Reactivity of cyclic sulfamidates towards sulfur-stabilised enolates. Stereocontrolled synthesis of functionalised lactams

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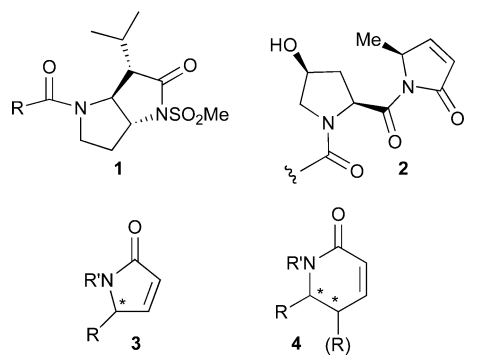
A structurally representative series of 1,2- and 1,3-cyclic sulfamidates react with enolates derived from methyl α-phenylthioacetate **9b** to give 5- and 6-substituted α-phenylthio lactams **20**–**24**. These products provide, *via* the corresponding sulfoxides, an entry to α,β-unsaturated lactams *e.g.* **12**, **27**, **29** and their α-phenylthio analogues *e.g.* **26** and **30**. With the enantiomerically pure 1,2-cyclic sulfamidates **10**, **15** and **17**, these reactions all proceed with no detectable loss of stereochemical integrity.

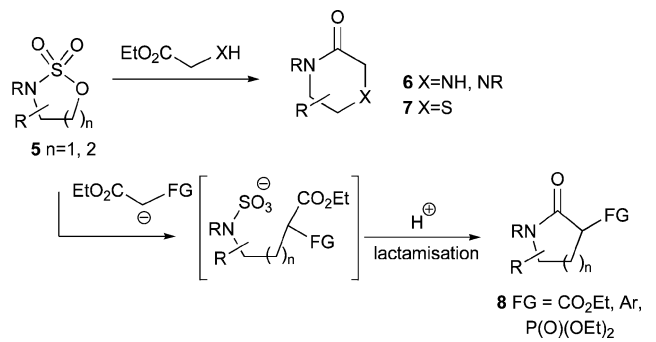
Introduction

Five and six-ring lactams, and the related saturated *N*-heterocycles, pyrrolidines and piperidines, represent important classes of molecules that find widespread applications throughout academia, the fine chemicals industry and, in particular, within the pharmaceutical sector.[1] Reports highlighting recent interest in the medicinal chemistry aspects of functionalised lactams include the *trans*-fused bicyclic serine protease inhibitors *e.g.* **1** reported by MacDonald and co-workers,[2] and the incorporation of α,β-unsaturated lactams units (derived from pyroglutamic acid) into microcolin A analogues **2** as described by Crews.[3] In both cases, enantiomerically pure substituted lactams represented key components of these biologically active entities.



We were attracted by two challenges in this area: (i) the synthesis of enantiomerically pure substituted 5- and 6-ring lactams and (ii) the ability to provide an entry to more highly functionalised lactams, such as the α,β-unsaturated variants. Currently, there are limited methods for accessing enantiomerically pure unsaturated 5- and 6-ring lactams **3** and **4**. The corresponding ω-carboxylic acid derivatives (pyroglutamic acid as well as the corresponding six-ring variant)[4] provide a valuable entry; pyroglutamic acid provided the starting point for the synthesis of **2**.[3] This approach, however, has inherent limitations in terms of the range of substrates that are accessible, and other recent reports have exploited the use of chiral auxiliaries or directing groups for the synthesis of a wider range of substituted and unsaturated lactam variants. These include use of (*R*)- and (*S*)-α-methyl benzylamine to direct a range of ring substitution reactions within a bicyclic framework,[5] and the exploitation of chiral anthracene cycloadducts (again incorporating α-methyl benzylamine) to generate 5-substituted α,β-unsaturated lactams *via* a retro Diels–Alder fragmentation.[6] The asymmetric Mannich reaction between imines and enol ethers provides a catalytic entry to 6-substituted six-ring lactams, as exemplified by a synthesis of (−)-sedamine.[7]

Our focus has been upon the application of substituted 1,2- and 1,3-cyclic sulfamidates **5** to the synthesis of enantiomerically pure substituted *N*-heterocycles, including lactams.[8,9] We have reported the synthesis of a range of enantiomerically pure scaffolds, such as piperazinones **6**, thiomorpholinones **7**,[8a] and a series of α-functionalised lactams **8**.[8b] The strategy that we have developed is outlined in Scheme 1.



Scheme 1

This involves the regioselective ring opening of a 1,2- or 1,3-cyclic sulfamidate with an α-amino ester (including α-substituted amino esters) or α-thiolester to give **6** and **7**, respectively. Alternatively, use of a functionalised enolate as the nucleophilic component provides a versatile entry to α-functionalised variants **8**. This methodology has also recently been applied to an efficient asymmetric synthesis of (−)-aphanorphine, which itself represents an entry to 3-benzazepines.[9]

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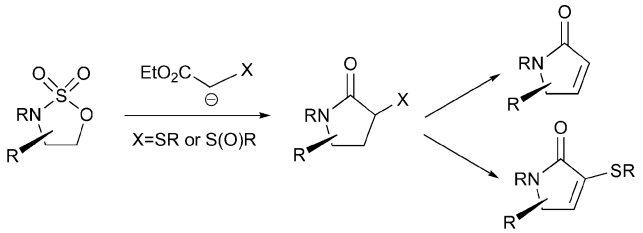
Results and discussion

A strategy for lactam synthesis using cyclic sulfamidates also offers an entry to α,β-unsaturated lactams and their α-thiophenyl derivatives based on the use of an α-sulfinyl (or an α-thio) enolate as the nucleophilic component (Scheme 2). Following ring opening of the cyclic sulfamidate, and subsequent lactamization, either (i) thermal elimination of RSOH or (ii) Pummerer oxidation would provide access to the target systems.

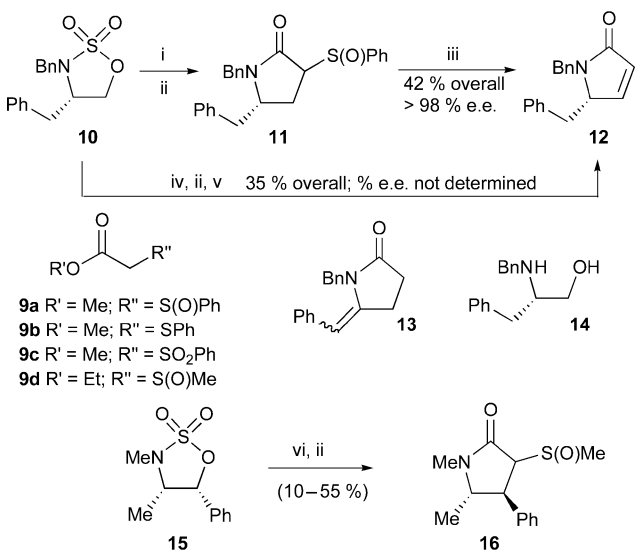


Scheme 2 Synthetic approach to unsaturated lactams *via* cyclic sulfamidates.

In this paper we report on the scope and limitations of this approach to functionalised and unsaturated substituted lactams, in terms of both the nucleophilic and electrophilic components.

Use of α-sulfinyl substituted enolates

We have previously investigated the ability of enolates derived from esters **9a**–**c** (see Scheme 3) carrying an α-sulfur-based electron withdrawing group (SR *vs* S(O)R *vs* SO_2R) to react with 1,2- and 1,3-cyclic sulfates,[10] and here we had encountered problems associated with the use of **9a** and **9b** (*i.e.* X = S(O)Ph and X = SPh, respectively). We were not able to achieve the desired transformations (nucleophilic ring opening of the cyclic sulfate substrate), although the analogous sulfone-based nucleophile **9c** was successfully employed. Although sulfoxide-stabilised enolates have been more successful with cyclic sulfamidates, we have nevertheless encountered issues in the reactions of **9a** (X=S(O)Ph) with some 1,2-cyclic sulfamidates which are described below (Scheme 3).



Scheme 3 Reagents and conditions: (i), **9a**, NaH, DMF, r.t.; (ii), 5 M HCl then $NaHCO_3$; (iii), PhMe, PS–PPh_3, 100 °C; (iv), **9d**, NaH, DMF, r.t.; (v), PhMe, $NaHCO_3$, reflux, 4 d; (vi), **9d**, KO*t*-Bu, *t*-BuOH, reflux.

Cyclic sulfamidate **10**, a representative and readily available substrate, reacted with the enolate derived from ester **9a** to give, after acidic hydrolysis (to cleave the intermediate *N*-sulfate) and neutralization (to achieve lactamization), lactam **11** in 48% yield as a mixture of diastereomers (Scheme 3). Issues associated with purification of the final product necessitated the use of a polystyrene-bound phosphine (PS–PPh_3)† scavenger for the subsequent sulfoxide elimination step, and in this way we were able to obtain **12** in 42% overall yield and in >98% e.e. (as judged by chiral HPLC). In the absence of a scavenger, alkene migration was facile and benzylidene derivative **13** was isolated as the major product; alkene **13** was a single geometric isomer although the alkene geometry has not been established.

We were, however, unable to generate a lactam adduct from 4,5-disubstituted cyclic sulfamidate **15** using ester **9a** because of competing and premature elimination of PhSOH. Nucleophilic ring cleavage appeared to proceed as expected, but the elevated temperatures required to achieve annulation led to problems associated with competing elimination. For this reason, the corresponding methyl sulfoxide derivative **9d** was investigated. Using **10** as a test substrate with **9d**, unsaturated lactam **12** was obtained in 35% yield although the enantiopurity of this product was not established. The drawback of the use of **9d** was the prolonged period (4 d) required for thermal elimination of MeSOH, and alternative reaction conditions (including use of higher temperatures or microwave-mediated thermolysis) resulted in unacceptable levels of decomposition. We also isolated significant amounts of amino alcohol **14** after the initial sulfamidate opening step using **9d**, which is possibly formed *via* competing *O*-alkylation (and subsequent hydrolysis) of the enolate species. In the case of the sterically more demanding disubstituted sulfamidate **15**, reaction with the enolate derived from **9d** led to poor and irreproducible yields of adduct **16** as a mixture of diastereomers which was not pursued further. In addition, we were unable to achieve thermal elimination of MeSOH from this substrate and the use of sulfoxide-based enolates was abandoned.

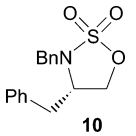
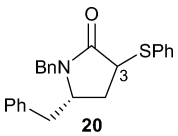
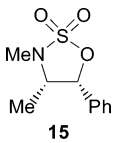
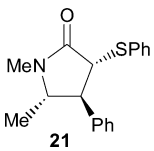
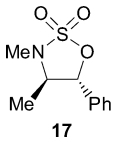
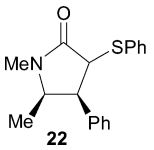
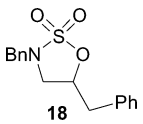
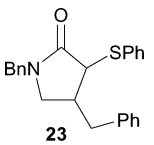
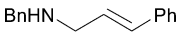
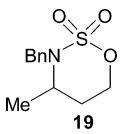
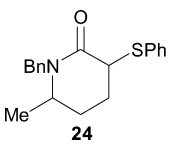
Use of α-sulfenyl substituted enolates

Enolates derived from α-thioesters have proven to be a more generally applicable class of nucleophiles, and use of ester **9b** with a series of cyclic sulfamidates (**10**, **15**, **17**–**19**) gave good yields of the corresponding α-phenylthio substituted lactams **20**–**24** A representative example based on cyclic sulfamidate **10** is illustrated in Scheme 4 and other details for additional substrates are presented in Table 1.

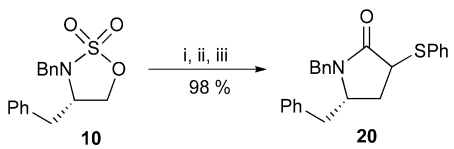
Certain experimental modifications were necessary in specific cases and these are detailed within the Experimental section. It should be noted that in some cases (*e.g.* formation of **21** and **22**) lactamisation occurred upon neutralization (following

† To the best of our knowledge PS–PPh_3 has not previously been used as a scavenger for thermal sulfoxide elimination reactions, although it has been widely applied to other processes, such as the Mitsunobu reaction.[11]

Table 1 Synthesis of α-sulfenyl substituted lactams

Entry	Cyclic sulfamidate[a]	*C*(3)-SPh lactam product[b]	Yield (%)	Comments
1	 **10**	 **20**	98	2 : 1 mixture of diastereomers at *C*(3) (see Scheme 4)
2	 **15**	 **21**	83	10 : 1 mixture of diastereomers at *C*(3); major isomer shown as determined by ^{1}H NMR
3	 **17**	 **22**	62	1 : 1 mixture of diastereomers at *C*(3)
4	 **18**	 **23**	23	3 : 2 mixture of diastereomers at *C*(3);  **25** (37 %)
5	 **19**	 **24**	80	1 : 1 mixture of diastereomers at *C*(3)

[a] Nucleophilic ring opening of **10**, **15**, **18** and **19** took place at room temperature, while **17** required 45 °C. [b] Lactamisation to give **21** and **22** took place at room temperature following neutralisation, whereas formation of **20**, **23** and **24** required thermal lactamisation conditions (see the Experimental section).



Scheme 4 Reagents and conditions: (i), **9b**, NaH DMF, r.t.; (ii), 5M HCl then $NaHCO_3$; (iii), PhMe, reflux. See Table 1 for other substrates studied.

nucleophilic cleavage and acidic hydrolysis) while in other examples (*e.g.* formation of **20** and **23**) the ring closure step was significantly slower and was best induced thermally. In the case of **24**, lactamisation was most efficiently achieved under basic (NaOEt, EtOH, heat) conditions.

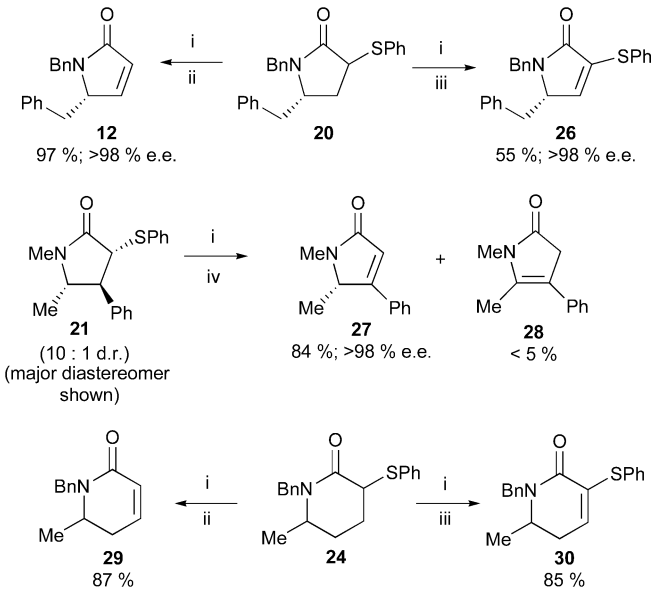
The substrates shown in Table 1 represent a range of readily available cyclic sulfamidate variants, which were chosen in order to define the scope of the underlying methodology. One limitation is obvious: use of the 5-benzyl derivative **18** leads to a significant amount of allylic amine **25**, which is the product of β-elimination of the precursor cyclic sulfamidate **18**. This is a side reaction that we had not previously encountered using **18** with other stabilised enolates, and this substrate appears to provide a good test as to the effectiveness of a given nucleophile towards a base sensitive substrate. It should also be pointed out that both the 1,2-cyclic sulfamidate **18** and the 1,3-cyclic sulfamidate **19** used in this study were most conveniently prepared in racemic form, while the other substrates (**10**, **15**, and **17**) employed here were derived using enantiomerically pure amino alcohols as starting materials.

Lactams **20**–**24** were all isolated as mixtures of diastereomers at *C*(3) and for the major isomer of **21**, the stereochemical assignment was based on correlations with related structures for which crystallographic data were available.[8b]

We have examined two transformations of representative α-phenylthiolactams shown in Table 1. These involved sulfide oxidation followed by either thermal elimination to give the α,β-unsaturated lactams, or Pummerer reaction of the sulfoxide intermediate which leads to the corresponding vinyl sulfides (see Scheme 2 and 5).

With lactams **20** and **21**, the key issue of interest associated with sulfoxide elimination was the enantiomeric integrity of the unsaturated products obtained. This is of particular significance in the five-ring series given the obvious possibilities associated with the allylic nature of *C*(5) present in *e.g.* **12** and **27**.

The oxidation/sulfoxide elimination reactions proceeded efficiently, and the unsaturated lactams **12**, **27** and **29** were obtained in high yields and for **12** and **27** with essentially no loss of enantiomeric integrity (Scheme 5). The enantiomeric purities of **12** and **27** were readily assessed using chiral HPLC with the corresponding racemic substrates being used as analytical standards. Generally, it was more convenient to use a polymer-supported phosphine to scavenge phenylsulfenic acid, but this was not essential to the



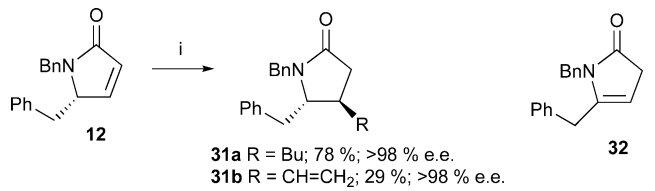
Scheme 5 Reagents and conditions: (i), *m*-CPBA, CH_2Cl_2, 0 °C; (ii), PhMe, PS–PPh_3, 100 °C; (iii), $(CF_3CO)_2O$, CH_2Cl_2, r.t.; (iv), $NaHCO_3$, MeCN, reflux.

success of these reactions. Interestingly, in the case of **21**, use of the resin-based scavenger led to approximately 50% of the enamine by-product **28**, but this side reaction was effectively suppressed when mildly basic conditions (use of $NaHCO_3$) were employed. In addition, the sulfoxide intermediate derived from the minor diastereomer of **21** did not undergo thermal elimination under a variety of conditions; this reflects upon the *trans* stereochemical relationship between the phenyl sulfoxide substituent and the β-proton. This observation also emphasises the importance of a favourable stereochemical outcome from the initial sulfamidate opening step to the overall efficiency of the sequence, as we were unable to achieve *in situ* equilibration of this stereocentre under the elimination conditions used. It is pertinent to point out that use of a 2-pyridyl variant of **9b** (*i.e.* R″ = S(2-Py)) for the initial sulfamidate opening/lactamisation sequence provides lactams which do undergo equilibration at *C*(3) under the mildly acidic oxidation conditions employed to form the requisite sulfoxide. This can be beneficial for the subsequent elimination step in cases where **9b** provides substrates with an unfavourable *C*(3) stereochemistry.

Sulfoxide-based Pummerer reactions also proceeded smoothly using the representative 5- and 6-ring lactams **20** and **24** to give **26** and **30**. In the case of **26**, which has an obvious sensitivity towards racemisation, no degradation of enantiomeric purity was detected (as judged by chiral HPLC).

It is also appropriate to mention that α,β-unsaturated lactams are valuable electrophiles in their own right. Accordingly, lactam **12** underwent a diastereoselective copper-mediated 1,4-addition of either *n*-BuLi or CH_2=CHMgBr to provide the 4,5-disubstituted lactams **31a** and **31b** (Scheme 6).

Again, no loss of enantiomeric purity was detected for **31a** and **31b** (based on chiral HPLC analysis). Similar 1, 4-additions involving *N*-alkyl lactams[12] have been reported but HMPA was required for these processes; in the absence of HMPA, the major product corresponded to base-mediated double bond isomerisation leading to enamine **32**. It is appropriate to note that work-up of these conjugate addition reactions involved exposure of the crude material to TBAF, since substantial amounts of *C*-silylated material were formed under the reaction conditions.



Scheme 6 Reagents and conditions: (i), *n*-BuLi or CH_2=CHMgBr, CuI, Me_3SiCl, HMPA, THF, r.t.

Conclusions

In summary, a range of variously substituted 1,2- and 1,3-cyclic sulfamidates react efficiently with sulfur-substituted enolates to give α-thiosubstituted lactams, which can then be used to generate the corresponding enones and vinyl sulfides. Thio-substituted enolates were the reagents of choice as these proved to be more generally applicable than the corresponding sulfoxide-substituted enolates. In cases where enantiomerically pure cyclic sulfamidates were used, clean inversion (where appropriate) was observed during the initial nucleophilic ring opening step and no erosion of enantiomeric integrity was encountered following lactam formation. In addition a series of other synthetically valuable reactions based on α,β-unsaturated lactams also proceeded without loss of enantiomeric purity. These transformations of cyclic sulfamidates demonstrate a new and straightforward approach to functionalised and enantiomerically pure lactams, and the further application of this chemistry to specific targets is underway.

Experimental

General

Starting materials sourced from commercial suppliers were used as received. Dry solvents, where necessary, were obtained by distillation using standard procedures or by passage through a column of anhydrous alumina using equipment from Anhydrous Engineering based on the Grubbs' design. Petrol refers to the fraction of petroleum ether boiling in the range of 40–60 °C. The removal of solvents *in vacuo* was achieved using both a Büchi rotary evaporator (bath temperatures up to 40 °C) at a pressure of either 15 mmHg (diaphragm pump) or 0.1 mmHg (oil pump), as appropriate, and a high vacuum line at room temperature. Reactions requiring anhydrous conditions were run under an atmosphere of dry nitrogen; glassware, syringes and needles were either flame dried immediately prior to use or placed in an oven (150 °C) for at least 2 h and allowed to cool either in a desiccator or under an atmosphere of dry nitrogen; liquid reagents, solutions or solvents were added *via* syringe through rubber septa; solid reagents were added *via* Schlenk type adapters. Commercially available Merck Kieselgel $60F_{254}$ aluminium backed plates were used for TLC analysis. Visualisation was achieved by either UV fluorescence, acidic $KMnO_4$ solution and heat, ammonium molybdate solution and heat or iodine vapour. Flash column chromatography (FCC) was performed using Fluorochem

60 silica: 230–400 mesh (40–63 μm). The crude material was applied to the column as a solution in CH_2Cl_2 or by pre-adsorption onto silica, as appropriate. Melting points were determined using a Reichert melting point table and temperature controller and are uncorrected. Optical rotations were measured using a Perkin-Elmer 241 polarimeter. Infra-red spectra were recorded in the range 4000–600 cm^{-1} on a Perkin Elmer Spectrum either as neat films or solids compressed onto a diamond window. Abbreviations used are: w (weak), m (medium), s (strong) and br (broad). NMR spectra were recorded on a JEOL GX270, JEOL GX400, JEOL Lambda 300, JEOL Eclipse 400 or JEOL Eclipse 300 spectrometer. Chemical shifts are quoted in parts per million (ppm); ^1H NMR spectra are referenced to TMS or residual protium of the deuterated solvent; ^{13}C NMR are referenced to TMS or the deuterated solvent. Coupling constants (J) are quoted to the nearest 0.5 Hz. Other abbreviations used are: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). Assignments of ^1H NMR and ^{13}C NMR signals were made where possible, using COSY, DEPT, HMQC and HMBC experiments. Where, *e.g.*, diastereomers have been characterised as a mixture, signals associated with the individual isomers are, where possible, referred to as *A* and *B*. Mass spectra were determined by the University of Bristol mass spectrometry service by either electron impact (EI) or chemical ionisation (CI) using a Fisons VG Analytical Autospec spectrometer, or by electrospray ionisation (ESI) using a Brüker Daltonics Apex IV spectrometer. Chiral HPLC was performed using the corresponding racemate as a standard on an Agilent 1100 LC system equipped with a quaternary pump, diode array detector and column thermostat under the conditions specified in each case.

For the preparation of cyclic sulfamidates **10**, **15**, **17**, **18** and **19** see earlier publications.[8] Lactam-based sulfoxide intermediates, which were formed as mixtures of 4 diastereomers, have only been characterised by mass spectrometry due to the complexity of NMR data obtained.

(5*S*)-3-Phenylsulfinyl-1,5-dibenzylpyrrolidin-2-one (11)

To a solution of methyl (phenylsulfinyl)acetate **9a** (143 mg, 0.72 mmol) in anhydrous DMF (3 cm^3) was added NaH (29 mg, 0.72 mmol, 60% dispersion in mineral oil) and the resulting suspension was stirred at r.t. for 10 min to form a pale yellow solution. Sulfamidate **10** (218 mg, 0.72 mmol) was added and the mixture was stirred at r.t. for 16 h. Aqueous 5 M HCl (0.37 cm^3) was added and the mixture was stirred at r.t. for 3 h. The mixture was neutralised by addition of saturated aq. $NaHCO_3$ (7 cm^3) and extracted with Et_2O (3 × 30 cm^3). The combined organic portions were washed with water (3 × 50 cm^3), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by FCC (Et_2O) to afford sulfoxide **11** (141 mg, 54%) as a colourless foam and as a mixture of four diastereoisomers; m/z (CI^+) 390 ($[M + H]^+$, 15%), 264 (100%).

(*S*)-1,5-Dibenzyl-1,5-dihydropyrrol-2-one (12) and 1-benzyl-5-benzylidene pyrrolidin-2-one (13)

Procedure A (one pot procedure from cyclic sulfamidate 10). To a solution of methyl (phenylsulfinyl)acetate **9a** (143 mg, 0.72 mmol) in anhydrous DMF (3 cm^3) was added NaH (29 mg, 0.72 mmol, 60% dispersion in mineral oil) and the resulting suspension was stirred at r.t. for 10 min to form a pale yellow solution. Sulfamidate **10** (218 mg, 0.72 mmol) was added and the mixture was stirred at r.t. for 16 h. Aq. 5 M HCl (0.37 cm^3) was then added and the mixture was stirred at r.t. for 3 h. The mixture was then neutralised by addition of saturated aq. $NaHCO_3$ (7 cm^3) and extracted with Et_2O (3 × 30 cm^3). The combined organic portions were washed with water (3 × 50 cm^3), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in anhydrous toluene (6 cm^3), added to a suspension of PS–PPh_3 (932 mg, 1–1.8 mmol g^{-1} loading, swelled for 2 h) in anhydrous toluene (4 cm^3), and then heated at 100 °C for 2.5 h. The mixture was cooled to r.t., filtered through Celite, washing with toluene (3 × 15 cm^3) and then CH_2Cl_2 (2 × 5 cm^3), and concentrated *in vacuo*. The residue was purified by FCC (Et_2O–petrol 7 : 3) to afford alkene **12** (74 mg, 42%, >98% e.e.) as a colourless oil. In the absence of a scavenger, **13** was formed as the major product.

Procedure B. PS–PPh_3 (173 mg, *ca.* 3.0 mmol g^{-1} loading) was allowed to swell in anhydrous toluene (2 cm^3) without stirring for 1.5 h. A solution of phenyl sulfoxide **11** (88 mg, 0.23 mmol) in anhydrous toluene (3 cm^3) was added and the resulting mixture was heated at 100 °C for 2 h. The reaction mixture was allowed to cool to r.t., filtered through Celite, washing with toluene (3 × 5 cm^3) followed by CH_2Cl_2 (4 × 5 cm^3), and concentrated *in vacuo*. The residue was purified by FCC (Et_2O–hexanes 7 : 3) to afford the product **12** (67 mg, 99%, >98% e.e.) as a colourless, viscous oil

Data for lactam **12**; $[a]_D^{20}$ −17.9 (*c* 0.7, $CHCl_3$); ν_{max}/cm^{-1} (film) 3028 (br w), 1676 (s), 1494 (m), 1405 (m), 1232 (m), 1028 (m); δ_H (400 MHz, $CDCl_3$) 2.57 (1 H, d d, J = 13.5 and 9.0, C5–CH_2Ph), 3.17 (1 H, d d, J = 13.5 and 5.0, C5–CH_2Ph), 4.10 (1 H, d d d d, J = 9.0, 5.0, 1.5 and 1.5, C5–*H*), 4.16 (1 H, d, J = 15.0, NCH_2Ph), 5.21 (1 H, d, J = 15.0, NCH_2Ph), 6.15 (1 H, d d, J = 6.0 and 1.5, C4–*H*), 6.89 (1 H, d d, J = 6.0 and 1.5, C5–*H*), 7.05 (2 H, d t, J = 6.0 and 2.0, ArC*H*), 7.18–7.36 (8 H, m ArC*H*); δ_C (75 MHz, $CDCl_3$) 37.6 (C5–*C*H_2Ph), 43.9 (N*C*H_2Ph), 62.8 (*C*-5), 127.0 (*C*-3), 127.1, 127.6, 127.9, 128.6, 128.8 and 129.1 (10 × Ar*C*H), 136.0 and 137.4 (2 × Ar*C*), 147.6 (*C*-4), 171.3 (*C*-2); m/z (CI^+) 264 ($[M + H]^+$, 100%); HRMS: (CI^+) Found: $[M + H]^+$ 264.1391, $C_{18}H_{18}NO$ requires 264.1388.

The enantiomeric purity of this compound was determined by chiral HPLC (Chiralcel OD, isocratic hexane–*i*-PrOH 93 : 7, 1.0 cm^3 min^{-1}, 20 °C); t_R (major) = 16.8 min and t_R (minor) = 20.4 min.

Data for exoalkene **13**; ν_{max}/cm^{-1} (film) 2920 (w), 1702 (s), 1635 (s), 1418 (m), 1342 (m), 1182 (m); δ_H (400 MHz, $CDCl_3$) 2.66–2.70 (2 H, m, C3–*H*), 3.01–3.06 (2 H, m, C4–*H*), 4.86 (2 H, s, NCH_2Ph), 5.78 (1 H, m, C5–CH_2Ph), 7.10–7.16 (3 H, m, ArC*H*), 7.25–7.40 (7 H, m, ArC*H*); δ_C (75 MHz, $CDCl_3$) 24.0 (*C*-4), 29.1 (*C*-3), 44.0 (N*C*H_2Ph), 104.1 (C5–*C*HPh), 125.7, 127.4, 127.6, 127.9, 128.6 and 128.9 (Ar*C*H × 10), 136.2 and 136.8 (Ar*C* × 2), 141.7 (*C*-5), 175.5 (*C*-2); m/z (CI^+) 264 ($[M + H]^+$, 100%); HRMS: (CI^+) Found: $[M + H]^+$ 264.1382, $C_{18}H_{18}NO$ requires 264.1388.

(5*S*)-1,5-Dibenzyl-3-methanesulfinylpyrrolidin-2-one and (2*S*)-2-benzyl amino-3-phenylpropan-1-ol (14)

To a solution of ethyl(methylsulfinyl)acetate **9d** (73 mg, 0.49 mmol) in anhydrous DMF (2 cm^3) at r.t. was added NaH (20 mg, 0.49 mmol, 60% dispersion in mineral oil) and the resulting

colourless suspension was stirred at r.t. for 20 min to form a pale yellow solution. Sulfamidate **10** (134 mg, 0.44 mmol) was added and the mixture was stirred at r.t. 18 h. Aqueous 5 M HCl (0.2 cm^3) was added and the resulting suspension was stirred at r.t. for 3 h. The reaction mixture was neutralised by addition of saturated aq. $NaHCO_3$, diluted by addition of water (10 cm^3) and extracted with Et_2O (3 × 10 cm^3). The organic extracts were combined, washed with water (3 × 10 cm^3), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in toluene (3 cm^3) and heated at 80 °C for 12 h, allowed to cool to r.t., and concentrated *in vacuo*. The residue was purified by FCC (CH_2Cl_2–MeOH 19 : 1) to afford (5*S*)-1,5-dibenzyl-3-methanesulfinylpyrrolidin-2-one (60 mg, 43%) as a pale oil and subsequently amino alcohol **14** (15 mg, 14%) as a colourless solid.

Data for (5*S*)-1,5-dibenzyl-3-methanesulfinylpyrrolidin-2-one: *m*/*z* (CI^+) 328 ($[M + H]^+$, 100%) 264 ($[M–SOMe]^+$, 90).

Data for **14**: δ_H (400 MHz, $CDCl_3$) 2.70–2.88 (2 H, m, C3–*H*), 2.96 (1 H, m, C2–*H*), 3.34 (1 H, d d, *J* = 10.5 and 5.5, C1–*H*), 3.65 (1 H, d d, *J* = 10.5 and 4.0, C1–*H*), 3.77 (2 H, s, NCH_2Ph), 7.14–7.36 (10 H, m, ArC*H*); *m*/*z* (CI^+) 242 ($[M + H]^+$, 100%). The spectroscopic properties of this compound were consistent with the data available in the literature.[13]

(4*S*,5*S*)-3-Methanesulfinyl-1,5-dimethyl-4-phenylpyrrolidin-2-one (16)

To a solution of ethyl(methylsulfinyl)acetate **9d** (173 mg, 1.15 mmol) in anhydrous *t*-BuOH (6 cm^3) at r.t. was added *t*-BuOK (136 mg, 1.15 mmol) and the resulting colourless suspension was stirred at r.t. for 20 min. Sulfamidate **15** (238 mg, 1.10 mmol) was added and the reaction mixture was heated at reflux for 46 h. The reaction mixture was allowed to cool to r.t. and aq. 5 M HCl (0.56 cm^3) was added and the mixture was stirred at r.t. for 4 h. The reaction mixture was neutralised by addition of saturated aq. $NaHCO_3$, diluted by addition of brine (30 cm^3) and extracted with CH_2Cl_2 (3 × 30 cm^3). The organics were combined, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by FCC (CH_2Cl_2–MeOH 10 : 1) to afford lactam **16** (152 mg, 55%) as a pale yellow oil and as a mixture of four diastereoisomers; *m*/*z* (CI^+) 252 ($[M + H]^+$, 100%).

(5*S*)-1,5-Dibenzyl-3-phenylsulfanylpyrrolidin-2-one (20)

To a solution of methyl(phenylthio)acetate **9b** (153 µl, 1.00 mmol) in anhydrous DMF (6 cm^3) was added NaH (40 mg, 1.00 mmol, 60% dispersion in mineral oil) and the resulting mixture was stirred at r.t. for 20 min to form a colourless suspension. Sulfamidate **10** (150 mg, 0.50 mmol) was added and the reaction mixture was stirred at r.t. for 20.5 h. Aqueous 5 M HCl (0.5 cm^3) was added and the resulting colourless suspension was stirred at r.t. for 3 h. The reaction mixture was neutralised by addition of saturated aq. $NaHCO_3$ and extracted with Et_2O (3 × 15 cm^3). The organic extracts were combined, washed with water (3 × 10 cm^3), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in toluene (8 cm^3) and heated at 100 °C for 18 h. Solvent was removed *in vacuo* and the residue was purified by FCC (Et_2O–petrol 1 : 1) to afford lactam **20** (183 mg, 98%, 2 : 1 d.r.) as a pale yellow oil; ν_{max}/cm^{-1} (thin film) 3028 (w), 2924 (w), 1686 (s), 1438 (m), 1249 (m), 733 (s), 691 (m); δ_H (400 MHz, $CDCl_3$) 1.79 (1 H, d d d, *J* = 13.5, 6.5 and 6.5, C4–*H* of *A*), 1.94 (1 H, d d d, *J* = 13.5, 8.0 and 8.0, C4–*H* of *B*), 2.20 (1 H, d d d, *J* = 13.5, 9.0 and 3.5, C4–*H* of *B*), 2.26 (1 H, d d, *J* = 13.0 and 10.0, C5–CH_2Ph of *A*), 2.33 (1 H, d d d, *J* = 13.5, 8.5 and 7.5, C4–*H* of *A*), 2.60 (1 H, d d, *J* = 13.5 and 8.0, C5–CH_2Ph of *B*), 2.93 (1 H, d d, *J* = 13.5 and 4.0, C5–CH_2Ph of *B*), 3.12 (1 H, d d, *J* = 13.0 and 4.5, C5–CH_2Ph of *A*), 3.49–3.62 (3 H, m, C5–*H* of *A* and *B* and C3–*H* of *B*), 3.84 (1 H, d d, *J* = 10.0 and 7.5, C3–*H* of *A*), 3.97 (1 H, d, *J* = 15.0, NCH_2Ph of *B*), 4.15 (1 H, d, *J* = 15.0, NCH_2Ph of *A*), 5.03 (1 H, d, *J* = 15.0, NCH_2Ph of *A*), 5.15 (1 H, d, *J* = 15.0, NCH_2Ph of *B*), 6.97 (2 H, d, *J* = 6.5, ArC*H* of *A*), 7.02 (2 H, d, *J* = 7.0, ArC*H* of *B*), 7.08–7.41 (22 H, m, ArC*H*), 7.46–7.52 (2 H, m, ArC*H*), 7.57–7.63 (2 H, m, ArC*H*); δ_C (100 MHz, $CDCl_3$) 31.8 (*C*-4 of *B*), 32.0 (*C*-4 of *A*), 38.9 (C5–*C*H_2Ph of *B*), 40.3 (C5–*C*H_2Ph of *A*), 45.0 (N*C*H_2Ph of *B*), 45.4 (N*C*H_2Ph of *A*), 46.9 (*C*-3 of *B*), 47.3 (*C*-3 of *A*), 55.7 (*C*-5 of *B*), 56.8 (*C*-5 of *A*), 126.8, 127.0, 127.7, 127.8 (2 signals), 128.1, 128.2, 128.7, 128.8 (2 signals), 129.0 (2 signals), 129.1, 129.2, 129.3 and 132.7 (16 × Ar*C*H), 133.0 (Ar*C*), 133.3 (2 × Ar*C*H), 134.1, 136.1, 136.5 (2 signals) and 136.9 (Ar*C*), 172.3 (*C*-2 of *B*), 172.8 (*C*-2 of *A*); *m*/*z* (CI^+) 374 ($[M + H]^+$, 100%); HRMS: (ESI) Found: $[M + Na]^+$ 396.1393, $C_{24}H_{23}NOSNa$ requires 396.1420.

Lactam **20** was oxidised to generate sulfoxide **11** as follows: To a solution of **20** (96 mg, 0.26 mmol) in CH_2Cl_2 (8 cm^3), at 0 °C, was added *m*-CPBA (64 mg, *ca.* 0.26 mmol, 70–75% purity) to form a colourless solution which was stirred at 0 °C for 2 h. The reaction mixture was quenched by addition of saturated aqueous potassium metabisulfite (10 cm^3). The organic portion was isolated, washed with saturated aq. $NaHCO_3$ (2 × 10 cm^3), dried (Na_2SO_4) and concentrated *in vacuo* to afford the sulfoxide **11** (98 mg, 97%) as a colourless foam. This was identical to the product obtain by reaction of **9** with **10** (see above).

(4*S*, 5*S*)-1,5-Dimethyl-4-phenyl-3-phenylsulfanylpyrrolidin-2-one (21)

To a solution of methyl(phenylthio)acetate **9b** (215 µl, 1.38 mmol) in anhydrous DMF (8.3 cm^3) was added NaH (55 mg, 1.38 mmol, 60% dispersion in mineral oil) and the resulting mixture was stirred at r.t. for 15 min to form a pale yellow suspension. Sulfamidate **15** (150 mg, 0.69 mmol) was added and the reaction mixture was stirred at r.t. for 18.5 h. Aq. 5 M HCl (0.69 cm^3) was added and the resulting pale yellow suspension was stirred at r.t. for 3 h. The reaction mixture was neutralised by addition of saturated aq. $NaHCO_3$ and extracted with Et_2O (3 × 20 cm^3). The combined organic extracts were washed with water (3 × 10 cm^3), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by FCC (Et_2O) to afford lactam **21** (169 mg, 83%, 10 : 1 d.r. *A* : *B*) as a colourless oil which crystallised on standing; m.p. 93–95 °C (Et_2O–petrol); ν_{max}/cm^{-1} (thin film) 3059 (w), 2969 (w), 1697 (s), 1396 (m), 751 (m), 694 (m); δ_H (400 MHz, $CDCl_3$) 1.08 (3 H, d, *J* = 6.0, C5–CH_3 of *A*), 1.26 (3 H, d, *J* = 6.5, C5–CH_3 of *B*), 2.77 (2 H, d d, *J* = 9.0 and 7.0, C4–*H* of *A*; 1 H, m, C4–*H* of *B*), 2.87 (3 H, s, NCH_3 of *A*), 2.90 (3 H, s, NCH_3 of *B*), 3.40 (1 H, d q, *J* = 7.0 and 6.5, C5–*H* of *B*), 3.51 (1 H, d q, *J* = 6.0 and 6.0, C5–*H* of *A*), 3.82 (1 H, d, *J* = 9.0, C3–*H* of *A*), 4.13 (1 H, d, *J* = 8.0, C3–*H* of *B*), 7.12–7.54 (20 H, m, ArC*H*); δ_C (100 MHz, $CDCl_3$) (data for major isomer *A* only) 18.4 (C5–*C*H_3), 28.1 (N*C*H_3), 53.9 (*C*-3), 56.3 (*C*-4), 60.1 (*C*-5), 127.6, 127.8, 127.9, 128.9 and 129.0

(8 × ArCH), 133.1 (ArC), 133.6 (2 × ArCH), 139.7 (ArC), 171.3 (C-2); *m/z* (CI$^+$) 298 ([M + H]$^+$, 100%); HRMS: (ESI) Found: [M + H]$^+$ 298.1260, $C_{18}H_{20}NOS$ requires 298.1249.

(4*S*, 5*R*)-1,5-Dimethyl-4-phenyl-3-phenylsulfanylpyrrolidin-2-one (22)

To a solution of methyl(phenylthio)acetate **9b** (215 μL, 1.38 mmol) in anhydrous DMF (8.3 cm^3) was added NaH (55 mg, 1.38 mmol, 60% dispersion in mineral oil) and the resulting mixture was stirred at r.t. for 20 min to form a pale yellow suspension. Sulfamidate **17** (150 mg, 0.69 mmol) was added and the reaction mixture was stirred at 45 °C for 18 h. Aq. 5 M HCl (0.69 cm^3) was added and the resulting pale yellow suspension was stirred at r.t. for 3 h. The reaction mixture was neutralised by addition of saturated aq. $NaHCO_3$ and extracted with Et_2O (3 × 25 cm^3). The organic extracts were combined, washed with water (3 × 10 cm^3), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by FCC (Et_2O–hexanes 1 : 1) to afford lactam **22** (126 mg, 62%, 1 : 1 d.r. *A* : *B*) as a colourless, viscous oil; ν_{max}/cm^{-1} (film) 2929 (br m), 1687 (s), 1395 (m), 1258 (w), 739 (s), 701 (s); δ_H (400 MHz, $CDCl_3$) 0.75 (3 H, d, *J* = 6.5, C5–CH_3 of *A*), 0.89 (3 H, d, *J* = 6.5, C5–CH_3 of *B*), 2.83 (3 H, s, NCH_3 of *A*), 2.87 (3 H, s, NCH_3 of *B*), 3.61–3.74 (2 H, m, C5–*H* of *A* and C4–*H* of *B*), 3.89 (1 H, d q, *J* = 6.5 and 6.5, C5–*H* of *B*), 4.02 (1 H, d, *J* = 8.0, C3–*H of* A), 4.27 (1 H, d, *J* = 8.0, C3–*H* of *B*), 7.03–7.36 (16 H, m, ArC*H*), 7.43–7.56 (4 H, m, ArC*H*); δ_C (100 MHz, $CDCl_3$) 15.0 (C5–*C*H$_3$ of *A*), 15.7 (C5–*C*H$_3$ of *B*), 27.7 and 28.3 (2 × N*C*H$_3$), 49.4 (*C*-4 of *A*), 49.6 (*C*-4 of *B*), 52.2 (*C*-3 of *A*), 55.2 (*C*-3 of *B*), 56.9 (*C*-5 of *B*), 57.5 (*C*-5 of *A*), 126.9, 127.4, 127.7, 128.0, 128.2, 128.3, 128.7, 128.8, 129.0, 129.7, 131.4 and 133.5 (20 × Ar*C*H), 133.0, 136.1, 136.5 and 137.5 (4 × Ar*C*), 171.7 and 173.5 (2 × *C*-2); *m/z* (CI$^+$) 298 ([M + H]$^+$, 100%); HRMS: (CI$^+$) Found: [M + H]$^+$ 298.1266, $C_{18}H_{20}NOS$ requires 298.1266.

1,4-Dibenzyl-3-phenylsulfanylpyrrolidin-2-one 23 and benzyl-(3-phenylallyl)amine (25)

To a solution of methyl(phenylthio)acetate **9b** (306 μl, 2.00 mmol) in anhydrous DMF (12 cm^3) was added NaH (80 mg, 2.00 mmol, 60% dispersion in mineral oil) and the resulting mixture was stirred at r.t. for 20 min to form a pale yellow suspension. Sulfamidate **18** (300 mg, 1.0 mmol) was added and the reaction mixture was stirred at r.t. for 16.5 h. Aq. 5 M HCl (0.5 cm^3) was added and the resulting pale yellow emulsion was stirred at r.t. for 3 h. The reaction mixture was neutralised by addition of saturated aq. $NaHCO_3$ and extracted with Et_2O (3 × 20 cm^3). The combined organic portions were washed with water (3 × 20 cm^3), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in toluene (16 cm^3) and heated at reflux for 3 h. Solvent was removed *in vacuo* and the residue was purified by FCC (Et_2O–hexanes 1 : 2 → Et_2O 100%) to afford the lactam **23** (84 mg, 23%, 3 : 2 d.r.) as a pale yellow oil. Continued elution provided alkene **25** (82 mg, 37%) as a yellow oil.

Data for lactam **23**: ν_{max}/cm^{-1} (thin film) 3027 (w), 2918 (w), 1688 (s), 1438 (m), 1426 (m), 1264 (br m), 740 (s), 698 (s); δ_H (400 MHz, $CDCl_3$) 2.44 (1 H, m, C4–*H* of *A*), 2.57 (1H, d d, *J* = 14.5 and 9.5, C5–*H* of *A*), 2.57 (1 H, d d, *J* = 14.5 and 10.0, C5–*H* of *B*), 2.80 (1 H, m, C4–*H* of *B*), 2.86 (1 H, d d, *J* = 10.0 and 6.0, C4–CH_2Ph of *A*), 2.88–3.07 (4 H, m, C4–CH_2Ph of *A* and *B* and C5–*H* of *A*), 3.11 (1 H, d d, *J* = 14.5 and 6.0, C5–*H* of *B*), 3.54 (1 H, d, *J* = 7.0, C3–*H* of *A*), 3.98 (1 H, d d, *J* = 14.5 and 6.5, C3–*H* of *B*), 4.28 (1 H, d, *J* = 14.5, NCH_2Ph of *B*), 4.34 (1 H, d, *J* = 14.5, NCH_2Ph of *A*), 4.45 (1 H, d, *J* = 14.5, NCH_2Ph of *A*), 4.50 (1 H, d, *J* = 14.5, NCH_2Ph of *B*), 6.95–7.02 (4 H, m, ArC*H*), 7.09–7.37 (22 H, m, ArC*H*), 7.54 (2 H, d d, *J* = 8.5 and 2.0, ArC*H* of *A*), 7.61 (2 H, d d, *J* = 8.5 and 1.5, ArC*H* of *B*); δ_C (100 MHz, $CDCl_3$) 35.1 (*C*-5 of *B*), 39.1 (*C*-5 of *A*), 39.8 (*C*-4 of *B*), 40.5 (*C*-4 of *A*), 46.9 (N*C*H$_2$Ph of *B*), 47.1 (N*C*H$_2$Ph of *A*), 49.5 (2 signals) (C4–*C*H$_2$Ph of *A* and *B*), 126.7, 127.6, 127.7, 127.8, 128.1, 128.2, 128.3, 128.6, 128.7, 128.8 (3 signals), 128.9, 129.1 (2 signals) and 132.4 (28 × Ar*C*H), 132.9 (Ar*C*), 133.7 (2 × Ar*C*H), 134.3, 136.1, 136.3, 138.3 and 139.2 (Ar*C*), 171.6 and 172.3 (*C*-2); *m/z* (CI$^+$) 374 ([M + H]$^+$, 100%); HRMS: (CI$^+$) Found: [M + H]$^+$ 374.1577, $C_{24}H_{24}NOS$ requires 374.1579.

Data for alkene **25**: δ_H (400 MHz, $CDCl_3$) 1.63 (1 H, br s, N*H*), 3.42 (2 H, d, *J* = 6.0, C1–*H*), 3.82 (2 H, s, NCH_2Ph), 6.30 (1 H, d t, *J* = 16.0 and 6.0, C2–*H*), 6.53 (1 H, d, *J* = 16.0, C3–*H*), 7.18–7.39 (10 H, m, ArC*H*); *m/z* (CI$^+$) 224 ([M + H]$^+$, 100%). The spectroscopic properties of this compound were consistent with the data available in the literature.[14]

1-Benzyl-6-methyl-3-phenylsulfanylpiperidin-2-one (24)

To a solution of methyl(phenylthio)acetate **9b** (537 μl, 3.45 mmol) in anhydrous DMF (21 cm^3) was added portionwise NaH (138 mg, 3.45 mmol, 60% dispersion in mineral oil) and the resulting mixture was stirred at r.t. for 20 min to form a pale yellow suspension. Sulfamidate **19** (416 mg, 1.73 mmol) was added and the reaction mixture was stirred at r.t. for 14.5 h. Aq. 5 M HCl (0.5 cm^3) was added and the resulting pale yellow suspension was stirred at r.t. for 3 h. The reaction mixture was neutralised by addition of saturated aq. $NaHCO_3$ and extracted with Et_2O (3 × 30 cm^3). The organic extracts were combined, washed with water (3 × 50 cm^3), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was dissolved in 0.2 M ethanolic NaOEt (20 cm^3) and heated at reflux for 11 h. The reaction mixture was quenched by addition of saturated aq. NH_4Cl (30 cm^3) and was extracted with CH_2Cl_2 (2 × 20 cm^3). The organic extracts were combined, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by FCC (Et_2O–hexanes 1 : 1) to afford lactam **24** (431 mg, 80%, 1 : 1 d.r.) as a pale yellow oil; ν_{max}/cm^{-1} (thin film) 2946 (m), 1639 (s), 1439 (m), 745 (m), 694 (m); δ_H (400 MHz, $CDCl_3$) 1.10 (3 H, d, *J* = 6.5, C6–CH_3), 1.20 (3 H, d, *J* = 6.5, C6–CH_3), 1.51 (1 H, m, C4–*H*), 1.74–1.85 (2 H, m, C5–*H*), 1.89 (1 H, m, C4–*H*), 2.00–2.09 (2 H, m, C5–*H*), 2.14–2.32 (2 H, m, C4–*H*), 3.38–3.50 (2 H, m, C6–*H*), 3.89–3.98 (3 H, m, NCH_2Ph and C3–*H* × 2), 4.11 (1 H, d, *J* = 15.0, NCH_2Ph), 5.22 (1 H, d, *J* = 15.0, NCH_2Ph), 5.41 (1 H, d, *J* = 15.0, NCH_2Ph), 7.21–7.35 (16 H, m, ArC*H*), 7.54–7.61 (4 H, m, ArC*H*); δ_C (100 MHz, $CDCl_3$) 19.7 and 20.0 (C6–*C*H$_3$), 24.8 (*C*-4), 25.6 (*C*-5), 27.0 (*C*-4), 28.6 (*C*-5), 47.4 and 47.9 (N*C*H$_2$Ph), 48.9 and 49.1 (*C*-3), 51.0 and 51.6 (*C*-6), 127.3 (2 signals), 127.6, 127.7 (2 signals), 127.9, 128.6 (2 signals), 128.9, 129.0, 132.8 and 133.1 (Ar*C*H × 20), 134.5, 134.8, 137.5 and 137.7 (Ar*C*), 168.7 and 169.0 (C-2); *m/z* (CI$^+$) 312 ([M + H]$^+$, 100%); HRMS: (CI$^+$) Found: [M + H]$^+$ 312.1420, $C_{19}H_{22}NOS$ requires 312.1422.

(*S*)-1,5-Dibenzyl-3-phenylsulfanyl-1,5-dihydropyrrol-2-one (26)

To a solution of phenylsulfoxide **11** (80 mg, 021 mmol) in anhydrous CH_2Cl_2 (2 cm^3) at 0 °C was added, *via* syringe, TFAA (59 μl, 0.42 mmol). The resulting clear solution was stirred at r.t. for 2 h to form a dark red solution which was then diluted by addition of saturated aq. $NaHCO_3$ (2 cm^3) and water (10 cm^3) and extracted with CH_2Cl_2 (2 × 10 cm^3). The combined organic portions were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by FCC (Petrol–Et_2O 4 : 1) to afford the product **26** (43 mg, 55%, >98% e.e.) as a red oil; $[\alpha]_D^{20}$ +141.2 (*c* 0.51, $CHCl_3$); ν_{max}/cm^{-1} (film) 2923 (br w), 1684 (s), 1406 (m), 1179 (m), 1024 (m); δ_H (400 MHz, $CDCl_3$) 2.58 (1 H, d d, *J* = 13.5 and 9.0, C5–C*H*$_2$Ph), 2.99 (1 H, d d, *J* = 13.5 and 5.0, C5–C*H*$_2$Ph), 3.95 (1 H, m, C5–*H*), 4.11 (1 H, d, *J* = 15.0, NC*H*$_2$Ph), 5.18 (1 H, d, *J* = 15.0, NC*H*$_2$Ph), 6.10 (1 H, d, *J* = 2.0, C3–*H*), 6.95–6.99 (2 H, m, ArC*H*), 7.15–7.42 (13 H, m ArC*H*); δ_C (100 MHz, $CDCl_3$) 37.7 (C5–*C*H$_2$Ph), 44.7 (N*C*H$_2$Ph), 61.5 (*C*-5), 127.0, 127.7, 128.2, 128.5, 128.6, 128.8, 129.2, 129.5 and 132.7 (15 × Ar*C*H), 134.9, 136.3, 136.6 and 136.9 (3 × Ar*C* and *C*-3), 136.9 (*C*-4), 168.2 (*C*-2); *m*/*z* (CI^+) 372 ([M + H]$^+$, 100%); HRMS: (CI^+) Found: [M + H]$^+$ 372.1423, $C_{24}H_{22}NOS$ requires 372.1422.

The enantiomeric purity of this compound was determined by chiral HPLC (Chiralcel OD, isocratic hexane–*i*-PrOH 95 : 5, 1.0 cm^3 min^{-1}, 20 °C); t_R (major) = 24.5 min and t_R (minor) = 34.5 min.

(4*S*, 5*S*)-1,5-Dimethyl-4-phenyl-3-phenylsulfinylpyrrolidin-2-one

To a solution of **21** (93 mg, 0.31 mmol) in CH_2Cl_2 (7 cm^3), at 0 °C, was added *m*-CPBA (76 mg, *ca.* 0.31 mmol, 70–75%) to form a colourless solution which was stirred at 0 °C for 1 h. The reaction mixture was quenched by addition of saturated aq. potassium metabisulfite (5 cm^3). The organics were isolated, washed with saturated aq. $NaHCO_3$ (2 × 5 cm^3), dried (Na_2SO_4) and concentrated *in vacuo* to afford the corresponding sulfoxide (93 mg, 96%, 10 : 10 : 1 : 1 d.r.) as a colourless foam; *m*/*z* (CI^+) 314 ([M + H]$^+$, 38%), 188 ([M–SOPh]$^+$, 100).

(5*S*)-1,5-Dimethyl-4-phenyl-1,5-dihydropyrrol-2-one (27) and 1,5-Dimethyl-4-phenyl-1,3-dihydropyrrol-2-one (28)

Procedure A. PS–PPh_3 (310 mg, *ca.* 3.0 mmol g^{-1} loading) was allowed to swell in anhydrous toluene (1.3 cm^3) without stirring for 1.5 h. A solution of (4*S*, 5*S*)-1,5-dimethyl-4-phenyl-3-phenylsulfinylpyrrolidin-2-one (53 mg, 0.17 mmol) in anhydrous toluene (2 cm^3) was added and the resulting mixture was heated at 100 °C for 1.5 h. The reaction mixture was allowed to cool to r.t., filtered through Celite (washing with toluene (3 × 5 cm^3) followed by CH_2Cl_2 (3 × 5 cm^3)) and concentrated *in vacuo*. ^{1}H NMR of the crude material showed **27** : **28** as a 11 : 9 mixture. Analytical samples were isolated by preparative TLC (Et_2O–petrol 1 : 1).

Procedure B. A suspension of (4*S*, 5*S*)-1,5-dimethyl-4-phenyl-3-phenylsulfinylpyrrolidin-2-one (135 mg, 0.43 mmol) and $NaHCO_3$ (160 mg, 1.90 mmol) in MeCN (8 cm^3) was heated at reflux for 10 h. The mixture was then cooled to r.t., filtered through Celite (washing with CH_2Cl_2 (3 × 5 cm^3)) and concentrated *in vacuo*. The residue was purified by FCC (EtOAc–hexanes 2 : 1) to afford the alkene **27** (68 mg, 84%, >98% e.e.) as a colourless, crystalline solid.

Data for **27**; m.p. 129–131 °C (EtOAc–hexanes); $[\alpha]_D^{20}$ +85.5 (*c* 1.31, $CHCl_3$); ν_{max}/cm^{-1} (thin film) 2925 (w), 1672 (s), 1448 (m), 1425 (m), 1395 (m), 767 (m), 693 (m); δ_H (400 MHz, $CDCl_3$) 1.34 (3 H, d, *J* = 7.0, C5–C*H*$_3$), 3.05 (3 H, s, NC*H*$_3$), 4.51 (1 H, q, *J* = 7.0, C5–*H*), 6.34 (1 H, s, C3–*H*), 7.36–7.48 (5 H, m, ArC*H*). The spectroscopic properties of this compound were consistent with the data available in the literature.[15]

The enantiomeric purity of this compound (synthesised via Procedure B) was determined by chiral HPLC (Chiralcel OJ-H, gradient hexane–*i*-PrOH 100 : 0–95 : 5 over 90 min, 1.0 cm^3 min^{-1}, 20 °C); t_R (major) = 68.2 min and t_R (minor) = 57.4 min.

Data for **28**; ν_{max}/cm^{-1} (thin film) 2960 (m), 1679 (br s), 1447 (m), 1436 (m), 1065 (m), 1023 (m), 764 (m), 696 (s); δ_H (400 MHz, $CDCl_3$) 2.18 (3H, t, *J* = 2.5, C5–C*H*$_3$), 3.10 (3 H, s, NC*H*$_3$), 3.34 (2 H, q, *J* = 2.5, C3–*H*), 7.17–7.39 (5 H, m, ArC*H*); δ_C (75 MHz, $CDCl_3$) 12.1 (C5–*C*H$_3$), 26.7 (N*C*H$_3$), 39.4 (*C*-3), 112.9 (*C*-4), 126.2, 127.2 and 128.7 (5 × Ar*C*H), 135.1 and 136.1 (*C*-5 and Ar*C*), 176.5 (*C*-2); *m*/*z* (CI^+) 188 ([M + H]$^+$, 100%); HRMS: (CI^+) Found: [M + H]$^+$ 188.1068, $C_{12}H_{14}NO$ requires 188.1075.

3-Phenylsulfinyl-1-benzyl-6-methylpiperidin-2-one

To a solution of **24** (341 mg, 1.10 mmol) in CH_2Cl_2 (25 cm^3), at 0 °C, was added *m*-CPBA (271 mg, *ca.* 1.10 mmol, 70–75%) to form a pale yellow solution which was stirred at 0 °C for 1 h. The reaction mixture was quenched by addition of saturated aq. potassium metabisulfite (25 cm^3). The organics were isolated, washed with saturated aq. $NaHCO_3$ (2 × 25 cm^3), dried (Na_2SO_4) and concentrated *in vacuo* to afford the corresponding sulfoxide (344 mg, 96%) as a pale yellow gum; *m*/*z* (CI^+) 328 ([M + H]$^+$, 100%).

1-Benzyl-6-methyl-5,6-dihydro-1*H*-pyridin-2-one (29)

PS–PPh_3 (210 mg, *ca.* 3 mmol g^{-1} loading) was allowed to swell in anhydrous toluene (2 cm^3) for 3.5 h without stirring. A solution of 3-phenylsulfinyl-1-benzyl-6-methylpiperidin-2-one (93 mg, 0.28 mmol) in anhydrous toluene (3 cm^3) was added and the resulting mixture was heated at reflux for 1.5 h. The reaction mixture was allowed to cool to r.t., filtered through Celite (washing with toluene (3 × 5 cm^3) followed by CH_2Cl_2 (4 × 5 cm^3)) and concentrated *in vacuo*. The residue was purified by FCC (Et_2O–hexanes 6 : 1) to afford product **29** (49 mg, 87%) as a colourless oil; ν_{max}/cm^{-1} (thin film) 2932 (m), 1664 (s), 1605 (s), 1449 (m), 1141 (m), 830 (m), 717 (m), 697 (m); δ_H (270 MHz, $CDCl_3$) 1.19 (3 H, d, *J* = 7.0, C6–C*H*$_3$), 2.09 (1 H, d d d d, *J* = 18.0, 6.0, 3.0 and 0.5, C5–*H*), 2.58 (1 H, d d d d, *J* = 18.0, 7.0, 2.5 and 2.5, C5–*H*), 3.56 (1 H, q d d d, *J* = 7.0, 7.0, 2.5 and 1.5, C6–*H*), 3.90 (1 H, d, *J* = 15.0, NC*H*$_2$Ph), 5.35 (1 H, d, *J* = 15.0, NC*H*$_2$Ph), 6.02 (1 H, d d d, *J* = 10.0, 3.0 and 0.5, C3–*H*), 6.44 (1 H, d d d, *J* = 10.0, 6.0, 2,5 and 1.5, C4–*H*), 7.18–7.27 (5 H, m, ArC*H*); δ_C (100 MHz, $CDCl_3$) 17.7 (C6–*C*H$_3$), 30.9 (*C*-5), 47.3 (N*C*H$_2$Ph), 49.8 (*C*-6), 125.0 (*C*-4), 127.3, 127.9 and 128.6 (Ar*C*H × 5), 137.2 (*C*-3), 138.3 (Ar*C*), 163.7 (C-2); *m*/*z* (CI^+) 202 ([M + H]$^+$, 100%); HRMS: (CI^+) Found: [M + H]$^+$ 202.1230, $C_{13}H_{16}NO$ requires 202.1232.

1-Benzyl-6-methyl-3-phenylsulfanyl-5,6-dihydro-1*H*-pyridin-2-one (30)

To an ice-cooled (0 °C) solution of 3-phenylsulfinyl-1-benzyl-6-methylpiperidin-2-one (99 mg, 0.30 mmol) in anhydrous CH_2Cl_2 (3 cm^3) was added, dropwise, TFAA (85 μl, 0.60 mmol) to form a pale yellow solution which was allowed to warm slowly to r.t. and stirred for 14.5 h. Saturated aq. $NaHCO_3$ (3 cm^3) was added, the reaction mixture was stirred at r.t. for 2 h and then extracted with CH_2Cl_2 (3 × 10 cm^3). The organic extracts were combined, washed with aq. 1 M HCl (10 cm^3), saturated aq. $NaHCO_3$ (10 cm^3), dried (Na_2SO_4) and concentrated *in vacuo* to afford the product **30** (79 mg, 85%) as a pale yellow gum; ν_{max}/cm^{-1} (thin film) 2968 (m), 1734 (m), 1639 (s), 1603 (s) 1439 (m), 1215 (m), 1073 (m), 1025 (m), 730 (s), 694 (s); δ_H (400 MHz, $CDCl_3$) 1.21 (3 H, d, J = 6.5, C6–CH_3), 2.06 (1 H, d d d, J = 17.5, 6.5 and 2.5, C5–*H*), 2.57 (1 H, d d d, J = 17.5, 7.0 and 3.0, C5–*H*), 3.57 (1 H, q d d d, J = 7.0, 6.5, 3.0 and 1.0, C6–*H*), 3.97 (1 H, d, J = 14.5, NCH_2Ph), 5.36 (1 H, d, J = 14.5, NCH_2Ph), 5.79 (1 H, d d d, J = 6.5, 2.5 and 1.0, C4–*H*), 7.20–7.45 (8 H, m, ArC*H*), 7.51–7.58 (2 H, d d, J = 6.0 and 4.5, ArC*H*); δ_C (100 MHz, $CDCl_3$) 17.6 (C6–*C*H_3), 31.4 (*C*-5), 48.0 (N*C*H_2Ph), 50.0 (*C*-6), 127.3, 127.9, 128.3 and 128.5 (Ar*C*H × 8), 129.4 (*C*-4), 132.4 and 133.7 (Ar*C* and *C*-3), 134.3 (Ar*C*H × 2), 137.9 (Ar*C*), 161.6 (C-2); m/z (CI^+) 310 ([M + H]$^+$, 100%); HRMS: (CI^+) Found: [M + H]$^+$ 310.1262, $C_{19}H_{20}NOS$ requires 310.1266.

(4*R*,5*S*)-1,5-Dibenzyl-4-butylpyrrolidin-2-one (31a) and 1,5-dibenzyl-1,3-dihydropyrrol-2-one (32)

To a stirred suspension of CuI (209 mg, 1.10 mmol) in anhydrous THF (1 cm^3) at 0 °C was added, *via* syringe, *n*-BuLi (1.6 M in hexanes, 1.31 cm^3, 2.10 mmol) to form a brown suspension. After 10 min the mixture was cooled to −78 °C and TMSCl (65 μl, 0.52 mmol) and HMPA (122 μl, 0.7 mmol) were sequentially added *via* syringe. After a further 5 min a solution of alkene **12** (91 mg, 0.35 mmol) in anhydrous THF (1.4 cm^3) was added, *via* syringe, and the mixture was stirred at r.t. for 2 h. Saturated aq. NH_4Cl (10 cm^3) was added and the mixture was diluted with Et_2O (15 cm^3). The organic portion was isolated and washed with saturated aq. NH_4Cl (10 cm^3) and water (2 × 10 cm^3), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in THF (1 cm^3), TBAF (1 M in THF, 0.25 cm^3, 0.25 mmol) was added and the mixture was stirred at r.t. for 15 min. The mixture was then diluted with water (5 cm^3) and extracted with Et_2O (2 × 5 cm^3). The organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to afford a residue which was purified by FCC (Et_2O–petrol 1 : 1) to yield the enamine **32** (5 mg, 6%) as a colourless oil and continued elution provided lactam **31a** (80 mg, 78%, >98% e.e.) as a colourless oil.

Data for **32**; ν_{max}/cm^{-1} (film) 2925 (br w), 1705 (s), 1646 (m), 1348 (m), 1183 (w); δ_H (400 MHz, $CDCl_3$) 3.15 (2 H, q, J = 2.5, C5–CH_2Ph), 3.43–3.47 (2 H, m C3–*H*), 4.59 (2 H, s, NCH_2Ph), 4.89–4.91 (1 H, m, C4–*H*), 7.11–7.19 (4 H, m, ArC*H*), 7.22–7.35 (6 H, m, ArC*H*); δ_C (100 MHz, $CDCl_3$) 34.3 (*C*-3), 36.9 (C5–*C*H_2Ph), 43.4 (N*C*H_2Ph), 101.4 (*C*-4), 126.8, 127.0, 127.4, 128.7 (2 signals) and 128.8 (10 × Ar*C*H), 136.2, 137.8 and 144.3 (*C*-5 and 2 × Ar*C*), 178.3 (*C*-2); m/z (CI^+) 264 ([M + H]$^+$, 100%); HRMS: (CI^+) Found: [M + H]$^+$ 264.1378, $C_{18}H_{18}NO$ requires 264.1388.

Data for **31a**: $[\alpha]_D^{20}$ −16.7 (*c* 0.48, $CHCl_3$); ν_{max}/cm^{-1} (film) 2927 (br m), 1686 (s), 1454 (m), 1365 (w); δ_H (400 MHz, $CDCl_3$) 0.70 (3 H, t, J = 7.5, $(CH_2)_3CH_3$), 0.82–1.10 (6 H, m, $(CH_2)_3CH_3$), 1.94–2.03 (2 H, m, C3–*H* and C4–*H*), 2.43 (1 H, d d, J = 17.0 and 8.5, C3–*H*), 2.63 (1 H, d d, J = 13.5 and 8.0, C5–CH_2Ph), 2.94 (1 H, d d, J = 13.5 and 4.5, C5–CH_2Ph), 3.25 (1 H, d d d, J = 8.0, 4.5 and 2.5, C5–*H*), 3.89 (1 H, d, J = 15.0, NCH_2Ph), 5.12 (1 H, d, J = 15.0, NCH_2Ph), 7.03–7.07 (2 H, m, ArC*H*), 7.18–7.36 (8 H, m ArC*H*); δ_C (100 MHz, $CDCl_3$) 13.8 ($(CH_2)_3CH_3$), 22.3, 28.8 and 34.5 ($(CH_2)_3CH_3$), 35.8 (*C*-4), 36.5 (*C*-3), 39.0 (C5–*C*H_2Ph), 44.5 (N*C*H_2Ph), 63.5 (*C*-5), 126.8, 127.9, 128.3, 128.6, 128.7 and 129.3 (10 × Ar*C*H), 136.7 and 137.3 (2 × Ar*C*), 174.5 (*C*-2); m/z (CI^+) 322 ([M + H]$^+$, 100%); HRMS: (CI^+) Found: [M + H]$^+$ 322.2177, $C_{22}H_{28}NO$ requires 322.2171.

The enantiomeric purity of this compound was determined by chiral HPLC (Chiralpak AD, isocratic hexane–*i*-PrOH 98 : 2, 1.0 cm^3/min, 15 °C); t_R (major) = 21.7 min and t_R (minor) = 28.2 min.

(4*S*,5*S*)-1,5-Dibenzyl-4-vinylpyrrolidin-2-one (31b)

To a stirred suspension of CuI (139 mg, 0.73 mmol) in anhydrous THF (0.6 cm^3) at 0 °C was added, *via* syringe, vinyl magnesium bromide (1 M in THF, 1.40 cm^3, 1.40 mmol) to form a brown suspension. After 10 min the mixture was cooled to −78 °C and TMSCl (43 μl, 0.34 mmol) and HMPA (81 μl, 0.46 mmol) were sequentially added *via* syringe. After a further 5 min a solution of alkene **12** (60 mg, 0.21 mmol) in anhydrous THF (1.0 cm^3) was added, *via* syringe, and the mixture was stirred at r.t. for 2 h. Saturated aq. NH_4Cl (10 cm^3) was added and the mixture was diluted with Et_2O (15 cm^3). The organic portion was isolated and washed with saturated aq. NH_4Cl (10 cm^3) and water (2 × 10 cm^3), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was dissolved in THF (1 cm^3), TBAF (1 M in THF, 0.20 cm^3, 0.20 mmol) was added and the mixture was stirred at r.t. for 15 min. The mixture was then diluted with water (5 cm^3) and extracted with Et_2O (2 × 5 cm^3). The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a residue which was purified by FCC (Et_2O–petrol 1 : 1) to yield the lactam **31b** (18 mg, 29%, >98% e.e.) as a colourless oil; $[\alpha]_D^{20}$ +19.0 (*c* 0.63, $CHCl_3$); ν_{max}/cm^{-1} (film) 2926 (br m), 1681 (s), 1420 (m), 1247 (m), 1079 (w), 912 (m); δ_H (400 MHz, $CDCl_3$) 2.21 (1 H, d d, J = 17.0 and 4.5, C3–*H*), 2.47 (1 H, d d d, J = 17.0, 9.0 and 1.0, C3–*H*), 2.66 (1 H, d d d d, J = 9.0, 7.5, 4.5 and 3.5, C4–*H*), 2.76 (1 H, d d, J = 14.0 and 7.5, C5–CH_2Ph), 2.95 (1 H, d d, J = 14.0 and 5.0, C5–CH_2Ph), 3.43 (1 H, d d d, J = 7.5, 5.0 and 3.5, C5–*H*), 3.92 (1 H, d, J = 15.0, NCH_2Ph), 4.81 (1 H, d t, J = 17.0 and 1.0, C4–CH=CH_2), 4.85 (1 H, d t, J = 10.0 and 1.0, C4–CH=CH_2), 5.12 (1 H, d, J = 15.0, NCH_2Ph), 5.52 (1 H, d d d, J = 17.0, 10.0 and 7.5, C4–C*H*=CH_2), 7.05–7.07 (2 H, m, ArC*H*), 7.14–7.17 (2 H, m ArC*H*), 7.21–7.34 (6 H, m ArC*H*); δ_C (100 MHz, $CDCl_3$) 35.9 (*C*-3), 38.4 (C5–*C*H_2Ph), 40.0 (*C*-4), 44.5 (N*C*H_2Ph), 63.2 (C-5), 115.0 (C4–CH=*C*H_2), 126.9, 127.7, 128.5, 128.8 (2 signals) and 129.4 (10 × Ar*C*H), 136.5 and 136.9 (2 × Ar*C*), 138.8 (C4–*C*H=CH_2), 174.0 (*C*-2); m/z (CI^+) 292 ([M + H]$^+$, 100%); HRMS: (CI^+) Found: [M + H]$^+$ 292.1698, $C_{20}H_{22}NO$ requires 292.1701.

The enantiomeric purity of this compound was determined by chiral HPLC (Chiralpak AD, isocratic hexane–*i*-PrOH 98 : 2,

1.0 cm^3/min, 15 °C); t_R (major) = 28.0 min and t_R (minor) = 42.3 min.

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References

1 M. G. P. Buffat, *Tetrahedron*, 2004, **60**, 1701–1729; P. M. Weintraub, J. S. Sabol, J. M. Kane and D. R. Borcherding, *Tetrahedron*, 2003, **59**, 2953–2989.
2 S. J. F. MacDonald, G. D. E. Clarke, M. D. Dowle, L. A. Harrison, S. T. Hodgson, G. G. A. Inglis, M. R. Johnson, P. Shah, R. J. Upton and S. B. Walls, *J. Org. Chem.*, 1999, **64**, 5166–5175; S. J. F. Macdonald, M. D. Dowle, L. A. Harrison, J. E. Spooner, P. Shah, M. R. Johnson, G. G. A. Inglis, G. D. E. Clarke, D. J. Belton, R. A. Smith, C. R. Molloy, M. Dixon, G. Murkitt, R. E. Godward, T. Skarzynski, O. M. P. Singh, K. A. Kumar, S. T. Hodgson, E. McDonald, G. W. Hardy and H. Finch, *Bioorg. Med. Chem. Lett.*, 2001, **11**, 243–246; S. J. F. Macdonald, G. G. A. Inglis, D. Bentley and M. D. Dowle, *Tetrahedron Lett.*, 2002, **43**, 5057–5060.
3 A. K. Mandal, J. Hines, K. Kuramochi and C. M. Crews, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 4043–4047.
4 For some recent applications, see: P. Armstrong, S. Feutren, H. McAlonan, G. O'Mahony and P. J. Stevenson, *Tetrahedron Lett.*, 2004, **45**, 1627–1630; J. Marin, C. Didierjean, A. Aubry, J.-R. Casimir, J.-P. Briand and G. Guichard, *J. Org. Chem.*, 2004, **69**, 130–141.
5 D. François, E. Poupon, N. Kunesch and H.-P. Husson, *Eur. J. Org. Chem.*, 2004, 4823–4829; M. Amat, C. Escolano, N. Llor, M. Huguet, M. Pérez and J. Bosch, *Tetrahedron: Asymmetry*, 2003, **14**, 1679–1683.
6 A. Sanyal, Q. Yuan and J. K. Snyder, *Tetrahedron Lett.*, 2005, **46**, 2475–2478.
7 N. S. Josephsohn, M. L. Snapper and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2004, **126**, 3734–3735.
8 (*a*) A. J. Williams, S. Chakthong, D. Gray, R. M. Lawrence and T. Gallagher, *Org. Lett.*, 2003, **5**, 811–814; (*b*) J. F. Bower, J. Švenda, A. J. Williams, J. P. H. Charmant, R. M. Lawrence, P. Szeto and T. Gallagher, *Org. Lett.*, 2004, **6**, 4727–4730.
9 J. F. Bower, P. Szeto and T. Gallagher, *Chem. Commun.*, 2005, **46**, 5793–5795.
10 M. Eskici and T. Gallagher, *SYNLETT*, 2000, 1360–1362; B. J. Littler, T. Gallagher, I. K. Boddy and P. D. Riordan, *SYNLETT*, 1997, 22–24.
11 A. R. Tunoori, D. Dutta and G. I. Georg, *Tetrahedron Lett.*, 1998, **39**, 8751–8754.
12 I. Baussanne and J. Royer, *Tetrahedron Lett.*, 1998, **39**, 845–848.
13 S. R. Hitchcock, G. P. Nora, C. Hedberg, D. M. Casper, L. S. Buchanan, M. D. Squire and D. X. West, *Tetrahedron*, 2000, **56**, 8799–8807.
14 J. Blid, P. Brandt and P. Somfai, *J. Org. Chem.*, 2004, **69**, 3043–3049.
15 G. Chelucci and A. Saba, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 78–79.