The synthesis of 5-substituted proline derivatives and of 5-substituted pyrrole-2-carboxylates by 5-*endo* cyclisations featuring a method for effectively favouring these with respect to 5-*exo* cyclisations

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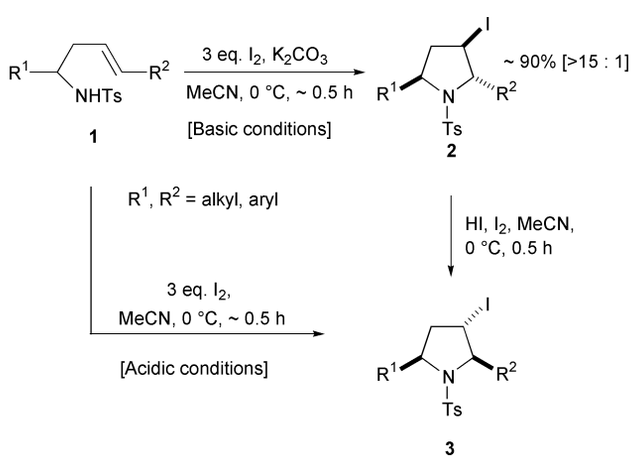
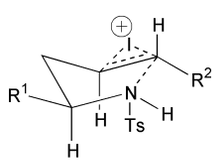
Overall 5-*endo* cyclisations of the *C*-allylic glycine sulfonamides **5** lead to usually excellent yields of the 2,5-*cis*- or 2,5-*trans*-pyrrolidine-2-carboxylates **11** and **12** respectively, depending upon whether base is absent or present. While reductions to the corresponding pyrrolidine-2-methanols **13** proved efficient, subsequent eliminations of the elements of hydrogen iodide gave mixtures of products **14**–**16**. Suitably positioned hydroxy groups compete successfully with the sulfonamide *via* a 5-*exo* cyclisation mode. However, when such a substrate contains a furan ring attached to the alkene function (**21**), then cyclisation does occur at the sulfonamide, presumably by participation of the furan oxygen, to give an iodopyrrolidine-2-methanol **13a**. Finally, base-induced elimination of both hydrogen iodide and toluene-*p*-sulfinic acid from the initial iodopyrrolidines **11** and **12** leads to 5-substituted pyrrole-2-carboxylates **26**. Overall, this sequence is complementary to the Kenner pyrrole synthesis.

Electrophile-induced 5-*endo-trig* cyclisations are now well established as a viable and often highly stereoselective approach to tetrahydrofurans.[1–5] In line with these studies, we have shown that similar cyclisations of the (*E*)-homoallylic sulfonamides **1** by treatment with excess iodine in the presence of anhydrous potassium carbonate lead smoothly to the 2,5-*trans*-iodopyrrolidines **2**, most likely *via* the chair-like transition state **4**. An unexpected bonus was the discovery that if the same sulfonamides **1** were cyclised solely in the presence of iodine, then the corresponding 2,5-*cis*-isomers **3** were the only products formed (Scheme 1).[6] Good evidence was obtained to suggest



Scheme 1

that this occurred *via* isomerisation of the initially formed and therefore kinetic isomers **2**. Both of these cyclisation pathways are extremely efficient and give excellent isolated yields of the final products. However, one limitation of this model work was that we only investigated substrates having either alkyl or aryl substituents. We were therefore very interested to determine if other functional groups could be successfully incorporated into this chemistry, thereby significantly expanding its scope and utility. In this present paper,[7] we report in full that ester groups do not interfere with the cyclisations and indeed can be successfully incorporated, resulting in a new and flexible approach to 5-substituted proline derivatives. Further, these initial cyclisation products undergo smooth elimination to give the corresponding pyrrole-2-carboxylates.



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Results and discussion

We chose to extend the model work by investigating similar cyclisations of 2-allylglycine derivatives **5**. Based on our model work, we chose to protect the amino groups as the corresponding toluene-*p*-sulfonamides and in addition, to use simple methyl esters rather than any more elaborate derivatives as these might interfere with the relatively unfavoured but desired 5-*endo* process. To access these precursors, we used a short if not exceptionally efficient approach which features the palladium-catalysed alkylation[8] of the glycine derivative **7**[9] by allylic carbonates **6**. This turned out to be a simple and reliable method but suffered from a lack of regioselectivity. Such alkylations led to approximately 50–75% isolated yields of the desired isomers **8** which were always accompanied by 10–20% of the corresponding internally substituted products **9**. Fortunately, these undesired isomers were separable by column chromatography. Subsequent protecting group exchange by sequential hydrolysis of the imine group followed by *N*-tosylation of the resulting amino esters **10** then led to good isolated yields of the required substrates **5** for cyclisation.

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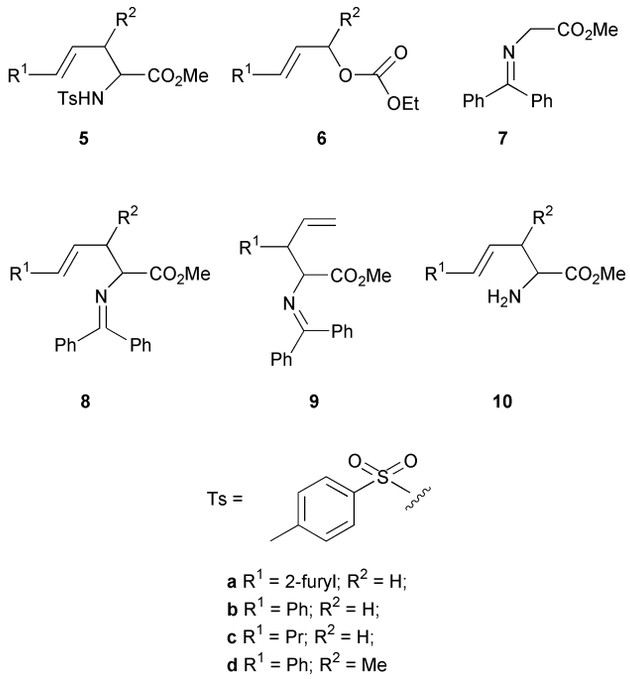
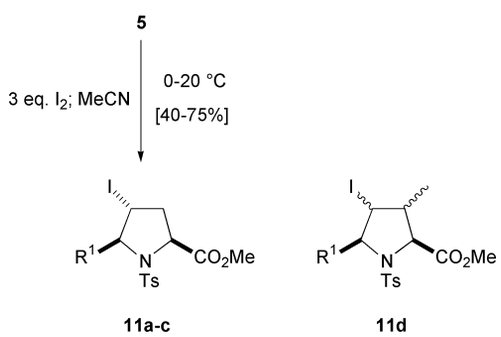


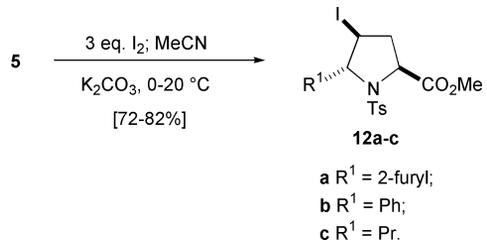
a R^1 = 2-furyl; R^2 = H;
b R^1 = Ph; R^2 = H;
c R^1 = Pr; R^2 = H;
d R^1 = Ph; R^2 = Me

We were delighted to find that simply exposing these substrates **5** to three equivalents of iodine in dry acetonitrile led smoothly in most cases to excellent isolated yields of the anticipated 2,5-*cis*-iodopyrrolidines **11** (Scheme 2). The yield



Scheme 2

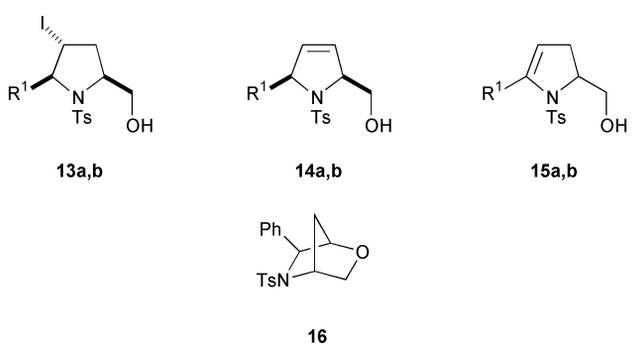
from the cyclisation of the furan derivative **5a** was somewhat lower, presumably by attack of the hydrogen iodide produced during the reaction on the furan ring. In these three cases (**11a**–**c**), only these isomers were detected in the crude products; inevitably however, the disubstituted precursor **5d**, a mixture of diastereoisomers, led to a gross mixture of isomers as expected. Therefore, these cyclisations which, in the absence of base clearly involve acidic conditions, appear to have led to the more thermodynamically stable isomers **11** presumably by a cyclisation–isomerization process similar to that outlined in Scheme 1. In complete contrast, when the same substrates were cyclised in the presence of potassium carbonate, the products were almost exclusively the corresponding 2,5-*trans*-isomers **12** (Scheme 3). It therefore appears that a similar pathway to that discovered during our initial model work[6] is being followed and that these are the kinetic products; concerns that the centre adjacent to the ester might be rather labile were evidently unfounded. In all cases, the detailed structures of the products **11** and **12** were determined by the usual analytical and spectroscopic data and in particular by detailed coupling constant analysis and NOE measurements and then comparisons with similar data obtained for related 2,5-dialkyl-3-iodopyrrolidines prepared during our initial work.[6] These structures were secured by extensive NMR studies and confirmed by selected X-ray crystallographic analysis.



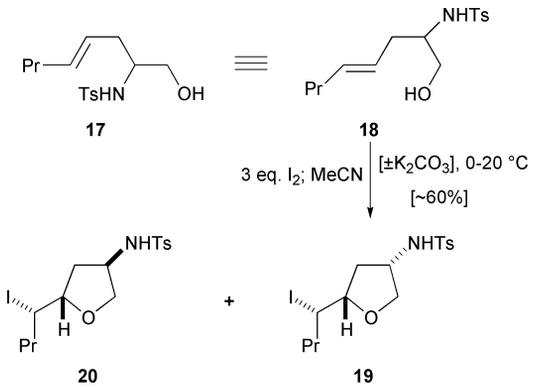
a R^1 = 2-furyl;
b R^1 = Ph;
c R^1 = Pr.

Scheme 3

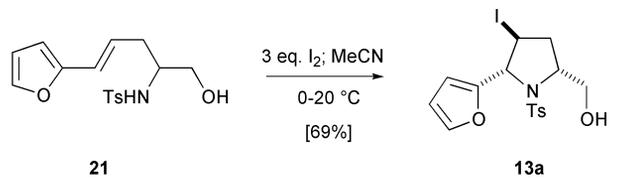
We briefly examined some chemistry of the initial cyclisation products. Thus, the ester function was smoothly reduced to the corresponding alcohol level using diisobutylaluminium hydride in toluene to give the pyrrolidine-2-methanols **13**. However, subsequent elimination reactions did not prove so productive. For example, exposure of the 5-furylpyrrolidine-2-methanol **13a** to DBU in refluxing toluene led to a 60% isolated yield of the 2,5-dihydropyrrole **14a** accompanied by approximately 30% of the corresponding 2,3-dihydropyrrole **15a**. In a similar fashion the phenyl-substituted analogue **13b** also gave these two dihydropyrroles (**14b**, **15b**) but in much lower yield. Interestingly, the major product was the azabicyclic system **16** which was isolated in 56% yield; quite why this substrate shows such a contrast in reactivity relative to the corresponding 5-furyl derivative **13a** is not clear. However, this type of intramolecular *O*-alkylation could represent a useful entry into this heterocyclic system; this is being pursued in a separate study.



Throughout our work on the 5-*endo*-cyclisations of homoallylic sulfonamides, we had naturally assumed that a second nucleophilic centre, positioned such that it could undergo a competing 5-*exo* cyclisation,[10] would react preferentially. Potentially, the ester group in substrates **5** could react in this manner, although previous results have shown that such methyl esters at least do not participate in this way. However, alcohol groups are well known to react in a 5-*exo* mode and we therefore chose to examine the iodocyclisation chemistry of the amino alcohol **17**, readily obtained by reduction of the corresponding ester **5c**. We were not surprised[10] to find that the products of iodocyclisations of the amino alcohol **17** under both acidic and basic conditions proceeded *via* conformation **18** (Scheme 4) and were the aminotetrahydrofurans **19** and **20**, isolated as a 1 : 1 mixture of diastereoisomers which were separated and tentatively assigned the structures shown. Thus, despite the evident facility with which a sulfonamide group undergoes 5-*endo* cyclisation, this is easily overridden by the competing and nonsereoselective 5-*exo* process involving the alcohol group.[11] NMR spectra of the crude products revealed the presence of only the merest traces (≤5%) of the iodopyrrolidines **11c** and **12c** respectively. In complete contrast, the related furyl-substituted amino alcohol **21**, similarly obtained by reduction of the corresponding ester **5a**, underwent iodocyclisation in the absence of potassium carbonate to give *only* the iodopyrrolidine **13a** (Scheme 5), the structure of which was secured by comparisons with spectral data of an authentic sample obtained by reduction of ester **11a**.[12]



Scheme 4

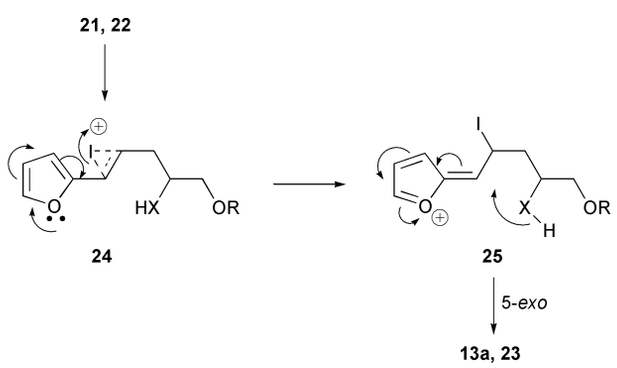


Scheme 5

Our motivation for carrying out these experiments was provided by the results of a Korean group[3] who reported that related furyl-substituted pent-4-ene-1,2-diol derivatives **22** undergo iodocyclisations, similar to that observed in the case of sulfonamide **21**, to give iodotetrahydrofurans **23** (Scheme 6) in

Scheme 6

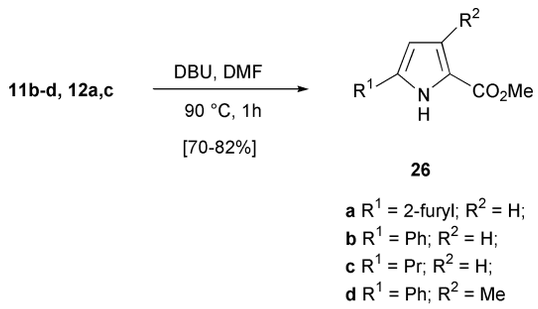
usually highly stereoselective fashion, depending on the exact conditions. At first sight, these appear extraordinary results as a 5-*endo* process appears to be favoured over a 5-*exo* cyclisation. Clearly, however, the furan substituents in both substrates **18** and **22** are having a controlling effect. Presumably, this involves formation of iodonium species **24** (Scheme 7) which are then



Scheme 7

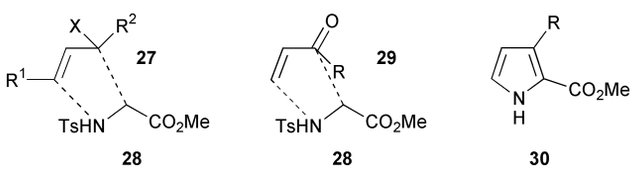
opened by participation of the furan oxygen at a rate faster than either of the two possible cyclisation modes. The activated intermediates **25** thus formed can also undergo two types of cyclisation but now the more favoured 5-*exo* mode wins out over the possible 6-*exo* cyclisations to give the observed products **13a** or **23**. As there are a number of possible cleavage reactions available for degradation of a furan nucleus, this could represent a useful synthetic tactic in some circumstances.

Finally, the partial success of the elimination reactions leading to the dihydropyrroles **14** and **15** led us to attempt similar reactions with the initial iodopyrrolidinecarboxylates **11** and **12**. After some experimentation, we were pleased to find that, irrespective of the pyrrolidine stereochemistry, exposure of the initial cyclisation products **11** or **12** to two equivalents of DBU in DMF at 90 °C for approximately one hour led to excellent isolated yields (70–82%) of the corresponding pyrrole-2-carboxylates **26** (Scheme 8) by the dual elimination of hydrogen



Scheme 8

iodide and toluene-*p*-sulfinic acid. Overall, this represents an approach to these useful compounds effectively from an *N*-tosylglycinate **28** and an allylic alcohol derivative **27**. In many respects, this method overall is complementary to the Kenner method for the elaboration of 3-substituted pyrrole-2-carboxylates **30** by sequential Michael and aldol condensations between enones **29** and glycinate **28** followed by a similar double elimination.[13]



In conclusion, we have shown that a methoxycarbonyl function is compatible with this type of cyclisation and does not undergo any competitive cyclisation. Both the approach to the cyclisation precursors **5**, effectively by *C*-alkylation of glycinates, together with the highly stereoselective nature of the 5-*endo* cyclisations under both sets of conditions, suggest that this methodology should be applicable to the elaboration of highly optically enriched pyrrolidine and proline derivatives. Efforts in this direction are continuing.

Experimental

General

Melting points were determined on a Kofler hot stage apparatus. Infra-red spectra were recorded on a Perkin Elmer 1600 series FTIR spectrometer using KBr discs for solid samples and thin films between NaCl plates in the cases of liquid samples. NMR spectra were recorded on a Bruker DPX 400 instrument operating at 400 MHz for ^{1}H spectra and 100 MHz for ^{13}C spectra. Unless otherwise stated, all such spectra were recorded at 300 K using dilute solutions in deuteriochloroform. Proton chemical shifts were determined relative to both tetramethylsilane (δ_H 0.00) and chloroform (δ_H 7.27) while carbon shifts were corrected to tetramethylsilane (δ_C 0.00) and the centre line of chloroform (δ_C 77.3). Coupling constants (J) are quoted in hertz (Hz) and multiplicities are expressed by the usual conventions; 'br' refers to a broadened resonance. NOE data are quoted for all enhancements in excess of 1%. Molecular weights and low resolution mass spectra were determined using a Fisons VG Platform II Quadrupole instrument using electrospray ionization (ES) unless otherwise stated. High resolution data was obtained courtesy of the EPSRC Mass Spectrometry

Service at University College, Swansea, using the ionization methods specified. Microanalyses were obtained using a Perkin Elmer 240C Elemental Analyzer.

Unless otherwise stated, reactions were performed under an atmosphere of dry nitrogen. Solvents and reagents were purified by the usual methods.[14] 'Petrol' refers to the fraction with bp 40–60 °C and 'ether' refers to diethyl ether. All organic solutions from work-ups were dried by brief exposure to dried magnesium sulfate. Column chromatography was carried out using 'Matrex Silica (35–70 mm) silica gel and the solvents specified.

Where relevant, all compounds referred to below were racemates.

Preparation of carbonates 6: general procedure

The alcohol (0.10 mol) was stirred with pyridine (0.12 mol, 1.2 eq.) in dichloromethane (125 ml) at 0 °C and ethyl chloroformate (0.11 mol, 1.1 eq.) added dropwise. The resulting mixture was stirred for 1 h and then allowed to warm to room temperature and stirred until complete according to TLC, typically 2 h. 2 M Hydrochloric acid (20 ml) was then added, the organic layer separated and the aqueous phase extracted with dichloromethane (3 × 50 ml). The combined organic solutions were washed with brine (50 ml), then dried, filtered and concentrated under reduced pressure to give the carbonate, which was purified by chromatography.

Ethyl (*E*)-3-(2-furyl)prop-2-enyl carbonate 6a. (*E*)-3-(2-Furyl)prop-2-en-1-ol (48 g, 0.387 mol)[15] was reacted with ethyl chloroformate according to the general procedure to give a crude product which was chromatographed (12 : 1 hexane–ethyl acetate) to give the *carbonate* **6a** (50.6 g, 67%) as a yellow oil, ν_{max}/cm^{-1} 2961 (m), 2874 (w), 1747 (s), 1466 (m), 1381 (m), 1260 (s) and 973 (m); δ_H 1.33 (3H, t, J = 7.1, CH_3), 4.23 (2H, q, J = 7.1, CH_2), 4.77 (2H, d, J = 6.4, 1-CH_2), 6.25 (1H, dt, J = 15.9 and 6.4, 2-H), 6.30 (1H, d, J = 3.3, 3′-H), 6.38 (1H, dd, J = 3.3 and 1.7, 4′-H), 6.50 (1H, d, J = 15.9, 3-H) and 7.37 (1H, d, J = 1.7, 5′-H); δ_C 14.2 (CH_3), 64.0, 67.8 (both CH_2), 109.0, 111.3, 120.9, 122.4, 142.4 (all CH), 151.6 (1′-C) and 154.9 (C=O).

Ethyl (*E*)-3-phenylprop-2-enyl carbonate 6b. (*E*)-Cinnamyl alcohol (6.00 g, 0.045 mol) was reacted with ethyl chloroformate according to the general procedure. The crude product was chromatographed (10 : 1 hexane–ethyl acetate) to give the *carbonate* **6b** (7.2 g, 78%) as a pale yellow oil, ν_{max}/cm^{-1} 2984 (m), 1750 (s), 1580 (w), 1448 (m), 1381 (m), 1248 (s) and 1110 (w); δ_H 1.27 (3H, t, J = 7.2, CH_3), 4.17 (2H, q, J = 7.2, OCH_2), 4.73 (2H, dd, J = 6.5 and 1.3, 1-CH_2), 6.25–6.35 (1H, m, 2-H), 6.63 (1H, d, J = 15.8, 3-H) and 7.19–7.35 (5H, m, 5 × Ar-H); δ_C 14.2 (CH_3), 64.4, 68.1 (both CH_2), 122.4, 126.6, 128.1, 128.5, 134.6 (all CH), 136.0 (Ar-C) and 155.0 (C=O); *m*/*z* [EI] 207 (M^+, 9%), 206 (26), 132 (48), 115 (41), 104 (100), 91 (61), 7.7 (67) and 55 (34).

Ethyl (*E*)-hex-2-en-1-yl carbonate 6c. (*E*)-2-Hexen-1-ol (10 g, 0.1 mol) was reacted with ethyl chloroformate according to the general procedure to give a crude product which was chromatographed (10 : 1 hexane–ethyl acetate) to give the *carbonate* **6c** (13.5 g, 78%) as a yellow oil, ν_{max}/cm^{-1} 2966 (m), 2238 (w), 1752 (s), 1466 (w), 1380 (m), 1363 (w), 1256 (s), 1150 (w) and 1025 (m); δ_H 0.90 (3H, t, J = 7.4, 6-CH_3), 1.29 (3H, t, J = 7.1, CH_3), 1.38 (2H, quin, J = 7.4, 5-CH_2), 2.03 (2H, app q, J = 6.6, 4-CH_2), 4.18 (2H, q, J = 7.1, OCH_2), 4.55 (2H, d, J = 6.6, 1-CH_2), 5.58 (1H, dt, J = 14.9 and 6.6, 3-H) and 5.80 (1H, dt, J = 14.9, and 6.6, 2-H); δ_C 13.5, 14.2 (both CH_3), 21.9, 34.2, 63.7, 68.4 (all CH_2), 123.3, 137.1 (both CH) and 155.0 (C=O).

Ethyl (*E*)-3-phenyl-1-methylprop-1-enyl carbonate 6d. (*E*)-1-Phenylbut-1-en-3-ol (5.5 g, 37 mmol) was reacted with ethyl chloroformate according to the general procedure to give a crude product which was chromatographed (10 : 1 hexane–ethyl acetate) to give the *carbonate* **6d** as a yellow oil (6.10 g, 81%), ν_{max}/cm^{-1} 2983 (m), 1749 (s), 1449 (m), 1372 (m), 1277 (s), 1149 (m) and 1037 (m); δ_H 1.12 (3H, t, J = 7.1, CH_3), 1.28 (3H, d, J = 6.6, 4-CH_3), 4.01 (2H, q, J = 7.1, OCH_2), 5.19 (1H, app quin, J = 6.6, 3-H), 6.02 (1H, dd, J = 16.0 and 6.6, 2-H), 6.46 (1H, d, J = 16.0, 1-H) and 7.14–7.29 (5H, m, 5 × Ar-H); δ_C 14.2, 20.4 (both CH_3), 63.7 (CH_2), 74.9, 126.6, 128.2, 128.5, 128.9, 132.1 (all CH), 136.1 (C) and 154.9 (C=O); *m*/*z* [EI] 205 (M + H^+, 11%), 172 (13), 147 (57), 131 (100), 105 (41), 91 (85) and 77 (74).

Palladium catalysed alkylation of Schiff's base: general procedure[8]

The allylic carbonate **6** (1 mmol, 1.0 eq.) and methyl 2-(*N*-benzhydrylideneamino)ethanoate **7** (1 mmol 1.0 eq.) were stirred in tetrahydrofuran (1 ml) under nitrogen at room temperature. A solution of tetrakis(triphenylphosphine)-palladium(0) (0.05 mmol, 0.05 eq.) and 1,2-bis(diphenylphosphino)ethane (0.1 mmol, 0.1 eq.) in THF (0.5 ml) was added. The mixture was then stirred until alkylation was complete according to TLC, typically for 24 h. The solvent was then evaporated and the residue triturated with ether. The resulting mixture and washings were filtered through Celite and the filtrate concentrated to give the crude imine, which was purified by column chromatography.

Methyl (*E*)-2-(*N*-benzhydrylideneamino)-5-(2-furyl)pent-4-enoate 8a. Ethyl (*E*)-3-(2-furyl)prop-2-enyl carbonate **6a** (3.40 g, 17.9 mmol) and methyl 2-*N*-benzhydrylideneamino)-ethanoate **7** (4.53 g, 17.9 mmol) were reacted according to the general procedure with tetrakis(triphenylphosphine)-palladium(0) (1.03 g, 0.9 mmol) and 1,2-bis(diphenylphosphino)ethane (0.71 g, 1.79 mmol) for 24 h. The residue was chromatographed (10 : 1 hexane–ethyl acetate) to give the *imine* **8a** (3.10 g, 50%) as a pale yellow oil, ν_{max}/cm^{-1} 3061 (w), 1739 (s), 1659 (s), 1598 (m), 1447 (m), 1278 (s), 1205 (m) and 1177 (m); δ_H 2.60–2.80 (2H, m, 3-CH_2), 3.65 (3H, s, CH_3), 4.08–4.14 (1H, m, 2-H), 6.80–6.89 (1H, m, 4-H), 6.15 (1H, d, J = 3.2, 3′-H), 6.14 (1H, d, J = 15.9, 5-H), 6.24 (1H, dd, J = 3.2 and 1.9, 4′-H) and 7.05–7.60 (11H, m, Ar-H); δ_C 37.0 (3-CH_2), 52.1 (OCH_3), 65.4 (2-CH), 106.7, 111.0, 121.2, 124.8, 127.8, 128.0, 128.4, 128.6, 130.0, 130.3, 132.3 (all CH), 136.2, 139.4 (both C), 141.5 (5′-CH), 152.8 (C), 171.1 (C=N) and 172.2 (C=O); *m*/*z* [EI] 359 (M^+, 9%), 300 (6), 252 (95), 192 (56), 165 (70) and 77 (100) [Found: M^+, 359.1520. $C_{23}H_{21}NO_3$ requires *M*, 359.1521].

Methyl (*E*)-2-(*N*-benzhydrylideneamino)-5-phenylpent-4-enoate 8b. Ethyl (*E*)-3-phenylprop-2-enyl carbonate **6b** (6.50 g, 31.6 mmol) and methyl 2-(*N*-benzhydrylideneamino)ethanoate **7** (8.00 g, 31.6 mmol) were reacted according to the general procedure with tetrakis(triphenylphosphine)palladium(0) (1.80 g, 1.58 mmol) and 1,2-bis(diphenylphosphino)ethane (1.30 g, 3.16 mmol) for 24 h. The residue was chromatographed (6 : 1 hexane–ethyl acetate) to give the *imine* **8b** (7.1 g, 63%) as a yellow oil, ν_{max}/cm^{-1} 3058 (m), 3026 (m), 2950 (m), 1739 (s), 1622 (s), 1492 (m), 1446 (s), 1278 (s), 1205 (s), 1174 (s), 1073 (m) and 967 (m); δ_H 2.73–2.88 (2H, m, 3-CH_2), 3.73 (3H, s, OCH_3), 4.24 (1H, dd, J = 8.1 and 4.9, 2-H), 6.01 (1H, ddd, J = 15.8, 7.5 and 7.5, 4-H), 6.39 (1H, d, J = 15.8, 5-H) and 7.10–7.64 (15H, m, Ar-H); δ_C 37.2 (3-CH_2), 52.2 (OCH_3), 65.5 (2-CH), 125.9, 126.0, 127.1, 127.8, 128.0, 128.2, 128.4, 128.6, 128.8, 130.3, 132.8 (all CH), 136.3, 137.2, 139.4 (all C), 170.8 (C=N) and 172.3 (C=O); *m*/*z* [EI] 369 (M^+, 19%), 310 (12), 252 (100), 192 (92), 165 (91) and 115 (42) [Found: M^+, 369.1729. $C_{25}H_{23}NO_2$ requires *M*, 369.1729] [Found: C, 80.95; H, 6.16; N, 3.37. $C_{25}H_{23}NO_2$ requires 81.27; H, 6.27; N, 3.79%].

Methyl (*E*)-2-(*N*-benzhydrylideneamino)oct-4-enoate 8c. Ethyl (*E*)-hex-2-enyl carbonate **6c** (9.0 g, 52.3 mmol) and methyl 2-(*N*-benzhydrylideneamino)ethanoate **7** (4.5 g, 52.3 mmol) were reacted together according to the general procedure with tetrakis(triphenylphosphine)palladium(0) (3.0 g, 0.9 mmol) and 1,2-bis(diphenylphosphino)ethane (2.1 g, 5.2 mmol) for 24 h. The residue was chromatographed (6 : 1 hexane–ethyl acetate) to give the *imine* **8c** (12.5 g, 74%) as a pale yellow oil, ν_{max}/cm^{-1} 3024 (w), 2956 (m), 1741 (s), 1660 (m), 1624 (m), 1598 (m), 1578 (m), 1447 (m), 1315 (m) and 1215 (m); δ_H 0.84 (3H, t, J = 7.4, 8-CH_3), 1.32 (2H, app sextet, J = 7.4, 7-CH_2), 1.94 (2H, app q, J = 7.4, 6-CH_2), 2.32–2.67 (2H, m, 3-CH_2), 3.72 (3H, s, OCH_3), 4.13 (1H, dd, J = 8.0 and 5.3, 2-H), 5.25 (1H, ddd, J = 14.9, 7.4 and 7.4, 4-H), 5.47 (1H, ddd, J = 14.9, 7.4 and 7.4, 5-H) and 7.15–7.83 (10H, m, Ar-H); δ_C 13.6 (8-CH_3), 22.5 (7-CH_2), 35.7 (6-CH_2), 37.2 (3-CH_2), 52.0 (OCH_3), 65.9 (2-CH), 125.5, 127.9, 128.0, 128.3, 128.4, 128.6, 128.8, 130.1, 130.3, 132.4, 132.5, 133.7 (all CH), 138.0, 139.0 (both C), 170.5 (C=N) and 172.2 (C=O); *m*/*z* [EI] 335 (M^+, 4%), 292 (43), 276 (77), 252 (87), 192 (90), 164 (100), 77 (98) and 55 (61) [Found: M^+, 335.1885. $C_{22}H_{25}NO_2$ requires *M*, 335.1885] [Found: C, 78.99; H, 7.56; N, 4.03. $C_{22}H_{25}NO_2$ requires C, 78.77; H, 7.51; N, 4.18%].

Methyl (*E*)-2-(*N*-benzhydrylideneamino)-5-phenyl-3-methylpent-4-enoate 8d. Ethyl (*E*)-3-phenyl-1-methylprop-1-enyl carbonate **6d** (6.0 g, 24.6 mmol) and methyl 2-(*N*-benzhydrylideneamino)ethanoate **7** (6.2 g, 24.6 mmol) were reacted according to the general procedure with tetrakis(triphenylphosphine)palladium(0) (1.4 g, 1.23 mmol) and 1,2-bis(diphenylphosphino)ethane (0.98 g, 2.46 mmol) for 24 h. The residue was chromatographed (6 : 1 hexane–ethyl acetate) to give the *imine* **8d** (7.1 g, 75%) as a yellow oil which contained a mixture of diastereoisomers and showed ν_{max}/cm^{-1} 3025 (m), 2951 (m), 1740 (s), 1660 (m), 1447 (m), 1277 (s), 1197 (m), 1173 (m) and 1038 (m); the major diastereoisomer exhibited δ_H 0.98 (3H, d, J = 6.9, 3-CH_3), 2.95–3.10 (1H, m, 3-H), 3.63 (3H, s, OCH_3), 4.00 (1H, d, J = 6.6, 2-H), 6.12 (1H, dd, J = 16.0 and 8.5, 4-H), 6.35 (1H, d, J = 16.0, 5-H), 6.92–7.59 (13H, m, Ar-H) and 7.72 (2H, d, J = 7.3, Ar-H); δ_C 17.6 (3-CH_3), 41.6 (3-CH), 52.0 (OCH_3), 70.8 (2-CH), 126.1–132.4 (17 × CH), 136.4, 137.5 and 139.6 (all C), 171.1 (C=N) and 172.0 (C=O); *m*/*z* [EI] 388 (M^+, 21%), 324 (16), 252 (89), 192 (84), 165 (100), 131 (63), 91 (97) and 77 (56) [Found: M^+, 383.1885. $C_{26}H_{25}NO_2$ requires *M*, 383.1885] [Found: C, 81.37; H, 6.45; N, 3.53. $C_{26}H_{25}NO_2$ requires C, 81.42; H, 6.58; N, 3.65%].

Hydrolysis of imines 8: general procedure

The imine (1 mmol) was vigorously stirred in 2 M hydrochloric acid (4 ml) and ether (6 ml) until the hydrolysis was complete according to TLC (approximately 1 h). The organic layer was then separated and discarded and the aqueous layer washed with ether (5 ml). The aqueous layer was then taken to pH 9 with solid sodium carbonate and the resulting mixture extracted with ether (4 × 5 ml). The combined organic extracts were dried, filtered and concentrated under reduced pressure to yield the crude homoallylic amine **10**, which was used without further purification in the tosylation reaction.

Methyl (*E*)-5-(2-furyl)-2-aminopent-4-enoate 10a. The imine **8a** (14.0 g, 39 mmol) was hydrolysed according to the general procedure to give the *homoallylic amine* **10a** (5.00 g, 66%) as a pale yellow oil, ν_{max}/cm^{-1} 3378 (m), 2952 (m), 1738 (s), 1437 (m), 1203 (s), 1175 (s), 1013 (m) and 965 (m); δ_H 1.66 (2H, br s, NH_2), 2.41 (1H, ddd, J = 14.1, 7.2 and 7.2, 3-H_a), 2.50–2.54 (1H, m, 3-H_b), 3.54 (1H, dd, J = 7.2 and 5.9, 2-H), 3.64 (3H, s, OCH_3), 5.91–5.99 (1H, m, 4-H), 6.11 (1H, d, J = 3.2, 3′-H), 6.20 (1H, d, J = 15.7, 5-H), 6.24 (1H, dd, J = 3.2 and 1.9, 4′-H) and 7.21 (1H, app br s, 5′-H); δ_C 38.1 (3-CH_2), 52.0 (OCH_3), 54.1 (2-CH), 107.2, 111.1, 122.0, 123.4, 141.6 (all CH), 152.3 (1′-C) and 175.4 (C=O); *m*/*z* [ES] 196 (M^+H^+, 100%), 179 (11), 154 (15) and 128 (41) [Found: M + H^+, 196.0974. $C_{10}H_{14}NO_3$ requires *M*, 196.0974].

Methyl (*E*)-2-amino-5-phenylpent-4-enoate 10b. The imine **8b** (12.0 g, 37.1 mmol) was hydrolysed according to the general procedure to give the *homoallylic amine* **10b** (4.00 g, 52%) as a pale yellow oil, ν_{max}/cm^{-1} 3379 (m), 3026 (m), 2952 (m), 1739 (s), 1598 (m), 1495 (m), 1437 (m) and 1200 (s); δ_H 1.69 (2H, br s, NH_2), 2.49–2.70 (2H, m, 3-CH_2), 3.61 (1H, dd, J = 7.0 and 5.3, 2-H), 3.74 (3H, s, OCH_3), 6.14 (1H, ddd, J = 15.7, 7.8 and 7.8, 4-H), 6.50 (1H, d, J = 15.7, 5-H) and 7.19–7.37 (5H, m, Ar-H); δ_C 30.1 (3-CH_2), 52.0 (OCH_3), 55.2 (2-CH), 124.0, 126.5, 127.0, 128.5, 135.0 (all CH), 151.0 (C) and 168.5 (C=O); *m*/*z* [EI] 205 (M^+, 2%), 167 (2), 149 (11), 129 (8), 117 (26) and 88 (100) [Found: M + H^+, 206.1181. $C_{12}H_{16}NO_2$ requires *M*, 206.1181].

Methyl (*E*)-2-aminooct-4-enoate 10c. The imine **8c** (12.0 g, 37.1 mmol) was hydrolysed according to the general procedure to give the *homoallylic amine* **10c** (4.80 g, 76%) as a pale yellow oil, ν_{max}/cm^{-1} 3191 (m), 2953 (m), 2361 (m), 1734 (s), 1674 (m), 1457 (w), 1436 (m), 1198 (m) and 970 (m); δ_H 0.91 (3H, t, J = 7.2, 8-CH_3), 1.37 (2H, sextet, J = 7.2, 7-CH_2), 1.67 (2H, br res, NH_2), 1.99 (2H, app q, J = 7.2, 6-CH_2), 2.31–2.45 (2H, m, 3-CH_2), 3.51 (1H, dd, J = 6.8 and 5.2, 2-H), 3.72 (3H, s, OCH_3), 5.30 (1H, ddd, J = 15.2, 6.8 and 6.8, 4-H) and 5.55 (1H, ddd, J = 15.2, 7.2 and 7.2, 5-H); δ_C 13.6 (8-CH_3), 22.5, 34.7, 38.0 (all CH_2), 51.9 (OCH_3), 54.2 (2-CH), 124.5 (5(4)-CH), 135.1 (4(5)-CH) and 175.9 (C=O); *m*/*z* [CH_4CI] 343 (2M + 1^+, 100%) and 172 (M + H^+, 40%) [Found [CH_4CI]: M + H^+, 172.1338. $C_9H_{18}NO_2$ requires *M*, 172.1338].

Methyl (*E*)-2-amino-3-methyl-5-phenylpent-4-enoate 10d. The imine **8d** (4.00 g, 10 mmol) was hydrolysed according to the general procedure to give the *homoallylic amine* **10d** (0.90 g, 41%) as a pale yellow oil, ν_{max}/cm^{-1} 3376 (m), 3026 (m), 2952 (m), 1737 (s), 1679 (m), 1494 (m), 1209 (m) and 1171 (m); the major diastereoisomer showed δ_H 1.12 (3H, d, J = 6.9, 3-CH_3), 1.54 (2H, br res, NH_2), 2.64–2.73 (1H, m, 3-H), 3.38 (1H, d, J = 5.6, 2-H), 6.01 (1H, dd, J = 15.8 and 8.1, 4-H), 6.40 (1H, d, J = 15.8, 5-H) and 7.13–7.30 (5H, m, Ar-H); δ_C 17.0 (3-CH_3), 41.4 (3-CH), 52.0 (OCH_3), 59.3 (2-CH), 127.3, 127.8, 128.4, 130.1, 131.2, 131.6 (all CH), 138.0 (C) and 172.0 (C=O). The whole sample showed *m*/*z* [EI] 219 (M^+, 18%), 160 (47), 143 (35), 128 (99), 115 (90), 91 (77), 88 (100) and 77 (52) [Found: M^+, 219.1259. $C_{13}H_{17}NO_2$ requires *M*, 219.1259].

Preparation of toluenesulfonamides 5: general procedure

The homoallylic amine (1 mmol, 1 eq.) was stirred in dichloromethane (3.5 ml) at room temperature. Tosyl chloride (1.1 mmol, 1.1 eq.) and a crystal of DMAP were added, followed by the dropwise addition of triethylamine (1.2 mmol, 1.2 eq.). The resulting mixture was stirred overnight at room temperature then acidified with 2 M hydrochloric acid (5 ml) and the resulting layers separated. The aqueous phase was extracted with dichloromethane (2 × 5 ml). The combined organic solutions were washed with brine (5 ml), dried, then filtered and concentrated under reduced pressure to give the crude toluenesulfonamide **5**, which was purified by column chromatography.

Methyl (*E*)-5-(2-furyl)-2-(4-tolylsulfonylamino)pent-4-enoate 5a. Homoallylic amine **10a** (5.00 g, 27.3 mmol) was reacted with tosyl chloride (5.73 g, 30.0 mmol) in the presence of triethylamine (4.6 ml, 32.8 mmol) according to the general procedure The crude residue was chromatographed (6 : 1 hexane–ethyl acetate) to give the *homoallylic toluenesulfonamide* **5a** (6.50 g, 70%) as a pale yellow solid, mp 87–88 °C, ν_{max}/cm^{-1} 3286 (m), 2959 (w), 1726 (s), 1598 (w), 1492 (w), 1425 (m), 1356

(s), 1339 (s), 1303 (w), 1256 (w), 1213 (m), 1163 (s), 1092 (m) and 1015 (w); δ_H 2.42 (3H, s, Ar-CH_3), 2.60 (2H, m, 3-CH_2), 3.57 (3H, s, OCH_3), 4.10 (1H, ddd, J = 8.8, 5.7 and 5.7, 2-H), 5.26 (1H, d, J = 8.8, NH), 5.88 (1H, ddd, J = 15.5, 7.7 and 7.7, 4-H), 6.20 (1H, d, J = 15.5, 5-H), 6.27 (1H, d, J = 3.4, 3′-H), 6.35 (1H, dd, J = 3.4 and 1.8, 4′-H), 7.20 (2H, d, J = 8.2, 2 × Ar-H), 7.32 (1H, app br s, 5′-H) and 7.73 (2H, d, J = 8.2, 2 × Ar-H); δ_C 21.6 (Ar-CH_3), 36.7 (3-CH_2), 52.6 (OCH_3), 55.4 (2-CH), 107.8, 111.2, 122.9, 124.0 (all CH), 127.3 (2 × Ar-CH), 129.7 (2 × Ar-CH), 137.3 (C), 141.9 (5′-CH), 143.7, 151.6 (both C) and 171.6 (C=O); *m/z* [EI] 349 (M^+, 2%), 290 (2), 242 (19), 178 (49), 155 (64), 107 (80) and 91 (100) [Found [NH_4 CI]: M + NH_4^+, 367.1328. $C_{17}H_{23}N_2O_5S$ requires M, 367.1327] [Found: C, 58.14; H, 5.73; N, 3.89. $C_{17}H_{19}NO_5S$ requires C, 58.44; H, 5.48; N, 4.01%].

Methyl (*E*)-5-phenyl-2-(4-tolylsulfonylamino)pent-4-enoate 5b. Homoallylic amine **10b** (2.60 g, 12.7 mmol) was reacted with tosyl chloride (2.65 g, 13.9 mmol) in the presence of triethylamine (2.14 ml, 15.3 mmol) in dichloromethane (45 ml) according to the general procedure. The crude residue was chromatographed (4 : 1 hexane–ethyl acetate) to give the *homoallylic toluenesulfonamide* **5b** (1.70 g, 40%) as a colourless solid, mp 95 °C, ν_{max}/cm^{-1} 3278 (m), 3031 (w), 1736 (s), 1598 (w), 1446 (m), 1431 (m), 1420 (m), 1366 (m), 1348 (m), 1324 (s), 1224 (m), 1153 (s), 1094 (s) and 966 (m); δ_H 2.41 (3H, s, Ar-CH_3), 2.64–2.70 (2H, m, 3-CH_2), 3.57 (3H, s, OCH_3), 4.11 (1H, ddd, J = 8.8, 5.9 and 5.9, 2-H), 5.10 (1H, d, J = 8.8, NH), 5.96 (1H, ddd, J = 15.5, 7.6 and 7.6, 4-H), 6.40 (1H, d, J = 15.5, 5-H), 7.23–7.34 (7H, m, Ar-H), and 7.74 (2H, d, J = 8.2, 2 × Ar-H); δ_C 21.6 (Ar-CH_3), 36.9 (3-CH_2), 52.6 (OCH_3), 55.4 (2-CH), 122.6, 126.3, 127.3, 127.7, 128.5, 129.7, 134.6 (all CH), 136.4, 136.5, 143.7 (all C) and 171.4 (C=O); *m/z* [EI] 359 (M^+, 14%), 300 (10), 242 (51), 188 (61), 155 (72), 117 (59), 115 (65), 91 (100) and 65 (63) [Found [CH_4 CI]: M + H^+, 360.1270. $C_{19}H_{22}NO_4S$ requires M, 360.1269] [Found: C, 63.63; H, 6.12; N. 3.81. $C_{19}H_{21}NO_4S$ requires C, 63.49; H, 5.89; N, 3.90%].

Methyl (*E*)-2-(4-tolylsulfonylamino)oct-4-enoate 5c. Homoallylic amine **10c** (4.80 g, 28.1 mmol) was reacted with tosyl chloride (5.89 g, 30.9 mmol) in the presence of triethylamine (4.7 ml, 33.7 mmol) in dichloromethane (100 ml) according to the general procedure. The crude residue was chromatographed (4 : 1 hexane–ethyl acetate) to give the *homoallylic toluenesulfonamide* **5c** (7.5 g, 81%) as a colourless solid, mp 63–65 °C, ν_{max}/cm^{-1} 3261 (m), 2955 (m), 2928 (w), 2870 (w) 1743 (s), 1598 (w), 1496 (w), 1440 (w), 1431 (m), 1333 (s), 1281 (m), 1244 (m), 1161 (s), 1093 (m), 1010 (w) and 970 (w); δ_H 0.87 (3H, t, J = 7.2, 8-CH_3), 1.32 (2H, sextet, J = 7.2, 7-CH_2), 1.92 (2H, q, J = 7.2, 6-CH_2), 2.39 (2H, m, 3-CH_2), 2.42 (3H, s, Ar-CH_3), 3.53 (3H, s, OCH_3), 3.98 (1H, ddd, J = 8.9, 5.7 and 5.7, 2-H), 5.10 (1H, d, J = 8.9, NH), 5.19 (1H, ddd, J = 15.0, 7.4 and 7.4, 4-H), 5.46 (1H, ddd, J = 15.0, 7.0 and 7.0, 5-H), 7.29 (2H, d, J = 8.2, 2 × Ar-H) and 7.72 (2H, d, J = 8.2, 2 × Ar-H); δ_C 13.6 (8-CH_3), 21.6 (Ar-CH_3), 22.3 (7-CH_2), 34.6 (6-CH_2), 36.5 (3-CH_2), 52.4 (OCH_3), 55.5 (2-CH), 122.4 (5(4)-CH), 127.3 (4(5)-CH), 129.6 (2 × Ar-CH), 136.2 (2 × Ar-CH), 137.0, 143.6 (both C) and 171.5 (C=O); *m/z* [NH_4 CI] 343 (M + NH_4^+, 100%) and 327 (M + H^+, 10%) [Found: M + NH_4^+, 343.1692. $C_{16}H_{27}N_2O_4S$ requires M 343.1691] [Found: C, 59.25; H, 7.30; N, 4.27. $C_{16}H_{23}NO_4S$ requires C, 59.05; H, 7.12; N, 4.30%].

Methyl (*E*)-3-methyl-5-phenyl-2-(4-tolylsulfonylamino)pent-4-enoate 5d. Homoallylic amine **10d** (0.70 g, 3.20 mmol) was reacted with tosyl chloride (0.67 g, 3.52 mmol) and triethylamine (0.54 ml, 3.8 mmol) in dichloromethane (11 ml) according to the general procedure. The crude residue was chromatographed (6 : 1 hexane–ethyl acetate) to give the *homoallylic toluenesulfonamide* **5d** (0.96 g, 81%) as a colourless solid which consisted of a mixture of diastereoisomers. The mixture showed ν_{max}/cm^{-1} 3280 (m), 3028 (w), 2953 (m), 2361 (m), 1743 (s), 1598 (m), 1448 (m), 1339 (s), 1164 (s) and 1093 (m). The major diastereoisomer showed δ_H 1.18 (3H, d, J = 6.9, 3-CH_3), 2.39 (3H, s, Ar-CH_3), 2.78–2.86 (1H, m, 3-H), 3.48 (3H, s, OCH_3), 3.90–3.94 (1H, m, 2-H), 5.91 (1H, dd, J = 16.0 and 8.0, 4-H), 6.36 (1H, d, J = 16.0, 5-H), 7.21–7.33 (7H, m, Ar-H) and 7.70 (2H, d, J = 8.3, 2 × Ar-H) while visible resonances due to the minor diastereoisomer were δ_H 1.11 (3H, d, J = 6.9, CH_3), 2.37 (3H, s, Ar-CH_3), 2.54–2.57 (1H, m, 3-H), 3.43 (3H, s, OCH_3), 4.10 (1H, dd, J = 9.5 and 7.0, 2-H), 5.05–5.10 (1H, m, =CH) and 5.40–5.50 (1H, m, =CH); δ_C 21.5 (Ar-CH_3), 40.1 (3-CH), 52.3 (OCH_3), 60.4 (2-CH) and 171.0 (C=O). The whole sample showed *m/z* [EI] 374 (M + H^+, 5%), 314 (7), 242 (27), 202 (42), 154 (58), 130 (100), 114 (45), 90 (95) and 64 (57) [Found: M + H^+, 374.1426. $C_{20}H_{24}NO_4S$ requires M, 374.1426].

Iodocyclisations of homoallylic sulfonamides 5 under acidic conditions: general procedure

To a stirred solution of the cyclisation precursor (1 mmol, 1.0 eq.) in dry acetonitrile (20 ml) was added a solution of iodine (3 mmol, 3.0 eq.) in dry acetonitrile (10 ml) at 0 °C. The reaction was then stirred without cooling until complete by TLC analysis. The mixture was then quenched with saturated aqueous sodium thiosulfate, which was added until decolorisation was complete, and the resulting mixture extracted with dichloromethane (3 × 10 ml). The combined organic extracts were dried, filtered and the solvent evaporated to yield the crude product, which was purified by column chromatography.

Methyl (2*RS*,4*SR*,5*RS*)-5-(2-furyl)-4-iodo-1-(4-tolylsulfonyl)-pyrrolidine-2-carboxylate 11a. Homoallylic toluenesulfonamide **5a** (0.20 g, 0.59 mmol) was cyclised with iodine (0.45 g, 1.77 mmol) according to the general procedure and the reaction was complete after 5 minutes. The crude product was chromatographed (4 : 1 hexane–ethyl acetate) to yield the *pyrrolidine* **11a** (0.11 g, 40%) as a colourless solid, mp 107–109 °C, ν_{max}/cm^{-1} 2920 (w), 1758 (s), 1741 (s), 1598 (w), 1052 (w), 1440 (w), 1348 (s), 1300 (m), 1198 (m), 1163 (s), 1093 (m), 1025 (m), 1013 (m) and 978 (w); δ_H 2.38 (3H, s, Ar-CH_3), 2.43 (1H, ddd, J = 13.7, 8.4 and 5.1, 3-H_a), 2.57 (1H, ddd, J = 13.7, 6.9 and 3.6, 3-H_b), 3.78 (3H, s, OCH_3), 4.35 (1H, ddd, J = 5.1 and 3.6 and 3.6, 4-H), 4.63 (1H, m, 2-H), 5.06 (1H, d, J = 3.6, 5-H), 6.21 (1H, dd, J = 3.2 and 1.9, 4′-H), 6.56 (1H, d, J = 3.2, 3′-H), 7.22 (1H, d, J = 1.9, 5′-H), 7.24 (2H, d, J = 8.3, 2 × Ar-H) and 7.69 (2H, J = 8.3, 2 × Ar-H); δ_C 21.5 (Ar-CH_3), 21.6 (4-CH), 40.6 (3-CH_2), 52.8 (OCH_3), 61.0 (2-CH), 68.4 (5-CH), 109.5 (4′-CH), 110.6 (3′-CH), 128.0 (2 × Ar-CH), 129.5 (2 × Ar-CH), 134.4 (C), 142.5 (5′-CH), 144.0, 151.7 (both C) and 171.5 (C=O); *m/z* [EI] 475 (M^+, 2%), 419 (16), 293 (30), 149 (81), 129 (36), 85 (32), 71 (75) and 56 (100) [Found [CI]: M + H^+, 476.002. $C_{17}H_{19}INO_5S$ requires M, 476.003].

NOE data: 2-H_a–3-H_a, 4%; 3-H_a–3-H_b, 12%; 3-H_b–4-H_b, 6%.

Methyl (2*RS*,4*SR*,5*RS*)-4-iodo-5-phenyl-1-(4-tolylsulfonyl)-pyrrolidine-2-carboxylate 11b. Homoallylic toluenesulfonamide **5b** (3.0 g, 8.85 mmol) was cyclised with iodine (11.2 g, 44.3 mmol, 5.0 eq.) according to the general procedure and the reaction was complete after 16 h. The crude product was chromatographed (5 : 1 hexane–ethyl acetate) to give the *pyrrolidine* **11b** (3.20 g, 75%) as a colourless solid, mp 99–100 °C, ν_{max}/cm^{-1} 2954 (w), 1747 (s), 1597 (w), 1494 (w), 1442 (m), 1348 (s), 1296 (s), 1254 (w), 1162 (s), 1140 (m), 1093 (m), 1030 (m) and 1012 (m); δ_H 2.41 (3H, s, Ar-CH_3), 2.43–2.48 (1H, m, 3-H_a), 2.55 (1H, ddd, J = 12.1, 7.0 and 7.0, 3-H_b), 3.87 (3H, s, OCH_3), 4.15–4.19 (1H, m, 4-H), 4.75 (1H, dd, J = 7.0 and 7.0, 2-H), 5.02 (1H, d, J = 4.6, 5-H), 7.23 (2H, d, J = 8.1, 2 × Ar-H), 7.27–7.28 (3H, m,

Ar-H), 7.51–7.53 (2H, m, Ar-H) and 7.60 (2H, d, J = 8.1, 2 × Ar-H); δ_C 21.5 (Ar-CH_3), 25.6 (4-CH), 40.4 (3-CH_2), 52.7 (OCH_3), 61.4 (2-CH), 74.4 (5-CH), 127.1, 127.8, 127.9, 128.4, 129.4 (all CH), 134.4, 138.9, 143.9 (all C) and 172.0 (C=O); *m/z* [EI] 485 (M^+, 5%), 426 (59), 358 (12), 300 (17), 203 (14), 155 (56), 115 (56), 91 (100) and 65 (65) [Found: M^+, 485.0158. $C_{19}H_{20}INO_4S$ requires *M*, 485.0160] [Found: C, 47.09; H, 4.23; N, 2.95. $C_{19}H_{20}INO_4S$ requires C, 47.01; H, 4.16; N, 2.89%].

NOE data: 2-H_a–3-H_a, 6%; 3-H_a–3-H_b, 8%; 3-H_b–4-H_b, 5%.

Methyl (2*RS*,4*SR*,5*RS*)-4-iodo-5-propyl-1-(4-tolylsulfonyl)-pyrrolidine-2-carboxylate 11c. Homoallylic toluenesulfonamide **5c** (0.20 g, 0.65 mmol) was cyclised using iodine (0.50 g, 1.95 mmol) according to the general procedure and the reaction was complete after 16 h. The crude product was purified by chromatography (6 : 1 hexane–ethyl acetate) to yield the *pyrrolidine* **11c** (0.20 g, 70%) as a colourless solid, mp 94–97 °C, ν_{max}/cm^{-1} 2958 (m), 1743 (s), 1599 (w), 1493 (w), 1440 (m), 1345 (s), 1291 (m), 1160 (s), 1091 (m) and 1024 (m); δ_H 0.94 (3H, t, J = 7.3, 3′-CH_3), 1.41 (2H, m, 2′-CH_2), 1.79–1.89 (2H, m, 1′-CH_2), 2.27 (1H, ddd, J = 14.0, 7.0 and 2.9, 3-H_a), 2.44 (3H, s, Ar-CH_3), 2.52 (1H, ddd, J = 14.0, 8.5 and 5.4, 3-H_b), 3.80 (3H, s, OCH_3), 3.92–3.99 (1H, m, 5-H), 4.10–4.16 (1H, m, 4-H), 4.38–4.43 (1H, m, 2-H), 7.35 (2H, d, J = 8.1, 2 × Ar-H) and 7.73 (2H, d, J = 8.2, 2 × Ar-H); δ_C 13.9 (3′-CH_3), 19.9 (2′-CH_2), 21.6 (4-CH and Ar-CH_3), 38.9 (1′-CH_2), 41.1 (3-CH_2), 52.8 (OCH_3), 61.0 (2-CH), 72.5 (5-CH), 128.2 (2 × Ar-CH), 129.8 (2 × Ar-CH), 134.0, 144.1 (both C) and 172.0 (C=O) [Found [NH_4 CI]: M + NH_4^+, 469.0658. $C_{16}H_{26}IN_2O_4S$ requires *M*, 469.0658].

NOE data: 2-H_a–3-H_a, 6%; 3-H_a–3-H_b, 9%; 3-H_b–4-H_b, 4%.

Methyl 4-iodo-3-methyl-5-phenyl-1-(4-tolylsulfonyl)pyrrolidine-2-carboxylate 11d. Homoallylic toluenesulfonamide **5d** (1.20 g, 3.23 mmol) was cyclised using iodine (2.48 g, 9.70 mmol) in acetonitrile (110 ml) according to the general procedure and the reaction was complete after 16 h. The crude product was chromatographed in (6 : 1 hexane–ethyl acetate) to give the *pyrrolidine* **11d** (1.19 g, 74%) as an oil which consisted of a mixture of 4 diastereoisomers, ν_{max}/cm^{-1} 2952 (m), 1746 (s), 1452 (m), 1356 (s), 1162 (s) and 1092 (m). The major diastereoisomer showed δ_H 1.23 (3H, d, J = 6.8, 3-CH_3), 2.33 (3H, s, Ar-CH_3), 3.61 (3H, s, OCH_3), 4.05 (1H, d, J = 9.0, 2-H), 4.20–4.22 (1H, m, 4-H), 4.60–4.65 (1H, m, 3-H), 5.17 (1H, d, J = 1.9, 5-H) and 7.02–7.66 (9H, m, Ar-H); *m/z* [EI] 498 (M^+, 3%), 440 (75), 372 (30), 217 (12), 158 (59), 130 (73), 90 (100) and 64 (31) [Found: M^+, 498.0238. $C_{20}H_{21}INO_4S$ requires *M*, 498.0238] [Found: C, 47.98; H, 4.43; N, 2.61%. $C_{20}H_{21}INO_4S$ requires C, 48.19; H, 4.25; N, 2.81%].

Iodocyclisations of homoallylic sulfonamides 5 under basic conditions: general procedure

To a stirred mixture of the cyclisation precursor **5** (1 mmol, 1 eq.) and anhydrous potassium carbonate (3 mmol, 3 eq.) in dry acetonitrile (20 ml) was added a solution of iodine (3 mmol, 3 eq.) in acetonitrile (10 ml) at 0 °C. The resulting mixture was stirred at room temperature until cyclisation was complete, according to TLC analysis. The mixture was then quenched with saturated aqueous sodium thiosulfate, which was added until decolorisation occurred, and the resulting mixture extracted with dichloromethane (3 × 10 ml). The combined organic extracts were dried, filtered and the solvent evaporated to give a crude product which was purified by column chromatography.

Methyl (2*RS*,4*RS*,5*SR*)-5-(2-furyl)-4-iodo-1-(4-tolylsulfonyl)-pyrrolidine-2-carboxylate 12a. Homoallylic toluenesulfonamide **5a** (0.37 g, 1.05 mmol) was cyclised with iodine (0.80 g, 3.16 mmol) and potassium carbonate (0.45 g, 3.16 mmol) according to the general procedure and the reaction was complete after 3 h. The crude product was chromatographed (6 : 1 hexane–ethyl acetate) to yield the *pyrrolidine* **12a** (0.388 g, 76%) as a colourless solid, mp 101–103 °C, ν_{max}/cm^{-1} 2950 (w), 2900 (w), 1748 (s), 1598 (w), 1436 (m), 1348 (m), 1168 (s), 1099 (m), 1034 (m) and 1015 (m); δ_H 2.38 (3H, s, Ar-CH_3), 2.54 (1H, ddd, J = 15.0, 6.1 and 4.8, 3-H_a), 3.10 (1H, ddd, J = 15.0, 8.6 and 7.6, 3-H_b), 3.86 (3H, s, OCH_3), 4.29–4.31 (1H, m, 4-H), 4.65 (1H, dd, J = 8.6 and 4.8, 2-H), 5.05 (1H, d, J = 6.1, 5-H), 6.24 (1H, dd, J = 3.2 and 1.8, 4′-H), 6.40 (1H, d, J = 3.2, 3′-H), 6.98 (1H, d, J = 1.8, 5′-H), 7.14 (2H, d, J = 8.2, 2 × Ar-H) and 7.69 (2H, d, J = 8.2, 2 × Ar-H); δ_C 19.1 (4-CH), 21.0 (Ar-CH_3), 40.7 (3-CH_2), 52.8 (OCH_3), 61.5 (2-CH), 66.9 (5-CH), 110.4 (4′-CH), 112.2 (3′-CH), 127.3 (2 × Ar-CH), 129.1 (2 × Ar-CH), 137.0, 138.3 (both C), 142.9 (5′-CH), 148.0 (C) and 171.0 (C=O); *m/z* [EI] 475 (M^+, 0.1%), 416 (45), 348 (40), 320 (28), 208 (26), 193 (50), 155 (68), 133 (99) and 90 (100) [Found [CI]: M + H^+, 476.0029. $C_{17}H_{19}INO_5S$ requires *M*, 476.0030] [Found: C, 42.88; H, 3.96; N, 2.81. $C_{17}H_{18}INO_5S$ requires C, 42.95; H, 3.82; N, 2.95%].

NOE data: 2-H_a–3-H_a, 7%; 3-H_a–3-H_b, 18%; 3-H_a–4-H_a, 4%.

Methyl (2*RS*,4*SR*,5*SR*)-4-iodo-5-phenyl-1-(4-tolylsulfonyl)-pyrrolidine-2-carboxylate 12b. Homoallylic toluenesulfonamide **5b** (50 mg, 0.140 mmol) was cyclised with iodine (107 mg, 0.421 mmol) and potassium carbonate (58 mg, 0.421 mmol) according to the general procedure and the reaction was complete after 16 h. The crude product was chromatographed (6 : 1 hexane–ethyl acetate) to give the *pyrrolidine* **12b** (59 mg, 72%) as a colourless solid, mp 93–95 °C, ν_{max}/cm^{-1} 2951 (w), 1748 (s), 1597 (m), 1436 (m), 1342 (s), 1208 (m), 1156 (s), 1098 (m) and 1036 (m); δ_H 2.57 (3H, s, Ar-CH_3), 2.83 (1H, ddd, J = 14.4, 6.2 and 4.6, 3-H_a), 3.32 (1H, ddd, J = 14.4, 8.1 and 8.1, 3-H_b), 4.13 (3H, s, OCH_3), 4.35–4.46 (1H, m, 4-H), 5.05 (1H, dd, J = 8.1 and 4.6, 2-H), 5.38 (1H, d, J = 6.2, 5-H) and 7.25–7.49 (9H, m, Ar-H); δ_C 21.4 (Ar-CH_3), 23.8 (4-CH), 40.2 (3-CH_2), 52.6 (OCH_3), 62.5 (2-CH), 74.1 (5-CH), 127.2, 127.9, 128.3, 128.4, 128.8 (all Ar-CH), 136.1, 137.8, 142.9 (all C) and 172.3 (C=O); *m/z* [EI] 485 (M^+, 1%), 426 (49), 358 (11), 203 (7), 149 (26), 143 (38), 115 (34), 91 (100) and 56 (51) [Found [CI]: M + H^+, 486.0237. $C_{19}H_{21}INO_4S$ requires *M*, 486.0236].

NOE data: 2-H_a–3-H_a, 7%; 3-H_a–3-H_b, 20%; 3-H_a–4-H_a, 5%.

Methyl (2*RS*,4*RS*,5*SR*)-4-iodo-5-propyl-1-(4-tolylsulfonyl)-pyrrolidine-2-carboxylate 12c. Homoallylic toluenesulfonamide **5c** (1.00 g, 3.25 mmol) was cyclised with iodine (2.49 g, 9.74 mmol) and potassium carbonate (1.34 g, 9.74 mmol) according to the general procedure and the reaction was complete after 3 h. The crude product was chromatographed (6 : 1 hexane–ethyl acetate) to give the *pyrrolidine* **12c** (1.20 g, 82%) as a colourless solid, mp 73–76 °C, ν_{max}/cm^{-1} 2956 (s), 1750 (s), 1560 (m), 1495 (m), 1450 (m), 1372 (m), 1344 (s), 1281 (m), 1209 (s), 1157 (s), 1054 (m), 1133 (s), 1094 (m), 1080 (m) and 1015 (m); δ_H 0.83 (3H, t, J = 7.2, 3′-CH_3), 1.25 (2H, sextet, J = 7.2, 2′-CH_2), 1.34–1.44 (1H, m, 1′-Ha), 1.94–2.04 (1H, m, 1′-Hb), 2.40–2.52 (4H, m, 3-H_a and Ar-CH_3), 2.87 (1H, ddd, J = 14.9, 9.1 and 7.1, 3-H_b), 3.73 (3H, s, OCH_3), 4.01–4.13 (1H, m, 5-H), 4.17 (1H, ddd, J = 7.1 and 3.1 and 3.1, 4-H), 4.64 (1H, dd, J = 9.1 and 2.9, 2-H), 7.36 (2H, d, J = 8.2, 2 × Ar-H) and 7.86 (2H, d, J = 8.2, 2 × Ar-H); δ_C 13.8 (3′-CH_3), 18.4 (2′-CH_2), 19.8 (4-CH), 21.5 (Ar-CH_3), 35.0 (1′-CH_2), 40.0 (3-CH_2), 52.3 (OCH_3), 60.9 (2-CH), 71.4 (5-CH), 127.6 (2 × Ar-CH), 129.5 (2 × Ar-CH), 137.6, 143.5 (both C) and 171.9 (C=O); *m/z* [EI] 452 (M + H^+, 1%), 408 (43), 392 (52), 324 (13), 222 (20), 155 (62) and 91 (100); *m/z* [NH_4 CI] 469 (M + NH_4^+, 100) and 452 (M + H^+, 9%) [Found: M + NH_4^+, 469.0658. $C_{16}H_{26}IN_2O_4S$ requires *M*, 469.0660] [Found: C, 42.70; H, 4.85; N, 3.14. $C_{16}H_{22}INO_4S$ requires C, 42.57; H, 4.92; N, 3.10%].

NOE data: 2-H_a–3-H_a, 7%; 3-H_a–3-H_b, 9%; 3-H_a–4-H_a, 5%.

Reductions: general procedure

The pyrrolidine-2-carboxylate (1 mmol, 1.0 eq.) was stirred in

toluene (1 ml) at 0 °C and a solution of 1.5 M DIBAL-H in toluene (2.1 eq.) was added dropwise. The reaction was stirred until complete by TLC, typically 3 h, then methanol (0.1 ml) was added dropwise, followed by 2 M hydrochloric acid (2 ml). The aluminium salts were filtered off and the organic layer was separated. The aqueous solution was extracted with ether (3 × 5 ml) and the combined organic solutions were dried, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography.

(2*RS*,4*SR*,5*RS*)-5-(2-Furyl)-4-iodo-1-(4-tolylsulfonyl)pyrrolidine-2-methanol 13a. The pyrrolidine-2-carboxylate **11a** (40 mg, 0.086 mmol) was reduced with 1.5 M DIBAL-H in toluene (0.12 ml, 0.18 mmol) according to the general procedure to give a crude product which was chromatographed (3 : 1 hexane–ethyl acetate) to give the *alcohol* **13a** (26 mg, 70%), as an oil, ν_{max}/cm^{-1} 3513 (s), 2926 (s), 2854 (m), 1594 (m), 1495 (m), 1348 (s), 1165 (s) and 1015 (m); δ_H 1.61 (1H, br s, OH), 2.17 (1H, ddd, J = 13.8, 7.0 and 4.4, 3-H$_a$), 2.42 (3H, s, Ar-CH$_3$), 2.50 (1H, ddd, J = 13.8, 7.5 and 5.7, 3-H$_b$), 3.79 (1H, dd, J = 12.1 and 4.3, C*H*$_a$H$_b$OH), 3.97 (1H, dd, J = 12.1 and 3.1, CH$_a$*H*$_b$OH), 4.05 (1H, m, 2-H), 4.34–4.38 (1H, m, 4-H), 5.02 (1H, d, J = 3.2, 5-H), 6.31 (1H, dd, J = 3.3 and 1.9, 4′-H), 6.40 (1H, d, 3.3, 3′-H), 7.31–7.33 (3H, m, 2 × Ar-CH and 5′-H) and 7.73 (2H, d, J = 8.3, 2 × Ar-CH); δ_C 21.0 (Ar-CH$_3$), 21.5 (4-CH), 41.0 (3-CH$_2$), 64.0 (2-CH), 66.0 (CH$_2$OH), 70.5 (5-CH), 111.0 (3′-CH), 108.8 (4′-CH), 128.1 (2 × Ar-CH), 129.9 (2 × Ar-CH), 142.6 (5′-CH), 136.0, 122.1 and 130.1 (all C); *m*/*z* [EI] 447 (M$^+$, 0.5%), 416 (78), 320 (12), 256 (21), 160 (21), 155 (100), 134 (90) and 85 (74) [Found: M$^+$, 447.0003. $C_{16}H_{18}INO_4S$ requires *M*, 447.0003].

(2*RS*,4*SR*,5*RS*)-4-Iodo-5-phenyl-1-(4-tolylsulfonyl)pyrrolidine-2-methanol 13b. The pyrrolidine-2-carboxylate **11b** (1.40 g, 3.90 mmol) was reduced with 1.5 M DIBAL-H (5.46 ml, 8.19 mmol), according to the general procedure for 2 h and the crude product chromatographed (3 : 1 hexane–ethyl acetate) to give the *alcohol* **13b** (1.00 g, 76%) as a pale yellow solid, mp 97–98 °C, ν_{max}/cm^{-1} 3425 (m), 1597 (w), 1448 (w), 1343 (m), 1162 (s), 1092 (m) and 1031 (m); δ_H 2.11 (1H, ddd, J = 13.7, 6.8 and 5.0, 3-H$_a$), 2.32 (1H, ddd, J = 13.7, 7.2 and 5.6, 3-H$_b$), 2.45 (3H, s, Ar-CH$_3$), 3.07 (1H, br s, OH), 4.00 (2H, app br s, CH$_2$OH), 4.04–4.10 (1H, m, 2-H), 4.15–4.19 (1H, m, 4-H), 5.02 (1H, d, J = 3.6, 5-H), 7.29–7.44 (7H, m, Ar-H) and 7.76 (2H, d, J = 8.3, 2 × Ar-H); δ_C 21.5 (CH$_3$), 25.9 (4-CH), 40.0 (3-CH$_2$), 63.0 (2-CH), 65.2 (CH$_2$OH), 75.9 (5-CH), 126.4, 128.1, 128.2, 128.7, 129.9 (all Ar-CH), 133.9, 156.7 and 145.0 (all C); *m*/*z* [EI] 457 (M$^+$, 1%), 426 (42), 155 (18), 143 (28), 115 (27), 91 (100) and 64 (44) [Found [NH$_4$ CI]: M + H$^+$, 458.0289. $C_{18}H_{21}INO_3S$ requires *M*, 458.0289] [Found: C, 47.49; H, 4.70; N, 2.85. $C_{18}H_{20}INO_3S$ requires C, 47.26; H, 4.41; N, 3.06%].

(2*RS*,5*SR*)-5-(2-Furyl)-1-(4-tolylsulfonyl)-2,5-dihydropyrrole-2-methanol 14a and (±)-5-(2-furyl)-1-(4-tolylsulfonyl)-2,3-dihydropyrrole-2-methanol 15a. To a stirred solution of iodopyrrolidine **13a** (0.50 g) in toluene (10 ml) at room temperature was added DBU (0.17 ml, 2.1 mmol), dropwise. The resulting solution was heated to reflux for 2 h, then cooled to room temperature, acidified using 2 M hydrochloric acid (10 ml) and was extracted with hexane (4 × 20 ml). The combined organic extracts were dried, filtered and concentrated to give a crude product which was separated by column chromatography (3 : 1 hexane–ethyl acetate) and gave the *2,5-dihydropyrrole* **14a** (0.20 g, 59%) as an oil which showed δ_H 2.42 (3H, s, Ar-CH$_3$), 2.66 (1H, br s, OH), 3.69–3.80 (1H, m, C*H*$_a$H$_b$-OH), 3.81–3.90 (1H, m, CH$_a$*H*$_b$OH), 4.60–4.63 (1H, m, 2-H), 5.58 (1H, d, J = 2.0, 5-H), 5.72 (2H, app s, 3- and 4-H), 6.32 (2H, app d, J = 1.4, 3′- and 4′-H), 7.29 (2H, d, J = 8.1, 2 × Ar-H), 7.35 (1H, d, J = 1.3, 5′-H) and 7.68 (2H, d, J = 8.1, 2 × Ar-H); δ_C 21.6 (Ar-CH$_3$), 64.4 (2(5)-CH), 65.4 (5(2)-CH), 69.6 (CH$_2$OH), 108.1 (3′-CH), 110.6 (4′-CH), 127.5 (2 × Ar-CH), 127.7 (3(4)-CH), 128.0 (4(3)-CH), 134.8 (2 × Ar-CH), 135.0, 142.7 (both C), 144.0 (5′-CH) and 152.7 (C); *m*/*z* [NH$_4$ CI] 337 (M + NH$_4^+$, 100%) and 320 (M + H$^+$, 24%) [Found: M + NH$_4^+$, 337.1220. $C_{16}H_{21}N_2O_4S$ requires *M*, 337.1222].

The minor 2,3-dihydropyrrole **15a** was not obtained in a sufficiently pure state to permit full characterization.

6-Phenyl-5-(4-tolylsulfonyl)-2-oxa-5-azabicyclo[2.2.1]heptane 16. To a stirred solution of iodopyrrolidine **13b** (0.46 g, 1.0 mmol) in toluene (10 ml) at room temperature was added DBU (0.17 ml, 2.1 mmol), dropwise. The resulting solution was refluxed for 2 h then cooled to room temperature. 2 M Hydrochloric acid (10 ml) was added and the resulting mixture extracted with hexane (4 × 20 ml). The combined extracts were dried, filtered and evaporated to give a crude product (0.18 g, 56%), which was purified by column chromatography (3 : 1 hexane–ethyl acetate) and gave a pure sample of the major product **16** which showed ν_{max}/cm^{-1} 2962 (m), 1598 (m), 1495 (m), 1346 (s), 1160 (s), 1092 (s) and 1055 (s); δ_H 1.31 (1H, app dd, J = 10.2 and 2.0, 7a-H), 1.72 (1H, app dd, J = 10.2 and 2.4, 7b-H), 2.37 (3H, s, Ar-CH$_3$), 3.70 (1H, dd, J = 7.8 and 2.0, 5a-H), 3.99 (1H, app d, J = 7.8, 5b-H), 4.32 (1H, app s, 6-H), 4.50 (2H, app s, 2- and 3-H), 7.18–7.35 (7H, m, Ar-H) and 7.65 (2H, d, J = 8.2, 2 × Ar-H); δ_C 21.0 (CH$_3$), 36.5 (7-CH$_2$), 62.0, 71.0 (both CH), 64.5 (CH$_2$), 81.0 (CH), 126.8, 127.7, 127.8, 128.2, 129.9 (all Ar-CH), 137.6, 141.0 and 153.0 (all C); *m*/*z* [EI] 329 (M$^+$, 2%), 174 (13), 106 (58), 90.9 (100), 64.9 (49) [Found: M$^+$, 329.1086. $C_{18}H_{21}NO_3S$ requires *M*, 329.1086].

The two minor dihydropyrroles **14b** and **15b** were not separated in sufficiently pure states to allow characterization.

(*E*)-2-(4-Tolylsulfonylamino)oct-4-en-1-ol 17. The ester **5c** (2.0 g, 6.43 mmol, 1.0 eq.) was reduced using the foregoing general method, with DIBAL-H (1.5 M, 9.0 ml, 13.5 mmol, 2.1 eq.) in toluene (4 ml) to give the *alcohol* **17** (1.5 g, 79%) as a colourless oil, ν_{max}/cm^{-1} 3510 (m), 3283 (m), 2958 (m), 1599 (w), 1434 (m), 1325 (m), 1159 (s), 1093 (m) and 972 (m); δ_H 0.83 (3H, t, J = 7.4, 8-CH$_3$), 1.19 (2H, sextet, J = 7.4, 7-CH$_2$), 1.82 (2H, app q, J = 7.4, 6-CH$_2$), 2.01–2.17 (2H, m, 3-CH$_2$), 2.42 (3H, s, Ar-CH$_3$), 2.71 (1H, br s, OH), 3.14–3.25 (1H, m, 2-H), 3.52 (1H, dd, J = 11.4 and 5.4, 1-H$_a$), 3.54 (1H, dd, J = 11.4 and 4.9, 1-H$_b$), 4.98 (1H, ddd, J = 14.8, 7.4 and 7.4, 4-H), 5.18 (1H, br s, NH), 5.36 (1H, ddd, J = 14.8, 7.4 and 7.4, 5-H), 7.30 (2H, d, J = 8.1, 2 × Ar-H) and 7.72 (2H, d, J = 8.1, 2 × Ar-H), δ_C 13.6 (9-CH$_3$), 21.5 (Ar-CH$_3$), 22.2 (7-CH$_2$), 34.5 (6(3)-CH$_2$), 34.8 (3(6)-CH$_2$), 55.2 (2-CH), 64.4 (1-CH$_2$), 124.4 (4(5)-CH), 127.1 (2 × Ar-CH), 129.6 (2 × Ar-CH), 134.9 (5(4)-CH), 137.2 (C), and 143.4 (C); *m*/*z* [CI] 315 (M + NH$_4^+$, 100%) and 298 (M + H$^+$, 30%) [Found: M + H$^+$, 298.1477. $C_{15}H_{24}NO_3S$ requires *M*, 298.1477] [Found: C, 60.29; H, 7.75; N, 4.65. $C_{15}H_{23}NO_3S$ requires C, 60.58; H, 7.79; N, 4.65%].

(*E*)-5-(2-Furyl)-2-(4-tolylsulfonylamino)pent-4-en-1-ol 21. The ester **5a** (0.12 g, 0.35 mmol, 1.0 eq.) was stirred in toluene (0.35 ml) at 0 °C and DIBAL-H (1.5 M, 0.50 ml, 0.74 mmol, 2.1 eq.) was added dropwise. The resulting solution was stirred at 0 °C for 3 hours, when toluene (1.0 ml) was added followed by the dropwise addition of methanol (0.5 ml). 2 M Hydrochloric acid (2 ml) was added, the aluminium salts were then filtered off and the organic layer was separated. The aqueous layer was extracted with ether (3 × 2 ml) and the combined organic solutions were dried, filtered and concentrated under reduced pressure. The crude product was chromatographed (3 : 1 hexane–ethyl acetate) to give the *alcohol* **21** (0.06 g, 52%), as an oil, ν_{max}/cm^{-1} 3470 (m), 3292 (m), 2925 (w), 1598 (m), 1424 (m), 1324 (m), 1157 (s), 1092 (m), 1013 (m) and 965 (m); δ_H 2.28–2.36 (2H, m, 3-CH$_2$), 2.40 (3H, s, Ar-CH$_3$), 3.30–3.34 (1H, m, 2-H), 3.59 (1H, dd, J = 11.2 and 5.1, 1-H$_a$), 3.66 (1H, dd,

J = 11.2 and 4.1, 1-H_b), 5.15 (1H, d, J = 7.4, 5-H), 5.71 (1H, ddd, J = 13.5, 7.4 and 7.4, 4-H), 6.11 (1H, d, J = 3.4, 3′-H), 6.35 (1H, dd, J = 3.4 and 1.6, 4′-H), 7.23 (2H, d, J = 8.2, 2 × Ar-H), 7.29 (1H, d, J = 1.6, 5′-H) and 7.74 (2H, d, J = 8.2, 2 × Ar-H); δ_C 21.5 (Ar-CH_3), 34.9 (3-CH_2), 55.2 (2-CH), 64.5 (1-CH_2), 107.2 (3′-CH), 111.1 (4′-CH), 122.0 (5(4)-CH), 123.4 (4(5)-CH), 127.1 (2 × Ar-CH), 129.6 (2 × Ar-CH), 137.0 (C), 141.6 (5′-CH), and 143.5 (C); *m/z* [ES] 322 (M + H^+, 100%), 255 (30), 149 (12) and 83 (82) [Found [NH_4 CI]: M + NH_4^+, 339.1378. $C_{16}H_{23}N_2O_2S$ requires *M*, 339.1378].

(1′*S*,2*SR*,4*SR*)- and (1′*S*,2*SR*,4*RS*)-2-(1-Iodobutan-1-yl)-4-(4-tolylsulfonylamino)tetrahydrofuran 19 and 20. *i) Under acidic conditions.* Homoallylic toluenesulfonamide **17** (0.20 g, 0.738 mmol, 1.0 eq.) was cyclised by treatment with iodine (0.56 g, 2.21 mmol, 3.0 eq.) according to the general procedure with no added base and the reaction was complete after 2 h. The crude product (0.18 g, 56%) was a 1 : 1 mixture of isomers and was chromatographed (6 : 1 hexane–ethyl acetate) to yield small amounts of these in a pure state for characterisation: the *cis* isomer **19** showed, ν_{max}/cm^{-1} 3274 (s), 2958 (s), 1598 (m), 1456 (m), 1333 (m), 1161 (s) and 1092 (s); δ_H 0.90 (3H, t, J = 7.4, 4′-CH_3), 1.25–1.67 (5H, m, 2′- and 3′-CH_2 and 3-H_a), 2.32 (1H, ddd, J = 13.6, 7.4 and 7.4, 3-H_b), 2.44 (3H, s, Ar-CH_3), 3.53 (1H, app q, J = 7.4, 2-H), 3.65–3.75 (2H, m, 5-CH_2), 3.96 (1H, m, 4-H), 4.20 (1H, m, 1′-H), 5.25 (1H, d, J = 8.7, NH), 7.33 (2H, d, J = 8.2, 2 × Ar-H) and 7.77 (2H, d, J = 8.2, 2 × Ar-H); δ_C 13.2 (4′-CH_3), 21.6 (Ar-CH_3), 22.6 (3′-CH_2), 38.2 (2′-CH_2), 38.7 (3-CH_2), 45.1 (1′-CH), 53.4 (4-CH), 72.5 (5-CH_2), 81.2 (2-CH), 127.1 (2 × Ar-CH), 129.9 (2 × Ar-CH), 137.4 and 143.8 (both C); *m/z* [EI] 424 (M + H^+, 4%), 296 (36), 252 (4), 214 (45), 172 (25), 155 (53) and 125 (100); [NH_4CI] 441 (M + NH_4^+, 100%) and 424 (M + H^+, 55%) [Found: M + H^+, 424.0443. $C_{15}H_{23}INO_3S$ requires *M*, 424.0445]; *trans* isomer **20**, ν_{max}/cm^{-1} 3268 (s), 2958 (s), 1598 (m), 1447 (m), 1331 (m), 1161 (s) and 1093 (s); δ_H 0.92 (3H, t, J = 7.4, 4′-CH_3), 1.25–1.68 (4H, m, 2′- and 3′-CH_2), 1.91 (1H, ddd, J = 13.7, 8.3 and 6.9, 3-H_a), 2.07 (1H, ddd, J = 13.7, 6.4 and 2.5, 3-H_b), 2.44 (3H, s, Ar-CH_3), 3.57 (1H, dd, J = 9.0 and 2.4, 5-H_b), 3.75–3.82 (1H, m, 2-H), 3.89–3.98 (2H, m, 4-H and 5-H_a), 4.10 (1H, app q, J = 6.8, 1′-H), 5.05 (1H, d, J = 7.0, NH), 7.33 (2H, d, J = 8.1, 2 × Ar-H) and 7.76 (2H, d, J = 8.1, 2 × Ar-H); δ_C 10.5 (4′-CH_3), 21.6 (Ar-CH_3), 22.6 (3′-CH_2), 38.1 (2′-CH_2), 42.2 (1′-CH), 54.1 (4-CH), 73.6 (5-CH_2), 80.8 (2-CH), 127.1 (2 × Ar-CH), 129.9 (2 × Ar-CH), 137.2 and 143.8 (both C); *m/z* [EI] 424 (M + H^+, 5%), 392 (12), 296 (13), 252 (12), 214 (62), 172 (76), 155 (82) and 125 (100); [NH_4 CI] 441 (M + NH_4^+) (100) and 424 (M + H^+, 90%) (Found: M + H^+, 424.0443).

ii) Under basic conditions. Homoallylic toluenesulfonamide **17** (0.20 g, 0.738 mmol, 1.0 eq.) was cyclised with iodine (0.57 g, 2.21 mmol, 3.0 eq.) in acetonitrile (22 ml), according to the general procedure and the reaction was complete after 1 h. The crude product (0.19 g, 61%) was again a 1 : 1 mixture of isomers, pure samples of which showed spectral and analytical data identical to the foregoing samples.

(2*RS*,4*SR*,5*RS*)-5-(2-Furyl)-4-iodo-1-(4-tolylsulfonyl)-pyrrolidine-2-methanol 13a by cyclisation of homoallylic toluenesulfonamide 21. Homoallylic toluenesulfonamide **21** (25 mg, 0.80 mmol, 1.0 eq.) was iodocyclised with iodine (61 mg, 2.41 mmol, 3.0 eq.) according to the general procedure in the absence of potassium carbonate and the reaction was complete after 2 h. The crude product was chromatographed (6 : 1 hexane–ethyl acetate) to yield the *title compound* **13a** (26 mg, 69%) as an oil which showed identical spectroscopic and analytical data to those displayed by the sample of pyrrolidine-2-methanol **13a** obtained by reduction of ester **11a**.

Preparation of pyrroles 26: general procedure

To a stirred solution of iodopyrrolidine-2-carboxylate (1 mmol, 1 eq.) in DMF (6 ml) at room temperature was added DBU (2.1 mmol, 2.1 eq.), dropwise. The solution was then heated to 90 °C until elimination was complete according to TLC analysis. The cooled solution was acidified with 2 M hydrochloric acid (6 ml) and the resulting mixture extracted with hexane (4 × 20 ml). The combined extracts were dried, filtered and concentrated under reduced pressure. The crude product was purified by dissolving in ethyl acetate and filtering through a small pad of silica, followed by evaporation of the filtrate.

Methyl 5-(2-furyl)pyrrole-2-carboxylate 26a. Iodopyrrolidine **12a** (0.20 g, 0.42 mmol) underwent eliminated according to the general procedure with DBU (100 μl, 0.88 mmol) in DMF (2.5 ml) and the reaction was complete after 1 h. The usual work-up gave the *pyrrole* **26a** (65 mg, 82%) as a colourless solid, mp 125–127 °C, ν_{max}/cm^{-1} 3297 (s), 2950 (m), 1694 (s), 1507 (w), 1440 (w), 1280 (s), 1270 (m) and 1190 (m); δ_H 3.89 (3H, s, OCH_3), 6.45 (1H, dd, J = 3.8 and 2.5, 4-H), 6.48 (1H, dd, J = 3.4 and 1.8, 4′-H), 6.55 (1H, d, J = 3.3, 3′-H), 6.93 (1H, dd, J = 3.8 and 2.5, 3-H), 7.3 (1H, app br s, 5′-H) and 9.33 (1H, br res, NH); δ_C 51.6 (OCH_3), 105.3, 107.0, 111.8, 116.7 (all CH), 137.0 (C), 141.8 (5′-CH), 146.0, 148.0 (both C) and 162.0 (C=O); *m/z* [EI] 191 (M^+, 54%), 159 (52), 131 (28), 103 (100), 76 (66) and 64 (63) [Found: M^+, 191.0582. $C_{10}H_9NO_3$ requires *M*, 191.0582].

Methyl 5-phenylpyrrole-2-carboxylate 26b. Iodopyrrolidine-2-carboxylate **11b** (50 mg, 0.103 mmol) underwent elimination with DBU (32 μl, 0.216 mmol) according to the general procedure and the reaction was complete after 1 h. The crude product was purified in the usual manner to give the *pyrrole* **26b** (14 mg, 81%) as a colourless solid, mp 144–146 °C (lit.[16] mp 142–143.5 °C); ν_{max}/cm^{-1} 3278 (s), 2950 (m), 1698 (s), 1436 (m), 1338 (m), 1163 (s) and 1092 (m); δ_H 3.89 (3H, s, OCH_3), 6.58 (1H, dd, J = 3.6 and 2.6, 4-H), 6.90 (1H, dd, J = 3.6 and 2.6, 3-H), 7.10–7.59 (5H, m, Ar-H) and 9.50 (1H, br res, NH).

Methyl 5-propylpyrrole-2-carboxylate 26c. Iodopyrrolidine-2-carboxylate **11c** (50 mg, 0.111 mmol) underwent elimination according to the general procedure with DBU (40 μl, 0.266 mmol) in DMF (0.5 ml) and the reaction was complete in 1 h. The usual work-up gave the *pyrrole* **26c** (14 mg, 78%) as a colourless oil, ν_{max}/cm^{-1} 3313 (s), 2958 (m), 1682 (s), 1494 (s), 1439 (s), 1329 (s), 1225 (s) and 1144 (m) δ_H 0.70 (3H, t, J = 7.5, 3′-CH_3), 1.68 (2H, sextet, J = 7.5, 2′-CH_2), 2.60 (2H, t, J = 7.5, 1′-CH_2), 3.84 (3H, s, OCH_3), 5.98 (1H, dd, J = 3.4 and 3.4, 4-H), 6.84 (1H, dd, J = 3.4 and 3.4, 3-H) and 8.94 (1H, br res, NH); δ_C 13.8 (3′-CH_3), 22.6 (2′-CH_2), 28.8 (1′-CH_2), 51.3 (OCH_3), 106.2 (4-CH), 116.0 (3-CH), 139.9, 130.0 (both C) and 171.0 (C=O) [Found [NH_4 CI]: M + NH_4^+, 185.1290. $C_9H_{17}N_2O_2$ requires *M*, 185.1290].

Under identical conditions and on the same scale, the 2,5-*trans*-3-iodopyrrolidine **12c** underwent elimination to give the *pyrrole* **26c** (15 mg, 76%) which displayed spectroscopic and analytical data identical to the foregoing.

Methyl 3-methyl-5-phenylpyrrole-2-carboxylate 26d. Iodopyrrolidine-2-carboxylate **11d** (0.46 g, 0.92 mmol) underwent elimination according to the general procedure with DBU (0.29 ml, 1.94 mmol) in DMF (9 ml) and the reaction was complete within 1 h to give the *pyrrole* **26d** (0.14 g, 70%) as a colourless solid, mp 124–126 °C; ν_{max}/cm^{-1} 3426 (s), 2924 (m), 1680 (s), 1453 (m) and 1268 (m); δ_H 2.39 (3H, s, 3-CH_3), 3.89 (3H, s, OCH_3), 6.40 (1H, d, J = 2.9, 4-H), 7.29–7.47 (5H, m, Ar-H) and 9.08 (1H, br s, NH); δ_C 12.9 (3-CH_3), 51.2 (OCH_3), 110.2 (4-CH), 124.6, 127.7, 129.0 (all Ar-CH), 129.1, 131.0, 135.0, 149.0 (all C) and 171.0 (C=O); *m/z* [EI] 215 (M^+, 100%), 182 (94), 154 (77), 139 (73), 128 (83), 114 (77), 101 (39), 90 (47) and 76 (84) [Found: M^+, 215.0946. $C_{13}H_{13}NO_2$ requires *M*, 215.0946] [Found: C, 72.32; H, 6.26; N, 6.45. $C_{13}H_{13}NO_2$ requires C, 72.53; H, 6.09; N, 6.51%].

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