Reactions of methyl 2-aryl-2*H*-azirine-3-carboxylates with nucleophiles

M. José Alves,[ab] Thomas L. Gilchrist *[a] and João H. Sousa [b]

[a] *Chemistry Department, The University of Liverpool, Liverpool, UK L69 7ZD*
[b] *Departamento de Química, Universidade do Minho, 4710 Braga, Portugal*

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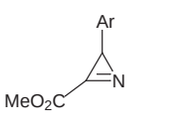
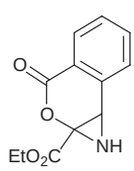
Reactions of the methyl 2-aryl-2*H*-azirine-3-carboxylates **1a** and **1b** with nucleophiles are described. Thiols add to the C=N bond to give aziridines **4**–**6**. Propargyl alcohol similarly gives the aziridine **7**. Primary and secondary aliphatic amines react with the azirines to give methyl 3-aminoacrylates **8**–**12**. 4-Cyclohexen-1-ylmorpholine and 1-cyclopenten-1-ylpyrrolidine react with the azirine **1a** to give products formulated as the aziridine **13** and the vinylidenecyclopentanone **14,** respectively, in contrast to previously reported reactions of enamines with azirines from which pyrroles were isolated. Acetylacetone gives a pyrrole-3-carboxylate **15** in low yield with the azirine **1a**. All these products have been rationalised by invoking initial addition of the nucleophile to the C=N bond of the azirine. The tetrahydrofuran-2-yl radical also adds to the C=N bond of the azirine **1a**, giving the aziridine **16** as a single diastereoisomer. X-Ray crystal structures of methyl (*E*)-3-amino-3-(2,6-dichlorophenyl)-2-morpholin-4-ylpropenoate **8** and of methyl 3-(2,6-dichlorophenyl)-2-(tetrahydrofuran-2-yl)aziridine-2-carboxylate **16** are reported.

We have described the reactions of methyl 2-aryl-2*H*-azirine-3-carboxylates **1** as dienophiles in the Diels–Alder reaction.[1] Electron deficient azirines of this type have also been reported to undergo phototrimerisation[2,3] and intramolecular ene reactions.[4] These azirines are highly susceptible to nucleophilic attack and do not survive exposure to protic solvents.[1] There are, however, few specific examples of characterised products resulting from nucleophilic attack. The aziridine **2** was isolated as a product of the thermolysis of ethyl 2-azido-3-(2-carboxyphenyl)propenoate and was formed, it was suggested, by intramolecular nucleophilic addition to the C=N bond of an intermediate azirine **3**.[5] Dimethyl 2*H*-azirine-2,3-dicarboxylate is reported to react with enamines[6,7] and with α-acylphosphonium ylides[6] to give pyrroles. The intermolecular addition of nucleophiles to azirines of other types has been reported several times; occasionally the product isolated is the aziridine resulting from addition to the C=N bond but more commonly the products are derived from the aziridine by ring opening and further reaction.[8] This paper records the results of a survey of the scope and potential synthetic applications of the reactions of the azirines **1** with simple nucleophiles, the principal aim being to identify which, if any, of these types of reactions are general and high yielding.



1 **a**; Ar = $C_6H_3Cl_2$-2,6
b; Ar = C_6H_4Me-4



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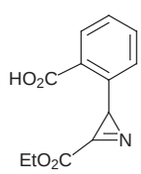

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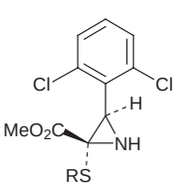
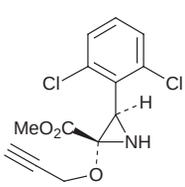


4; R = Ph
5; R = C_6H_4Cl-4
6; R = CH_2CO_2Me



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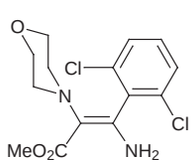

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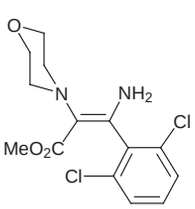

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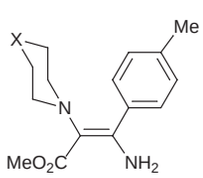
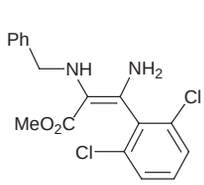


10; X = O
11; X = CH_2



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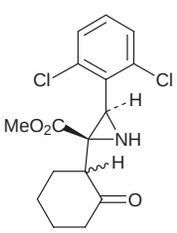

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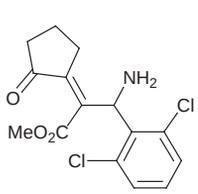

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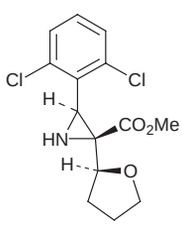


16

Results and discussion

Reactions with thiols

Benzenethiol reacted readily with the azirine **1a** at room temperature and gave a single product in good yield. The product was assigned the structure **4** mainly on the basis of its ^1H and ^{13}C NMR spectra, the relative stereochemistry at C-2 and C-3 being based on the assumption that the thiol will attack from the less hindered face of the azirine. The ^1H NMR spectrum shows signals for H-3 and NH as broad doublets at δ 3.66 and 3.31; with D_2O the signal at δ 3.66 collapses to a singlet and that at δ 3.31 disappears. In the ^{13}C NMR spectrum the signals for C-2 and C-3 appear at δ 51.0 and 45.0. Similar aziridines **5** and **6** were isolated from the reaction of the azirine **1a** with 4-chlorobenzenethiol and with ethyl mercaptoacetate. The

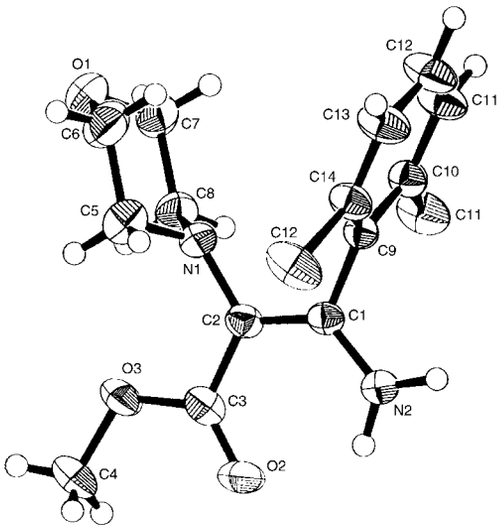


Fig. 1 The structure of **8**.

isolation of aziridines from these reactions is in accord with previous examples of the addition of thiols to azirines.[9]

Reactions with alcohols

The azirines **1** reacted rapidly at room temperature with simple alcohols such as methanol and ethanol. The reactions were performed under a variety of conditions in attempts to obtain characterisable products from the reactions but we were unable to do so. Propan-2-ol and benzyl alcohol reacted slowly with the azirines but again, we failed to characterise the reaction products. With propargyl alcohol (prop-2-yn-1-ol), however, a 1 : 1 adduct was isolated in good yield and was characterised as the aziridine **7**. The assignment of stereochemistry to the aziridine was supported by an NOE experiment: irradiation of the signal for the side chain methylene group produced an enhancement in the intensity of the signal at δ 3.54 assigned to the aziridine ring hydrogen, indicating that they are on the same side of the ring.

2*H*-Azirines have previously been observed to react with sodium alkoxides, but not with the corresponding alcohols, to give 2-alkoxyaziridines.[10]

Reactions with amines

The azirine **1a** reacted rapidly with morpholine at room temperature, the reaction being complete after 15 min. Two solid products were isolated from the reaction mixture. These were identified as the *E*- and *Z*-3-aminoacrylates **8** and **9** from their spectra. The major product (isolated in 44% yield) was shown to be the *E*-isomer **8** by X-ray crystallography (Fig. 1); the minor product (10%) was assigned the structure **9** because the spectra of the two compounds were closely similar. Minor differences in the NMR spectra did, however, allow structural assignments to be made to reaction products with other amines, as indicated below. The methyl signal in the ^{1}H NMR spectrum of compound **8** has a chemical shift of 3.80 ppm whereas the corresponding signal in the spectrum of the isomeric acrylate **9** is at 3.51 ppm. In the ^{13}C spectra the chemical shifts of C-3 and C=O are greater for compound **8** (155.3 and 170.6 ppm) than for its isomer **9** (149.5 and 166.0 ppm).

A single product was isolated (57%) from the reaction mixture of the azirine **1b** with morpholine. This was identified as the *E*-isomer **10** on the basis of a comparison of its NMR spectra [δ (CH_3) 3.77; δ (C-3) 160.9; δ (C=O) 172.0] with those of compound **8**. Piperidine also reacted with the azirine **1b** to give a single product (72%) that was also identified as an *E*-aminoacrylate **11** on the basis of the chemical shift of the CH_3 signal (3.75 ppm). Thus, in all three reactions with secondary amines the major or exclusive products were the *E*-aminoacrylates. In contrast, benzylamine reacted with the azirine **1a** to give a single product (65%) for which the spectra clearly pointed to its assignment as the *Z*-isomer **12** [δ (CH_3) 3.46; δ (C-3) 146.2; δ (C=O) 166.4]. It appears likely that these reactions all lead initially to the formation of aziridines analogous to those isolated from reactions with thiols, but that the aziridines rapidly isomerise to the aminoacrylates. The factors that determine the isomer composition have not been established. The crystal structure of compound **8** is consistent with the presence of an intramolecular hydrogen bond between the amino and carbonyl functions. When allowed to stand for 24 h in DCM containing a drop of acetic acid, the aminoacrylate **12** was partially converted into a second compound which, from the ^{1}H NMR spectrum, appeared to be the *E*-isomer, so the *E*-isomers may be the products of thermodynamic control.

Reactions with carbon nucleophiles

Pyrroles have previously been isolated from the reactions of enamines with azirines bearing alkoxycarbonyl or similar functions at the tetrahedral carbon C-2, formally by way of [2 + 2] addition of the enamines to the C=N bond of the azirines.[6,7] The azirine **1a** was allowed to react at RT with two enamines, 4-cyclohexen-1-ylmorpholine and 1-cyclopenten-1-ylpyrrolidine, but in neither case were pyrroles isolated from the reaction mixture. 4-Cyclohexen-1-ylmorpholine gave an aziridine **13**, a product to be expected from nucleophilic addition of the enamine to the azirine. The aminoacrylates **8** and **9** were also detected as reaction products. 1-(Cyclopenten-1-yl)pyrrolidine reacted rapidly and exothermically with the azirine **1a** at RT. A single product was isolated in 62% yield; it has tentatively been assigned the structure **14** on the basis of its IR and NMR spectra. In particular the appearance of a 1 H triplet (*J* 2.7 Hz) at δ 5.68 in the ^{1}H NMR spectrum, which has been assigned to the benzylic hydrogen in structure **14**, is inconsistent with alternative 3-aminoacrylate structures. The *Z*-stereochemistry would also preclude its cyclisation to a pyrrole whereas such a cyclisation might be expected to take place readily with the *E*-isomer. The most likely route by which compound **14** is formed is by way of an aziridine analogous to **13**, but the aziridine was not detected as an intermediate in this reaction.

The azirine **1a** also reacted slowly with acetylacetone. After 2 days at RT the azirine had been consumed and from the reaction mixture one product was isolated pure in low yield. This proved to be the pyrrole **15**, which is possibly formed by the sequence shown in Scheme 1. Pyrroles have previously been isolated as the products of the reactions of carbanions (as sodium salts) with 2*H*-azirines.[11]

Reactions with other activated methylene compounds were attempted but the reactions were slow and led to complex mixtures. An unexpected by-product was isolated from reactions carried out in THF over several days. The crystalline product was subjected to X-ray analysis and it proved to be the aziridine **16** (Fig. 2), a formal 1 : 1 adduct of the azirine and THF. This is probably the result of radical addition of THF to the C=N bond since the same product was formed when the azirine **1a** was heated under reflux for 30 min in THF containing benzoyl peroxide. Such radical additions to activated double bonds[12] and to iminium ions[13] are known, but the high stereoselectivity of the addition (only one isomer was detected) is surprising. As far as we are aware, the addition of radicals to the C=N bond of azirines has not previously been reported. Imines do not generally undergo intermolecular radical addition although intramolecular addition to imines[14] and intermolecular addition to oxime ethers[15] † are synthetically useful reactions.

† We thank a referee for drawing this work to our attention.

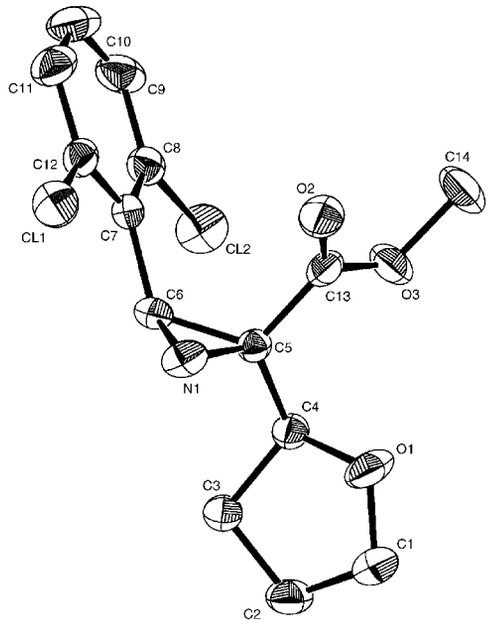
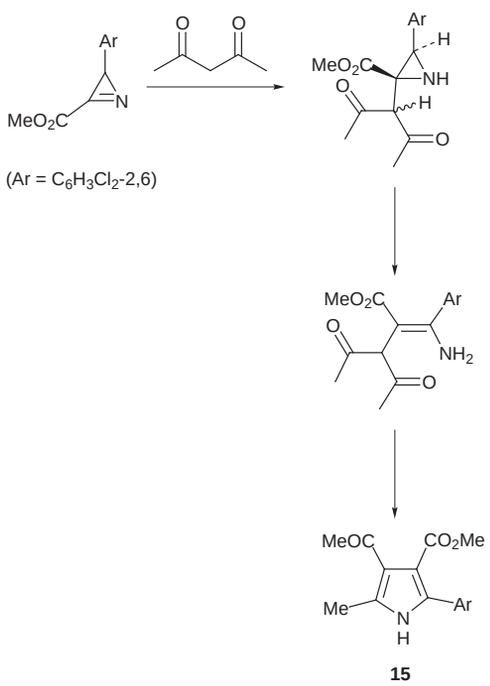


Fig. 2 The structure of **16**.



Scheme 1

Conclusions

Of the reactions surveyed only those with thiols and aliphatic secondary amines consistently gave products of a specific type. The reactions with alcohols, enamines and activated methylene compounds were unpredictable. All of the products isolated can be rationalised as being formed by initial nucleophilic addition to the C=N bond of the azirine, as expected, and some of these aziridines can be isolated. The ready reaction of the tetrahydrofuranyl radical with the azirine **1a** indicates that the C=N bond may also be highly susceptible to radical addition.

Experimental

General

^{1}H NMR spectra were recorded either on a Bruker AC 200 (200 MHz) or on a Varian Gemini 2000 (300 MHz) spectrometer. Multiplicities are recorded as broad peaks (br), singlets (s), doublets (d), triplets (t), quartets (q) and multiplets (m). *J* values are in Hz. Infrared spectra were recorded either on a Perkin-Elmer 298 or on a Perkin-Elmer 1720-X FTIR spectrometer. Solid samples were run as Nujol mulls, and liquids as thin films. Mass spectra were recorded on a VG Micromass 7070E machine as electron impact spectra (70 eV). Microanalyses were performed in the University of Liverpool Microanalysis Laboratory. Melting points (mp) were determined on a Kofler block and are uncorrected. Dry column flash chromatography was carried out using Kieselgel 60 and water pump vacuum. Thin layer chromatography (TLC) was carried out on Merck 10 × 2 cm aluminium-backed plates with a 0.2 mm layer of Kieselgel 60 F_{254}. The azirines **1a** and **1b** were prepared as described earlier.[1]

Methyl 3-(2,6-dichlorophenyl)-2-phenylthioaziridine-2-carboxylate 4

Thiophenol (149 mg, 1.35 mmol) was added to a solution of the azirine **1a** (300 mg, 1.23 mmol) in THF (5 ml) at RT. After 2 h the solvent was removed to leave a yellow oil. Flash column chromatography gave [with hexane–ether (19 : 1)] the aziridine **4** (310 mg, 71%) as a pale yellow oil (Found: C, 53.8; H, 3.6; N, 4.0. $C_{16}H_{13}Cl_2NO_2S$ requires C, 54.25; H, 3.7; N, 3.95%); ν_{max} (Nujol)/cm^{-1} 3285 (NH) and 1719 (C=O); δ_H (300 MHz) 3.31 (1 H, br d, exchanges with D_2O), 3.47 (3 H, s), 3.66 (1 H, br d), 7.13–7.34 (6 H, m) and 7.51–7.58 (2 H, m); δ_C (75.5 MHz) 45.0 (C-3), 51.00 (C-2), 53.6 (CH_3), 128.0, 128.5, 129.1, 129.1, 129.6, 130.5, 132.4, 136.0 and 170.0; *m*/*z* 353/355/357 (M^+) and 244 (100%; M^+ − PhS).

Methyl 2-(4-chlorophenylthio)-3-(2,6-dichlorophenyl)aziridine-2-carboxylate 5

By the method described for compound **4**, the azirine **1a** (300 mg, 1.23 mmol) and 4-chlorothiophenol (180 mg, 1.23 mmol) gave the *aziridine* **5**. This was obtained directly by evaporation of the reaction mixture and crystallisation as a colourless solid (340 mg, 71%), mp 128–129 °C (from ether–hexane) (Found: C, 49.3; H, 3.25; N, 3.7. $C_{16}H_{12}Cl_3NO_2S$ requires C, 49.4; H, 3.1; N, 3.6%); ν_{max} (Nujol)/cm^{-1} 3270 (NH) and 1714 (C=O); δ_H (300 MHz) 3.30 (1 H, br d), 3.35 (3 H, s), 3.37 (1 H, br d), 7.15–7.21 (1 H, m), 7.26–7.33 (4 H, m) and 7.52–7.55 (2 H, m); δ_C (75.5 MHz) 47.3 (C-3), 53.1 (CH_3), 53.8 (C-2), 127.2, 127.9, 128.0, 129.3, 130.9, 132.3, 133.7, 134.2 and 164.2; *m*/*z* 387/389 (M^+).

Methyl 3-(2,6-dichlorophenyl)-2-methoxycarbonylmethylthioaziridine-2-carboxylate 6

By the method described for compound **4**, the azirine **1a** (600 mg, 2.46 mmol) and methyl mercaptoacetate (260 mg, 2.46 mmol) gave, after isolation by chromatography, the *aziridine* **6** (380 mg, 44%), mp 101–102 °C (from ether–hexane) (Found: C, 44.5; H, 3.9; N, 4.1. $C_{13}H_{13}Cl_2NO_4S$ requires C, 44.6; H, 3.7; N, 4.0%); ν_{max} (Nujol)/cm^{-1} 3281 (NH), 1732 and 1720 (C=O); δ_H (300 MHz) 3.20 (1 H, d, *J* 10.2 Hz, signal removed by D_2O shake), 3.40 (1 H, d, *J* 14.7 Hz), 3.60–3.70 (2 H, m), 3.62 (3 H, s), 3.72 (3 H, s), 7.17 (1 H, t, *J* 7.8 Hz) and 7.29 (2 H, d, *J* 7.8 Hz); δ_C (75.5 MHz) 32.1 (CH_2), 49.0 (C-2), 49.7 (C-3), 52.4 (CH_3), 53.7 (CH_3), 128.3 (CH), 129.6 (CH), 130.4, 135.5, 169.5 and 170.5; *m*/*z* 349/351 (M^+).

Methyl 3-(2,6-dichlorophenyl)-2-prop-2-ynyloxyaziridine-2-carboxylate 7

The azirine **1a** (900 mg, 3.69 mmol) in dry DCM (0.5 ml) and prop-2-yn-1-ol (960 mg, 17.2 mmol) were mixed and the solution was allowed to stand at RT until the azirine could no longer be detected (19 h). The solvent was evaporated to leave a solid that was washed with hexane–ether (1 : 1). The residue (1.04 g, 94%) was essentially pure by NMR. Crystallisation of a sample gave the *aziridine* **7**, mp 127.5–128.5 °C (from ether–

hexane) (Found: C, 52.0; H, 3.85; N, 4.7. $C_{13}H_{11}Cl_2NO_3$ requires C, 52.0; H, 3.7; N, 4.7%); ν_{max} (Nujol)/cm^{-1} 3309 (CH), 3294 (NH), 2120w (C≡C) and 1727 (C=O); δ_H (300 MHz) 2.46 (1 H, t, *J* 2.0 Hz), 2.76 (1 H, br d), 3.54 (1 H, d, *J* 10.8 Hz), 3.69 (3 H, s), 4.48 (2 H, d, *J* 2.0 Hz), 7.17 (1 H, t, *J* 7.2 Hz) and 7.28 (2 H, d, *J* 7.2 Hz); with D_2O the d at δ 2.76 disappears and the d at δ 3.54 collapses to a s; δ_C (75.5 MHz) 47.0 (C-3), 53.2 (CH_3), 55.2 (CH_2), 72.9 (C-2), 75.0 (CH), 79.0 (C), 128.5 (CH), 129.6 (CH), 130.5, 135.7 and 169.4; *m*/*z* 260/262 ($M^+ - C_3H_3$).

Methyl (*E*)-3-amino-3-(2,6-dichlorophenyl)-2-morpholin-4-ylpropenoate 8 and methyl (*Z*)-3-amino-3-(2,6-dichlorophenyl)-2-morpholin-4-ylpropenoate 9

Morpholine (120 mg, 1.38 mmol) was added to a stirred solution of the azirine **1a** (300 mg, 1.23 mmol) in THF (3 ml) at RT. The reaction was complete after 15 min. The solvent was removed to leave an oil. Flash chromatography gave [with ether–hexane (1 : 1)] the *E*-isomer **8** (180 mg, 44%) followed by the *Z*-isomer **9** (40 mg, 10%).

The 3-aminopropenoate 8. Mp 174–176 °C (from ether–hexane) (Found: C, 50.9; H, 4.9; N, 8.2. $C_{14}H_{16}Cl_2N_2O_3$ requires C, 50.8; H, 4.9; N, 8.5%); ν_{max} (Nujol)/cm^{-1} 3394, 3281, and 1665; δ_H (300 MHz) 2.40–3.90 (8 H, br m), 3.80 (3 H, s), 6.11 (2 H, br s) and 7.19–7.37 (3 H, m); δ_C (75.5 MHz) 50.3 (CH_3), 51.4 (CH_2), 68.0 (CH_2), 110.3 (C-2), 127.8 (CH), 129.6 (CH), 133.3, 137.0, 155.3 (C-3) and 170.6; *m*/*z* 330/332 (M^+).

The 3-aminopropenoate 9. Mp 153–170 °C (melts then resolidifies) (from ether–hexane) (Found: C, 50.9; H, 4.9; N, 8.4%); ν_{max} (Nujol)/cm^{-1} 3425, 3306 and 1658; δ_H (300 MHz) 3.02 (4 H, br s), 3.51 (3 H, s), 3.80 (4 H, br s), 5.08 (2 H, br s) and 7.19–7.34 (3 H, m); δ_C (75.5 MHz) 49.9 (CH_2), 50.2 (CH_3), 68.5 (CH_2), 113.8 (C-2), 127.8 (CH), 129.7 (CH), 133.5, 135.7, 149.5 (C-3) and 166.0; *m*/*z* 330/332 (M^+).

Methyl (*E*)-3-amino-3-(4-methylphenyl)-2-morpholin-4-yl-propenoate 10

Morpholine (90 mg, 1.03 mmol) was added to a stirred solution of the azirine **1b** (220 mg, 1.16 mmol) in THF (4 ml) at RT. The reaction was complete after 15 min. The solvent was removed to leave an oil. Flash chromatography gave [with ether–hexane (1 : 3)] the *3-aminopropenoate* **10** (160 mg, 56%), mp 154–155 °C (from ether–hexane) (Found: C, 64.95; H, 7.3; N, 10.1. $C_{15}H_{20}N_2O_3$ requires C, 65.2; H, 7.3; N, 10.1%); ν_{max} (film)/cm^{-1} 3410, 3306 and 1661; δ_H (200 MHz) 2.39 (3 H), 2.30–3.40 (8 H, br s), 3.77 (3 H, s), 6.25 (2 H, br s), 7.18 (2 H, d, *J* 8.0 Hz) and 7.27 (2 H, d, *J* 8.0 Hz); δ_C (75.5 MHz) 21.3 (CH_3), 50.1 (CH_3), 51.7 (CH_2), 67.4 (CH_2), 110.0 (C-2), 127.5 (CH), 128.3 (CH), 135.7, 138.5, 160.9 (C-3) and 172.0; *m*/*z* 276 (M^+).

Methyl (*E*)-3-amino-3-(4-methylphenyl)-2-piperidin-1-yl-propenoate 11

Piperidine (90 mg, 1.06 mmol) was added to a stirred solution of the azirine **1b** (220 mg, 1.16 mmol) in THF (5 ml) at 5 °C. The reaction was complete after 15 min. The solvent was removed to leave an oil. Flash chromatography gave [with ether–hexane (1 : 3)] the *3-aminopropenoate* **11** (210 mg, 72%) as an oil (Found: M^+; 274.168. $C_{16}H_{22}N_2O_2$ requires M, 274.168); ν_{max} (film)/cm^{-1} 3435, 3322 and 1660; δ_H (200 MHz) 0.85 (6 H, br s), 2.38 (3 H, s), 3.36 (4 H, br s), 3.77 (3 H, s), 6.25 (2 H, br s), 7.18 (2 H, d, *J* 8.0 Hz) and 7.27 (2 H, d, *J* 8.0 Hz); *m*/*z* 274 (M^+).

Methyl (*Z*)-3-amino-2-benzylamino-3-(2,6-dichlorophenyl)-propenoate 12

Benzylamine (120 mg, 1.12 mmol) was added to a stirred solution of the azirine **1a** (300 mg, 1.23 mmol) in DCM (10 ml) at RT. The reaction was slightly exothermic and was complete after 1 h. The solvent was removed to leave a solid. It was washed with cold ether–hexane (1 : 1) and the residue was crystallised to give the *3-aminopropenoate* **12** (280 mg, 71%), mp 83–84 °C (from ether–hexane) (Found: C, 58.0; H, 4.5; N, 7.9. $C_{17}H_{16}Cl_2N_2O_2$ requires C, 58.1; H, 4.6; N, 8.0%); ν_{max} (Nujol)/cm^{-1} 3450, 3333 and 1642; δ_H (300 MHz) 3.46 (3 H, s), 3.99 (2 H, s), 4.76 (2 H, br s) and 7.18–7.46 (8 H, m); δ_C (75.5 MHz) 51.0, 52.1, 111.1 (C-2), 127.0, 127.9, 128.2, 128.5, 129.7, 133.9, 135.9, 140.7, 146.2 (C-3) and 166.4; *m*/*z* 350/352 (M^+).

A sample of the aminopropenoate **12** was allowed to stand for 24 h in DCM containing 1 drop of acetic acid. The ^{1}H NMR spectrum showed additional signals at δ 3.72 (s), 3.79 (s) and 5.97 (s) in the ratio 2 : 3 : 2 which are tentatively assigned to the *E*-isomer.

Methyl 3-(2,6-dichlorophenyl)-2-(2-oxocyclohexyl)aziridine-2-carboxylate 13

4-Cyclohexen-1-ylmorpholine (200 mg, 1.20 mmol) was added to a solution of the azirine **1a** (300 mg, 1.23 mmol) in THF (3 ml) at RT. The solution was kept under N_2 for 19 h, after which period none of the azirine **1a** could be detected. The solvent was then removed and the residue was subjected to flash column chromatography which gave [with hexane–ether, gradient polarity] the *aziridine* **13** (98 mg, 24%), mp 73–74 °C (from ether–hexane) (Found: C, 56.2; H, 5.0; N, 4.1. $C_{16}H_{17}Cl_2NO_3$ requires C, 56.2; H, 5.0; N, 4.1%); ν_{max} (Nujol)/cm^{-1} 3305 (NH), 1722 (C=O) and 1702 (C=O); δ_H (300 MHz) 1.45–1.95 (3 H, m), 1.95–2.20 (3 H, m), 2.30–2.55 (2 H, m), 2.97 (1 H, d, *J* 9.5 Hz, exchanges with D_2O), 3.19 (1 H, d, *J* 9.5 Hz), 3.44 (3 H, s), 3.65 (1 H, dd, *J* 13.2 and 6.0 Hz), 7.15 (1 H, t, *J* 7.8 Hz) and 7.25 (2 H, d, *J* 7.8 Hz); δ_C (75.5 MHz) 24.7 (CH_2), 26.6 (CH_2), 27.1 (CH_2), 40.6 (C-3), 42.1 (CH_2), 45.4 (C-2), 49.5 (CH), 52.5 (CH_3), 127.7, 129.1, 131.9, 135.1, 171.4 and 209.8. The morpholine adducts **8** and **9** were also detected as reaction products.

Methyl (*E*)-3-amino-3-(2,6-dichlorophenyl)-2-(2-oxocyclopentylidene)propanoate 14

1-Cyclopenten-1-ylpyrrolidine (170 mg, 1.24 mmol) was added to a stirred solution of the azirine **1a** (300 mg, 1.23 mmol) in THF (5 ml) at RT. The reaction was complete after 15 min. The solvent was removed to leave an oil. Flash chromatography gave [with ether–hexane (1 : 3)] the *3-aminopropanoate* **14** (250 mg, 62%) as an oil (Found: C, 54.7; H, 4.6; N, 4.25. $C_{15}H_{15}Cl_2NO_3$ requires C, 54.9; H, 4.6; N, 4.3%); ν_{max} (film)/cm^{-1} 3398, 3331, 1725 and 1631; δ_H (300 MHz) 1.60–1.90 (3 H, m), 1.95 (2 H, br s), 2.05–2.15 (3 H, m), 3.87 (3 H, s), 5.68 (1 H, t, *J* 2.7 Hz), 7.17 (1 H, t, *J* 8.1 Hz) and 7.33 (2 H, d, *J* 8.1 Hz); δ_C (75.5 MHz) 19.4 (CH_2), 27.1 (CH_2), 37.8 (CH_2), 52.2 (CH_3), 53.4 (CH), 129.3 (CH), 129.4 (CH), 133.5 (C), 135.0 (C), 138.2 (C), 141.8 (C), 169.1 (C=O) and 205.5 (C=O); *m*/*z* 327/329 (M^+).

Methyl 4-acetyl-2-(2,6-dichlorophenyl)-5-methylpyrrole-3-carboxylate 15

Pentane-2,4-dione (130 mg, 1.30 mmol) was added to a stirred solution of the azirine **1a** (300 mg, 1.23 mmol) in dry THF (5 ml) at RT. After 2 days the solvent was removed under reduced pressure. Flash chromatography of the residue [ether–hexane (gradient elution)] gave a fraction that after crystallisation was identified as the *pyrrole* **15** (90 mg, 22%), mp 162–164 °C (from hexane) (Found: C, 55.5; H, 4.0; N, 4.3. $C_{15}H_{13}Cl_2NO_3$ requires C, 55.2; H, 4.0; N, 4.3%); ν_{max} (Nujol)/cm^{-1} 3252 (NH), 1679 (C=O) and 1660 (C=O); δ_H (300 MHz) 2.37 (3 H, s), 2.43 (3 H, s), 3.60 (3 H, s), 7.26 (1 H, t, *J* 7.5 Hz), 7.36 (2 H, d, *J* 7.5 Hz) and 9.07 (1 H); δ_C (75.5 MHz) 12.9, 31.0, 51.3, 114.6, 122.7, 127.9, 129.3, 130.6, 130.8, 134.4, 136.5, 164.6 and 198.5; *m*/*z* 325/327 (M^+).

Methyl 3-(2,6-dichlorophenyl)-2-(tetrahydrofuran-2-yl)aziridine-2-carboxylate 16

(a) Diethyl malonate (220 mg, 1.37 mmol) was added to a solution of the azirine **1a** (300 mg, 1.23 mmol) in THF (5 ml) at RT. The solution was kept under N_2 until the azirine **1a** could no longer be detected (3 days). The solvent was then removed and the residue was subjected to flash column chromatography which gave [with hexane–ether (gradient elution)] the *aziridine* **16** (50 mg, 13%), mp 73–74 °C (from ether–hexane) (Found: C, 53.45; H, 4.8; N, 4.4. $C_{14}H_{15}Cl_2NO_3$ requires C, 53.2; H, 4.8; N, 4.4%); ν_{max} (Nujol)/cm^{-1} 3295 (NH) and 1724 (C=O); δ_H (300 MHz) 1.40–1.80 (2 H, m), 1.80–2.20 (3 H, m), 3.09 (1 H, s), 3.55 (3 H, s), 3.80–3.90 (2 H, m), 4.90 (1 H, br s), 7.13 (1 H, t, *J* 7.8 Hz) and 7.27 (2 H, d, *J* 7.8 Hz); δ_C (75.5 MHz) 26.2 (CH_2), 27.2 (CH_2), 41.2 (C-3), 47.6 (C-2), 52.6 (CH_3), 68.8 (CH_2), 76.2 (CH), 128.4, 129.1, 131.8, 135.9 and 170.9.

(b) A solution of the azirine **1a** (300 mg, 1.23 mmol) and benzoyl peroxide (150 mg, 0.62 mmol) in THF (5 ml) was heated under reflux for 0.5 h, after which time none of the azirine **1a** remained. Flash chromatography gave [with ether–hexane (3:17)] the aziridine **16** (100 mg, 26%), which was identical (mp, NMR) to the sample from (a).

Crystal data for 8

$C_{14}H_{16}Cl_2N_2O_3$, $M = 331.20$. Monoclinic, $a = 9.620(2)$, $b = 14.594(2)$, $c = 11.666(2)$ Å, $\beta = 94.72(1)°$, $V = 1632.3(4)$ Å^3, $F(000)$ 688, $\lambda = 0.710\ 69$ Å, $T = 293.0$ K, space group $P2_1/n$ (#14), $Z = 4$, $D_c = 1.348$ g cm^{-3}, clear prism, 0.300 × 0.100 × 0.200 mm.

Data collection and processing. Rigaku AFC6S diffractometer, graphite-monochromated Mo-Kα radiation, ω–2θ scans to a maximum 2θ value of 50.1°; 3196 reflections collected of which 3013 were unique ($R_{int} = 0.031$). The intensities of three representative reflections which were measured after every 150 reflections remained constant throughout data collection; no decay correction was applied. An empirical absorption correction, based on azimuthal scans of several reflections, was applied which resulted in transmission factors ranging from 0.72 to 1.00. The data were corrected for Lorentz and polarization effects.

Structure solution and refinement. The structure was solved by direct methods.[16] Non-H atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 1905 observed reflections ($I > 2.00\sigma(I)$) and 190 variable parameters and converged (largest parameter shift was 0.00 times its esd) with weighted and unweighted agreement factors of:

$$R = \Sigma||F_o| - |F_c||/\Sigma|F_o| = 0.050$$

$$R_w = [(\Sigma w(|F_o| - |F_c|)^2/\Sigma wF_o^2)]^{1/2} = 0.053$$

The standard deviation of an observation of unit weight was 1.72. The weighting scheme was based on counting statistics and included a factor ($p = 0.030$) to downweight the intense reflections. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.25 and −0.34 e Å^{-3}, respectively. All calculations were performed using the TEXSAN crystallographic structure package of the Molecular Structure Corporation.[17]

CCDC reference number 207/317.

Crystal data for 16

$C_{14}H_{15}Cl_2NO_3$, $M = 316.18$. Monoclinic, $a = 9.517(3)$, $b = 8.184(5)$, $c = 19.218(3)$ Å, $\beta = 100.13(2)°$, $V = 1473.5(9)$ Å^3, $F(000)$ 656, $\lambda = 0.710\ 69$ Å, $T = 153.0$ *K*, space group $P2_1/c$ (#14), $Z = 4$, $D_c = 1.425$ g cm^{-3}, clear prism.

Data collection and processing. Rigaku AFC6S diffractometer, graphite-monochromated Mo-Kα radiation, ω–2θ scans to a maximum 2θ value of 45.1°; 2251 reflections collected of which 2107 were unique ($R_{int} = 0.149$). No decay correction was applied. Azimuthal scans of several reflections indicated no need for an absorption correction. The data were corrected for Lorentz and polarization effects.

Structure solution and refinement. The structure was solved by and expanded using Fourier techniques.[18] Non-H atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement was based on 1937 observed reflections ($I > 0.00\sigma(I)$) and 181 variable parameters and converged (largest parameter shift was 0.01 times its esd) with weighted and unweighted agreement factors of:

$$R = \Sigma||F_o| - |F_c||/\Sigma|F_o| = 0.067$$

$$R_w = [(\Sigma w(|F_o| - |F_c|)^2/\Sigma wF_o^2)]^{1/2} = 0.121$$

The standard deviation of an observation of unit weight was 2.52. The weighting scheme was based on counting statistics and included a factor ($p = 0.030$) to downweight the intense reflections. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.61 and −0.65 e Å^{-3}, respectively. All calculations were performed using the TEXSAN crystallographic structure package of the Molecular Structure Corporation.[17]

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