Synthesis F. M. Ribeiro Laia, T. M. V. D. Pinho e Melo Special Topic

Synthesis and Reactivity of Aziridines with Internal Dipolarophiles: An Approach to 1,4-Dihydrochromeno[4,3-*b*]pyrroles and 3-Methylenechromano[4,3-*b*]pyrroles

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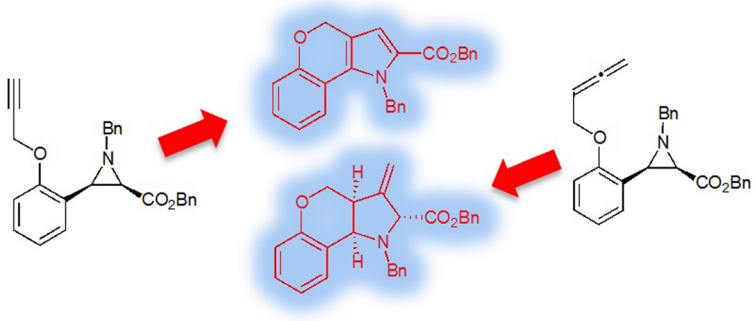

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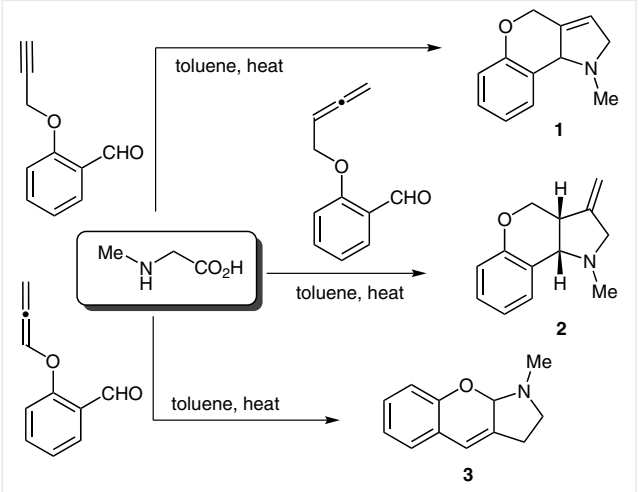
Abstract Aziridines derived from 2-(prop-2-yn-1-yloxy)- and 2-(buta-2,3-dien-1-yloxy)chalcones and from benzyl 2-(prop-2-yn-1-yloxy)- and 2-(buta-2,3-dien-1-yloxy)phenylacrylates were prepared in a stereoselective fashion. Their reactivity as azomethine ylide precursors was examined, leading to the synthesis of 1,4-dihydrochromeno[4,3-*b*]pyrrole and 3-methylenechromano[4,3-*b*]pyrrole derivatives through intramolecular 1,3-dipolar cycloaddition reactions.

Key words polycycles, heterocycles, allenes, alkynes, cycloadditions, ylides, pyrroles, chromenes

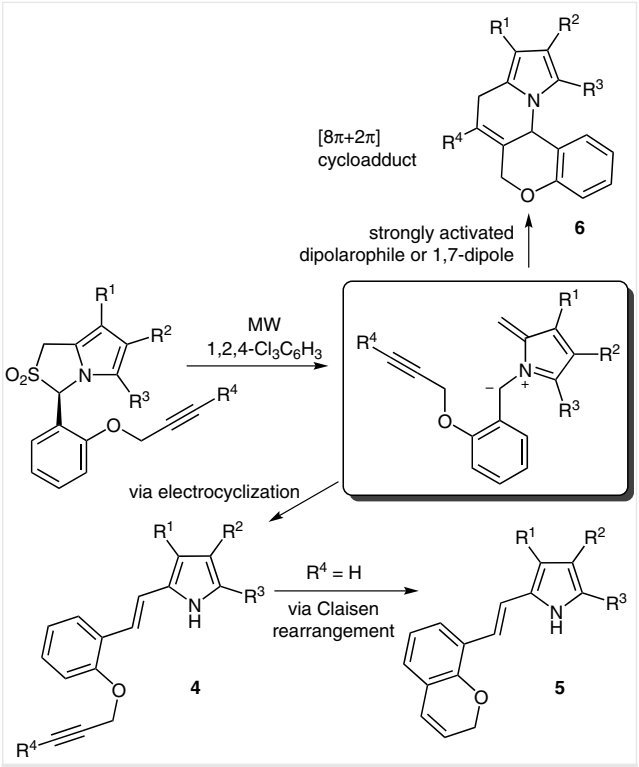
The chromene moiety is present in a variety of naturally occurring compounds, many of which exhibit interesting biological activities.[1–3] Chromene-based derivatives have been reported to show a broad spectrum of pharmacological activities, including anticancer, antimicrobial, and antihypertensive activities, making them important target molecules in medicinal chemistry.

We recently reported the reactivities of sarcosine and 1,3-thiazolidine-4-carboxylic acid toward salicylaldehyde-derived alkynes and allenes, which gave access to chromeno[4,3-*b*]pyrrole and chromeno[2,3-*b*]pyrrole derivatives (for example, compounds **1**–**3**; Scheme 1). Decarboxylative condensation of these secondary amino acids with 2-(prop-2-yn-1-yloxy)benzaldehyde gave tetrahydrochromeno[4,3-*b*]pyrroles through intramolecular 1,3-dipolar cycloaddition, whereas chromeno[2,3-*b*]pyrroles were obtained from the reaction with 2-(propa-1,2-dien-1-yloxy)benzaldehyde. On the other hand, sarcosine reacted with 2-(buta-2,3-dien-1-yloxy)benzaldehyde to give the corresponding 3-methylenechromano[4,3-*b*]pyrrole **2** (Scheme 1).[4]



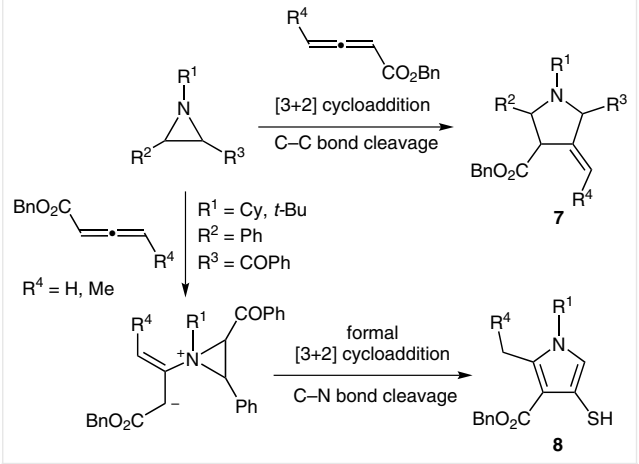
Scheme 1 Synthesis of chromeno[4,3-*b*]pyrrole and chromeno[2,3-*b*]pyrrole derivatives from sarcosine and salicylaldehyde-derived alkynes or allenes

In continuation of our interest in the chemistry of chromenes, we reported the synthesis of chromene derivatives by pericyclic reactions of azafulvenium methides bearing internal dipolarophiles (Scheme 2).[5] Azafulvenium methides bearing the (prop-2-yn-1-yloxy)phenyl substituent were converted into 2-[2-(2*H*-chromen-8-yl)vinyl]-1*H*-pyrroles **5** through a sequence of rearrangements. These reactive intermediates, which contain a more activated dipolarophile as well as the more activated 5-(trifluoromethyl)azafulvenium methide, participate in [8π+2π] cycloadditions to give 8,12a-dihydro-6*H*-chromeno[4,3-*e*]indolizines **6**. A synthesis of chiral 3-(2*H*-chromen-8-yl)-1*H*,3*H*-pyrrolo[1,2-*c*]thiazoles by microwave-induced rearrangement of 3-[2-(prop-2-yn-1-yloxy)phenyl]-1*H*,3*H*-pyrrolo[1,2-*c*]thiazoles was also described.



Scheme 2 Synthesis of chromene derivatives by pericyclic reactions of azafulvenium methides

We surmised that the thermolysis of aziridines bearing prop-2-yn-1-yloxyphenyl or buta-2,3-dien-1-yloxyphenyl substituents might permit the synthesis of chromeno[4,3-*b*]pyrroles with unusual substitution patterns. We recently described the reactivity of buta-2,3-dienoates toward aziridines (Scheme 3).[6] We observed that allenoates can react as the 2π-component in a [3+2] cycloaddition with azomethine ylides generated from aziridines to give the corresponding methylenepyrrolidines **7**, but they can also react by formal [3+2] cycloadditions to give functionalized pyrroles **8**. The substitution pattern of the aziridine determines the outcome of the reaction. In contrast with the reactivity observed in toluene as a solvent, carrying out the reaction in supercritical carbon dioxide resulted in formal [3+2] cycloaddition becoming the preferred pathway.[6c]

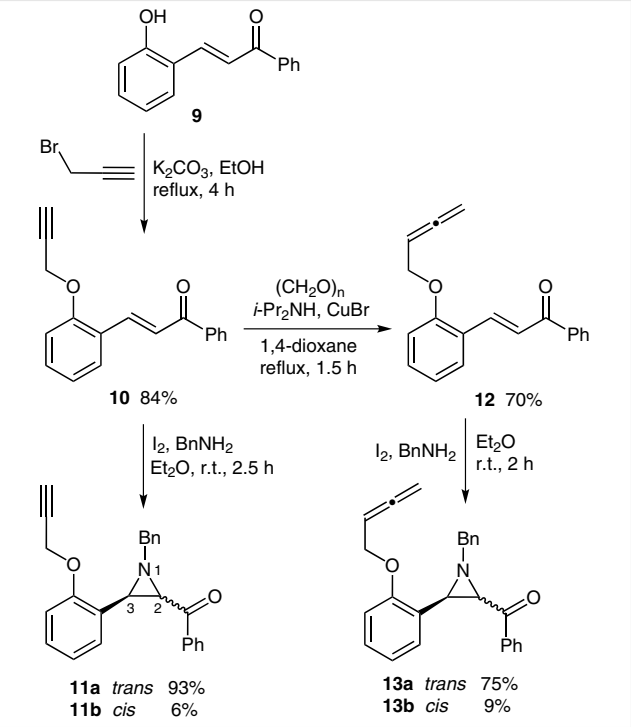


Scheme 3 Cycloadditions of aziridines with allenoates to give methylenepyrrolidines and pyrroles

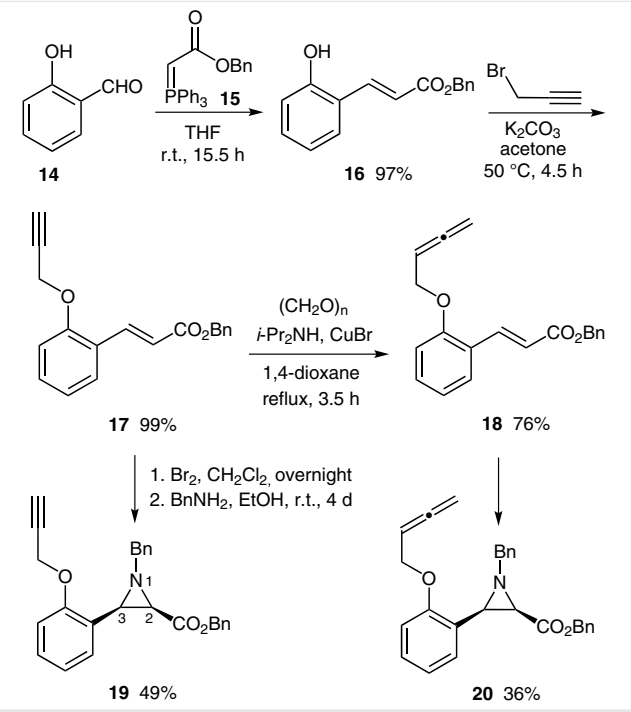
Intramolecular cycloadditions of azomethine ylides generated from aziridines containing double and triple C–C bonds are known.[7] However, the importance of chromene derivatives justifies further exploration of the chemistry of salicylaldehyde-derived aziridines with the aim of achieving greater structural diversity. In this context, we describe thermal reactions of aziridines bearing terminal alkyne and allene groups to give chromeno[4,3-*b*]pyrrole derivatives, including 3-methylenechromano[4,3-*b*]pyrroles.

The synthesis of the target aziridines is outlined in Schemes 4 and 5. (2*E*)-1-Phenyl-3-[2-(prop-2-yn-1-yloxy)phenyl]prop-2-en-1-one (**10**) was obtained from the reaction of (2*E*)-3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one (**9**) with propargyl bromide in refluxing ethanol in the presence of potassium carbonate (Scheme 4). Treatment of enone **10** with iodine and benzylamine, following a known general procedure,[8] gave *trans*-aziridine **11a** as the major product (93%), together with the corresponding *cis*-isomer **11b**, isolated in 6% yield. In the NOESY spectrum of aziridine **11a**, no connectivity was observed between protons H-2 and H-3, whereas the NOESY spectrum of aziridine **11b** showed cross-peaks between protons H-2 and H-3, confirming the assignment of their stereochemistry. Chalcone **10** was converted into (2*E*)-3-[2-(buta-2,3-dien-1-yloxy)phenyl]-1-phenylprop-2-en-1-one (**12**) by Crabbé homologation.[9] The product was subsequently treated with iodine and benzylamine to give aziridines **13** in good overall yield. The synthesis of the aziridine-2-carboxylates **19** and **20** required the initial preparation of benzyl (2*E*)-3-(2-hydroxyphenyl)acrylate (**16**) through Wittig reaction of phosphorus ylide **15** and salicylaldehyde (**14**). Compound **16** reacted with propargyl bromide in acetone at 50 °C in the presence of a base to give the functionalized acrylate **17** in 99% yield. Attempts to obtain the corresponding aziridine by treating acrylate **17** with iodine and benzylamine were unsuccessful. However, bromination of alkene **17** with dibromine followed by treatment with benzylamine gave the *cis*-aziridine **19** in moderate yield.[10] The NOESY spectrum of aziridine **19** corroborated the assignment of its stereochemistry. Allene **18** was obtained from alkyne **17** in 76% yield by the Crabbé reaction,[9] and was then converted into *cis*-aziridine **20** by successive reactions with dibromine and benzylamine.[10]

Initially, we examined the thermal reactivity of aziridine **11a** (Table 1). The reaction was performed in *tert*-butyl alcohol in the absence or presence of potassium *tert*-butoxide. The latter reaction conditions permitted the in situ



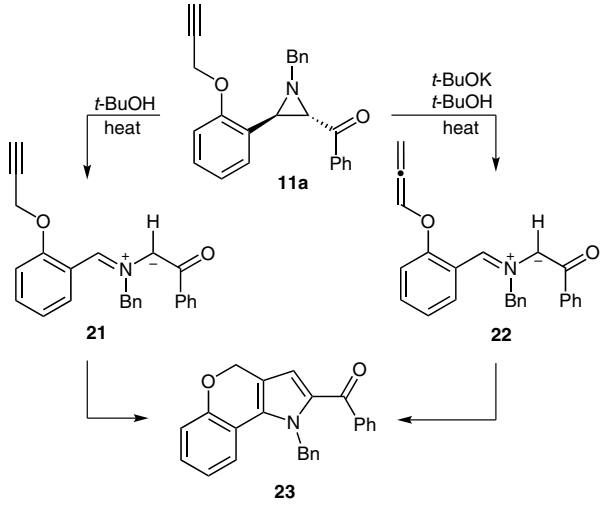
Scheme 4 Synthesis of functionalized aziridines **11** and **13**



Scheme 5 Synthesis of functionalized aziridines **19** and **20**

generation of an allene moiety through isomerization of the propargyl group. The optimized synthetic procedure for the thermolysis in the presence of potassium *tert*-butoxide allowed the synthesis of 1,4-dihydrochromeno[4,3-*b*]pyrrole **23** in 54% yield (Table 1, entry 4). Heterocycle **23** was obtained on carrying out the reaction of aziridine **11a** in the absence of potassium *tert*-butoxide (entries 6–8). A more efficient process was obtained by heating aziridine **11a** in refluxing *tert*-butyl alcohol for 27 hours, giving the target compound in 64% yield (entry 8). When the reaction was carried out in refluxing toluene for 27 hours or under microwave irradiation (toluene, 150 °C, 15 min), 1,4-dihydrochromeno[4,3-*b*]pyrrole **23** was obtained in modest yield (29%).

Table 1 Synthesis of 1,4-Dihydrochromeno[4,3-*b*]pyrrole **23** from Aziridine **11a** in *tert*-Butyl Alcohol



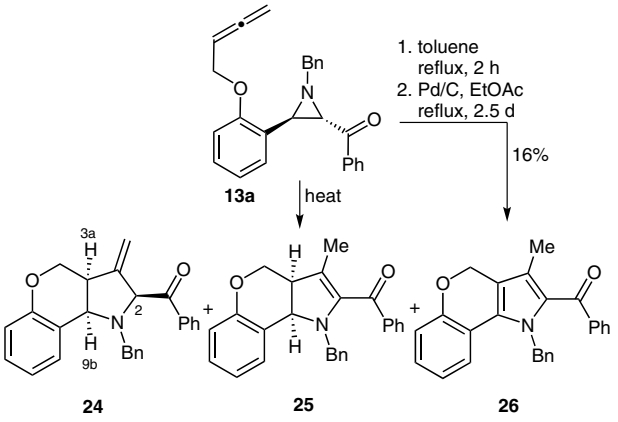
Entry	*t*-BuOK (equiv)	Temp (°C)	Time	Yield[a] (%)
1	0.5	60	27 h	42
2	0.5	reflux	5 h	38
3	0.5	80 (MW)	20 min	26
4	1.0	60	47 h	54
5	2.0	60	24 h	36
6	–	reflux	3.5 h	32
7	–	reflux	5 h	32
8	–	reflux	27 h	64

[a] Isolated yield.

These results indicated that both the in situ generated allene and the carbon–carbon triple bond can act as dipolarophiles in the cycloaddition of the azomethine ylide generated by conrotatory electrocyclic ring opening of aziridine **11a** to give 1,4-dihydrochromeno[4,3-*b*]pyrrole **23** after aromatization of the five-membered ring.

The reactivity of aziridine **13a**, which contains both an aziridine ring and an allenic moiety, was also studied (Table 2). When the reaction was performed in refluxing *tert*-butyl alcohol for four hours, no products could be isolated (Table 2, entry 1). However, on carrying out the reaction in refluxing toluene for three hours, three products were obtained: cycloadduct **24** (22% yield) and a 52:48 mixture of the corresponding tautomeric derivative **25** and 1,4-dihydrochromeno[4,3-*b*]pyrrole **26** in 14% overall yield (entry 2). With a longer reaction time, this mixture was obtained in 40% yield (entry 3). Derivatives **24**, **25**, and **26** were also obtained by microwave irradiation at 150 °C for 15 minutes (entry 4). The assignment of the stereochemistry of compound **24** was supported by its NOESY spectrum (400 MHz), in which cross-peaks were observed between protons H-3a and H-9b. The reaction of aziridine **13a** in refluxing toluene for two hours with subsequent oxidation by using palladium/carbon in refluxing ethyl acetate for 2.5 days gave cycloadduct **26** in 16% overall yield.

Table 2 Synthesis of Compounds **24**–**26** from Aziridine **13a**

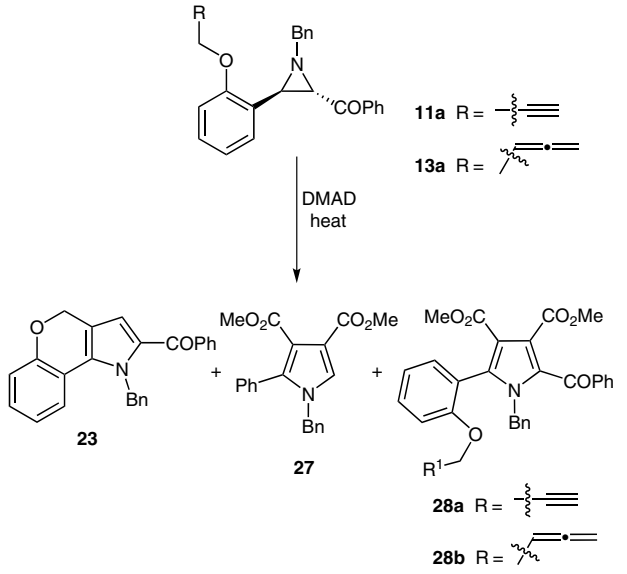


Entry	Solvent	Temp	Time	Yield[a] (%)	
				24	**25** + **26**[b]
1	*t*-BuOH	reflux	4 h	–	–
2	toluene	reflux	3 h	22	14 (52:48)[c]
3	toluene	reflux	21 h	–	40 (55:45)[c]
4	toluene	150 °C (MW)	15 min	<4	18 (43:57)[c]

[a] Isolated yield.
[b] Obtained together with **12**, formed by elimination of $BnNH_2$ from aziridine **13a** in variable amounts.
[c] Ratio determined by ^1H NMR spectroscopy.

To evaluate the efficiency of the generation of the azomethine ylides under the studied reaction conditions, we carried out the thermal reactions of aziridines **11a** and **13a** in the presence of dimethyl acetylenedicarboxylate. On performing the reaction of **11a** in refluxing *tert*-butyl alcohol for 23 hours, we obtained the three products **23**, **27**, and **28a** in 80% overall yield (Table 3, entry 1). Pyrrole **28a** and 1,4-dihydrochromeno[4,3-*b*]pyrrole **23**, resulting from the inter- and intramolecular 1,3-dipolar cycloaddition, respectively, were each obtained in 38% yield, and pyrrole **27** was also isolated in a low yield. Similar results were obtained when the reaction was carried out in refluxing toluene (entry 2). In the case of aziridine **13a**, dimethyl acetylenedicarboxylate efficiently trapped the azomethine ylide, giving pyrrole **28b** in 74% yield together with pyrrole **27** in 10% yield (entry 3). Pyrrole **27** was also obtained in low yield by sealed-tube thermolysis of pyrrole **28b** (240 °C, 4 h), indicating that it is derived from compounds **28a** and **28b**.

Table 3 Thermolysis of Aziridines **11a** and **13a** in the Presence of Dimethyl Acetylenedicarboxylate[a]

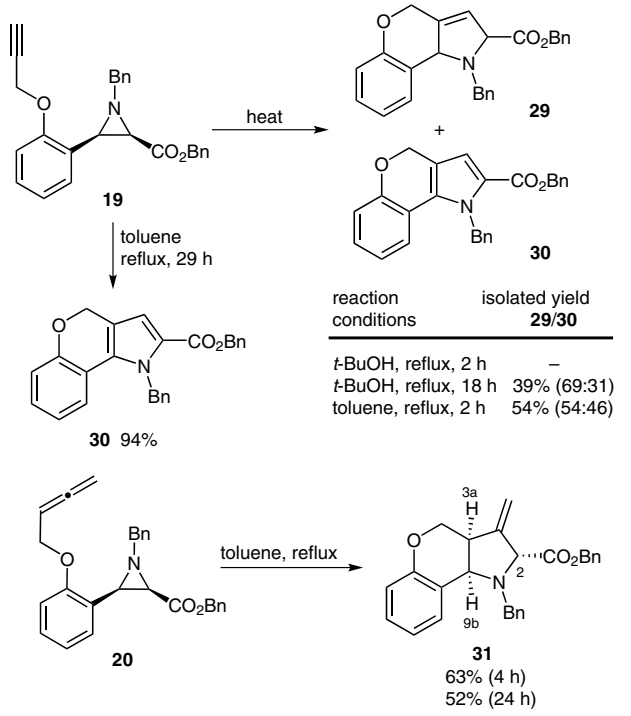


Entry	Aziridine	Solvent	Yield[b] (%)		
			23	**27**	**28**
1	**11a**	*t*-BuOH	38	4	38 (**28a**)
2	**11a**	toluene	24	7	30 (**28a**)
3	**13a**	*t*-BuOH	–	10	74 (**28b**)

[a] Reaction conditions: reflux, 23 h.
[b] Isolated yield.

These results indicate that the terminal alkyne of aziridine **11a** is a more activated dipolarophile than the allenic group of aziridine **13a**. On the other hand, a more activated dipole might ensure more-efficient synthesis of the chromene derivatives. With this in mind, we extended our study to other aziridines in which a carboxylate group replaced the benzoyl group (Scheme 6). Thermolysis of aziridine **19** in refluxing *tert*-butyl alcohol for two hours did not lead to any products. However, on increasing the reaction time to 18 hours, we obtained a 69:31 mixture of compounds **29** and **30** in 39% overall yield. The yield was improved by performing the reaction in refluxing toluene for

two hours. Interestingly, when we carried out the thermolysis of aziridine **19** in refluxing toluene for 29 hours, we obtained the 1,4-dihydrochromeno[4,3-*b*]pyrrole **30** in high yield (94%).



Scheme 6 Synthesis of chromeno[4,3-*b*]pyrrole derivatives from aziridines **19** and **20** by intramolecular 1,3-dipolar cycloaddition

Finally, we studied the reactivity of the *cis*-1-benzyl-3-(buta-2,3-dien-1-yloxyphenyl)aziridine **20**. On carrying out the reaction in toluene at reflux for four hours, we obtained the 3-methylenechromano[4,3-*b*]pyrrole **31** stereoselectively in 63% yield. With a longer reaction time, a decrease in the isolated yield was observed (52%). In the NOESY spectrum of compound **31**, connectivity was observed between protons H-9b and H-3a.

In conclusion, salicylaldehyde-derived aziridines bearing terminal alkyne and allene groups were prepared, and their thermal reactivity was explored. On thermolysis, the azomethine ylides generated from the aziridines by conrotatory electrocyclic ring opening participated in intramolecular cycloadditions to give chromeno[4,3-*b*]pyrrole derivatives. Aziridine-2-carboxylates gave higher yields of the target heterocycles than did the corresponding 2-benzoylaziridines. On the other hand, the carbon–carbon triple bond proved to be a more activated dipolarophile, leading to the corresponding 1,4-dihydrochromeno[4,3-*b*]pyrroles after aromatization of the initially formed cycloadducts. Aziridines bearing terminal allenes allowed the stereoselective synthesis of 3-methylenechromano[4,3-*b*]pyrrole derivatives.

Flash column chromatography was performed on silica gel 60 as the stationary phase. ^{1}H NMR spectra were recorded on a Bruker Avance III instrument operated at 400 MHz. ^{13}C NMR spectra were recorded on the same instrument operated at 100 MHz. Chemical shifts are expressed in ppm relatively to internal TMS. IR spectra were recorded on a Nicolet 6700 Fourier-transform spectrophotometer. HRMS spectra were obtained by electron impact (EI) or electrospray (ESI) methods using a Waters Micromass Autospec M (EI) and on a Bruker FTMS APEXIII (ESI) ToF mass spectrometer. Melting points were determined in open glass capillaries. Ylide **15** was prepared according to a reported procedure.[11]

Benzyl (2*E*)-3-(2-Hydroxyphenyl)acrylate (16)

Salicylaldehyde (**14**; 1.56 mL, 14.62 mmol) was added to a solution of ylide **15** (6.0 g, 14.62 mmol) in THF (100 mL), and the mixture was stirred at r.t. for 15.5 h. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography [silica gel, EtOAc–hexane (1:3 then 1:2)] to give a white solid; yield: 3.603 g (97%); mp 86.1–88.0 °C (EtOAc–hexane).

IR (KBr): 3213, 1674, 1628, 1448, 1379, 1300, 1277, 1174 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.28 (s, 2 H), 6.72 (d, ^3J = 16.0 Hz, 1 H), 6.78–6.80 (m, 1 H, Ar-H), 6.86–6.90 (m, 1 H, Ar-H), 7.13 (br s, 1 H), 7.18–7.22 (m, 1 H, Ar-H), 7.33–7.45 (m, 6 H, Ar-H), 8.11 (d, ^3J = 16.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 66.6, 116.5, 117.8, 120.6, 121.6, 128.3, 128.3, 128.7, 129.4, 131.6, 136.0, 141.7, 155.8, 168.7.

HRMS (EI): *m/z* [M$^+$] calcd for $C_{16}H_{14}O_3$: 254.0943; found: 254.0944.

(2*E*)-1-Phenyl-3-[2-(prop-2-yn-1-yloxy)phenyl]prop-2-en-1-one (10)

Anhydrous K_2CO_3 (1.356 g, 9.81 mmol) was added to a solution of enone **9** (2.0 g, 8.92 mmol) in EtOH (20 mL), and the mixture was stirred for 5 min at r.t. An 80% solution of propargyl bromide in toluene (1.46 mL, 13.54 mmol) was added and the mixture was refluxed for 4 h under N_2, then cooled to r.t. H_2O (100 mL) was added to the mixture and the aqueous layer was extracted with CH_2Cl_2 (3 × 80 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash chromatography [silica gel, EtOAc–hexane (1:4)] gave a yellow solid; yield: 1.968 g (84%); mp 63.0–64.6 °C (EtOAc–hexane).

IR (KBr): 3249, 2116, 1655, 1601, 1570, 1277, 1217, 1020 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.55 (t, ^4J = 2.2 Hz, 1 H), 4.79 (d, ^4J = 2.2 Hz, 2 H), 7.02–7.06 (m, 2 H, Ar-H), 7.35–7.40 (m, 1 H, Ar-H), 7.47–7.51 (m, 2 H, Ar-H), 7.55–7.58 (m, 1 H, Ar-H), 7.64–7.65 (m, 1 H, Ar-H), 7.66 (d, ^3J = 16.0 Hz, 1 H), 8.02–8.04 (m, 2 H, Ar-H), 8.09 (d, ^3J = 16.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.3, 76.0, 78.2, 112.8, 121.7, 123.4, 124.6, 128.5, 128.6, 129.5, 131.5, 132.6, 138.4, 140.0, 156.7, 191.0.

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{18}H_{14}O_2$: 262.0994; found: 262.0990.

Benzyl (2*E*)-3-[2-(Prop-2-yn-1-yloxy)phenyl]acrylate (17)

Anhydrous K_2CO_3 (1.584 g, 11.46 mmol) was added to a solution of acrylate **16** (2.650 g, 10.42 mmol) in acetone (25 mL), and the mixture was stirred for 5 min at r.t. An 80% soln of propargyl bromide in toluene (1.23 mL, 11.46 mmol) was added, and the mixture was heated at 50 °C for 4.5 h under N_2 then cooled to r.t. H_2O (120 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash chromatography [silica gel, EtOAc–hexane (1:4)] gave a white solid; yield: 3.025 g (99%); mp 37.5–39.2 °C (EtOAc–hexane).

IR (KBr): 3224, 2114, 1705, 1628, 1308, 1275, 1219, 1167 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.54 (t, ^4J = 2.4 Hz, 1 H), 4.77 (d, ^4J = 2.4 Hz, 2 H), 5.28 (s, 2 H), 6.60 (d, ^3J = 16.2 Hz, 1 H), 7.00–7.07 (m, 2 H, Ar-H), 7.33–7.46 (m, 6 H, Ar-H), 7.54 (dd, ^3J = 7.8 Hz, ^4J = 1.4 Hz, 1 H, Ar-H), 8.09 (d, ^3J = 16.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.1, 66.2, 76.1, 78.2, 112.8, 118.8, 121.7, 124.0, 128.2, 128.3, 128.6, 129.0, 131.4, 136.3, 140.3, 156.3, 167.2.

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{19}H_{16}O_3$: 292.1099; found: 292.1088.

Allenes 12 and 18; General Procedure

Allenes **12** and **18** were prepared according to a reported procedure.[9] A mixture of the appropriated alkyne, paraformaldehyde, *i*-Pr_2NH, and anhydrous CuBr in 1,4-dioxane was refluxed for the appropriate time then cooled to r.t. The mixture was then filtered and the precipitate was washed with Et_2O (25 mL). The organic phases were combined and concentrated under reduce pressure to give a gum-like residue that was treated with 1 M aq HCl to adjust its pH to 2–3. The mixture was extracted with Et_2O (3 × 30 mL) and the ether extracts were combined, washed to neutrality with H_2O (2 × 50 mL), and then washed with sat. brine (2 × 50 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to give a crude product that was purified by flash column chromatography [silica gel; EtOAc–hexane].

(2*E*)-3-[2-(Buta-2,3-dien-1-yloxy)phenyl]-1-phenylprop-2-en-1-one (12)

Prepared from alkyne **10** (2.004 g, 7.64 mmol), paraformaldehyde (0.574 g, 19.10 mmol), *i*-Pr_2NH (2.14 mL, 15.28 mmol), and anhyd CuBr (0.548 g, 3.82 mmol) in 1,4-dioxane (12 mL). The mixture was stirred for 1.5 h, and the crude product was purified by flash column chromatography [silica gel; EtOAc–hexane (1:4)] to give a yellow oil; yield: 1.486 g (70%).

IR (film): 3062, 1957, 1660, 1600, 1213, 1017 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.66–4.68 (m, 2 H), 4.86–4.89 (m, 2 H), 5.41–5.47 (m, 1 H), 6.95 (d, ^3J = 8.4 Hz, 1 H, Ar-H), 6.98–7.02 (m, 1 H, Ar-H), 7.33–7.37 (m, 1 H, Ar-H), 7.47–7.51 (m, 2 H, Ar-H), 7.55–7.59 (m, 1 H, Ar-H), 7.62–7.69 (m, 2 H), 8.01–8.03 (m, 2 H, Ar-H), 8.11 (d, ^3J = 15.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 66.3, 76.9, 86.9, 112.8, 121.1, 123.2, 124.4, 128.5, 129.5, 131.6, 132.5, 138.6, 140.5, 157.7, 191.2, 209.5.

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{19}H_{16}O_2$: 276.1150; found: 276.1155.

Benzyl (2*E*)-3-[2-(Buta-2,3-dien-1-yloxy)phenyl]acrylate (18)

Prepared from alkyne **17** (1.165 g, 3.99 mmol), paraformaldehyde (0.299 g, 9.96 mmol), *i*-Pr_2NH (1.12 mL, 7.98 mmol), and anhyd CuBr (0.287 g, 2.0 mmol) in 1,4-dioxane (15 mL) according to the general procure. The mixture was stirred for 3.5 h, and the crude product was purified by flash column chromatography [silica gel, EtOAc–hexane (1:4)] to give a yellow oil; yield: 0.929 g (76%).

IR (film): 1957, 1711, 1161 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.61–4.64 (m, 2 H), 4.85–4.88 (m, 2 H), 5.25 (s, 2 H), 5.36–5.42 (m, 1 H), 6.60 (d, ^3J = 16.4 Hz, 1 H), 6.89–6.97 (m, 2 H, Ar-H), 7.29–7.43 (m, 6 H, Ar-H), 7.48–7.51 (m, 1 H, Ar-H), 8.05 (d, ^3J = 16.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 66.1, 66.2, 77.0, 86.9, 112.7, 118.5, 121.0, 123.8, 128.2, 128.3, 128.6, 129.1, 131.4, 136.3, 140.7, 157.2, 167.4, 209.4.

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{20}H_{18}O_3$: 306.1256; found: 306.1254.

Aziridines 11, 13, 19, and 20; General Procedures

Method A: A solution of $BnNH_2$ (4.7 equiv) in Et_2O was slowly added to a solution of I_2 (1.1 equiv) and the appropriate chalcone in Et_2O, and the mixture was stirred at r.t. for the appropriate time. When the reaction was complete (TLC), the mixture was filtered and the solution was washed several times with H_2O. The organic layer was dried (Na_2SO_4) and the solvent was evaporated. The crude product was purified by flash column chromatography [silica gel, EtOAc–hexane (1:4)].

Method B: Br_2 was added dropwise to a solution of the appropriated alkene in CH_2Cl_2 at 0 °C. The mixture was stirred overnight at r.t., and 40% aq $NaHSO_3$ solution was added. The organic phase was separated and dried (Na_2SO_4), and the solvent was evaporated. The resulting dibromide was dissolved in EtOH (5 mL/mmol), $BnNH_2$ (4.0 equiv) was added, and mixture was stirred at r.t. for 4 d. When the reaction was complete (TLC), H_2O (10–15 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by flash column chromatography [silica gel, EtOAc–hexane (1:4)].

{*trans*-1-Benzyl-3-[2-(prop-2-yn-1-yloxy)phenyl]aziridin-2-yl}(phenyl)methanone (11a) and {*cis*-1-Benzyl-3-[2-(prop-2-yn-1-yloxy)phenyl]aziridin-2-yl}(phenyl)methanone (11b)

Prepared by Method A from I_2 (1.426 g, 5.62 mmol) and chalcone **10** (1.340 g, 5.11 mmol) in Et_2O (30 mL) and $BnNH_2$ (2.62 mL, 24.02 mmol) in Et_2O (4 mL). The mixture was stirred for 2.5 h and the product was purified by flash chromatography [silica gel, EtOAc–hexane (1:4)] to give, in order of elution, compound **11a** [yield: 1.747 g (93%)] as a yellow oil and compound **11b** [yield: 0.120 g (6%)] as a white solid.

11a

IR (film): 3292, 2121, 1668, 1493, 1452, 1228, 1024 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.40 (br s, 1 H), 3.57 (d, ^3J = 2.0 Hz, 1 H), 3.92 (d, ^3J = 2.0 Hz, 1 H), 4.04 (d, ^2J = 13.6 Hz, 1 H), 4.18 (d, ^2J = 13.6 Hz, 1 H), 4.65 (d, ^4J = 1.6 Hz, 2 H), 6.95–6.97 (m, 2 H, Ar-H), 7.14–7.23 (m, 4 H, Ar-H), 7.34–7.41 (m, 5 H, Ar-H), 7.48–7.52 (m, 1 H, Ar-H), 7.91–7.92 (m, 2 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.1, 46.9, 55.1, 56.2, 75.6, 78.7, 112.1, 121.6, 126.9, 127.1, 127.9, 128.2, 128.3, 128.4, 128.5, 128.5, 133.1, 138.4, 139.4, 156.1, 195.3.

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{25}H_{21}NO_2$: 367.1572; found: 367.1575.

11b

Mp 102.7–103.8 °C (EtOH).

IR (KBr): 3282, 2129, 1680, 1450, 1242, 1230 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.45 (t, ^4J = 2.4 Hz, 1 H), 3.46 (d, ^3J = 7.2 Hz, 1 H), 3.59 (d, ^3J = 7.2 Hz, 1 H), 3.75 (d, ^2J = 13.6 Hz, 1 H), 4.03 (d, ^2J = 13.6 Hz, 1 H), 4.48 (dd, ^2J = 15.6 Hz, ^4J = 2.4 Hz, 1 H), 4.57 (dd, ^2J = 15.6 Hz, ^4J = 2.4 Hz, 1 H), 6.73 (d, ^3J = 8.0 Hz, 1 H, Ar-H), 6.87–6.91 (m, 1 H, Ar-H), 7.07–7.11 (m, 1 H, Ar-H), 7.22–7.26 (m, 1 H, Ar-H), 7.30–7.39 (m, 4 H, Ar-H), 7.44–7.51 (m, 4 H, Ar-H), 7.93–7.95 (m, 2 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.1, 50.6, 55.7, 63.9, 75.5, 78.5, 110.6, 121.3, 123.6, 127.2, 128.0, 128.3, 128.4, 129.6, 132.8, 137.1, 138.2, 155.7, 193.4.

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{25}H_{21}NO_2$: 367.1572; found: 367.1580.

{*trans*-1-Benzyl-3-[2-(buta-2,3-dien-1-yloxy)phenyl]aziridin-2-yl}(phenyl)methanone (13a) and {*cis*-1-Benzyl-3-[2-(buta-2,3-dien-1-yloxy)phenyl]aziridin-2-yl}(phenyl)methanone (13b)

Prepared by Method A from I_2 (0.276 g, 1.09 mmol) and chalcone **12** (0.272 g, 0.99 mmol) in Et_2O (6 mL) and $BnNH_2$ (0.51 mL, 4.65 mmol) in Et_2O (0.5 mL). The mixture was stirred for 2 h and the product was purified by flash chromatography [silica gel, EtOAc–hexane (1:4)] to give, in order of elution, compound **13a** [yield: 0.285 g (75%)] as a yellow oil and compound **13b** [yield: 0.035 g (9%)] as a pale-yellow solid.

13a

IR (film): 1957, 1668, 1493, 1452, 1230 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.58 (d, ^3J = 2.6 Hz, 1 H), 3.92 (d, ^3J = 2.6 Hz, 1 H), 4.06 (d, ^2J = 13.8 Hz, 1 H), 4.21 (d, ^2J = 13.8 Hz, 1 H), 4.55–4.56 (m, 2 H), 4.77–4.79 (m, 2 H), 5.25–5.32 (m, 1 H), 6.85 (d, ^3J = 8.0 Hz, 1 H, Ar-H), 6.91–6.95 (m, 1 H, Ar-H), 7.15–7.25 (m, 4 H, Ar-H), 7.31–7.37 (m, 3 H, Ar-H), 7.41–7.45 (m, 2 H, Ar-H), 7.52–756 (m, 1 H, Ar-H), 7.93–7.94 (m, 2 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.5, 46.8, 55.1, 65.9, 76.7, 87.2, 111.8, 120.9, 126.9, 127.0, 127.7, 128.2, 128.3, 128.5, 128.6, 133.1, 138.5, 139.5, 156.9, 195.4, 209.2.

HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{26}H_{24}NO_2$: 382.18042; found: 382.18016.

13b

Mp 88.6–90.3 °C (EtOH).

IR (KBr): 1959, 1682, 1244, 1227 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.45 (d, ^3J = 7.0 Hz, 1 H), 3.59 (d, ^3J = 7.0 Hz, 1 H), 3.76 (d, ^2J = 13.8 Hz, 1 H), 4.03 (d, ^2J = 13.8 Hz, 1 H), 4.35–4.41 (m, 1 H), 4.46–4.52 (m, 1 H), 4.82–4.87 (m, 2 H), 5.24–5.30 (m, 1 H), 6.65 (d, ^3J = 8.0 Hz, 1 H, Ar-H), 6.83–6.87 (m, 1 H, Ar-H), 7.05–7.09 (m, 1 H, Ar-H), 7.22–7.26 (m, 1 H, Ar-H), 7.30–7.37 (m, 4 H, Ar-H), 7.45–7.50 (m, 4 H, Ar-H), 7.92–7.95 (m, 2 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.3, 50.6, 64.0, 65.5, 76.7, 87.2, 110.5, 120.5, 123.3, 127.1, 128.0, 128.2, 128.2, 128.3, 128.4, 129.5, 132.7, 137.2, 138.2, 156.4, 193.4, 209.2.

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{26}H_{23}NO_2$: 381.1729; found: 381.1726.

Benzyl *cis*-1-Benzyl-3-[2-(prop-2-yn-1-yloxy)phenyl]aziridine-2-carboxylate (19)

Prepared by Method B from alkene **17** (0.246 g, 0.84 mmol) and Br_2 (0.05 mL, 0.88 mmol) in CH_2Cl_2 (5 mL). Purification by flash chromatography [silica gel, EtOAc–hexane (1:4)] gave a white solid; yield: 0.164 g (49%); mp 86.6–87.8 °C (EtOAc–hexane).

IR (KBr): 3253, 2129, 1734, 1194, 1169 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.44 (t, ^4J = 2.4 Hz, 1 H), 2.73 (d, ^3J = 6.8 Hz, 1 H), 3.26 (d, ^3J = 6.8 Hz, 1 H), 3.66 (d, ^2J = 13.6 Hz, 1 H), 3.92 (d, ^2J = 13.6 Hz, 1 H), 4.53 (dd, ^2J = 15.6 Hz, ^4J = 2.4 Hz, 1 H), 4.59 (dd, ^2J = 15.6 Hz, ^4J = 2.4 Hz, 1 H), 4.92 (d, ^2J = 12.4 Hz, 1 H), 4.96 (d, ^2J = 12.4 Hz, 1 H), 6.86–6.92 (m, 2 H, Ar-H), 7.04–7.07 (m, 2 H, Ar-H), 7.17–7.22 (m, 1 H, Ar-H), 7.24–7.27 (m, 4 H, Ar-H), 7.29–7.33 (m, 2 H, Ar-H), 7.42–7.43 (m, 2 H, Ar-H), 7.47–7.49 (m, 1 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 44.3, 45.2, 56.0, 63.7, 66.3, 75.4, 78.7, 111.5, 121.2, 124.1, 127.3, 127.9, 128.1, 128.1, 128.3, 128.4, 128.4, 129.8, 135.8, 137.9, 156.0, 168.3.

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{26}H_{23}NO_3$: 397.1678; found: 397.1683.

Benzyl *cis*-1-Benzyl-3-[2-(buta-2,3-dien-1-yloxy)phenyl]aziridine-2-carboxylate (20)

Prepared by Method B from alkene **18** (0.90 g, 2.94 mmol) and Br_2 (0.17 mL, 3.23 mmol) in CH_2Cl_2 (16 mL). Purification by flash chromatography [silica gel, EtOAc–hexane (1:4)] gave a colorless oil; yield: 0.430 g (36%).

IR (film): 1957, 1749, 1720, 1495, 1454, 1184, 1167 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.72 (d, ^3J = 6.8 Hz, 1 H), 3.26 (d, ^3J = 6.8 Hz, 1 H), 3.66 (d, ^2J = 13.6 Hz, 1 H), 3.92 (d, ^2J = 13.6 Hz, 1 H), 4.40–4.51 (m, 2 H), 4.80–4.83 (m, 2 H), 4.94 (s, 2 H), 5.25–5.32 (m, 1 H), 6.75 (d, ^3J = 8.0 Hz, 1 H, Ar-H), 6.85–6.89 (m, 1 H, Ar-H), 7.03–7.06 (m, 2 H, Ar-H), 7.15–7.19 (m, 1 H, Ar-H), 7.23–7.27 (m, 4 H, Ar-H), 7.29–7.33 (m, 2 H, Ar-H), 7.42–7.47 (m, 3 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 44.5, 45.3, 63.8, 65.9, 66.3, 76.5, 87.3, 111.3, 120.5, 123.9, 127.3, 127.9, 128.1, 128.3, 128.4, 128.4, 129.5, 135.8, 138.0, 156.8, 168.4, 209.2.

HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{27}H_{26}NO_3$: 412.19072; found: 412.19074.

Thermolysis of Aziridines 11a, 13a, 19, and 20; General Procedures

Method C: A solution of the appropriate aziridine in *t*-BuOH or toluene was refluxed until the reaction was complete (TLC). The solvent was removed under reduced pressure and the crude product was purified by preparative TLC [EtOAc–hexane] or by flash chromatography [silica gel, EtOAc–hexane].

Method D: A solution of *t*-BuOK (1.0 equiv) in *t*-BuOH (2 mL) was added dropwise to a solution of the appropriate aziridine in *t*-BuOH (8 mL). The mixture was heated at 60 °C for 47 h under N_2 then cooled to r.t. H_2O (15 mL) was added, and the aqueous layer was extracted with Et_2O (3 × 15 mL). The organic layer was washed with sat. aq NH_4Cl (15 mL), dried (Na_2SO_4), and concentrated in vacuum. The crude product was purified by flash chromatography [silica gel, EtOAc–hexane].

(1-Benzyl-1,4-dihydrochromeno[4,3-*b*]pyrrol-2-yl)(phenyl)methanone (23)

Prepared by Method C from aziridine **11a** (78 mg, 0.21 mmol) in *t*-BuOH (8 mL). The mixture was stirred for 27 h and the product was purified by flash chromatography [silica gel, EtOAc–hexane (1:5)] to give a pale-orange solid; yield: 50 mg (64%).

Alternatively, the product was prepared by Method D from aziridine **11a** (78 mg, 0.21 mmol) and *t*-BuOK (24 mg, 0.21 mmol). Purification by flash chromatography [silica gel, EtOAc–hexane (1:5)] gave a pale-orange solid; yield: 42 mg (54%); mp 104.9–106.5 °C (Et_2O–PE).

IR (KBr): 1630, 1464, 1392, 1275, 725 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.16 (s, 2 H), 5.98 (br s, 2 H), 6.66 (s, 1 H), 6.83–6.87 (m, 1 H, Ar-H), 7.01 (dd, ^3J = 8.0 Hz, ^4J = 1.2 Hz, 1 H, Ar-H), 7.13–7.18 (m, 3 H, Ar-H), 7.22–7.35 (m, 4 H, Ar-H), 7.40–7.44 (m, 2 H, Ar-H), 7.49–7.53 (m, 1 H, Ar-H), 7.75–7.77 (m, 2 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.4, 65.2, 116.9, 117.6, 118.0, 118.4, 122.1, 122.9, 125.7, 127.2, 128.0, 128.9, 129.3, 129.4, 131.4, 132.0, 132.8, 138.3, 140.2, 155.1, 185.7.

HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{25}H_{20}NO_2$: 366.14886; found: 366.14873.

{1-Benzyl-3-methylene-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrol-2-yl}(phenyl)methanone (24), (1-Benzyl-3-methyl-1,3a,4,9b-tetrahydrochromeno[4,3-*b*]pyrrol-2-yl)(phenyl)methanone (25), and (1-Benzyl-3-methyl-1,4-dihydrochromeno[4,3-*b*]pyrrol-2-yl)(phenyl)methanone (26)

Prepared by Method C from aziridine **13a** (100 mg, 0.26 mmol) in toluene (12 mL). The mixture was stirred for 3 h. Purification by preparative TLC [EtOAc–hexane (1:4)] gave, in order of elution, compound **24** [yield: 21.9 mg (22%)] as an orange oil and a 52:48 mixture of compounds **25** and **26** [yield: 13.9 mg (14%)], also as an orange oil.

24

IR (film): 1658, 1610, 1489, 1450, 1257, 1223 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.02–3.07 (m, 1 H), 3.98 (d, ^2J = 12.4 Hz, 1 H), 4.05–4.17 (m, 2 H), 4.35 (d, ^2J = 12.4 Hz, 1 H), 4.71–4.72 (m, 1 H), 4.79 (d, ^3J = 5.2 Hz, 1 H), 5.01 (br s, 1 H), 5.07–5.08 (m, 1 H), 6.92–6.98 (m, 2 H, Ar-H), 7.10–7.14 (m, 5 H, Ar-H), 7.22–7.26 (m, 1 H, Ar-H), 7.30–7.34 (m, 2 H, Ar-H), 7.38 (dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1 H, Ar-H), 7.42–7.44 (m, 2 H, Ar-H), 7.46–7.50 (m, 1 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.9, 49.8, 56.8, 63.0, 65.8, 109.7, 116.0, 117.0, 119.4, 126.0, 127.2, 127.5, 128.0, 128.1, 131.7, 131.8, 136.2, 137.7, 145.6, 154.0, 199.9.

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{26}H_{23}NO_2$: 381.1729; found: 381.1733.

Mixture of 25 + 26

^{1}H NMR (400 MHz, $CDCl_3$): δ (**25**; major product) = 1.75 (s, 3 H), 2.99–3.03 (m, 1 H), 3.94 (d, ^2J = 15.6 Hz, 1 H), 4.01–4.07 (m, 3 H), 4.24 (d, ^3J = 8.4 Hz, 1 H), 6.75–7.48 (m, 12 H, Ar-H), 7.70–7.72 (m, 2 H, Ar-H); δ (**26**; minor product) = 1.70 (s, 3 H), 5.12 (s, 2 H), 5.77 (s, 2 H), 6.84–6.87 (m, 1 H, Ar-H), 7.01 (d, ^3J = 8.0 Hz, 1 H, Ar-H), 7.06–7.08 (m, 2 H, Ar-H), 7.12–7.16 (m, 1 H, Ar-H), 7.18–7.22 (m, 1 H, Ar-H), 7.25–7.30 (m, 3 H, Ar-H), 7.38–7.42 (m, 2 H, Ar-H), 7.48–7.52 (m, 1 H, Ar-H), 7.63–7.65 (m, 2 H, Ar-H).

Benzyl 1-Benzyl-1,4-dihydrochromeno[4,3-*b*]pyrrole-2-carboxylate (30)

Prepared by Method C from aziridine **19** (100 mg, 0.25 mmol) in toluene (5 mL). The mixture was stirred for 29 h, and the product was purified by flash chromatography [silica gel, EtOAc–hexane (1:4)] to give a pale-yellow solid; yield: 93 mg (94%); mp 115.0–116.6 °C (EtOAc–hexane).

IR (KBr): 1703, 1697, 1271, 1211, 1184 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.15 (s, 2 H), 5.20 (s, 2 H), 5.88 (br s, 2 H), 6.79–6.83 (m, 1 H, Ar-H), 6.98–7.00 (m, 2 H), 7.07–7.13 (m, 3 H, Ar-H), 7.17–7.19 (m, 1 H, Ar-H), 7.22–7.34 (m, 8 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.0, 65.3, 65.7, 113.9, 116.7, 117.9, 118.0, 122.0, 122.2, 123.7, 125.6, 127.2, 128.0, 128.1, 128.6, 128.8, 128.9, 131.3, 136.3, 138.1, 154.8, 160.5.

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{26}H_{21}NO_3$: 395.1521; found: 395.1524.

Benzyl 1-Benzyl-1,2,4,9b-tetrahydrochromeno[4,3-*b*]pyrrole-2-carboxylate (29) and Benzyl 1-Benzyl-1,4-dihydrochromeno[4,3-*b*]pyrrole-2-carboxylate (30)

Prepared by Method C from aziridine **19** (80 mg, 0.20 mmol) in toluene (5 mL). The reaction mixture was stirred for 2 h, and the product was purified by flash chromatography [silica gel, EtOAc–hexane (1:4)] to give a 54:46 mixture of compounds **29** and **30** as a yellow oil; total yield: 43 mg (54%).

^{1}H NMR (400 MHz, $CDCl_3$): δ (**29**; major product) = 4.30 (d, ^2J = 14.0 Hz, 1 H), 4.50 (br s, 1 H), 4.59 (d, ^2J = 14.0 Hz, 1 H), 4.73 (d, ^2J = 13.8 Hz, 1 H), 4.83 (d, ^2J = 13.8 Hz, 1 H), 5.01–5.08 (m, 2 H), 5.17 (br s, 1 H), 5.66 (br s, 1 H), 6.90 (d, ^3J = 8.0 Hz, 1 H, Ar-H), 6.94–6.98 (m, 1 H, Ar-H), 7.07–7.33 (m, 11 H, Ar-H), 7.46 (d, ^3J = 7.6 Hz, 1 H, Ar-H); δ (**30**; minor product) = 5.15 (s, 2 H), 5.20 (s, 2 H), 5.88 (br s, 2 H), 6.79–6.83 (m, 1 H, Ar-H), 6.98–7.00 (m, 2 H), 7.07–7.13 (m, 3 H, Ar-H), 7.17–7.19 (m, 1 H, Ar-H), 7.22–7.34 (m, 8 H, Ar-H).

Benzyl 1-Benzyl-3-methylene-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2-carboxylate (31)

Prepared by Method C from aziridine **20** (90 mg, 0.22 mmol) in toluene (5 mL). The mixture was stirred for 4 h, and the product was purified by flash chromatography [silica gel, EtOAc–hexane (1:8)] to give a colorless oil; yield: 57 mg (63%).

IR (film): 1732, 1153, 1119, 1045 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.94–3.00 (m, 1 H), 3.87 (d, ^2J = 12.8 Hz, 1 H), 4.00–4.04 (m, 2 H), 4.06 (s, 1 H), 4.29 (d, ^2J = 12.8 Hz, 1 H), 4.52 (d, ^3J = 4.8 Hz, 1 H), 5.10 (d, ^2J = 12.0 Hz, 1 H), 5.15–5.18 (m, 2 H), 5.22–5.23 (m, 1 H), 6.89–6.95 (m, 2 H, Ar-H), 7.04–7.06 (m, 2 H, Ar-H), 7.15–7.17 (m, 3 H, Ar-H), 7.20–7.40 (m, 7 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 39.9, 49.5, 56.5, 62.8, 65.3, 65.6, 109.8, 116.0, 118.9, 118.9, 126.0, 127.2, 127.3, 127.4, 127.5, 127.6, 128.1, 131.7, 134.7, 137.5, 144.5, 154.0, 170.1.

HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{27}H_{26}NO_3$: 412.19072; found: 412.19039.

(1-Benzyl-3-methyl-1,4-dihydrochromeno[4,3-*b*]pyrrol-2-yl)(phenyl)methanone (26)

A solution of aziridine **13a** (110 mg, 0.29) in toluene (5 mL) was refluxed for 2 h then cooled to r.t. The solvent was removed under reduced pressure, and the crude product was dissolved in EtOAc (5 mL) and treated with 5% Pd/C (62 mg, 0.03 mmol). The resulting mixture was refluxed for 2.5 d then cooled to r.t. The mixture was filtered on Celite to remove the oxidant and the solvent was evaporated under reduced pressure. The crude product was purified by preparative TLC [EtOAc–hexane (1:6)] to give a yellow oil; yield: 17 mg (16%).

IR (film): 1616, 1450, 1396 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.70 (s, 3 H), 5.12 (s, 2 H), 5.77 (s, 2 H), 6.84–6.87 (m, 1 H, Ar-H), 7.01 (d, ^3J = 8.0 Hz, 1 H, Ar-H), 7.06–7.08 (m, 2 H, Ar-H), 7.12–7.16 (m, 1 H, Ar-H), 7.18–7.22 (m, 1 H, Ar-H), 7.25–7.30 (m, 3 H, Ar-H), 7.38–7.42 (m, 2 H, Ar-H), 7.48–7.52 (m, 1 H, Ar-H), 7.63–7.65 (m, 2 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.8, 50.0, 64.2, 117.4, 117.8, 122.0, 122.7, 123.9, 125.7, 127.1, 128.4, 128.6, 128.8, 128.9, 129.1, 130.9, 131.6, 131.9, 138.7, 140.8, 155.0, 187.9.

HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{26}H_{22}NO_2$: 380.16451; found: 380.16491.

Thermolysis of Aziridines 11a and 13a in the Presence of Dimethyl Acetylenedicarboxylate; General Procedure

A solution of the appropriate aziridine and DMAD (1.5 equiv) in *t*-BuOH (15 mL) was refluxed for 23 h. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography [silica gel, EtOAc–hexane (1:4)].

(1-Benzyl-1,4-dihydrochromeno[4,3-*b*]pyrrol-2-yl)(phenyl)methanone (23), Dimethyl 1-Benzyl-4-phenyl-1*H*-pyrrole-2,3-dicarboxylate (27), and Dimethyl 2-Benzoyl-1-benzyl-5-[2-(prop-2-yn-1-yloxy)phenyl]-1*H*-pyrrole-3,4-dicarboxylate (28a)

Prepared from aziridine **11a** (100 mg, 0.27 mmol) and DMAD (0.05 mL, 0.41 mmol). Purification by flash chromatography [silica gel, EtOAc–hexane (1:4)] gave, in order of elution, compound **23** [yield: 38 mg (38%),] compound **27** [yield: 3 mg (4%)] as a yellow oil, and compound **28a** [yield: 52 mg (38%)] as a dark-orange oil.

23

Identified by comparison with the specimen previously prepared (see above).

27

IR (film): 1730, 1711, 1263, 1209 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.80 (s, 3 H), 3.82 (s, 3 H), 5.53 (s, 2 H), 6.94 (s, 1 H), 7.18–7.19 (m, 2 H, Ar-H), 7.23–7.39 (m, 8 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.8, 52.4, 52.5, 121.1, 122.3, 124.1, 125.7, 127.0, 127.3, 127.4, 127.9, 128.6, 128.8, 133.3, 136.9, 160.7, 167.3.

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{21}H_{19}NO_4$: 349.1314; found: 349.1314.

28a

IR (film): 3286, 2121, 1724, 1213 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.48 (t, ^4J = 2.4 Hz, 1 H), 3.20 (s, 3 H), 3.58 (s, 3 H), 4.65 (d, ^4J = 2.4 Hz, 2 H), 5.13 (d, ^2J = 15.4 Hz, 1 H), 5.40 (d, ^2J = 15.4 Hz, 1 H), 6.83–6.85 (m, 2 H, Ar-H), 7.01–7.08 (m, 4 H, Ar-H), 7.12 (d, ^3J = 8.0 Hz, 1 H, Ar-H), 7.25–7.27 (m, 1 H, Ar-H), 7.33–7.37 (m, 2 H, Ar-H), 7.41–7.50 (m, 2 H, Ar-H), 7.60–7.62 (m, 2 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 49.3, 51.5, 51.7, 55.8, 75.9, 78.3, 112.5, 113.6, 119.2, 121.2, 123.8, 127.0, 127.4, 128.1, 128.3, 129.0, 130.7, 131.1, 132.7, 132.9, 137.0, 138.6, 139.1, 155.5, 163.6, 164.8, 188.1.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{31}H_{26}NO_6$: 508.17546; found: 508.17568.

Dimethyl 1-Benzyl-4-phenyl-1*H*-pyrrole-2,3-dicarboxylate (27) and Dimethyl 2-Benzoyl-1-benzyl-5-[2-(buta-2,3-dien-1-yloxy)phenyl]-1*H*-pyrrole-3,4-dicarboxylate (28b)

Prepared from aziridine **13a** (200 mg, 0.52 mmol) and DMAD (0.1 mL, 0.79 mmol). Purification by flash chromatography [silica gel, EtOAc–hexane (1:4)] gave, in order of elution, compound **27** [yield: 19 mg (10%)] and compound **28b** [yield: 3 mg (4%)] as a yellow oil.

27

Identified by comparison with the specimen previously prepared (see above).

28b

IR (film): 1957, 1722, 1647, 1454, 1209, 1165 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.20 (s, 3 H), 3.59 (s, 3 H), 4.53–4.56 (m, 2 H), 4.83–4.86 (m, 2 H), 5.12 (d, ^2J = 15.4 Hz, 1 H), 5.20–5.27 (m, 1 H), 5.38 (d, ^2J = 15.4 Hz, 1 H), 6.84–6.86 (m, 2 H, Ar-H), 6.96–7.02 (m, 2 H, Ar-H), 7.05–7.11 (m, 3 H, Ar-H), 7.26–7.28 (m, 1 H, Ar-H), 7.33–7.42 (m, 3 H, Ar-H), 7.46–7.50 (m, 1 H, Ar-H), 7.59–7.61 (m, 2 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 49.4, 51.4, 51.7, 65.8, 76.9, 86.9, 112.5, 113.4, 119.1, 120.6, 123.9, 127.0, 127.4, 128.1, 128.3, 129.0, 130.5, 131.1, 132.6, 132.9, 137.1, 138.6, 139.7, 156.4, 163.6, 164.9, 188.1, 209.2.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{32}H_{28}NO_6$: 522.19111; found: 522.19127.

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Supporting Information

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