Observations on the ring opening reactions of 2-methyleneaziridines with acid chlorides and alkyl chloroformates

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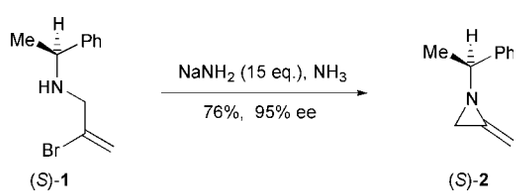
A variety of 1-alkyl-2-methyleneaziridines react with alkyl chloroformates (MeO_2CCl, $PhCH_2O_2CCl$) or acid chlorides (AcCl, *p*-$NO_2C_6H_4COCl$) at room temperature in nonpolar solvents (CH_2Cl_2, THF, toluene) to produce ring opened enamide products in moderate to good yields. Mechanistic studies using 3-deuterio-*N*-(1-phenylethyl)-2-methyleneaziridine suggest the reactions proceed by initial *N*-acylation to form the corresponding aziridinium cation (*e.g.* **27**) which subsequently undergoes regiospecific ring opening by chloride ion at the sp^3 hybridised aziridine carbon atom to produce the observed products.

Introduction

2-Methyleneaziridines are small but densely functionalised heterocycles which possess a substantial amount of ring strain. Despite the fact that this unusual ring system has been known for over 40 years, rather little is known about its chemistry. Methyleneaziridines were unknowingly first made in 1951 by Pollard and Parcell when they treated *N*-(2-bromoallyl)alkylamines with sodium amide in liquid ammonia.[1] It was several years later before Bottini and Roberts correctly identified the products from these reactions as the corresponding 1-alkyl-2-methyleneaziridines.[2] We have used this methodology to make a variety of chiral, nonracemic methyleneaziridines which we hope may ultimately find use in asymmetric synthesis.[3,4] For example, we have prepared methyleneaziridine (*S*)-**2** as a single enantiomer by ring closure of the corresponding *N*-(2-bromoallyl)amine **1**, itself readily derived from (*S*)-α-methylbenzylamine (Scheme 1).[3] Few other general methods for the



Scheme 1

preparation of 2-methyleneaziridines currently exist. De Kimpe *et al.* have reported that these heterocycles can be made by dehydrobromination of 2-(bromomethyl)aziridines using potassium *tert*-butoxide.[5] Alternatively, nitrene additions to allenes have been shown to furnish 2-methyleneaziridines albeit in very poor yields.[6,7]

To date, most investigations into the reactivity of the methyleneaziridine ring system have focused on cycloaddition chemistry of the exocyclic double bond. Methyleneaziridines react with tetracyanoethylene to produce 1,1,2,2-tetracyano-5-azaspiro[3.2]hexanes *via* [2π + 2π] cycloaddition reactions.[8,9] Akasaka *et al.* have shown that reaction of 2-adamantylidene-*N*-*tert*-butylaziridine with singlet oxygen produces the corresponding 1,2-dioxetane as an unstable intermediate by a related [2π + 2π] cycloaddition.[10] Methyleneaziridines also react with alkyl[11] and sulfonyl azides[5] to give triazoles and 2-(sulfonylimino)azetidines respectively. These observations have been rationalised in terms of initial [3π + 2π] cycloaddition between the azide moieties and the alkene, followed by subsequent rearrangements of the resulting spirotriazolines. In other chemistry, Alper and Hamel have shown that methyleneaziridines undergo palladium catalysed ring expansion reactions in the presence of carbon monoxide yielding the corresponding α-methylene-β-lactams.[12] Despite the fact that simple aziridines undergo a diverse range of ring cleavage reactions, few articles relating to ring opening reactions of the more strained methyleneaziridine ring system have been published.[2,11,13,14] Bottini and Roberts have reported that 1-ethyl-2-methyleneaziridine, upon treatment with hydrochloric acid, yields chloroacetone presumably *via* ring opening of the protonated methyleneaziridine and subsequent hydrolysis. Chloroacetone from this reaction was isolated as its 2,4-dinitrophenylhydrazone derivative although the overall yield for this sequence was not disclosed.[2] Crandall *et al.* have reported that phenol effects ring opening of 1-isopropyl-2-methyleneaziridine by initial Markovnikov addition to the alkene double bond and subsequent fission of the ring to give *N*-isopropylaminopropan-2-one diphenyl acetal after addition of a second equivalent of phenol.[11] A detailed mechanistic study relating to the protonation and subsequent ring opening reactions of 1-methyl-2-methyleneaziridine using FSO_3H–SbF_5 has been described.[13] Finally, it has been postulated that the decomposition of 3-lithio-1-*tert*-butyl-2-methyleneaziridine involves nucleophilic ring opening of 1-*tert*-butyl-2-methyleneaziridine by this organolithium species.[14] In this paper, we disclose studies from our laboratories which establish that methyleneaziridines can be induced to undergo smooth nucleophilic ring opening reactions in the presence of a variety of alkyl chloroformates and acid chlorides under relatively mild reaction conditions and provide some mechanistic insights into the ring opening reactions of 2-methyleneaziridines.[15]

Results and discussion

Several new 2-substituted methyleneaziridines were made for the purposes of this investigation. These were made in two simple steps by *N*-alkylation of the appropriate primary amine with 2,3-dibromopropene in the presence of potassium carbonate and subsequent ring closure using excess sodium amide in

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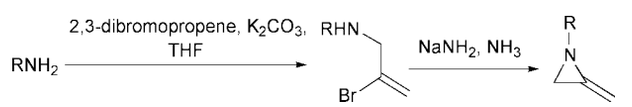
liquid ammonia (Table 1).[1,2] Pure methyleneaziridines were obtained in modest but acceptable yields after chromatography on basic alumina (**8**) or bulb to bulb distillation (**7**, **9**, **10**). The successful synthesis of 1-benzyl-2-methyleneaziridine **7** by this method is notable as we had previously incorrectly reported that it cannot be made using the Pollard and Parcell cyclisation protocol.[3] It transpires that careful control of the reaction conditions are essential if this compound is to be successfully produced and isolated. This discovery followed earlier work in which we had determined that the optimal time for ring closure can be highly dependent on the structure of the substrate {1-trityl-2-methyleneaziridine = 6 h[3] *cf.* 1-[1-(1-phenyl-2-phenylmethoxy)ethyl]-2-methyleneaziridine = 90 s[4]). Under optimised conditions [$NaNH_2$ (5 equiv.), 15 min] amine **3** yielded a 8 : 73 : 19 ratio of starting material, 1-benzyl-2-methyleneaziridine **7** and the corresponding acetylene ($PhCH_2NHCH_2$-CCH). The unwanted secondary amines could be conveniently removed by washing with 0.1 M acetic acid prior to distillation to give pure 1-benzyl-2-methyleneaziridine in 38% isolated yield. Other methyleneaziridines used in this study, (*S*)-**2**, (*S*)-**11**, (*S*)-**12** and (*S*)-**13** were made in accordance with published methods.[3,4]

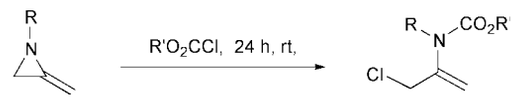
Table 1 Synthesis of 2-methyleneaziridines



R	*N*-(2-Bromopropenyl)amine (yield, %)	Methyleneaziridine (yield, %)
$-CH_2Ph$	**3** (68)	**7** (38)
–cyclohexyl	**4** (86)	**8** (78)
$-CH_2CH_2CH_2CH_2OH$	**5** (55)	**9** (36)
$-CH_2CH_2CH_2CH(OMe)_2$	**6** (72)	**10** (40)

With a variety of methyleneaziridines in hand, we began to examine their ring opening reactions. Our initial investigations focused on the use of alkyl chloroformates in such reactions.[16] Treatment of methyleneaziridine (*S*)-**2** with methyl chloroformate (1.1 equiv.) in dichloromethane at room temperature gave enamide **14** in 85% yield (Table 2). Other solvents have been used for this transformation including toluene (63%) and THF (69%), although in general, it appears that the best yields are obtained in dichloromethane. The structure of enamide **14** was readily elucidated using a combination of spectroscopic techniques. The formation of an addition product and the incorporation of one chlorine atom was readily ascertained by mass spectrometry. The presence of the new carbamate group was readily established by infrared (1701 cm^{-1}) and ^{13}C NMR spectroscopy (δ_C 155.3). Detailed analysis of the ^1H NMR spectrum of **14** revealed a pair of doublets centred at δ 3.67 and 3.93 displaying a large geminal coupling constant (*J* 13.5 Hz), and singlets at δ 4.91 and 5.40, which we assigned to the CH_2Cl and the enamide double bond respectively. Particularly noteworthy was the quartet arising from the methine hydrogen adjacent to the nitrogen atom which was significantly further downfield than in the corresponding methyleneaziridine (δ 5.48 *cf.* 2.93). Additional evidence in support of this structure comes from the fact that the ^1H NMR spectrum for **14** closely resembles that of related *N*-benzyl-*N*-vinylcarbamates prepared by Tamura *et al.* using an alternative route.[17] Further studies have established that the ring opening reaction of methyleneaziridines with methyl chloroformate is quite general. Considerable variation in the structure of the methyleneaziridine can be accommodated without detrimental effects (Table 2). The only unsuccessful reaction was found to be that with sterically encumbered 1-trityl-2-methylenaziridine **11**. Treatment of this compound with 1.1 equivalents of methyl chloroformate in toluene failed to give the desired ring opened product. Even after 4 days at reflux only starting material was recovered. Whilst we have not studied the use of a wide variety of alkyl chloroformates in this process, we have ascertained that benzyl chloroformate can also be used (**2**→**21**). All the reactions involving homochiral methyleneaziridines produce enamides which display significant optical rotations although the enantiomeric purities of the products have not been determined at the present time.

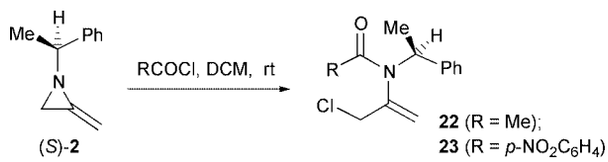
Table 2 Ring opening reactions of 2-methyleneaziridines with alkyl chloroformates



Starting material	R	R′	Product (yield, %)
2	(*S*)–CH(Me)Ph	Me	**14** (85)[a]
7	$-CH_2Ph$	Me	**15** (51)[a]
8	–cyclohexyl	Me	**16** (68)[b]
9	$-CH_2CH_2CH_2CH_2OH$	Me	**17** (57)[a]
10	$-CH_2CH_2CH_2CH(OMe)_2$	Me	**18** (40)[a]
11	$-CPh_3$	Me	—
12	(*S*)-CH(Ph)CH_2OBn	Me	**19** (52)[b]
13	(*S*)-CH(^{i}Pr)CH_2OBn	Me	**20** (74)[a]
2	(*S*)-CH(Me)Ph	CH_2Ph	**21** (63)[b]

[a] Performed in dichloromethane. [b] Performed in toluene.

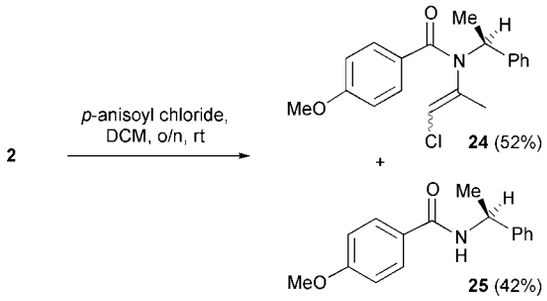
Next, we chose to examine whether acid chlorides would react with 2-methyleneaziridines in a similar fashion. Treatment of methyleneaziridine (*S*)-**2** with acetyl chloride (1.1 equiv.) for 3 hours proceeded smoothly to furnish enamide **22** in 67% isolated yield after column chromatography (Scheme 2). All



Scheme 2

spectroscopic data were in complete agreement with the assigned structure. However, we did observe line broadening in the ^1H NMR spectrum, presumably due to relatively slow rotation around the amide bond. It should be stressed that enamide **22** proved much less stable than the corresponding carbamate **14**, and it was essential to use shorter reaction times and perform the purification quickly to obtain reasonable yields of product. Similarly, when (*S*)-**2** was reacted with *p*-nitrobenzoyl chloride (1.1 equiv., DCM, 4 h) the expected enamide **23** was produced in 76% yield after aqueous work-up and subsequent silica gel chromatography.

Interestingly, attempts to isolate the corresponding enamide products by reaction of (*S*)-**2** with more electron-rich aromatic acid chlorides (benzoyl chloride, *p*-anisoyl chloride) were complicated by side reactions. For example, treatment of (*S*)-**2** with *p*-anisoyl chloride (1.1 equiv., DCM, 24 h) produced enamide **24** and amide **25** as the only isolable products (Scheme 3). Isomerised enamide **24** was obtained as a single, and as yet undetermined, geometric isomer as judged by ^1H NMR spectroscopy. We speculate that this reaction proceeds along similar lines to that observed with *p*-nitrobenzoyl chloride (Scheme 2), but that the initially formed enamide product, being more electron-rich, is prone to *C*-protonation by traces of acid present in the reaction mixture. Further loss of a proton from the resulting *N*-acyliminium cation leads to the observed conjugated enamide **24**, whereas hydrolysis of this intermediate

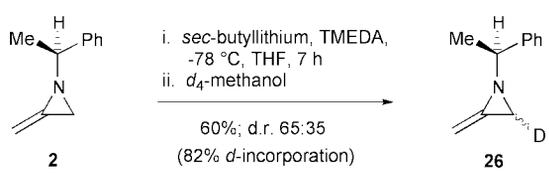


Scheme 3

N-acyliminium cation by adventitious water accounts for the formation of amide **25**.

We postulate that all the ring opening reactions proceed *via* an *N*-acylaziridinium cation which is subsequently ring opened by the chloride anion generated in the reaction mixture (*vide infra*). The lack of reactivity of 1-trityl-2-methyleneaziridine **11** towards methyl chloroformate is consistent with this mechanism, since the sterically blocked nitrogen lone pair of this substrate precludes formation of the reactive *N*-acylaziridinium cation. We reasoned that other reagents capable of acylating or alkylating the nitrogen atom might induce related ring opening reactions. However, treatment of methyleneaziridine (*S*)-**2** with acetic anhydride (1.1 equiv., toluene), even at elevated temperatures, yielded only recovered starting material as determined by ^{1}H NMR spectroscopy. Other reagents such as methanesulfonyl chloride (1.1 equiv., DCM, rt or −78 °C), diphenylphosphoryl azide (1.1 equiv., DCM, rt), trimethylsilyl chloride (1.1 equiv., DCM, rt) or *tert*-butyldiphenylsilyl chloride (1.1 equiv., DCM, rt) produced complex mixtures of products from which no discernible products could be isolated.

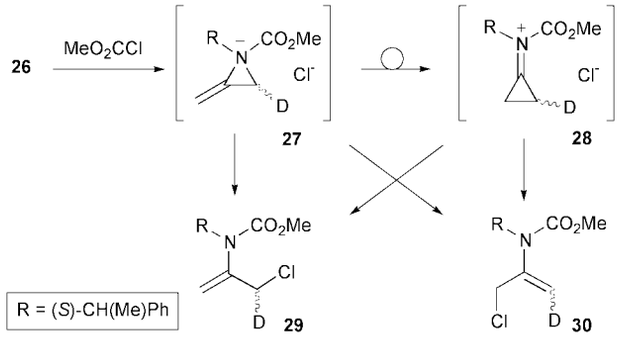
In order to elucidate the mechanism of the ring opening reactions observed with acid chlorides and alkyl chloroformates, we prepared deuterium labelled methyleneaziridine **26** in a regiospecific fashion. This compound was made by lithiation of methyleneaziridine (*S*)-**2** with 1.1 equivalents of *sec*-butyllithium and subsequent deuteration with d_4-methanol according to published methods (Scheme 4).[14,18] The extent of



Scheme 4

deuterium incorporation was estimated to be approximately 82% by ^{1}H NMR analysis. Furthermore, it was judged to be a 65 : 35 mixture of diastereomers by integration of the remaining diastereotopic aziridine hydrogens at δ 2.08 (0.65H, s) and 1.99 (0.35H, s). Clearly, the α-methylbenzyl group of (*S*)-**2** exerts a modest stereochemical influence on this lithiation–deuteration process.

After initial formation of the *N*-acylaziridinium cation, ring fission could proceed by several alternative pathways which can be differentiated using *C*-3 deuterated methyleneaziridine **26** (Scheme 5). Direct nucleophilic attack by a chloride anion at the methylene carbon atom of the aziridine ring of **27** would be expected to produce enamide **29**, whereas the alternative S_N' process involving chloride anion attack at the exocyclic carbon of the double bond would lead to the isomeric enamide **30**. On the basis of the work undertaken by Jongejan *et al*. on the rearrangement reactions of 2-methyleneaziridinium cations, one must also consider the possible involvement of cyclopropaniminium cation **28**.[13] If ring opening was to occur *via* such an intermediate, nearly equal quantities of the two enamides **29** and **30** would be expected. In fact, treatment of deuterated



Scheme 5

methyleneaziridine **26** with methyl chloroformate in toluene yields enamide **29** in 65% yield as the sole product. The deuterium atom was located exclusively at the sp^3 hybridised carbon atom as determined by both ^{1}H and ^{13}C NMR spectroscopy. This study suggests that these ring opening reactions proceed *via* direct ring opening of the initially formed aziridinium cation.

In summary, we have established that 2-methyleneaziridines can readily be ring opened to a variety of functionalised enamide products using alkyl chloroformates and acid chlorides under mild reaction conditions. In future work, we wish to establish if Lewis acids will complex to and hence activate 2-methyleneaziridines to ring opening with external nucleophiles. The outcome of these studies will be disclosed in due course.

Experimental

General

Reactions requiring anhydrous conditions were performed using oven-dried glassware and conducted under a positive pressure of nitrogen. Anhydrous solvents were prepared in accordance with standard protocols, or alternatively purchased from Aldrich in Sure/Seal™ bottles. Light petroleum refers to petroleum spirit with a boiling point in the range 40–60 °C. IR spectra were recorded (4000–600 cm^{-1}) on a Nicolet FT-205 spectrometer or a Nicolet Magna-550 FT-IR spectrometer with internal calibration. Spectra were recorded as thin films, as solutions in DCM or as Nujol® mulls. NMR spectra were recorded on a JEOL GSX-270 instrument or alternatively on Bruker ACF-250, ACF-300 or DRX 400 spectrometers with either TMS or residual protic solvent as internal reference. Multiplicities in ^{13}C NMR spectra refer to the signals in the off-resonance spectra and were elucidated using the distortionless enhancement by polarisation transfer (DEPT) spectral editing technique, with secondary pulses at 90 and 135°. Elemental analyses were carried out on a Perkin-Elmer 2400 CHN elemental analyser. Mass spectra and accurate masses were recorded under EI$^+$ or CI$^+$ conditions on a VG Analytical ZAB-E instrument at the EPSRC Mass Spectrometry Centre, University College, Swansea or under EI$^+$ conditions on a Kratos Profile HV-3 mass spectrometer. Optical rotations were determined on the sodium D-line using an AA-1000 polarimeter and are given in 10^{-1} deg cm^2 g^{-1}. Analytical thin layer chromatography (TLC) was performed on precoated aluminium backed silica plates (Fluka Kieselgel 60 F_{254}).

N-(2-Bromoprop-2-enyl)benzylamine 3

To a stirred solution of benzylamine (5.0 g, 46.7 mmol) in THF (40 ml) was added 2,3-dibromopropene (4.66 g, 23.3 mmol) dropwise and the resulting solution heated under reflux for 12 hours. Potassium carbonate (12.8 g, 92.6 mmol) was then added and the mixture heated for a further 12 hours. On cooling, the mixture was filtered and the precipitate washed with diethyl ether. The filtrate was washed with 10% sodium hydroxide solution (2 × 10 ml) and extracted with diethyl ether (3 × 25 ml).

The combined organic extracts were washed with water (2 × 10 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (5% ethyl acetate–light petroleum using silica pretreated with triethylamine) gave **3** (3.60 g, 68%) as an orange oil. ν_{max} (film)/cm^{-1} 3500–3300, 2900, 1626, 1454, 736; δ_H (270 MHz, $CDCl_3$) 7.35–7.25 (5H, m, ArH), 5.81 (1H, d, *J* 1.6, =CH), 5.61 (1H, d, *J* 1.6, =CH), 3.75 (2H, s, CH_2Ph), 3.48 (2H, s, CH_2N), 1.76 (1H, br s, NH); δ_C (67.5 MHz, $CDCl_3$) 140.1 (s), 133.9 (s), 129.0 (d), 128.7 (d), 127.7 (d), 118.3 (t), 57.0 (t), 51.9 (t); *m*/*z* 227/225 (M^+), 146 ($M^+ - Br$), 120, 91, 77 (Found: M^+, 225.0153. $C_{10}H_{12}BrN$ requires 225.0154).

N-(2-Bromoprop-2-enyl)cyclohexylamine 4

To a stirred solution of cyclohexylamine (4.0 g, 40.3 mmol) in THF (50 ml) was added 2,3-dibromopropene (3.66 g, 18.3 mmol) dropwise and the resultant solution was heated under reflux for 24 hours. Potassium carbonate (5.57 g, 40.3 mmol) was added and the mixture refluxed for a further 7 hours. On cooling, the mixture was filtered and the precipitate washed with diethyl ether. The filtrate was washed with 10% sodium hydroxide (2 × 10 ml) and the aqueous layer re-extracted with diethyl ether (3 × 20 ml). The combined organic extracts were washed with water (2 × 10 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (60% light petroleum–diethyl ether) gave **4** (3.43 g, 86%) as an orange oil. ν_{max} (film)/cm^{-1} 3390, 2927, 1626, 1450; δ_H (250 MHz, $CDCl_3$) 5.78 (1H, d, *J* 1.5, =CH), 5.54 (1H, d, *J* 1.5, =CH), 3.48 (2H, s, CH_2N), 2.49 (1H, m, CHN), 1.70–0.85 (11H, m, 5 × CH_2 and NH); δ_C (62.9 MHz, $CDCl_3$) 134.1 (s), 117.0 (t), 54.4 (t), 54.2 (d), 33.2 (t), 26.0 (t), 24.7 (t); *m*/*z* 219/217 (M^+), 174, 138, 82, 55 (Found: M^+, 217.0463. $C_9H_{16}BrN$ requires 217.0466).

4-[*N*-(2-Bromoprop-2-enyl)amino]butan-1-ol 5

2,3-Dibromopropene (5.56 g, 27.8 mmol) was added to a stirred solution of 4-aminobutan-1-ol (5.00 g, 56.1 mmol), potassium carbonate (3.87 g, 28.0 mmol) and THF (60 ml). The resultant mixture was stirred under reflux for 48 hours. On cooling, the reaction mixture was filtered and the precipitate washed with diethyl ether. 10% NaOH solution was added to the filtrate and the organic layer was separated. Sodium chloride was added to the aqueous layer and after 2 minutes, the solution was filtered and extracted with DCM (3 × 15 ml). The combined organic extracts were dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (2% methanol–DCM using silica pre-treated with triethylamine) gave **5** (3.20 g, 55%) as a reddish-orange oil. ν_{max} (film)/cm^{-1} 3500–3200, 2924, 1623, 1449, 1050, 891; δ_H (400 MHz, $CDCl_3$) 5.73 (1H, s, =CH), 5.25 (1H, s, =CH), 3.56 (2H, t, *J* 5.4, C*H*$_2$OH), 3.40 (2H, s, NC*H*$_2$C(Br)=), 3.11 (2H, br s, OH and NH), 2.56 (2H, t, *J* 6.0, CH_2N), 1.62–1.54 (4H, m, 2 × CH_2); δ_C (100.6 MHz, $CDCl_3$) 132.1 (s), 118.2 (t), 62.4 (t), 57.0 (t), 47.4 (t), 31.6 (t), 27.5 (t); *m*/*z* 210/208 (MH^+), 190, 148, 136 (Found: M^+, 207.0254. $C_7H_{14}NOBr$ requires 207.0259).

N-(2-Bromoprop-2-enyl)-4,4-dimethoxybutylamine 6

2,3-Dibromopropene (1.20 g, 6.00 mmol) was added to a stirred solution of 4-aminobutyraldehyde dimethyl acetal (1.62 g, 12.2 mmol), potassium carbonate (0.84 g, 6.1 mmol) and THF (50 ml) and the resultant mixture stirred under reflux for 72 hours. On cooling, the reaction mixture was filtered and the precipitate washed with DCM. The filtrate was washed with 10% NaOH (2 × 10 ml) and the combined aqueous phases extracted with DCM (3 × 10 ml). The organic extracts were washed with water (3 × 10 ml), dried over $MgSO_4$ and filtered. Removal of the solvent under reduced pressure and subsequent column chromatography (2% methanol–DCM using silica pre-treated with triethylamine) gave **6** (1.10 g, 72%) as a light orange oil. ν_{max} (film)/cm^{-1} 3300, 2947, 1627, 1457, 1296; δ_H (300 MHz, $CDCl_3$) 5.70 (1H, s, =CH), 5.56 (1H, s, =CH), 4.32 (1H, t, *J* 5.4, CH), 3.46 (2H, s, $NCH_2C(Br)$=), 3.27 (6H, s, 2 × OCH_3), 2.51 (2H, t, *J* 7.0, NCH_2), 1.61–1.45 (5H, m, 2 × CH_2 and NH); δ_C (75 MHz, $CDCl_3$) 133.7 (s), 117.4 (t), 104.3 (d), 57.4 (t), 52.7 (q), 47.4 (t), 30.2 (t), 24.9 (t); *m*/*z* 254/252 (MH^+), 238, 236, 190, 188, 75 (Found: MH^+, 252.0606. $C_9H_{19}NO_2{}^{79}Br$ requires 252.0599).

1-Benzyl-2-methyleneaziridine 7[5]

To a three-necked flask fitted with a dry ice condenser, calcium chloride drying flask and gas inlet was added sodium amide (1.89 g, 48.4 mmol) and the system flushed with ammonia. A dry ice–acetone mixture was added to the condenser and ammonia (50 ml) condensed into the flask. Compound **3** (2.19 g, 9.69 mmol) was added to the mixture in one portion and the resulting solution stirred for 15 minutes. The reaction mixture was diluted with diethyl ether (10 ml) and quenched by the dropwise addition of water (10 ml) (CAUTION). After the ammonia had been evaporated, water (10 ml) and diethyl ether (10 ml) were added. The organic phase was separated and the aqueous phase extracted with diethyl ether (3 × 15 ml). The combined organic extracts were washed with 10% sodium hydroxide (2 × 10 ml), then water (2 × 10 ml), followed by washing with 0.1 M acetic acid (2 × 10 ml). The combined organic extracts were finally washed with sodium hydrogen carbonate (2 × 10 ml) and dried over $MgSO_4$. Bulb to bulb distillation (bp 100 °C/0.9 mmHg) gave **7** (0.54 g, 38%) as a colourless oil. δ_H (300 MHz, $CDCl_3$) 7.35–7.29 (5H, m, ArH), 4.70 (2H, t, *J* 1.1, =CH_2), 3.68 (2H, s, C*H*$_2$Ph), 2.12 (2H, t, *J* 1.1, aziridine CH_2); *m*/*z* 144 ($M - H^+$), 105, 91, 77, 54 (Found: M^+, 145.0892. $C_{10}H_{11}N$ requires 145.0891). Data consistent with those described in the literature.[5]

1-(Cyclohexyl)-2-methyleneaziridine 8

To a three-necked flask fitted with a dry ice condenser, calcium chloride drying flask and gas inlet was added sodium amide (20.55 g, 527 mmol). The system was flushed with ammonia. A dry ice–acetone mixture was then added to the condenser and ammonia condensed into the flask (200 ml). Compound **4** (7.66 g, 35.1 mmol) was added and the reaction mixture allowed to stir for 3 hours. Diethyl ether (30 ml) was added followed by the dropwise addition of water (40 ml) (CAUTION) and the ammonia was allowed to evaporate overnight. Water (20 ml) was added followed by diethyl ether (20 ml) and the mixture was stirred for 2 minutes. The organic phase was separated and the aqueous phase extracted with diethyl ether (2 × 30 ml). The combined organic extracts were washed with 10% sodium hydroxide (2 × 30 ml), then water (2 × 30 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (light petroleum using basic alumina {Brockmann Grade I}) gave **8** (3.78 g, 78%) as a yellow oil. ν_{max} (film)/cm^{-1} 2930, 1770, 1450; δ_H (250 MHz, $CDCl_3$) 4.73 (1H, m, =CH), 4.62 (1H, br s, =CH), 1.99 (2H, br s, aziridine CH_2), 1.91–1.19 (11H, m, 5 × CH_2 and CH); δ_C (62.9 MHz, $CDCl_3$) 137.1 (s), 82.1 (t), 67.1 (d), 32.4 (t), 28.7 (t), 25.6 (t), 24.3 (t); *m*/*z* 137 (M^+), 83, 28 (Found: MH^+, 138.1281. $C_9H_{16}N$ requires 138.1282).

4-(2-Methyleneaziridin-1-yl)butan-1-ol 9

To a three-necked flask fitted with a dry ice condenser, calcium chloride drying flask and gas inlet was added sodium amide (3.03 g, 77.7 mmol) and the system flushed with ammonia. A dry ice–acetone mixture was added to the condenser and ammonia (50 ml) was condensed into the flask. Compound **5** (1.08 g, 5.19 mmol) was added in a small volume of diethyl ether to the mixture dropwise and the solution stirred for 30

minutes. The reaction mixture was then diluted with diethyl ether (10 ml) and quenched by the dropwise addition of water (*ca*. 15 ml) (CAUTION). After the ammonia had evaporated overnight, water (10 ml) and DCM (10 ml) were added and the mixture stirred for 2 minutes. The organic phase was separated and the aqueous phase extracted with DCM (3 × 10 ml). The combined organic extracts were washed with 10% NaOH (2 × 10 ml), 0.1 M acetic acid, dried over $MgSO_4$ and the solvent removed under reduced pressure to give the crude product. Purification by bulb to bulb distillation (bp *ca.* 100 °C/2 mmHg) gave **9** (0.24 g, 36%) as a pale yellow oil. ν_{max} (film)/cm^{-1} 3400–3200, 2939, 2864, 1771; δ_H (300 MHz, $CDCl_3$) 4.67 (1H, s, =CH), 4.61 (1H, s, =CH), 3.90 (1H, br s, OH), 3.53 (2H, t, *J* 6.0, C*H*$_2$OH), 2.46 (2H, t, *J* 6.5, CH_2N), 1.97 (2H, s, aziridine CH_2), 1.57 (4H, m 2 × CH_2); δ_C (100.6 MHz, C_6D_6) 137.5 (s), 82.3 (t), 62.1 (t), 59.3 (t), 30.8 (t), 30.2 (t), 26.7 (t); *m*/*z* 127 (M^+), 126, 110, 98, 96, 73, 72, 71, 60, 55 (Found: M^+, 127.0995. $C_7H_{13}NO$ requires 127.0997).

1-(4,4-Dimethoxybutyl)-2-methyleneaziridine 10

To a three-necked flask fitted with a dry ice condenser, calcium chloride drying flask and gas inlet was added sodium amide (1.37 g, 35.1 mmol) and the system flushed with ammonia. A dry ice–acetone mixture was added to the condenser and ammonia (40 ml) was condensed into the flask. Compound **6** (0.59 g, 2.34 mmol) in a small volume of diethyl ether was added dropwise to the mixture and the resultant solution stirred for 30 minutes. The mixture was then diluted with diethyl ether (10 ml) and the reaction quenched by the dropwise addition of water (20 ml) (CAUTION). After the ammonia had evaporated overnight, water (10 ml) and DCM (10 ml) were added and the mixture stirred for 2 minutes. The organic phase was separated and the aqueous phase extracted with DCM (3 × 10 ml). The combined organic extracts were washed with 10% NaOH (2 × 10 ml), 0.1M acetic acid, dried over $MgSO_4$ and the solvent removed under reduced pressure to give the crude product. Purification by bulb to bulb distillation (bp *ca.* 100 °C/2 mmHg) gave **10** (0.16 g, 40%) as colourless oil. ν_{max} (film)/cm^{-1} 2954, 1769, 1649; δ_H (300 MHz, $CDCl_3$) 4.66 (1H, s, =CH), 4.60 (1H, s, =CH), 4.34 (1H, t, *J* 5.4, $CH(OMe)_2$), 3.26 (6H, br s, OCH_3) 2.47 (2H, t, *J* 6.6, CH_2N), 1.97 (2H, br s, aziridine CH_2), 1.64–1.59 (4H, m, 2 × CH_2); δ_C (100 MHz, $CDCl_3$) 137.5 (s), 117.2 (d), 82.6 (t), 59.3 (t), 52.6 (q), 30.6 (t), 30.1 (t), 24.6 (t); *m*/*z* 172 (MH^+), 156, 140, 124, 75 (Found: C, 63.10; H, 10.27; N, 8.12%. $C_9H_{17}NO_2$ requires C, 63.13; H, 10.01; N, 8.18%).

(*S*)-Methyl *N*-(3-chloroprop-1-en-2-yl)-*N*-(1-phenylethyl)-carbamate 14

To a solution of (*S*)-**2** (0.20 g, 1.26 mmol) in DCM (10 ml) was added methyl chloroformate (0.10 ml, 1.29 mmol) and the reaction mixture stirred at room temperature for 24 hours. Water (10 ml) was added and the mixture extracted with DCM (3 × 10 ml). The combined organic extracts were washed with water (2 × 5 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (10% ethyl acetate–light petroleum) gave (*S*)-**14** (0.27 g, 85%) as a pale yellow oil. $[\alpha]_D$ −15.7 (*c* 1.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 1701, 1654, 1486, 1191; δ_H (300 MHz, $CDCl_3$) 7.37–7.25 (5H, m, ArH), 5.48 (1H, q, *J* 7.0, NC*H*CH_3), 5.40 (1H, s, =CH), 4.91 (1H, s, =CH), 3.93 (1H, d, *J* 14, C*H*HCl), 3.79 (3H, s, OCH_3), 3.67 (1H, d, *J* 14, CH*H*Cl), 1.62 (3H, d, *J* 7.0, CH_3); δ_C (100.6 MHz, $CDCl_3$) 155.3 (s), 141.6 (s), 141.3 (s), 128.4 (d), 127.5 (d), 127.2 (d), 116.0 (t), 56.1 (d), 52.9 (q), 44.9 (t), 17.8 (q); *m*/*z* 255/253 (M^+), 218 (M^+ − Cl), 105, 77, 51 (Found: M^+, 253.0875. $C_{13}H_{16}ClNO_2$ requires 253.0869).

Methyl *N*-(3-chloroprop-1-en-2-yl)-*N*-benzylcarbamate 15

To a stirred solution of **7** (0.16 g, 1.10 mmol) in DCM (10 ml) was added methyl chloroformate (0.11 g, 1.16 mmol) and the reaction mixture stirred at room temperature for 24 hours. Water (10 ml) was added and the reaction mixture extracted with DCM (3 × 10 ml). The combined organic extracts were washed with water (2 × 5 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (5% ethyl acetate–light petroleum) gave **15** (0.135 g, 51%) as a pale green oil. ν_{max} (film)/cm^{-1} 3031, 2954, 1714, 1644, 1448, 1095, 726; δ_H (300 MHz, $CDCl_3$) 7.32–7.27 (5H, m, Ph), 5.16 (1H, s, =CH), 4.90 (1H, s, =CH), 4.72 (2H, s, CH_2Ph), 4.24 (2H, br s, CH_2Cl), 3.76 (3H, s, OCH_3); δ_C (100.6 MHz, $CDCl_3$) 155.4 (s), 144.6 (s), 138.0 (s), 128.8 (d), 127.8 (d), 127.4 (d), 113.3 (t), 54.1 (t), 53.1 (q), 45.1 (t); *m*/*z* 241, 239, 205, 204, 91 (Found: M^+, 239.0711. $C_{12}H_{14}ClNO_2$ requires 239.0713).

Methyl *N*-(3-chloroprop-1-en-2-yl)-*N*-cyclohexylcarbamate 16

To a solution of **8** (0.28 g, 2.04 mmol) in toluene (5 ml) was added methyl chloroformate (0.17 ml, 2.20 mmol) and the reaction mixture stirred at room temperature for 6 hours. Water (10 ml) was added and the mixture extracted with diethyl ether (3 × 10 ml). The combined organic extracts were washed with water (2 × 5 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (10% ethyl acetate–light petroleum) gave **16** (0.32 g, 68%) as a colourless oil. ν_{max} (film)/cm^{-1} 2930, 1720, 1668, 1477, 1093; δ_H (300 MHz, $CDCl_3$) 5.48 (1H, s, =CH), 5.14 (1H, s, =CH), 4.07 (2H, s, CH_2Cl), 3.83–3.74 (1H, m, CH), 3.69 (3H, s, OCH_3), 2.08–1.01 (10H, m, cyclohexyl); δ_C (100.6 MHz, $CDCl_3$) 155.0 (s), 142.3 (s), 115.8 (t), 58.6 (d), 52.6 (q), 45.2 (t), 31.5 (t), 26.0 (t), 25.4 (t); *m*/*z* 232 (MH^+), 196, 114, 55 (Found: M^+, 231.1034. $C_{11}H_{18}ClNO_2$ requires 231.1026).

Methyl *N*-(3-chloroprop-1-en-2-yl)-*N*-(4-hydroxybutyl)-carbamate 17

Methyl chloroformate (0.14 g, 1.48 mmol) was added to a stirred solution of **9** (0.16 g, 1.26 mmol) in DCM (10 ml) and the resultant mixture was stirred overnight at room temperature. The reaction was quenched by the addition of water (5 ml) and the layers separated. The aqueous layer was extracted with DCM (3 × 10 ml), then the combined organic extracts dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (2% MeOH–DCM) gave **17** (0.16 g, 57%) as pale yellow oil. ν_{max} (film)/cm^{-1} 3500–3200, 2952, 2870, 1700, 1646, 773; δ_H (400 MHz, $CDCl_3$) 5.25 (1H, s, =CH), 5.07 (1H, s, =CH), 4.23 (2H, s, CH_2Cl), 3.68 (3H, s, OMe), 3.62 (2H, t, *J* 6.4, C*H*$_2$OH), 3.49 (2H, t, *J* 7.4, CH_2N), 2.13 (1H, br s, OH), 1.70–1.65 (2H, m, CH_2), 1.57–1.50 (2H, m, CH_2); δ_C (100.6 MHz, $CDCl_3$) 155.2 (s), 144.5 (s), 113.2 (t), 62.2 (t), 52.8 (q), 49.9 (t), 44.1 (t), 29.6 (t), 25.1 (t); *m*/*z* 223, 221, 214, 206, 204, 186 (Found: M^+, 221.0815. $C_9H_{16}ClNO_3$ requires 221.0819).

Methyl *N*-(3-chloroprop-1-en-2-yl)-*N*-(4,4-dimethoxybutyl)-carbamate 18

Methyl chloroformate (0.67 g, 7.1 mmol) was added to a stirred solution of **10** (0.112 g, 0.65 mmol) in DCM (10 ml) and the reaction mixture stirred at room temperature for 48 hours. Water (10 ml) was added and the mixture extracted with DCM (3 × 10 ml). The combined organic extracts were washed with water (2 × 5 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (2% MeOH–DCM using silica pretreated with triethylamine) gave **18** (69 mg, 40%) as a pale yellow oil. ν_{max} (film)/cm^{-1} 3500–3200, 2953, 1700, 1646, 1539, 1448; δ_H (300 MHz, $CDCl_3$) 5.26 (1H, s, =CH), 5.08 (1H, s, =CH), 4.37 (1H, t, *J* 5.5, C*H*$(OMe)_2$), 4.24 (2H, br s, CH_2Cl), 3.70 (3H, s, OMe), 3.52 (2H, t, *J* 6.7, CH_2N), 3.30 (6H, s, 2 × OMe), 1.67–1.58 (4H, m, 2 × CH_2); δ_C (75 MHz, $CDCl_3$) 155.2 (s), 144.6 (s), 113.2 (t), 104.2 (d), 52.9 (q, 3 coincident OMe), 50.0 (t), 45.0 (t), 29.7 (t), 23.9 (t); *m*/*z* 266

(MH$^+$), 265 (M$^+$), 85, 75 (Found: M$^+$, 265.1073. $C_{11}H_{20}ClNO_4$ requires 265.1080).

(*S*)-Methyl *N*-(3-chloroprop-1-en-2-yl)-*N*-(1-phenyl-2-phenylmethoxy)ethylcarbamate 19

To a solution of (*S*)-**12** (0.20 g, 0.75 mmol) in toluene (5 ml) was added methyl chloroformate (81 mg, 0.86 mmol) and the reaction mixture stirred at room temperature for 24 hours. Water (5 ml) was added and the mixture extracted with diethyl ether (3 × 10 ml). The combined organic extracts were washed with water (2 × 5 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (10% ethyl acetate–light petroleum) gave (*S*)-**19** (0.14 g, 52%) as a pale yellow oil. $[\alpha]_D$ +25.6 (*c* 1.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 3055, 1711, 1654, 1458, 1271; δ_H (300 MHz, $CDCl_3$) 7.50–7.25 (10H, m, ArH), 5.47 (1H, s, =CH), 5.42 (1H, dd, *J* 8.9, 5.5, NC*H*Ph), 5.03 (1H, s, =CH), 4.59 (2H, br s, CH_2Ph), 4.07 (1H, dd, *J* 10.1, 8.9, C*H*OBn), 3.92 (1H, d, *J* 13.9, CHCl), 3.88 (1H, dd, *J* 10.1, 5.5, C*H*OBn), 3.75 (1H, d, *J* 13.9, CHCl), 3.71 (3H, s, OCH_3); δ_C (100.6 MHz, $CDCl_3$) 155.5 (s), 142.3 (s), 138.0 (s), 137.8 (s), 128.5 (d), 128.4 (d), 128.0 (d), 127.8 (d), 127.7 (d), 127.5 (d), 116.3 (t), 73.0 (t), 69.2 (t), 60.8 (d), 52.9 (q), 44.4 (t); *m*/*z* 361/359 (M$^+$), 324 (M$^+$ − Cl), 238, 104, 91, 51 (Found: M$^+$, 359.1297. $C_{20}H_{22}ClNO_3$ requires 359.1288).

(*S*)-Methyl *N*-(3-chloroprop-1-en-2-yl)-*N*-(3-methyl-1-phenylmethoxy)butan-2-ylcarbamate 20

To a solution of (*S*)-**13** (0.20 g, 0.86 mmol) in DCM (5 ml) was added methyl chloroformate (90 mg, 0.95 mmol) and the reaction mixture stirred at room temperature for 24 hours. Water (5 ml) was added and the mixture extracted with diethyl ether (3 × 10 ml). The combined organic extracts were washed with water (2 × 5 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (10% ethyl acetate–light petroleum) gave (*S*)-**20** (0.21 g, 74%) as a colourless oil. $[\alpha]_D$ −22.8 (*c* 1.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 2967, 1720, 1654, 1447; δ_H (300 MHz, $CDCl_3$) 7.36–7.25 (5H, m, ArH), 5.52 (1H, s, =CH), 5.29 (1H, s, =CH), 4.51 (1H, d, *J* 12, A of AB, CHPh), 4.46 (1H, d, *J* 12, B of AB, CHPh), 4.19 (1H, d, *J* 13, A of AB, C*H*Cl), 4.12 (1H, d, *J* 13, B of AB, C*H*Cl), 3.71–3.57 (3H, m, CH_2OBn, NCH), 3.68 (3H, s, OCH_3), 2.00–1.98 (1H, m, C*H*(CH_3)$_2$), 1.00 (3H, d, *J* 6.7, CH_3), 0.94 (3H, d, *J* 6.7, CH_3); δ_C (100.6 MHz, $CDCl_3$) 155.5 (s), 143.9 (s), 138.0 (s), 128.3 (d), 127.61 (d), 127.60 (d), 115.1 (t), 72.9 (t), 69.2 (t), 66.4 (d), 52.7 (q), 44.6 (t), 29.0 (d), 20.6 (q), 20.3 (q); *m*/*z* 327/325 (M$^+$), 290 (M$^+$ − Cl), 204, 91, 55 (Found: M$^+$, 325.1446. $C_{17}H_{24}ClNO_3$ requires 325.1444).

(*S*)-Benzyl *N*-(3-chloroprop-1-en-2-yl)-*N*-(1-phenylethyl)-carbamate 21

To a solution of (*S*)-**2** (0.30 g, 1.88 mmol) in toluene (5 ml) was added benzyl chloroformate (0.30 ml, 2.10 mmol) and the reaction mixture stirred at room temperature for 24 hours. Water (10 ml) was added and the mixture extracted with diethyl ether (3 × 10 ml). The organic layers were collected, washed with water (2 × 5 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (10% ethyl acetate–light petroleum) gave (*S*)-**21** (0.39 g, 63%) as a colourless oil. $[\alpha]_D$ −3.7 (*c* 1.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 3028, 1710, 1643, 1405, 1317; δ_H (300 MHz, $CDCl_3$) 7.34–7.25 (10H, m, ArH), 5.47 (1H, q, *J* 5.2, C*H*CH_3), 5.39 (1H, s, =CH), 5.18 (1H, d, *J* 12.5, CO_2C*H*HPh), 5.12 (1H, d, *J* 12.5, CO_2CH*H*Ph), 4.93 (1H, s, =CH), 3.95 (1H, d, *J* 14, CHCl), 3.70 (1H, d, *J* 14, CHCl), 1.63 (3H, d, *J* 5.2, CH_3); δ_C (100.6 MHz, $CDCl_3$) 154.1 (s), 141.7 (s), 141.4 (s), 136.2 (s), 128.5 (d), 128.4 (d), 128.0 (d), 127.7 (d), 127.5 (d), 127.2 (d), 116.0 (t), 67.5 (t), 56.2 (d), 45.0 (t), 17.9 (q); *m*/*z* 331/329 (M$^+$), 294, 238, 194, 91, 77, 51 (Found: M$^+$, 329.1196. $C_{19}H_{20}ClNO_2$ requires 329.1182).

(*S*)-*N*-(3-Chloroprop-1-en-2-yl)-*N*-(1-phenylethyl)acetamide 22

To a solution of (*S*)-**2** (0.50 g, 3.14 mmol) in DCM (5 ml) was added acetyl chloride (0.25 ml, 3.52 mmol) and the reaction mixture stirred at room temperature for 3 hours. Water (10 ml) was added and the mixture extracted with DCM (3 × 10 ml). The combined organic extracts were washed with water (2 × 5 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (10% ethyl acetate–light petroleum) gave (*S*)-**22** (0.50 g, 67%) as a pale yellow oil which slowly decomposes at room temperature. $[\alpha]_D$ −29.6 (*c* 1.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 2979, 1670, 1380, 1308, 1110; δ_H (400 MHz, $CDCl_3$) 7.34–7.25 (5H, m, ArH), 5.99 (1H, br s, C*H*CH_3), 5.57 (1H, s, =CH), 5.06 (1H, s, =CH), 3.43–3.39 (2H, br m, CH_2Cl), 2.12 (3H, s, CH_3), 1.52 (3H, d, *J* 7.0, CH_3CH), peak broadening due to amide rotamers; δ_C (100.6 MHz, $CDCl_3$) 169.9 (s), 142.2 (s), 140.8 (s), 128.4 (d), 128.1 (d), 127.8 (d), 120.8 (t), 51.5 (d), 45.2 (t), 22.5 (q), 16.8 (q); *m*/*z* 239/237 (M$^+$), 202, 105, 77 (Found: M$^+$, 237.0914. $C_{13}H_{16}ClNO$ requires 237.0920).

(*S*)-*N*-(3-Chloroprop-1-en-2-yl)-*N*-(1-phenylethyl)-4-nitrobenzamide 23

To a solution of (*S*)-**2** (0.20 g, 1.26 mmol) in DCM (3.0 ml) was added *p*-nitrobenzoyl chloride (0.25 g, 1.35 mmol) dissolved in DCM (1 ml) and the reaction stirred for 3.5 hours at room temperature. Water (5 ml) was added and the mixture extracted with DCM (3 × 10 ml). The combined organic extracts were washed with water (2 × 5 ml), dried over $MgSO_4$, and the solvent removed under reduced pressure. Column chromatography (15% ethyl acetate–light petroleum) gave (*S*)-**23** (0.33 g, 76%) as a yellow oil. $[\alpha]_D$ +2.46 (*c* 1.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 1640, 1510, 1350; δ_H (300 MHz, $CDCl_3$) 8.24 (2H, d, *J* 7.0, ArH), 7.67 (2H, d, *J* 7.0, ArH), 7.41–7.26 (5H, m, ArH), 5.59 (1H, br s, C*H*CH_3), 5.40 (1H, s, =CH), 4.91 (1H, s, =CH), 3.60 (1H, br d, *J* 14, CHCl), 3.45 (1H, br d, *J* 14, CHCl), 1.70 (3H, d, *J* 7.0, CH_3); δ_C (100.6 MHz, $CDCl_3$) 168.6 (s), 148.3 (s), 142.5 (s), 141.2 (s), 140.0 (s), 128.6 (d), 128.0 (d), 127.7 (d), 127.5 (d), 126.3 (d), 120.3 (t), 53.8 (d), 44.8 (t), 16.9 (q); *m*/*z* 346/344 (M$^+$), 309 (M$^+$ − Cl), 150, 105, 77 (Found: M$^+$, 344.0936. $C_{18}H_{17}ClN_2O_3$ requires 344.0927).

Nucleophilic ring opening of (*S*)-*N*-(1-phenylethyl)-2-methyleneaziridine 2 with *p*-anisoyl chloride

To a stirred solution of (*S*)-**2** (0.31 g, 1.95 mmol) in DCM (4 ml) was added *p*-anisoyl chloride (0.37 g, 2.17 mmol) dissolved in DCM (1 ml) and the resulting mixture stirred overnight at room temperature. The solvent was removed under reduced pressure to give a crude, cherry coloured oil. Column chromatography (10% ethyl acetate–light petroleum) gave (*S*)-**24** (0.33 g, 51%) as a pale yellow oil. ν_{max} (film)/cm^{-1} 3015, 1652, 1607, 1508, 1330, 1253 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.45–7.27 (7H, m, Ar), 6.83 (2H, d, *J* 8.9, Ar), 6.13 (1H, q, *J* 7.0, C*H*CH_3), 5.65 (1H, s, =CH), 3.80 (3H, s, OMe), 1.61 (3H, d, *J* 7.0, CHCH_3), 1.49 (3H, s, =CCH_3); δ_C (100.6 MHz, $CDCl_3$) 169.8 (s), 160.9 (s), 141.1 (s), 137.9 (s), 129.5 (d), 129.1 (s), 128.5 (d), 127.7 (d), 127.6 (d), 126.6 (d), 113.4 (d), 55.2 (q), 53.3 (d), 19.6 (q), 16.8 (q); *m*/*z* 332 (MH$^+$ ^{37}Cl), 331 (M$^+$ ^{37}Cl), 330 (MH$^+$ ^{35}Cl), 329 (M$^+$ ^{35}Cl), 294, 225, 135, 105, 77 (Found: M$^+$, 329.1183. $C_{19}H_{20}ClNO_2$ requires 329.1183). Further elution gave (*S*)-**25** (0.21 g, 42%) as a white flaky powder. ν_{max} (DCM)/cm^{-1} 3339, 2924, 2853, 1623, 1456, 1377, 1256; δ_H (300 MHz, $CDCl_3$) 7.75 (2H, d, *J* 9.0, Ar), 7.41–7.27 (5H, m, Ar), 6.93 (2H, d, *J* 9.0, Ar), 6.24 (1H, br s, NH), 5.37 (1H, q, *J* 7.0, C*H*CH_3), 3.84 (3H, s, OCH_3), 1.62 (3H, d, *J* 7.0, CH_3); δ_C (100.6 MHz, $CDCl_3$) 166.2 (s), 162.1 (s), 143.4 (s), 128.8 (d), 128.7 (d), 127.4 (d), 126.8 (s), 126.3 (d), 113.7 (d), 55.4 (q), 49.1 (d), 21.8 (q); *m*/*z* 256 (MH$^+$), 255 (M$^+$), 151, 135, 120, 77 (Found: M$^+$, 255.1268. $C_{16}H_{17}NO_2$ requires 255.1260).

3-Deuterio-*N*-(1-phenylethyl)-2-methyleneaziridine 26

To a solution of (*S*)-**2** (0.60 g, 3.77 mmol) in anhydrous THF at −78 °C was added *sec*-butyllithium (1.3 M, 3.19 ml, 4.15 mmol) followed by TMEDA (0.62 ml, 4.11 mmol), and the reaction mixture stirred at −78 °C for 7 hours. The reaction was quenched with d_4-methanol (0.17 ml, 4.19 mmol) and allowed to warm to room temperature. The organic phase was separated and the aqueous phase extracted with diethyl ether (2 × 10 ml). The combined organic extracts were washed with water (2 × 10 ml), dried over $MgSO_4$, and the solvent removed under reduced pressure. Bulb to bulb distillation (bp 150 °C/10 mmHg) gave **26** (0.36 g, 60%) as a colourless oil and as a 65 : 35 mixture of diastereomers. The extent of deuterium incorporation was estimated to be 82%. These measurements were made using ^{1}H NMR spectroscopy. ν_{max} (film)/cm^{-1} 3076, 1749, 1599, 1449, 699; δ_H (300 MHz, $CDCl_3$) 7.39–7.24 (5H, m, ArH), 4.63 (2H, m, $=CH_2$), 2.94 (1H, q, *J* 6.6, NC*H*CH_3), 2.08 (0.65H, s, aziridine CD*H*), 1.99 (0.35H, s, aziridine CD*H*), 1.51 (3H, d, *J* 6.6, CHC*H*$_3$); δ_C (100.6 MHz, $CDCl_3$) 143.9 (s), 137.0 (s), 128.3 (d), 127.2 (d), 126.7 (d), 83.0 (t), 68.5 (d), 29.5 (t, *J* 26 in ^{13}C{^{1}H} spectrum), 23.4 (q); *m*/*z* 160 (M^+), 105, 77, 57 (Found: M^+, 160.1118. $C_{11}H_{12}DN$ requires 160.1110).

(*S*)-Methyl *N*-(3-chloro-3-deuterioprop-1-en-2-yl)]-*N*-(1-phenylethyl)carbamate 29

To a solution of **26** (0.15 g, 0.94 mmol) in toluene (5 ml) was added methyl chloroformate (0.08 ml, 1.03 mmol) and the reaction mixture stirred at room temperature for 24 hours. Water (5 ml) was added and the reaction mixture extracted with diethyl ether (3 × 5 ml). The combined organic extracts were washed with water (2 × 5 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (15% ethyl acetate–light petroleum) gave **29** (0.15 g, 63%) as a pale yellow oil. ν_{max} (film)/cm^{-1} 1701, 1654, 1486, 1191; δ_H (300 MHz, $CDCl_3$) 7.37–7.25 (5H, m, ArH), 5.48 (1H, q, *J* 7.1, NC*H*CH_3), 5.40 (1H, s, =CH), 4.91 (1H, s, =CH), 3.72 (3H, br s, OCH_3), 3.94 and 3.69 (1H, br s, CD*H*Cl {2 diastereomers}), 1.63 (3H, d, *J* 7.1, CH_3); δ_C (100.6 MHz, $CDCl_3$) 155.3 (s), 141.6 (s), 141.3 (s), 128.3 (d), 127.5 (d), 127.2 (d), 116.0 (t), 56.0 (d), 52.9 (q), 44.7 (t, *J* 23 in ^{13}C{^{1}H} spectrum), 17.8 (q); *m*/*z* 256/254 (M^+), 219 (M^+ − Cl), 105, 77, 51 (Found: M^+, 254.0941. $C_{13}H_{15}ClDNO_2$ requires 254.0932).

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