Reaction of 4-ethoxycarbonyl-2-phenyl-4,5-dihydrooxazol-5-one with organolead(IV) triacetates. A route to some α-arylglycine and α-vinylglycine derivatives

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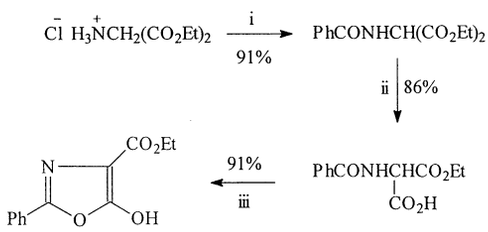
4-Ethoxycarbonyl-2-phenyl-4,5-dihydrooxazol-5-one undergoes rapid arylation and vinylation with arylead triacetates and (*E*)-styryllead triacetates, respectively. The resulting moisture-sensitive 4-aryl- and 4-styryl-oxazolones undergo hydrolysis and decarboxylation under mild conditions to provide a short efficient route to derivatives of α-arylglycines and α-vinylglycines.

In a preliminary communication[1] we reported the use of aryllead triacetates, compounds which we have developed as electrophilic arylating agents,[2,3] in the synthesis of *N*-benzoyl derivatives of α-arylglycines. We now report that work in detail, together with the results of our attempts to employ vinyllead triacetates[4,5,6] and alk-1-ynyllead triacetates[7] in the synthesis of α-vinyl- and α-alkynyl-glycine derivatives.

In our initial attempts to access α-arylglycines we examined the reaction of aryllead triacetates with diethyl acetamidomalonate and its enolate salt but, unlike the α-alkylmalonates,[8] α-arylation was not observed. Since we had found that the arylation reaction proceeds best for the more acidic β-dicarbonyl compounds,[8] we sought to achieve the desired syntheses by the use of more acidic malonate derivatives. In a search limited to compounds readily available from inexpensive starting materials we were attracted to the possibility of employing 4-ethoxycarbonyl-2-phenyl-4,5-dihydrooxazol-5-one,[9] which was found by NMR spectroscopy to exist in $CDCl_3$ as the enol tautomer **1**. The route to compound **1** is shown in Scheme 1 and, as indicated, all steps are high yielding (71% overall). We found it necessary to employ trifluoroacetic anhydride (TFAA) in the dehydration step rather than acetic anhydride as reported,[9] since in our hands yields for this step did not exceed 35%.



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Scheme 1 *Reagents and conditions:* i, PhCOCl, Na_2CO_3, H_2O, 5–10 °C; ii, KOH, EtOH; iii, TFAA

Arylation results

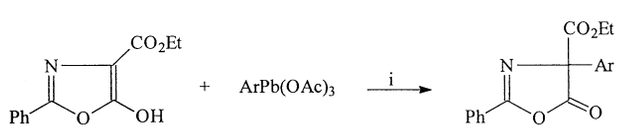
The oxazolone **1** proved to be highly reactive towards phenyllead triacetate **2a** under our standard chloroform–pyridine conditions; phenylation was complete after 1 h at 40 °C and the 4-phenyloxazolone **3a** was shown to be formed (^{1}H NMR spectroscopy) in almost quantitative yield. The product **3a** proved to be even more sensitive to hydrolytic ring opening than the starting material **1**, thus excluding its isolation for full characterisation. For this reason, the reaction mixture was heated directly with alkali in order to effect ring opening, hydrolysis of the ethyl ester group and decarboxylation of the resulting malonic acid. With this procedure we were able to isolate *N*-benzoyl-α-phenylglycine **4a** in 87% yield (Scheme 2, entry 1, Table 1).

Table 1 Yields of *N*-benzoyl-α-arylglycines **4** obtained by reaction of the oxazolone **1** with aryllead(IV) triacetates and subsequent hydrolysis of the 4-aryl-4-ethoxycarbonyl-2-phenyl-4,5-dihydrooxazol-5-one produced

		Yield (%) of compound **4**[a]	
Entry	$ArPb(OAc)_3$	With isolated $ArPb(OAc)_3$	With $ArPb(OAc)_3$ formed *in situ*
1	**2a**	87	94
2	**2b**	—	93
3	**2c**	88	—
4	**2d**	75	70
5	**2e**	—	83
6	**2f**	87	—
7	**2g**	90	—
8	**2h**	89	75

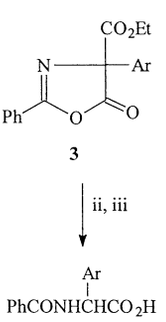
[a] Yields are for pure material based on oxazolone **1**.

As found in previous studies,[2,3] the arylation reaction was not significantly affected by changes in the nature of the aryl group; excellent yields were obtained for the *N*-benzoyl-α-arylglycines **4a**–**4h** (see Table 1) from reactions of oxazolone **1** with the aryllead triacetates **2a**–**2h**, respectively, followed by *in situ* hydrolysis and decarboxylation of the arylated oxazolones **3a**–**3h** as outlined in Scheme 2. In only one case was the



1 **2** **3**

a Ar = Ph
b Ar = *o*-FC_6H_4
c Ar = *p*-FC_6H_4
d Ar = *p*-$CF_3C_6H_4$
e Ar = *o*-$MeOC_6H_4$
f Ar = *p*-$MeOC_6H_4$
g Ar = 2,4-$(MeO)_2C_6H_3$
h Ar = 3,4-$(MeO)_2C_6H_3$



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Scheme 2 *Reagents and conditions:* i, $CHCl_3$, pyridine, 40 °C; ii, NaOH, EtOH, H_2O, steam bath; iii, H_3O^+

moisture-sensitive arylated oxazolone isolated. This was 4-(2,4-dimethoxyphenyl)-4-ethoxycarbonyl-2-phenyl-4,5-dihydro-oxazol-5-one **3g**, which was slower to hydrolyse possibly due to the steric effect of the *ortho* methoxy group.

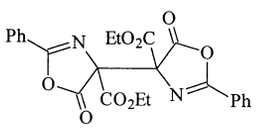
The ready availability of aryllead triacetates containing a wide range of substituents by tin–lead exchange [10,11] and boron–lead exchange [12] (Scheme 3) thus permits ready access to a wide

$$ArSnBu_3 + Pb(OAc)_4 \xrightarrow{i} ArPb(OAc)_3 + Bu_3SnOAc$$

$$ArB(OH)_2 + Pb(OAc)_4 \xrightarrow{i} ArPb(OAc)_3 + AcOB(OH)_2$$

Scheme 3 *Reagents and conditions:* i, $Hg(OAc)_2$ catalyst, $CHCl_3$

range of α-arylglycines. The efficiency of the overall procedure can be further improved by the generation of the aryllead triacetate *in situ*. This is best achieved by reacting the corresponding arylboronic acid with lead tetraacetate (LTA) in chloroform at 40 °C in the presence of a catalytic amount of mercury(II) acetate, rather than by the slower tin–lead exchange which generally requires an overnight reaction, followed by separation of the product from tributyltin acetate. The method has been demonstrated by syntheses of α-phenylglycine **4a** (entry 1, Table 1), *o*-fluorophenylglycine **4b** (entry 2), *p*-trifluoromethylphenylglycine **4d** (entry 4), *o*-methoxyphenylglycine **4e** (entry 5) and 3,4-dimethoxyphenylglycine **4h** (entry 8). When employing the latter procedure, it is necessary to ensure that excess LTA is not present when the oxazolone **1** is added, since it is oxidised rapidly by LTA to a mixture which would appear from the NMR spectrum to be a mixture of the two isomeric C4-linked dimers **5**. In the two cases where aryllead triacetates



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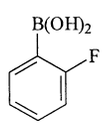

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were produced *in situ*, we found that the addition of a small amount of formic acid on completion of the boron–lead exchange destroyed excess LTA and this method was employed in two of the examples in Table 1 (entries 2 and 5).

Synthesis of *o*-fluorophenylboronic acid. Attempts to prepare *o*-fluorophenylboronic acid **6** by direct lithiation of fluorobenzene with butyllithium by the reported method [13] led, in our hands, to a poor yield of the desired product, which was contaminated by butylboronic acid. We have found that, if the lithiation is conducted with *sec*-butyllithium at −78 °C, followed by reaction with triisopropyl borate at the same temperature, the boronic acid **6** can be produced in a crude yield of 93%. This material, which contained 1.3% of triphenylene (by ^{1}H NMR spectroscopy), was suitable for our needs; however, it is readily purified by recrystallisation from water.

Vinylation results

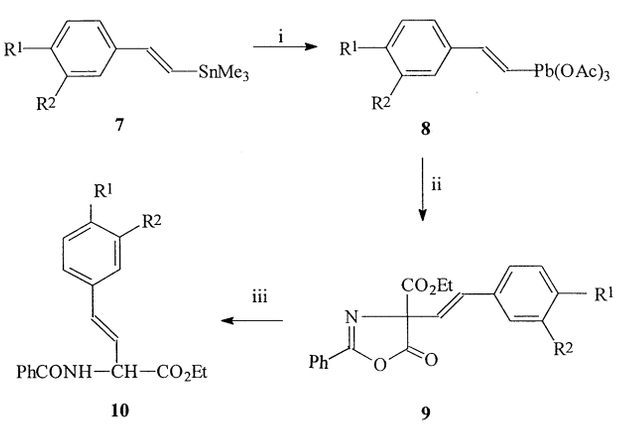
Our first attempts to achieve the vinylation of the oxazolone **1** were carried out with (*E*)-styryllead triacetate **8a** under conditions we had developed in earlier work.[4,5,6] This entailed the addition of trimethyl[(*E*)-styryl]stannane **7a** (1.1 equiv.) in chloroform to a stirred chloroform solution of LTA (1.1 equiv.), and allowing 1 min for the Sn–Pb exchange before adding the resulting solution to a stirred solution of the oxazolone **1** (1.0 equiv.) in chloroform–pyridine at 0 °C; however, the reaction produced only a small amount of the expected product **9a**.

A detailed study of the Sn–Pb exchange reaction of **7a** indicated that it was incomplete under our previously developed conditions, and it also showed that the yield of **9a** could not be significantly improved by use of a longer exchange time because of the instability of the vinyllead reagent **8a**. The slower Sn–Pb exchange reaction observed in the present work was eventually traced to a change in the preparation of the LTA. In our earlier work [4,5,6] the removal of acetic acid was clearly less rigorous than in the current study, and its presence was shown to increase significantly the rate of the exchange reaction. Thus, it should be noted that vinyllead triacetates are best prepared by adding 1% w/w acetic acid to the chloroform solution of acetic acid-free LTA. With this modification the Sn–Pb exchange reaction of the vinylstannane **7a** was complete (^{1}H NMR spectroscopy) in less than 2.5 min, and when a solution of the vinyllead compound **8a**, generated in this way, was reacted with the oxazolone **1** as outlined in Scheme 4, the vinylated oxazolone **9a**

Table 2 Yields of vinylated oxazolones **9** and *N*-benzoyl-α-styrylglycine ethyl esters **10** obtained by reaction of the oxazolone **1** with the (*E*)-styryllead(IV) triacetates **8**

		Yield (%)	
Entry	$RPb(OAc)_3$	**9** + **10**	**10**
1	**8a**	62[a]	28[b]
2	**8b**	41[a]	29[b]
3	**8c**	57[a]	30[b]
4	**8d**	45[a]	17[b]

[a] Determined by ^{1}H NMR spectroscopy with CH_2Br_2 as internal standard. [b] Yield for pure material separated by HPLC.



Scheme 4 *Reagents and conditions:* i, LTA, 1% HOAc, $CHCl_3$, room temp., 2.5 min; ii, **1**, $CHCl_3$; iii, EtOH, H_2O

and α-vinylglycine ethyl ester **10a** were produced in a combined yield of 62% (by ^{1}H NMR spectroscopy). Because of its moisture sensitivity, the isolation of oxazolone **9a** was not attempted; instead, the mixture was heated in aqueous ethanol to complete the hydrolysis and decarboxylation to the glycine ethyl ester **10a**, which was isolated by HPLC in modest yield (entry 1, Table 2).

The reaction sequence outlined in Scheme 4 was applied to the three substituted (*E*)-styryltrimethylstannanes **7b**, **7c** and **7d**. In each case the corresponding Sn–Pb exchange was rapid (<2.5 min), and the vinyllead triacetates, which were generated in high yield (shown by ^{1}H NMR) reacted rapidly with oxazolone **1** to give mixtures of vinylated oxazolones **9** and the *N*-benzoyl-α-vinylglycine esters **10b**, **10c** and **10d**, respectively, in moderate yield (Table 2). As in the first example the mixtures were not separated, but treated with hot aqueous ethanol to allow isolation and characterisation of the *N*-benzoyl-α-vinylglycine esters.

Previously we had shown that alk-1-ynyllead triacetates

could be generated *in situ* from the corresponding alkynyltrimethylstannanes in a manner analogous to that shown in Scheme 4, and then reacted with a range of carbon nucleophiles.[7] We attempted to employ this alkynylation procedure with the oxazolone **1** to access α-alkynylglycine derivatives; however, attempts to achieve the desired alkynylation with phenylethynyllead triacetate resulted only in the oxidative dimerisation of compound **1**, previously observed when it was treated with LTA.

Experimental

Mps 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 (ε values are given in units of $dm^3\ mol^{-1}\ cm^{-1}$). 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 HPLC was performed on a Brownlee SI 100 5μ column (0.46 cm id ×25 cm) and preparative HPLC was carried out on a Whatman Partisil 10 column (2.2 cm id ×50 cm). Phenyllead triacetate,[10] *p*-fluorophenyllead triacetate,[10] *p*-trifluoromethylphenyllead triacetate,[10] *p*-methoxyphenyllead triacetate,[14] 2,4-dimethoxyphenyllead triacetate,[15] 3,4-dimethoxyphenyllead triacetate,[10] *p*-trifluoromethylphenylboronic acid,[12] *o*-methoxyphenylboronic acid[12] and 3,4-dimethoxyphenylboronic acid[16] were prepared by previously reported methods. Phenylboronic acid was purchased from Aldrich Chemical Company. Ether refers to diethyl ether.

Preparation of 4-ethoxycarbonyl-2-phenyl-4,5-dihydrooxazol-5-one 1

Ethyl hydrogen benzamidomalonate[9] (94.5 g, 0.376 mol) was suspended in rapidly stirred ether (1 dm^3), trifluoroacetic anhydride (79.0 g, 0.376 mol) was then added, and the mixture stirred for 30 min at room temperature. The thick yellow suspension was collected at the pump in a large sintered funnel and compressed to remove filtrate. The pale yellow material was then washed well with dry cold ether (2 × 500 cm^3) by resuspending it in the solvent in the filter funnel. Finally, the solid was washed with dry cold acetonitrile (200 cm^3) containing pyridine (1%) in a similar manner and dried *in vacuo* to constant weight over silica gel and KOH pellets. 4-Ethoxycarbonyl-2-phenyl-4,5-dihydrooxazol-5-one **1** (79.9 g, 91%), which was stored over silica gel and KOH pellets, was obtained as a moisture-sensitive pale yellow solid, mp 126–128 °C (lit.,[9] 147–148 °C); $\delta_H(CDCl_3–C_5D_5N, 3:1)$ 1.37 (3 H, t, ^3J 7.09, CH_3CH_2), 4.35 (2 H, q, ^3J 7.09. CH_3CH_2), 7.24–7.60 (3 H, m, phenyl 3-, 4- and 5-H), 8.01 (2 H, m, phenyl 2- and 6-H) and 8.23 (1 H, br s, enol OH).

Preparation of *o*-fluorophenylboronic acid 6

sec-Butyllithium (100 mmol in cyclohexane) was added dropwise over 25 min to a stirred solution of fluorobenzene (10.32 cm^3, 110 mmol) in dry THF (250 cm^3) at −78 °C under nitrogen, and the mixture was stirred at −78 °C for a further 2 h. Triisopropyl borate (23.1 cm^3, 100 mmol) was added with stirring over 5 min at −78 °C and the mixture stirred under nitrogen at −78 °C for 2 h and then at room temperature overnight.

The reaction mixture was carefully acidified (Congo Red) with hydrochloric acid (3 M; *ca*. 150 cm^3), then water (250 cm^3) was added, and the solution extracted with ether (1 dm^3). The ether extract was shaken thoroughly with hydrochloric acid (3 M; 400 cm^3) and brine (400 cm^3), then dried (Na_2SO_4) and the solvent evaporated on a water bath at 35 °C. The product was air-dried overnight at room temperature to give crude *o*-fluorophenylboronic acid (13.87 g, 99%). The crude material was further purified by stirring it with ice-cold pentane (2 × 50 cm^3) and discarding the washings. When dried again as above, the boronic acid **6** was obtained as colourless crystals (13.07 g, 93%) which contained 1.3% triphenylene (w/w) (by ^{1}H NMR spectroscopy). This material, which was suitable for our purposes, was readily freed of triphenylene by recrystallisation from water, but the yield of the pure compound was reduced to 57%; $\delta_H(CDCl_3–[^2H_6]DMSO)$ 7.00 (1 H, m, aryl 3-H), 7.05 approx. (2 H, br s, exch., 2 × OH), 7.10 (1 H, m, aryl 5-H), 7.38 (1 H, m, aryl 4-H) and 7.77 (1 H, m, aryl 6-H).

Preparation of *N*-benzoyl-α-arylglycines 4

Method (a). The aryllead triacetate (3.0 mmol, 1.2 mol equiv.) and dry pyridine (0.712 g, 9.0 mmol, 3.6 mol equiv.) were dissolved in dry chloroform (4 cm^3) and 4-ethoxycarbonyl-2-phenyl-4,5-dihydrooxazol-5-one **1** (0.583 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, 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 aq. sodium hydrogen carbonate (25 cm^3). The chloroform solution was filtered and evaporated at 40 °C and then finally subjected to high vacuum to yield a pale yellow oil. Ethanol (12 cm^3) and aq. sodium hydroxide (1.25 M; 4 cm^3, 2 mol 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 evaporated at 40 °C. Carbon tetrachloride (20 cm^3) was added to the residue for azeotropic removal of water, and the solvent was evaporated under vacuum. The residue was pumped at high vacuum to yield the *N*-benzoyl-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 mol equiv.) over 15 min at 40 °C to a stirred mixture of dry lead tetraacetate (LTA) (1.33 g, 3.0 mmol, 1.2. mol equiv.) and mercury(II) acetate (0.0956 g, 0.3 mmol, 0.12 mol 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 mol equiv.) was added to the mixture followed by the oxazolone **1** (0.583 g, 2.5 mmol) added over 5 min at 40 °C. The mixture was stirred for 1 h at 40 °C and the work-up and hydrolysis were carried out as in method (a).

***N*-Benzoyl-α-phenylglycine 4a.** The title compound was prepared by method (a) in 87% yield and by method (b) in 94% yield, as colourless crystals, mp 168–169 °C (chloroform–light petroleum) (lit.,[17] 172–173 °C); ν_{max}(Nujol)/cm^{-1} 3316, 1700 and 1635; $\delta_H([^2H_6]DMSO)$ 5.71 (1 H, d, ^3J 7.5, CH), 7.24–7.62 (8 H, m, 5 × phenyl H and benzoyl 3-, 4- and 5-H), 7.95 (2 H, m, benzoyl 2- and 6-H) and 8.86 (1 H, d, ^3J 7.5, NH); $\delta_C([^2H_6]DMSO)$ 57.0 (CH), 127.8 (2 × phenyl CH), 128.0 (α-phenyl C-4), 128.21 (2 × phenyl CH), 128.26 (2 × phenyl CH), 128.46 (2 × phenyl CH), 131.5 (phenyl C-4), 133.8 (phenyl C-1), 137.2 (α-phenyl C-1), 166.4 (CONH) and 172.0 (CO_2H); *m/z* 255 (M^+, 0.4%), 210 (10), 133 (22) and 105 (PhCO, 100).

***N*-Benzoyl-α-(2-fluorophenyl)glycine 4b.** Method (b) was employed, with the modifications that 1.5 mol equiv of the 2-fluorophenylboronic acid **6** and 0.24 mol equiv. of mercury(II) acetate were used, and the duration of the boron–lead exchange reaction was increased to 24 h at 40 °C. The *title compound* was obtained in 93% yield as colourless crystals, mp 156–157 °C (chloroform) (Found: C, 65.8; H, 4.6; N, 5.1. $C_{15}H_{12}FNO_3$ requires C, 65.9; H, 4.4; N, 5.1%); ν_{max}(Nujol)/cm^{-1} 3325, 1713 and 1637; $\delta_H([^2H_6]DMSO)$ 5.91 (1 H, d, ^3J 7.8, CH), 7.15–7.28 (2 H, m, 2 × aryl H), 7.32–7.60 (5 H, m, 2 × aryl H and benzoyl

3-, 4- and 5-H), 7.90 (2 H, m, benzoyl 2- and 6-H) and 9.12 (1 H, d, ^3J 7.8, exch., NH); δ_C([$^2H_6$]DMSO) 50.0 (d, $^3J_{C,F}$ 2.9, CH), 115.4 (d, $^2J_{C,F}$ 21.8, aryl C-3), 124.5 (d, $^4J_{C,F}$ 3.2, aryl C-5), 124.7 (d, $^2J_{C,F}$ *ca.* 15.4, aryl C-1), 127.7 (2 × phenyl CH), 128.3 (2 × phenyl CH), 129.6 (d, $^3J_{C,F}$ 3.1, aryl C-6), 130.1 (d, $^3J_{C,F}$ 8.3, aryl C-4), 131.6 (phenyl C-4), 133.6 (phenyl C-1), 160.1 (d, $J_{C,F}$ 246, aryl C-2), 166.3 (CONH) and 171.2 (CO_2H); *m*/*z* 274 (M^+ + 1, 0.7%), 273 (M^+, 0.4), 255 (3), 229 (21), 228 (63), 151 (18), 122 (17), 106 (19) and 105 (PhCO, 100).

***N*-Benzoyl-α-(4-fluorophenyl)glycine 4c.** The title compound was prepared by method (a) in 88% yield as colourless crystals, mp 171–172 °C (chloroform) (lit.,[18] 165 °C) (Found: C, 65.8; H, 4.3; N, 5.1. $C_{15}H_{12}FNO_3$ requires C, 65.9; H, 4.4; N, 5.1%); ν_{max}(Nujol)/cm^{-1} 3323, 1734 and 1627; δ_H([$^2H_6$]DMSO) 5.61 (1 H, d, ^3J 7.5, CH), 7.20 (2 H, m, aryl 3- and 5-H), 7.38–7.62 (5 H, m, aryl 2- and 6-H and benzoyl 3-, 4- and 5-H), 7.90 (2 H, m, benzoyl 2- and 6-H) and 9.02 (1 H, d, ^3J 7.5, exch., NH); δ_C([$^2H_6$]DMSO) 56.2 (CH), 115.2 (d, $^2J_{C,F}$ 21.4, aryl C-3 and -5), 127.8 (2 × phenyl CH), 128.3 (2 × phenyl CH), 130.3 (d, $^3J_{C,F}$ 8.3, aryl C-2 and -6), 131.6 (phenyl C-4), 133.5 (aryl or phenyl C-1), 133.8 (phenyl or aryl C-1), 161.9 (d, $J_{C,F}$ 244, C-F), 166.4 (CONH) and 171.9 (CO_2H); *m*/*z* 273 (M^+, 0.4%), 151 (22), 122 (17) and 105 (PhCO, 100).

***N*-Benzoyl-α-(4-trifluoromethylphenyl)glycine 4d.** The *title compound* was prepared by method (a) in 75% yield and by method (b) in 70% yield, as a pale yellow solid, mp 197–198 °C (chloroform–light petroleum) (Found: C, 59.2; H, 3.9; N, 4.3. $C_{16}H_{12}F_3NO_5$ requires C, 59.4; H, 3.7; N, 4.3%); ν_{max}(Nujol)/cm^{-1} 3266, 1712 and 1649; δ_H([$^2H_6$]DMSO) 5.73 (1 H, d, ^3J 7.5, CH), 7.48 (3 H, m, benzoyl 3-, 4- and 5-H), 7.73 (4 H, s, 4 × aryl H), 7.91 (2 H, m, benzoyl 2- and 6-H) and 9.16 (1 H, d, ^3J 7.5, exch., NH); δ_C([$^2H_6$]DMSO) 57.0 (CH), 124.3 (q, $J_{C,F}$ 273, CF_3), 125.0 (aryl C-3 and -5), 127.5 (2 × aromatic CH), 128.3 (2 × aromatic CH), 128.6 (2 × aromatic CH), 131.5 (phenyl C-4), 133.9 (phenyl C-1), 143.3 (quaternary C), 166.0 (CONH) and 171.2 (CO_2H); *m*/*z* 324 (M^+ + 1, 0.5%), 323 (M^+, 0.3), 278 (25), 201 (17), 172 (10), 106 (17) and 105 (PhCO, 100).

***N*-Benzoyl-α-(2-methoxyphenyl)glycine 4e.** The *title compound* was prepared by method (b) in 83% yield as colourless crystals, mp 145–145.5 °C (ethyl acetate) (Found: C, 67.3; H, 5.5; N, 5.0. $C_{16}H_{15}NO_4$ requires C, 67.4; H, 5.3; N, 4.9%); λ_{max}(EtOH)/nm 273 and 281sh (ε 3150 and 2500); ν_{max}(Nujol)/cm^{-1} 3328, 1723 and 1645; δ_H([$^2H_6$]DMSO) 3.82 (3 H, s, OMe), 5.98 (1 H, d, ^3J 7.5, CH), 6.91–7.10 (2 H, m, 2 × aryl H), 7.28–7.59 (5 H, m, 2 × aryl H and benzoyl 3-, 4- and 5-H), 7.88 (2 H, m, benzoyl 2- and 6-H), 8.84 (1 H, d, ^3J 7.5, exch., NH); δ_C([$^2H_6$]DMSO) 51.1 (CH), 55.8 (OMe), 111.3 (aryl C-3), 120.4 (aryl C-6), 125.5 (aryl C-1), 127.7 (2 × phenyl CH), 128.3 (2 × phenyl CH), 129.0 (aryl CH), 129.5 (aryl CH), 131.5 (phenyl C-4), 134.0 (phenyl C-1), 157.0 (*C*–OMe), 166.4 (CONH) and 172.3 (CO_2H); *m*/*z* 285 (M^+, 0.3%), 267 (3), 241 (40), 240 (23), 180 (19), 136 (22), 134 (13), 106 (16) and 105 (PhCO, 100).

***N*-Benzoyl-α-(4-methoxyphenyl)glycine 4f.** The title compound was prepared by method (a) in 87% yield as colourless crystals, mp 171–173 °C (ethyl acetate) (lit.,[17] 166 °C) Found: C, 67.6; H, 5.3; N, 5.0. $C_{16}H_{15}NO_4$ requires C, 67.4; H, 5.3; N, 4.9%); λ_{max}(EtOH)/nm 275 and 282 (ε 2300 and 1600); ν_{max}(Nujol)/cm^{-1} 3282, 1708 and 1634; δ_H([$^2H_6$]DMSO) 3.74 (3 H, s, OMe), 5.52 (1 H, d, ^3J 7.3, CH), 6.93 (2 H, m, aryl 3- and 5-H), 7.36–7.59 (5 H, m, aryl 2- and 6-H and benzoyl 3-, 4- and 5-H) and 7.91 (2 H, m, benzoyl 2- and 6-H); δ_C([$^2H_6$]DMSO) 55.3 (OMe), 56.2 (CH), 114.0 (aryl C-3 and -5), 127.9 (2 × phenyl CH), 128.3 (2 × phenyl CH), 129.2 (aryl C-1), 129.6 (aryl C-2 and -6), 131.6 (phenyl C-4), 134.0 (phenyl C-1), 159.2 (*C*–OMe), 166.5 (CONH) and 172.4 (CO_2H); *m*/*z* 285 (M^+, 2%), 241 (20), 180 (30), 134 (38) and 105 (PhCO, 100).

Preparation of 4-(2,4-dimethoxyphenyl)-4-ethoxycarbonyl-2-phenyl-4,5-dihydrooxazol-5-one 3g. The general method (a) for preparation of compounds **4** was followed using 2,4-dimethoxyphenyllead triacetate **2g** (1.563 g, 3.0 mmol). The crude arylated oxazolone **3g** was not subjected to alkaline hydrolysis, but was dissolved in dry ether (15 cm^3), filtered through silica gel (2.5 g), and the solvent removed under anhydrous conditions to give a yellow oil (0.91 g, 98%) which was crystallised from chloroform–pentane to give the *title compound* **3g** as moisture-sensitive colourless crystals, mp 91.5–93 °C (Found: C, 64.5; H, 5.2; N, 3.7; M^+, 369.1213. $C_{20}H_{19}NO_6$ requires C, 65.0; H, 5.2; N, 3.8%; *M*, 369.1212); λ_{max}(EtOH)/nm 251 and 279sh (ε 29 900 and 17 400); ν_{max}($CHCl_3$)/cm^{-1} 1842, 1823, 1746, 1646 and 1614; δ_H($CDCl_3$) 1.31 (3 H, t, ^3J 7.0, Me), 3.79 (3 H, s, OMe), 3.81 (3 H, s, OMe), 4.34 (2 H, q, ^3J 7.0, CH_2), 6.49 (2 H, m, 3- and 5-ArH), 7.22 (1 H, m, 6-ArH), 7.43–7.65 (3 H, m, phenyl 3-, 4- and 5-H) and 8.12 (2 H, m, phenyl 2- and 6-H); δ_C($CDCl_3$) 14.0 (Me), 55.4 (OMe), 55.9 (OMe), 62.9 (CH_2), 99.8 (aryl C-3), 104.8 (aryl C-5), 115.6 (quaternary C), 125.5 (quaternary C), 128.4 (2 × phenyl CH), 128.6 (aryl C-6), 128.8 (2 × phenyl CH), 133.2 (phenyl C-4), 158.3 (*C*–OMe), 161.8 (*C*–OMe), 163.3 (quaternary C), 166.0 (quaternary C) and 172.5 (quaternary C); *m*/*z* 369 (M^+, 2%), 296 (12), 165 (25) and 105 (100).

***N*-Benzoyl-α-(2,4-dimethoxyphenyl)glycine 4g.** The *title compound* was obtained by method (a) in 90% yield as colourless crystals, mp 110–113 °C (ethyl acetate–light petroleum) (Found: C, 64.5; H, 5.7; N, 4.2. $C_{17}H_{17}NO_5$ requires C, 64.8; H, 5.4; N, 4.4%); λ_{max}(EtOH)/nm 276 (ε 4400); ν_{max}(Nujol)/cm^{-1} 3308, 1720 and 1640; δ_H([$^2H_6$]DMSO) 3.76 (3 H, s, OMe), 3.79 (3 H, s, OMe), 5.82 (1 H, d, ^3J 7.5, CH), 6.56 (2 H, m, aryl 3- and 5-H), 7.28 (1 H, d, ^3J 8.3, aryl 6-H), 7.46 (3 H, m, benzoyl 3-, 4- and 5-H), 7.87 (2 H, m, benzoyl 2- and 6-H) and 8.69 (1 H, d, ^3J 7.5, exch., NH); δ_C([$^2H_6$]DMSO) 50.6 (CH), 55.2 (OMe), 55.7 (OMe), 98.5 (aryl C-3), 104.8 (aryl C-5), 117.6 (quaternary C), 127.6 (2 × phenyl CH), 128.1 (2 × phenyl CH), 129.6 (aryl C-6), 131.3 (phenyl C-4), 133.9 (quaternary C), 158.0 (*C*–OMe), 160.5 (*C*–OMe), 166.1 (CONH) and 172.4 (CO_2H); *m*/*z* 315 (M^+, 0.25%), 271 (M − CO_2, 46), 270 (22), 210 (23), 166 (23), 164 (17), 106 (14) and 105 (PhCO, 100).

***N*-Benzoyl-α-(3,4-dimethoxyphenyl)glycine 4h.** The *title compound* was prepared by method (a) in 89% yield and by method (b) in 75% yield as yellow crystals, mp 210–211 °C (ethyl acetate) (Found: C, 64.7; H, 5.5; N, 4.4. $C_{17}H_{17}NO_5$ requires C, 64.8; H, 5.4; N, 4.4%); λ_{max}(EtOH)/nm 274 (ε 12 000); ν_{max}(Nujol)/cm^{-1} 3353, 1713 and 1622; δ_H([$^2H_6$]-DMSO) 3.74 (3 H, s, OMe), 3.75 (3 H, s, OMe), 5.51 (1 H, d, ^3J 7.5, CH), 6.94 (1 H, d, ^3J 8.3, aryl 5-H), 7.02 (1 H, dd, ^3J 8.3, ^4J 2.0, aryl 6-H), 7.12 (1 H, d, ^4J 2.0 aryl 2-H), 7.35–7.59 (3 H, m, benzoyl 3-, 4- and 5-H), 7.90 (2 H, m, benzoyl 2- and 6-H) and 8.92 (1 H, d, ^3J 7.5, exch., NH); δ_C([$^2H_6$]DMSO) 55.6 (2 × OMe), 56.7 (CH), 111.7 (aryl C-5 or -2), 112.0 (aryl C-2 or -5), 120.6 (aryl C-6), 127.7 (2 × phenyl CH), 128.2 (2 × phenyl CH), 129.4 (aryl C-1), 131.4 (phenyl C-4), 133.9 (phenyl C-1), 148.7 (2 × *C*–OMe), 166.3 (CONH) and 172.2 (CO_2H); *m*/*z* 315 (M^+, 1%), 271 (M − CO_2, 30), 210 (18), 164 (24) and 105 (PhCO, 100).

Synthesis of trimethyl(vinyl)stannanes

The method employed by us in a previous study[6] to produce trimethyl[(*E*)-styryl]stannane **7a** and [(*E*)-*p*-methoxystyryl]trimethylstannane **7c** was used.

The following compounds were prepared by the same general method.

[(*E*)-*p*-Methylstyryl]trimethylstannane 7b. Yield 40%, bp 59 °C/0.2 mmHg (Kugelrohr) (lit.,[19] 89 °C/0.35 mmHg); δ_H($CDCl_3$) 0.23 (9 H, s, ^{119}Sn and ^{117}Sn satellites gave $^2J_{Sn,Me}$ 52.9 and 55.1 respectively, $SnMe_3$), 2.36 (3 H, s, Me), 6.86 (2 H, s, ^{119}Sn and ^{117}Sn satellites gave $^2J_{Sn,H}$ and $^3J_{Sn,H}$ average 74.9, 2 × vinyl H), 7.15 and 7.34 (4 H, AA′BB′, 4 × aryl H).

[(*E*)-3,4-Dimethoxystyryl]trimethylstannane 7d. Yield 65%, a moisture-sensitive waxy pale yellow solid, bp 67 °C/0.18 mmHg (Kugelrohr), mp 63–65 °C (Found: M^+ 328.0485. $C_{13}H_{20}O_2$ ^{120}Sn

requires *M*, 328.0485); $\nu_{max}(CHCl_3)/cm^{-1}$ 4210, 3020, 2400, 1600, 1570, 1510, 1460, 1260 and 1210 cm^{-1}; $\delta_H(CDCl_3)$ 0.20 (9 H, s, ^{119}Sn and ^{117}Sn satellites gave $^2J_{Sn,Me}$ 55.2 and 53.2 respectively, $SnMe_3$), 3.88 (3 H, s, OMe), 3.91 (3 H, s, OMe), 6.71 (1 H, d, $^3J_{trans}$ 19.3 vinyl H), 6.84 (1 H, d, $^3J_{trans}$ 19.3, vinyl H), 6.81 (1 H, m, aryl 6-H) and 6.97 (2 H, m, aryl 2 and 5-H); *m*/*z* 328 (M^+, 7%), 313 (100), 283 (11), 163 (19), 151 (31) and 135 (17).

Preparation of *N*-benzoyl-α-vinylglycine ethyl esters 10

The trimethyl(vinyl)stannane **7** (1–5 mmol, 1.1 mol equiv.) in chloroform (2 cm^3) was added to a stirred solution of dry LTA (1.0 mol equiv.) and acetic acid (1% w/w) in chloroform (7 cm^3) at room temperature. The solution was stirred at room temperature for 2–3 min (as indicated), and then added to a solution of the oxazolone **1** (1.0 mol equiv.) in chloroform (5 cm^3) and pyridine (3.3 mol 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 sonicated in deoxygenated ethanol–water (1:4) at <40 °C for 11 h under an atmosphere of nitrogen. The mixture was extracted with chloroform and then the extract was dried (Na_2SO_4) and the solvent was evaporated. The pure product was isolated by preparative HPLC in the solvent system indicated.

The following compounds were prepared by the above general method.

Ethyl (*E*)-2-benzamido-4-phenylbut-3-enoate 10a. Prepared from trimethyl[(*E*)-styryl]stannane **7a** (0.500 g, 1.87 mmol), LTA (0.755 g, 1.70 mmol) and the oxazolone **1** (0.397 g, 1.70 mmol). Fractionation by HPLC in methanol–dichloromethane (0.2:99.8) afforded a colourless solid (0.147 g, 28%), mp 91–93 °C (Found: C, 73.4; H, 5.9; N, 4.7. $C_{19}H_{19}NO_3$ requires C, 73.8; H, 6.2; N, 4.5%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3430, 3020, 1730, 1670, 1510 and 1480; $\delta_H(CDCl_3)$ 1.30 (3 H, t, ^3J 7.08, $CH_2C\mathit{H}_3$), 4.25 (2 H, m, OCH_2), 5.49 (1 H, m, CH), 6.30 (1 H, dd, $^3J_{vic}$ 6.35, $^3J_{trans}$ 15.9, vinyl H), 6.73 (1 H, dd, $^4J_{allylic}$ 1.4, $^3J_{trans}$ 15.9, vinyl H), 7.13 (1 H, br d, ^3J 7.21, NH), 7.20–7.55 (8 H, m, 8 × phenyl H), 7.87 (2 H, m, benzoyl 2- and 6-H); *m*/*z* 309 (M^+, <5%), 236 (17), 204 (55), 105 (100) and 77 (64).

Ethyl (*E*)-2-benzamido-4-(*p*-methylphenyl)but-3-enoate 10b. Prepared from trimethyl[(*E*)-*p*-methylstyryl]stannane **7b** (0.450 g, 1.60 mmol), LTA (0.646 g, 1.46 mmol) and the oxazolone **1** (0.340 g, 1.46 mmol). Fractionation by HPLC in methanol–dichloromethane (0.2:99.8) afforded a colourless solid (0.138 g, 29%), mp 85–87 °C (Found: C, 74.6; H, 6.7; N, 4.3. $C_{20}H_{21}NO_3$ requires C, 74.3; H, 6.6; N, 4.3%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3430, 3010, 1740, 1670, 1510 and 1480; $\delta_H(CDCl_3)$ 1.31 (3 H, t, ^3J 7.15, $CH_2C\mathit{H}_3$), 2.32 (3 H, s, Me), 4.28 (2 H, m, OCH_2), 5.46 (1 H, m, CH), 6.23 (1 H, dd, $^3J_{vic}$ 6.40, $^3J_{trans}$ 15.9, vinyl H), 6.69 (1 H, d, $^3J_{trans}$ 15.9, vinyl H), 6.97 (1 H, br d, ^3J 7.15, NH), 7.11 and 7.27 (4 H, AA′BB′, 4 × phenyl H), 7.35–7.59 (3 H, m, phenyl 3-, 4- and 5-H) and 7.86 (2 H, m, phenyl 2- and 6-H); *m*/*z* 323 (M^+, 14%), 277 (11), 250 (25), 218 (68), 144 (62), 105 (100) and 77 (88).

Ethyl (*E*)-2-benzamido-4-(*p*-methoxyphenyl)but-3-enoate 10c. Prepared from trimethyl[(*E*)-*p*-methoxystyryl]stannane **7c** (0.425 g, 1.43 mmol), LTA (0.577 g, 1.30 mmol) and the oxazolone **1** (0.304 g, 1.30 mmol). Fractionation by HPLC in ethyl acetate–light petroleum (15:85) gave a colourless solid (0.133 g, 30%), mp 59–61 °C (Found: C, 70.8; H, 6.5; N, 4.0. $C_{20}H_{21}NO_4$ requires C, 70.8; H, 6.2; N, 4.1%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3430, 3010, 1730, 1660, 1510 and 1480; $\delta_H(CDCl_3)$ 1.32 (3 H, t, ^3J 7.14, $CH_2C\mathit{H}_3$), 3.80 (3 H, s, OMe), 4.28 (2 H, m, OCH_2), 5.45 (1 H, m, CH), 6.14 (1 H, dd, $^3J_{vic}$ 6.4, $^3J_{trans}$ 15.8, vinyl H), 6.68 (1 H, d, $^3J_{trans}$ 15.8, vinyl H), 6.95 (1 H, br d, ^3J 7.4, NH), 6.84 and 7.31 (4 H, AA′BB′, 4 × aryl H), 7.40–7.58 (3 H, m, phenyl 3-, 4- and 5-H) and 7.88 (2 H, m, phenyl 2- and 6-H); *m*/*z* 339 (M^+, <5%), 234 (42), 160 (17), 105 (100) and 77 (24).

Ethyl (*E*)-2-benzamido-4-(3,4-dimethoxyphenyl)but-3-enoate 10d. Prepared from trimethyl[(*E*)-3,4-dimethoxystyryl]stannane **7d** (0.400 g, 1.22 mmol), LTA (0.493 g, 1.11 mmol) and the oxazolone **1** (0.259 g, 1.11 mmol). Fractionation by HPLC in methanol–dichloromethane (0.3:99.7) afforded a colourless solid (0.071 g, 17%), mp 93–94 °C (Found: M^+, 369.1576. $C_{21}H_{23}NO_5$ requires *M*, 369.1576); $\nu_{max}(CHCl_3)/cm^{-1}$ 3430, 3010, 1740, 1670, 1510 and 1480; $\delta_H(CDCl_3)$ 1.33 (3 H, t, ^3J 7.10, $CH_2C\mathit{H}_3$), 3.88 (3 H, s, OMe), 3.89 (3 H, s, OMe), 4.29 (2 H, m, OCH_2), 5.46 (1 H, m, CH), 6.29 (1 H, dd, $^3J_{vic}$ 6.42, $^3J_{trans}$ 16.0, vinyl H), 6.69 (1 H, dd, $^4J_{allylic}$ 1.15, $^3J_{trans}$ 16.0, vinyl H), 6.80 (1 H, m, aryl 6-H), 6.91 (3 H, m, aryl 2- and 5-H and NH), 7.40–7.60 (3 H, m, phenyl 3-, 4- and 5-H) and 7.88 (2 H, m, phenyl 2- and 6-H); *m*/*z* 369 (M^+, 5%), 264 (33), 218 (11), 175 (29), 105 (100) and 77 (43).

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