Reaction of organolead triacetates with 4-ethoxycarbonyl-2-methyl-4,5-dihydro-1,3-oxazol-5-one. The synthesis of α-aryl- and α-vinyl-*N*-acetylglycines and their ethyl esters and their enzymic resolution

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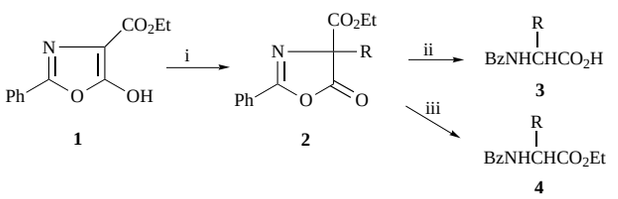
4-Ethoxycarbonyl-2-methyl-4,5-dihydro-1,3-oxazol-5-one 7, which may be readily obtained from diethyl acetamidomalonate, undergoes high-yielding arylation and vinylation at the 4-position with organolead triacetates to give compounds which may be hydrolysed to give either the α-aryl- or α-vinyl-*N*-acetylglycine or the corresponding ethyl ester. The kinetic resolution of a number of these derivatives by enzymic hydrolysis of either the amide or ester function has been demonstrated.

In a recent paper[1] we reported that 4-ethoxycarbonyl-2-phenyl-4,5-dihydro-1,3-oxazol-5-one, which in chloroform exists predominantly as the enol **1**, undergoes ready arylation and vinylation at the 4-position with aryllead and vinyllead triacetates to give substituted oxazolones **2**. These compounds undergo hydrolysis and decarboxylation under very mild conditions to give either α-substituted *N*-benzoylglycines **3** or the corresponding ethyl esters **4** (Scheme 1).



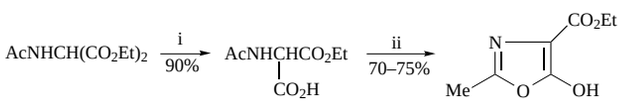
1 **2** **3** **4**

Scheme 1 *Reagents and conditions:* i, $RPb(OAc)_3$; ii, NaOH, EtOH, H_2O, then H_3O^+; iii, H_2O, heat

Having established the potential of the above route to efficiently access α-arylglycine and α-vinylglycine derivatives, compounds in which there is considerable interest for their therapeutic usefulness,[2–5] we addressed the possibility of employing such a route to produce the *N*-acetyl analogues of **3** and **4**. With the former compounds there was the potential to carry out an enantioselective hydrolysis with an acylase enzyme such as porcine kidney acylase (PKA) or *Aspergillus* acylase (AA),[6,7] and so develop a simple route to a variety of natural and unnatural amino acids. In a preliminary communication[8] we established the success of this approach and we now report this work in detail.

Results and discussion

The synthesis of the required 2-methyloxazolone **7**, which like the 2-phenyl analogue **1** exists in chloroform–pyridine as the enol, was achieved by a route similar to that used to obtain compound **1**. The starting point is commercially available diethyl acetamidomalonate **5**, which on partial hydrolysis yields the monoethyl malonate **6** (Scheme 2). The cyclodehydration of compound **6** to give the oxazolone **7** was only achieved in acceptable yield (70–75%) by employing 2.2 equiv. of trifluoroacetic anhydride in diethyl ether. This afforded a solution of the oxazolone enol trifluoroacetate, which was hydrolysed by the careful addition of water (1.1 equiv.) at 0 °C, resulting in precipitation of the sparingly diethyl ether soluble, but highly moisture sensitive, enol form of **7**.†



5 **6** **7**

Scheme 2 *Reagents and conditions:* i, KOH (1.0 equiv.), EtOH, H_2O, room temp., then H_3O^+; ii, $(CF_3CO)_2O$, Et_2O, N_2, room temp., then H_2O, 0 °C

Arylation and vinylation

The 2-methyloxazolone **7** reacted rapidly with phenyllead triacetate **8a** under our standard chloroform–pyridine conditions to give the 4-phenylated oxazolone **9a** in almost quantitative yield (by ^{1}H NMR spectroscopy) after less than 1 h at 40 °C. The oxazolone **9a** proved to be too sensitive to hydrolytic ring opening to be readily isolated, and therefore the crude reaction product was hydrolysed directly, with concomitant decarboxylation, to the *N*-acetylglycine or its ethyl ester (Scheme 3); treatment of the crude oxazolone **9a** with alkali at 40 °C produced *N*-acetyl-α-phenylglycine **10a** in an overall yield of 93%, while simply warming it with water led to an identical yield of *N*-acetyl-α-phenylglycine ethyl ester **11a** (Table 1, entry 1).

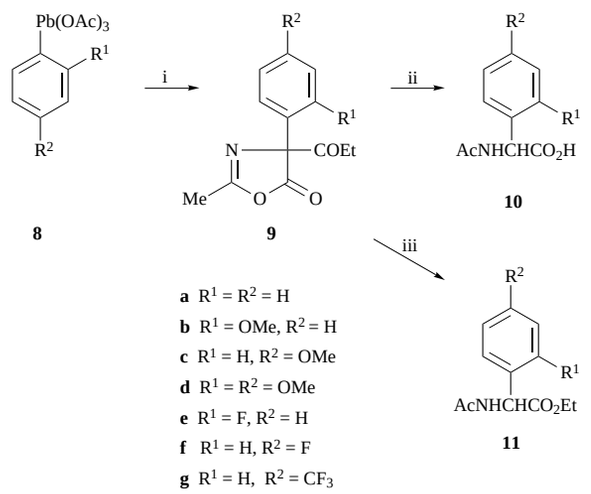
The route outlined in Scheme 3 was shown to be generally applicable to a range of aryllead triacetates, and as can be seen from the results recorded in Table 1 the reaction of oxazolone **7** with the aryllead triacetates **8b**–**g** produced the corresponding *N*-acetyl-α-arylglycines **10b**–**g** in similar high yields to that obtained with phenyllead triacetate **8a**. In accord with our previous experience with the arylation of other carbon nucleophiles, the yields of arylated products were not noticeably affected by the nature and position of substituents in the aromatic ring; the yields obtained with *p*-methoxyphenyllead triacetate **8c** (entry 3) and *p*-trifluoromethylphenyllead triacetate **8g** (entry 7) were very similar. Only one other glycine ethyl ester derivative, namely *N*-acetyl-2,4-dimethoxyphenylglycine ethyl ester **11d** (entry 4), was produced in this work, but clearly, from the high yields obtained in the two cases examined, the method

† This material must be washed free of trifluoroacetic acid with a large volume of dry diethyl ether before being stored in an anhydrous atmosphere.

Table 1 Yields of *N*-acetyl-α-substituted glycines and their ethyl esters obtained by reaction of the oxazolone **7** with aryllead and vinyllead triacetates and subsequent hydrolysis of the 4-substituted 4-ethoxycarbonyl-2-methyl-4,5-dihydro-1,3-oxazol-5-ones produced

		Product (yield, %)[a]	
Entry	$RPb(OAc)_3$	$AcNHCHRCO_2H$	$AcNHCHRCO_2Et$
1	**8a**	**10a** (93)	**11a** (93)
2	**8b**	**10b** (81)	
3	**8c**	**10c** (86)	
4	**8d**	**10d** (82)	**11d** (87)
5	**8e**	**10e** (90)	
6	**8f**[b]	**10f** (83)	
7	**8g**	**10g** (92)	
8	**13a**[c]	**15a** (60)	**14a** (62)
9	**13b**[c]		**14b** (63)
10	**13c**[c]		**14c** (60)
11	**13d**[c]		**14d** (44)

[a] Yields are for pure material based on compound **7**. [b] *p*-$FC_6H_4Pb(OAc)_3$ **8f** was produced *in situ* by B–Pb exchange. [c] The vinyllead triacetates were produced *in situ* by Sn–Pb exchange



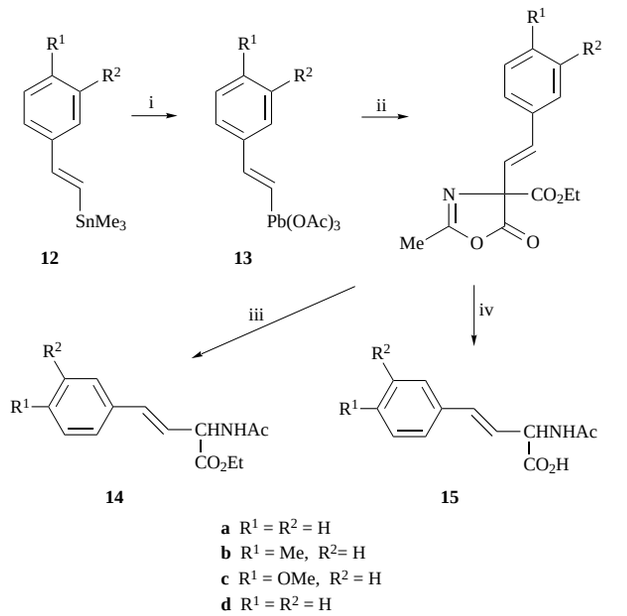
Scheme 3 *Reagents and conditions:* i, $CHCl_3$, pyridine, 40 °C; ii, NaOH, EtOH, H_2O, then H_3O^+; iii, H_2O, 100 °C

provides an efficient and general high-yielding route to such compounds.

The oxazolone **7** also behaved like the 2-phenyl analogue **1** in its reaction with a number of vinyllead triacetates. The study has been confined so far to (*E*)-styryllead triacetate **13a** and its three derivatives **13b–d**, which were generated from the corresponding trimethyl(vinyl)stannanes **12a–d**, respectively, as outlined in Scheme 4 and previously described by us.[1] In all cases the oxazolone **7** reacted rapidly to give the 4-vinylated oxazolones (by ^{1}H NMR spectroscopy) which, on hydrolysis in water, produced the *N*-acetyl-α-vinylglycine ethyl esters **14a–d**, respectively, in moderate yield (Table 1, entries 8–11). Alkaline hydrolysis to the corresponding *N*-acetyl-α-vinylglycine **15** is also possible; however, this route was only employed to obtain *N*-acetyl-α-[(*E*)-styryl]glycine **15a** to examine its reactivity with the acylase enzyme preparations.

Enzymic resolution

In a major study and review of the scope of the hydrolysis of α-substituted *N*-acyl glycines by commercially available acylase 1 enzymes from porcine kidney (PKA) and *Aspergillus* species (AA), Whitesides[7] stated that *N*-acetyl-α-phenylglycine **10a** was accepted as a substrate by AA, but its acceptance by PKA was only fair. The percentage enantiomeric excesses achieved for the recovered L-amino acid and the *N*-acetyl D-amino acid were not recorded. However, Polish workers had previously reported[9] that immobilized PKA could be employed in a potentially useful industrial system to produce *N*-acetyl-D-α-phenylglycine (D-**10a**) and *N*-acetyl-D-α-(*p*-hydroxyphenyl)glycine in high optical purity from the corresponding racemic mixtures. Of the other *N*-acetyl-α-arylglycines produced in our study, only the α-*p*-methoxyphenyl compound **10c** has been reported[10] to have been resolved by use of an acylase enzyme.



Scheme 4 *Reagents and conditions*: i, LTA, 1% HOAc, $CHCl_3$, room temp., 2–3 min; ii, **7**, $CHCl_3$, pyridine; iii, EtOH, H_2O, < 40 °C; iv, NaOH, EtOH, H_2O, reflux, then H_3O^+

In view of the general nature of our route to *N*-acetyl-α-arylglycines and in light of the great interest in the synthesis of potentially useful unnatural and rarely occurring α-amino acids in homochiral form,[7,11–13] we decided to examine the effect of substitution in the aromatic ring on the efficiency of the enzyme-catalysed hydrolysis. We conducted initial rate studies for the *N*-acetyl-α-arylglycines **10a–g** with *N*-acetyl-DL-methionine as a standard under the same conditions as outlined by Whitesides.[7] In contrast to their brief statement concerning the hydrolysis of *N*-acetyl-α-phenylglycine **10a**, we found it to be more reactive to PKA than to AA, and this applied generally to the other *N*-acetyl-α-arylglycines which were accepted by PKA and AA. With some substrates, Whitesides found[7] that Co^{II} ions accelerated the rate of enzymic hydrolysis and its inclusion was examined in the present work. In the case of compound **10a** in the presence of PKA there was a small rate enhancement, and since no suppression of reactivity was observed for the other substrates, $CoCl_2$ was included routinely in the preparative resolutions reported below. From the initial rate studies with PKA, the order of reactivity of the *N*-acetyl-α-arylglycines with added $CoCl_2$ relative to *N*-acetyl-DL-methionine was as follows: phenyl (**10a**) > *p*-methoxyphenyl **10c** > *o*-fluorophenyl **10e**, *p*-trifluoromethylphenyl **10g** > *p*-fluorophenyl **10f**. The rate of hydrolysis of compound **10a** was approximately 25% of that of the standard, while the other four compounds which were hydrolysed at a synthetically useful rate showed activities of less than 5% of that of *N*-acetylmethionine.

From the results presented here, it is clear that certain *N*-acetyl-α-arylglycines will not be resolvable by this method, since neither PKA nor AA was active towards the two compounds containing *o*-methoxy groups, *N*-acetyl-α-(*o*-methoxyphenyl)glycine **10b** and *N*-acetyl-α-(2,4-dimethoxyphenyl)-glycine **10d**. In contrast, compound **10e** with the much smaller *o*-fluoro group was accepted by PKA. We also examined the possibility of resolving *N*-acetyl-α-[(*E*)-styryl]glycine **15a** by employing the acylase enzyme preparations; however, both

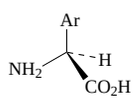
Table 2 Enzymic resolution of some α-substituted *N*-acetylglycines by porcine kidney acylase (PKA) and of their ethyl esters by the esterase subtilisin Carlsberg[a,b]

		PKA		Subtilisin Carlsberg	
Entry	DL-Glycine derivative	L-Amino acid (% yield, % ee)	D-Amido acid (% yield, % ee)	L-Amido acid (% yield, % ee)	D-Amido ester (% yield, % ee)
1	**10a**	**16** (89, 99)	D-**10a** (94, 95)		
2	**10g**	**17** (86, 94)	D-**10g** (100, 95)		
3	**11a**			L-**10a** (93, 97)	D-**11a** (100, 91)
4	**11d**			L-**10d** (89, 90)	D-**11d** (101, 95)
5	**14a**			L-**15a** (100, 82)	D-**14a** (95, 93)

[a] Yields are for isolated material. [b] Percentage ee was determined by GC on a Chirasil-Val-L column except for entry 5 where ^{1}H NMR spectroscopy with a chiral shift reagent was employed

PKA and AA showed only very slight activity towards this substrate.

Preparative resolutions were carried out for the phenyl derivative **10a** and the trifluoromethylphenyl compound **10g**, and as can be seen from the results listed in Table 2 (entries 1 and 2), both the yields and enantiomeric excesses obtained for L-α-phenylglycine and L-α-(*p*-trifluoromethylphenyl)glycine were very good. In both cases the recovered *N*-acetyl-D-α-arylglycines were obtained in high yield and with good optical purity (95% ee).



16 Ar = Ph
17 Ar = *p*-$CF_3C_6H_4$

Since our method also provided a simple and efficient route to the ethyl esters of α-aryl- and α-vinyl-*N*-acetylglycines we explored the possibility of employing an esterase to effect the resolution of those compounds which were not accepted by the acylase enzymes. A report[11] of the successful resolution of a number of *N*-acetyl-α-arylglycine methyl esters by the proteolytic enzyme subtilisin led us to explore a similar approach. We examined the hydrolysis of *N*-acetyl-α-phenylglycine ethyl ester **11a** (Table 2, entry 3), *N*-acetyl-α-(2,4-dimethoxyphenyl)glycine ethyl ester **11d** (Table 2, entry 4) and *N*-acetyl-α-[(*E*)-styryl]-glycine ethyl ester **14a** (Table 2, entry 5) with the enzyme preparation subtilisin Carlsberg, and in all cases obtained good yields and high enantiomeric excesses of the *N*-acetyl L-amino acids and *N*-acetyl D-amino acid ethyl esters.

Experimental

Melting points were determined on a Kofler hot stage and are uncorrected. IR spectra were recorded on a Digilab FTS-80 spectrometer and UV spectra were obtained on a Hitachi Model 150-20 apparatus. NMR spectra were determined with $SiMe_4$ as internal standard on Bruker AMX-400 and AC-200B spectrometers; *J* values are given in Hz. Microanalyses were performed by the microanalytical unit of the School of Chemistry, University of New South Wales, and mass spectra were recorded on an AEI model Ms902 double focusing instrument. Analytical high performance liquid chromatography (HPLC) was performed on a Brownlee SI 100 5μ column (0.46 cm × 25 cm) and preparative HPLC was carried out on a Whatman Partisil 10 column (2.2 cm × 50 cm). Gas chromatography (GC) was carried out on a Hewlett Packard 5890A instrument. Phenyllead triacetate,[14] *o*-methoxyphenyllead triacetate,[14] *p*-methoxyphenyllead triacetate,[15] 2,4-dimethoxyphenyllead triacetate,[16] *o*-fluorophenyllead triacetate,[10] *p*-fluorophenylboronic acid[17] and *p*-trifluoromethylphenyllead triacetate[14] were prepared by previously reported methods. The syntheses of the trimethyl(vinyl)stannanes **12a**, **12b**, **12c** and **12d** were carried out as previously described.[1,18] The acylase enzyme preparations from *Aspergillus melleus* (AA) and porcine kidney (PKA) were obtained from Sigma and Aldrich Chemical companies, respectively, while the protease, subtilisin Carlsberg, was obtained from Sigma. Light petroleum refers to that boiling in the range 60–80 °C.

Preparation of 4-ethoxycarbonyl-2-methyl-4,5-dihydro-1,3-oxazol-5-one 7

Ethyl hydrogen acetamidomalonate **6** (16.04 g, 84.8 mmol) and dry diethyl ether (200 cm^3) were stirred vigorously under dry N_2, and trifluoroacetic anhydride (39.3 g, 26.0 cm^3, 2.2 equiv.) was added *via* syringe over 10 min with stirring. Vigorous stirring was continued for 15 min, by which time a clear solution of the enol trifluoroacetate of oxazolone **7** had been formed. The reaction mixture was cooled to 0 °C and water (1.68 g, 1.1 equiv.) was added *via* syringe over 2 min with stirring. The reaction flask was then removed from the ice bath and the mixture was stirred at room temp. for 1 h. The pale yellow suspension was cooled to 0 °C, then transferred to a dry bag where it was collected at the pump under dry N_2 and washed with numerous small volumes of ice-cold dry diethyl ether (total of 1 dm^3). The product was dried *in vacuo* over fresh NaOH pellets for 3 days to give the title compound **7** (10.72 g, 73.8%) as moisture-sensitive pale yellow crystals, mp 121–122 °C (decomp.) (HRMS: Found M^+, 171.0532; $M^+ + H$, 172.0610. $C_7H_9NO_4$ requires M^+, 171.0532; $M^+ + H$, 172.0610); ν_{max}(Nujol)/cm^{-1} 1777, 1664 and 1629; δ_H($CDCl_3$–C_5D_5N, 3:1) 1.23 (3 H, t, *J* 7.1, CH_2CH_3), 2.34 (3 H, s, CH_3), 4.23 (2 H, q, *J* 7.1, CH_2) and 17.2 (1 H, br s, OH); δ_C[$(CD_3)_2SO$] 13.02, (CH_3), 14.75 (CH_3), 58.71 (CH_2), 84.35 (C-4), 151.65 (C-2), 160.47 (C=O or C-5) and 160.69 (C=O or C-5); *m*/*z* 172 (M + 1, 1%), 171 (M, 0.5), 99 (54), 98 (10), 71 (32) and 43 (100). The compound was stored *in vacuo* over sodium hydroxide and the vacuum released with dry N_2.

Preparation of *N*-acetyl-α-arylglycines 10

Method A. The aryllead triacetate (3.0 mmol, 1.2 equiv.) and dry pyridine (0.712 g, 9.0 mmol, 3.6 equiv.) were dissolved in dry chloroform (4 cm^3) and 4-ethoxycarbonyl-2-methyl-4,5-dihydroxy-1,3-oxazol-5-one **7** (0.428 g, 2.5 mmol) was added over 5 min at 40 °C with stirring. The mixture was stirred in a stoppered flask for 1 h at 40 °C and then diluted with chloroform (25 cm^3) and washed with sulfuric acid (3 M; 15 cm^3). The aqueous layer was washed with chloroform (25 cm^3) and the chloroform extracts were combined and washed with saturated aqueous sodium hydrogen carbonate (25 cm^3). The chloroform solution was filtered and the solvent evaporated at 40 °C, and the residue was dried *in vacuo* to yield the crude arylated oxazolone **9** as a pale yellow oil. Ethanol (12 cm^3) and aqueous sodium hydroxide (1.25 M; 4 cm^3, 2 equiv.) were added to the oil and the mixture was heated at reflux for 0.5 h. The mixture was cooled, diluted with water (20 cm^3) and the ethanol was evaporated at 40 °C. The aqueous mixture was washed with ethyl acetate (2 × 20 cm^3), acidified with an excess of hydrochloric

acid (3 M) and extracted with ethyl acetate (3 × 40 cm^3). The combined extracts were dried (Na_2SO_4), filtered and the solvent evaporated at 40 °C. Carbon tetrachloride (20 cm^3) was added to the residue for azeotropic removal of water and the solvent was evaporated *in vacuo*. The residue was dried *in vacuo* to yield the *N*-acetyl-α-arylglycine as a crystalline solid.

Method B. The aryllead triacetate was generated *in situ* by adding the arylboronic acid (3.5 mmol, 1.4 equiv.) over 15 min at 40 °C to a stirred mixture of dry lead tetraacetate (LTA) (1.33 g, 3.0 mmol, 1.2 equiv.) and mercury(II) acetate (0.0956 g, 0.3 mmol, 0.12 equiv.) in dry chloroform (4 cm^3). The mixture was stirred for 1 h at 40 °C, after which a test for residual LTA was negative. Pyridine (0.712 g, 9.0 mmol, 3.6 equiv.) was added to the mixture followed by the oxazolone **7** (0.428 g, 2.5 mmol) added over 5 min at 40 °C. The mixture was stirred for 1 h at 40 °C, after which the work-up and hydrolysis were carried out as in method A.

***N*-Acetyl-α-phenylglycine 10a.** The title compound was prepared by method A in 93% yield as a crystalline solid, mp 201–202 °C (ethyl acetate) (lit.,[19] 201 °C); ν_{max}(Nujol)/cm^{-1} 3335, 1714 and 1600; δ_H[$(CD_3)_2SO$] 1.90 (3 H, s, Me), 5.34 (1 H, d, ^3J 7.5, CH), 7.36 (5 H, m, 5 × aryl H) and 8.63 (1 H, d, ^3J 7.5, exchanges in D_2O, NH); δ_C[$(CD_3)_2SO$] 22.2 (Me), 56.3 (CH), 127.6 (2 × phenyl CH), 127.9 (phenyl C-4), 128.5 (2 × phenyl CH), 137.3 (phenyl C-1), 169.1 (CONH) and 172.0 (CO_2H); *m*/*z* (M^+, 1%), 175 (25), 150 (20), 148 (31), 133 (21), 107 (16), 106 (100), 105 (23), 104 (44), 79 (22), 77 (24) and 43 (59).

***N*-Acetyl-α-(2-methoxyphenyl)glycine 10b.** The title compound was prepared by method A in 81% yield as a crystalline solid, mp 175–176 °C (ethyl acetate) (Found: C, 59.2; H, 6.1; N, 6.2. $C_{11}H_{13}NO_4$ requires C, 59.2; H, 5.9; N, 6.3%); λ_{max}(EtOH)/nm 273 and 278 sh (ε 2400 and 2200); ν_{max}(Nujol)/cm^{-1} 3356, 1739 and 1600; δ_H[$(CD_3)_2SO$] 1.87 (3 H, s, Me), 3.79 (3 H, s, OMe), 5.66 (1 H, d, ^3J 7.9, CH), 6.89–7.08 (2 H, m, aryl 3-H and 5-H), 7.24–7.38 (2 H, m, aryl 4-H and 6-H) and 8.34 (1 H, d, ^3J 7.9, exchanges in D_2O, NH); δ_C[$(CD_3)_2SO$] 22.3 (Me), 50.4 (CH), 55.6 (OMe), 111.3 (aryl C-3), 120.4 (aryl CH), 125.7 (aryl C-1), 128.6 (aryl CH), 129.4 (aryl CH), 156.7 (*C*OMe), 169.1, (CONH) and 172.4 (CO_2H); *m*/*z* 224 (M + 1, 0.4%), 223 (0.2%), 179 (25), 178 (17), 137 (11), 136 (100), 134 (17), 121 (21), 107 (13), 77 (12) and 43 (37).

***N*-Acetyl-α-(4-methoxyphenyl)glycine 10c.** The title compound was prepared by method A in 86% yield as a crystalline solid, mp 221–222 °C (ethyl acetate) (lit.,[20] 215 °C) (Found: C, 58.9; H, 6.1; N, 6.2. $C_{11}H_{13}NO_4$ requires C, 59.2; H, 5.9; N, 6.3%); λ_{max}(EtOH)/nm 275 and 281 (ε 1400 and 1200); ν_{max}(Nujol)/cm^{-1} 3339, 1720 and 1599; δ_H[$(CD_3)_2SO$] 1.88 (3 H, s, Me), 3.73 (3 H, s, OMe), 5.26 (1 H, d, ^3J 7.3, CH), 6.92 and 7.31 (4 H, AA′BB′, aryl 3-H and 5-H, and 2-H and 6-H, respectively) and 8.55 (1 H, d, ^3J 7.3, exchanges in D_2O, NH); δ_C[$(CD_3)_2SO$] 22.3 (Me), 55.2 (CH), 55.8 (OMe), 114.0 (aryl C-3 and C-5), 129.0 (aryl C-2 and C-6), 129.2 (aryl C-1), 159.0 (aryl C-4), 169.1 (CONH) and 172.4 (CO_2H); *m*/*z* 223 (M, 2%), 205 (15), 180 (17), 179 (19), 137 (14), 136 (100), 135 (24), 134 (61), 121 (10), 109 (11) and 43 (44).

***N*-Acetyl-α-(2,4-dimethoxyphenyl)glycine 10d.** The title compound was prepared by method A in 82% yield as a crystalline solid, mp 202–203 °C (ethyl acetate) (Found: C, 57.2; H, 6.3; N, 5.4. $C_{12}H_{15}NO_5$ requires C, 56.9; H, 6.0; N, 5.5%); λ_{max}(EtOH)/nm 277 (ε 2500); ν_{max}(Nujol)/cm^{-1} 3339, 1721 and 1608; δ_H[$(CD_3)_2SO$] 1.86 (3 H, s, Me), 3.76 (3 H, s, OMe), 3.78 (3 H, s, OMe), 5.56 (1 H, d, ^3J 7.7, CH), 6.48–6.60 (2 H, m, aryl 3-H and 5-H), 7.17 (1 H, m, aryl 6-H) and 8.28 (1 H, d, ^3J 7.7, exchanges in D_2O, NH); δ_C[$(CD_3)_2SO$] 22.3 (Me), 50.0 (CH), 55.3 (OMe), 55.7 (OMe), 98.6 (aryl C-3), 104.9 (aryl C-5), 117.9 (aryl C-1), 129.3 (aryl C-6), 157.8 (*C*-OMe), 160.5 (*C*-OMe), 169.1 (CONH) and 172.6 (CO_2H); *m*/*z* 253 (M, 0.5%), 210 (11), 209 (40), 208 (18), 167 (14), 166 (100), 164 (19), 151 (17) and 43 (39).

***N*-Acetyl-α-(2-fluorophenyl)glycine 10e.** The title compound was prepared by method A in 90% yield as colourless crystals, mp 222–223 °C (ethyl acetate) (Found: C, 56.8; H, 5.1; N, 6.4. $C_{10}H_{10}FNO_3$ requires C, 56.9; H, 4.8; N, 6.6%); λ_{max}(EtOH)/nm 263 and 269 (ε 1000 and 850); ν_{max}(Nujol)/cm^{-1} 3341, 1715 and 1599; δ_H[$(CD_3)_2SO$] 1.90 (3 H, s, Me), 5.66 (1 H, d, ^3J 7.9, CH), 7.21 (2 H, m, aryl 3-H and 5-H), 7.32–7.47 (2 H, m, aryl 4-H and 6-H) and 8.70 (1 H, d, ^3J 7.9, NH); δ_C[$(CD_3)_2SO$] 22.3 (Me), 49.7 (d, J_{CF} 3.2, CH), 115.6 (d, J_{CF} 21.5, aryl C-3), 124.6 (d, J_{CF} 3.3, aryl C-5), 125.1 (d, J_{CF} 15.1, aryl C-1), 129.4 (d, J_{CF} 3.5, aryl C-6), 130.1 (d, J_{CF} 8.5, aryl C-4), 159.9 (d, J_{CF} 246.0, C–F), 169.3 (CONH) and 171.4 (CO_2H); *m*/*z* 211 (M, 0.3%), 166 (34), 125 (10), 124 (100), 122 (20), 97 (12) and 43 (36).

***N*-Acetyl-α-(4-fluorophenyl)glycine 10f.** The title compound was prepared by method B in 83% yield as a crystalline solid, mp 188–189.5 °C (water) (lit.,[19] 189 °C); ν_{max}(Nujol)/cm^{-1} 3347, 1724 and 1609; δ_H[$(CD_3)_2SO$] 1.88 (3 H, s, Me), 5.34 (1 H, d, ^3J 7.5, CH), 7.19 (2 H, m, aryl 3-H and 5-H), 7.42 (2 H, m, aryl 2-H and 6-H) and 8.62 (1 H, d, ^3J 7.5, exchanges in D_2O, NH); δ_C[$(CD_3)_2SO$] 22.3 (Me), 55.5 (CH), 115.3 (d, J_{CF} 21.9, aryl C-3 and C-5), 129.7 (d, J_{CF} 8.4, aryl C-2 and C-6), 133.6 (aryl C-1), 161.8 (d, J_{CF} 244, C–F), 169.1 (CONH) and 171.9 (CO_2H); *m*/*z* 211 (M^+, 1%), 193 (15), 168 (13), 166 (11), 151 (17), 125 (11), 124 (100), 123 (24), 122 (50) and 43 (79).

***N*-Acetyl-α-(4-trifluoromethylphenyl)glycine 10g.** The title compound was prepared by method A in 92% yield as colourless crystals, mp 205.5–206.5 °C (ethyl acetate–light petroleum) (Found: C, 50.7; H, 4.1; N, 5.2. $C_{11}H_{10}F_3NO_3$ requires C, 50.6; H, 3.9; N, 5.4%); ν_{max}(Nujol)/cm^{-1} 3356, 1726 and 1599; δ_H[$(CD_3)_2SO$] 1.91 (3 H, s, Me), 5.48 (1 H, d, ^3J 7.6, CH), 7.62 and 7.74 (4 H, AA′BB′, aryl 2-H and 6-H, and 3-H and 5-H, respectively) and 8.75 (1 H, d, ^3J 7.6, exchanges in D_2O, NH); δ_C[$(CD_3)_2SO$] 22.4 (Me), 56.1 (CH), 124.3 (q, J_{CF} 272, CF_3), 125.5 (q, J_{CF} 3.7, aryl C-3 and C-5), 128.6 (aryl C-2 and C-6), 128.7 (q, J_{CF} 32, aryl C-4), 142.4 (aryl C-1), 169.5 (CONH) and 171.6 (CO_2H); *m*/*z* 262 (M + 1, 0.3%), 216 (14), 201 (12), 174 (75), 173 (17), 172 (33), 127 (16) and 43 (100).

***N*-Acetyl-α-(2,4-dimethoxyphenyl)glycine ethyl ester 11d.** The crude arylated oxazolone **9d** (1.0 g, 3.25 mmol), prepared as in method A was refluxed with distilled water (13.5 cm^3) with stirring for 1.5 h. Water (25 cm^3) was added to the mixture which was then extracted with chloroform (2 × 50 cm^3). Evaporation of the solvent at 40 °C gave a pale yellow solid which was crystallized from ethyl acetate to give the title compound as cream needles (1.643 g, 87%), mp 112–113 °C (Found: C, 60.0; H, 7.0; N, 5.0. $C_{14}H_{19}NO_5$ requires C, 59.8; H, 6.8; N, 5.0%); ν_{max}(Nujol)/cm^{-1} 3254, 1745, 1645, 1539 and 1514; δ_H($CDCl_3$) 1.17 (3 H, t, ^3J 7.1, Me), 2.01 (3 H, s, COMe), 3.79 (3 H, s, OMe), 3.80 (3 H, s, OMe), 4.16 (2 H, q, ^3J 7.1, CH_2), 5.68 (1 H, d, ^3J 8.4, CH), 6.40–6.60 (3 H, m, 3 × aryl H) and 7.26 (1 H, m, exchanges in D_2O, NH); δ_C($CDCl_3$) 13.9 (Me), 23.0 (CH_3CO), 52.6 (CH), 55.24 (OMe), 55.27 (OMe), 61.3 (CH_2), 98.9 (aryl CH), 104.2 (aryl CH), 118.1 (aryl C-1), 131.0 (aryl CH), 157.8 (*C*-OMe), 160.9 (*C*-OMe), 169.2 (CONH) and 171.2 (CO_2); *m*/*z* 281 (M, 4%), 238 (10), 209 (13), 208 (95), 167 (14), 166 (100), 164 (12) and 43 (14).

Synthesis of *N*-acetyl-α-vinylglycines and their ethyl esters

Method A. The trimethyl(vinyl)stannane **12** (1–5 mmol, 1.1 equiv.) in chloroform (2 cm^3) was added to a stirred solution of dry lead tetraacetate (1.0 equiv.)–acetic acid (1% w/w) in chloroform (7 cm^3). The solution was stirred at room temperature for 2–3 min (depending on the stannane) and then added to a solution of the oxazolone **7** (1.0 equiv.) in chloroform (5 cm^3) and pyridine (3.3 equiv.) at 0 °C. The mixture was stirred at 0 °C for 0.5 h and then at room temperature for 3 h. The solution was diluted with chloroform (50 cm^3) and washed in turn with dilute sulfuric acid (1 M; 2 × 30 cm^3), water (40 cm^3) and brine (40 cm^3), and the solvent was then evaporated. The resulting crude material was refluxed gently in ethanol (28 cm^3) and aqueous

sodium hydroxide (1.5 M; 2.5 equiv.) for 40 min. The mixture was allowed to cool, diluted with water (40 cm^3) and the ethanol was evaporated *in vacuo* at 40 °C. The pH at this stage was 9–10. The mixture was washed with ethyl acetate (2 × 40 cm^3) to remove neutral impurities, and the aqueous solution made acid with excess 3 M hydrochloric acid. The resulting precipitate was extracted into ethyl acetate (3 × 80 cm^3) and the solvent was evaporated below 40 °C to yield a solid which was dried by azeotroping with carbon tetrachloride.

Method B. As for method A except that hydrolysis of the crude product was effected by sonication in a deoxygenated ethanol–water mixture (20:80) at < 40 °C for 11 h under an atmosphere of nitrogen. The reaction mixture was extracted with chloroform and the solvent was evaporated. The pure product was then isolated by HPLC with the solvent system indicated.

***N*-Acetyl-α-[(*E*)-styryl]glycine 15a.** The title compound was prepared by method A in 60% yield, as a crystalline solid, mp 166.5–167.5 °C (Found: C, 66.0; H, 5.9; N, 6.3. $C_{12}H_{13}NO_3$ requires C, 65.7; H, 6.0; N, 6.4%); λ_{max}(EtOH)/nm 254 (ε 20 700); δ_H[$(CD_3)_2SO$] 1.90 (3 H, s, Me), 4.93 (1 H, ddd, $^3J_{H,NH}$ 7.7, $^3J_{H,vinylic}$ 6.7, $^4J_{allylic}$ 1.0, CH), 6.30 (1 H, dd, $^3J_{trans}$ 15.9, $^3J_{vic}$ 6.7, vinyl H), 6.63 (1 H, dd, $^3J_{trans}$ 15.9, $^4J_{allylic}$ 1.0, vinyl H), 7.20–7.50 (5 H, m, 5 × phenyl H) and 8.43 (1 H, d, ^3J 7.7, exchanges in D_2O, NH); δ_C[$(CD_3)_2SO$] 22.3 (Me), 54.4 (CH), 124.6 (vinyl C), 126.3 (2 × phenyl CH), 127.9 (phenyl C-4), 128.7 (2 × phenyl CH), 131.7 (vinyl C), 135.9 (phenyl C-1), 169.0 (CONH) and 171.9 (CO_2H); *m*/*z* 220 (M + 1, 1%), 219 (2), 175 (10), 159 (14), 133 (18), 132 (100), 131 (94), 130 (42), 117 (17), 115 (23), 105 (14), 104 (10), 103 (35), 91 (17), 77 (46) and 43 (82).

***N*-Acetyl-α-[(*E*)-styryl]glycine ethyl ester 14a.** The title compound was prepared by method B in 62% yield. Fractionation by HPLC with an ethyl acetate–light petroleum (1:1) solvent system afforded pale yellow crystals, mp 68–70 °C (Found: C, 67.8; H, 7.10; N, 5.5. $C_{14}H_{17}NO_3$ requires C, 68.0; H, 6.9; N, 5.7%); δ_H($CDCl_3$) 1.30 (3 H, t, ^3J 7.1, Me), 2.08 (3 H, s, COMe), 4.24 (2 H, m, CH_2), 5.28 (1 H, ddd, $^3J_{H,NH}$ 7.5, $^3J_{H,vinylic}$ 6.3, $^4J_{allylic}$ 1.2, CH), 6.18 (1 H, dd, $^3J_{trans}$ 16.0, $^3J_{vic}$ 6.3, vinyl H), 6.36 (1 H, br d, ^3J 7.5, exchanges in D_2O, NH), 6.65 (1 H, dd, $^3J_{trans}$ 16.0, $^4J_{allylic}$ 1.2, vinyl H) and 7.33 (5 H, m, 5 × phenyl H); δ_C($CDCl_3$) 14.0 (Me), 23.0 (CH_3CO), 54.2 (CH), 61.9 (CH_2), 123.4 (vinyl C), 126.5 (2 × phenyl CH), 128.1 (phenyl C-4), 128.5 (2 × phenyl CH), 133.0 (vinyl C), 135.8 (phenyl C-1), 169.6 (CONH) and 170.8 (CO_2); *m*/*z* 247 (M, 10%), 204 (39), 201 (30), 174 (38), 159 (27), 132 (12), 133 (100), 131 (22), 115 (49), 103 (10), 77 (15) and 43 (44).

***N*-Acetyl-α-[(*E*)-*p*-methylstyryl]glycine ethyl ester 14b.** Trimethyl[(*E*)-*p*-methylstyryl]stannane **12b** (0.562 g, 2.0 mmol), LTA (0.806 g, 1.82 mmol) and oxazol-5-one **7** (0.311 g, 1.82 mmol) were reacted according to method B. Fractionation by HPLC with an ethyl acetate–light petroleum (1:1) solvent system afforded the title compound (0.299 g, 63%), mp 86–88 °C (Found: C, 68.7; H, 7.6; N, 5.2. $C_{15}H_{19}NO_3$ requires C, 68.9; H, 7.3; N, 5.4%); ν_{max}($CHCl_3$)/cm^{-1} 3430, 2980, 2250, 1740, 1680 and 1500; δ_H($CDCl_3$) 1.30 (3 H, t, ^3J 7.11, CH_2CH_3), 2.09 (3 H, s, Me), 2.33 (3 H, s, *p*-Me), 4.24 (2 H, m, OCH_2), 5.26 (1 H, m, CH), 6.13 (1 H, dd, $^3J_{vic}$ 6.7, $^3J_{trans}$ 15.6, vinyl H), 6.30 (1 H, br d, $^3J_{H,CH}$ 7.8, NH), 6.62 (1 H, d, $^3J_{trans}$ 15.6, vinyl H), 7.12 and 7.26 (4 H, AA′BB′, Ar-H); *m*/*z* 261 (M, 10%), 218 (25), 188 (12), 146 (100), 129 (45) and 43 (36).

***N*-Acetyl-α-[(*E*)-*p*-methoxystyryl]glycine ethyl ester 14c.** Trimethyl[(*E*)-*p*-methoxystyryl]stannane **12c** (0.594 g, 2.0 mmol), LTA (0.806 g, 1.82 mmol) and oxazol-5-one **7** (0.311 g, 1.82 mmol) were reacted according to method B. Purification of the crude product by HPLC with an ethyl acetate–light petroleum (1:1) solvent system afforded the title compound, mp 67–69 °C (0.302 g, 60%) (HRMS: Found M^+, 277.1314. $C_{15}H_{19}NO_4$ requires M^+, 277.1314); ν_{max}($CHCl_3$)/cm^{-1} 3430, 2990, 2250, 1740, 1680, 1610 and 1510; δ_H($CDCl_3$) 1.30 (3 H, t, ^3J 7.14, CH_2CH_3), 2.08 (3 H, s, Me), 3.81 (3 H, s, OMe), 4.25 (2 H, m, OCH_2), 5.24 (1 H, m, CH), 6.03 (1 H, dd, $^3J_{vic}$ 6.45, $^3J_{trans}$ 15.8, vinyl H), 6.25 (1 H, br d, $^3J_{H,CH}$ 7.55, NH), 6.60 (1 H, d, $^3J_{trans}$ 15.8, vinyl H), 6.84 and 7.30 (4 H, AA′BB′, Ar-H); δ_C($CDCl_3$) 14.73 (CH_3CH_2), 23.70 (CH_3CONH), 54.96 (OCH_3), 55.89 (CH), 62.47 (CH_2), 114.64 (aryl C-2 and C-6), 121.76 (vinyl C), 128.49 (aryl C-3 and C-5), 129.27 (aryl C-1), 133.33 (vinyl C), 160.28 (aryl C-4), 170.22 (CONH) and 171.67 (CO_2); *m*/*z* 277 (M, 10%), 234 (45), 204 (12), 189 (40), 162 (100), 145 (60) and 43 (33).

***N*-Acetyl-α-[(*E*)-3,4-dimethoxystyryl]glycine ethyl ester 14d.** Trimethyl[(*E*)-3,4-dimethoxystyryl]stannane **12d** (0.654 g, 2.0 mmol), LTA (0.806 g, 1.82 mmol) and oxazol-5-one **7** (0.311 g, 1.82 mmol) were reacted by method B. Purification of the crude product by HPLC with an ethyl acetate–dichloromethane (15:85) solvent system afforded the title compound (0.248 g, 44%), mp 114–114 °C (Found: C, 62.4; H, 6.8; N, 4.4. $C_{16}H_{21}NO_5$ requires C, 62.5; H, 6.9; N, 4.6%); ν_{max}($CHCl_3$)/cm^{-1} 3430, 2980, 2250, 1740, 1680, 1600, 1590 and 1510; δ_H($CDCl_3$) 1.30 (3 H, t, ^3J 7.2, CH_2CH_3), 2.09 (3 H, s, Me), 3.88 (3 H, s, OMe), 3.89 (3 H, s, OMe), 4.29 (2 H, m, OCH_2), 5.24 (1 H, m, CH), 6.04 (1 H, dd, $^3J_{vic}$ 6.49, $^3J_{trans}$ 15.8, vinyl H), 6.24 (1 H, br d, $^3J_{H,CH}$ 7.1, NH), 6.59 (1 H, dd, $^4J_{allylic}$ 1.25, $^3J_{trans}$ 15.8, vinyl H), 6.80 (1 H, m, aryl 6-H) and 6.91 (2 H, m, aryl 2 and 5-H); *m*/*z* 307 (M, 20%), 264 (24), 219 (67), 192 (45), 175 (100) and 43 (86).

Method used to assay the activity of enzyme preparations AA and PKA towards the *N*-acetyl-α-arylglycines 10a–g

The basic method of Whitesides[7] was followed with some minor modifications. The specific activities of both enzyme preparations were determined with *N*-acetyl-DL-methionine, without added Co^{2+}, as the standard. The activity of PKA, which in all cases was the more active catalyst, was found to be close to that reported by Whitesides and showed little change during the course of the work. With all substrates the addition of Co^{2+} (1 mM) enhanced the activity of PKA and it was employed in all cases. The concentration of PKA was extended to cover the range 0.01–4.0 mg per 2 cm^3 of reaction volume to permit the appraisal of poor substrates.

Resolution of *N*-acetyl-DL-α-phenylglycine 10a

Compound **10a** (2.90 g, 15 mmol) was suspended in distilled water (20 cm^3) and $CoCl_2·6H_2O$ solution (150 mm^3, 0.2 M, 0.03 mmol) in a vessel equipped with a pH electrode, a magnetic stirrer bar and a septum. The mixture was stirred under N_2 in a bath maintained at 37 °C and concentrated aqueous LiOH was added *via* syringe to produce a pH of 7.5–8.0. The enzyme PKA (94 mg) was introduced and the pH of the solution was adjusted to 7.5 and maintained by the intermittent addition of aqueous LiOH. A dense crystalline precipitate formed rapidly and stirring was continued, with pH adjustment, for 50 h. The mixture was cooled in ice and the pH was adjusted to 7.5 by addition of a small volume of dilute HCl. The precipitate was collected, washed with small portions of ice-cold water and dried to yield L-α-phenylglycine **16** (1.011 g, 89%, 99% ee), mp 260 °C, $[\alpha]_D^{20}$ +162.4 (*c* 2.0, 1 M HCl) (lit.,[21] +164.2 in 5 M HCl).

The filtrate was adjusted to pH 5.0 with 10 M HCl and heated to 60 °C with Norit. The coagulated protein and Norit were filtered off and the filtrate was adjusted to pH 1.5 with 10 M HCl. The resultant dense white suspension was stirred at 0 °C for 30 min and then collected at the pump. It was then washed with small portions of ice-cold water and dried over KOH *in vacuo* to yield *N*-acetyl-D-α-phenylglycine D-**10a**. The filtrate was extracted with ethyl acetate (2 × 30 cm^3), the extract was dried (Na_2SO_4) and filtered, and the solvent was evaporated to give a further quantity of *N*-acetyl-D-α-phenyl-glycine which was obtained as colourless crystals (total of 1.364 g, 94%, 95% ee), mp 180.5–181.5 °C (lit.,[22] 187 °C), $[\alpha]_D$ −218.9 (*c* 2.0 in

MeOH) (lit.,[22] −206 in H_2O and lit.,[11] +219.3 for L-enantiomer in MeOH).

Resolution of *N*-acetyl-DL-(*p*-trifluoromethylphenyl)glycine 10g

Compound **10g** was resolved in a similar manner to compound **10a** above with minor modifications. A substrate concentration of 0.2 M, a $CoCl_2$ concentration of 1 mM and PKA (80 mg) were used for 0.83 g (3.18 mmol) of substrate. Reaction time was 3.5 days at 37 °C. Work-up was the same as for compound **10a** to give L-(*p*-trifluoromethylphenyl)glycine **17** (0.301 g, 86%) as a white powder, mp 251–253 °C; 95% ee by GC, $[\alpha]_D$ + 107.4 (*c* 2.0 in 1 M HCl) (lit.,[23] +104). *N*-Acetyl-D-(*p*-trifluorophenyl)-glycine D-**10g** (0.256 g, 62%) was obtained as colourless crystals, mp 183–185 °C, 97% ee by GC; $[\alpha]_D$ −160.2 (*c* 2.0 in MeOH). Further product extracted from the filtrate (0.158 g, 38%) had an ee of 93% (GC).

Resolution[24] of *N*-acetyl-DL-α-phenylglycine ethyl ester 11a

The powdered racemic ester **11a** (2 mmol) was added to a solution of KCl (0.1 M) and KH_2PO_4 (10^{-4} M) in water (14 cm^3) at room temperature and under N_2 and the pH was adjusted to 7.6. Subtilisin Carlsberg (10.0 mg) was added with stirring, and the pH was maintained at ≤ 7.6 by the addition of 0.5 M aqueous NaOH from a micrometer burette. The time for complete reaction, which was judged from the stability of the pH and stoichiometry of the base addition, was approximately 2 h. The reaction mixture was then extracted with chloroform (2 × 25 cm^3), the extract was dried (Na_2SO_4) and filtered, and the solvent was evaporated at 40 °C to give *N*-acetyl-D-α-phenylglycine ethyl ester D-**11a** (0.22 g, 100%, 91% ee by GC) as colourless crystals, mp 88–89 °C (from ethyl acetate–light petroleum) (lit.,[22] 88–89 °C), $[\alpha]_D$ −142 (*c* 0.888 in EtOH) (lit.,[22] −149).

The aqueous layer was acidified with HCl (3 M, 1.0 cm^3) and extracted with ethyl acetate (3 × 25 cm^3). The organic extracts were dried (Na_2SO_4) and filtered, then the solvent was removed and the residue dried *in vacuo* to give *N*-acetyl-L-α-phenylglycine L-**10a** (0.180 g, 93%, 97% ee by GC), mp 189–190.5 °C (lit.,[22] 194–195 °C), $[\alpha]_D$ −189 (*c* 0.7 in MeOH) (lit.,[11] +195.3).

Resolution of *N*-acetyl-DL-α-(2,4-dimethoxyphenyl)glycine ethyl ester 11d

The powdered racemate **11d** (1.422 mmol) was treated with subtilisin Carlsberg as for compound **11a** above, but with a higher enzyme concentration (14.2 mg) and a reaction temperature of 37 °C. The reaction mixture was worked up as for compound **11a** to give *N*-acetyl-D-α-(2,4-dimethoxyphenyl)glycine ethyl ester D-**11d** (0.2025 g, 101%, 95% ee by GC), mp 113.5–114.5 °C, $[\alpha]_D$ −207.2 (*c* 2.0 in EtOH). The ^{1}H NMR spectrum was identical to that of the DL-ester above.

N-Acetyl-L-α-(2,4-dimethoxyphenyl)glycine L-**10d** was obtained as colourless crystals (0.160 g, 89%, 90% ee by GC), mp 204–206 °C (from water), $[\alpha]_D$ +75.9 (*c* 1.18 in MeOH). The ^{1}H NMR spectrum was identical to that of the racemate **10d** above.

Resolution of *N*-acetyl-DL-α-[(*E*)-styryl]glycine ethyl ester 14a

The powdered racemic ester **14a** (495 mg, 2.0 mmol) was treated as in the resolution of compound **11a** above except that subtilisin Carlsberg (20 mg) and a reaction temperature of 37 °C were used. The reaction mixture was worked up in the same way after a reaction time of approximately 1 h to give *N*-acetyl-D-α-[(*E*)-styryl]glycine ethyl ester D-**14a** (0.235 g, 95%, 93% ee by ^{1}H NMR spectroscopy in the presence of optical shift reagent as outlined below), mp 84–85 °C, $[\alpha]_D$ −121.7 (*c* 2.0 in EtOH). The ^{1}H NMR spectrum was identical to that of the racemate.

N-Acetyl-L-α-[(*E*)-styryl]glycine L-**15a** (0.220 g, 100%, 82% ee by ^{1}H NMR spectroscopy on the methyl ester in the presence of optical shift reagent as outlined below), mp 172–174 °C, $[\alpha]_D$ +150.8 (*c* 2.0 in MeOH). The ^{1}H NMR spectrum was identical to that of the racemate above.

Determination of ee values by gas chromatography

N-Acetyl-α-arylglycines **10a** and **10g** were methylated by treatment of a small sample (*ca.* 5 mg) dissolved in methanol with excess diazomethane in diethyl ether. The amido acid methyl esters were analysed by gas chromatography on a Chrompak Chirasil-Val-L column (25 m × 0.25 mm × 0.12 μm film thickness), using injector and detector temperatures of 270 °C and a temperature programme rising from 60 °C to 190 °C at 5 °C min^{-1}, and then maintained at 190 °C for 20 min.

α-Arylglycines (*ca.* 1 mg) were alkylated using propan-2-ol in 3.2 M HCl (250 mm^3) in a glass bomb at 110 °C for 1 h. The derived esters were dried in a stream of nitrogen and then converted to amido esters by reaction with pentafluoropropionic anhydride (50 mm^3) in dichloromethane (0.3 cm^3) in the same glass bomb at 110 °C for 10 min. The product was dried thoroughly in a stream of nitrogen, then dissolved in dichloromethane (*ca.* 0.5 cm^3) and analysed by GC under the conditions described above. Enantiomeric excess values were determined from the peak areas of the D- and L-enantiomers, which in all cases were well resolved.

Determination of ee values by ^{1}H NMR spectroscopy

The enantiomeric purity of *N*-acetyl-D-α-[(*E*)-styryl]glycine ethyl ester D-**14a** was determined from its ^{1}H NMR spectrum run in the presence of (R_P)-*tert*-butylphenylphosphinothioic acid.[25] The ee for *N*-acetyl-L-α-[(*E*)-styryl]glycine L-**15a** was obtained in the same way on the methyl ester produced by treating the glycine derivative with diazomethane in diethyl ether.

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