Palladium-catalysed asymmetric allylic substitution: synthesis of α- and β-amino acids

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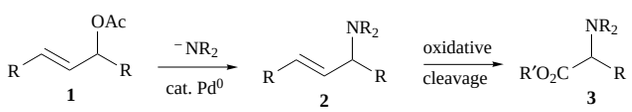
Methodology has been established for the formation of enantiomerically enriched α-amino acids using palladium-catalysed allylic amination. The formation of enantiomerically enriched allylamines has been achieved with high enantioselectivity. Oxidative cleavage of the allylamines provides arylglycine and glutamic acid derivatives. Additionally, enantiomerically enriched β-amino acids have been prepared in high enantiomeric excess. Palladium-catalysed asymmetric allylic substitution is used as the key synthetic transformation.

Palladium-catalysed allylic substitution has found numerous applications in the synthesis of compounds with important biological activity.[1] However, there have been relatively few reported syntheses of enantiomerically enriched amino acids by the use of this reaction.[2–4]

Herein, we report the use of palladium-catalysed allylic substitution in the preparation of enantiomerically enriched protected and deprotected α- and β-amino acids.

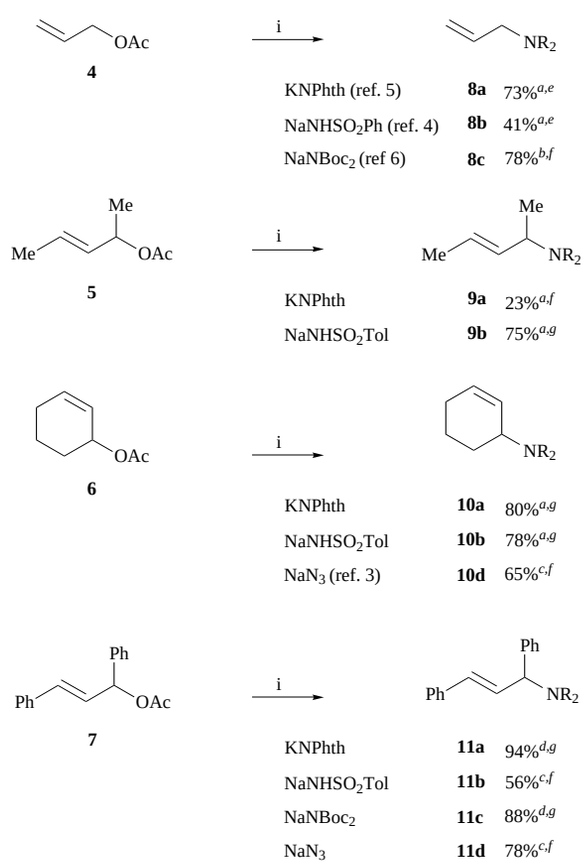
For the synthesis of α-amino acids, the methodology comprises of two principal synthetic steps. Firstly, the reaction of an allyl acetate **1** with a nitrogen nucleophile to afford an allylamine derivative **2**, followed by oxidative cleavage of the alkene to give an *N*-protected amino acid or ester **3** (Scheme 1).



Scheme 1

Our initial interests lay in the construction of a general methodology to provide a useful approach to the synthesis of achiral and enantiomerically enriched *α*-amino acids. Azide,[5] sulfonamide,[6] phthalimide[7] and di-*tert*-butyl iminodicarbonate[8] have all been reported to be effective nitrogen nucleophiles in palladium-catalysed allylic substitutions and were also successful in our hands. This allows a wide scope in the choice of nitrogen nucleophile and the resulting *N*-protected amine.[9] The reaction of the allyl acetates **4**–**7** with various nitrogen nucleophiles in the presence of catalytic amounts of palladium and an achiral phosphine afforded the corresponding allylamine derivatives **8**–**11** (Scheme 2).

With the formation of allylamines in hand, we required oxidative methods for the cleavage of alkenes into carboxylic acids and esters. The oxidative cleavage of alkenes by ozonolysis in the presence of methanolic sodium hydroxide (2.5 M) at −78 °C has been reported by Marshall and co-workers, in which the cleavage of enantiomerically enriched allylic ethers and amines yielded the corresponding methyl esters without loss of stereochemical purity.[10] Using this procedure we were able to convert allylic amine derivatives into the corresponding *N*-protected amino esters **14**–**20** (Table 1). However, allyl azides **10d** and **11d** were found to decompose under these reaction conditions. In an additional step the azide groups were converted into the corresponding amides **12** and **13** in modest yield by using thioacetic acid prior to the oxidative cleavage (Scheme 3).[11]



Scheme 2 *Conditions:* i, palladium catalyst, ligand, solvent. [a] THF–DMSO (80:20), 60 °C, 19 h. [b] DMF, 60 °C, 19 h. [c] THF–H_2O (80:20), 20 °C, 19 h. [d] THF, 50 °C, 19 h. [e] $Pd(dba)_2$ was employed as the catalyst (5 mol%) with Ph_3P (10 mol%). [f] $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ was employed as the catalyst (2.5 mol%) with Ph_3P (10 mol%). [g] $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ was employed as the catalyst (2.5 mol%) with dppe (5 mol%).

The resultant allyl amides **12** and **13** were smoothly converted into the corresponding amino acid derivatives **18** and **20** by ozonolysis in basic methanol. The results of the oxidative cleavage by this method are listed in Table 1.[12] **CAUTION:** On one

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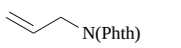
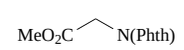
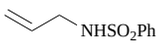
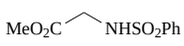
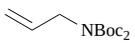
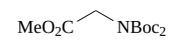
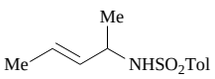
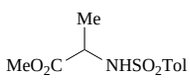
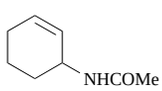
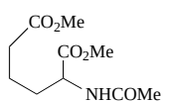
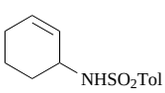
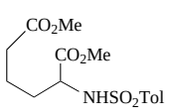
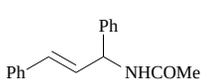
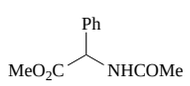
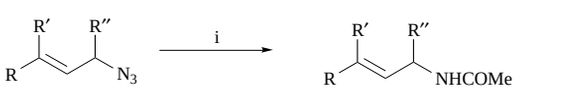
Table 1 Conversion of allylamine derivatives into amino acid derivatives by ozonolysis

Allyl amine derivative		Amino acid derivative[a]	Yield(%)
	**8a**		**14** 6
	**8b**		**15** 66
	**8c**		**16** 95
	**11b**		**17** 73
	**12**		**18** 49
	**10b**		**19** 73
	**13**		**20** 66

[a] Standard reaction conditions used O_3 bubbled through NaOH (2.5 M in methanol), −78 °C, 2.5 h.

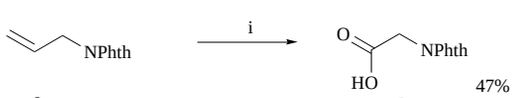


6	R = H, R′, R″ = -$(CH_2)_3$-	**12**	R = H , R′, R″ = -$(CH_2)_3$- 46%
7	R = R″ = Ph, R′ = H	**13**	R = R″ = Ph, R′ = H 32%

Scheme 3 *Conditions:* i, CH_3COSH, 20 °C, 12 h

occasion, we experienced a small explosion whilst conducting the ozonolysis, and we therefore recommend the use of a blast shield for this procedure.

Additionally, alkenes may be oxidatively cleaved using periodate in the presence of a ruthenium catalyst.[13] Thus, the allylphthalimide **8** was subjected to oxidation with catalytic $RuCl_3$ and stoichiometric $NaIO_4$ and afforded the expected product **21** (47%) (Scheme 4). Higher yields were obtained with substituted allylphthalimides (*vide infra*).



Scheme 4 *Conditions:* i, catalytic $RuCl_3$, $NaIO_4$, CCl_4–MeCN–H_2O, 20 °C, 18 h

Having established the synthetic methodology for the formation of achiral *N*-protected amino esters, we wished to investigate the formation of enantiomerically enriched amino acids. In the first step, the formation of enantiomerically enriched allylamines was achieved by palladium-catalysed allylic amination with a protected nitrogen nucleophile in the presence of the enantiomerically pure phosphine oxazoline ligand **22**. Ligand **22** has previously been found by this group and by others to induce very high enantioselectivity in palladium-catalysed allylations with carbon nucleophiles.[14,15] We therefore chose to use this ligand with a variety of nitrogen nucleophiles, and these results are summarised in Table 2. THF appears to be the most appropriate solvent for good yields and high enantiomeric excess of allylamines. DMF and the mixtures of THF and DMSO (80:20) both led to diminished enantioselectivity.

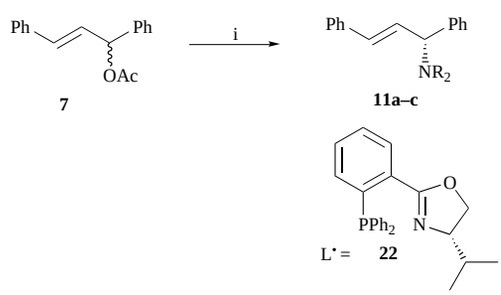
Table 2 Palladium-catalysed enantioselective amination of compound **7** to afford compounds **11a–c**

Solvent	K^{+-}NPhth	$Na^{+-}NHSO_2$-$ArCH_3$	$Na^{+-}NBoc_2$
THF	70% (96–98% ee)	90% (95% ee)	90% (54% ee)
THF–DMSO	34% (84% ee)	84% (90% ee)	88% (12% ee)
DMSO	Recovered SM*	62% (94% ee)	—
DMF	Recovered SM	32% (68% ee)	—

* SM = starting material.

Furthermore, it can be seen that not all of the nitrogen nucleophiles used achieved high enantioselectivity in the amination. The sodium salt of di-*tert*-butyl iminodicarbonate yielded the amination product **11c** with only 54% ee (Scheme 5) in comparison to the high enantiomeric excess achieved using potassium phthalimide or sodium toluene-*p*-sulfonamide when the respective reactions were carried out in THF.

During the course of this investigation, von Matt *et al.* and Jumnah *et al.* also reported palladium-catalysed enantioselective allylic amination using ligand **22**.[16,17]



Scheme 5 *Conditions:* i, $[Pd(C_3H_5)Cl]_2$ (2 mol%), L* (**22**) (4 mol%), MNR_2 (see Table 2) 50 °C, 24 h, solvent (see Table 2)

Other substrates were also investigated in the palladium-catalysed enantioselective allylic amination. Fig. 1 summarises

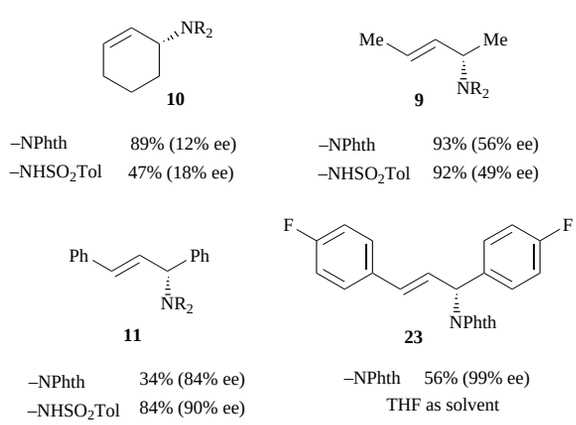
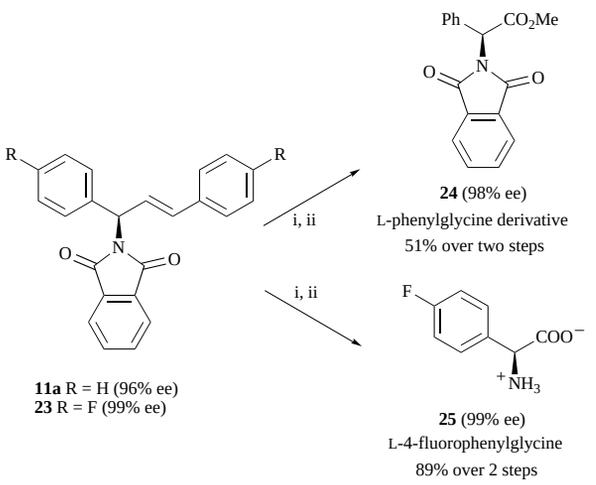


Fig. 1 Products formed by palladium-catalysed allylic amination using THF–DMSO (80:20)

the products formed and the nitrogen nucleophiles used in a solvent mixture of THF–DMSO (80:20). It is clear that the allyl system with a phenyl terminus gives superior results, and this would appear to be a limitation of this chemistry. However, the use of substrates which do not proceed through symmetrical allyl systems allows this problem to be overcome with some nucleophiles (*vide infra*).

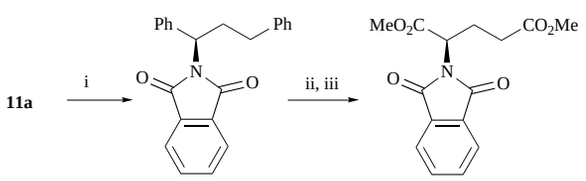
In order to prepare enantiomerically pure amino acid derivatives, an oxidative cleavage of the alkene moiety was required. Treatment of compound **11a** with periodic acid in the presence of a ruthenium catalyst effected oxidative cleavage to give the carboxylic acid.[13] The carboxylic acid could only be purified by crystallisation, and since this could enhance the enantiomeric excess of the product, we converted it directly into

the methyl ester to give the protected phenylglycine derivative **24** (this compound was readily purified by column chromatography) (Scheme 6). Alternatively, deprotection of the phthalimide group in the presence of sodium borohydride yielded the free amino acid **25** from allylamine **23**.[18] In both arylglycine products **24** and **25**, there was no observed erosion of stereochemical purity. Amino acid **25** was confirmed to be the L-enantiomer from optical rotation data.[19]



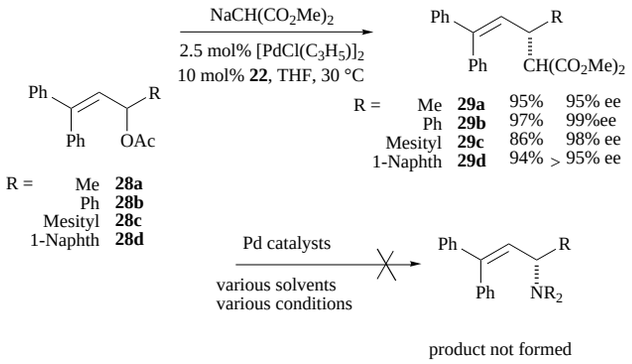
Scheme 6 *Conditions:* i, 2 mol% $RuCl_3 \cdot 3H_2O$, H_5IO_6 (4.2 equiv.), CCl_4–MeCN–H_2O (2:2:3), 18 h, 35–40 °C; ii, Me_3SiCl (4 equiv.), MeOH, 18 h, 50 °C; iii, $NaBH_4$, Pr^iOH–H_2O, room temp., AcOH, 80 °C, chromatography on Amberlite 120

In a differing synthetic strategy, a D-glutamic acid derivative was prepared. The alkene **11a** was reduced by heterogeneous hydrogenation in the presence of a palladium catalyst to give the corresponding alkane **26**. The benzylic phthalimide group proved to be inert to the hydrogenation conditions employed. Oxidative cleavage of the phenyl groups was carried out in the presence of periodic acid and a ruthenium catalyst to yield the dicarboxylic acid,[20] which was further transformed to the diester **27** with preservation of stereochemical purity (Scheme 7). It was found that the selective oxidative cleavage of the phenyl rings could be achieved without the cleavage of the phthalimide group. This is consistent with the fact that electron-deficient aryl groups are less susceptible to oxidative cleavage under these conditions,[20] although elevation of the temperature to over 50 °C led to degradation of the product.



Scheme 7 *Conditions:* i, H_2 (1 atm.), 5% Pd–C, EtOAc; ii, 2 mol% $RuCl_3 \cdot 3H_2O$, H_5IO_6 (28.4 equiv.), CCl_4–MeCN–H_2O (2:2:3), 18 h, 35–40 °C; iii, Me_3SiCl (4 equiv.), MeOH, 18 h, 50 °C

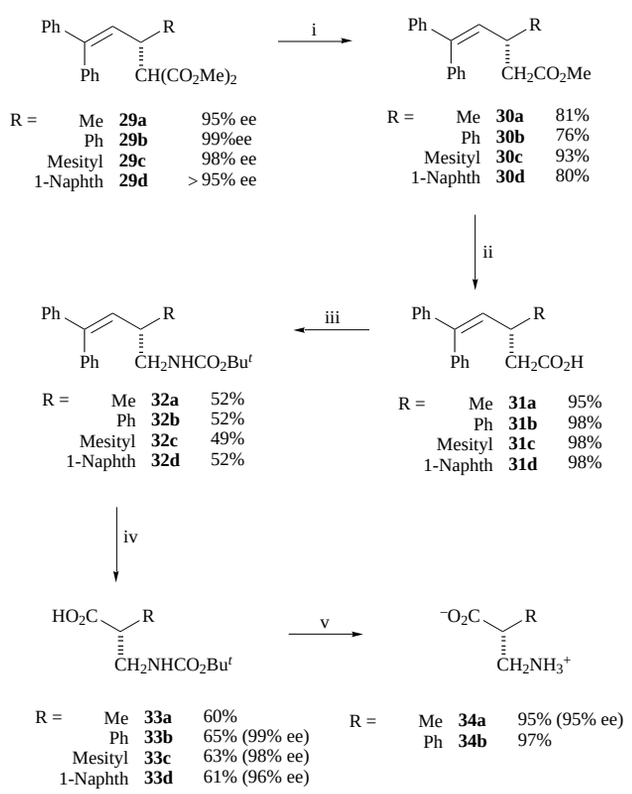
Several research groups have shown that unsymmetrical allylic acetates such as compounds **28a–d** undergo palladium-catalysed enantioselective allylic substitutions.[21] We have recently successfully applied the ligand **22** to this reaction,[22] which provides a convenient access to the products **29a–d** in high yield and excellent enantioselectivity (Scheme 8). However, we were unable to obtain a reaction between allylic acetate **28a** or **28b** and a nitrogen nucleophile using a palladium-catalysed reaction. This is unfortunate, since substrates of this type are easily prepared from β-phenylcinnamaldehyde[22] and would have allowed a greater range of *α*-amino acids to be prepared.



Scheme 8

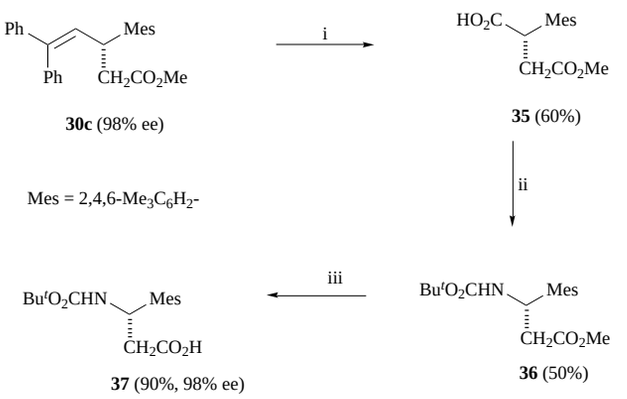
Nevertheless, we felt that the use of substrates **28a–d** (and related structures) may offer some potential for the synthesis of β-amino acids. Indeed, this has proved to be successful and the results are described below.

The enantiomerically pure products **29a–d** were decarboxylated using the Krapcho procedure[23] affording the mono-esters **30a–d** (Scheme 9). Hydrolysis of the decarboxylated products **30a–d** afforded the mono-acid compounds **31a–d** in high yield. These carboxylic acids were subjected to a modified Curtius reaction.[24] Thus, treatment of mono-acids **31a–d** with diphenylphosphoryl azide and triethylamine in refluxing *tert*-butyl alcohol afforded the *tert*-butoxycarbonylamino products **32a–d** in reasonable yield. Oxidation of compounds **32a–d** with sodium metaperiodate and a ruthenium catalyst[13] afforded the corresponding protected β-amino acids **33a–d** in reasonable yield. In order to demonstrate that this methodology can be used to access free β-amino acids, the substrates **33a** and **33b** were converted into the free β-amino acids **34a** and **34b** by acid hydrolysis in good yield. There was no loss of stereochemical purity in the synthesis of compound **34a** indicating that this methodology does not lead to significant racemisation.



Scheme 9 *Conditions:* i, DMSO–H_2O, NaCl, 180 °C, sealed tube, 7 h; ii, NaOH–H_2O–MeOH, reflux, 2 h; iii, $(PhO)P(O)N_3$, NEt_3, Bu^tOH, reflux, 16 h; iv, 2.5 mol% $RuCl_3 \cdot (H_2O)_n$, $NaIO_4$ (4.1 equiv.), MeCN–CCl_4–H_2O (2:2:3), 40 °C, 2 h; v, 4 M HCl–dioxane, DOWEX, 4 h

Chiral β-amino acids can have their asymmetric centre either α or β to the carbonyl group. In the examples above, the asymmetric centre is generated in the α-position. However, by modification of the reaction sequence, β-amino acids may be prepared in which the asymmetric centre is in the β-position. Thus, the mono-ester **30c** was subjected to catalytic ruthenium–sodium metaperiodate oxidising conditions, producing the product **35** in reasonable yield (Scheme 10). Treatment of **35** under modified Curtius reaction conditions afforded the *tert*-butoxycarbonylamino compound **36** in reasonable yield (which proceeds with retention of configuration). Finally, hydrolysis of the mono-ester **36** afforded the desired product **37** in good yield and with excellent enantioselectivity, as determined by chiral HPLC [Chiralcel OD, hexane–isopropyl alcohol (80 : 20)].



Scheme 10 *Conditions:* i, 2.5 mol% $RuCl_3 \cdot (H_2O)_n$, $NaIO_4$ (4.1 equiv.), MeCN–CCl_4–H_2O (2 : 2 : 3), 40 °C, 2 h; ii, $(PhO)P(O)N_3$, NEt_3, Bu^{t}OH, reflux, 16 h; iii, NaOH, H_2O–MeOH, reflux, 2 h

In summary, we have described an effective and highly enantioselective synthesis of α- and β-amino acids. Palladium-catalysed asymmetric allylic substitution was the key step in the preparation of both classes of compound.

Experimental

Commercially available solvents and reagents were used throughout without further purification, except for those detailed below which were purified as described. Light petroleum refers to the fraction boiling in the range 40–60 °C, and was distilled through a 36 cm Vigreux column before use. Diethyl ether (referred to as ether) was dried by storage over sodium wire for several days. THF was distilled from sodium benzophenone ketyl under nitrogen, prior to use. Dichloromethane was distilled from phosphorus pentoxide. In order to dry DMF, it was stirred over calcium hydride for 15 h, decanted and distilled under reduced pressure before storage over 4 Å molecular sieves under nitrogen.

Analytical thin layer chromatography was carried out using aluminium-backed plates coated with Merck Kieselgel 60 GF_{254}. Plates were visualised under UV light (at 254 and/or 360 nm) or by staining with phosphomolybdic acid reagent, followed by heating. Flash chromatography was carried out using Merck Kieselgel 60 H silica or Sorbsil C 60 silica gel. Pressure was applied at the column head with hand bellows. Samples were applied pre-adsorbed on silica or as a saturated solution in an appropriate solvent.

IR Spectra were recorded in the range 4000–600 cm^{-1} using a Nicolet FT-205 spectrometer, with internal calibration. Spectra were recorded as solutions in chloroform. Elemental analyses were carried out on a Perkin-Elmer 2400 Elemental Analyser. ^{1}H and ^{13}C NMR spectra were recorded using Bruker AC-250 and Bruker WH-400 (SERC NMR Spectroscopy Centre, Warwick) instruments. High- and low-resolution mass spectra were recorded on a Kratos MS80 instrument or on a VG Analytical ZAB-E instrument (EPSRC mass spectrometry service, Swansea). Optical rotations were carried out on an Optical Activity AA100 polarimeter and are recorded as 10^{-1} degrees cm^2 g^{-1}. Mps were measured on an Electrothermal digital melting point apparatus and are uncorrected. The preparations of ligand **22**, allyl acetates **4**–**7** and **28a**–**d** and the substitution products **29a**–**d** have been detailed elsewhere.[16,22]

Typical procedure for palladium-catalysed allylic amination of allyl acetates

(−)-(*E*)-*N*-Pent-3-en-2-yltoluene-*p*-sulfonamide 9b.[16] To a solution of (*E*)-2-acetoxypent-3-ene **5** (0.100 g, 0.78 mmol, 1 equiv.) in THF–DMSO (80 : 20; 4 cm^3) was added $[PdCl(C_3H_5)]_2$ (0.0061 g, 0.016 mmol, 0.02 equiv.) and ligand **22** (0.010 g, 0.032 mmol, 0.04 equiv.). The solution was stirred at room temperature for 5–10 min after which *N*-sodiotoluene-*p*-sulfonamide (0.211 g, 1.09 mmol, 1.4 equiv.) was added to it. The reaction mixture was then heated under N_2 at 50 °C for 18 h, after which it was diluted with ether (40 cm^3) and washed with water (20 cm^3 × 3); the aqueous layer was then back-extracted with ether (20 cm^3 × 3). The combined organic extracts were washed with brine (40 cm^3), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which was purified by silica gel column chromatography using (light petroleum–ether, 4 : 1) to yield the title compound **9b** as a colourless oil (0.190 g, 92%) (Found: M^+, 239.0983. $C_{12}H_{17}NO_2S$ requires M^+, 239.0978); $[\alpha]_D^{25}$ −13.4 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3293 (NH); δ_H(250 MHz; $CDCl_3$) 1.14 (3 H, d, *J* 6.7, NCHC*H*$_3$), 1.43 (3 H, d, *J* 8.5, CHC*H*$_3$), 2.41 (3 H, s, CH_3), 3.83 (1 H, m, CH_3C*H*N), 5.02 (1 H, br d, *J* 7.4, NH), 5.17 (1 H, dd, *J* 15.7 and 6.6, CH_3CHC*H*), 5.40 (1 H, dq, *J* 15.7 and 6.2, CH_3C*H*CH) and 7.26–7.77 (4 H, m, ArH); δ_C(63 MHz; $CDCl_3$) 17.4 (Ar*C*H$_3$), 21.4 (CH_3), 21.8 (CH_3), 51.4 (CHN), 126.3 (CH*C*H), 127.2 (Arom CH × 2), 129.3 (Arom CH × 2), 131.8 (*C*HCH), 138.0 (Arom C) and 142.9 (Arom C); *m*/*z* (EI) 239.0 (M^+, 1.5%) and 91 (100); 49% ee [determined by chiral shift ^{1}H NMR in the presence of 40 equiv. of (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol].

(−)-(*E*)-4-Phthalimidopent-2-ene 9a. Colourless oil (0.116 g, 93%) (Found: M^+, 215.0946. $C_{13}H_{13}NO_2$ requires M^+, 215.0959); $[\alpha]_D^{25}$ −12.1; ν_{max}/cm^{-1} 1708 (C=O); δ_H(250 MHz; $CDCl_3$) 1.55 (3 H, d, *J* 7.1, C*H*$_3$CHN), 1.68 (3 H, d, *J* 7.0, C*H*$_3$CHCH), 4.86 (1 H, apparent quintet, *J* 7.1, CHN), 5.71 (1 H, dq, *J* 15.4 and 7.1, CH_3CHC*H*), 5.91 (1 H, dd, *J* 15.3 and 7.0, CH_3C*H*CH-) and 7.66–7.85 (4 H, m, ArH); δ_C(63 MHz; $CDCl_3$) 17.5 (CH_3), 18.8 (CH_3), 48.7 (CHN), 122.9 (Arom CH × 2), 127.8 (CH*C*H), 129.8 (*C*HCH), 132.0 (Arom C), 133.7 (Arom CH × 2), 134.1 (Arom C × 2) and 168.0 (C=O × 2); *m*/*z* (EI) 215.0 (M^+, 90.2%) and 200 (100); HPLC: 56% ee; t_R 7/11 min [Chiralcel OJ, hexane–Pr^{i}OH (96 : 4), 1.0 cm^3 min^{-1}, 254 nm].

(*Z*)-1-Phthaloylimidocyclohex-2-ene 10a. Crystalline colourless solid (0.227 g, 89%), mp 111–113 °C (Found: M^+, 227.0948. $C_{14}H_{13}NO_2$ requires M^+, 227.0946); ν_{max}/cm^{-1} 1721 (C=O); δ_H(250 MHz; $CDCl_3$) 1.67–1.95 (6 H, m, CH_2 × 3), 4.88 (1 H, m, CHN), 5.56 (1 H, br d, *J* 10.2, CHC*H*=CH), 5.93 (1 H, m, NCHCH=C*H*) and 7.64–7.84 (4 H, m, ArH); δ_C(63 MHz; $CDCl_3$) 21.7 (CH_2), 24.2 (CH_2), 27.0 (CH_2), 47.4 (CHN), 122.9 (Arom CH × 2), 126.5 (*C*H=CH), 129.9 (CH=*C*H), 132.0 (Arom C), 133.8 (Arom CH × 2) and 168.0 (C=O); *m*/*z* (EI) 227.0 (M^+, 24.7%) and 80 (100); HPLC: 12% ee; t_R 12/15 min [Chiracel OJ, hexane–Pr^{i}OH (90 : 10), 1.0 cm^3 min^{-1}, 254 nm].

(*Z*)-*N*-Cyclohex-2-enyltoluene-*p*-sulfonamide 10b.[7] Crystalline colourless solid (0.084 g, 47%), mp 100–101 °C (Found: M^+, 251.0968. $C_{13}H_{17}NO_2S$ requires M^+, 251.0980); ν_{max}/cm^{-1} 3270 (NH); δ_H(250 MHz; $CDCl_3$) 1.48–1.91 (6 H, m, CH_2 × 3), 2.41 (3 H, s, CH_3), 4.78 (1 H, br s, CHN), 5.11 (1 H, d, *J* 8.4, NH), 5.36 (1 H, m, CHC*H*CHNH), 5.74 (1 H, m, C*H*CH-CHNH), 7.29 (2 H, d, *J* 8.1, Arom CH × 2) and 7.89 (2 H, d, *J* 8.1, Arom CH × 2); δ_C(63 MHz; $CDCl_3$) 19.3 (CH_2), 21.4 (CH_3), 24.4 (CH_2), 30.1 (CH_2), 48.9 (CHN), 126.9 (Arom CH), 127.0 (CH=*C*H), 129.5 (Arom CH), 131.2 (*C*H=CH), 138.3

(Arom C) and 143.2 (Arom C); *m*/*z* (EI) 251.0 (M^+, 5.7%) and 91 (100); HPLC: 18% ee; t_R 15/17 min [Chiracel OJ, hexane–Pr^{i}OH (93:7), 1.0 cm^3 min^{-1}, 254 nm].

(−)-(*E*)-1-Phthaloylimido-1,3-diphenylprop-2-ene 11a. Colourless crystalline solid (3.702 g, 92%), mp 101–102 °C; $[\alpha]_D^{25}$ −19.9 (*c* 1.5 in $CHCl_3$) (Found: M^+, 339.1259. $C_{23}H_{17}NO_2$ requires M^+, 339.1254); ν_{max}/cm^{-1} 1720 (C=O); δ_H(250 MHz; $CDCl_3$) 6.13 (1 H, d, *J* 8.6, ArC*H*N), 6.71 (1 H, d, *J* 15.9, ArC*H*=CH), 7.07 (1 H, dd, *J* 8.6 and 15.9, ArCH=C*H*) and 7.23–7.85 (14 H, m, Arom H); δ_C(63 MHz; $CDCl_3$) 56.4 (CHN), 123.3 (Arom CH × 2), 125.2 (CH=*C*H), 126.7 (Arom CH), 127.4 (Arom CH), 127.7 (Arom CH), 128.0 (Arom CH), 128.5 (Arom CH), 128.6 (Arom CH), 133.2 (C), 134.0 (Arom CH × 2), 134.3 (*C*H=CH), 136.2 (C), 138.0 (C) and 168.2 (C=O); *m*/*z* (EI) 339.1 (M^+, 13.5%) and 192 (100); HPLC: 96% ee; t_R 11/13 min [Chiralcel OD, hexane–Pr^{i}OH (99:1), 0.5 cm^3 min^{-1}, 254 nm].

(−)-(*E*)-*N*-(1,3-Diphenylprop-2-enyl)toluene-*p*-sulfonamide 11b.[16] Colourless crystalline solid (0.156 g, 90%), mp 153–154 °C (Found: M^+, 363.1289. $C_{22}H_{21}NO_2S$ requires M^+, 363.1293); $[\alpha]_D^{25}$ −31.4 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 3288 (NH); δ_H(250 MHz; $CDCl_3$) 2.29 (3 H, s, CH_3), 4.94 (1 H, d, *J* 7.2, NH), 5.10 (1 H, apparent t, *J* 7.2, CHN), 6.05 (1 H, dd, *J* 6.8 and 15.8, ArCHC*H*), 6.33 (1 H, d, *J* 15.9, ArC*H*CH), 7.10–7.24 (12 H, m, ArH) and 7.65 (2 H, d, *J* 8.3, Arom CH × 2); δ_C(63 MHz; $CDCl_3$) 21.4 (CH_3), 53.7 (CHN), 126.5 (Arom CH × 2), 127.0 (Arom CH × 2), 127.1 (Arom CH × 2), 127.8 (Arom CH × 2), 128.6 (Arom CH × 2), 129.4 (CH=*C*H), 132.0 (*C*H=CH), 136.0 (Arom C), 137.6 (Arom C), 139.6 (Arom C) and 143.1 (Arom C); *m*/*z* (EI) 363.1 (M^+, 3.9%) and 208 (100); HPLC: 95% ee; t_R 17/27 min [Chiralcel OD, hexane–Pr^{i}OH (99:1), 0.5 cm^3 min^{-1}, 254 nm].

(+)-(*E*)-*N*,*N*-Di-*tert*-butoxycarbonyl-1,3-diphenylprop-2-enamine 11c. Colourless crystalline solid (0.180 g, 90%), mp 96–97 °C, $[\alpha]_D^{25}$ +23.4 (*c* 1.0 in $CHCl_3$); ν_{max}/cm^{-1} 1739 (C=O), 1723 (C=O), 1696 (C=O) and 1600 (ArH); δ_H(250 MHz; $CDCl_3$) 1.39 [18 H, s, C(CH_3)$_3$ × 2], 6.10 (1 H, d, *J* 8.1, CHN), 6.66 (1 H, d, *J* 16.0, ArC*H*CH), 6.78 (1 H, dd, *J* 16.0 and 8.1, ArCH-C*H*) and 7.23–7.46 (10 H, m, ArH); δ_C(63 MHz; $CDCl_3$) 27.8 [(CH_3)C], 61.3 (CHN), 82.5 [(CH_3)$_3$C], 126.4 (CH), 126.6 (CH), 126.9 (CH), 127.8 (CH), 128.1 (CH), 128.5 (CH), 134.3 (CH), 136.6 (Arom C), 140.6 (Arom C) and 152.3 (C=O); *m*/*z* (EI) 410.0 (M^+, 0.1%), 192 (90) and 57 (100); HPLC: 54% ee; t_R 8/15 min [Chiralcel OD, hexane–Pr^{i}OH (99:1), 0.5 cm^3 min^{-1}, 254 nm].

(−)-(*E*)-1-Phthalimido-1,3-bis(4-fluorophenyl)prop-2-ene 23. Colourless oil (0.364 g, 56%) (Found: M^+, 375.1099. $C_{23}H_{15}F_2NO_2$ requires M^+, 375.1071); $[\alpha]_D^{25}$ −31.3 (*c* 1.6 in $CHCl_3$); ν_{max}/cm^{-1} 1712 (C=O); δ_H(400 MHz; $CDCl_3$) 6.08 (1 H, d, *J* 8.4, CHN), 6.64 (1 H, d, *J* 15.9, ArC*H*=CH), 6.99–7.36 (11 H, m, ArH and ArCH=C*H*) and 7.69–7.87 (4 H, m, ArH); δ_C(63 MHz; $CDCl_3$) 55.8 (CHN), 115.4 (Arom CH), 115.5 (Arom CH), 115.6 (Arom CH), 123.4 (Arom CH), 124.9 (ArCH=*C*H), 128.1 (Arom CH), 129.3 (Arom CH), 129.4 (Arom CH), 131.6 (Ar*C*H=CH), 134.0 (Arom CH), 161.1 (Arom C), 161.5 (Arom C) and 164.0 (Arom C); *m*/*z* (EI) 375.1 (M^+, 8.2%) and 228 (100); HPLC: 99% ee; t_R 16/24 min [Chiracel OD, hexane–Pr^{i}OH (99:1), 0.5 cm^3 min^{-1}, 254 nm].

***N*-Allylphthalimide 8a.**[7] Colourless solid (0.276 g, 73%), mp 192–193 °C (lit.,[19] mp 192–194 °C) (Found: M^+, 187.0623. $C_{11}H_9NO_2$ requires M^+, 187.0633); ν_{max}/cm^{-1} 1708.1 (C=O); δ_H(250 MHz; $CDCl_3$) 4.26 (2 H, br d, *J* 5.6, NCH_2), 5.20 (2 H, m, CH=CH_2), 5.86 (1 H, m, C*H*=CH_2) and 7.68–7.83 (4 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 39.9 (NCH_2), 117.5 (CH=*C*H_2), 123.1 (Arom CH × 2), 131.4 (Arom C), 131.9 (CH=*C*H_2), 133.8 (Arom CH × 2) and 167.7 (C=O); *m*/*z* (EI) 187.0 (M^+, 100%), 169 (30) and 160 (25).

***N*-Allylphenyl-*p*-sulfonamide 8b.** Colourless oil (0.917 g, 41%) (Found: M^+, 197.0511. $C_9H_{11}NO_2S$ requires M^+, 197.0517); ν_{max}/cm^{-1} 3550 (NH); δ_H(250 MHz; $CDCl_3$) 4.09 (2 H, br d, *J* 7.1, NCH_2), 5.00 (1 H, br s, NH), 5.13 (2 H, m, CH=CH_2), 5.58 (1 H, m, C*H*=CH_2) and 7.47–7.85 (5 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 49.3 (NCH_2), 119.1 (CH=*C*H_2), 127.1 (Arom CH), 129.1 (Arom CH), 132.4 (Arom CH), 132.4 (Arom CH) and 140.0 (C); *m*/*z* (EI) 197 (M^+, 8%) and 77 (100).

***N*,*N*-Di-*tert*-butoxycarbonylprop-2-enamine 8c.**[8] Colourless crystalline solid (0.985 g, 78%), mp 45 °C (lit.,[2] 47–48 °C); ν_{max}/cm^{-1} 1699 (C=O); δ_H(250 MHz; $CDCl_3$) 1.50 (18 H, s, CH_3 × 6), 4.17 (2 H, m, NCH_2), 5.14 (2 H, m, NCH_2CH=CH_2) and 5.83 (1 H, m, CH); δ_C(62.5 MHz; $CDCl_3$) 27.9 [(*C*H_3)C × 3], 48.4 (NCH_2), 82.2 [(CH_3)$_3$*C*], 116.1 (NCH_2-CH=*C*H_2), 133.7 (NCH_2*C*H) and 152.7 (C=O); *m*/*z* (EI) 258.0 (MH^+, 60%), 219 (28) and 202 (100).

(*E*)-1-Azido-1,3-diphenylprop-2-ene 11d.[25] To a solution of (*E*)-1,3-diphenyl-1-acetoxyprop-2-ene **7** (1.200 g, 4.76 mmol, 1 equiv.) in THF (8.5 cm^3) was added $[PdCl(C_3H_5)]_2$ (0.026 g, 0.07 mmol, 0.03 equiv.) and triphenylphosphine (0.075 g, 0.47 mmol, 0.09 equiv.). The solution was stirred for 5–10 min at room temperature before sodium azide (0.465 g, 7.14 mmol, 1.5 equiv.) in water (2.5 cm^3) was added to it. The reaction mixture was stirred for a further 3 h at room temperature after which it was diluted with ether (50 cm^3) and washed with water (30 cm^3 × 3); the aqueous layer was back-extracted with ether (30 cm^3 × 3). The combined organic extracts were washed with brine (90 cm^3), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which was purified by silica gel column chromatography (light petroleum) to yield the title compound **11d** as a pale yellow oil (0.862 g, 77%); ν_{max}/cm^{-1} 2100 (N_3) and 696.5; δ_H(250 MHz; $CDCl_3$) 5.22 (1 H, d, *J* 6.3, CHN), 6.30 (1 H, dd, *J* 15.5 and 8.4, PhCH=C*H*), 6.72 (1 H, d, *J* 15.5, PhC*H*=CH) and 7.25–7.43 (10 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 67.0 (CHN), 126.6 (CH), 126.9 (CH), 128.1 (CH), 128.5 (CH), 128.7 (CH), 132.8 (CH), 135.7 (CH) and 138.2 (CH); *m*/*z* (EI) 193 [MH^+ (−N_3), 70%], 130 (40) and 115 (100).

1-Azidocyclohex-2-ene 10d.[25] Colourless oil (0.064 g, 65%); δ_H(250 MHz; $CDCl_3$) 1.65–1.88 (6 H, m, CH_2 × 3), 3.86 (1 H, s, CHN), 5.69 (1 H, m, CHC*H*CHN) and 5.98 (1 H, m, C*H*CHCHN).

1-Acetamido-1,3-diphenylprop-2-ene 13. To the azide **11d** (1.010 g, 4.32 mmol, 1 equiv.) was added thioacetic acid (2.620 g, 34.4 mmol, 8 equiv.) and the reaction mixture was stirred at room temperature for 36 h. The crude product, precipitated by adding ether and light petroleum to the reaction mixture, was recrystallised from dichloromethane–light petroleum to yield the title compound **13** as a colourless crystalline solid (0.232 g, 32%), mp 93 °C (Found: M^+, 251.1320. $C_{17}H_{17}NO$ requires M^+, 251.1310); ν_{max}/cm^{-1} 1638 (NC=O) and 3293 (NH); δ_H(250 MHz; $CDCl_3$) 2.06 (3 H, s, $COCH_3$), 5.82 (2 H, br s, CHN and NH), 6.34 (1 H, dd, *J* 15.9 and 2.6, ArCHC*H*), 6.53 (1 H, d, *J* 15.9, ArC*H*CH) and 7.19–7.38 (10 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 23.3 (CH_3), 54.8 (CHN), 126.5 (CH), 127.2 (CH), 127.6 (CH), 127.7 (CH), 128.6 (CH), 128.8 (CH), 129.0 (CH), 131.3 (CH), 136.5 (Arom C), 140.9 (Arom C) and 169.2 (C=O); *m*/*z* (EI) 251.1 (M^+, 6.8%), 208 (34) and 160 (100).

1-Acetamidocyclohex-2-ene 12.[26] Colourless crystalline compound (0.064 g, 46%); δ_H(250 MHz; $CDCl_3$) 1.63–2.35 (6 H, m, CH_2 × 3), 2.03 (3 H, s, NHCOCH_3), 4.39 (1 H, apparent q, *J* 6.1, CHN), 5.54–5.65 (2 H, m, CH=CH) and 6.18 (1 H, d, *J* 7.0, NH).

Procedures for oxidative cleavage

(i) Ozonolysis: a typical procedure. N,N-*Di*-tert-*butoxycarbonylglycine methyl ester* **16**.—*N*,*N*-Di-*tert*-butoxycarbonylprop-2-enamine **8c** (0.128 g, 0.50 mmol, 1 equiv.) was added to 2.5 M methanolic sodium hydroxide (2.8 cm^3 × 2) in dichloromethane (12 cm^3). The reaction mixture was stirred at −78 °C as ozone was passed through it for 2.5 h until a pale blue colour persisted. After passage of N_2 through the reaction mixture for 1 min, it was diluted with dichloromethane (10 cm^3) and water (10 cm^3) and allowed to warm to room temperature over 16 h.

The organic layer was separated and the aqueous layer was extracted with dichloromethane (20 cm^3 × 4). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product, which was purified by silica gel column chromatography (light petroleum–ether, 1:1) to give the title compound **16** as a colourless oil (0.137 g, 95%); ν_{max}/cm^{-1} 3400 (NH) and 1770 (C=O); δ_H(250 MHz; $CDCl_3$) 1.50 (18 H, s, CH_3 × 6), 3.78 (3 H, s, CO_2CH_3) and 4.34 (2 H, s, CH_2); δ_C(62.5 MHz; $CDCl_3$) 28.0 [$(CH_3)_3C$], 47.2 (CH_2), 52.1 (CO_2CH_3), 83.1 [$(CH_3)_3C$], 152.7 (C=O × 2) and 169.9 (CO_2CH_3); *m*/*z* (EI) 290 (MH^+, 1%), 234 (12), 178 (12) and 57 (100).

N-*Phthaloylglycine methyl ester* **14**.—Pale yellow oil (0.087 g, 6%) (Found: M^+, 219.0500. $C_{11}H_9NO_4$ requires M^+, 219.0532); ν_{max}/cm^{-1} 1708.1 (NC=O) and 1740.7 (C=O); δ_H(250 MHz; $CDCl_3$) 3.77 (3 H, s, CO_2CH_3), 4.45 (2 H, s, CH_2) and 7.73–7.91 (4 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 38.8 (CH_2), 52.8 (CO_2CH_3), 123.6 (Arom CH × 2), 128.8 (Arom C × 2), 134.3 (Arom CH × 2) and 173.7 (C=O); *m*/*z* (EI) 219.0 (M^+, 15.2%), 160 (100) and 147 (17).

N-*Phenylsulfonylglycine methyl ester* **15**.—Colourless oil (0.177 g, 67%) (Found: M^+, 229.0479. $C_9H_{11}NO_4S$ requires M^+, 229.0487); ν_{max}/cm^{-1} 3400 (NH) and 1754.7 (C=O); δ_H(250 MHz; $CDCl_3$) 3.64 (3 H, s, CO_2CH_3), 4.19 (2 H, s, CH_2) and 7.47–6.85 (5 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 48.2 (CH_2), 52.3 (CO_2CH_3), 123.1 (C), 127.3 (Arom CH × 2), 129.0 (Arom CH × 2), 133.0 (Arom CH), 133.9 (C) and 169.1 (C=O); *m*/*z* (EI) 229.0 (M^+, 0.4%), 160 (45), 141 (37) and 42 (100).

Dimethyl-2-*tosylaminohexanedioate* **19**.—Colourless oil (0.111 g, 73%) (Found: M^+, 343.4008. $C_{15}H_{21}NO_6S$ requires M^+, 343.4008); ν_{max}/cm^{-1} 3273 (NH) and 1738.8 (C=O); δ_H(250 MHz; $CDCl_3$) 1.17–2.32 (6 H, m, CH_2 × 3), 2.42 (3 H, s, $ArCH_3$), 3.49 (3 H, s, $CH_2CO_2CH_3$), 3.66 (3 H, s, $NCHCO_2CH_3$), 3.93 (1 H, br s, CHN), 5.36 (1 H, br d, *J* 14.3, NH) and 7.27–7.73 (4 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 20.4 (CH_2), 21.5 (CH_3), 32.4 (CH_2), 33.0 (CH_2), 51.6 (CH_3), 52.5 (CH_3), 55.4 (CHN), 127.3 (Arom CH × 2), 129.6 (Arom CH × 2), 171.9 (C=O) and 173.4 (C=O); *m*/*z* (EI) 343.0 (M^+, 1.4%), 171 (36), 155 (33) and 91 (100).

N-*Tosylalanine methyl ester* **17**.—Colourless crystalline solid (0.093 g, 73%), mp 187–188 °C (Found: M^+, 257.0724. $C_{11}H_{15}NO_4S$ requires M^+, 257.0724); ν_{max}/cm^{-1} 1738 (C=O); δ_H(250 MHz; $CDCl_3$) 1.38 (3 H, d, CH_3), 2.42 (3 H, s, $ArCH_3$), 3.54 (3 H, s, CO_2CH_3), 3.99 (1 H, m, CH_3CH), 5.28 (1 H, d, *J* 8.9, NH) and 7.27–7.75 (4 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 19.7 (CH_3), 21.5 ($ArCH_3$), 51.4 (CHN), 52.5 (CO_2CH_3), 127.1 (Arom *m*-CH × 2), 129.6 (Arom *o*-CH × 2), 137.7 (C), 143.6 (C) and 173.3 (C=O); *m*/*z* (EI) 257.0 (M^+, 0.1%), 171 (38) and 91 (100).

Dimethyl 2-*acetamidohexanedioate* **18**.—Pale yellow oil (0.023 g, 49%), ν_{max}/cm^{-1} 1692.3 (NC=O), 1739.6 (C=O) and 3264 (NH); δ_H(250 MHz; $CDCl_3$) 1.63–2.35 (6 H, m, CH_2 × 3), 2.03 (3 H, s, $NHCOCH_3$), 3.67 (3 H, s, $NCHCO_2CH_3$), 3.73 (3 H, s, $CH_2CO_2CH_3$), 4.59 (1 H, apparent q, *J* 6.1, CHN) and 6.18 (1 H, d, *J* 7.0, NH); δ_C(62.5 MHz; $CDCl_3$) 15.3 (CH_2), 28.0 (CH_2), 29.8 (CH_2), 38.7 (CH_3N), 51.7 (CO_2CH_3), 52.7 (CHN), 65.9 (CO_2CH_3), 168.0 (C=O) and 168.2 (C=O); *m*/*z* (EI) 232.0 (MH^+, 100%), 218 (6) and 172 (70).

Methyl acetamido(*phenyl*)*acetate* **20**.—Colourless oil (0.068 g, 66%) (Found: M^+, 207.0888. $C_{11}H_{13}NO_3$ requires M^+, 207.0895); ν_{max}/cm^{-1} 3290 (NH), 1751 (C=O) and 1658 (NC=O); δ_H(250 MHz; $CDCl_3$) 2.02 (3 H, s, $COCH_3$), 3.72 (3 H, s, CO_2CH_3), 5.59 (1 H, d, *J* 7.3, CHN), 6.81 (1 H, br s, NH) and 7.27–7.42 (5 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 23.0 ($NHCOCH_3$), 52.7 (CO_2CH_3), 56.4 (CHN), 127.3 (Arom CH), 128.6 (Arom CH), 129.0 (Arom CH), 136.6 (C), 169.4 (CO_2CH_3) and 171.5 (C=O); *m*/*z* (EI) 207.0 (M^+, 2.3%) and 106 (100).

(ii) With ruthenium tetroxide: a typical procedure. N-*Phthaloylglycine* **21**.—Allylphthalimide **8a** (0.187 g, 1.00 mmol, 1 equiv.) was added to sodium periodate (0.877 g, 2.16 mmol, 2.2 equiv.) and ruthenium trichloride (0.007 g, 0.03 mmol, 0.03 equiv.) in a solvent mixture of acetonitrile (2 cm^3), tetrachloromethane (2 cm^3) and water (3 cm^3). The reaction mixture was stirred at room temperature for 19 h, after which it was filtered through a silica column (eluent ether) and concentrated *in vacuo* to yield a white solid. This was recrystallised from water to yield the title compound **21** as a colourless crystalline solid (47%), mp 191–192 °C (Found: M^+, 205.0370. $C_{10}H_7NO_4$ requires M^+, 205.0375); ν_{max}/cm^{-1} 3532 (OH) and 1717.4 (C=O); δ_H(250 MHz; $CDCl_3$) 4.31 (2 H, s, CH_2) and 7.65–7.96 (4 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 38.9 (CH_2), 123.4 (Arom CH × 2), 131.9 (Arom C), 133.9 (Arom CH × 2), 167.5 (CO_2H) and 169.1 (C=O); *m*/*z* (EI) 205.0 (M^+, 1.2%) and 160 (100).

(S)-N-*Phthaloylphenylglycine methyl ester* **24.**—To **11a** (0.207 g, 0.610 mmol, 1 equiv.) was added periodic acid (0.616 g, 2.70 mmol, 4.4 equiv.) in a solvent mixture of CCl_4 (1 cm^3), MeCN (1 cm^3) and water (1.5 cm^3). The reaction mixture was stirred for 10 min to give two clear phases, before ruthenium trichloride (0.003 g, 0.012 mmol, 0.02 equiv.) was added to it. After this the reaction mixture was stirred at 35–40 °C for 18 h before being diluted with water (40 cm^3); the layers were separated and the aqueous layer was extracted with ether (20 cm^3 × 3). The combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The yellow residue was dissolved in methanol (4 cm^3) and trimethylsilyl chloride (0.30 cm^3, 2.36 mmol, 3.8 equiv.) was added to the solution. The reaction mixture was stirred at 50 °C for 18 h after which it was diluted with ether (40 cm^3) and washed with water (20 cm^3 × 2); the aqueous layer was back-extracted with ether (20 cm^3 × 3). The combined organic extracts were washed with brine (60 cm^3), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which was purified by silica gel column chromatography (light petroleum–ether, 1:1) to yield the title compound **24** as a colourless oil (0.092 g, 51%) (Found: M^+, 295.0848. $C_{17}H_{13}NO_4$ requires M^+, 295.0845); ν_{max}/cm^{-1} 1714 (C=O) and 1739 (C=O); δ_H(250 MHz; $CDCl_3$) 3.81 (3 H, s, CO_2CH_3), 6.02 (1 H, s, CHN), 7.32–7.53 (5 H, m, ArH) and 7.69–7.86 (4 H, m, ArH); δ_C(63 MHz; $CDCl_3$) 53.0 (CH_3), 55.7 (CHN), 123.5 (Arom CH × 2), 128.4 (Arom CH), 128.7 (Arom CH), 129.7 (Arom CH), 134.2 (Arom *C*H × 2), 167.3 (C=O) and 171.2 (C=O); *m*/*z* (EI) 295.0 (M^+, 1.1%) and 236 (100).

(+)-4-*Fluorophenylglycine* **25**.[19]—To (−)-1-phthalimido-1,3-bis(4-fluorophenyl)prop-2-ene **23** (0.305 g, 0.814 mmol, 1 equiv.) was added periodic acid (0.778 g, 3.416 mmol, 4.2 equiv.) in a solvent mixture of CCl_4 (2 cm^3), MeCN (2 cm^3) and water (3 cm^3). The reaction mixture was stirred for 10 min to give two clear phases after which ruthenium trichloride (0.003 g, 0.014 mmol, 0.01 equiv.) was added to it. The reaction mixture was then stirred at 35–40 °C for 18 h before being diluted with water (40 cm^3); the aqueous layer was then separated and extracted with ether (20 cm^3 × 3). The combined organic extracts were washed with brine (50 cm^3), dried ($MgSO_4$) and concentrated *in vacuo* to give a colourless oil. This was dissolved in propan-2-ol (7.7 cm^3) and water (1.3 cm^3), and treated with sodium borohydride (0.225 g, 6.02 mmol, 7.4 equiv.). The reaction mixture was stirred for 24 h at room temperature after which it was treated with acetic acid (0.9 cm^3) and stirred at 80 °C for 2 h. The reaction mixture was purified by column chromatography on Amberlite 120 (eluent water). The Ninhydrin-active fractions were concentrated *in vacuo* to yield the title compound **25** as a colourless crystalline solid (0.172 g, 89%; 99% ee); $[\alpha]_D^{25}$ +104.5 (*c* 0.3 in 1 M HCl) (lit.,[19] 105.5); δ_H(250 MHz; CH_3CO_2D) 5.59 (1 H, s, CH) and 7.33–7.70 (4 H, m, ArH).

Dimethyl (+)-N-*phthaloylglutamate* **27.**—To compound **26** (0.217 g, 0.64 mmol, 1 equiv.) was added periodic acid (4.223 g, 18.52 mmol, 28.9 equiv.) in a solvent mixture of CCl_4 (2 cm^3), MeCN (2 cm^3) and water (3 cm^3). The reaction mixture was stirred for 10 min to give two clear phases before ruthenium

trichloride (0.003 g, 0.012 mmol, 0.02) was added to it. The reaction mixture was stirred at 30–35 °C for 18 h and then diluted with water (40 cm^3); the aqueous layer was separated and extracted with ether (20 cm^3 × 3). The combined organic extracts were washed with brine (50 cm^3), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in methanol (4 cm^3) and trimethylsilyl chloride (0.30 cm^3, 2.36 mmol, 3.6 equiv.) was added to the solution. The reaction mixture was stirred at 50 °C for 18 h before being diluted with ether (40 cm^3) and washed with water (20 cm^3 × 3). The aqueous layer was separated and back-extracted with ether (20 cm^3 × 3). The combined organic extracts were washed with brine (40 cm^3), dried ($MgSO_4$) and concentrated *in vacuo* to give a pale yellow oil, which was purified by silica column chromatography (light petroleum–diethyl ether, 1:1) to yield the title compound **27** as a colourless oil (0.088 g, 47%); $[\alpha]_D^{25}$ +173.6 (*c* 1.4 in $CHCl_3$); ν_{max}/cm^{-1} 1714 (C=O), 1743 (C=O) and 1746 (C=O); δ_H(250 MHz; $CDCl_3$) 2.36–2.66 (4 H, m, CH_2 × 2), 3.61 (3 H, s, CO_2CH_3), 3.75 (3 H, s, CO_2CH_3), 4.94 (1 H, dd, *J* 10 and 5.3, CHN) and 7.75–7.90 (4 H, m, ArH); δ_C(63 MHz; $CDCl_3$) 24.2 (CH_2CH_2CHN), 30.5 (CH_2CH_2CHN), 51.0 (CHN), 51.6 (CO_2CH_3), 52.7 (CO_2CH_3), 123.5 (Arom *C*H × 2), 132.7 (Arom C), 134.2 (Arom *C*H × 2), 164.7 (C=O), 168.9 (C=O) and 172.5 (C=O); *m/z* (EI) 305.0 (M^+, 0.1%), 273 (18) and 186 (100).

(+)-1-*Phthalimido*-1,3-*diphenylpropane* **26**.—Compound **11a** (0.213 g, 0.78 mmol, 1 equiv.) was stirred in ethyl acetate (8 cm^3) in the presence of 5% Pd–C (0.041 g) under H_2 (1 atm) at room temperature for 18 h. The reaction mixture was filtered and concentrated *in vacuo* to yield the crude product, which was purified by silica column chromatography (light petroleum–ether, 4:1) to yield the title compound **26** as a colourless oil (0.196 g, 90%); $[\alpha]_D^{25}$ +7.9 (*c* 1.2 in $CHCl_3$); ν_{max}/cm^{-1} 1709 (C=O); δ_H(250 MHz; $CDCl_3$) 2.53–3.19 (4 H, m, CH_2 × 2), 5.36 (1 H, dd, *J* 6.1 and 5.2, CHN), 7.10–7.53 (10 H, m, ArH) and 7.63–7.78 (4 H, m, ArH); δ_C(63 MHz; $CDCl_3$) 32.5 (CH_2), 33.4 (CH_2), 54.7 (CHN), 123.1 (Arom CH × 2), 127.8 (C), 127.9 (Arom CH), 128.1 (Arom CH), 128.3 (Arom CH), 128.4 (Arom CH), 128.5 (Arom CH), 128.6 (Arom CH), 131.8 (Arom C), 133.9 (Arom CH × 2), 139.6 (Arom C), 140.9 (Arom C) and 168.3 (C=O); *m/z* (EI) 341.0 (M^+, 30%) and 236 (100).

Typical procedure for decarboxylation of malonates 29a–d

A degassed solution of the appropriate alkylated product **29a–d** (1.0 mmol), NaCl (2.6 mmol) and water (2.8 mmol) in DMSO (5 cm^3) was heated in a sealed tube at 180 °C for 6 h. After cooling to room temperature, the mixture was diluted with dichloromethane (30 cm^3) and brine (100 cm^3) and then thrice extracted with dichloromethane (30 cm^3). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification of the residue by 'flash' column chromatography (eluent, light petroleum–ether, 3:1) gave the title compounds as described.

Methyl 3-methyl-5,5-diphenylpent-4-enoate 30a. (81%) as a colourless oil (Found: M^+, 280.1463. $C_{19}H_{20}O_2$ requires M^+, 280.1463); $[\alpha]_D^{20}$ −67.15 (*c* 0.83, $CHCl_3$); ν_{max}/cm^{-1} 3024, 2980, 1738 (C=O) and 1433; δ_H(400 MHz; $CDCl_3$) 1.08 (d, 3 H, *J* 6.6, CH_3), 2.30–2.38 (m, 2 H, $CH_2CO_2CH_3$), 2.81–2.85 (m, 1 H, $CHCH_3$), 3.59 (s, 3 H, CO_2CH_3), 5.88 (d, 1 H, *J* 10.1, C*H*=CPh_2), 7.15–7.24 (m, 6 H, ArH) and 7.32–7.36 (m, 4 H, ArH); δ_C(100 MHz; $CDCl_3$) 21.1 (CH_3), 31.2 ($CHCH_3$), 41.9 ($CH_2CO_2CH_3$), 51.6 (CO_2CH_3), 127.1 (Arom CH), 127.3 (Arom CH), 127.5 (Arom CH), 128.2 (Arom CH), 128.4 (Arom CH), 130.1 (Arom CH), 133.2 (*C*H=CPh_2), 139.9 (Ph_2C=CH), 141.4 (Arom C), 142.4 (Arom C) and 172.5 (C=O); *m/z* (EI) 280 (M^+, 13%), 206 (100) and 129 (60).

Methyl 3,5,5-triphenylpent-4-enoate 30b. Colourless solid (79%), mp 117–119 °C (Found: M^+, 342.1619. $C_{24}H_{22}O_2$ requires M^+, 342.1619); $[\alpha]_D^{20}$ −125.0 (*c* 0.96, $CHCl_3$); ν_{max}/cm^{-1} 3054, 1736 (C=O), 1438 and 1265; δ_H(400 MHz; $CDCl_3$) 2.73 (d, 2 H, *J* 7.6, $CH_2CO_2CH_3$), 3.58 (s, 3 H, CO_2CH_3), 3.93–3.99 (m, 1 H, C*H*Ph), 6.24 (d, 1 H, *J* 10.4, C*H*=CPh_2) and 7.11–7.37 (m, 15 H, ArH); δ_C(100 MHz; $CDCl_3$) 44.3 (*C*HPh), 44.4 ($CH_2CO_2CH_3$), 53.9 (CO_2CH_3), 128.9 (Arom CH), 129.5 (Arom CH), 129.6 (Arom CH), 129.7 (Arom CH), 129.8 (Arom CH), 130.6 (Arom CH), 131.1 (Arom CH), 131.6 (Arom CH), 132.1 (Arom CH), 132.7 (*C*H=CPh_2), 142.0 (Ph_2C=CH), 144.6 (Arom C), 144.8 (Arom C), 145.9 (Arom C) and 174.2 (C=O); *m/z* (EI) 342 (M^+, 1%), 268 (100) and 191 (82).

Methyl 5,5-diphenyl-3-(2,4,6-trimethylphenyl)pent-4-enoate 30c. A colourless solid (93%), mp 100–102 °C (Found: M^+, 384.2089. $C_{27}H_{28}O_2$ requires M^+, 384.2089); $[\alpha]_D^{20}$ +153.1 (*c* 1.9, $CHCl_3$); ν_{max}/cm^{-1} 3023, 2919, 1738 (C=O), 1440 and 1160; δ_H(400 MHz; $CDCl_3$) 2.03 (br s, 6 H, 2 × ArCH_3), 2.19 (s, 3 H, ArCH_3), 2.57 (dd, 1 H, *J* 5.3 and 14.7, C*H*HCO_2CH_3), 2.86 (dd, 1 H, *J* 10.2 and 14.7, CH*H*CO_2CH_3), 3.62 (s, 3 H, CO_2CH_3), 4.34–4.39 (m, 1 H, C*H*-Mes), 6.54 (d, 1 H, *J* 8.6, C*H*=CPh_2), 6.70 (s, 2 H, ArH), 6.93–6.95 (m, 2 H, ArH) and 7.18–7.25 (m, 8 H, ArH); δ_C(100 MHz; $CDCl_3$) 20.6 (ArCH_3), 21.2 (2 × ArCH_3), 37.5 (*C*H-Mes), 39.4 ($CH_2CO_2CH_3$), 51.5 (CO_2CH_3), 126.3 (Arom CH), 126.9 (Arom CH), 127.1 (Arom CH), 127.4 (Arom CH), 128.1 (Arom CH), 128.3 (Arom CH), 128.5 (Arom CH), 129.5 (Arom CH), 130.6 (*C*H=CPh_2), 135.4 (Ph_2C=CH), 136.0 (Arom C), 137.6 (Arom C), 139.9 (Arom C), 142.1 (Arom C), 142.8 (Arom C) and 172.5 (C=O); *m/z* (EI) 384 (M^+, 17%), 311 (100) and 191 (45).

Methyl 5,5-diphenyl-3-(1-naphthyl)pent-4-enoate 30d. A colourless solid (80%), mp 107–109 °C (Found: M^+, 392.1776. $C_{28}H_{24}O_2$ requires M^+, 392.1776); $[\alpha]_D^{20}$ +110.8 (*c* 1.37, $CHCl_3$); ν_{max}/cm^{-1} 3020, 1734 (C=O), 1443 and 1216; δ_H(250 MHz; $CDCl_3$) 2.77 (dd, 1 H, *J* 8.9 and 14.7, C*H*HCO_2CH_3), 2.91 (dd, 1 H, *J* 5.9 and 14.7, CH*H*CO_2CH_3), 3.55 (s, 3 H, CO_2CH_3), 4.76–4.86 (m, 1 H, C*H*-Naphth), 6.45 (d, 1 H, *J* 10.0, C*H*=CPh_2), 7.02–7.06 (m, 1 H, ArH), 7.22–7.29 (m, 8 H, ArH), 7.38–7.44 (m, 5 H, ArH) and 7.50–7.75 (m, 3 H, ArH); δ_C(62.5 MHz; $CDCl_3$) 37.1 (*C*H-Naphth), 42.4 ($CH_2CO_2CH_3$), 51.5 (CO_2CH_3), 123.2 (Arom CH), 124.0 (Arom CH), 125.5 (Arom CH), 125.5 (Arom CH), 125.9 (Arom CH), 127.1 (Arom CH), 127.2 (Arom CH), 127.3 (Arom CH), 127.4 (Arom CH), 127.5 (Arom CH), 128.1 (Arom CH), 128.8 (Arom CH), 129.7 (Arom CH), 130.3 (*C*H=CPh_2), 134.2 (Ph_2C=CH), 139.1 (Arom C), 140.0 (Arom C), 142.0 (Arom C), 142.5 (Arom C) and 172.1 (C=O); *m/z* (EI) 392 (M^+, 29%), 319 (100), 241 (80), 191 (90) and 165 (60).

Typical procedure for conversion of the mono-esters 30a–d into the corresponding mono-acids 31a–d

A solution of the appropriate mono-ester **30a–d** (1 mmol) and sodium hydroxide (5 mmol) in MeOH (5 cm^3)–water (4 cm^3) was heated to reflux with TLC monitoring (light petroleum–ether, 3:1) which indicated when all of the starting material had been consumed (2 h). The reaction mixture was then acidified (1 M HCl) and the aqueous phase separated and extracted with dichloromethane (3 × 30 cm^3). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield a brown oil, purification of which by 'flash' column chromatography (eluent, light petroleum–ether, 2:1) gave the title compounds as described.

3-Methyl-5,5-diphenylpent-4-enoic acid 31a. A colourless oil (95%) (Found: M^+, 266.1306. $C_{18}H_{18}O_2$ requires M^+, 266.1306); $[\alpha]_D^{20}$ −62.4 (*c* 0.82, $CHCl_3$); ν_{max}/cm^{-1} 3100 (CO_2H), 2999, 1708 (C=O), 1444 and 1296; δ_H(400 MHz; $CDCl_3$) 1.09 (d, 3 H, *J* 6.7, CH_3), 2.29–2.41 (m, 2 H, CH_2CO_2H), 2.79–2.87 (m, 1 H, $CHCH_3$), 5.89 (d, 1 H, *J* 10.1, C*H*=CPh_2), 7.13–7.35 (m, 10 H, ArH) and 8.70–10.0 (br s, 1 H, CO_2H); δ_C(100 MHz; $CDCl_3$) 20.9 (CH_3), 30.9 ($CHCH_3$), 41.7 (CH_2CO_2H), 127.1 (Arom CH), 127.1 (Arom CH), 127.3 (Arom CH), 127.9 (Arom CH), 128.3 (Arom CH), 129.6 (Arom CH), 132.8 (*C*H=CPh_2), 139.9 (Ph_2C=CH), 141.7 (Arom C), 142.2 (Arom C) and 178.4 (C=O);

m/z (EI) 266 (M^+, 18%), 206 (100), 191 (40), 129 (65) and 69 (60).

3-Phenyl-5,5-diphenylpent-4-enoic acid 31b. A colourless solid (98%), mp 129–131 °C (Found: M^+, 328.1463. $C_{23}H_{20}O_2$ requires M^+, 328.1463); $[\alpha]_D^{20}$ −121.8 (*c* 0.78, $CHCl_3$); ν_{max}/cm^{-1} 3054 (CO_2H), 2987, 1709 (C=O) and 1265; δ_H(400 MHz; $CDCl_3$) 2.73 (d, 2 H, *J* 7.2, C$H_2$$CO_2H$), 3.90–3.96 (m, 1 H, C*H*Ph), 6.22 (d, 1 H, *J* 10.4, C*H*=CPh_2), 7.05–7.33 (m, 15 H, ArH) and 9.0–10.1 (br s, 1 H, CO_2H); δ_C(100 MHz; $CDCl_3$) 41.6 (*C*HPh), 41.7 (*C*H_2CO_2H), 126.6 (Arom CH), 127.2 (Arom CH), 127.3 (Arom CH), 127.4 (Arom CH), 128.1 (Arom CH), 128.3 (Arom CH), 128.4 (Arom CH), 128.7 (Arom CH), 129.7 (Arom CH), 130.1 (*C*H=CPh_2), 139.5 (Ph_2C=CH), 142.0 (Arom C), 142.7 (Arom C), 143.2 (Arom C) and 177.2 (C=O); *m/z* (EI) 328 (M^+, 7%), 268 (100) and 191 (89).

5,5-Diphenyl-3-(2,4,6-trimethylphenyl)pent-4-enoic acid 31c. A colourless solid (98%), mp 136–138 °C (Found: M^+, 370.1932. $C_{26}H_{26}O_2$ requires M^+, 370.1932); $[\alpha]_D^{20}$ +160.0 (*c* 0.90, $CHCl_3$); ν_{max}/cm^{-1} 3058 (CO_2H), 2921, 1768 (C=O) and 1265; δ_H(400 MHz; $CDCl_3$) 2.03 (br s, 6 H, 2 × ArCH_3), 2.19 (s, 3 H, ArCH_3), 2.59 (dd, 1 H, *J* 5.1 and 15.0, C*H*HCO_2H), 2.88 (dd, 1 H, *J* 10.0 and 15.0, CH*H*CO_2H), 4.33–4.39 (m, 1 H, C*H*-Mes), 6.55 (d, 1 H, *J* 8.6, C*H*=CPh_2), 6.87 (s, 2 H, ArH), 6.91–6.93 (m, 2 H, ArH), 7.17–7.24 (m, 8 H, ArH) and 9.0–10.0 (br s, 1 H, CO_2H); δ_C(100 MHz; $CDCl_3$) 20.6 (Ar*C*H_3), 21.2 (2 × Ar*C*H_3), 37.3 (*C*H-Mes), 39.4 (*C*H_2CO_2H), 126.9 (Arom CH), 126.9 (Arom CH), 127.1 (Arom CH), 127.9 (Arom CH), 128.1 (Arom CH), 128.3 (Arom CH), 129.5 (Arom CH), 129.9 (Arom CH), 130.4 (*C*H=CPh_2), 135.5 (Ph_2C=CH), 136.0 (Arom C), 137.5 (Arom C), 139.7 (Arom C), 141.9 (Arom C), 143.0 (Arom C) and 178.2 (C=O); *m/z* (EI) 370 (M^+, 35%), 311 (100), 191 (40) and 91 (75).

5,5-Diphenyl-3-(1-naphthyl)pent-4-enoic acid 31d. A colourless solid (98%), mp 85–87 °C (Found: M^+, 378.1619. $C_{27}H_{22}O_2$ requires M^+, 378.1620); $[\alpha]_D^{20}$ +146.8 (*c* 0.94, $CHCl_3$); ν_{max}/cm^{-1} 3000 (CO_2H), 2592, 1735 (C=O) and 1252; δ_H(400 MHz, $CDCl_3$) 2.79 (dd, 1 H, *J* 8.7 and 15.1, C*H*HCO_2H), 2.91 (dd, 1 H, *J* 5.9 and 15.1, CH*H*CO_2H), 4.75–4.81 (m, 1 H, C*H*-Naphth), 6.40 (d, 1 H, *J* 10.1, C*H*=CPh_2), 6.98–7.01 (m, 2 H, ArH), 7.18–7.25 (m, 8 H, ArH), 7.37–7.47 (m, 4 H, ArH), 7.63–7.69 (m, 2 H, ArH), 7.74–7.77 (m, 1 H, ArH) and 9.0–10.0 (br s, 1 H, CO_2H); δ_C(100 MHz; $CDCl_3$) 37.4 (*C*H-Naphth), 42.4 (*C*H_2CO_2H), 123.6 (Arom CH), 124.4 (Arom CH), 125.9 (Arom CH), 126.4 (Arom CH), 127.7 (Arom CH), 127.8 (Arom CH), 127.9 (Arom CH), 128.5 (Arom CH), 128.6 (Arom CH), 129.2 (Arom CH), 130.1 (Arom CH), 130.5 (*C*H=CPh_2), 131.1 (Ph_2C=CH), 134.5 (Arom C), 139.8 (Arom C), 140.2 (Arom C), 142.6 (Arom C), 143.5 (Arom C) and 178.1 (C=O); *m/z* (EI) 378 (M^+, 47%), 319 (92), 241 (75), 191 (70) and 167 (100).

Typical procedure for the modified Curtius reaction

A solution of **31b** (90 mg, 0.27 mmol), triethylamine (30 mg, 0.30 mmol) and diphenylphosphoryl azide (83 mg, 0.30 mmol) in *tert*-butyl alcohol (3 cm^3) was refluxed for 16 h, cooled and then poured into saturated aqueous sodium hydrogen carbonate (10 cm^3). The solution was extracted with dichloromethane (3 × 15 cm^3) and the combined extracts were washed with water (20 cm^3) and brine (30 cm^3), dried ($MgSO_4$), filtered and evaporated to yield a brown oil. Purification of this by 'flash' column chromatography with light petroleum–ether (5:1) gave compound **32b**.

***N*-(*tert*-Butoxycarbonyl)-2-methyl-4,4-diphenylbut-3-enamine 32a.** A colourless solid (52%), mp 88–90 °C (Found: M^+, 337.2042. $C_{22}H_{27}NO_2$ requires M^+, 337.2042); $[\alpha]_D^{20}$ −58.3 (*c* 0.7, $CHCl_3$); ν_{max}/cm^{-1} 3359 (NH), 2965, 1712 (C=O), 1249 and 1172; δ_H(400 MHz; $CDCl_3$) 1.01 (d, 3 H, *J* 6.6, CH_3), 1.41 [s, 9 H, $NHCO_2C(CH_3)_3$], 2.44–2.49 (m, 1 H, C*H*CH_3), 2.97–3.03 (m, 1 H, C*H*HNHBoc), 3.03–3.15 (m, 1 H, CH*H*NHBoc), 4.45 (br s, 1 H, N*H*Boc), 5.84 (d, 1 H, *J* 10.2, C*H*=CPh_2) and 7.16–7.38 (m, 10 H, ArH); δ_C(100 MHz; $CDCl_3$) 18.5 (CH_3), 28.4 [$C(CH_3)_3$], 35.2 (*C*HCH_3), 46.5 (*C*H_2NHBoc), 79.0 [*C*$(CH_3)_3$], 127.0 (Arom CH), 127.1 (Arom CH), 127.2 (Arom CH), 128.1 (Arom CH), 128.4 (Arom CH), 129.7 (Arom CH), 132.5 (*C*H=*C*Ph_2), 140.1 (Ph_2C=CH), 142.1 (Arom C), 142.7 (Arom C) and 155.9 (C=O); *m/z* (EI) 337 (M^+, 0.3%), 281 (20), 207 (100), 129 (45) and 57 (90).

***N*-(*tert*-Butoxycarbonyl)-2,4,4-triphenylbut-3-enamine 32b.** A colourless solid (61%), mp 118–120 °C (Found: M^+, 399.2198. $C_{27}H_{29}NO_2$ requires M^+, 399.2198); $[\alpha]_D^{20}$ −87.2 (*c* 0.86, $CHCl_3$); ν_{max}/cm^{-1} 3443 (NH), 3054, 2984, 1711 (C=O), 1265 and 1170; δ_H(400 MHz; $CDCl_3$) 1.39 [s, 9 H, $NHCO_2(CH_3)_3$], 3.38–3.48 (m, 2 H, CH_2NHBoc), 3.55–3.59 (m, 1 H, C*H*Ph), 4.44 (br s, 1 H, N*H*Boc), 6.25 (d, 1 H, *J* 10.3, C*H*=CPh_2) and 7.12–7.36 (m, 15 H, ArH); δ_C(100 MHz; $CDCl_3$) 28.4 [$C(CH_3)_3$], 46.0 (*C*H_2NHBoc), 46.3 (*C*HPh), 79.2 [*C*$(CH_3)_3$], 126.7 (Arom CH), 127.2 (Arom CH), 127.3 (Arom CH), 127.4 (Arom CH), 127.5 (Arom CH), 128.1 (Arom CH), 128.3 (Arom CH), 128.8 (Arom CH), 129.4 (Arom CH), 129.8 (*C*H=CPh_2), 139.8 (Ph_2C=CH), 142.1 (Arom C), 142.1 (Arom C), 143.6 (Arom C) and 155.8 (C=O); *m/z* (EI) 399 (M^+, 10%), 269 (100) and 191 (62).

***N*-(*tert*-Butoxycarbonyl)-2-(2,4,6-trimethylphenyl)but-3-enamine 32c.** A colourless oil (49%) (Found: M^+, 441.2667. $C_{30}H_{35}NO_2$ requires M^+, 441.2667); $[\alpha]_D^{20}$ +155.1 (*c* 0.25, $CHCl_3$); ν_{max}/cm^{-1} 3362 (NH), 2975, 1712 (C=O) and 1265; δ_H(400 MHz; $CDCl_3$) 1.46 [s, 9 H, $NHCO_2C(CH_3)_3$], 2.07 (br s, 6 H, 2 × ArCH_3), 2.24 (s, 3 H, ArCH_3), 3.25–3.29 (m, 1 H, C*H*HNHBoc), 3.48–3.54 (m, 1 H, CH*H*NHBoc), 4.00–4.06 (m, 1 H, C*H*Mes), 4.55 (br s, 1 H, N*H*Boc), 6.65 (d, 1 H, *J* 10.0, C*H*=CPh_2), 6.75 (s, 2 H, ArH), 6.95–6.97 (m, 2 H, ArH) and 7.23–7.29 (m, 8 H, ArH); δ_C(100 MHz; $CDCl_3$) 20.6 (Ar*C*H_3), 21.3 (2 × Ar*C*H_3), 28.4 [$C(CH_3)_3$], 42.1 (*C*HMes), 43.6 (*C*H_2NHBoc), 79.2 [*C*$(CH_3)_3$], 126.9 (Arom CH), 127.1 (Arom CH), 128.1 (Arom CH), 128.2 (Arom CH), 129.7 (Arom CH), 129.8 (Arom CH), 129.9 (Arom CH), 129.9 (*C*H=CPh_2), 135.6 (Ph_2C=CH), 135.9 (Arom C), 136.6 (Arom C), 139.8 (Arom C), 142.0 (Arom C), 143.7 (Arom C) and 155.9 (C=O); *m/z* (EI) 441 (M^+, 0.2%), 311 (100), 191 (30) and 57 (50).

***N*-(*tert*-Butoxycarbonyl)-2-(1-naphthyl)but-3-enamine 32d.** A colourless oil (52%) (Found: M^+, 450.2433. $C_{31}H_{31}NO_2$ requires M^+, 450.2433); $[\alpha]_D^{20}$ +118.2 (*c* 0.44, $CHCl_3$); ν_{max}/cm^{-1} 3446 (NH), 3054, 2983, 2932, 1710 (C=O) and 1265; δ_H(250 MHz; $CDCl_3$) 1.39 [s, 9 H, $NHCO_2C(CH_3)_3$], 3.43–3.58 (m, 2 H, CH_2NHBoc), 4.47–4.54 (m, 2 H, C*H*Naphth and N*H*Boc), 6.45 (d, 1 H, *J* 10.1, C*H*=CPh_2), 7.06–7.23 (m, 2 H, ArH), 7.25–7.30 (m, 8 H, ArH), 7.36–7.48 (m, 4 H, ArH) and 7.66–7.85 (m, 3 H, ArH); δ_C(62.5 MHz; $CDCl_3$) 28.3 [$C(CH_3)_3$], 41.0 (*C*HNaphth), 46.1 (*C*H_2NHBoc), 79.1 [*C*$(CH_3)_3$], 123.2 (Arom CH), 124.4 (Arom CH), 125.5 (Arom CH), 125.9 (Arom CH), 127.2 (Arom CH), 127.2 (Arom CH), 127.5 (Arom CH), 128.0 (Arom CH), 128.2 (Arom CH), 128.7 (Arom CH), 129.5 (*C*H=CPh_2), 129.8 (Arom CH), 134.2 (Ph_2C=CH), 138.2 (Arom C), 138.2 (Arom C), 139.3 (Arom C), 139.3 (Arom C) and 153.5 (C=O); *m/z* (EI) 450 (M^+, 0.2%), 393 (12), 319 (100) and 241 (40).

Typical procedure for the conversion of the alkenes 32a–d into the corresponding carboxylic acids 33a–d

To a solution of **32b** (50 mg, 0.125 mmol) and sodium metaperiodate (117 mg, 0.513 mmol) in the solvent system CCl_4 (1 cm^3), MeCN (1 cm^3) and water (1.5 cm^3) was added ruthenium trichloride hydrate (0.57 mg, 0.0027 mmol). The reaction mixture was stirred at 40 °C for 2 h after which it was diluted with water (10 cm^3); the aqueous layer was then separated and extracted with dichloromethane (3 × 15 cm^3). The combined organic layer and extracts were washed with brine (30 cm^3), dried ($MgSO_4$), filtered and evaporated to yield a dark brown oil. Purification of this by 'flash' column chromatography, eluting with light petroleum–ethyl acetate (1:1) gave compound **33b**.

3-*tert*-Butoxycarbonylamino-2-methylpropanoic acid 33a. A

colourless solid (60%), mp 81–83 °C (Found: M^+, 203.1157. $C_9H_{17}NO_4$ requires M^+, 203.1157); $[\alpha]_D^{20}$ +63.1 (*c* 0.25, $CHCl_3$); ν_{max}/cm^{-1} 3343 (NH), 3300–3000 (CO_2H), 2938, 1712 (C=O acid), 1698 (C=O carbamate) and 1252; δ_H(400 MHz; $CDCl_3$) 1.20 (d, 3 H, *J* 6.9, CH_3), 1.44 [s, 9 H, $NHCO_2C(CH_3)_3$], 2.69 (br s, 1 H, $CHCH_3$), 3.32 (m, 2 H, CH_2NHBoc), 5.07 and 6.35 (br s, 1 H, NHBoc) and 9.79 (br s, 1 H, CO_2H); δ_C(100 MHz; $CDCl_3$) (some of the peaks were doubled up, probably due to the presence of rotamers) 14.6 (CH_3), 28.1 and 28.3 [$C(CH_3)_3$], 40.0 and 40.1 ($CHCH_3$), 42.8 and 44.2 (CH_2NHBoc), 79.6 and 81.1 [$C(CH_3)_3$], 156.1 and 157.7 (C=O carbamate) and 179.5 and 180.6 (C=O acid); *m/z* (EI) 203 (M^+, 0.2%), 148 (70), 130 (40) and 57 (100).

3-*tert*-Butoxycarbonylamino-2-phenylpropanoic acid 33b. A colourless solid (65%), mp 144–146 °C (Found: M^+, 265.1314. $C_{14}H_{19}NO_4$ requires M^+, 265.1314); $[\alpha]_D^{20}$ +88.2 (*c* 1.25, $CHCl_3$); ν_{max}/cm^{-1} 3448 (NH), 3338–3054 (CO_2H), 2892, 1718 (C=O acid), 1708 (C=O carbamate) and 1264; δ_H(400 MHz; $CDCl_3$) 1.42 [s, 9 H, $NHCO_2C(CH_3)_3$], 3.49 (m, 2 H, CH_2NHBoc), 3.84 (m, 1 H, CHPh), 5.00 and 6.72 (br s, 1 H, NHBoc), 7.09–7.4 (m, 5 H, ArH) and 9.78 (br, 1 H, CO_2H); δ_C(100 MHz; $CDCl_3$) (some of the peaks were doubled up, probably due to the presence of rotamers) 27.8 and 28.4 [$C(CH_3)_3$], 43.2 and 44.7 (CH_2NHBoc), 51.6 and 52.5 (CHPh), 79.8 and 81.4 [$C(CH_3)_3$], 127.8 (Arom CH), 128.1 (Arom CH), 128.9 (Arom CH), 135.9 (Arom C), 155.9 and 158.1 (C=O carbamate), 176.3 and 177.4 (C=O acid); *m/z* (EI) 265 (M^+, 1%), 236 (18), 217 (20), 155 (40), 51 (70) and 28 (100).

3-*tert*-Butoxycarbonylamino-2-(2,4,6-trimethylphenyl)propanoic acid 33c. A colourless solid (63%), mp 160–162 °C (Found: M^+, 307.1784. $C_{17}H_{25}NO_4$ requires M^+, 307.1784); $[\alpha]_D^{20}$ −142.0 (*c* 0.15, $CHCl_3$); ν_{max}/cm^{-1} 3331 (NH), 3400–2976 (CO_2H), 1728 (C=O acid), 1688 (C=O carbamate) and 1251; δ_H(400 MHz, $CDCl_3$) 1.43 [$NHCO_2C(CH_3)_3$], 2.24 (s, 3 H, $ArCH_3$), 2.32 (br s, 6 H, 2 × $ArCH_3$), 3.36–3.40 (m, 1 H, CHNHBoc), 3.63–3.73 (m, 1 H, CHNHBoc), 4.01–4.05 (m, 1 H, CH-Mes), 4.19 and 5.09 (br s, 1 H, NHBoc), 6.85 (s, 2 H, ArH) and 9.0–10.1 (br s, 1 H, CO_2H); δ_C(100 MHz, $CDCl_3$) (some of the peaks were doubled up, probably due to the presence of rotamers) 20.5 ($ArCH_3$), 20.8 (2 × $ArCH_3$), 28.2 and 28.4 [$C(CH_3)_3$], 40.5 and 41.3 (CH_2NHBoc), 46.8 and 48.7 (CH-Mes), 79.6 and 81.3 [$C(CH_3)_3$], 129.9 (2 × Arom CH), 130.4 (Arom C), 130.7 (Arom C), 136.9 (Arom C), 137.0 (Arom C), 155.9 and 157.7 (C=O carbamate) and 177.3 and 178.9 (C=O acid); *m/z* (EI) 307 (M^+, 0.8%), 178 (55), 133 (45) and 57 (100).

3-*tert*-Butoxycarbonylamino-2-(1-naphthyl)propanoic acid 33d. A colourless solid (61%), mp 140–142 °C (Found: M^+, 315.1471. $C_{18}H_{21}NO_4$ requires M^+, 315.1470); $[\alpha]_D^{20}$ −130.0 (*c* 0.5, $CHCl_3$); ν_{max}/cm^{-1} 3400 (NH), 3390–3000 (CO_2H), 2900, 1720 (C=O acid), 1695 (C=O carbamate) and 1265; δ_H(250 MHz; $CDCl_3$) 1.34 [s, 9 H, $NHCO_2C(CH_3)_3$], 3.55–3.60 (m, 2 H, CH_2NHBoc), 4.52–4.56 (m, 1 H, CH-Naphth), 4.70 and 6.50 (br s, 1 H, NHBoc), 7.12–8.21 (m, 7 H, ArH) and 9.0–10.5 (br s, 1 H, CO_2H); δ_C(62.5 MHz; $CDCl_3$) (some of the peaks were doubled up, probably due to the presence of rotamers) 27.9 and 28.3 [$C(CH_3)_3$], 46.1 and 47.5 (CH_2NHBoc), 54.5 and 55.8 (CH-Naphth), 79.4 and 80.6 [$C(CH_3)_3$], 123.1 (Arom CH), 125.3 (Arom CH), 126.1 (Arom CH), 126.3 (Arom CH), 127.7 (Arom CH), 128.7 (Arom CH), 128.9 (Arom CH), 129.1 (Arom C), 134.0 (Arom C), 155.6 and 156.1 (C=O carbamate) and 177.2 and 178.1 (C=O acid); *m/z* (EI) 315 (M^+, 10%), 297 (50), 200 (55) and 57 (100).

3-Amino-2-methylpropanoic acid 34a.[27] The Boc-protected amino acid **33a** (50 mg, 0.246 mmol) was dissolved in a 4.0 M HCl–dioxane solution (8 cm^3) and stirred at room temperature for 4 h. The reaction mixture was then evaporated to dryness and the resulting colourless crystalline solid passed down a DOWEX ion-exchange column (50X8–200 resin) with water (containing 1% ammonia). The fractions which tested positive with ninhydrin were evaporated to dryness to give **34a** (90%) as a colourless solid, mp 182–184 °C (lit.,[27] mp 185–186 °C) (Found: M^+, 103.0633. $C_4H_9NO_2$ requires M^+, 103.0633); $[\alpha]_D^{20}$ −13.5 (*c* 0.5, water); δ_H(400 MHz; D_2O) 1.25 (d, 3 H, *J* 6.0, CH_3CHCO_2H), 2.90 (m, 1 H, $CHCH_3$), 3.12 (m, 1 H, $CHHNH_3^+$) and 3.21 (m, 1 H, $CHHNH_3^+$); δ_C(100 MHz; D_2O) 14.6 (CH_3), 37.4 ($CHCH_3$), 41.6 ($CH_2NH_3^+$) and 177.9 (CO_2H).

3-Amino-2-phenylpropanoic acid 34b.[28] A colourless solid (85%), mp 220–222 °C (lit.,[8] mp 222–224 °C) (Found: M^+, 165.0789. $C_9H_{11}O_2$ requires M^+, 165.0789); $[\alpha]_D^{20}$ −95.0 (*c* 0.18, water) [lit.,[28] $[\alpha]_D^{20}$ −94.0 (*c* 0.20, water]; ν_{max}/cm^{-1} 1660 (C=O); δ_H(400 MHz; D_2O) 3.39 (dd, 1 H, *J* 7.1 and 13.1, $CHHNH_3^+$), 3.62 (dd, 1 H, *J* 7.7 and 13.1, $CHHNH_3^+$), 4.08 (t, 1 H, *J* 7.4, CHPh) and 7.37–7.48 (m, 5 H, ArH); δ_C(100 MHz; D_2O) 43.9 ($CH_2NH_3^+$), 51.6 (CHPh), 130.9 (Arom CH), 131.5 (Arom CH), 132.3 (Arom CH), 137.3 (Arom C) and 177.8 (C=O); *m/z* (EI) 166 (MH^+, 30%), 118 (40), 91 (40) and 30 (100).

Methyl hydrogen 2-(2,4,6-trimethylphenyl)malonate 35. To a vigorously stirred solution of the decarboxylated compound **30c** (754 mg, 1.96 mmol) and sodium periodate (1.72 g, 8.04 mmol) in a solvent mixture of acetonitrile (3 cm^3), carbon tetrachloride (3 cm^3) and water (4.5 cm^3) was added ruthenium trichloride hydrate (8.95 mg, 0.043 mmol). The reaction mixture was stirred until TLC monitoring (light petroleum–ether, 3:1; silica plates stained with bromocresol, green–yellow colouration developed for carboxylic acid functionality) indicated that all of the starting material had been consumed (2 h). The reaction mixture was then diluted with dichloromethane (25 cm^3) and washed with water (20 cm^3). The organic layer was separated, dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield a dark-brown oil. Purification of this by 'flash' column chromatography (eluent, light petroleum–ether, 1:1) gave the title compound (319 mg, 65%) as a pale yellow oil (Found: M^+, 250.1205. $C_{14}H_{18}O_4$ requires M^+, 250.1205); $[\alpha]_D^{20}$ +230.3 (*c* 0.35, $CHCl_3$); ν_{max}/cm^{-1} 3250–2900 (CO_2H), 2956, 1739 (C=O ester), 1708 (C=O acid) and 1167; δ_H(400 MHz; $CDCl_3$) 2.27 (s, 3 H, $ArCH_3$), 2.31 (br s, 6 H, 2 × $ArCH_3$), 2.43 (dd, 1 H, *J* 4.6 and 16.7, $CHHCO_2CH_3$), 3.26 (dd, 1 H, *J* 7.8 and 16.7, $CHHCO_2CH_3$), 3.68 (s, 3 H, CO_2CH_3), 4.68–4.71 (m, 1 H, CHMes) and 6.85 (s, 2 H, ArH); δ_C(100 MHz; $CDCl_3$) 20.5 ($ArCH_3$), 20.8 (2 × $ArCH_3$), 34.9 ($CH_2CO_2CH_3$), 41.3 (CO_2CH_3), 52.0 (CH-Mes), 129.9 (Arom CH), 129.9 (Arom CH), 132.2 (Arom C), 136.4 (Arom C), 137.1 (Arom C), 172.4 (C=O ester) and 179.3 (C=O acid); *m/z* (EI) 250 (M^+, 10%), 163 (40), 133 (100) and 119 (37).

Methyl 3-*tert*-butoxycarbonylamino-3-(2,4,6-trimethylphenyl)propanoate 36. A solution of the carboxylic acid **35** (176 mg, 0.70 mmol), triethylamine (78 mg, 0.78 mmol) and diphenylphosphoryl azide (213 mg, 0.78 mmol) in *tert*-butyl alcohol (1.5 cm^3) was refluxed under nitrogen until TLC analysis (light petroleum–ether, 3:1) indicated that all of the starting material had been consumed (16 h). The reaction mixture was then cooled to room temperature and poured onto saturated aqueous sodium hydrogen carbonate (30 cm^3). The resulting milky white precipitate was extracted with dichloromethane (3 × 30 cm^3) and the combined organic extracts were washed with brine (50 cm^3), dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield a brown oil. Purification of this by 'flash' column chromatography (eluent, light petroleum–ether, 3:1) gave the title compound (113 mg, 50%) as a colourless oil (Found: M^+, 321.1939. $C_{18}H_{27}NO_4$ requires M^+, 321.1940); $[\alpha]_D^{20}$ +115.0 (*c* 0.25, $CHCl_3$); ν_{max}/cm^{-1} 3350 (NH), 3071, 1737 (C=O ester), 1711 (C=O carbamate) and 1227; δ_H(250 MHz; $CDCl_3$) 1.38 [s, 9 H, $NHCO_2C(CH_3)_3$], 2.22 (br s, 6 H, 2 × $ArCH_3$), 2.27 (s, 3 H, $ArCH_3$), 2.75 (dd, 1 H, *J* 4.8 and 16.7, $CHHCO_2CH_3$), 2.92 (dd, 1 H, *J* 7.6 and 16.7, $CHHCO_2CH_3$), 3.64 (s, 3 H, CO_2CH_3), 4.96 (m, 1 H, CH-Mes), 5.50 (br s, 1 H, NHBoc) and 6.80 (s, 2 H, ArH); δ_C(62.5 MHz; $CDCl_3$) 20.4 ($ArCH_3$), 20.8 (2 × $ArCH_3$), 28.3 [$C(CH_3)_3$], 34.9 ($CH_2CO_2CH_3$), 41.0 (CO_2CH_3), 46.0 (CH-Mes), 128.6 (Arom CH), 129.0 (Arom CH), 136.2 (Arom C),

137.0 (Arom C), 137.5 (Arom C), 150.4 (C=O carbamate) and 170.2 (C=O ester); *m/z* (EI) 321 (M^+, 0.6%), 233 (20), 170 (30), 94 (40) and 65 (65).

3-*tert*-Butoxycarbonylamino-3-(2,4,6-trimethylphenyl)-propanoic acid 37. A solution of the mono-ester **36** (87 mg, 0.27 mmol) and sodium hydroxide (54 mg, 1.35 mmol) in MeOH (1 cm^3)–water (0.75 cm^3) was heated to reflux until TLC analysis (light petroleum–ether, 3:1) indicated that all of the starting material had been consumed (2 h). The reaction mixture was then extracted with dichloromethane (3 × 30 cm^3). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield a brown oil. Purification of this by 'flash' column chromatography (eluent, light petroleum–ether, 1:1) gave the title compound (76 mg, 91%) as a colourless solid, mp 158–160 °C (Found: M^+, 307.1783. $C_{17}H_{25}NO_4$ requires M^+, 307.1784); $[\alpha]_D^{20}$ +100.5 (*c* 0.43, $CHCl_3$); ν_{max}/cm^{-1} 3300 (NH), 3300–2900 (CO_2H), 2931, 1700 (C=O acid), 1690 (C=O carbamate) and 1252; δ_H(400 MHz; $CDCl_3$) 1.43 [s, 9 H, $NHCO_2C(CH_3)_3$], 2.24 (s, 3 H, $ArCH_3$), 2.34 (br s, 6 H, 2 × $ArCH_3$), 2.65 (dd, 1 H, *J* 5.1 and 15.0, $CHHCO_2H$), 2.92 (dd, 1 H, *J* 10.1 and 15.0, $CHHCO_2H$), 4.39–4.45 (m, 1 H, C*H*-Mes), 5.0 (br s, 1 H, N*H*Boc), 6.85 (s, 2 H, ArH) and 9.0–10.0 (br s, 1 H, CO_2H); δ_C(100 MHz; $CDCl_3$) 20.5 ($ArCH_3$), 20.8 (2 × $ArCH_3$), 28.2 and 28.4 [$C(CH_3)_3$], 40.5 and 41.3 (CH_2CO_2H), 46.9 and 48.7 (*C*H-Mes), 79.6 and 81.3 [$C(CH_3)_3$], 129.9 (Arom CH), 130.3 (Arom CH), 136.8 (Arom C), 137.0 (Arom C), 155.8 and 157.7 (C=O carbamate) and 177.3 and 178.9 (C=O acid); *m/z* (EI) 307 (M^+, 2%), 178 (55), 133 (50) and 57 (100).

Acknowledgements

We thank the EPSRC for an earmarked QUOTA (to J. F. B.), and the EPSRC, DTI and Lilly Research Centre for a studentship (to R. J.) under the LINK Asymmetric Synthesis Programme.

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Paper 6/06586D
Received 25*th September* 1996
Accepted 4*th December* 1996