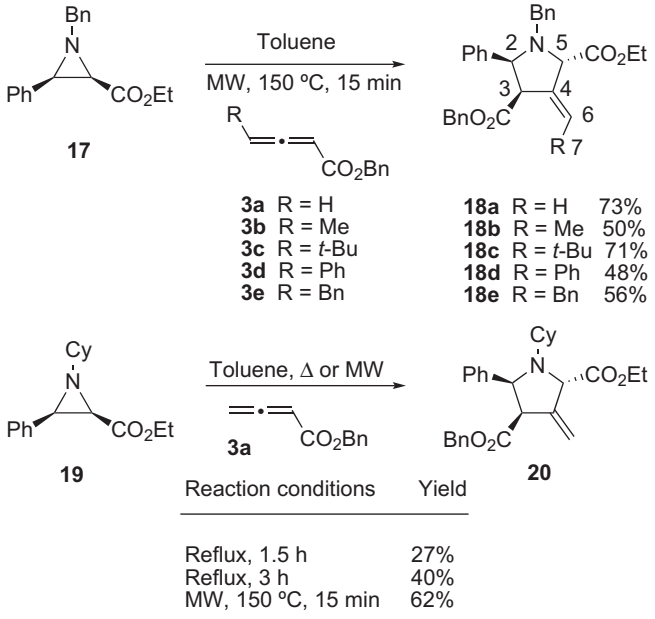
temperature no reaction was observed and the reaction in refluxing methanol gave only pyrrole **5b** in 31% yield.

Then, the reactivity of *trans*-2,3-dibenzoyl-1-benzylaziridine (**14**)[17] in the presence of buta-2,3-dienoate **3a** was studied (Scheme 5). From the thermolysis at 80 °C no product could be isolated. However, when the reaction was carried out in refluxing toluene for 3 h, methylenepyrrolidine **15** was obtained in 39% yield. With a longer reaction time (5.5 h) compound **15** was obtained in 52% together with the formation of methylenepyrrolidine **16** in 4% yield. The stereochemistry assignment was based on ^{1}H NMR data. In fact, the coupling constant between protons H-2 and H-3 observed for compound **15** was 8.0 Hz, whereas the value for compound **16** was 4.4 Hz. The microwave induced [3+2] cycloaddition of the azomethine ylide generated from aziridine **14** with allene **3a** was also site- and regio-selective but not stereoselective. Carrying out the reaction at 150 °C for 15 min gave methylenepyrrolidine **15** and methylenepyrrolidine **16** in 49% and 12% yield, respectively.



Scheme 5. Synthesis of 4-methylenepyrrolidines **15** and **16** via [3+2] cycloaddition.

Finally, the reactivity of *N*-benzyl- and *N*-cyclohexyl-*cis*-3-phenylaziridine-2-carboxylates towards allenoates was explored (Scheme 6). The microwave induced conrotatory electrocyclic ring opening of aziridine **17** was followed by 1,3-dipolar cycloaddition of the in situ generated azomethine ylide with allenoates **3a**–**e** in a site-, regio- and stereo-selective fashion affording methylenepyrrolidines **18** in good yields. The NOESY spectrum of compound **17b** shows connectivity of H-6 with H-5 and H-7, H-7 shows connectivity with H-3, and H-2 shows connectivity with H-3, but no connectivity was observed between H-2 and H-5 or between H-3 and H-5. On the other hand, methylenepyrrolidines **18** are characterized by a coupling constant between H-2 and H-3 in the range of 7.6–8.4 Hz. A similar chemical behaviour was observed between ethyl *N*-cyclohexyl-*cis*-3-phenylaziridine-2-carboxylate (**19**) and benzyl buta-2,3-dienoate (**3a**). Under microwave irradiation methylenepyrrolidine **20** was obtained in 62% yield, whereas the conventional thermolysis afforded the same product in lower yield.



Scheme 6. Synthesis of 4-methylenepyrrolidines **18** and **20** via [3+2] cycloaddition.

3. Conclusion

Site-, regio- and stereoselective synthesis of 4-methylenepyrrolidines was achieved via [3+2] cycloaddition of allenoates with azomethine ylides generated from *cis*-1-benzyl-2-benzoyl-3-phenylaziridine, *N*-benzyl- and *N*-cyclohexyl-*cis*-3-phenylaziridine-2-carboxylates.

Reaction of *N*-cyclohexyl- or *N*-*tert*-butyl-2-benzoyl-3-phenylaziridines with buta-2,3-dienoates led to a different outcome. In these cases pyrroles were obtained as the only or the major product resulting from formal [3+2] cycloadditions via aziridine C–N bond cleavage.

These reactions can be carried out under microwave irradiation or with conventional heating.

4. Experimental section

4.1. General

^{1}H NMR spectra were recorded on an instrument operating at 400 MHz. ^{13}C spectra were recorded on an instrument operating at 100 MHz. The solvent is deuteriochloroform except where otherwise indicated. IR spectra were recorded on a Perkin–Elmer 1720X FTIR spectrometer. Mass spectra were recorded on a Bruker FTMS APEXIII instrument under electrospray ionization (ESI) except where indicated otherwise. Melting points were recorded on a Reichert hot stage and are uncorrected. Flash column chromatography was performed with Merck 9385 silica as the stationary phase.

4.2. General procedure for the synthesis of ethyl 3-phenylaziridine-2-carboxylates

A suspension of the appropriated amine (35.7 mmol) and ethyl 2,3-dibromo-3-phenylpropanoate (3.0 g, 8.9 mmol) in ethanol (12 mL) was stirred at room temperature (for 4.5 days, starting from benzylamine; for 6 days starting from cyclohexylamine). The reaction mixture was diluted with water and extracted with dichloromethane. The organic layer was dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography [ethyl acetate–hexane].

*4.2.1. Ethyl 1-benzyl-3-phenylaziridine-2-carboxylate (**17**).* Purification by flash column chromatography [ethyl acetate–hexane (1:5)] afforded **17** as a white solid in 62% yield. Mp 63.5–66.0 °C (from ethyl acetate–hexane). IR (KBr) 2978, 1734, 1261 and 1163 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) 0.96 (3H, t, *J*=7.2 Hz), 2.63 (1H, d, *J*=6.8 Hz), 3.06 (1H, d, *J*=6.8 Hz), 3.64 (1H, d, *J*=13.6 Hz), 3.87–4.02 (3H, m), 7.19–7.43 (10H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 13.9, 46.0, 47.7, 60.7, 63.5, 127.3, 127.4, 127.9, 128.0, 128.4, 135.1, 137.7, 168.1; MS (ESI) *m*/*z* 282 (MH^+, 100%) and 201 (81). HRMS (ESI) *m*/*z* 282.14895 ($C_{18}H_{20}NO_2$ [MH^+], 282.14886).

*4.2.2. Ethyl 1-cyclohexyl-3-phenylaziridine-2-carboxylate (**19**).* Purification by flash column chromatography [ethyl

acetate–hexane (1:9)] afforded **19** as a white solid in 59% yield. Mp 34.0–36.0 °C (from ethyl acetate–hexane). IR (KBr) 2922, 1738, 1250 and 1173 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 0.93 (3H, t, *J*=7.2 Hz), 1.19–1.30 (3H, m), 1.49–1.61 (4H, m), 1.82–1.84 (4H, m), 2.47 (1H, d, *J*=6.8 Hz), 2.93 (1H, d, *J*=6.8 Hz), 3.84–3.92 (1H, m), 3.96–4.04 (1H, m), 7.19–7.29 (3H, m, Ar–H), 7.38–7.40 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 13.9, 24.5, 24.5, 26.0, 31.8, 32.3, 44.6, 47.0, 60.5, 68.7, 127.3, 127.8, 127.9, 135.9, 168.7; MS (ESI) *m/z* 274 (MH^+, 100%) and 201 (30). HRMS (ESI) *m/z* 274.18009 ($C_{17}H_{24}NO_2$ [MH^+], 274.18016).

4.3. General procedure for [3+2] cycloaddition of aziridines with allenes

Method A: A suspension of the appropriated aziridine and allene in toluene (1 mL) was irradiated in the microwave reactor (CEM—Focused Synthesis System, Discover S-Class) for 15 min with the temperature set to 150 °C. The solvent was removed under reduced pressure and the crude product was purified by crystallization, by flash column chromatography [ethyl acetate–hexane] or by preparative thin layer chromatography [ethyl acetate–hexane (1:10)] followed by recrystallization, as indicated for each case.

Method B: A solution of the appropriated aziridine and allene in toluene (6 mL) was heated at reflux for 1.5 h. The solvent was removed under reduced pressure and the crude product was purified by crystallization or by flash column chromatography [ethyl acetate–hexane] followed by recrystallization, as indicated for each case.

*4.3.1. Benzyl 5-benzoyl-1-benzyl-4-methylene-2-phenylpyrrolidine-3-carboxylate (**4a**).* Prepared by *methods A* or *B* from aziridine **1** (100 mg, 0.32 mmol) and allene **3a** (0.48 mmol). Crystallization from methanol afforded **4a** as a yellow solid in 73% (*method A*) or 31.5% (*method B*) yield. Mp 111.0–113.0 °C (from methanol). IR (film) 3030, 1734, 1680, 1218 and 1157 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 3.58 (1H, d, *J*=13.2 Hz), 3.84 (1H, d, *J*=13.2 Hz), 4.18 (1H, d, *J*=8.0 Hz), 4.41 (1H, d, *J*=12.4 Hz), 4.78 (1H, d, *J*=12.4 Hz), 4.99 (1H, br s), 5.15 (1H, br s), 5.17 (1H, d, *J*=8.0 Hz), 5.35 (1H, s), 7.02 (2H, br s, Ar–H), 7.18 (5H, br s, Ar–H), 7.28–7.36 (8H, m, Ar–H), 7.46–7.58 (5H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 51.5, 55.0, 66.6, 67.2, 68.8, 112.6, 127.1, 128.0, 128.1, 128.3, 128.4, 128.5, 128.6, 129.0, 133.0, 135.4, 136.7, 138.3, 138.5, 144.3, 170.8, 201.3; LC–MS (ESI) *m/z* 488 (MH^+, 57%), 470 (35), 396 (100) and 380 (73). HRMS (ESI) *m/z* 488.22112 ($C_{33}H_{30}NO_3$ [MH^+], 488.22202).

*4.3.2. Benzyl 5-benzoyl-1-benzyl-4-ethylidene-2-phenylpyrrolidine-3-carboxylate (**4b**).* Prepared by *method A* from aziridine **1** (100 mg, 0.32 mmol) and allene **3b** (0.48 mmol). Crystallization from methanol afforded **4b** as a yellow solid in 59% yield. Mp 138.8–140.9 °C (from methanol). IR (film) 3030, 1736, 1672, 1217 and 1146 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 1.40 (3H, d, *J*=6.8 Hz), 3.58 (1H, d, *J*=13.2 Hz), 3.91 (1H, d, *J*=13.2 Hz), 4.07 (1H, d, *J*=8.0 Hz), 4.37 (1H, d, *J*=12.0 Hz), 4.79 (1H, d, *J*=12.0 Hz), 5.23–5.30 (2H, m), 5.42 (1H, s), 7.01–7.03 (2H, m, Ar–H), 7.16–7.38 (13H, m, Ar–H), 7.44–7.57 (5H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 15.0, 51.1, 53.6, 65.3, 66.5, 69.2, 122.3, 127.1, 127.9, 128.0, 128.2, 128.3, 128.3, 128.4, 128.5, 129.0, 132.9, 135.6, 137.3, 138.5, 171.0, 202.2; MS (ESI) *m/z* 502 (MH^+, 100%). HRMS (ESI) *m/z* 502.23665 ($C_{34}H_{32}NO_3$ [MH^+], 502.23767).

*4.3.3. Benzyl 5-benzoyl-1-benzyl-4-(2,2-dimethylpropylidene)-2-phenylpyrrolidine-3-carboxylate (**4c**).* Prepared by *method A* from aziridine **1** (100 mg, 0.32 mmol) and allene **3c** (0.48 mmol). Crystallization from methanol afforded **4c** as a yellow solid in 46% yield. Mp 143.0–144.0 °C (from methanol). IR (KBr) 3030, 1732, 1675, 1222 and 1152 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 0.81 (9H, s), 3.54 (1H, d, *J*=13.6 Hz), 3.93 (1H, d, *J*=13.6 Hz), 4.20 (1H, d, *J*=7.6 Hz), 4.29 (1H, d, *J*=12.0 Hz), 4.81 (1H, d, *J*=12.0 Hz), 5.04 (1H, s), 5.26 (1H, d, *J*=7.6 Hz), 5.40 (1H, s), 7.02 (2H, br s, Ar–H), 7.17–7.55 (18H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 29.7, 33.7, 50.9, 53.6, 66.4, 66.6, 70.0, 127.0, 128.0, 128.1, 128.2, 128.3, 128.4, 128.6, 129.0, 132.6, 133.2, 135.4, 137.7, 138.2, 138.6, 171.8, 203.7; MS (ESI) *m/z* 544 (MH^+, 100%). HRMS (ESI) *m/z* 544.28363 ($C_{37}H_{38}NO_3$ [MH^+], 544.28462).

*4.3.4. Benzyl 5-benzoyl-1-benzyl-4-benzylidene-2-phenylpyrrolidine-3-carboxylate (**4d**).* Prepared by *methods A* or *B* from aziridine **1** (100 mg, 0.32 mmol) and allene **3d** (0.38 mmol). Purification by flash column chromatography [ethyl acetate–hexane (1:9)] afforded **4d** as a yellow solid in 43% (*method A*) or 39% (*method B*) yield. Mp 141.9–143.7 °C (from ethyl ether). IR (KBr) 3028, 1737, 1676, 1224 and 1150 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 3.61 (1H, d, *J*=13.2 Hz), 3.97 (1H, d, *J*=13.2 Hz), 4.12 (1H, d, *J*=12.0 Hz), 4.43 (1H, d, *J*=8.0 Hz), 4.63 (1H, d, *J*=12.0 Hz), 5.38 (1H, d, *J*=8.0 Hz), 5.60 (1H, s), 6.22 (1H, s), 6.92–6.93 (2H, m, Ar–H), 7.02–7.04 (2H, m, Ar–H), 7.10–7.12 (3H, m, Ar–H), 7.19–7.38 (13H, m, Ar–H), 7.48–7.49 (3H, m, Ar–H), 7.56–7.57 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 51.2, 54.5, 66.5, 67.1, 70.1, 127.1, 127.2, 127.3, 128.0, 128.0, 128.1, 128.3, 128.3, 128.4, 128.4, 128.6, 129.0, 133.0, 135.4, 136.1, 137.4, 137.9, 138.4, 170.2, 202.2; MS (ESI) *m/z* 564 (MH^+, 100%) and 201 (74). HRMS (ESI) *m/z* 564.25488 ($C_{39}H_{34}NO_3$ [MH^+], 564.25332).

*4.3.5. Benzyl 5-benzoyl-1-benzyl-4-phenethylidene-2-phenylpyrrolidine-3-carboxylate (**4e**) and benzyl 1-cyclohexyl-2-phenethyl-4-phenyl-1H-pyrrole-3-carboxylate (**5a**).* Prepared by *method A* from aziridine **1** (100 mg, 0.32 mmol) and allene **3e** (0.48 mmol). Purification by preparative thin layer chromatography [ethyl acetate–hexane (1:10)] afforded **4e** as a yellow solid in 30% yield and **5a** as a yellow oil in 23% yield. *Benzyl 5-benzoyl-1-benzyl-4-phenethylidene-2-phenylpyrrolidine-3-carboxylate* (**4e**). Mp 139.9–141.1 °C (from methanol). IR (KBr) 3029, 1735, 1680, 1235 and 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 3.13 (2H, d, *J*=7.2 Hz), 3.60 (1H, d, *J*=13.6 Hz), 3.94 (1H, d, *J*=13.6 Hz), 4.17 (1H, d, *J*=8.4 Hz), 4.36 (1H, d, *J*=12.0 Hz), 4.76 (1H, d, *J*=12.0 Hz), 5.32–5.34 (2H, m), 5.47 (1H, s), 6.87–6.88 (2H, m, Ar–H), 7.01–7.03 (2H, m, Ar–H), 7.18–7.27 (19H, m, Ar–H), 7.56–7.58 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 35.5, 51.0, 53.7, 65.4, 65.5, 69.1, 125.9, 126.0, 126.5, 127.0, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.8, 129.3, 132.8, 135.3, 137.2, 137.6, 138.2, 138.4, 139.1, 170.9, 202.3; MS (ESI) *m/z* 578 (MH^+, 100%), 494 (6) and 413 (6). HRMS (ESI) *m/z* 578.26698 ($C_{40}H_{36}NO_3$ [MH^+], 578.26897); *Benzyl 1-cyclohexyl-2-phenethyl-4-phenyl-1H-pyrrole-3-carboxylate* (**5a**). IR (film) 3028, 1696, 1282 and 1181 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 2.74 (2H, t, *J*=7.8 Hz), 3.12 (2H, t, *J*=7.8 Hz), 4.81 (2H, s), 5.18 (2H, s), 6.52 (1H, s), 6.96–6.98 (2H, m, Ar–H), 7.02–7.04 (2H, m, Ar–H), 7.12–7.37 (16H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 28.3, 36.2, 50.4, 65.5, 110.5, 120.9, 126.1, 126.2, 126.7, 127.7, 127.9, 128.3, 128.5, 128.6, 128.7, 129.1, 129.5, 135.9, 136.3, 136.9, 140.2, 141.4, 165.2; MS (ESI) *m/z* 472 (MH^+, 25%), 429 (17), 301 (29) and 201 (48). HRMS (ESI) *m/z* 472.22769 ($C_{33}H_{30}NO_2$ [MH^+], 472.22711).

*4.3.6. Benzyl 1-cyclohexyl-2-methyl-4-phenyl-1H-pyrrole-3-carboxylate (**5b**).* Prepared by *method B* of general procedure from aziridine **7** and allene **3a**. Purification by preparative thin layer chromatography [ethyl acetate–hexane (1:10)] afforded **5b** as a yellow oil in 54% yield. IR (film) 2932, 1696, 1411, 1272 and 1155 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 1.21–2.01 (10H, m), 2.55 (3H, s), 3.88 (1H, t, *J*=12.0 Hz), 5.14 (2H, br s), 6.61 (1H, s), 7.06 (2H, br s, Ar–H), 7.22–7.32 (8H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 11.3, 25.4, 25.8, 34.0, 55.3, 65.2, 109.9, 116.0, 126.0, 127.5, 127.6, 127.9, 128.2, 129.3, 135.8, 136.4, 136.5, 165.8; GC–MS (EI) *m/z* 373 (M^+, 72%), 283 (25), 282 (100), 200 (55) and 91 (21). HRMS (ESI) *m/z* 374.21127 ($C_{25}H_{28}NO_2$ [MH^+], 374.21146).

*4.3.7. Benzyl 1-cyclohexyl-2-ethyl-4-phenyl-1H-pyrrole-3-carboxylate (**5c**) and benzyl 5-benzoyl-1-cyclohexyl-4-ethylidene-2-*

*phenylpyrrolidine-3-carboxylate (**4f**).* Prepared by *method B* from aziridine **6** and allene **3b**. Purification by preparative thin layer chromatography [ethyl acetate–hexane (1:10)] afforded **5c** as a yellow oil in 62% yield and **4f** as a yellow oil in 19% yield. *Benzyl* 1-*cyclohexyl*-2-*ethyl*-4-*phenyl*-1*H*-*pyrrole*-3-*carboxylate* (**5c**). IR (film) 2932, 1700, 1281 and 1154 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 1.20 (3H, t, J=7.2 Hz), 1.38–2.00 (10H, m), 2.99 (2H, q, J=7.2 Hz), 3.85–3.91 (1H, m), 5.14 (2H, s), 6.60 (1H, s), 7.06 (2H, br s, Ar–H), 7.20–7.36 (8H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 14.8, 18.5, 25.4, 25.9, 34.6, 55.0, 65.2, 116.2, 126.0, 127.5, 127.6, 128.0, 128.2, 128.3, 128.4, 128.6, 129.3, 136.4, 136.5, 141.6, 165.5; MS (ESI) m/z 388 (MH^+, 100%). HRMS (ESI) m/z 388.22696 ($C_{26}H_{30}NO_2$ [MH^+], 388.22711). *Benzyl* 5-*benzoy*-1-*cyclohexyl*-4-*ethylidene*-2-*phenylpyrrolidine*-3-*carboxylate* (**4f**). IR (film) 2930, 1735, 1669, 1212 and 1148 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 0.80–1.85 (10H, m), 2.61–2.66 (1H, m), 4.19 (1H, d, J=8.4 Hz), 4.28 (1H, d, J=12.0 Hz), 4.64 (1H, d, J=12.0 Hz), 5.45–5.49 (2H, m), 5.66 (1H, s), 7.04–7.06 (2H, m, Ar–H), 7.26–7.50 (11H, m, Ar–H), 8.09–8.11 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 15.3, 25.4, 25.7, 25.9, 30.7, 33.1, 52.6, 56.8, 66.3, 66.9, 122.1, 127.4, 127.7, 127.9, 128.2, 128.6, 128.8, 128.9, 132.9, 135.4, 136.3, 137.0, 139.6, 170.5, 204.0; MS (ESI) m/z 494 (MH^+, 100%), 442 (12), 285 (14) and 254 (24). HRMS (ESI) m/z 494.26825 ($C_{33}H_{36}NO_3$ [MH^+], 494.26897).

*4.3.8. Benzyl 2-benzyl-1-cyclohexyl-4-phenyl-1H-pyrrole-3-carboxylate (**5d**) and benzyl 5-benzoyl-4-benzylidene-1-cyclohexyl-2-phenylpyrrolidine-3-carboxylate (**4g**).* Prepared by *method A* from aziridine **6** and allene **3d**. Purification by preparative thin layer chromatography [ethyl acetate–hexane (1:10)] afforded **5d** as a yellow oil in 64% yield and **4g** as a yellow solid in 10% yield. *Benzyl* 2-*benzyl*-1-*cyclohexyl*-4-*phenyl*-1*H*-*pyrrole*-3-*carboxylate* (**5d**). IR (film) 2931, 1734, 1696, 1268 and 1149 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 0.84–1.77 (10H, m), 3.79–3.85 (1H, m), 4.44 (2H, s), 5.13 (2H, s), 6.64 (1H, s), 7.20–7.36 (15H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 25.2, 25.8, 31.0, 34.2, 55.4, 65.3, 110.5, 116.8, 126.0, 126.1, 127.5, 127.7, 127.9, 128.0, 128.2, 128.4, 128.5, 128.6, 129.0, 129.3, 129.5, 129.8, 131.8, 133.6, 136.3, 137.1, 139.2, 165.7; MS (ESI) m/z 450 (MH^+, 41%), 342 (7), 273 (27) and 233 (10). HRMS (ESI) m/z 450.24321 ($C_{31}H_{32}NO_2$ [MH^+], 450.24276). *Benzyl* 5-*benzoyl*-4-*benzylidene*-1-*cyclohexyl*-2-*phenylpyrrolidine*-3-*carboxylate* (**4g**). Mp 139.0–140.5 °C (from methanol). IR (film) 2930, 1733, 1675, 1267 and 1145 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 0.85–1.59 (8H, m), 1.80–1.90 (2H, m), 2.66–2.71 (1H, m), 3.86 (1H, d, J=12.4 Hz), 4.19 (1H, d, J=12.4 Hz), 4.66 (1H, d, J=8.8 Hz), 5.53 (1H, d, J=8.8 Hz), 5.81 (1H, s), 6.51 (1H, s), 6.77–6.79 (2H, m, Ar–H), 7.05–7.35 (13H, m, Ar–H), 7.49–7.60 (3H, m, Ar–H), 8.15–8.17 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 25.5, 25.9, 26.0, 31.1, 33.4, 53.5, 57.1, 66.4, 67.9, 126.7, 127.0, 127.6, 127.8, 127.9, 128.0, 128.1, 128.2, 128.5, 128.8, 128.9, 129.0, 133.2, 135.3, 136.3, 136.8, 137.2, 139.9, 169.4, 203.5; MS (ESI) m/z 556 (MH^+, 100%), 557 (45), 201 (17) and 195 (10). HRMS (ESI) m/z 556.28482 ($C_{38}H_{38}NO_3$ [MH^+], 556.28462).

*4.3.9. Benzyl 1-cyclohexyl-2-phenethyl-4-phenyl-1H-pyrrole-3-carboxylate (**5e**) and benzyl 5-benzoyl-1-cyclohexyl-4-phenethylidene-2-phenylpyrrolidine-3-carboxylate (**4h**).* Prepared by *method B* from aziridine **6** and allene **3e**. Purification by preparative thin layer chromatography [ethyl acetate–hexane (1:10)] afforded **5e** as a yellow oil in 26% yield and **4h** as a yellow oil in 23% yield. *Benzyl* 1-*cyclohexyl*-2-*phenethyl*-4-*phenyl*-1*H*-*pyrrole*-3-*carboxylate* (**5e**). IR (film) 2932, 1696, 1274 and 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 1.11–1.84 (10H, m), 2.90 (2H, t, J=7.6 Hz), 3.22 (2H, t, J=7.6 Hz), 3.59–3.65 (1H, m), 5.17 (2H, s), 6.57 (1H, s), 7.09–7.10 (2H, m, Ar–H), 7.23–7.36 (13H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 25.3, 25.9, 34.3, 36.7, 55.3, 65.3, 109.3, 116.4, 126.0, 126.1, 127.6, 127.9, 128.1, 128.3, 128.5, 128.6, 129.0, 129.4, 129.8, 131.8, 134.5, 136.3, 136.4, 139.2, 141.5, 165.4; MS (ESI) m/z 464 (MH^+, 75%), 303 (11), 287 (80) and 201 (11). HRMS (ESI) m/z 464.25909 ($C_{32}H_{34}NO_2$ [MH^+], 464.25845). *Benzyl* 5-*benzoyl*-1-*cyclohexyl*-4-*phenethylidene*-2-*phenylpyrrolidine*-3-*carboxylate* (**4h**). IR (film) 2929, 1735, 1670, 1211 and 1149 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 0.80–1.89 (10H, m), 2.63–2.68 (1H, m), 3.08 (1H, dd, J=8.0 Hz and 16 Hz), 3.14 (1H, dd, J=6.4 Hz and 16.0 Hz), 4.23 (1H, d, J=8.8 Hz), 4.27 (1H, d, J=12.4 Hz), 4.63 (1H, d, J=12.4 Hz), 5.46 (1H, d, J=8.8 Hz), 5.55 (1H, approx. t, J=7.0 Hz), 5.67 (1H, s), 6.78–6.80 (2H, m, Ar–H), 7.08–7.36 (16H, m, Ar–H), 8.09–8.11 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 25.5, 25.9, 26.0, 30.9, 33.2, 35.8, 52.8, 57.0, 66.6, 67.2, 126.0, 126.4, 127.7, 127.9, 128.1, 128.2, 128.3, 128.5, 128.6, 128.7, 128.8, 129.0, 133.0, 135.4, 136.6, 137.0, 139.6, 170.6, 207.1; MS (ESI) m/z 570 (MH^+, 100%), 518 (8), and 254 (4). HRMS (ESI) m/z 570.30053 ($C_{39}H_{40}NO_3$ [MH^+], 570.30027).

*4.3.10. Benzyl 2-benzyl-1-cyclohexyl-4-phenyl-1H-pyrrole-3-carboxylate (**5d**) and benzyl 5-benzoyl-4-benzylidene-1-cyclohexyl-2-phenylpyrrolidine-3-carboxylate (**8a**).* Prepared by *methods A or B* from aziridine **7** and allene **3d**. Purification by preparative thin layer chromatography [ethyl acetate–hexane (1:10)] afforded by *method B* **5d** as a yellow oil in 41% yield and **8a** as a yellow oil in 35% yield [*method A*: **5d** (53%) and **8a** (35%)]. Compound **5d** was identified by comparison with the specimen previous prepared (see above). *Benzyl* 5-*benzoyl*-4-*benzylidene*-1-*cyclohexyl*-2-*phenylpyrrolidine*-3-*carboxylate* (**8a**). IR (film) 2930, 1735, 1669, 1210 and 1147 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 0.86–1.90 (10H, m), 2.66–2.71 (1H, m), 3.88 (1H, d, J=12.0 Hz), 4.21 (1H, d, J=12.0 Hz), 4.69 (1H, d, J=9.2 Hz), 5.55 (1H, d, J=9.2 Hz), 6.53 (1H, s), 6.79–6.81 (2H, m, Ar–H), 7.09–7.53 (16H, m, Ar–H), 8.18–8.20 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 25.5, 25.9, 26.0, 31.1, 33.4, 53.5, 57.1, 66.4, 67.9, 126.8, 127.1, 127.6, 127.8, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.8, 128.9, 129.0, 133.2, 135.3, 136.3, 136.8, 137.3, 139.9, 169.4, 203.5; MS (ESI) m/z 556 (MH^+, 100%), 504 (6), 466 (8) and 254 (23). HRMS (ESI) m/z 556.28373 ($C_{38}H_{38}NO_3$ [MH^+], 556.28462).

*4.3.11. Benzyl 1-cyclohexyl-2-phenethyl-4-phenyl-1H-pyrrole-3-carboxylate (**5e**) and benzyl 5-benzoyl-1-cyclohexyl-4-phenethylidene-2-phenylpyrrolidine-3-carboxylate (**8b**).* Prepared by *method B* from aziridine **7** and allene **3e**. Purification by preparative thin layer chromatography [ethyl acetate–hexane (1:10)] afforded by *method B* **5e** as a yellow oil in 43% yield and **8b** as a yellow oil in 33% yield [*method A*: **5e** (75%)]. Compound **5e** was identified by comparison with the specimen previous prepared (see above). *Benzyl* 5-*benzoyl*-1-*cyclohexyl*-4-*phenethylidene*-2-*phenylpyrrolidine*-3-*carboxylate* (**8b**). IR (film) 2928, 1732, 1669, 1212 and 1143 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 0.82–1.88 (10H, m), 2.63–2.68 (1H, m), 3.06 (1H, dd, J=8.0 and 16.0 Hz), 3.14 (1H, dd, J=6.8 and 16 Hz), 4.24 (1H, d, J=8.8 Hz), 4.27 (1H, d, J=12.4 Hz), 4.63 (1H, d, J=12.4 Hz), 5.46 (1H, d, J=8.8 Hz), 5.55 (1H, approx. t, J=7.0 Hz), 5.67 (1H, s), 6.78–6.80 (2H, m, Ar–H), 7.09–7.36 (16H, m, Ar–H), 8.09–8.11 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 25.5, 25.9, 26.1, 30.9, 33.2, 35.8, 52.8, 57.0, 66.6, 67.2, 126.0, 126.4, 127.7, 127.9, 128.1, 128.2, 128.3, 128.5, 128.6, 128.7, 128.8, 129.0, 133.0, 135.4, 136.6, 137.0, 139.6, 170.6, 204.0; MS (ESI) m/z 570 (MH^+, 100%), 518 (10) and 254 (7). HRMS (ESI) m/z 570.30060 ($C_{39}H_{40}NO_3$ [MH^+], 570.30027).

*4.3.12. Benzyl 2,5-dibenzoyl-1-benzyl-4-methylenepyrrolidine-3-carboxylate (**15**) and benzyl 2,5-dibenzoyl-1-benzyl-4-methylenepyrrolidine-3-carboxylate (**16**).* Prepared by *methods A* or *B* from aziridine **14** (100 mg, 0.29 mmol) and allene **3a** (0.44 mmol). Compound **15** crystallized from the crude mixture of **15** and **16** as a white solid in 49% (method A) or 52% (method B; reaction time, 5.5 h) yield. The remaining mixture was purification by flash column chromatography [ethyl acetate–hexane (1:9)] affording **16** as a yellow oil in 12% (method A) or 4% (method B; reaction time, 5.5 h) yield. *Benzyl* 2,5-*dibenzoyl*-1-*benzyl*-4-*methylenepyrrolidine*-

3-*carboxylate* (**15**). Mp 117.0–118.0 °C (from methanol). IR (film) 3063, 1740, 1675, 1228 and 1151 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 3.63 (1H, d, *J*=12.8 Hz), 3.86 (1H, d, *J*=12.8 Hz), 4.28–4.30 (1H, m), 4.61 (1H, d, *J*=12.4 Hz), 4.85 (1H, d, *J*=12.4 Hz), 5.06 (1H, br s), 5.27 (1H, d, *J*=8.0 Hz), 5.30 (1H, br s), 5.48 (1H, s), 7.02–7.15 (7H, m, Ar–H), 7.22–7.24 (3H, m, Ar–H), 7.31–7.34 (2H, m, Ar–H), 7.42–7.46 (2H, m, Ar–H), 7.49–7.58 (2H, m, Ar–H), 7.65–7.67 (2H, m, Ar–H), 7.92–7.94 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 51.9, 53.4, 63.4, 66.9, 71.0, 111.6, 127.4, 128.1, 128.2, 128.3, 128.4, 128.5, 129.0, 129.3, 133.0, 133.1, 134.8, 136.4, 137.5, 142.8, 169.0, 199.5, 200.3; MS (ESI) *m*/*z* 516 (MH^+, 100%), 517 (35) and 518 (5). HRMS (ESI) *m*/*z* 516.21632 ($C_{34}H_{30}NO_4$ [MH^+], 516.21693); *Benzyl* 2,5-*dibenzoyl*-1-*benzyl*-4-*methylenepyrrolidine*-3-*carboxylate* (**16**). IR (film) 3063, 1737, 1686, 1228 and 1159 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 3.78–3.79 (1H, m), 3.85 (1H, d, *J*=12.4 Hz), 3.94 (1H, d, *J*=12.4 Hz), 5.04 (1H, br s), 5.15 (2H, s), 5.30 (1H, br s), 5.34 (1H, br s), 5.53 (1H, d, *J*=4.4 Hz), 7.15–7.39 (14H, m, Ar–H), 7.50–7.56 (2H, m, Ar–H), 7.84–7.90 (4H, m, Ar–H); MS (ESI) *m*/*z* 516 (MH^+, 100%), 201 (44), 233 (14) and 207 (15). HRMS (ESI) *m*/*z* 516.21749 ($C_{34}H_{30}NO_4$ [MH^+], 516.21693).

*4.3.13. 4-Benzyl 2-ethyl 1-benzyl-3-methylene-5-phenylpyrrolidine-2,4-dicarboxylate (**18a**).* Prepared by *method A* from aziridine **17** (100 mg, 0.36 mmol) and allene **3a** (0.43 mmol). Crystallization from methanol afforded **18a** as a yellow solid in 73% yield. Mp 84.0–86.0 °C (from methanol). IR (KBr) 3026, 1738, 1247 and 1152 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 1.24 (3H, t, *J*=7.2 Hz), 3.55 (1H, d, *J*=13.6 Hz), 3.81 (1H, d, *J*=13.6 Hz), 4.09 (1H, d, *J*=8.4 Hz), 4.13–4.18 (2H, m), 4.38 (1H, s), 4.43 (1H, d, *J*=12.4 Hz), 4.77 (1H, d, *J*=12.4 Hz), 4.94 (1H, d, *J*=8.4 Hz), 5.23 (1H, br s), 5.39 (1H, br s), 7.01–7.02 (2H, m, Ar–H), 7.29–7.32 (11H, m, Ar–H), 7.39–7.41 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 14.3, 51.6, 54.6, 60.6, 66.5, 66.7, 68.6, 112.1, 127.1, 128.0, 128.1, 128.2, 128.3, 128.4, 128.6, 135.4, 138.2, 138.3, 143.7, 170.7, 171.8; MS (ESI) *m*/*z* 456 (MH^+, 100%), 201 (17) and 195 (15). HRMS (ESI) *m*/*z* 456.21580 ($C_{29}H_{30}NO_4$ [MH^+], 456.21693).

*4.3.14. 4-Benzyl 2-ethyl 1-benzyl-3-ethylidene-5-phenylpyrrolidine-2,4-dicarboxylate (**18b**).* Prepared by *method A* from aziridine **17** (100 mg, 0.36 mmol) and allene **3b** (0.43 mmol). Purification by flash column chromatography [ethyl acetate–hexane (1:9)] afforded **18b** as a white solid in 50% yield. Mp 72.0–74.0 °C (from methanol). IR (film) 3031, 1733, 1256 and 1151 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 1.22 (3H, t, *J*=7.2 Hz), 1.52 (3H, d, *J*=6.8 Hz), 3.55 (1H, d, *J*=14.0 Hz), 3.86 (1H, d, *J*=14.0 Hz), 3.99 (1H, d, *J*=8.0 Hz), 4.14 (2H, q, *J*=7.2 Hz), 4.35 (1H, s), 4.40 (1H, d, *J*=12.0 Hz), 4.78 (1H, d, *J*=12.0 Hz), 5.04 (1H, d, *J*=8.0 Hz), 5.72 (1H, q, *J*=6.8 Hz), 7.02–7.03 (2H, m, Ar–H), 7.23–7.34 (11H, m, Ar–H), 7.48–7.50 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 14.3, 15.0, 51.1, 53.0, 60.3, 65.9, 66.5, 69.0, 122.0, 127.0, 128.0, 128.2, 128.3, 128.3, 128.4, 128.4, 135.6, 136.1, 138.2, 138.5, 170.8, 172.3; MS (ESI) *m*/*z* 470 (MH^+, 100%), 211 (12) and 201 (28). HRMS (ESI) *m*/*z* 470.23076 ($C_{30}H_{32}NO_4$ [MH^+], 470.23258).

*4.3.15. 4-Benzyl 2-ethyl 1-benzyl-3-(2,2-dimethylpropylidene)-5-phenylpyrrolidine-2,4-dicarboxylate (**18c**).* Prepared by *method A* from aziridine **17** (100 mg, 0.36 mmol) and allene **3c** (0.43 mmol). Crystallization from methanol afforded **18c** as a white solid in 71% yield. Mp 138.0–140.0 °C (from methanol). IR (KBr) 2952, 1724, 1257 and 1146 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 0.96 (9H, s), 1.21 (3H, t, *J*=7.2 Hz), 3.53 (1H, d, *J*=13.6 Hz), 3.88 (1H, d, *J*=13.6 Hz), 4.05–4.22 (3H, m), 4.34 (1H, d, *J*=12.0 Hz), 4.35 (1H, s), 4.81 (1H, d, *J*=12.0 Hz), 5.03 (1H, d, *J*=7.6 Hz), 5.62 (1H, s), 7.02–7.03 (2H, m, Ar–H), 7.22–7.34 (11H, m, Ar–H), 7.46–7.48 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 14.3, 29.8, 33.6, 50.8, 53.1, 60.1, 66.6, 67.1, 69.9, 127.0, 128.1, 128.3, 128.4, 128.5, 131.5, 135.4, 137.1, 138.3, 138.6, 171.6, 172.6; MS (ESI) *m*/*z* 512 (MH^+, 100%), 201 (76) and 195 (25). HRMS (ESI) *m*/*z* 512.27993 ($C_{33}H_{38}NO_4$ [MH^+], 512.27954).

*4.3.16. 4-Benzyl 2-ethyl 1-benzyl-3-benzylidene-5-phenylpyrrolidine-2,4-dicarboxylate (**18d**).* Prepared by *method A* from aziridine **17** (100 mg, 0.36 mmol) and allene **3d** (0.43 mmol). Crystallization from methanol afforded **18d** as a white solid in 48% yield. Mp 118.6–119.9 °C (from methanol). IR (KBr) 3031, 1730, 1257 and 1154 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 1.26 (3H, t, *J*=7.2 Hz), 3.59 (1H, d, *J*=13.6 Hz), 3.92 (1H, d, *J*=13.6 Hz), 4.14–4.21 (3H, m), 4.35 (1H, d, *J*=8.0 Hz), 4.54 (1H, s), 4.65 (1H, d, *J*=12.4 Hz), 5.13 (1H, d, *J*=8.0 Hz), 6.68 (1H, s), 6.93–6.95 (2H, m, Ar–H), 7.18–7.35 (16H, m, Ar–H), 7.49–7.51 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 14.4, 51.1, 54.1, 60.5, 66.5, 67.7, 69.8, 126.7, 127.1, 127.4, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 135.4, 136.1, 136.3, 138.0, 138.3, 170.1, 171.9; MS (ESI) *m*/*z* 532 (MH^+, 100%) and 201 (28). HRMS (ESI) *m*/*z* 532.24948 ($C_{35}H_{34}NO_4$ [MH^+], 532.24824).

*4.3.17. 4-Benzyl 2-ethyl 1-benzyl-3-phenethylidene-5-phenylpyrrolidine-2,4-dicarboxylate (**18e**).* Prepared by *method A* from aziridine **17** (100 mg, 0.36 mmol) and allene **3e** (0.43 mmol). Crystallization from methanol afforded **18e** as a white solid in 56% yield. Mp 94.3–95.2 °C (from methanol). IR (KBr) 2931, 1722, 1603, 1277 and 1159 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 1.17 (3H, t, *J*=7.2 Hz), 3.23 (2H, d, *J*=7.6 Hz), 3.59 (1H, d, *J*=14.0 Hz), 3.89 (1H, d, *J*=14.0 Hz), 4.08–4.14 (3H, m), 4.38 (1H, d, *J*=12.4 Hz), 4.41 (1H, s), 4.75 (1H, d, *J*=12.4 Hz), 5.09 (1H, d, *J*=8.0 Hz), 5.84 (1H, t, *J*=7.6 Hz)), 7.03–7.05 (4H, m, Ar–H), 7.20–7.33 (14H, m, Ar–H), 7.49–7.51 (2H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 14.3, 35.6, 51.0, 53.3, 60.4, 65.9, 66.6, 69.1, 125.9, 126.2, 127.1, 127.7, 127.9, 128.1, 128.3, 128.4, 128.7, 135.4, 136.4, 138.0, 138.4, 139.4, 170.8, 172.1; MS (ESI) *m*/*z* 546 (MH^+, 100%), 287 (3) and 201 (6). HRMS (ESI) *m*/*z* 546.26447 ($C_{36}H_{36}NO_4$ [MH^+], 546.26389.

*4.3.18. 4-Benzyl 2-ethyl 1-cyclohexyl-3-methylene-5-phenylpyrrolidine-2,4-dicarboxylate (**20**).* Prepared by *method A* from aziridine **19** (100 mg, 0.37 mmol) and allene **3a** (0.44 mmol). Crystallization from methanol afforded **20** as a white solid in 62% yield. Prepared by *method B* hating the toluene solution of aziridine **19** (100 mg, 0.37 mmol) and allene **3a** (0.44 mmol) for 3 h. Purification by flash column chromatography [ethyl acetate–hexane (1:8)] afforded **20** as a yellow oil in 40% yield. Mp 96.5–98.0 °C (from methanol). IR (KBr) 2930, 1745, 1237 and 1187 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 1.25 (3H, br s), 1.29 (3H, t, *J*=7.2 Hz), 1.45–1.48 (1H, m), 1.55–1.62 (3H, m), 1.78–1.86 (3H, m), 2.41–2.46 (1H, m), 4.21 (2H, q, *J*=7.2 Hz), 4.25–4.28 (1H, m), 4.54 (1H, d, *J*=12.0 Hz), 4.54 (1H, s), 4.76 (1H, d, *J*=12.0 Hz), 4.92 (1H, d, *J*=8.4 Hz), 5.42 (1H, br s), 5.50 (1H, br s), 7.12–7.13 (4H, m, Ar–H), 7.20–7.22 (3H, m, Ar–H), 7.29–7.31 (3H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 14.2, 25.0, 25.4, 25.8, 31.0, 32.5, 52.2, 57.5, 60.9, 66.2, 66.5, 68.1, 112.0, 127.5, 127.9, 128.1, 128.3, 128.4, 135.5, 139.7, 142.5, 169.3, 174.3; MS (ESI) *m*/*z* 448 (MH^+, 100%) and 274 (8). HRMS (ESI) *m*/*z* 448.24723 ($C_{28}H_{34}NO_4$ [MH^+], 448.24824).

4.4. General procedure for formal [3+2] cycloaddition of 2-benzoyl-1-*tert*-butyl-3-phenylaziridine (9) with allenes

A solution of aziridine **9** (100 mg, 0.36 mmol) and the appropriated buta-2,3-dienoate (0.54 mmol) in toluene (6 mL) was heated at 80 °C for 4 h. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography [ethyl acetate–hexane (1:9)].

*4.4.1. Benzyl 1-tert-butyl-2-methyl-4-phenyl-1H-pyrrole-3-carboxylate (**10a**).* Cycloadduct **10a** was obtained as a yellow oil in 65% yield. IR (film) 2980, 1696, 1209 and 1143 cm^{-1}; ^1H NMR ($CDCl_3$,

400 MHz) 1.64 (9H, s), 2.75 (3H, s), 5.12 (2H, s), 6.72 (1H, s), 7.00–7.02 (2H, m, Ar–H), 7.20–7.30 (8H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 14.7, 30.7, 57.0, 65.3, 112.4, 117.7, 124.3 125.9, 127.5, 127.7, 128.0, 128.2, 129.2, 136.4, 136.5, 166.1; MS (EI) *m*/*z* 347 (M^+, 24%), 256 (14), 201 (14), 200 (100) and 184 (16). HRMS (EI) *m*/*z* 347.1894 ($C_{23}H_{25}NO_2$ [M^+], 347.1885).

*4.4.2. Benzyl 1-tert-butyl-2-ethyl-4-phenyl-1H-pyrrole-3-carboxylate (**10b**).* Cycloadduct **10b** was obtained as a colourless oil in 38% yield. IR (film) 2980, 1696, 1210 and 1145 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) 1.28 (3H, t, *J*=7.2 Hz), 1.64 (9H, s), 3.17 (2H, q, *J*=7.2 Hz), 5.12 (2H, s), 6.66 (1H, s), 7.01–7.02 (2H, m, Ar–H), 7.20–7.36 (8H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) 15.5, 21.0, 26.1, 31.3, 57.1, 65.2, 67.2, 111.5, 117.6, 124.7, 125.9, 127.5, 127.6, 128.0, 128.2, 128.3, 128.4, 128.6, 129.3, 136.4, 136.6, 143.2, 165.5; MS (EI) *m*/*z* 361 (M^+, 25%), 214 (52), 196 (100) and 91 (41). HRMS (EI) *m*/*z* 361.2037 ($C_{24}H_{27}NO_2$ [M^+], 361.2042).

4.5. Crystal data

*4.5.1. Crystal data for 2-benzoyl-1-benzyl-3-phenylaziridine (**1**).* The X-ray data were collected on a Bruker Apex II single crystal diffractometer, using room temperature using Mo Kα radiation. The structures were solved by direct methods as implemented in SHELXS97 and refined by full-matrix least-squares using SHELXL97.[17] All the crystals available were ill-formed and showed signs of twinning. Examination of the structure with PLATON revealed a twin law that was used in the last refinements (the BASF parameter refined to 0.17).

$C_{22}H_{19}NO$, *M*=313.38, triclinic, *P*-1 with unit cell, *a*=5.7129 (10) Å, *b*=10.7002(17) Å, *c*=14.740(2) Å, α=88.373(12)°, β=77.814 (13)°, γ=74.337(12)°, *V*=847.6(2) Å^3. It contains two molecules/unit cell. ρ_{calcd}=1.228 g cm^{-3}, *Z*=2, μ=0.075 mm^{-1}. *R* (*I*>2σ(*I*))=0.1228 and R_w=0.3693 for 3226 independent reflections. H atoms were placed at calculated positions and refined as riding on their parent atoms.

*4.5.2. Crystal data for benzyl 5-benzoyl-1-benzyl-4-benzylidene-2-phenylpyrrolidine-3-carboxylate (**4d**).* The X-ray data were collected on a Bruker Apex II single crystal diffractometer, using room temperature using Mo Kα radiation. The structures were solved by direct methods as implemented in SHELXS97 and refined by full-matrix least-squares using SHELXL97.[18] Examination of the structure with PLATON revealed voids capable of containing solvent molecules. Such molecules could not be modelled and the SQUEEZE function was used to account for the extra charge density.

$C_{39}H_{33}NO_3$, *M*=563.66, monoclinic, *P*21/*c* with unit cell, *a*=11.2176(4) Å, *b*=15.7551(6) Å, *c*=19.3159(7) Å, β=99.281(2)°, *V*=3369.1(2) Å^3. It contains four molecules/unit cell. ρ_{calcd}=1.111 g cm^{-3}, *Z*=4, μ=0.070 mm^{-1}. *R* (*I*>2σ(*I*))=0.0477 and R_w=0.1418 for 6657 independent reflections. H atoms were placed at calculated positions and refined as riding on their parent atoms.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.09.081.

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