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Graphical Abstract

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Enantioselective Synthesis of Non-Proteinogenic 2-Arylallyl α-Amino Acids via Pd/In Catalytic Cascades

Ronald Grigg[a*], Shaun McCaffrey[a], Visuvanathar Sridharan[a],Colin W. G. Fishwick[a], Colin Kilner[a], Stewart Korn[b], Kevin Bailey[b] and John Blacker[b]

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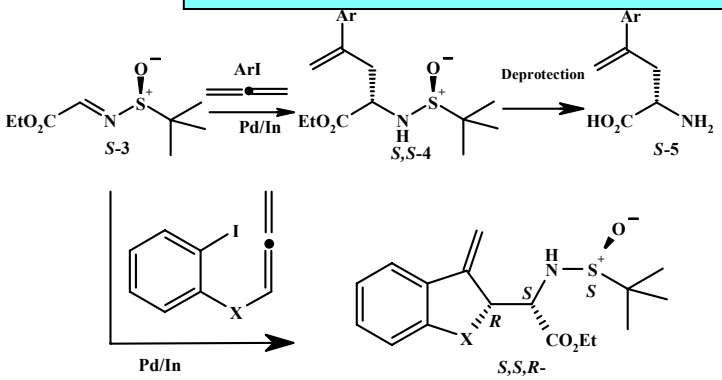

TETRAHEDRON

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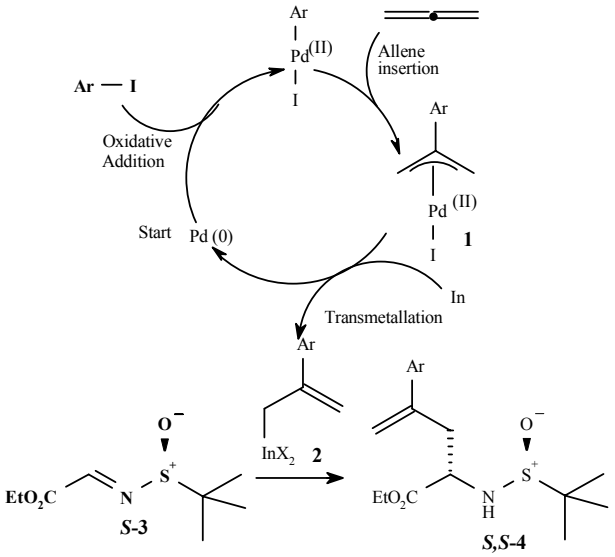
Abstract— An efficient synthesis of both *R*- and *S*- enantiomers of 2-arylallyl-α-amino acids *via* a diastereoselective Pd/In mediated catalytic allylation of chiral *N*-sulfinyl-α-imino esters is described. The potential for further enhancing molecular complexity and creating contiguous chiral centers by interfacing these processes with catalytic cyclisation-anion capture methodology is demonstrated.

The synthesis of peptides and proteins containing non-natural α-amino acids vastly increases the structural and chemical diversity of polypeptides.



Scheme 1. Reaction Mechanism

Conditions: (i) ArI (0.75 mmol), allene (1 atm) In (0.75 mmol), $Pd(OAc)_2$ (10 mol %), tri-2-furyl phosphine (20 mol %), CuI (20 mol %), piperidine (0.5 mmol), DMF (20 ml/mmol), 40 ^oC, 24 h; (ii) 4M HCl/dioxane (5 mol eqv), EtOH (10 ml/mmol), 30 min, rt; NaOH (2 mol eqv), 1:1 v/v EtOH/H_2O (10 ml/mmol) reflux, 2 h.

Novel α-amino acid side-chains and the availability of both *R*- and *S*- stereoisomers enable tuning of pharmacokinetics, formation of β-sheets and other peptide structural motifs that effect biological activity and structural properties.

The synthesis of "designer" peptidomimetics, incorporating and/or modifying the beneficial aspects of the parent polypeptides whilst also possessing enhanced metabolic stability and/or improved pharmacokinetics is an area of burgeoning interest.[1-3]

The asymmetric alkylation of glycine cation equivalents is a general, efficient route to non-proteinogenic α-amino acid derivatives. Previously, our group reported highly regio- and diastereo- selective Pd/In mediated cascade allylations of carbonyl compounds including a highly stereoselective allylation of chiral *N*-sulfinyl aldimines.[4-10] We now report further applications of the *tert*-butyl sulfinyl chiral auxilliary, which has been widely used in the synthesis of chiral amines including 1,2-amino alcohols and α-and β-amino acids,[11-13] to a new approach to unusual α-amino acids.

The Pd/In bimetallic cascade process involves generation of an electrophilic π-allyl palladium species **1** that undergoes transmetallation in the presence of indium, furnishing nucleophillic η^1-allylindium species **2**. Allylation of the enantiopure *N*-sulfinyl-α-imino ester **3**, affords *N*-sulfinyl-α-alkyl-α-amino esters **4** as single diastereoisomers (Scheme 1). Initial

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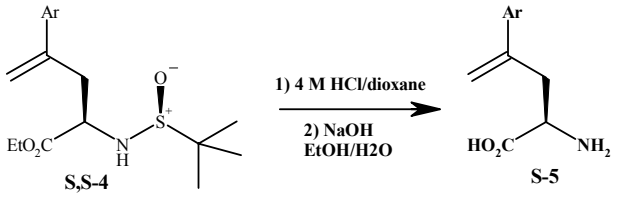
experiments employing iodobenzene and a catalyst system comprising of 10 mol % $Pd(OAc)_2$, 20 mol % tris-2-furylphosphine and 20 mol % CuI in DMF at 40 °C confirmed these expectations (Table 1, entry 1).

The scope of the reaction was explored through a series of aryl iodides (Table 1). X-Ray crystal structures of one such pair ***S,S*–6** and ***R,R*–6** (Fig. 1), derived by partial deprotection of ***S,S*–4g** and ***R,R*–4g**, established that the *S*-sulfinimine engenders *S* stereochemistry at the new chiral centre and the *R*-sulfinimine provides *R* stereochemistry at the new chiral centre.[14] Non-proteinogenic α-amino acids **5** are obtained in good to excellent yield (Table 1) from **4** *via* a two-step deprotection process (Scheme 2).



Scheme 2. deprotection of *N*-sulfinyl esters

Cleavage of the chiral sulfinyl auxilliary is carried out first by treatment with 4M HCl in dioxane (5 mol eqv) for 30 min. Following removal of the solvent the crude material is treated with 1M aqueous NaOH solution (2 mol eqv) in a 1:1 v/v EtOH:H_2O under reflux for 2 h. The amino acids **5a - h** are isolated using an Amberlyst H^+ ion exchange resin (Table 1).

A rationale for the stereochemical outcome of the cascade **3** → **4** is summarised in Fig. 2. The four possible Zimmerman-Traxler, chair-like transition states **7** – **10** have been modelled using semi-empirical calculations.[15] These correspond to additions of the allyl indium intermediate to either the *re* or *si* face of the *S*-sulphoximine, each of which can involve two possible chair-like arrangements. The heats of formation (ΔHf) and imaginary vibrational frequencies (ν_i) for transition states corresponding to additions to the *S*-sulphoximine indicate a marked preference for transition state **10**, which locates the ester moiety axially. Closer inspection of this transition state reveals that the ester carbonyl oxygen is located near to the indium atom (O – In distance of 2.80Å) indicating coordination to the indium atom. This transition state leads to the product possessing *S* stereochemistry at the newly created chiral centre. Interestingly, transition state **10** also locates the sulphoxide oxygen near to the metal centre (at a distance of 2.75Å) and this, although now involving a 4-membered ring, may also further stabilise the transition state. This type of chelation appears to be energetically important as the next most favourable transition state **8** locates the sulphoxide oxygen close to the metal centre at a distance of 2.75 Å. (Note: The calculations employed parameters for In(III) although the valence state of the In in this chemistry is not yet established).

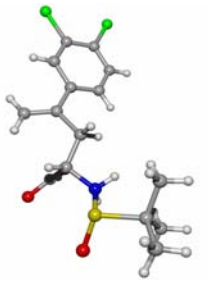
Table 1. Bimetallic cascade synthesis of chiral 4a-h and 5a-h[a].

Entry	ArI	Cascade Product		Amino acid	
		Confg	Yield (%)[b]	Confg	Yield (%)[c]
1		4a *S,S*	92	5a *S*	100
		4a *R,R*	80	5a *R*	100
2		4b *S,S*	69	5b *S*	-
		4b *R,R*	55	5b *R*	100
3		4c *S,S*	68	5c *S*	50
		4c *R,R*	68	5c *R*	54
4		4d *S,S*	54	5d *S*	99
		4d *R,R*	49	5d *R*	99
5		4e *S,S*	72	5e *S*	97
		4e *R,R*	67	5e *R*	80
6		4f *S,S*	52	5f *S*	85
		4f *R,R*	69	5f *R*	79
7		4g *S,S*	73	5g *S*	73
		4g *R,R*	74	5g *R*	82
8		4h *S,S*	69	5h *S*	89
		4h *R,R*	76	5h *R*	68

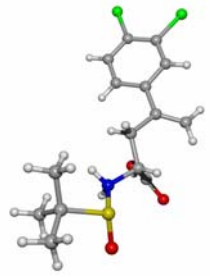
a. Conditions as for Scheme 1. b. Isolated yield. c. Isolated overall yield for the 2-step deprotection.

To further extend the scope of our chemistry, we have utilised bifunctional aryl iodide/allenes **13 – 16** (Scheme 3) allowing access to our catalytic cyclisation – anion capture methodology.[16] The cyclisation – allylation reaction is entirely regio- and diastereo- selective generating two contiguous chiral centres with complete stereocontrol, affording **17 – 20** in moderate to good yield (Table 2).

A matched pair of X-ray crystal structures ***S,S,R*-18** and ***R,R,S*-18**[14] established that the *R*-sulfinimine engenders *R* stereochemistry at the 5-position and *S* stereochemistry at the 6-position (Table 2, entries 3 and 4, Fig. 3). Semi-empirical calculations reveal a similar trend to those described above. In this case, four chair-like transition states are possible giving rise to four possible diastereoisomeric products.



***S,S*-6**

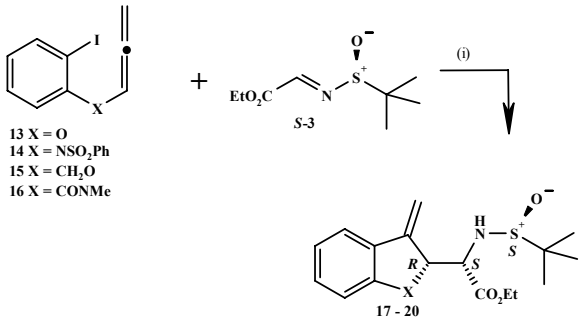


***R,R*-6**

Figure 1. X-Ray crystal structures of a matched pair of enantiomers.

The most energetically favourable transition state **21** leads to the formation of **18**. As in the case of **10** (Fig. 2), this

The most energetically favourable transition state **21** leads to the formation of **18**. As in the case of **10** (Fig. 2), this transition state appears to be stabilised by coordination to the indium involving both the sulphoxide and ester (Fig. 4). This transition state is calculated to be nearly 8 kcal/mol lower in energy than the next most energetically favoured transition state, thus acounting for the observed stereochemical preference in this reaction.

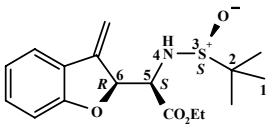
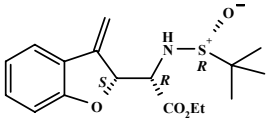
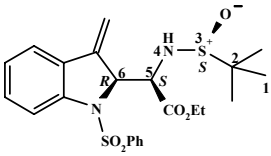
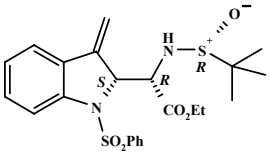
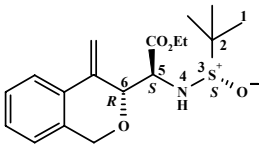
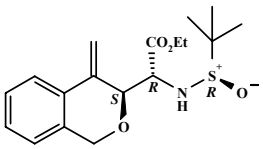
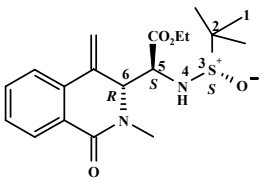
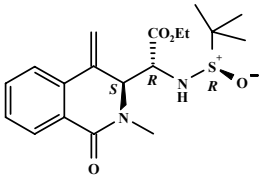


Scheme 3. Tandem cyclisation –imine capture cascade

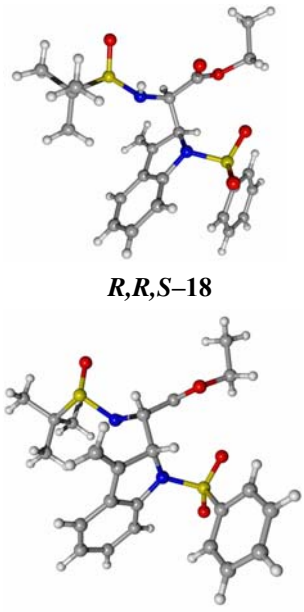
Conditions: (i) ArI (0.75 mmol), In (0.75 mmol), $Pd(OAc)_2$ (10 mol %), tri-2-furyl phosphine (20 mol %), CuI (20 mol %), piperidine (0.5 mmol), DMF (20 ml/mmol), 80 ^{o}C, 24 h.

In conclusion, we have described a short, efficient, diastereoselective synthesis of 2-arylallyl-α-amino acids as single enantiomers with either *R* or *S* stereochemistry. Application of bifunctional allene/aryl iodides as substrates furnishes enantiopure *N*-sulfinyl-α-amino esters with two contiguous chiral centres *via* a regioselective process. The stereochemical outcome of both types of process has been modelled by semi-empirical calculations which highlight the key transition state influence of chelation to indium by both the sulfoxide and carbonyl oxygen atoms.

Table 2. Tandem cyclisation – allylation cascades

Entry	Allene	Imine	Product	Yield (%)[b]
1	**13**	***S*-3**	 ***S,S,R* – 17**	64
2	**13**	***R*-3**	 ***R,R,S* – 17**	62
3	**14**	***S*-3**	 ***S,S,R* – 18**	44
4	**14**	***R*-3**	 ***R,R,S* – 18**	48
5	**15**	***S*-3**	 ***S,S,R* – 19**	62
6	**15**	***R*-3**	 ***R,R,S* – 19**	64
7	**16**	***S*-3**	 ***S,S,R* – 20**	28
8	**16**	***R*-3**	 ***R,R,S* – 20**	32

a. General conditions as for Scheme 3 b. Isolated yield.



***R,R,S*–18**

***S,S,R*-18**

Figure 3. X-Ray crystal structures of ***R,R,S*–18** and ***S,S,R*-18**

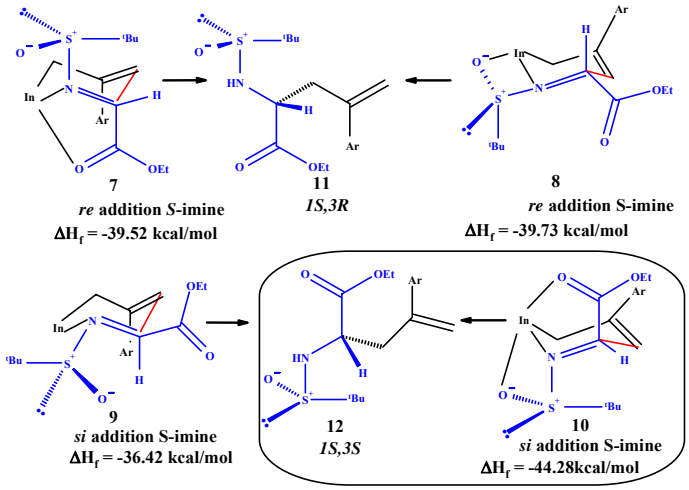


Figure 2. Stereochemical rationale for Scheme 2.

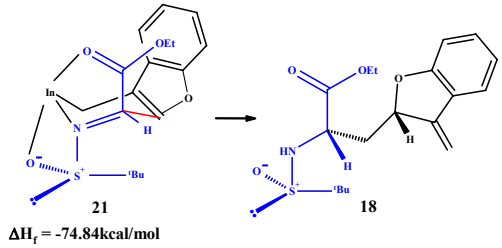


Figure 4. Stereochemical rationale for Scheme 3.

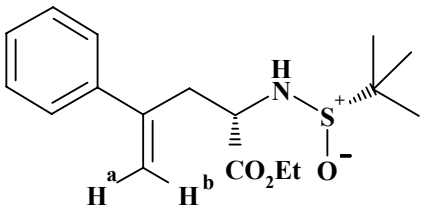
Experimental

Unless otherwise noted all reagents were obtained from commercial suppliers and used without further purification. All solvents were dried or purified by literature procedures[i]. Chromatography columns were prepared using Fisher chemicals 60A 35 – 70 micron silica gel. Nuclear magnetic resonance spectra were recorded using Bruker DPX300 and DRX500 MHz spectrometers. Chemical shifts are reported in parts per million (δ) downfield relative to the internal reference tetramethylsilane. Unless otherwise specified NMR spectra were recorded in deuterochloroform at room temperature. Abbreviations used; Ar = aromatic, d = doublet, dd = doublet of doublets, dq = doublet of quartets, dt = doublet of triplets, m = multiplet, q = quartet, s = singlet, t = triplet. Mass spectra were recorded using a micromass ZMD 2000 spectrometer employing the electrospray (ES+) ionisation technique. Accurate molecular masses were obtained from the EPSRC Swansea Mass Spectroscopy service using perfluorotributylamine or polyethylenimine as an internal standard. Infra-red spectra were recorded using a Perkin-Elmer FT-IR spectrometer. IR spectra of liquids were recorded as thin films on sodium chloride plates. IR spectra of solids were recorded using the "golden gate" apparatus. Optical rotations were measured on an Optical Activity AA-1000 polarimeter.

Rotations are quoted in 10^{-1} deg cm^2 g^{-1} and the concentration (c) is expressed in g per 100 mL. Unless otherwise stated chloroform was the solvent. Microanalysis was performed using a Carlo-Erber 1108 elemental analyser and, for sulfur, by titration against barium perchlorat

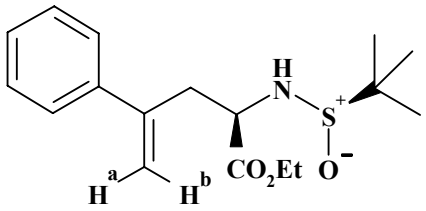
General procedure for synthesis of *N*-sulfinylamino esters 4a – h

Aryl iodide (0.75 mmol) was added to a suspension of chiral α-iminoester **3** (0.5 mmol), indium metal powder (0.088 g, 0.75 mmol), $Pd(OAc)_2$ (0.011g, 0.05 mmol), tri-2-furyl phosphine (0.024 g, 0.1 mmol), CuI (0.019 g, 0.1 mmol) and piperidine (0.05 ml, 0.5 mmol) in DMF (10 ml) in a Schlenk tube. The mixture was subjected to two freeze, pump, thaw cycles and then charged, using standard Schlenk techniques, with allene gas (0.5 bar). The mixture was stirred and heated to 40 ^oC (oil bath temperature) for 24 h, left to cool and vented. Ethyl acetate (20 ml) and 5 % HCl aqueous solution (10 ml) added and the mixture stirred for 20 mins. The phases were separated and the aqueous layer extracted with ethyl acetate (20 ml). The organic extracts were combined and washed with water (3 x 40 ml), dried over magnesium sulfate, filtered and the filtrate concentrated *in vacuo*. The residue was purified by flash chromatography to give the *N-sulfinylamino esters*.



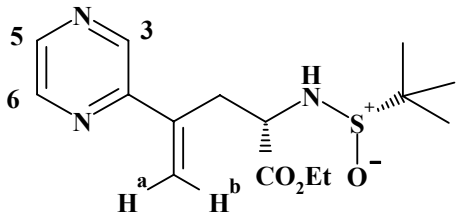
Ethyl 2*S*,4*S*-(2-methyl-propane-2-sulfinylamino)-4-phenyl-pent-4-enoate (*S*,*S*-4a)

Obtained as a pale yellow oil (0.149 g, 92 %) after flash chromatography (9:1 v/v diethyl ether : hexane); R_F 0.43 (diethyl ether); $[a]_D^{20}$ + 81.4 (*c* 1.2); Found; C, 62.90; H, 7.80; N, 4.35; S, 9.90, $C_{17}H_{25}NO_3S$ requires; C, 63.13; H, 7.79; N, 4.33; S, 9.91 %; ν_{max}/cm^{-1}; 3294, 2983, 2253, 1794, 1732, 1630; δ_H (500 MHz, $CDCl_3$); 7.37 – 7.34 (3H, m, ArH), 7.29 – 7.27 (2H, m, ArH), 5.34 (1H, s, =CH^a), 5.12 (1H, s, =CH^b), 4.10 – 4.01 (4H, m, OCH_2CH$_3$**,** N*HCH*), 3.04 (1H, dd, NCHC*H*, *J*, 1.0, 2.9 Hz,), 2.85 (1 H, dd, NCHC*H*, *J*, 1.0, 3.2 Hz), 1.26 (3H, t, OCH$_2$C*H*$_3$, *J*, 7.1 Hz,), 1.16 (9H, s, C(CH$_3$)$_3$); δ_c (75 MHz, $CDCl_3$); 173.3 (*C*O), 144.1(H$_2$C=*C*), 140.5 (Ar), 128.9 (Ar), 128.2 (Ar), 126.6 (Ar), 117.0 (=*C*H$_2$), 62.1 (OC), 57.3 (NC), 56.5(S*C*), 40.8 (NC*C*), 23.0 (SC(*C*H$_3$)$_3$), 14.5 (OC*C*); m/z (ES$^+$); 324 (MH$^+$).



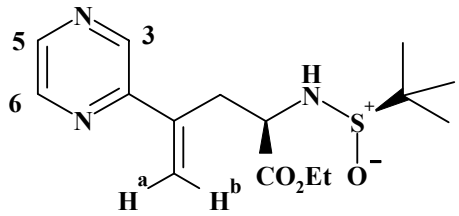
Ethyl 2*R*,4*R*-(2-methyl-propane-2-sulfinylamino)-4-phenyl-pent-4-enoate (*R*,*R*-4a)

Obtained as a pale yellow oil (0.130 g, 80 %) after flash chromatography (9:1 v/v diethyl ether : hexane); R_F 0.43 (diethyl ether); $[a]_D^{20}$ - 79.9 (*c* 1.6); Found; C, 63.00; H, 7.80; N, 4.40; S, 9.90, $C_{17}H_{25}NO_3S$ requires; C, 63.13; H, 7.79; N, 4.33; S, 9.91 %; ν_{max}/cm^{-1}; 3294, 2983, 2253, 1794, 1732, 1630; δ_H (500 MHz, $CDCl_3$); 7.37 – 7.34 (3H, m, ArH), 7.29 – 7.27 (2H, m, ArH), 5.34 (1H, s, =CH^a), 5.12 (1H, s, =CH^b), 4.10 – 4.01 (4H, m, OCH_2CH$_3$**,** N*HCH*), 3.04 (1H, dd, NCHC*H*, *J*, 1.0, 2.9 Hz,), 2.85 (1 H, dd, NCHC*H*, *J*, 1.0, 3.2 Hz), 1.26 (3H, t, OCH$_2$C*H*$_3$, *J*, 7.1 Hz,), 1.16 (9H, s, C(CH$_3$)$_3$); δ_c (75 MHz, $CDCl_3$); 173.3 (*C*O), 144.1(H$_2$C=*C*), 140.5 (Ar), 128.9 (Ar), 128.2 (Ar), 126.6 (Ar), 117.0 (=*C*H$_2$), 62.1 (OC), 57.3 (NC), 56.5(SC), 40.8 (NC*C*), 23.0 (SC(*C*H$_3$)$_3$), 14.5 (OC*C*); m/z (ES$^+$); 324 (MH$^+$).



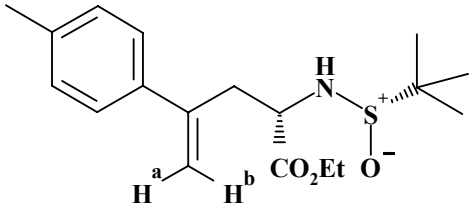
Ethyl 2*S*,4*S*-(2-methyl-propane-2-sulfinylamino)-4-pyrazin-2-yl-pent-4-enoate (*S*,*S*-4b)

Obtained as a pale yellow oil (0.112 g, 69 %) after flash chromatography (ethyl acetate); R_F 0.37 (ethyl acetate); $[a]_D^{20}$ + 63.5 (*c* 0.9); Found; C, 54.40; H, 6.90; N, 12.70, $C_{15}H_{23}N_3O_3S$.0.25 M H_2O requires; C, 54.61; H, 7.18; N, 12.74 %; ν_{max}/cm^{-1}; 3584, 3436 (NH), 3289, 2982, 2963, 2240, 1734 (C=O), 1468, 1367, 1067; δ_H (500 MHz, $CDCl_3$); 8.74 (1H, s, pyrazinyl-3H), 8.47 (1H, d, pyrazinyl-6H, *J*, 1.3 Hz), 8.39 (1H, d, pyrazinyl-5H, *J*, 1.3 Hz), 5.81 (1H, s, =CH^a), 5.42 (1H, s, =CH^b), 4.14 – 4.04 (4H, m, br, OCH_2, N*HCH*), 3.05 (1H, dd, NCHC*H*, *J*, 5.3, 14.3 Hz), 2.93 (1H, dd, NHCHC*H*, *J*, 8.2, 14.3 Hz), 1.18 (3H, t, OCH$_2$C*H*$_3$, *J*, 7.2 Hz), 1.08 (9H, s, C(CH$_3$)$_3$); δ_c (75 MHz, $CDCl_3$); 172.00 (CO), 152.02 (H$_2$C=*C*), 142.29 (Ar), 141.91 (Ar), 141.22 (Ar), 140.08 (Ar), 119.35 (=*C*H$_2$), 60.69 (O*C*), 55.82 (NC), 55.13 (SC), 37.13 (NC*C*), 21.54 (C(*C*H$_3$)$_3$), 13.08 (OC*C*); m/z (ES$^+$); 326 (MH$^+$).



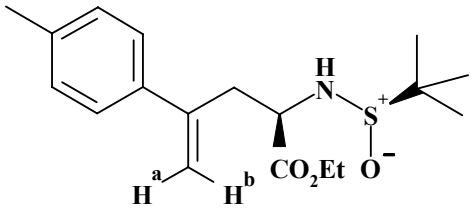
Ethyl 2*R*,4*R*-(2-methyl-propane-2-sulfinylamino)-4-pyrazin-2-yl-pent-4-enoate (*R*,*R*-4b)

Obtained as a pale yellow oil (0.169 g, 35 %) after flash chromatography (ethyl acetate); R_F 0.37 (ethyl acetate); $[a]_D^{20}$ - 63.6 (*c* 1.1); Found; C, 54.40; H, 6.85; N, 12.65, $C_{15}H_{23}N_3O_3S$. 0.25M H_2O requires; C, 54.61; H, 7.18; N, 12.74 %; ν_{max}/cm^{-1}; 3447, 2981, 1734, 1633, 1519, 1469; δ_H (500 MHz, $CDCl_3$); 8.75 (1H, s, pyrazinyl-3H), 8.46 (1H, d, pyrazinyl-6H, *J*, 1.3 Hz), 8.39 (1H, d, pyrazinyl-5H, *J*, 1.3 Hz), 5.81 (1H, s, =CH^a), 5.42 (1H, s, =CH^b), 4.17 – 4.04 (4H, m, br, OCH_2, N*HCH*), 3.05 (1H, dd, NCHC*H*, *J*, 5.3 Hz, 14.3 Hz), 2.93 (1H, dd, NCHC*H*, *J*, 8.2 Hz, 14.3 Hz), 1.18 (3H, t, OCH$_2$C*H*$_3$, *J*, 7.2 Hz), 1.08 (9H, s, C(CH$_3$)$_3$); δ_c (75 MHz, $CDCl_3$); 171.95 (CO), 152.02 (H$_2$C=*C*), 142.32 (Ar), 141.89 (Ar), 141.19 (Ar), 140.57 (Ar), 119.35 (=*C*H$_2$), 60.63 (O*C*), 55.85 (NC), 55.19 (SC), 37.09 (NC*C*), 21.76 (C(*C*H$_3$)$_3$), 13.08 (OC*C*); m/z (ES$^+$); 326 (MH$^+$).



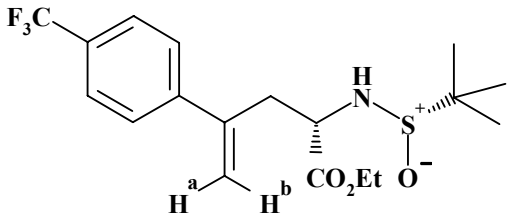
Ethyl 2*S*,4*S*-(2-methyl-propane-2-sulfinylamino)-4-*p*-tolyl-pent-4-enoate (*S*,*S*-4c)

Obtained as a colourless oil (0.230 g, 68 %) after flash chromatography (8:1 v/v Et_2O : hexane); R_F 0.53 (8:1 v/v Et_2O : hexane); $[a]_D^{20}$ + 87.2 (*c* 2.4); Found; C, 63.90; H, 8.40; N, 3.90; S, 9.40, $C_{18}H_{27}NO_3S$ requires; C, 64.06; H, 8.06; N, 4.15; S, 9.50 %; ν_{max}/cm^{-1}; 3456, 3280 (NH), 3082, 1733(CO), 1626, 1563, 1511; δ_H (500 MHz, $CDCl_3$); 7.25 (2H, d, ArH, *J*, 7.9 Hz), 7.14 (2H, d, ArH, *J*, 7.9 Hz), 5.31 (1H, s, =CH^a), 5.07 (1H, s, =CH^b), 4.12 (2H, q, OCH_2, *J*, 7.1 Hz), 4.03 (1H, d, NH, *J*, 8.3 Hz), 4.02 – 3.91 (1H, m, NCH), 3.00 (1H, dd, NCHC*H*, *J*, 5.4, 14.3 Hz), 2.80 (1H, dd, NCHC*H*, *J*, 7.6, 14.3 Hz), 2.35 (3H, s, ArCH_3), 1.25 (3H, t, OCH_2CH_3, *J*, 7.1 Hz), 1.17 (9H, s, $C(CH_3)_3$); δ_c (75 MHz, $CDCl_3$); 171.29 (CO), 142.42 (H_2C=*C*), 136.50 (Ar), 136.05 (Ar), 128.11 (Ar), 125.21 (Ar), 114.65 (=*C*H_2), 60.54 (O*C*), 55.87 (NC), 55.08 (SC), 39.41 (NC*C*), 21.52 (C(*C*H_3)$_3$), 20.05 (OC*C*), 13.05 (Ar*C*H_3); m/z (ES^+); 338 (MH^+).



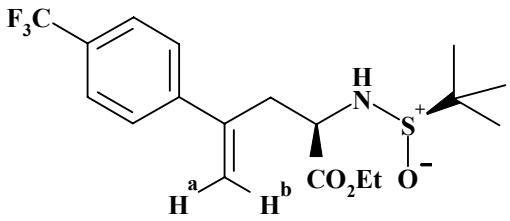
Ethyl 2*R*,4*R*-(2-methyl-propane-2-sulfinylamino)-4-*p*-tolyl-pent-4-enoate (*R*,*R*-4c)

Obtained as a colourless oil (0.233 g, 68 %) after flash chromatography (8:1 v/v Et_2O : hexane); R_F 0.53 (8:1 v/v Et_2O : hexane); $[a]_D^{20}$ - 88.6 (*c* 1.5); Found; C, 64.00; H, 8.40; N, 4.10; S, 9.40, $C_{18}H_{27}NO_3S$ requires; C, 64.06; H, 8.06; N, 4.15; S, 9.50 %; ν_{max}/cm^{-1}; 3276, 3085, 2980, 2958, 2926, 2869, 1737; δ_H (500 MHz, $CDCl_3$); 7.25 (2H, d, ArH, *J*, 7.9 Hz), 7.14 (2H, d, ArH, *J*, 7.9 Hz), 5.30 (1H, s, =CH^a), 5.07 (1H, s, =CH^b), 4.14 – 4.10 (2H, q, OCH_2, *J*, 7.1 Hz), 4.03 (1H, d, NH, *J*, 8.3 Hz), 4.0 – 3.9 (1H, m, NCH), 3.00 (1H, dd, NCHC*H*, 5.4, 14.3 Hz), 2.80 (1H, dd, NCHC*H*, *J*, 7.6, 14.3 Hz), 2.35 (3H, s, ArCH_3), 1.24 (3H, t, OCH_2CH_3, *J*, 7.1 Hz), 1.16 (9H, s, $C(CH_3)_3$); δ_c (75 MHz, $CDCl_3$); 173.34 (CO), 143.84 (H_2C=*C*), 137.96 (Ar), 137.48 (Ar), 129.54 (Ar), 126.63 (Ar), 116.09 (=*C*H_2), 61.99 (O*C*), 57.28 (NC), 56.52 (SC), 40.85 (NC*C*), 22.96 (C(*C*H_3)$_3$), 21.48 (OC*C*), 14.47 (Ar*C*H_3); m/z (ES^+); 338 (MH^+).



Ethyl 2*S*,4*S*-(2-methyl-propane-2-sulfinylamino)- 4-(4-trifluoromethyl-phenyl)-pent-4-enoate (*S*,*S*-4d)

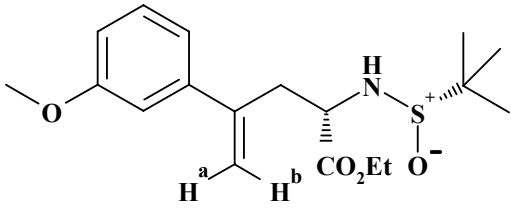
Obtained as a colourless oil (0.422 g, 54 %) after flash chromatography (Et_2O); R_F 0.16 (Et_2O); $[a]_D^{20}$ + 82.2 (*c* 1.1); Found; C, 55.00; H, 6.30; N, 3.60; S, 8.10, $C_{18}H_{24}NSO_4F_3$ requires; C, 55.23; H, 6.18; N, 3.58; S, 8.19; F, 14.56 %; ν_{max}/cm^{-1}; 3453, 3283 (NH), 3088, 2982, 2961, 2907, 2871, 1738 (CO), 1616; δ_H (500 MHz, $CDCl_3$); 7.60 (2H, ArH, d, *J*, 8.2 Hz), 7.47 (2H, ArH, d, *J*, 8.2 Hz), 5.41 (1H, s, =CH^a), 5.23 (1H, s, =CH^b), 4.12 (2H, m, OCH_2), 4.04 (1H, d, N*H*, 7.5 Hz), 3.97 (1H, dt, NCH, *J*, 5.6, 7.5 Hz), 3.05 (1H, dd, NCHC*H*, *J*, 5.6, 14.3 Hz), 2.86 (1H, dd, NCHC*H*, *J*, 7.5, 14.3 Hz), 1.25 (3H, t, OCH_2CH_3, *J*, 7.2 Hz), 1.16 (9H, s, $C(CH_3)_3$); δ_c (75 MHz, $CDCl_3$); 172.99 (CO), 149.37 (Ar), 143.13 (H_2C=*C*), 130.17 (q, CF_3, *J*, 32.39 Hz), 127.16 (Ar), 126.85 (Ar), 125.86 (q, F_3CC, 4.06 Hz), 118.89 (=CH_2), 62.20 (OC), 57.02 (NC), 56.52 (SC), 40.54 (NC*C*), 22.89 (C(*C*H_3)$_3$), 14.44 (OCC); m/z (ES^+); 392 (MH^+).



Ethyl 2*R*,4*R*-(2-methyl-propane-2-sulfinylamino)- 4-(4-trifluoromethyl-phenyl)-pent-4-enoate (*R*,*R*-4d)

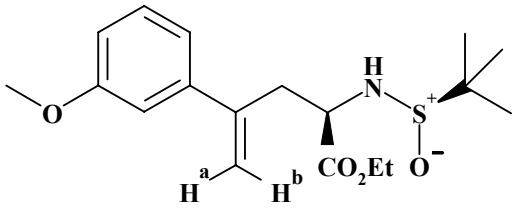
Obtained as a colourless oil (0.385 g, 49 %); after flash chromatography (Et_2O); R_F 0.16 (Et_2O); $[a]_D^{20}$ - 80.4 (*c* 0.7); Found; C, 55.00; H, 6.20; N, 3.70; S, 8.30, $C_{18}H_{24}NSO_4F_3$ requires; C, 55.23; H, 6.18; N, 3.58; S, 8.19; F, 14.56 %; ν_{max}/cm^{-1}; 3459, 3282 (NH), 2982, 3088, 2982, 2961, 2907, 2871, 1738 (CO), 1616, 1573; δ_H (500 MHz, $CDCl_3$); 7.60 (2H, ArH, d, *J*, 8.2 Hz), 7.47 (2H, ArH, d, *J*, 8.2 Hz), 5.41 (1H, s, =CH^a), 5.23 (1H, s, =CH^b), 4.19 – 4.06 (2H, m, OCH_2), 4.03 (1H, d, NH, *J*, 7.5 Hz), 3.97 (1H, dt, NCH, *J*, 5.6, 7.5 Hz), 3.04 (1H, dd, NCC*H*, *J*, 5.6, 14.3 Hz), 2.87 (1H, dd, NCC*H*, *J*, 7.5 Hz, 14.3 Hz); 1.25 (3H, t, OCH_2CH_3, *J*, 7.19); 1.16 (9H, s, $C(CH_3)_3$); δ_c (75 MHz, $CDCl_3$); 172.99 (CO), 149.37 (Ar), 143.13 (H_2C=*C*), 130.17 (q, CF_3, *J*, 32.39 Hz), 127.16 (Ar), 126.85 (Ar),

125.86 (q, F_3CC, 4.06 Hz), 118.89 (=CH_2), 62.20 (OC), 57.02 (NC), 56.52 (SC), 40.54 (NC*C*), 22.89 (C(CH_3)$_3$, 14.44 (OCC); m/z (ES^+); 392 (MH^+).



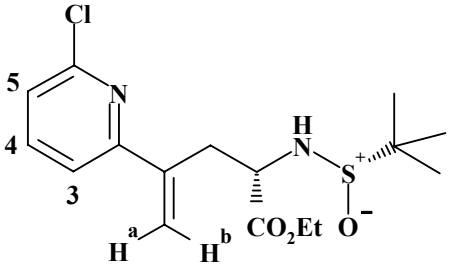
Ethyl 2*S*,4*S*-(3-methoxy-phenyl)-2-(2-methyl-propane-2-sulfinylamino)-pent-4-enoate (*S*,*S*-4e)

Obtained as a pale yellow oil (0.130 g, 72 %) after flash chromatography (9:1 v/v diethyl ether : hexane); R_F 0.47 (3:1 v/v ethyl acetate : hexane); $[a]_D^{20}$ + 78.3 (*c* 2.1); Found; C, 60.40; H, 7.80; N, 3.70, $C_{18}H_{27}NO_4S$.0.25 M H_2O requires; C, 60.39; H, 7.74; N, 3.91 %; Found; 376.1552; $C_{18}H_{27}NO_4S$.Na requires 376.1559; ν_{max}/cm^{-1}; 3583, 3453 (NH), 3283, 2978, 2836, 1736 (CO), 1628; δ_H (500 MHz, $CDCl_3$); 7.19 (1H, t, Ar-5H, *J*, 7.7 Hz), 6.87 (1H, s, Ar-2H), 6.82 (1H, d, Ar-4H *J*, 7.7 Hz), 6.75 (1H, d, Ar-6H, *J*, 7.7 Hz), 5.27 (1H, s, =CH^a), 5.04 (1H, s, =CH^b), 4.07 – 4.03 (2H, m, OCH_2,), 3.97 – 3.92 (2H, m, N*HCH*), 3.74 (3H, s, OCH_3), 2.93 (1H, dd, NCC*H*, *J*, 5.3, 14.0 Hz), 2.74 (1H, dd, NCC*H*, *J*, 7.5 Hz, 14.0 Hz), 1.17 (3H, t, OCH_2CH_3, *J*, 4.8 Hz), 1.09 (9H, s, C(CH_3)$_3$); δ_c (75 MHz, $CDCl_3$); 171.85 (CO), 158.60 (H_2C=*C*), 150.48 (Ar), 142.52 (Ar), 140.55 (Ar), 134.76 (Ar), 117.83 (Ar), 115.61 (=CH_2), 111.91 (Ar), 60.72 (NC*C*), 55.85 (ArO*C*), 55.09 (NC), 54.19 (SC), 21.61 (C(CH_3)$_3$, 13.15 (OC*C*); m/z (ES^+); 354 (MH^+).



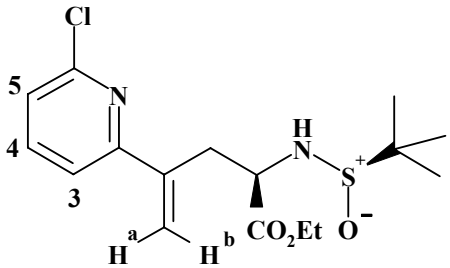
Ethyl 2*R*,4*R*-(3-methoxy-phenyl)-2-(2-methyl-propane-2-sulfinylamino)-pent-4-enoate (*R*,*R*-4e)

Obtained as a pale yellow oil (0.119 g, 67 %) after flash chromatography (9:1 v/v diethyl ether : hexane); R_F 0.47 (3:1 v/v ethyl acetate : hexane); $[a]_D^{20}$ - 77.1 (*c* 1.2); Found; C, 61.30; H, 7.80; N, 4.00, 9.20, $C_{18}H_{27}NO_4S$ requires; C, 61.16; H, 7.70; N, 3.96; S, 9.07 %; ν_{max}/cm^{-1}; 3282, 3082, 2980, 2958, 2907, 2869, 2836, 1737(CO), 1627, 1598, 1577; δ_H (500 MHz, $CDCl_3$); 7.18 (1H, t, Ar-5H, *J*, 7.9 Hz), 6.87 (1H, d, Ar-2H, 7.9 Hz), 6.82 (1H, s, Ar-4H), 6.76 (1H, d, Ar-6H, *J*, 7.9 Hz), 5.27 (1H, s, =CH^a), 5.04 (1H, s, =CH^b), 4.07 – 4.03 (2H, m, OCH_2,), 3.97 – 3.92 (2H, m, N*HCH*), 3.74 (3H, s, OCH_3), 2.93 (1H, dd, NCC*H*, *J*, 5.3, 14.0 Hz), 2.74 (1H, dd, NCC*H*, *J*, 7.5 Hz, 14.0 Hz), 1.17 (3H, t, OCH_2CH_3, *J*, 7.1 Hz), 1.09 (9H, s, C(CH_3)$_3$); δ_c (75 MHz, $CDCl_3$); 171.85 (CO), 158.61 (H_2C=*C*), 142.22 (Ar), 140.55 (Ar), 128.44 (Ar), 117.43 (Ar), 115.61 (=CH_2), 111.92 (Ar), 111.42 (Ar), 60.62 (O*C*), 55.87 (OCH_3), 55.10 (SC), 54.19 (NC), (NC*C*), 21.55 (C(CH_3)$_3$), 13.05 (OC*C*); m/z (ES^+); 354 (MH^+).



Ethyl 2S,4S-(6-chloro-pyridin-2-yl)-2-(2-methyl-propane-2-sulfinylamino)-pent-4-enoate (*S*,*S*-4f)

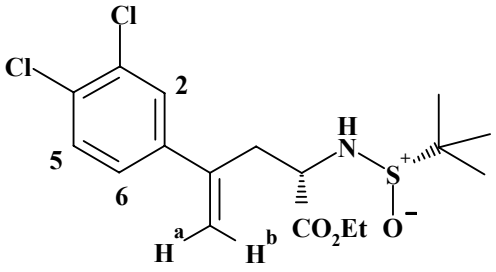
Obtained as a pale yellow oil (0.187 g, 52 %) after flash chromatography (6:1 v/v ethyl acetate : hexane); R_F 0.41 (6:1 v/v ethyl acetate : hexane); $[a]_D^{20}$ + 86.7 (*c* 1.8); Found; C, 53.30; H, 6.60; N, 7.80; S, 9.00, $C_{16}H_{23}ClN_2O_3S$ requires; C, 53.55; H, 6.46; Cl, 9.88; N, 7.81; S, 8.93 %; ν_{max}/cm^{-1}; 3417, 3209, 2981, 2961, 1737 (CO); δ_H (500 MHz, $CDCl_3$); 8.40 (1H, d, pyridyl-5H, *J*, 2.3 Hz), 7.63 (1H, d, pyridyl-3H, *J*, 8.4 Hz), 7.32 (1H, dd, pyridyl-4H, *J*, 2.3, 8.4 Hz), 5.41 (1H, s, =CH^a), 5.27 (1H, s, =CH^b), 4.17 – 4.09 (3H, m, br, NH, OCH_2), 3.96 (1H, m, NHC*H*), 3.00 (1H, dd, NCC*H*, 0.6, 5.0 Hz), 2.86 (1H, dd, H_2C=CC*H*, *J*, 0.6, 7.7Hz), 1.26 (3H, t, OCH_2CH_3, *J*, 7.2 Hz), 1.18 (9H, s, C(CH_3)$_3$); δ_c (75 MHz, $CDCl_3$); 172.82 (CO), 151.06 (H_2C=*C*), 147.96 (Ar), 140.11 (Ar), 136.86 (Ar), 135.10 (Ar), 124.36 (Ar), 119.32 (=CH_2), 62.36 (O*C*), 56.74 (NC), 56.61 (SC), 22.95 (C(CH_3)$_3$), 14.48 (O_2CC); m/z (ES^+); 359 (^{35}Cl MH^+), 361 (^{37}Cl MH^+).



Ethyl 2*R*,4*R*-(6-chloro-pyridin-2-yl)-2-(2-methyl-propane-2-sulfinylamino)-pent-4-enoate (*R*,*R*-4f)

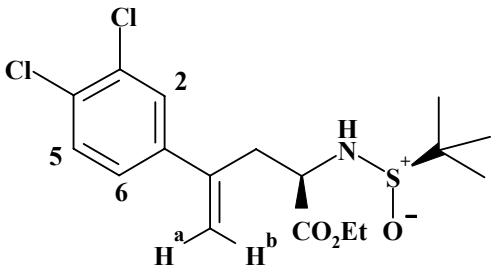
Obtained as a pale yellow oil (0.088 g, 49 %) after flash chromatography (6:1 v/v ethyl acetate : hexane); R_F 0.41 (6:1 v/v ethyl acetate : hexane); $[a]_D^{20}$ - 84.9 (*c* 2.5); Found; C, 53.50; H, 7.00; Cl, 9.70; N, 7.70; S, 8.80, $C_{16}H_{23}ClN_2O_3S$ requires; C, 53.55; H, 6.46; Cl, 9.88; N,

7.81; S, 8.93 %; ν_{max}/cm^{-1}; 3448, 3429, 2983, 1737 (CO), 1461, 1366; δ_H (500 MHz, $CDCl_3$); 8.32 (1H, d, pyridyl-5H, *J*, 2.5 Hz), 7.57 (1H, dd, pyridyl-3H, *J*, 2.5, 8.3 Hz), 7.25 (1H, d, pyridyl-4H, *J*, 8.3 Hz), 5.34 (1H, s, =CH^a), 5.19 (1H, s, =CH^b), 4.06 – 4.01 (3H, m, br, NH, OCH_2), 3.89 (1H, dd, NC*H J*, 5.0, 7.7 Hz), 2.92 (1H, dd, NCC*H*, *J*, 0.6, 5.0 Hz), 2.78 (1H, dd, NCC*H*, *J*, 0.6, 7.7Hz), 1.19 (3H, t, OCH_2CH_3, *J*, 7.2 Hz), 1.10 (9H, s, $C(CH_3)_3$); δ_c (75 MHz, $CDCl_3$); 171.39 (CO), 149.61 (H_2C=*C*), 146.53 (Ar), 138.68 (Ar), 135.47 (Ar), 133.69 (Ar), 117.92 (=CH_2), 60.72 (O*C*), 55.35 (N*C*), 54.94 (SC), 38.81 (NC*C*), 21.61 ($C(CH_3)_3$), 13.06 (OC*C*); m/z (ES^+); 359 (^{35}Cl MH^+), 361 (^{37}Cl MH^+).



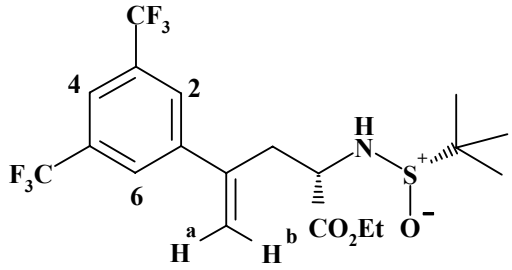
Ethyl 2*S*,4*S*-(3,4-dichloro-phenyl)-2-(2-methyl-propane-2-sulfinylamino)-pent-4-enoate (*S,S*-4g)

Obtained as a pale yellow oil (0.144 g, 73 %) after flash chromatography (9:1 v/v diethyl ether : hexane); R_F 0.22 (9:1 v/v diethyl ether : hexane); $[a]_D^{20}$ + 68.3 (*c* 1.1); Found; C, 52.20; H, 6.10; Cl, 17.80; N, 3.60, S, 7.90, $C_{17}H_{23}Cl_2NO_3S$ requires; C, 52.04; H, 5.91; Cl, 18.07; N, 3.57; S, 8.17 %; ν_{max}/cm^{-1}; 3583, 3450 (NH), 3282, 2981, 2960, 1736 (CO), 1474, 1367, 1074; δ_H (500 MHz, $CDCl_3$); 7.37 (1H, s, Ar-2H), 7.33 (1H, d, Ar-5H, *J*, 8.3 Hz), 7.12 (1H, d, Ar-6H, *J*, 8.3 Hz), 5.29 (1H, s, =CH^a), 5.11 (1H, s, =CH^b), 4.06 (2H, dq, OCH_2, *J*, 7.2, 13.1 Hz), 3.89 (1H, dd, NC*H*, 7.7, 6.2 Hz) 2.90 (1H, dd, NCHC*H*, *J*, 6.2, 14.5 Hz), 2.75 (1H, dd, NCHC*H*, *J*, 7.7, 14.5 Hz), 1.18 (3H, t, OCH_2CH_3, *J*, 7.2 Hz), 1.10 (9H, s, $C(CH_3)_3$); δ_c (75 MHz, $CDCl_3$); 171.51 (CO), 140.68 (*C*=CH_2), 131.57 (Ar), 130.73 (Ar), 129.87 (Ar), 128.87 (Ar), 127.77 (Ar), 124.67 (Ar), 117.79 (=CH_2), 60.58 (O*C*), 55.55 (N*C*), 55.14 (SC), 38.96 (NC*C*), 21.62 ($C(CH_3)_3$), 13.05 (OC*C*); m/z (ES^+); 393 ($^{35/35}Cl$ MH^+), 395 ($^{35/37}Cl$ MH^+), 397 ($^{37/37}Cl$ MH^+).



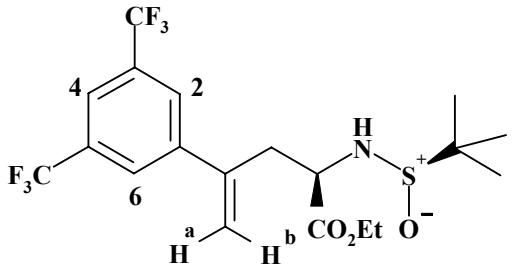
Ethyl 2*R*,4*R*-(3,4-dichloro-phenyl)-2-(2-methyl-propane-2-sulfinylamino)-pent-4-enoate (*R,R*-4g)

Obtained as a pale yellow oil (0.146 g, 74 %) after flash chromatography (9:1 v/v diethyl ether : hexane); R_F 0.22 (9:1 v/v diethyl ether : hexane); $[a]_D^{20}$ - 70.8 (*c* 1.2); Found; C, 52.04; H, 5.91; Cl, 18.07; N, 3.57; S, 8.17, $C_{17}H_{23}Cl_2NO_3S$ requires; C, 52.00; H, 5.90; Cl, 18.10; N, 3.60; S, 8.20 %; ν_{max}/cm^{-1}; 3583, 3450 (NH), 3274, 2978, 2956, 1736 (CO), 1473, 1366, 1070; δ_H (500 MHz, $CDCl_3$); 7.37 (1H, d, Ar-2H, *J*, 2.0 Hz), 7.33 (1H, d, Ar-5H, *J*, 8.3 Hz), 7.13 (1H, dd, Ar-6H, *J*, 2, 8.3 Hz), 5.29 (1H, s, =CH^a), 5.11 (1H, s, =CH^b), 4.06 (2H, dq, OCH_2, *J*, 7.6, 10.7 Hz), 3.89 (1H, dd, NC*H*, *J*, 5.5, 7.4 Hz), 2.90 (1H, dd, NCHC*H*, *J*, 5.5, 14.5 Hz), 2.73 (1H, dd, NCHC*H*, *J*, 7.4, 14.5 Hz), 1.19 (3H, t, OCH_2CH_3, *J*, 7.2 Hz), 1.10 (9H, s, $C(CH_3)_3$); δ_c (75 MHz, $CDCl_3$); 171.50 (CO), 140.68 (*C*=CH_2), 131.55 (Ar), 130.71 (Ar), 129.39 (Ar), 128.87 (Ar), 127.35 (Ar), 124.68 (Ar), 117.02 (=CH_2), 60.82 (O*C*), 55.55 (N*C*), 55.13 (SC), 38.95 (NC*C*), 21.51 ($C(CH_3)_3$), 13.05 (OC*C*); m/z (ES^+); 393 ($^{35/35}Cl$ MH^+), 395 ($^{35/37}Cl$ MH^+), 397 ($^{37/37}Cl$ MH^+).



Ethyl 2*S*,4*S*-(3,5-bis-trifluoromethyl-phenyl)-2-(2-methyl-propane-2-sulfinylamino)-pent-4-enoate (*S,S*-4h)

Obtained as a pale yellow oil (0.159 g, 69 %) after flash chromatography (3:1 v/v ethyl acetate : hexane to 6:1 v/v ethyl acetate : hexane); R_F 0.58 (3:1 v/v ethyl acetate : hexane); $[a]_D^{20}$ + 55.2 (*c* 3.2); Found; C, 49.50; H, 5.00; N, 3.00; S, 6.80, $C_{19}H_{23}F_6NO_3S$ requires; C, 49.67; H, 5.05; F, 24.81; N, 3.05; S, 6.98 %; ν_{max}/cm^{-1}; 3583, 3454 (NH), 2983, 2963, 1739 (CO), 1632, 1378, 1279, 1180, 1136, 1078; δ_H (500 MHz, $CDCl_3$); 7.72 (3H, s, ArH), 5.41 (1H, s, =CH^a), 5.28 (1H, s, =CH^b), 4.13 – 4.01 (3H, m, br, O-CH_2, NH), 3.91 – 3.88 (1H, m, NCH), 3.07 (1H, dd, NCHC*H*, *J*, 5.1, 14.5 Hz), 2.93 (1H, dd, NCHC*H*, *J*, 7.3, 14.5 Hz), 1.18 (3H, t, OCH_2CH_3, *J*, 7.2 Hz), 1.07 (9H, s, $C(CH_3)_3$; δ_c (75 MHz, $CDCl_3$); 171.35 (CO), 141.74 (H_2C=*C*), 140.72 (Ar), 13.90 (q, Ar, *J*, 33.3 Hz), 125.86 (Ar), 122.2 (q, CF_3, *J*, 272.8 Hz), 119.94 (Ar), 118.75 (=CH_2), 60.98 (O*C*), 55.93 (NC), 55.12 (SC), 38.76 (NC*C*), 21.43 ($C(CH_3)_3$), 12.93 (OC*C*); m/z (ES^+); 460 (MH^+).

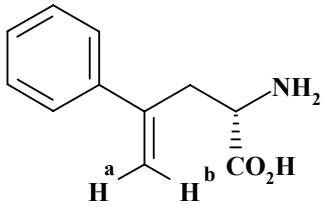


Ethyl 2*R*,4*R*-(3,5-bis-trifluoromethyl-phenyl)-2-(2-methyl-propane-2-sulfinylamino) -pent-4-enoate (*R*,*R*-4h)

Obtained as a pale yellow oil (0.151 g, 66 %) after flash chromatography (3:1 v/v ethyl acetate : hexane to 6:1 v/v ethyl acetate : hexane); R_F 0.58 (3:1 v/v ethyl acetate : hexane); $[a]_D^{20}$ - 53.0 (*c* 1.1); Found; C, 49.60; H, 5.10; N, 3.10; S, 6.80, $C_{19}H_{23}F_6NO_3S$ requires; C, 49.67; H, 5.05; F, 24.81; N, 3.05; S, 6.98 %; ν_{max}/cm^{-1}; 3450 (NH), 2978, 1739 (CO), 1629, 1374, 1278; δ_H (500 MHz, $CDCl_3$); 7.72 (3H, s, ArH), 5.41 (1H, s, $=CH^a$), 5.28 (1H, s, $=CH^b$), 4.13 – 4.02 (3H, m, br, OCH_2, NH), 3.91 – 3.88 (1H, m, NC*H*), 3.07 (1H, dd, NCHC*H*, *J*, 5.1, 14.5 Hz), 2.93 (1H, dd, NCHC*H*, *J*, 7.3, 14.5 Hz), 1.18 (3H, t, OCH_2CH_3, *J*, 7.2 Hz), 1. 07 (9H, s, $C(CH_3)_3$; δ_c (75 MHz, $CDCl_3$); 171.34 (CO), 141.75 ($H_2C=C$), 140.72 (Ar), 130.90 (q, Ar, *J*, 33.3 Hz), 125.54 (Ar), 122.23 (q, CF_3, *J*, 272.8 Hz), 119.94 (Ar), 118.75 ($=CH_2$), 60.98 (O*C*), 55.93 (NC), 55.12 (SC), 38.76 (NC*C*), 21.43 ($C(CH_3)_3$), 12.93(OC*C*); m/z (ES^+); 460 (MH^+).

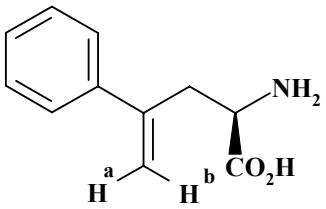
General procedure for the synthesis of α-amino acids 5a – h.

4M HCl in dioxane (5 eqv) was added to a 0.1 M solution of the *N*-sulfinyl α-aminoester in EtOH. The solution was stirred at room temperature for 2 h and the solvent removed *in vacuo*. 1M NaOH solution (2 eqv) was added to a 0.1 M solution of the ester in a 1:1 v/v H_2O : EtOH solvent system and the mixture stirred and heated to reflux (80 °C oil bath temperature) for 4 h. The solution was left to cool to room temperature and the solvent removed *in vacuo*. The residue was dissolved in deionised water and applied to the top of an amberlyst 15 H^+ form 20 – 50 mesh ion exchange column and eluted with distilled water followed by a 1 % NH_3 solution in deionised water. The ammonia fractions were visualised under UV light and the UV active fractions were collected and concentrated *in vacuo* to give the *amino acid products* as pale yellow to colourless solids.



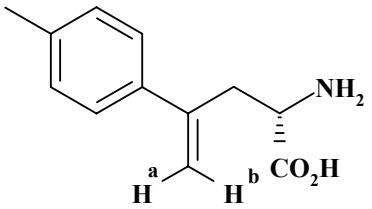
2-(*S*)-2-Amino-4-phenyl-pent-4-enoic acid (*S*-5a)

Obtained as colourless prisms (0.156 g, 100 %) after ion exchange chromatography. M.pt. 130 – 132 °C; $[a]_D^{20}$ + 26.4 (*c* 0.3, MeOH); Found; 192.1021; $C_{11}H_{13}NO_2$ requires; 192.1019; ν_{max}/cm^{-1}; 3030 (br, OH), 2065, 1590 (CO), 1395, 1340; δ_H (500 MHz, D_2O); 6.90 (2H, d, ArH, 7.8 Hz), 6.85 – 6.75 (3H, m, ArH), 4.98 (1H, s, $=CH^a$), 4.73 (1H, s, $=CH^b$), 3.45 (1H, dd, NCH, *J*, 5.1, 8.6 Hz), 2.76 (1H, dd, NCCH, *J*, 5.1, 15.4 Hz), 2.47 (1H, dd, NCCH, *J*, 8.6, 15.4 Hz); δ_c (75 MHz, D_2O); 171.00 (CO), 140.85 ($H_2C=C$), 137.72 (Ar), 128.62 (Ar), 128.36 (Ar), 126.12 (Ar), 118.04 ($=CH_2$), 51.23 (NC), 35.55 (NC*C*); m/z (ES^+); 192 (MH^+).



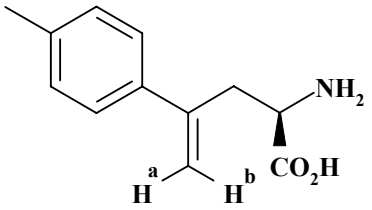
2-(*R*)-2-Amino-4-phenyl-pent-4-enoic acid (*R*-5a)

Obtained as colourless prisms (0.095 g, 100 %) after ion exchange chromatography. M.pt. 138 – 140 °C; $[a]_D^{20}$ - 26.2 (*c* 0.6, MeOH); Found; C, 66.70; H, 6.65; N, 6.95, $C_{11}H_{13}NO_2.0.33\ H_2O$ requires; C, 66.99; H, 6.98; N, 7.10 %; Found; 192.1022; $C_{11}H_{14}NO_2$ requires; 192.1025; ν_{max}/cm^{-1}; 3024 (br, OH), 2075, 1822, 1668, 1594 (CO), 1524, 1443, 1400, 1359; δ_H (500 MHz, D_2O); 7.15 (2H, d, ArH, 8.1 Hz), 7.09 – 6.98 (3H, m, ArH), 5.21 (1H, s, $=CH^a$), 4.95 (1H, s, $=CH^b$), 3.69 (1H, dd, NCH, *J*, 5.1, 8.6 Hz), 2.98 (1H, dd, NCC*H*, *J*, 5.1, 15.4 Hz), 2.71 (1H, dd, NCC*H*, *J*, 8.6, 15.4 Hz); δ_c (75 MHz, D_2O); 171.31 (CO), 141.18 ($H_2C=C$), 138.08 (Ar), 128.93 (Ar), 128.67 (Ar), 126.47 (Ar), 118.40 ($=CH_2$), 51.44 (NCH), 35.80 (NC*C*); m/z (ES^+); 192 (MH^+).



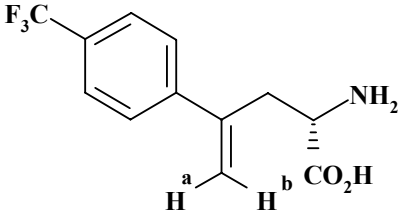
2-(*S*)-2-Amino-4-*p*-tolyl-pent-4-enoic acid (*S*-5c)

Obtained as colourless prisms (0.073 g, 61 %) after ion exchange chromatography. M.pt. 165 – 167 °C; $[a]_D^{20}$ + 10.8 (*c* 0.2, MeOH); Found; C, 68.70; H, 7.20; N, 6.60, $C_{12}H_{15}NO_2$.O.25 M H_2O requires; C, 68.71; H, 7.45; N, 6.68 %; Found; 205.1097; $C_{12}H_{15}NO_2$ requires; 205.1097; ν_{max}/cm^{-1}; 3034 (br, OH), 2089, 1912, 1818, 1671 (CO), 1594, 1518, 1450, 1400, 1359; δ_H (300 MHz, D_2O); 7.24 (2H, ArH, d, *J*, 8.0 Hz), 7.07 (2H, ArH, d, *J*, 8.0 Hz), 5.37 (1H, s, =CH^a), 5.10 (1H, s, =CH^b), 3.88 (1H, dd, NCH, *J,* 5.0, 8.7 Hz), 3.16 (1H, dd, NCCH, *J*, 5.0, 14.9 Hz), 2.87 (1H, dd, NCCH, *J*, 8.7, 14.9 Hz), 2.14 (3H, s, $ArCH_3$); δ_c (75 MHz, D_2O); 171.60 (CO), 141.2 (H_2C=*C*), 139.4 (Ar), 135.2 (Ar), 129.7 (Ar), 126.6 (Ar), 117.8 (=CH_2), 51.7 (Ar*C*H_3), 36.0 (NC), 20.4 (NC*C*); m/z (ES); 206 (MH^+).



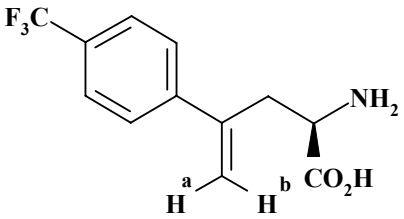
2-(*R*)-2-Amino-4-*p*-tolyl-pent-4-enoic acid (*S*-5c)

Obtained as colourless prisms (0.084 g, 51 %) after ion exchange chromatography. M.pt 165 – 167 °C; $[a]_D^{20}$ - 10.6 (*c* 0.3, MeOH); Found; 205.1099; $C_{12}H_{15}NO_2$ requires; 205.1097; ν_{max}/cm^{-1}; 3030 (br, OH), 2087, 1818, 1670 (CO), 1594, 1518, 1450, 1401, 1359; δ_H (300 MHz, D_2O); 7.30 (2H, ArH, d, *J*, 8.0 Hz), 7.13 (2H, ArH, d, *J*, 8.0 Hz), 5.43 (1H, s, =CH^a), 5.16 (1H, s, =CH^b), 3.93 (1H, dd, NCH, *J,* 5.0, 8.7 Hz), 3.22 (1H, dd, NCCH, *J*, 5.0, 14.9 Hz), 2.92 (1H, dd, NCCH, *J*, 8.7, 14.9 Hz), 2.20 (3H, s, $ArCH_3$); δ_c (75 MHz, D_2O); 171.66 (CO), 141.2 (H_2C=*C*), 139.4 (Ar), 135.3 (Ar), 129.8 (Ar), 126.6 (Ar), 117.8 (=CH_2), 51.7 (ArMe), 36.1 (NC), 20.5 (NC*C*); m/z (ES^+); 206 (MH^+).



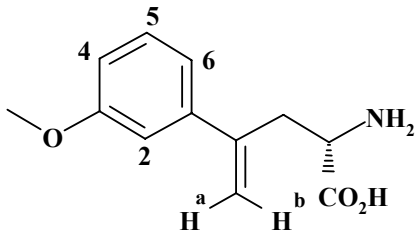
2-(*S*)-2-Amino-4-(4-trifluoromethyl-phenyl)-pent-4-enoic acid (*S*-5d)

Obtained as colourless prisms (0.223g, 99 %) after ion exchange chromatography. M.pt. 141 – 143 °C; $[a]_D^{20}$ + 31.1 (*c* 0.6, MeOH), Found; C, 55.50; H, 4.80; N, 5.30, $C_{12}H_{13}NO_2F_3$ requires; C, 55.60; H, 4.67; N, 5.40 %; ν_{max}/cm^{-1}; 3007 (br, OH), 2128, 1831, 1614 (CO), 1508, 1455, 1427, 1406, 1328; δ_H (500 MHz, CD_3OD); 7.95 (2H, d, ArH, *J*, 8.3 Hz), 7.88 (2H, d, ArH, *J*, 8.3 Hz), 5.86 (1H, s, =CH^a), 5.62 (1H, s, =CH^b), 3.73 (1H, dd, NC*H*, *J*, 3.6, 10.5 Hz), 3.66 (1H, dd, NCC*H*, *J*, 5.0, 15.1 Hz), 3.00 (1H, dd, NCC*H*, *J*, 10.5, 15.1 Hz); δ_c (75 MHz, D_2O); 171.25 (CO), 162.45 (q, CF_3, *J*, 36.8 Hz), 141.82 (H_2C=*C*), 129.32 (q, F_3C*C*, *J*, 32.25 Hz), 126.83 (Ar), 125.64 (Ar), 121.95 (Ar), 114.26 (=CH_2), 51.44 (NC), 35.70 (NC*C*); m/z (ES^+); 260 (MH^+).



2-(*R*)-2-Amino-4-(4-trifluoromethyl-phenyl)-pent-4-enoic acid (*R*-5d)

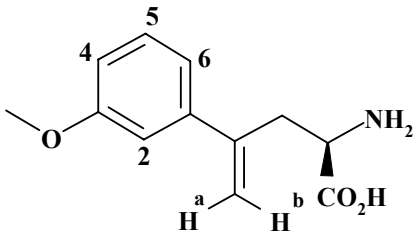
Obtained as colourless prisms (0.193 g, 99 %) after ion exchange chromatography. M.pt. 141 – 143 °C; $[a]_D^{20}$ - 32.7 (*c* 0.5, MeOH); Found; C, 54.80; H, 4.80; N, 5.20, $C_{12}H_{13}NO_2F_3$.0.25 M H_2O requires; C, 54.65; H, 4.78; F, 21.61; N, 5.31 %; Found; 260.0887; $C_{12}H_{13}NO_2F_3$ requires; 260.0898; δ_H (500 MHz, CD_3OD); 6.84 (2H, d, ArH, *J*, 8.3 Hz), 6.80 (2H, d, ArH, *J*, 8.3 Hz), 4.86 (1H, s, =CH^a), 4.66 (1H, s, =CH^b), 3.26 (1H, dd, NC*H*, *J*, 5.0, 9.1 Hz), 2.60 (1H, dd, NCC*H*, *J*, 5.0, 15.1 Hz), 2.30 (1H, dd, NCC*H*, *J*, 9.1, 15.1 Hz); δ_c (75 MHz, D_2O); 171.25 (CO), 162.45 (q, CF_3, *J*, 36.8 Hz), 141.82 (H_2C=*C*), 129.32 (q, F_3C*C*, *J*, 32.25 Hz), 126.83 (Ar), 125.64 (Ar), 121.95 (Ar), 114.26 (=CH_2), 51.44 (NC), 35.70 (NC*C*); m/z (ES^+); 260 (MH^+).



2-(*S*)-2-Amino-4-(3-methoxy-phenyl)-pent-4-enoic acid (*S*-5e)

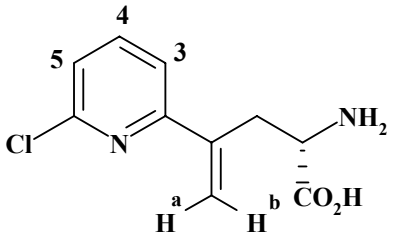
Obtained as colourless prisms (0.088 g, 97 %) after ion exchange chromatography. M.pt. 144 – 147 °C; $[a]_D^{20}$ + 10.9 (*c* 0.2, MeOH); Found; 222.1126; $C_{12}H_{15}NO_3$ requires; 222.1125; ν_{max}/cm^{-1}; 3009 (br, OH), 2593, 2288, 2085,

1843, 1576 (CO), 1491, 1457, 1398; δ_H (500 MHz, D_2O); 7.22 (1H, dd, Ar-5H, *J*, 7.7, 8.1 Hz), 6.99 (1H, d, Ar-4H, *J*, 7.7 Hz), 6.94 (1H, s, Ar-2H), 6.84 (1H, d, Ar-6H, *J*, 8.1 Hz), 5.45 (1H, s, =CH^a), 5.20 (1H, s, =CH^b), 3.93 (1H, dd, NCH, *J*, 5.1, 8.1 Hz), 3.69 (3H, s, OCH_3), 3.18 (1H, dd, NCC*H*, *J*, 5.1, 15.4 Hz), 2.96 (1H, dd, NCC*H*, *J*, 8.1, 15.4 Hz); δ_c (75 MHz, D_2O); 171.57 (CO), 159.40 (H_2C=*C*), 141.21 (Ar), 140.10 (Ar), 130.41 (Ar), 119.67 (Ar), 119.05 (=CH_2), 114.96 (Ar), 112.57 (Ar), 55.70 (OCH_3), 51.70 (NC), 36.09 (NC*C*); m/z (ES$^+$); 222 (MH^+).



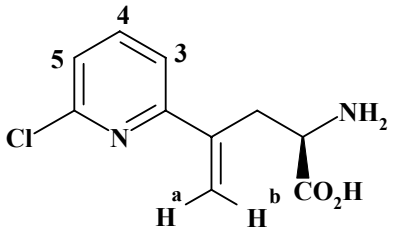
2-(*R*)-2-Amino-4-(3-methoxy-phenyl)-pent-4-enoic acid (*R*-5e)

Obtained as colourless prisms (0.115 g, 80 %) after ion exchange chromatography. M.pt. 147 – 149 ^oC; $[a]_D^{20}$ - 9.5 (*c* 0.3, MeOH); Found; C, 63.60; H, 6.80; N, 6.30, $C_{12}H_{15}NO_3$.0.25M H_2O requires; C, 63.84; H, 6.92; N, 6.20 %; Found; 222.1130; $C_{12}H_{15}NO_3$ requires; 222.1120; ν_{max}/cm^{-1}; 3009 (br, OH), 2593, 2086, 1818, 1668, 1575 (CO), 1525, 1493; δ_H (500 MHz, CD_3OD); 7.18 (1H, t, Ar-5H, *J*, 8.1 Hz), 7.01 (1H, d, Ar-4H, *J*, 7.7 Hz), 6.99 (1H, d, Ar-2H, *J*, 2.1 Hz), 6.77 (1H, dd, Ar-6H, *J*, 8.1 Hz), 5.41 (1H, s, =CH^a), 5.17 (1H, s, =CH^b), 3.71 (3H, s, OCH_3), 3.44 (1H, dd, NCH, *J*, 10.7, 11.1 Hz), 3.34 (1H, dd, NCCH, *J*, 10.7, 15.2 Hz), 2.61 (1H, dd, NCCH, *J*, 11.1 15.2 Hz); δ_c (75 MHz, D_2O); 174.37 (CO), 159.51 (H_2C=*C*), 142.38 (Ar), 140.55 (Ar), 130.48 (Ar), 119.65 (Ar), 118.16 (=CH_2), 114.26 (Ar), 112.57 (Ar), 55.79 (OCH_3), 53.67 (NC), 36.96 (NC*C*); m/z (ES$^+$); 222 (MH^+).



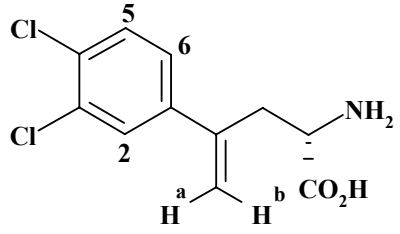
2-(*S*)-2-Amino-4-(6-chloro-pyridin-2-yl)-pent-4-enoic acid (*S*-5f)

Obtained as colourless prisms (0.066 g, 79 %) after ion exchange chromatography. M.pt. 193 – 195 ^oC; $[a]_D^{20}$ + 31.7 (*c* 0.1, MeOH); Found; C, 52.00; H, 5.00; N, 11.70, $C_{10}H_{11}ClN_2O_2$.0.25 M H_2O requires; C, 51.96; H, 5.01; N, 12.12 %; Found; 227.0579; $C_{10}H_{11}ClN_2O_2$ requires; 227.0587; ν_{max}/cm^{-1}; 3456, (br, OH), 3049, 2929, 1854, 1630 (CO), 1523; δ_H (500 MHz, D_2O); 8.43 (1H, d, pyridyl-5H, *J*, 2.1 Hz), 7.97 (1H, dd, pyridyl-4H, 2.1, 8.3 Hz), 7.51 (1H, d, pyridyl-3H, *J*, 8.3 Hz), 5.61 (1H, s, =CH^a), 5.43 (1H, s, =CH^b), 4.03 (1H, dd, NCH *J*, 6.0, 7.7 Hz), 3.21 (1H, dd, NCC*H*, *J*, 6.0, 15.4 Hz), 3.11 (1H, dd, NCC*H*, *J*, 7.7, 15.4 Hz); (75 MHz, D_2O); 174.32 (CO), 142.57 (H_2C=*C*), 138.76 (Ar), 129.28 (Ar), 128.55 (Ar), 126.72 (Ar), 125.77 (Ar), 117.75 (=CH_2), 52.97 (NC), 36.87 (NC*C*); m/z (ES$^+$); 227 ($^{35}Cl\ MH^+$), 229 ($^{37}Cl\ MH^+$).



2-(*R*)-2-Amino-4-(6-chloro-pyridin-2-yl)-pent-4-enoic acid (*R*-5f)

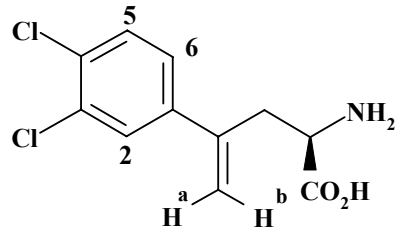
Obtained as colourless prisms (0.123 g, 79 %) after ion exchange chromatography. M.pt. 196 – 198 ^oC; $[a]_D^{20}$ - 32.1 (*c* 0.3, MeOH); Found; 227.0583; $C_{10}H_{11}ClN_2O_2$ requires; 227.0587; ν_{max}/cm^{-1}; 3051 (br, OH), 2093, 1893, 1607 (CO), 1555, 1474, 1454, 1410; δ_H (500 MHz, D_2O); 8.17 (1H, d, pyridyl-5H, *J*, 2.4 Hz), 7.89 (1H, dd, pyridyl-4H, *J*, 2.4, 8.8 Hz), 7.89 (1H, d, pyridyl-3H, *J*, 8.8 Hz), 5.23 (1H, s, =CH^a), 5.09 (1H, s, =CH^b), 3.54 (1H, dd, NCH, *J*, 6.2, 7.7 Hz), 2.74 (1H, dd, NCC*H*, *J*, 6.2, 15.5 Hz), 2.64 (1H, dd, NCC*H*, *J*, 7.7, 15.5 Hz); δ_c (75 MHz, D_2O); 174.19 (CO), 150.06 (H_2C=*C*), 147.16 (Ar), 138.55(Ar), 138.20 (Ar), 134.25 (Ar), 124.83 (Ar), 120.16 (=CH_2), 53.47 (NC), 36.45 (NC*C*); m/z (ES$^+$); 227 ($^{35}Cl\ MH^+$), 229 ($^{37}Cl\ MH^+$).



2-(*S*)-2-Amino-4-(3,4-dichloro-phenyl)-pent-4-enoic acid (*S*-5g)

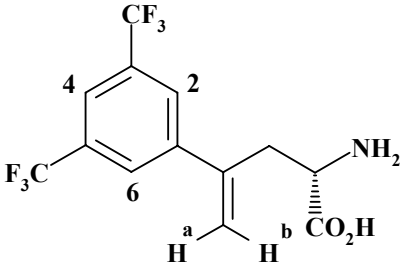
Obtained as colourless prisms (0.107 g, 82 %) after ion exchange chromatography. M.pt. 147 – 148 ^oC; $[a]_D^{20}$ + 33.1 (*c* 0.4, MeOH); Found; C, 50.80; H, 4.50; Cl, 27.40; N, 5.30, $C_{11}H_{11}Cl_2NO_2$ requires; C, 50.79; H, 4.26; Cl, 27.26; N, 5.38 %; ν_{max}/cm^{-1}; 3025 (br OH), 2064, 1899, 1840, 1761, 1670, 1579, 1517; δ_H (500 MHz, D_2O); 7.54 (1H, s, Ar-2H), 7.40 (1H, d, Ar-5H, *J*, 8.4 Hz), 7.26 (1H, d, Ar-6H, *J*, 8.4 Hz), 5.48 (1H, s, =CH^a), 5.26 (1H, s, =CH^b), 3.96 (1H, dd, NC*H*, *J*, 5.1, 5.5 Hz), 3.15 (1H, dd, NCC*H*, *J*, 5.5, 13.2 Hz), 2.98 (1H, dd, NCC*H*, *J*, 5.1, 13.2 Hz); δ_c (75 MHz, D_2O); 165.14 (CO), 142.0 (H_2C=*C*), 141.14 (Ar),

134.78 (Ar), 134.39 (Ar), 133.30 (Ar), 131.07 (Ar), 128.91 (Ar), 120.84 (=CH_2), 54.02 (NC), 38.21 (NC*C*), m/z (ES^+); 260 ($^{35/35}$Cl MH^+), 262 ($^{35/37}$Cl MH^+), 264 ($^{37/37}$Cl MH^+).



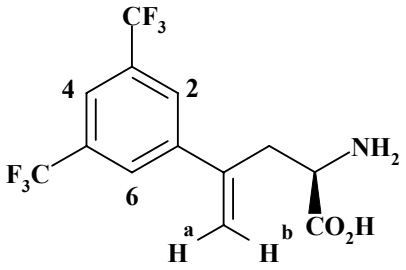
2-(*R*)-2-Amino-4-(3,4-dichloro-phenyl)-pent-4-enoic acid (*R*-5g)

Obtained as colourless prisms (0.094 g, 73 %) after ion exchange chromatography. M.pt. 146 – 148 ^oC $[a]_D^{20}$ - 31.4 (*c* 0.1, MeOH); Found; C, 49.30; H, 4.60; N, 4.70, $C_{11}H_{11}Cl_2NO_2$.0.5 M H_2O requires; C, 49.09; H, 4.49; N, 5.20 %; Found; 259.0164; $C_{11}H_{11}Cl_2NO_2$ requires; 259.0161; ν_{max}/cm^{-1}; 3033 (br, OH), 1669, 1576, 1516; δ_H (500 MHz, D_2O); 7.54 (1H, s, Ar-2H), 7.40 (1H, d, Ar-5H, *J*, 8.4 Hz), 7.26 (1H, d, Ar-6H, *J*, 8.4 Hz), 5.48 (1H, s, =CH^a), 5.26 (1H, s, =CH^b), 3.96 (1H, dd, NC*H*, *J*, 5.1, 5.5 Hz), 3.15 (1H, dd, NCC*H*, *J*, 5.5, 13.2 Hz), 2.98 (1H, dd, NCC*H*, *J*, 5.1, 13.2 Hz); δ_c (75 MHz, D_2O); 171.48 (CO), 142.0 (H_2C=*C*), 141.14 (Ar), 134.78 (Ar), 134.39 (Ar), 133.30 (Ar), 131.07 (Ar), 128.91 (Ar), 120.84 (=CH_2), 54.02 (NC), 38.21 (NC*C*); m/z (ES^+); 260 ($^{35/35}$Cl MH^+), 262 ($^{35/37}$Cl MH^+), 264 ($^{37/37}$Cl MH^+).



2-(*S*)-2-Amino-4-(3,5-bis-trifluoromethyl-phenyl)-pent-4-enoic acid (*S*-5h)

Obtained as colourless prisms (0.178 g, 89 %) after ion exchange chromatography. M.pt. 152 – 155 ^oC; $[a]_D^{20}$ + 10.9 (0.5, MeOH); Found; C, 47.65; H, 3.30; N, 4.05, $C_{13}H_{11}F_6NO_2$ requires; C, 47.72; H, 3.39; N, 4.28 %; Found; 328.0765; $C_{13}H_{11}F_6NO_2$ requires; 328.0767; ν_{max}/cm^{-1}; 3456 (NH), 3049 (br, OH), 2929, 1854, 1622 (CO), 1524, 1398, 1334, 1277; δ_H (500 MHz, CD_3OD); 8.01 (2H, s, Ar-2H, Ar-6H), 7.83 (1H, s, Ar-4H), 5.55 (1H, s, =CH^a), 5.40 (1H, s, =CH^b), 3.40 (1H, dd, NCH, *J*, 4.1, 9.7 Hz), 3.33 (1H, dd, NCC*H*, *J*, 4.1, 15.4 Hz), 2.79 (1H, dd, NCC*H*, *J*, 9.7, 15.4 Hz); δ_c (75 MHz, CD_3OD); 173.70 (CO), 143.83 (H_2C=*C*), 143.11 (Ar), 133.42 (q, F_3CC, *J*, 33.25 Hz), 128.64 (Ar), 125.14 (q, CF_3, *J*, 271.82 Hz), 122.96 (Ar), 121.14 (=CH_2), 54.63 (NC), 38.29 (NC*C*); m/z (ES^+); 328 (MH^+).

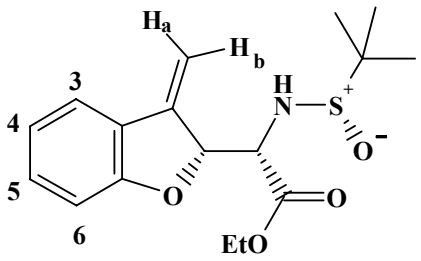


2-(R)-2-Amino-4-(3,5-bis-trifluoromethyl-phenyl)-pent-4-enoic acid (*R*-5h)

Obtained as colourless prisms (0.167 g, 68 %) after ion exchange chromatography. M.pt. 153 – 156 ^oC; $[a]_D^{20}$ - 9.5 (*c* 0.6, MeOH); Found; C, 47.50; H, 3.30; N, 4.20, $C_{13}H_{11}F_6NO_2$ requires; C, 47.72; H, 3.39; N, 4.28 %; ν_{max}/cm^{-1}; 3683, 2929 (br, OH), 2065, 1832, 1634 (CO), 1510, 1444; δ_H (500 MHz, D_2O); 7.40 (2H, s, Ar-2H, Ar-6H), 7.36 (1H, s, Ar-4H), 5.12 (1H, s, =CH^a), 4.95 (1H, s, =CH^b), 3.48 (1H, dd, NCH, *J*, 5.5, 8.0 Hz), 2.78 (1H, dd, NCC*H*, *J*, 5.5, 15.3 Hz), 2.79 (1H, dd, NCC*H*, *J*, 8.0, 15.4 Hz); δ_c (75 MHz, CD_3OD); 173.65 (CO), 143.64 (H_2C=*C*), 142.96 (Ar), 133.22 (q, F_3CC, *J*, 33.25 Hz), 128.56 (Ar), 125.14 (q, CF_3, *J*, 271.82 Hz), 122.94 (Ar), 121.15 (=CH_2), 54.46 (NC), 38.17 (NC*C*); m/z (ES^+); 328 (MH^+).

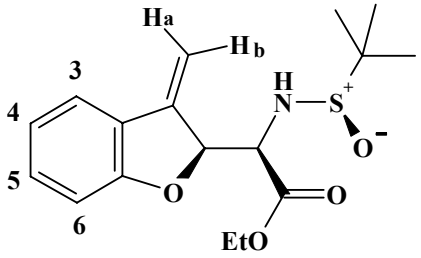
General procedure for synthesis of *N*-sulfinyl α-aminoesters 17 – 20

Bi-functional aryl iodide/allene (0.75 mmol), was added to a suspension of chiral α-iminoester (0.5 mmol), indium metal powder (0.088 g, 0.75 mmol), $Pd(OAc)_2$ (0.011g, 0.05 mmol), tri-2-furyl phosphine (0.024 g, 0.1 mmol), CuI (0.019 g, 0.1 mmol) and piperidine (0.05 ml, 0.5 mmol) in DMF (10 ml) in a Schlenk tube. The mixture was stirred and heated to 60 ^oC (oil bath temperature) for 24 h, left to cool and vented. Ethyl acetate (20 ml) and 5 % HCl solution (10 ml) added and the mixture stirred for 20 mins. The phases were separated and the aqueous layer extracted with ethyl acetate (20 ml). The organic extracts were combined and washed with water (3 x 100 ml), dried over magnesium sulphate, filtered and the filtrate concentrated *in vacuo*. The residue was purified by flash chromatography to give the *N-sulfinylamino esters*.



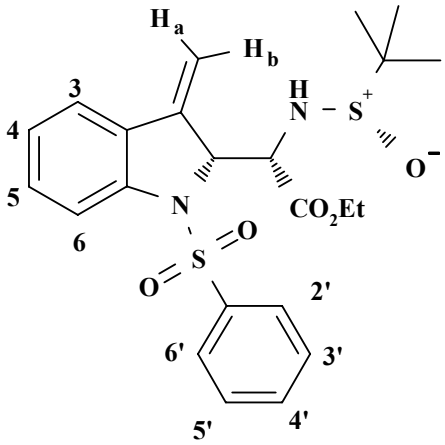
Ethyl 2*S*,5*S*,6*R*-(3-methylene-2,3-dihydro-benzofuran-2-yl)-(2-methyl-propane-2-sulfinylamino) acetate (*S*,*S*,*R*-17)

Obtained as a pale yellow oil (0.110 g, 64 %) after flash chromatography (Et_2O); R_F 0.11 (Et_2O); $[a]_D^{20}$ - 42.2 (*c* 1.1); Found; C, 58.60; H, 7.20; N, 4.10, $C_{17}H_{23}NO_4S.0.5\ H_2O$ requires; C, 58.94; H, 6.98; N, 4.04 %; ν_{max}/cm^{-1}; 3286, 3078, 2984, 2968, 2869, 2836, 1739 (CO), 1634; δ_H (500 MHz, $CDCl_3$); 7.33 (1H, d, Ar-6H, *J*, 7.6 Hz), 7.19 (1H, t, Ar-5H, *J*, 7.6 Hz), 6.87 (1H, t, Ar-4H, *J*, 7.6 Hz), 6.84 (1H, d, Ar-3H, *J*, 7.6 Hz), 5.54 (2H, m, NCH, =CH^a), 5.09 (1H, s, =CH^b), 4.32 (2H, q, OCH_2, *J*, 7.3 Hz), 4.21 (2H, m, NCH, OCH), 1.32 (3H, t, OCH_2CH_3, *J*, 7.3 Hz); δ_c (75 MHz, $CDCl_3$); 170.45 (CO), 163.13 (Ar), 144.48 (Ar), 131.14 (Ar), 126.52 (Ar), 124.27 (Ar), 121.39 (Ar), 121.11 (Ar), 110.67 (Ar), 102.69 (=CH_2), 85.78 (OCH), 62.99 (OCH_2), 62.65 (NC), 56.73 (S*C*), 22.57 ($C(CH_3)_3$), 14.50 (OCH_2CH_3); m/z (ES^+); 338 (MH^+).



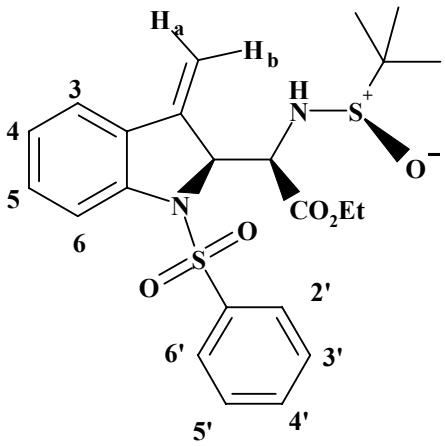
Ethyl 2*R*,5*R*,6*S*-(3-methylene-2,3-dihydro-benzofuran-2-yl)-(2-methyl-propane-2-sulfinylamino) acetate (*R*,*R*,*S*-17)

Obtained as a pale yellow oil (0.108 g, 64 %) after flash chromatography (Et_2O); R_F 0.11 (Et_2O); $[a]_D^{20}$ + 39.7 (*c* 0.5); Found; C, 59.60; H, 6.85; N, 4.25, $C_{17}H_{23}NO_4S.0.25\ H_2O$ requires; C, 59.71; H, 6.93; N, 4.10 %; ν_{max}/cm^{-1}; 3281, 3077, 2959, 2869, 2836, 1737 (CO), 1634; δ_H (500 MHz, $CDCl_3$); 7.33 (1H, d, Ar-6H, *J*, 7.6 Hz), 7.19 (1H, t, Ar-5H, *J*, 7.6 Hz), 6.87 (1H, t, Ar-4H, *J*, 7.6 Hz), 6.84 (1H, d, Ar-3H, *J*, 7.6 Hz), 5.54 (2H, m, NCH, =CH^a), 5.09 (1H, s, =CH^b), 4.32 (2H, q, OCH_2, *J*, 7.3 Hz), 4.21 (2H, m, NCH, OCH), 1.32 (3H, t, OCH_2CH_3, *J*, 7.3 Hz); δ_c (75 MHz, $CDCl_3$); 170.43 (CO), 163.12 (Ar*C*), 144.46 (Ar), 131.12 (Ar), 126.51 (Ar), 121.37 (Ar), 121.10 (Ar), 110.67 (Ar), 102.64 (=CH_2), 85.76 (OCH), 62.94 (OCH_2), 62.62 (NC), 56.68 (S*C*), 22.65 ($C(CH_3)_3$), 14.49 (OCH_2CH_3); m/z (ES^+); 338 (MH^+).



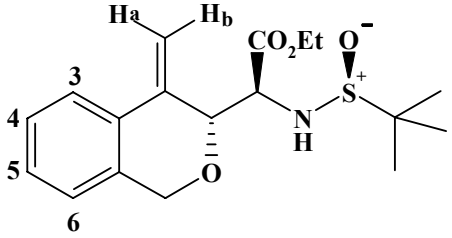
Ethyl 2*S*,5*S*,6*R*-(1-benzenesulfonyl-3-methylene-2,3-dihydro-1*H*-indol-2-yl)-(2-methyl-propane-2-sulfinylamino) acetate (*S*,*S*,*R*-18)

Obtained as colourless prisms (0.110 g, 46 %) after flash chromatography (Et_2O); R_F 0.14 (Et_2O); M.pt. 149 – 151°C; $[a]_D^{20}$ - 16.3 (*c* 0.6); Found; C, 57.85; H, 5.65; N, 5.80; S, 13.35, $C_{23}H_{28}N_2O_5S_2$ requires; C, 57.96; H, 5.92; N, 5.88; S, 13.45 %; ν_{max}/cm^{-1}; 3294 (NH), 3085, 3014, 2985, 1732 (CO), 1648, 1600, 1584; δ_H (500 MHz, $CDCl_3$); 7.71 (1H, d, Ar-6H, *J*, 8.1 Hz), 7.55 (2H, d, Ar-2'H, Ar-6'H, *J*, 7.7 Hz), 7.49 (1H, d, Ar-3H, *J*, 7.5 Hz), 7.34 (2H, t, Ar-3'H, Ar-5'H, *J*, 7.7 Hz), 7.27 – 7.23 (2H, m, Ar-4H, Ar-5H), 7.05 (1H, t, Ar-4'H, *J*, 7.7 Hz), 5.44 (1H, s, =CH^a), 5.08 (1H, s, =CH^b), 4.97 (1H, d, NH, *J,* 1.6 Hz), 4.37 (1H, d, $PhSO_2NCH$, *J*, 7.6 Hz), 4.33 (2H, m, OCH_2), 4.15 (1H, dd, SNC*H*, *J*, 1.6, 7.6 Hz), 1.32 (3H, t, OCH_2CH_3, *J*, 7.2 Hz), 0.91 (9H, s, $C(CH_3)_3$); δ_c (75 MHz, $CDCl_3$); 170.09 (CO), 144.73 (H_2C=*C*), 143.14 (Ar), 136.75 (Ar), 133.91 (Ar), 131.61 (Ar), 130.57 (Ar), 129.44 (Ar), 127.61 (Ar), 121.19 (Ar), 118.02 (H_2C=C), 68.14 (SO_2NC), 64.46 (SC), 62.90 (SNC), 56.45 (OCH_2), 22.50 ($C(CH_3)_3$), 14.41 (OCH_2CH_3); m/z (ES^+); 477 (MH^+).



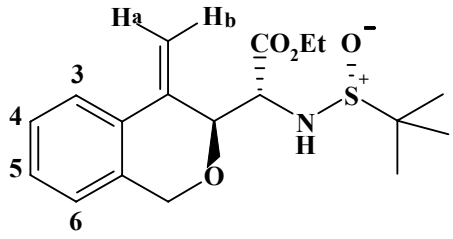
Ethyl 2*R*,5*R*,6*S*-(1-benzenesulfonyl-3-methylene-2,3-dihydro-1*H*-indol-2-yl)-(2-methyl-propane-2-sulfinylamino) acetate (*R,R,S*-18)

Obtained as colourless prisms (0.231g, 48 %) after flash chromatography (Et_2O); R_F 0.14 (Et_2O); 149 – 151°C; $[a]_D^{20}$ + 15.7 (*c* 0.8); Found, C, 58.0; H, 5.90; N, 5.90; S, 13.60, $C_{23}H_{28}N_2O_5S_2$ requires; C, 57.96; H, 5.92; N, 5.88; S, 13.45 %; ν_{max}/cm^{-1}; 3294 (NH), 3085, 3014, 2985, 1732 (CO), 1648, 1600, 1584; δ_H (500 MHz, $CDCl_3$); 7.71 (1H, d, Ar-6H, *J*, 8.1 Hz), 7.55 (2H, d, Ar-2'H, Ar-6'H, *J*, 8.2 Hz), 7.49 (1H, d, Ar-3H, *J*, 7.5 Hz), 7.34 (2H, t, Ar-3'H, Ar-5'H, *J*, 7.9 Hz), 7.27 – 7.23 (2H, m, Ar-4H, Ar-5H), 7.05 (1H, t, Ar-4'H, *J*, 7.5 Hz), 5.44 (1H, s, =CH^a), 5.08 (1H, s, =CH^b), 4.97 (1H, d, NH, *J,* 1.6 Hz), 4.37 (1H, d, SO_2NCH, *J*, 7.6 Hz), 4.33 (2H, m, OCH_2), 4.15 (1H, dd, NC*H*, *J*, 1.6, 7.6 Hz), 1.32 (3H, t, OCH_2CH_3, *J*, 7.2 Hz), 0.91 (9H, s, $C(CH_3)_3$); δ_c (75 MHz, $CDCl_3$); 170.09 (CO), 144.73 (H_2C=*C*), 143.14 (Ar), 136.75 (Ar), 133.91 (Ar), 131.61 (Ar), 130.57 (Ar), 129.44 (Ar), 127.61 (Ar), 121.19 (Ar), 118.02 (H_2C=C), 68.14 (SO_2NC), 64.46 (SC), 62.90 (SNC), 56.45 (OC), 22.50 ($C(CH_3)_3$), 14.41 (OCH_2CH_3); m/z (ES^+); 477 (MH^+).



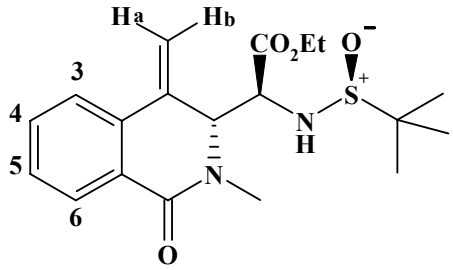
Ethyl 2*S*,5*S*,6*R*-(4-methylene-isochroman-3-yl)-(2-methyl-propane-2-sulfinylamino) acetate (*S,S,R*-19)

Obtained as a pale yellow oil (0.108 g, 62 %) after flash chromatography (Et_2O); R_F 0.14 (Et_2O); $[a]_D^{20}$ - 41.0 (*c* 0.7); Found; C, 61.80; H, 7.00; N, 3.70; S, 9.20, $C_{18}H_{25}NO_4S$ requires; C, 61.51; H, 7.17; N, 3.99; S, 9.12 %; ν_{max}/cm^{-1} 3296 (NH), 3126, 2980, 2960, 2905, 2868, 2841, 1738 (CO), 1628; δ_H (500 MHz, $CDCl_3$); 7.57 (1H, d, Ar-6H, *J*, 2.5 Hz), 7.25 – 7.22 (2H, m, Ar-4H, Ar-5H), 7.03 (1H, m, Ar-3H,), 5.72 (1H, s, =CH^a), 5.11 (1H, s, =CH^b), 4.89 (1H, dd, OCH, *J*, 1.7, 3.8 Hz), 4.75 (1H, d, ArCH, *J*, 14.5 Hz), 4.62 (1H, d, ArCH, *J*, 14.5 Hz), 4.32 (1H, dd, NCH, *J* 3.8, 8.6 Hz), 4.27 (2H, dq, CO_2CH_2, *J* 1.3, 7.3 Hz), 1.29 (3H, t, OCH_2CH_3, *J*, 7.1 Hz), 1.09 (9H, s, $C(CH_3)_3$); δ_c (75 MHz, $CDCl_3$); 171.49 (CO), 138.88 (=C), 134.58 (Ar), 132.32 (Ar), 128.33 (Ar), 127.83 (Ar), 124.89 (Ar), 124.14 (Ar), 110.09 (=CH_2), 79.17 (NC*C*), 66.91 (OCH_2), 62.40 (CO_2C), 62.06 (NC), 56.84 (SC), 22.96 ($C(CH_3)_3$), 14.51 (OCH_2CH_3); m/z (ES^+); 352 (MH^+).



Ethyl 2*R*,5*R*,6*S*-(4-methylene-isochroman-3-yl)-(2-methyl-propane-2-sulfinylamino) acetate (*R,R,S*-19)

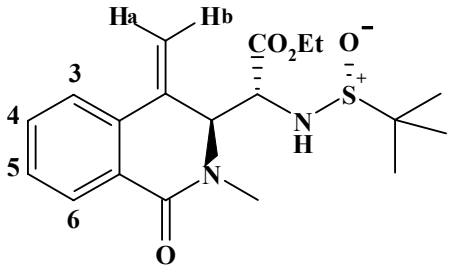
Obtained as a pale yellow oil (0.101 g, 58 %) after flash chromatography (Et_2O); R_F 0.14 (Et_2O); $[a]_D^{20}$ + 41.5 (*c* 1.3); Found; 374.1402; $C_{18}H_{25}NO_4S.Na$ requires; 374.1402; ν_{max}/cm^{-1}; 3450, 3297 (NH), 2959, 2868, 1738 (CO), 1628, 1576; δ_H (500 MHz, $CDCl_3$); 7.57 (1H, dd, Ar-6H, *J*, 4.3, 9.0 Hz), 7.23 (2H, m, Ar-4H, Ar-5H), 7.03 (1H, dd, Ar-3H, *J*, 4.3, 6.0 Hz), 5.72 (1H, s =CH^a), 5.11 (1H, s =CH^b), 4.89 (1H, m, NH), 4.75 (1H, d, OCH, *J*, 14.5 Hz), 4.62 (1H, d, OCH, *J*, 14.5 Hz), 4.32 (1H, dd, NCH, *J* 3.8, 8.6 Hz), 4.29 – 4.24 (3H, m, CO_2CH_2, OCH), 1.30 (3H, t, OCH_2CH_3, *J*, 7.1 Hz), 1.09 (9H, s, $C(CH_3)_3$); δ_c (75 MHz, $CDCl_3$); 170.08 (CO), 137.44 (=C), 133.15 (Ar), 130.89 (Ar), 126.90 (Ar), 126.40 (Ar), 123.46 (Ar), 122.71 (Ar), 108.66 (=CH_2), 77.74 (NC*C*), 65.48 (OCH_2), 60.98 (CO_2C), 60.92 (NC), 55.39 (SC), 21.53 ($C(CH_3)_3$), 13.09 (OCH_2CH_3); m/z (ES^+); 352 (MH^+).



Ethyl 2*S*,5*S*,6*R*-(2-methyl-4-methylene-1-oxo-1,2,3,4-tetrahydro-isoquinolin-3-yl)-(2-methyl-propane-2-sulfinylamino) acetate (*S,S,R*-20)

Obtained as a pale yellow oil (0.052 mg, 28 %) after flash chromatography (EtOAc); R_F 0.10 (EtOAc); $[a]_D^{20}$ - 7.3 (*c* 0.4); Found; C, 60.20; H, 6.90; N, 7,10; S, 8.40, $C_{19}H_{26}N_2O_4S$ requires; C, 60.29; H, 6.92; N, 7.40; S, 8.47 %; ν_{max}/cm^{-1}; 3459 (NH), 3274, 2961, 2239, 1739 (CO), 1648 (CO), 1602, 1573; δ_H (500 MHz, $CDCl_3$); 8.09 (1H, d, Ar-6H, *J*, 7.7 Hz), 7.51 (1H, d, Ar-3H, *J*, 7.7 Hz), 7.47 (1H, td, Ar-4H, *J*, 0.9, 7.7 Hz), 7.40 (1H, td, Ar-5H, *J*, 0.9, 7.7 Hz), 5.74 (1H, s, =CH^a), 5.31 (1H, s, =CH^b), 4.38 (1H, d, MeNC*H*, *J*, 4.7 Hz), 4.27 (1H, d, NH, *J*, 8.1 Hz), 4.11 (1H, dd, NCH, *J*, 4.7, 8.1 Hz), 3.90 (1H, dq, OCH, *J*, 7.3, 10.7 Hz), 3.54 (1H, dq, OCH, *J*, 7.3, 10.7 Hz), 3.22 (3H, s, NCH_3), 1.15 (9H, s, $C(CH_3)_3$), 1.13 (3H, t, OCH_2CH_3, *J*, 7.3 Hz); δ_c (75 MHz, $CDCl_3$); 170.53 (CO), 163.29 (NCO), 136.20 (=C), 134.46 (Ar), 132.19 (Ar), 128.10 (Ar), 127.83 (Ar), 127.27 (Ar), 123.68 (Ar), 115.76 (=CH_2), 68.33

(MeN*C*), 62.34 (OC), 59.54 (SNC), 56.22 (SC), 35.14 (NCH_3), 22.53 ($C(CH_3)_3$), 10.97 (OCH_2CH_3); m/z (ES^+); 379 (MH^+).



Ethyl (R)-((S)-2-methyl-4-methylene-1-oxo-1,2,3,4-tetrahydro-isoquinolin-3-yl)-((R)-2-methyl-propane-2-sulfinylamino) acetate (*R,R,S*-20)

Obtained as a pale yellow oil (0.130 g, 69 %) after flash chromatography (EtOAc); R_F 0.10 (EtOAc); $[a]_D^{20}$ + 9.2 (*c* 0.6); Found; C, 60.50; H, 7.20; N, 7,40; S, 8.40, $C_{19}H_{26}N_2O_4S$ requires; C, 60.29; H, 6.92; N, 7.40; S, 8.47 %; ν_{max}/cm^{-1}; 3459 (NH), 3274, 2964, 2239, 1744 (CO), 1658 (CO), 1602; δ_H (500 MHz, $CDCl_3$); 8.09 (1H, d, Ar-6H, *J*, 7.8 Hz), 7.51 (1H, d, Ar-3H, *J*, 7.7 Hz), 7.47 (1H, td, Ar-4H, *J*, 0.9, 7.7 Hz), 7.40 (1H, td, Ar-4H, *J*, 0.9, 7.7 Hz), 5.74 (1H, s, $=CH^a$), 5.31 (1H, s, $=CH^b$), 4.39 (1H, d, MeNC*H*, *J*, 4.7 Hz), 4.27 (1H, d, NH, *J*, 8.1 Hz), 4.14 (1H, dd, NCH, *J*, 4.5, 8.1 Hz), 3.90 (1H, dq, OCH, *J*, 7.3, 10.7 Hz), 3.54 (1H, dq, OCH, *J*, 7.3, 10.7 Hz), 3.23 (3H, s, NCH_3), 1.15 (9H, s, $C(CH_3)_3$), 1.13 (3H, t, OCH_2CH_3, *J*, 7.3 Hz); δ_c (75 MHz, $CDCl_3$); 170.53 (CO), 163.29 (NCO), 136.20 (=C), 134.46 (Ar), 132.19 (Ar), 128.10 (Ar), 127.83 (Ar), 127.27 (Ar), 123.68 (Ar), 115.76 ($=CH_2$), 68.33 (MeN*C*), 62.34 (OC), 59.54 (SNC), 56.22 (SC), 35.14 (NCH_3), 22.53 ($C(CH_3)_3$), 10.97 (OCH_2CH_3); m/z (ES^+); 379 (MH^+).

Acknowledgments

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14. Supplementary crystallographic data for *S,S*-6 (CCDC 277090), *R,R*-6 (CCDC 277091), and *R,R,S*-18 (CCDC 277092) can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/datarequest/cif.
15. Semi-empirical calculations were performed using MOPAC v7 by J.J.P. Stewart and the PM3 Hamiltonian. Approximate transition structures were located using the SADDLE routine within MOPAC following full conformational optimisation of the attached sub-structures (MM2). Transition structures were then fully optimised using the TS routine within MOPAC and these then characterised by observing them to have a single negative vibrational frequency following use of the FORCE calculation within MOPAC.
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