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Elaboration of the Side Chain of α-Amino Acids by Palladium-Catalysed Stille Couplings

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Abstract: The palladium-catalysed couplings of a γ-tri-*n*-butylstannylallylglycine derivative and an *E*-δ-tri-*n*-butylstannylallylglycine derivative with various organic electrophiles are described.

Unnatural and non-proteinogenic α-amino acids are important as enzyme inhibitors, therapuetic agents and chiral synthons.[1a-e] An important class of non-proteinogenic α-amino acids is that based on allylglycines, many of these compounds have been reported to act as irreversible, mechanism-based, inhibitors of pyridoxal phosphate dependent enzymes.[2a-d] Allylglycine derivatives have been prepared previously by routes such as allyl electrophiles reacting with glycine anions[3a-d], allyl nucleophiles reacting with glycine cations[4a-d] and Wittig reactions of *L*-aspartic acid semialdehyde derivatives.[5]

Stille coupling methodology should be ideally suited for the elaboration of the side-chain of α-amino acids since the reactions take place under mild conditions and are tolerant of a wide variety of functionality.[6] Palladium-catalysis has been used previously for the synthesis of allylglycine derivatives including allyl acetate coupling with glycine anions[3d,7], vinyl electrophiles coupling with an organozinc derivative of β-iodoalanine [8], rearrangements of imino acid allyl ester derivatives[9] and a Stille coupling of a bromoallylglycine derivative.[10]

We have previosly reported on the palladium-catalysed elaboration of a vinylglycine derivative via Heck reactions[11] and a propargylglycine derivative with organic electrophiles.[12]

In this paper we report that tri-*n*-butylstannylallylglycine derivatives undergo coupling with organic electrophiles in the presence of palladium catalysts and we have explored the scope and limitations of this methodology for the preparation of modified allylglycines.

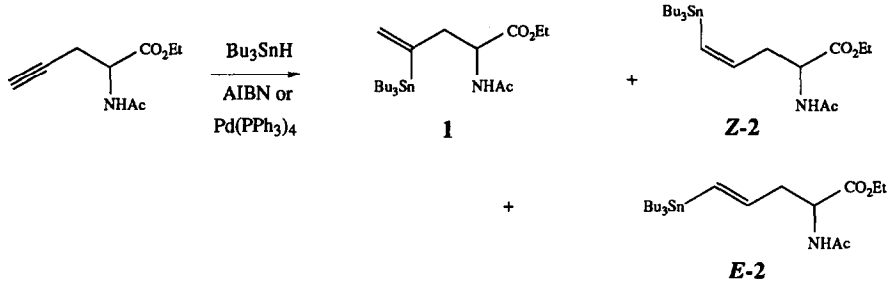
Results and Discussion

The preparations of the tri-*n*-butylstannylallylglycine derivatives **1**, ***E*-2** and ***Z*-2** have been reported briefly.[13] Palladium-catalysed hydrostannation of ethyl N-acetyl-*D,L*-propargylglycinate gave two products resulting from *syn*-addition, namely γ-tri-*n*-butylstannyl-*D,L*-allylglycinate **1** and the δ regioisomer ***E*-2**

(Scheme 1). The rapid reaction gave the two products in quantitative yield and a subsequent number of flash chromatographic purifications gave a clean separation of the two isomers. The ^{1}H nmr spectrum of the γ-isomer **1** is markedly different to that of the δ-isomer with the vinylic methylene protons resonating as broad singlets at δ5.26 and 5.74 and the diastereotopic β-protons as distinct doublets of doublets at δ2.51 and 2.79 respectively, all four of these protons with tin satellites. The vinylstannane **1** was air and temperature stable (distilled at *ca* 200°/0.03mm without decomposition).

Compound ***E*-2** (containing between 5-10% ***Z*-2**) can also be prepared by the hydrostannation of ethyl N-acetyl-*D,L*-propargylglycinate with tri-*n*-butyltin hydride in toluene at 100^0 (Scheme 1). The two isomeric vinylstannanes were easily distinguished in the ^{1}H nmr spectrum as ***E*-2** showed a coupling of 18.6Hz and ***Z*-2** a coupling of 12.6Hz for the respective vinylic protons. Satellites for the ^{117}Sn/^{119}Sn to ^{1}H coupling were evident for the vinylic protons. We were unable to separate ***E*-2** and ***Z*-2** by chromatography on silica gel. The stannanes were isolated as a colourless, clear oil, stable to the atmosphere for many months and to distillation at high temperature under reduced pressure (*ca* 200^0/0.03mm). Attempted isomerisation of the minor *Z*-isomer to the thermodynamically more stable *E*-isomer by a number of methods such as heating the mixture to 250° at atmospheric pressure (some decomposition), heating in toluene or dioxane at reflux in the presence of tri-*n*-butyltin hydride and AIBN or by sun lamp irradiation of the mixture at reflux in toluene had no significant effect on the proportion of *Z*-isomer present in the mixture.

The palladium catalysed hydrostannation was repeated on an enantiomerically enriched sample of ethyl N-acetyl-*L*-propargylglycinate and both ***L*-1** and ***L,E*-2** were optically active and a chiral Eu(III)(hfc)3 ^{1}H nmr shift experiment confirmed that no racemisation had taken place.

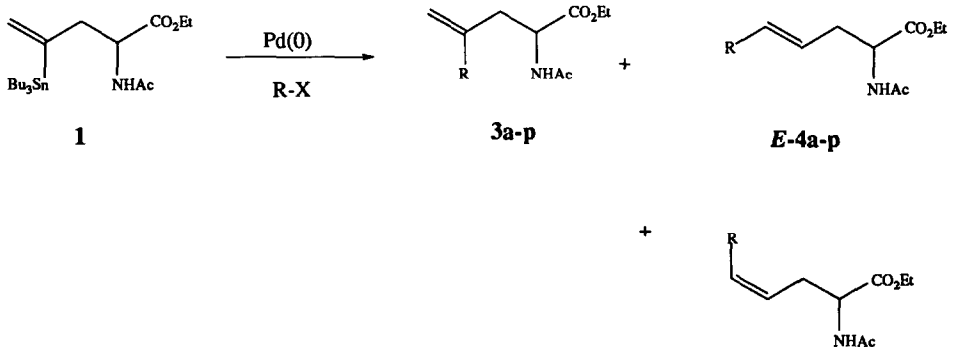


Scheme 1

Stille couplings of ethyl N-acetyl-γ-tri-n-butylstannylallylglycinate (1)

The Stille coupling of the γ-stannane (**1**) with iodobenzene was studied as a model reaction (Scheme 2). The reaction catalysed by Pd(PPh3)4 in DMF at 100°C (Table 1, entry 1) gave a number of different isomeric products: the anticipated γ-phenyl product **3a** arising from *ipso*-substitution as well as the unexpected *E* and *Z*-δ-isomers ***E*-4a** and ***Z*-4a** arising from *cine*-substitution. The three isomers were easily characterised by the vinylic proton signals in their ^{1}H nmr spectra. For the γ-phenyl isomer (**3a**) the vinylic protons resonated at δ5.02 and 5.25 as broad singlets, whereas the *E*-δ isomer (***E*-4a**) had a doublet (δ6.36, *J*15.7Hz) and doublet of triplets (δ5.98, *J*7.4, 15.7Hz) for the C5 and C4-hydrogens respectively and the *Z*-γ-isomer (***Z*-4a**) a doublet (δ6.53ppm, *J*11.6Hz) and doublet of triplets (δ5.50, *J*7.0, 11.7Hz) for the corresponding

vinylic protons. The resonances of the acetamido methyl group, the ethyl ester methylene and the α-proton were all shifted upfield for **3a** relative to ***E*-4a** and ***Z*-4a** (*ca* 0.17, 0.22 and 0.08 ppm respectively) indicating that those protons are positioned to some extent in the shielding zone of the phenyl ring. The reaction was repeated using a number of different conditions and in all instances the three isomeric products were obtained (Table 1, entries 2-4). The small amounts of δ-substituted isomers (***E*-4a** and ***Z*-4a**) did not arise from *ipso*-substitution reaction of small amounts of residual δ-stannane (***E*-2** and ***Z*-2**) in the starting material since ^{1}H nmr spectra confirmed the purity of the γ-stannane. Recovery of isomerically pure γ-stannane (**1**) from some of the reaction mixtures suggested that vinylstannanes ***E*-2** and ***Z*-2** were not formed *in situ*. The use of a catalyst derived from (Pd_2dba_3.$CHCl_3$) and eight equivalents of $AsPh_3$ resulted in a more active catalyst and a lower temperature reaction, however, this catalyst system produced significantly more *cine*-substitution (entry 4)



1 **3a-p** ***E*-4a-p**

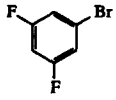
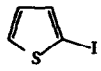
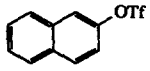
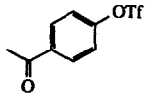
Z-4a-g

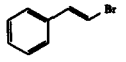
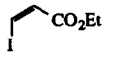
Scheme 2

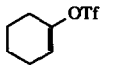
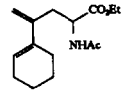
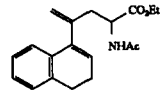
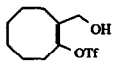
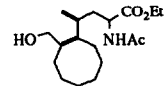
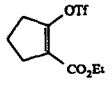
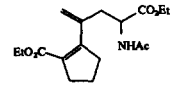
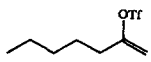
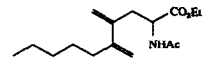
Cine-substitution of vinyl stannanes during Stille couplings has been reported in the literature in only a few instances and usually involves sterically hindered organostannanes where the rate of transmetallation might be expected to be slower.[14a,b,15] The formation of *cine*-substituted products could be the result of a Heck reaction between the terminal alkene portion of **1** and the organic electrophile, followed by a palladium-catalysed loss of tri-*n*-butyltin halide. When the reaction was repeated in the presence of triethylamine in an attempt to facilitate the Heck reaction the effect on product distribution was negligible (Table 1, compare entries 2 and 3).

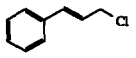
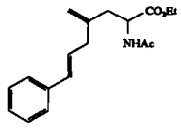
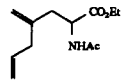
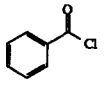
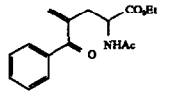
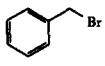
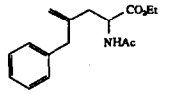
The reactions of other aryl halides were investigated using the $Pd(AsPh_3)_4$ in THF system (Table 1, entries 5,6). 3,5-Difluorobromobenzene reacted to give the desired *ipso*-substituted product (**3b**) as well as a small amount of γ-phenyl product (**3a**). Presumably formation of **3a** arose by a palladium catalysed transfer of a phenyl group from a triphenylarsine ligand. Transfer of aryl groups from phosphine ligands have been reported previously.[16a-c] No *cine*-isomers were observed for the reaction of 3,5-difluorobromobenzene. Reaction of 2-iodothiophene gave an almost 1:1 mixture of γ-(2-thienyl) and *E*-δ-isomers (**3c** and ***E*-4c**) (entry 6). Phenyl substituted products were also formed (tlc) but were separated from the desired products by flash chromatography.

Table 1. Stille coupling between γ-tri-*n*-butylstannylallylglycinate (**1**) and organic electrophiles

Entry	Substrate	Condition[a]	Yield % isolated	Ratio of products[b]				
				γ	*E*-δ	*Z*-δ	γ-Ph (**3a**)	*E*-δ-Ph (***E*-4a**)
1		A	52	80 (**3a**)	10 (***E*-4a**)	10 (***Z*-4a**)		
2		B	66	52	32	18		
3		B[c]	54	63	22	15		
4		C	55[d]	30	30	10		
5		C	56	100 (**3b**)	0	0	7	
6		C	53	54 (**3c**)	46 (***E*-4c**)	0	trace	
7		D	70	85 (**3d**)	15 (***E*-4d**)	0	0	0
8		B[e]	64	65	13		19	3
9		B	67	86	0		14	0
10		B[e]	69	95 (**3e**)	5 (***E*-4e**)		0	0
11		B	37	100	0		0	0

				γ	*E*-δ	γ-Ph (3a)	*E*-δ-Ph (*E*-4a)
12		B	68	8 (3f)	79 (*E*-4f)	10	0
13		B[f]	47	71	0	29	0
14		E	91	100	0	0	0
15		B	70	65 (*Z*-3g) 10 (*E*-3g)	18 (*Z*,*E*4g) 7 (*E*,*E*-4g)		

Entry	Substrate	Condition	%Yield	Product
16		B	79	 **3h**
17		B	98	 **3i**
18		B	44	 **3j**
19		B	91	 **3k**
20		B	91	 **3l**

21		B	99	 **3m**
22		B	80	 **3n**
23		B	69	 **3o**
24		B	100	 **3p**

a. A 5% $Pd(PPh_3)_4$, DMF, 100°

B 5% $Pd_2dba_3.CHCl_3/AsPh_3$ (1:8), THF,65°

C 5% $Pd_2dba_3.CHCl_3/P(2\text{-furyl})_3$ (1:8), THF,65°

D 5% $Pd(PPh_3)_4$, LiCl, DMF, 100°

E 5% $Pd(CH_3CN)_2Cl_2$, THF, 65°

b. Ratio determined by ^1H nmr spectra.

c. In addition, triethylamine (3 equivalents) added.

d. Another product, tentatively assigned as a 2-furyl derivative (30%) was isolated.

e. In addition LiCl was added.

f. In addition Ag_2CO_3 was added.

It is interesting to note the effect that the electron density of the aryl group has on the *ipso:cine* ratio of the aryl halide Stille reactions. The most electron deficient, 3,5-difluorobromobenzene, gave no *cine* substitution products (entry 5), yet the most electron rich, 2-iodothiophene, gave 46% of ***E*-4c** (entry 6). Iodobenzene gave up to 50% δ-isomers depending upon the reaction conditions. If transmetallation is considered as an electrophilic substitution reaction it would be expected to occur more rapidly for more electron deficient Pd(II) complexes. Thus, for relatively π-electron rich arylpalladium(II) complexes, such as would be formed after oxidative addition of 2-iodothiophene to Pd(0), transmetallation would occur relatively slowly because of the decreased electrophilicity of palladium(II) so competing processes, such as Heck-addition, can become more dominant.

Stille coupling of the γ-stannane (**1**) with two aryl triflates was examined and the results are summarised in Table 1. 2-Naphthyl triflate was initially investigated with a standard Stille catalyst system[17]

for organotriflates consisting of $Pd(PPh_3)_4$ and LiCl in DMF at 100° (entry 7). Once again a number of products were formed from *ipso* and *cine* substitution, γ-(2-naphthyl)allyl glycinate (**3d**) and *E*-δ-(2-naphthyl)allylglycinate (***E*-4d**). Repeating this reaction with $Pd(AsPh_3)_4$ and LiCl in THF (entry 8) gave four products , **3d** and ***E*-4d** as well as the corresponding phenyl substituted products **3a** and ***E*-4a**. This clearly shows the effect that the ligands have on the product distribution (*i.e.* triphenylarsine transfers a phenyl group in the presence of palladium, but triphenylphosphine does not). Although lithium chloride is reported as being necessary for the coupling reactions of aryl triflates[17] we investigated the reaction without this additive to see whether the phenyl substitution leading to by-products **3a** and ***E*-4a** was occurring through a non-transmetallative process. Surprisingly, in the absence of lithium chloride the reaction (entry 9) gave products arising only from *ipso*-substitution, namely the γ-naphthyl and the γ-phenylallylglycinate (**3d** and **3a**). This is, to the best of our knowledge, the first example of a Stille reaction of an *aryl* triflate occurring without the necessity for a halide source.

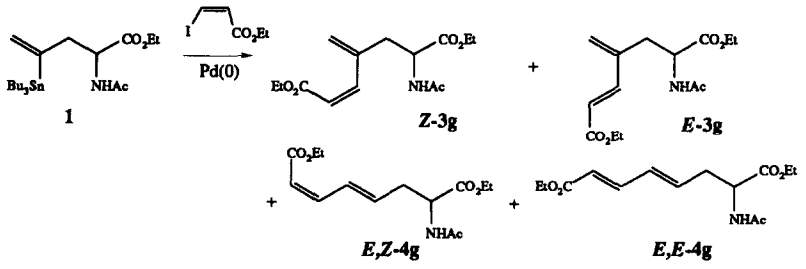
The coupling of *p*-acetylphenyl triflate with **1** in the presence and absence of lithium chloride gave an interesting result in that coupling with lithium chloride gave the expected *ipso*-substituted γ-isomer (**3e**) and a small amount of *E*-δ-isomer (***E*-4e**) (entry 10), whilst coupling in the absence of lithium chloride (entry 11) gave only the transmetallation product (**3e**). However, the catalyst was unstable under these conditions and often conversion of **1** was incomplete.

On the basis of these results with respect to electron density and the presence of halide, the reaction of vinyl halides with **1** could be expected to yield substantial amounts of *cine*-substituted product in addition to the expected *ipso*-substitution. Indeed, this was the case for *E*-β-bromo styrene which gave *predominantly* the *cine*-substituted *E,E*-δ-substituted product (***E*-4f**) and a minor amount of γ-styryl product (**3f**) when reacted under our standard conditions (Table 1, entry 12). Such a preference for *cine*-substitution was not observed for any other Stille reaction of **1**.

In an attempt to obtain a more electron-deficient palladium(II) intermediate, the reaction was repeated in the presence of silver carbonate as a halide abstractor. This procedure has previously been used in Heck reactions of vinyl*silanes* with vinyl and aryl halides where unexpected transmetallation-like products were eliminated by the addition of silver salts.[18] Although we are unaware of any previous use of silver salts in *Stille* reactions we postulated that coupling of organohalides in the presence of silver(I) would lead mainly, or exclusively, to *ipso*-substitution because the cationic intermediate would be more electrophilic and consequently would undergo transmetallation more efficiently. Thus reaction of *E*-β-bromostyrene with **1** in the presence of $Pd(AsPh_3)_4$ and silver carbonate in THF at reflux gave a modest yield of a mixture of γ-styryl and γ-phenyl products (**3f** and **3a**) (Table 1, entry 13). No *cine* substituted products were observed. Again, **3a** is formed by phenyl substitution from a triphenylarsine ligand, a process independent of halide. This reaction shows that Heck addition to a vinylstannane can be suppressed by the addition of silver salts and confirms that halide bound to palladium(II) is an important prerequisite for *cine*-substitution.

Reaction of *E*-β-bromostyrene with **1** using a modified procedure developed by Stille for vinylstannanes [$PdCl_2(CH_3CN)_2$, DMF, room temperature, entry 16][19] gave an excellent yield of the desired γ-styryl product (**3f**) with no side product formation.

Ethyl *Z*-2-iodoacrylate reacted with **1** to yield two *ipso* (**Z-3g, E-3g**) and two *cine* substituted (***E,Z*** **4g, *E,E*-4g**) isomers (Scheme 3, Table 1 entry 15). These isomers were inseparable by chromatography and were clearly assigned on the basis of their ^{1}H nmr coupling constants.



Scheme 3

Vinyl triflates proved to be very good substrates for the Stille reactions of the γ-stannane (**1**) (Table 1, entries 16-20). All coupled successfully and stereospecifically in good to excellent yields with the Pd(AsPh3)4 catalyst in THF without the need for addition of lithium chloride. Catalyst stability was excellent and the reaction mixtures remained clear and light yellow throughout the reaction. The reactive species in the transmetallation step is believed to be a strongly electrophilic cationic palladium(II) intermediate. No *cine*-substitution products were observed although in some instances small amounts of unidentified product were obtained, possibly double bond isomers.

Reaction of allyl halides (cinnamyl chloride and allyl bromide), benzoyl chloride and benzyl bromide with the γ-stannane (**1**) gave the desired products from *ipso*-substitution in good to quantitative yields (Table 1. entries 21-24). No isomers resulting from double bond migration were observed by ^{1}H nmr spectroscopy. The 1,4-dienes were clearly assigned by the presence of the doubly allylic methylene groups at δ2.97 and 2.70 respectively and the expected splitting pattern and *trans*-coupling between the C6 and C7 vinylic protons (*e.g.* **3m**: δ6.20, *dt*, C6; **3n**: δ5.70, *ddt*, C6). Although these reactions were with halides, no products arising from *cine*-substitution were observed. Presumably the palladium(II) intermediates are more electron deficient than the corresponding vinyl and aryl intermediates.

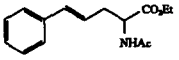
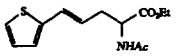
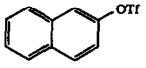
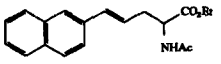
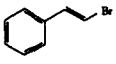
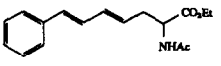
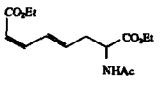
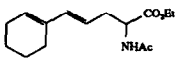
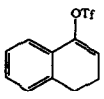
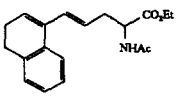
In order to show that these Stille reactions were not occurring with concomitant racemisation at the α-centre, we repeated one of the reactions using the enantiomerically enriched γ-stannane (*L*-**1**). We chose the reaction of *p*-acetylphenyl triflate with Pd(AsPh3)4 in the absence of lithium chloride since this had given a clean product (**3e**) with no unwanted isomers or byproducts. A ^{1}H nmr shift experiment with Eu(hfc)3 on the products of both racemic and chiral reaction products showed no racemization had taken place.

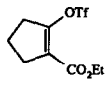
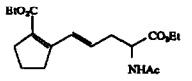
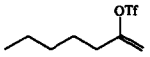
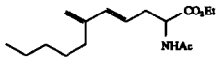
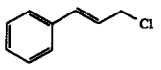
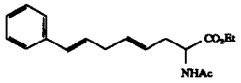
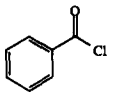
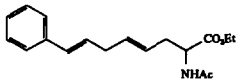
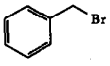
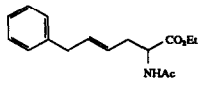
Stille coupling reactions of ethyl E,N-acetyl-δ-tri-n-butylstannylallylglycinate (E-2)

Stille coupling reactions were carried out on *E*-δ-tri-*n*-butylstannylallylglycinate (***E*-2**) with a selection of the organohalides and triflates which had successfully coupled with the γ-stannane (**1**). All reactions were performed using 5mol% of Pd(AsPh3)4. Generally these reactions proceeded to give good to excellent yields of the expected *ipso*-substituted products.

The reaction with aryl halides (Table 2, entries 1 and 2) gave the desired coupled products (***E*-4a** and ***E*-4c**) in good yields. If part the reason for *cine*-substitution of the γ-stannane (**1**) was because steric

Table 2. Stille coupling between *E*-δ-tri-*n*-butylstannylallylglycinate (**E-2**) and organic electrophiles[a]

Entry	Substrate	% Yield Isolated	Product
1		83	 **(*E*-4a)**
2		74	 **(*E*-4c)**
3		29[b]	 **(*E*-4d)**
4		76	**(*E*-4d)**
5		75	 **(*E*-4f)**
6		84	 **(*E,Z*-4g)**
7		47	 **(4h)**
8		53	 **(4i)**

9		93	 (4k)
10		58	 (4l)
11		96	 (4m)
12		80	 (4n)
13		68[c]	 (4o)

a. 5% $Pd_2dba_3.CHCl_3$, $AsPh_3$ (1:8), THF, 65°
b. Heated at 50° with 2 equivalents LiCl
c. Room temperature

hindrance retarded the efficiency of transmetallation and hence Heck addition became a competitive alternative process, we might expect that the less sterically encumbered *E*-δ-stannane (***E*-2**) would be less likely to undergo *cine*-substitution.

The only aryltriflate coupled was 2-naphthyl triflate which was reacted both in the presence and absence of lithium chloride. With lithium chloride present the Stille reaction gave a low yield of coupled product (***E*-4d**) (entry 3). However, ***E*-2** also reacted with 2-naphthyl triflate in the absence of lithium chloride and gave the product (***E*-4d**) in good yield (entry 4). The catalyst was not stable in this reaction and precipitated palladium black within two hours. However, this is an interesting result as it shows that Stille coupling of aryl triflates with quite sterically unencumbered vinylstannanes can occur without the addition of a halide source and may be quite general for a variety of stannanes, although catalyst instability may be a limiting factor in some reactions. Stille reactions of ***E*-2** with vinyl halides and triflates are summarised in Table 2. Reaction of *E*-β-bromo styrene and ethyl *Z*-2-iodoacrylate (entries 5 and 6) gave good yields of the expected products from *ipso*-substitution (***E*-4f** and ***E*,*Z*-4g**), although the product obtained from reaction of *E*-β-bromo styrene contained a minor impurity of unknown composition (*ca* 5%, probably isomeric). These two

vinyl halides were both compounds which had resulted in considerable *cine*-substitution in the corresponding coupling reactions of **1** (Table 1), but with ***E*-2** no *cine*-substituted products were observed. *Z*-2-Iodoacrylate coupled readily with ***E*-2** and gave only the *E,Z*-isomer (***E,Z*-4g**) in good yield (entry 6).

The reactions with vinyl triflates gave moderate to excellent yields of the expected *E*-δ-substituted products (entries 7-10). Again, all these triflates reacted with ***E*-2** without the need for the addition of lithium chloride. No phenyl substituted product (***E*-4a**) was isolated from any of these reactions, but small quantities may have formed which were separated from the major products by chromatography.

Reactions of cinnamyl chloride, benzoyl chloride and benzyl bromide with *E*-δ-stannane (***E*-2**) (Table 2, entries 11-13) yielded the expected *ipso*-substituted products (**4m, 4n** and **4o**) in good to excellent yields using the standard conditions of 5mol% of $Pd(AsPh_3)_4$ in THF. Benzoyl chloride reacted with ***E*-2** under these conditions within minutes at room temperature. The intermediate benzoylpalladium(II) chloride must be extremely electrophilic and this allowed for mild Stille coupling conditions.

Acknowledgements

We would like to thank the Australian Research Council for the award of an Australian Postgraduate Research Award to P.T.G.

Experimental Section

^1H and ^{13}C nmr spectra were recorded using either a Bruker ACP-300 or Bruker CXP-300 spectrometer as dilute solutions in deuteriochloroform, unless otherwise noted. Chemical shift values are given in parts per million (ppm) relative to tetramethylsilane. Nmr multiplicities are abbreviated as follows: *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *quin* = quintet, *m* = multiplet, *br* = broad. Infrared spectra were recorded using a Hitachi 270-30 spectrophotometer as neat films, nujol mulls or chloroform solutions as indicated. Peak shapes are abbreviated as follows: *s* = strong, *m* = medium, *w* = weak, *br* = broad. Electron impact mass spectra and accurate mass measurements were obtained using an AIG-GEC MS3074 spectrometer. Optical rotation data were obtained on a Perkin Elmer 141 Polarimeter measured with sodium D light (589nm). Melting points were determined using a Kofler hot stage with a Reichert microscope and are uncorrected. Elemental analyses were determined by Chemical and Micro Analytical Services, Melbourne, Australia. Thin layer chromatography was carried out on Merck Alufolien Kieselgel 60 PF_{254} plates which were visualised by ultraviolet light (254nm) and by staining with an acidic aqueous solution of ammonium molybdate, a 5% ethanolic solution of phosphomolybdic acid or a 5% ethanolic solution of vanillin followed by development with heat. Flash and 'squat' column chromatographies were carried out using Merck Silica Gel 60 (230-400 mesh) and Merck Silica Gel 60 PF_{254} respectively. All solvents were distilled prior to use. Tetrahydrofuran (THF) and diethyl ether were freshly distilled from sodium/benzophenone prior to use. Dimethyl formamide (DMF) was distilled from sodium sulphate under reduced pressure and stored over 4Å molecular sieves. Light petroleum refers to the fraction of boiling point 66-69°. Organic extracts were dried with magnesium sulphate.

The following compounds were prepared according to known procedures: tetrakis(triphenyl phosphine) palladium,[20] dichlorobis(acetonitrile)palladium,[21] tris(dibenzylidine)dipalladium chloroform complex,[22] tri(2-furyl)phosphine,[23] ethyl 2-{[(trifluoromethyl)sulphonyl]oxy}-1-cyclo pentene-1-carboxylate,[24] 1-hydroxy methyl-2-{[(trifluoromethyl)sulphonyl]oxy}-1-cyclooctene,[25] N-acetyl-*D,L*-

propargylglycine ,[26] α–tetralenyl triflate[27], 2-naphthyl triflate[27], *p*-acetylphenyl triflate[28] and ethyl Z-2-iodoacrylate[29].

Palladium catalysed hydrostannation: Tributyltin hydride (1.62ml, 6.00ml) was added *via* syringe over a ten minute period to a degassed solution of ethyl N-acetyl-*D,L*-propargylglycinate (1.0g, 5.46 mmol) and $Pd(PPh_3)_4$ (25mg, 0.022mmol) in benzene under nitrogen. The solution was stirred for a further five minutes at ambient temperature. The solvent was evaporated and the residue subjected to 'squat column' chromatography to yield a slightly impure mixture of γ-stannane (**1**) and *E*-δ-stannane (***E*-2**) (2.5g, *ca* 96%). These two isomers were separated by repeated flash chromatography gradient eluting with 20-50% ethyl acetate/light petroleum (**1**: 58%, ***E*-2**: 15%)

AIBN initiated radical hydrostannation: A solution of ethyl N-acetyl-*D,L*-propargylglycinate (3.05g, 16.6mmol) and AIBN (5mg) in toluene (30ml) was degassed by a stream of dry nitrogen. Tributyltin hydride (6.7ml, 25.0mmol) was added and the solution heated at reflux for 30 minutes. The solution was cooled and the solvent evaporated. 'Squat column' chromatography of the residue gave a slightly impure product (7.6g, *ca* 96%). A portion (3.6g) was purified by flash chromatography to yield the hydrostannation products ***E*-2** and ***Z*-2** (ratio 88:12) (3.15g, 84%).

Tributylborane initiated radical hydrostannation: Tributylborane (1.0M in THF, 0.55ml, 0.55 mmol) was added *via* syringe to a solution of ethyl N-acetyl-*D,L*-propargylglycinate (1.00g, 5.46 mmol) and tributyltin hydride (1.62ml, 6.00mmol) in dry toluene. The solution was stirred at room temperature open to the dry atmosphere. Two further charges of tributylborane (2x0.5ml) were added after 1 and 15 hours. The reaction was left for a total of three weeks after which time the solvent was evaporated. Crude 'squat column' chromatography gave a slightly impure product (1.94g, 75%) a portion (0.5g) of which was purified by flash chromatography to yield the hydrostannation product (433mg, 64%). By ^1H nmr this product was a mixture of (***E*-2** and ***Z*-2**) (ratio 58:42).

Ethyl N-acetyl-*D,L*-4-(tri-*n*-butylstannyl)allylglycinate (1). b.p. *ca* 200°/0.03 mm Hg; ^1H nmr: 0.80-1.05 (*m*, 15H), 1.25-1.40 (*m*, 9H), 1.40-1.60 (*m*, 6H), 2.00 (*s*, 3H), 2.51 (*dd*, *J*9.2, 14.1Hz, 1H), 2.79 (*dd*, *J*5.1, 14.1Hz, 1H), 4.19 (*q*, *J*7.2Hz, 2H), 4.48 (*m*, 1H), 5.26 (*br s*, 1H, (with Sn-H satellites, $^3J_{SnH}$=58Hz)), 5.74 (*br s*, 1H, (with Sn-H satellites, $^3J_{SnH}$=127Hz)), 5.89 (*d*, *J*7.0Hz, 1H); ^{13}C nmr: 9.58 ($\underline{C}H_2Sn$, (with Sn-C satellites, $^1J_{SnC}$=328Hz)), 13.61 ($\underline{C}H_3(CH_2)_3$), 14.07 ($\underline{C}H_3CH_2O$), 22.89 ($\underline{C}H_3CON$), 27.29 ($\underline{C}H_2CH_2Sn$, (with Sn-C satellites, $^2J_{SnC}$=59Hz)), 28.93 ($\underline{C}H_2CH_2CH_2Sn$, (with Sn-C satellites, $^3J_{SnC}$=20Hz)), 43.42, 51.99, 61.21, 128.74 (CH_2=CSn), 150.04 (CH_2=CSn), 169.63, 172.31; IR (neat): 3284*m*, 3032*w*, 2952*s*, 2924*s*, 2868*m*, 2848*m*, 1748*s*, 1656*s*, 1548*s*, 1464*m*, 1446*m*, 1376*s*, 1296*m*, 1270*m*, 1222*m*, 1192*s*, 1162*m*, 1028*m*, 920*m*, 864*w*; MS: 475 (M^+ (major isotope ^{119}Sn), 1%, calc. for $C_{21}H_{41}NO_3{}^{119}Sn$: 475.2108, found: 475.2125), 418 (100, $[M\text{-}Bu]^+$ (major isotope)), 416 (75), 343 (15), 178 (13); Analysis: calc. for $C_{21}H_{41}NO_3Sn$: C, 53.19; H, 8.71; N, 2.95; found: C, 52.95; H, 8.88; N, 2.85. Repetition of the palladium catalysed hydrostannation with enantiomerically

enriched ethyl N-acetyl-*L*-propargylglycinate yielded the optically active product (*L*-**1**) (49%). $[\alpha]_D$ = +22.3° (*c*1.04, $CHCl_3$).

Ethyl (*E*)-N-acetyl-*D,L*-5-(tri-*n*-butylstannyl)allylglycinate (*E*-2) b.p. *ca* 200°/0.03 mm Hg; ^1H nmr: 0.80-0.90 (*m*, 15H), 1.15-1.25 (*m*, 9H), 1.30-1.50 (*m*, 6H), 1.95 (*s*, 3H), 2.55 (*m*, 2H), 4.13 (*q*, *J*7.1Hz, 2H), 4.58 (*dq*, *J*5.9, 7.5Hz, 1H), 5.73 (*dt*, *J*5.6, 18.7Hz, 1H), 5.99 (*d*, *J*18.6Hz, 1H), 6.00 (*br d*, 1H); ^{13}C nmr: 9.33 ($\underline{C}H_2Sn$ (with Sn-C satellites, $^1J_{SnC}$=329Hz)), 13.63 ($\underline{C}H_3(CH_2)_3Sn$), 14.13 ($\underline{C}H_3CH_2O$), 23.03 ($\underline{C}H_3CON$), 27.17 ($\underline{C}H_2CH_2Sn$ (with Sn-C satellites, $^2J_{SnC}$=54Hz)), 28.99 ($\underline{C}H_2CH_2CH_2Sn$ (with Sn-C satellites, $^3J_{SnC}$=21Hz)), 40.35, 51.53, 61.29, 133.98 (CH=CHSn), 141.93 (CH=CHSn), 169.49, 172.89; IR (neat): 3288*m*, 3064*w*, 2952*s*, 2924*s*, 2868*m*, 2840*m*, 1746*s*, 1656*s*, 1600*w*, 1548*s*, 1466*m*, 1376*m*, 1198*s*, 1030*m*, 864*m*; MS: ; 475 (M^+ (major isotope with ^{119}Sn), 5%, calc. for $C_{28}H_{41}NO_3{}^{119}Sn$: 475.2108, found: 475.2094), 418 ([M-Bu]$^+$, major isotope, 100), 360 (7), 343 (5), 303 (10), 288 (7). Repetition of the palladium catalysed hydrostannation with enantiomerically enriched ethyl N-acetyl-*L*-propargylglycinate yielded the optically active product (*L*-*E*-**2**) (7%). $[\alpha]_D$ = +33.5° (*c*1.10, $CHCl_3$).

Ethyl (*Z*)-N-acetyl-*D,L*-5-(tri-*n*-butylstannyl)allylglycinate (*Z*-2) ^1H nmr: 0.83 (*m*, 15H), 1.22 (*m*, 9H), 1.40 (*m*, 6H), 1.95 (*s*, 3H), 2.40-2.60 (*m*, 2H), 4.13 (*m*, 2H), 4.61 (*m*, 1H, a), 5.97 (*d*, *J*12.6Hz, 1H), 6.00 (*br*, 1H, NH), 6.31 (*ddd*, *J*6.4, 7.3, 12.6Hz, 1H); ^{13}C nmr: 10.13 ($\underline{C}H_2Sn$, with satellites), 13.62 ($\underline{C}H_3(CH_2)_3Sn$), 14.12 ($\underline{C}H_3CH_2O$), 23.03 ($\underline{C}H_3CON$), 27.29 ($\underline{C}H_2CH_2Sn$, with satellites), 29.13 ($\underline{C}H_2(CH_2)_2Sn$, with satellites), 38.92 (beta C), 51.46 (alpha C), 61.43 ($CH_3\underline{C}H_2O$), 133.62 (CH=CHSn), 141.70 (CH=CHSn), 169.62 (C=O), 171.85 (C=O).

Ethyl 2-acetamido-4-phenylpent-4-enoate (3a) $Pd_2dba_3.CHCl_3$ (4.8mg, 5.3mmol) and triphenylarsine (13mg, 42mmol) were stirred in dry THF under a nitrogen atmosphere for 10 minutes by which time the solution had become canary yellow in colour. Iodobenzene (35µl, 0.136mmol) and **1** (100mg, 0.211mmol) were added and the solution heated at reflux for 6 hours then cooled to room temperature. Aqueous potassium fluoride (10%, 30ml) was added and the aqueous phase extracted with diethyl ether (4x30ml). The combined organic extracts were dried and the solvent evaporated. Flash chromatography of the residue on silica gel, gradient eluting with a mixture of ethyl acetate and light petroleum (30-50%), gave a mixture of isomers (29mg, 66% based on recovered vinylstannane (**1**) [20%]) consisting of the title compound and *E* and *Z*-5-phenylallyl glycinates (*E*-**4a** and *Z*-**4a**) (ratio 52:32:18). **3a**: ^1H nmr: 1.14 (*t*, *J*7.1Hz, 3H), 1.77 (*s*, 3H), 2.90 (*dd*, *J*6.3, 14.2Hz, 1H), 3.00 (*dd*, *J*5.9, 14.1Hz, 1H), 3.88 (*dq*, *J*7.2, 10.7Hz, 1H), 3.97 (*dq*, *J*7.1, 10.7Hz, 1H), 4.59 (*br dt*, *J*6.1, 7.7Hz, 1H), 5.02 (*br s*, 1H), 5.25 (*d*, *J*1.2Hz, 1H), 5.88 (*br d*, 1H), 7.10-7.35 (*m*, 5H); ^{13}C nmr: 14.00, 22.86, 37.60, 51.65, 61.32, 116.35, 126.27, 127.74, 128.33, 140.29, 143.90, 169.46, 171.64, ; IR (neat): 3284 (*br s*), 3056*w*, 2980*w*, 2928*w*, 1742*s*, 1656*s*, 1548*s*, 1498*w*, 1446*m*, 1376*m*, 1300*w*, 1200*s*, 1134*w*, 1028*m*, 906*w*, 780*m*, 704*m*; MS: 261 (M^+, 6%, calc. for $C_{15}H_{19}NO_3$: 261.1365, found: 261.1356), 218 (5), 215 (4), 178 (14), 146 (31), 129 (100), 102 (83), 43 (89).

Ethyl 2-acetamido-4-(3,5-difluorophenyl)pent-4-enoate (3b) Reaction of **1** (100mg, 0.211mmol) and 3,5-difluorobromobenzene (36μl, 0.316mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 20h yielded after workup the title compound as a thick oil (35.3mg, 56%). The product was contaminated with phenyl substituted product (**3a**) (6.5%). ^1H nmr: 1.16 (*t*, *J*7.2Hz, 3H), 1.84 (*s*, 3H), 2.84 (*dd*, *J*6.3, 14.2Hz, 1H), 2.93 (*dd*, *J*5.7, 14.1Hz, 1H), 3.95 (*dq*, *J*7.2, 10.8Hz, 1H), 4.03 (*dq*, *J*7.1, 10.8Hz, 1H), 4.58 (*br q*, *J*7.6Hz, 1H), 5.10 (*s*, 1H), 5.31 (*d*, *J*0.6Hz, 1H), 6.10 (*br d*, 1H), 6.65 (*tt*, *J*2.3, 8.8Hz, 1H), 6.84 (*m*, 2H); ^{13}C nmr: 13.93, 22.77, 37.42, 51.40, 61.48, 102.94 (*t*, *J*25.6Hz), 109.19 (*d*, *J*25.5Hz), 141.93, 143.71, 162.86 (*dd*, *J*12.6, 248.1Hz), 169.53, 171.48; IR (neat): 3288 (*br s*), 3080*w*, 2984*w*, 1736*s*, 1658*s*, 1622*m*,, 1586*m*, 1548*m*, 1446*m*, 1378*m*, 1324*w*, 1302*w*, 1248*w*, 1208*m*, 1118*s*, 1026*m*, 988*m*, 914*w*, 860*m*; MS: 297 (M^+, 85%, calc. for $C_{15}H_{17}NO_3F_2$: 297.1177, found: 297.1172), 237 (15), 223 (23), 182 (46), 165 (62), 102 (100), 43 (69).

Ethyl 2-acetamido-4-(thien-2-yl)pent-4-enoate (3c). Reaction of **1** (100mg, 0.211mmol) and 2-iodothiophene (35μl, 0.316mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 20h yielded after workup the title compound and *E*-5-(thien-2-yl)allylglycinate (***E*-4c**) as an inseparable mixture (30.1mg, 53%, 54:46 ratio). **3c**: ^1H nmr: 1.19 (*t*, *J*7.2Hz, 3H), 1.90 (*s*, 3H), 2.89 (*dd*, *J*6.3, 14.0Hz, 1H), 2.93 (*dd*, *J*6.4, 14.0Hz, 1H), 4.05 (*m*, 2H), 4.67 (*dt*, *J*6.3, 7.8Hz, 1H), 4.92 (*s*, 1H), 5.40 (*s*, 1H), 6.12 (*br d*, *J*7.7Hz, 1H), 6.94 (*dd*, *J*3.7, 5.1Hz, 1H), 7.04 (*dd*, *J*1.1, 3.7Hz, 1H), 7.14 (*dd*, *J*1.0, 5.2Hz, 1H); IR ($CHCl_3$): 3436*m*, 3016*s*, 2932*w*, 1734*s*, 1668*s*, 1510*s*, 1416*w*, 1376*m*, 1342*w*, 1094*w*, 1024*m*, 936*w*, 860*w*; MS: 268 ($[M+H]^+$, 8%, calc. for $C_{13}H_{17}NO_3S$: 267.0929, found: 267.0918), 267 (M^+, 13), 224 (8), 221 (10), 208 (68), 152 (20), 144 (18), 135 (100), 123 (55), 112 (63), 102 (73), 70 (70), 43 (25).

Ethyl 2-acetamido-4-(naphth-2-yl)pent-4-enoate (3d) Reaction of **1** (80mg, 0.169mmol) and 2-naphthyl triflate (70mg, 0.253mmol) with 1.5mol% $Pd(AsPh_3)_4$ in THF at reflux for 9h yielded after workup the title compound as a thick oil (36.4mg, 69%). The product was contaminated with phenyl substituted product (**3a**) (5%). ^1H nmr: 1.14 (*t*, *J*7.3Hz, 3H), 1.78 (*s*, 3H), 3.06 (*dd*, *J*6.2, 14.2Hz, 1H), 3.14 (*dd*, *J*6.0, 14.2Hz, 1H), 3.92 (*m*, 2H), 4.70 (*br dt*, *J*7.6Hz, 1H), 5.16 (*s*, 1H), 5.45 (*s*, 1H), 6.09 (*br d*, *J*7.6Hz, 1H), 7.40-7.50 (*m*, 3H), 7.70-7.85 (*m*, 4H); ^{13}C nmr: 13.93, 22.84, 37.59, 51.71, 61.31, 116.70, 124.47, 124.94, 126.00, 126.22, 127.41, 127.90, 128.08, 132.75, 133.14, 137.33, 143.58, 169.52, 171.67; IR (neat): 3292 (*s br*), 3056*m*, 2980*m*, 2932*w*, 1736*s*, 1654*s*, 1598*w*, 1546*s*, 1446*m*, 1376*m*, 1344*w*, 1300*w*, 1198*s*, 1136*w*, 1096*w*, 1026*s*, 968*m*, 908*m*, 860*m*, 820*m*, 752*m*, 732*w*, 704*w*; MS: 311 (M^+, 6%, calc. for $C_{19}H_{21}NO_3$: 311.1521, found: 311.1512), 252 (10), 217 (6), 214 (4), 188 (31), 179 (31), 146 (25), 129 (93), 102 (86), 88 (63), 86 (100), 49 (96), 43 (94).

Ethyl 2-acetamido-4-(*p*-acetylphenyl)pent-4-enoate (3e) Reaction of **1** (40mg, 0.084 mmol) and *p*-acetylphenyl triflate (34mg, 0.127mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 15h yielded after workup the title compound as a thick oil (18.7mg, 37%). ^1H nmr: 1.17 (*t*, *J*7.2Hz, 3H), 1.82 (*s*, 3H), 2.55 (*s*, 3H), 2.95 (*dd*, *J*6.3, 14.2Hz, 1H), 3.04 (*dd*, *J*6.3, 14.1Hz, 1H), 3.98 (*m*, 2H), 4.60 (*br q*, *J*7.6Hz, 1H), 5.16 (*s*, 1H), 5.38 (*d*, *J*0.8Hz, 1H), 5.96 (*br d*, J7.4Hz, 1H), 7.43 (*m*, 2H), 7.88 (*m*, 2H); ^{13}C nmr: 13.91, 22.74, 26.46, 37.51, 51.41, 61.31, 117.99, 126.31, 128.35, 136.07, 142.92, 144.75, 169.48,

171.48, 197.46; IR ($CHCl_3$): 3436*m*, 1734*s*, 1680*s*, 1604*m*, 1506*m*, 1404*w*, 1378*m*, 1360*w*, 1268*m*, 1218*s*, 1138*w*, 1016*w*, 956*w*, 914*w*, 848*w*; MS: 303 (M^+, 14%, calc. for $C_{17}H_{21}NO_4$: 303.1471, found: 303.1459), 259 (6), 256 (6), 243 (16), 230 (16), 229 (14), 188 (28), 171 (44), 160 (20), 115 (18), 102 (54), 43 (100). Reaction of ethyl N-acetyl-*L*-4-(tributylstannyl)allyl glycinate (*L*-**1**) (100mg, 0.211mmol) under identical conditions yielded *L*-**3e** (25.6mg, 40%). $[\alpha]_D$ = +56.6° (*c*0.26, $CHCl_3$).

Ethyl *E*-2-acetamido-4-methylene-6-phenylhex-5-enoate (3f) To a solution of **1** (80mg, 0.169mmol) and *E*-β-bromostyrene (100μl, 0.781mmol) in DMF (2ml) under a nitrogen atmosphere was added bis(acetonitrile)palladium(II) chloride (2.2mg, 8.5mmol) and the resultant mixture stirred at ambient temperature for 16h. Aqueous potassium fluoride (10%, 30ml) was added and the aqueous phase extracted with diethyl ether (4x30ml). The combined organic extracts were dried and the solvent evaporated. Flash chromatography of the residue on silica gel, gradient eluting with a mixture of ethyl acetate and light petroleum (30-50%), gave the title compound as a thick oil (44.2mg, 91%). ^1H nmr: 1.27 (*t*, *J*7.2Hz, 3H), 1.98 (*s*, 3H), 2.79 (*dd*, *J*6.2, 14.1Hz, 1H, C3-H), 2.86 (*dd*, *J*5.8, 14.1Hz, 1H, C3-H), 4.17 (*m*, 2H), 4.81 (*dt*, *J*7.8, 6.5Hz, 1H, C2-H), 5.06 (*br s*, 1H), 5.25 (*br s*, 1H), 6.20 (*br d*, *J*7.6Hz, 1H, NH), 6.70 (*d*, *J*16.4Hz, 1H), 6.78 (*d*, *J*16.4Hz, 1H), 7.20-7.45 (*m*, 5H); MS: 287 (M^+, 13%, calc. for $C_{17}H_{21}NO_3$: 287.1521, found: 287.1506), 260 (22), 228 (68), 188 (32), 155 (55), 131 (91), 44 (100).

Ethyl (*Z*)-2-acetamido-4-methylene-6-(carboethoxy)hex-5-enoate (*Z*-3g) Reaction of **1** (100mg, 0.211mmol) and ethyl *Z*-3-iodoacrylate (57mg, 0.253mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 15h yielded after workup the title compound in an isomeric mixture with ***E*-3g**, ***E*,*Z*-4g** and ***E*,*E*-4g** (42mg, 70%, ratio 65:18:10:7). ***Z*-3g**: ^1H nmr: 1.17 (*t*, *J*7.1Hz, 3H), 1.21 (*t*, *J*7.1Hz, 3H), 1.93 (*s*, 3H), 2.66 (*dd*, *J*5.7, 14.0Hz, 1H), 2.72 (*dd*, *J*5.9, 14.1Hz, 1H), 4.08 (*m*, 4H), 4.63 (*dt*, *J*8.3, 5.8Hz, 1H), 5.04 (*s*, 1H), 5.08 (*s*, 1H), 5.70 (*d*, *J*12.1Hz, 1H), 6.34 (*d*, *J*12.1Hz, 1H), 7.01 (*br d*, *J*8.2Hz, 1H); IR (neat): 3292 (*m br*), 3064*w*, 2980*m*, 2932*w*, 1740*s*, 1658*s*, 1548*s*, 1446*w*, 1376*m*, 1274*w*, 1182*s*, 1096*w*, 1028*m*, 968*w*, 920*w*, 860*w*, 824*w*; MS: 283 (M^+, 3%, calc. for $C_{14}H_{21}NO_5$: 283.1419, found: 283.1406), 238 (3), 237 (3), 224 (7), 210 (5), 209 (3), 196 (8), 195 (17), 168 (13), 167 (7), 164 (01), 139 (63), 122 (33), 102 (73), 43 (100).

Ethyl 2-acetamido-4-(cyclohex-1-en-1-yl)pent-4-enoate (3h) Reaction of **1** (100mg, 0.211mmol) and cyclohex-1-en-1-yl triflate (58mg, 0.253mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 2h yielded after workup the title compound as a thick oil (44mg, 79%). ^1H nmr: 1.20 (*t*, *J*7.1Hz, 3H), 1.45-1.70 (*m*, 4H), 1.92 (*s*, 3H), 2.07 (*m*, 4H), 2.57 (*dd*, *J*7.4, 14.0Hz, 1H), 2.68 (*dd*, *J*6.2, 13.9Hz, 1H), 4.08 (*m*, 2H), 4.58 (*br q*, *J*6.3Hz, 1H), 4.75 (*br s*, 1H), 4.98 (*br s*, 1H), 5.89 (*br*, 1H), 6.03 (*br d*, 1H); ^{13}C nmr: 14.02, 21.90, 22.64, 22.92, 25.74, 25.97, 36.25, 51.68, 61.12, 112.06, 125.34, 134.98, 143.44, 169.58, 172.24; IR (neat): 3288 (*br s*), 3064*w*, 2980*w*, 2928*s*, 2852*w*, 1742*s*, 1656*s*, 1548*s*, 1448*m*, 1376*m*, 1296*w*, 1192 (*br s*), 1136*w*, 1028*m*, 920*w*, 896*w*, 854*w*, 802*w*; MS: 265 (M^+, 7%, calc. for $C_{15}H_{23}NO_3$: 265.1678, found: 265.1668), 222 (8), 206 (50), 177 (15), 148 (23), 133 (100), 121 (33), 102 (57), 91 (43), 43 (74).

Ethyl 2-acetamido 4-(3,4-dihydronaphth-1-yl)pent-4-enoate (3i) Reaction of **1** (103mg, 0.217mmol) and α-tetralenyl triflate (88mg, 0.316mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 7h yielded after workup the title compound as a thick oil (66.5mg, 98%). ^1H nmr: 1.16 (*t*, *J*7.3Hz, 3H), 1.91 (*s*, 3H), 2.28 (*m*, 2H), 2.74 (*m*, 3H), 2.88 (*dd*, *J*5.4, 13.7Hz, 1H), 3.98 (*m*, 1H), 4.07 (*m*, 1H), 4.60 (*br q*, *J*6.4Hz, 1H), 5.14 (*br s*, 1H), 5.17 (*d*, *J*2.0Hz, 1H), 5.98 (*t*, *J*4.4Hz, 1H), 6.12 (*br d*, 1H), 7.05-7.20 (*m*, 4H); ^{13}C nmr: 13.90, 22.84, 22.98, 27.90, 37.33, 51.45, 61.19, 118.20, 124.63, 126.31, 127.00, 127.56, 133.25, 136.42, 139.36, 143.95 (N.B. one aromatic overlapping), 169.43, 171.79; IR (neat): 3284 (*br s*), 3060*m*, 2980*w*, 2932*m*, 2828*m*, 1736*s*, 1654*s*, 1544*s*, 1486*w*, 1450*m*, 1376*m*, 1298*m*, 1096*s*, 1130*m*, 1024*s*, 910*m*, 774*m*, 742*m*; MS: 314 ($[M+H]^+$, 6%, calc. for $C_{19}H_{24}NO_3$: 314.1756, found: 314.1765), 286 (6), 268 (4), 254 (6), 225 (6), 208 (12), 197 (10), 181 (61), 169 (47), 165 (33), 145 (100), 43 (49).

Ethyl 2-acetamido-4-(2-[hydroxymethyl]cyclooct-1-en-1-yl)pent-4-enoate (3j) Reaction of **1** (103mg, 0.217mmol) and 2-(hydroxymethylene)cyclooct-1-en-1-yl triflate (94mg, 0.326mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 15h yielded after workup the title compound as a thick oil (31mg, 44%). ^1H nmr: 1.23 (*t*, *J*7.2Hz, 3H), 1.30-1.60 (*m*, 8H), 1.96 (*s*, 3H), 2.18 (*m*, 2H), 2.30 (*m*, 2H), 2.55 (*dd*, *J*6.8, 14.4Hz, 1H), 2.72 (*dd*, *J*4.3, 14.4Hz, 1H), 4.00-4.20 (*m*, 4H), 4.56 (*d*, *J*2.4Hz, 1H), 4.61 (*m*, 1H), 4.96 (*br d*, *J*2.3Hz, 1H), 6.55 (*br d*, *J*8.4Hz, 1H); ^{13}C nmr: 14.07, 22.98, 26.14, 26.75, 27.51, 28.27, 28.30, 29.28, 37.17, 51.33, 60.80, 61.65, 118.31, 123.79, 137.00, 143.17, 170.29, 172.44; IR (neat): 3284 (*br s*), 3072*w*, 2920*s*, 2848*m*, 1736*s*, 1656*s*, 1550*s*, 1470*w*, 1448*m*, 1376*m*, 1298*m*, 1208*m*, 1186*m*, 1130*w*, 1004*s*, 912*m*, 732*m*; MS: 323 (M^+, 2%, calc. for $C_{18}H_{29}NO_4$: 323.2097, found: 323.2105), 305 ($[M-H_2O]^+$, 5), 262 (11), 259 (14), 246 (49), 232 (27), 218 (14), 217 (17), 190 (32), 179 (29), 173 (43), 165 (43), 161 (60), 145 (49), 91 (52), 43 (100).

Ethyl 2-acetamido-4-(2-[carboethoxy]cyclopent-1-en-1-yl)-pent-4-enoate (3k) Reaction of **1** (100mg, 0.211mmol) and 2-(carboethoxy)cyclopent-1-en-1-yl triflate (91mg, 0.316 mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 6h yielded after workup the title compound as a thick oil (62mg, 91%). ^1H nmr: 1.16 (*t*, *J*7.1Hz, 3H), 1.21 (*t*, *J*7.2Hz, 3H), 1.78 (*m*, 2H), 1.94 (*s*, 3H), 2.30-2.60 (*m*, 4H), 2.65 (*dd*, *J*5.6, 14.3Hz, 1H), 2.75 (*dd*, *J*5.8, 14.4Hz, 1H), 4.03 (*m*, 2H), 4.10 (*q*, *J*7.1Hz, 2H), 4.58 (*dt*, *J*5.7, 8.1Hz, 1H), 4.94 (*s*, 1H), 4.95 (*s*, 1H), 7.18 (*br d*, 1H); ^{13}C nmr: 13.92, 14.05, 21.71, 22.77, 34.06, 36.52, 38.78, 50.56, 60.15, 61.15, 117.06, 129.87, 140.55, 155.78, 165.97, 170.17, 171.61; IR (neat): 3300 (*br s*), 3076*w*, 2976*s*, 1740*s*, 1708*s*, 1656*s*, 1544*s*, 1446*m*, 1374*s*, 1254 (*s br*), 1192 (*s br*), 1138*m*, 1032*s*, 910*w*, 860*w*, 770*m*; MS: 323 (M^+, 29%, calc. for $C_{17}H_{25}NO_5$: 323.1733, found: 323.1723), 278 (8), 236 (17), 235 (21), 178 (100), 151 (25), 134 (21), 43 (33).

Ethyl 2-acetamido-4,5-(dimethylene)decanoate (3l) Reaction of **1** (100mg, 0.211mmol) and hept-1-en-2-yl triflate (78mg, 0.316mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 6h yielded after workup the title compound as a thick oil (54mg, 91%). ^1H nmr: 0.82 (*t*, *J*6.7Hz, 3H), 1.10-1.15 (*m*, 6H), 1.20 (*t*, *J*7.2Hz, 3H), 1.92 (*s*, 3H), 2.15 (*t*, *J*6.8Hz, 2H), 2.57 (*dd*, *J*7.4, 14.2Hz, 1H), 2.69 (*dd*, *J*5.9, 14.1Hz, 1H), 4.10 (*m*, 2H), 4.60 (*dt*, *J*6.1, 7.5Hz, 1H), 4.89 (*s*, 1H), 4.93 (*s*, 1H), 5.09 (*s*, 1H), 5.10 (*d*, *J*0.9Hz,

1H), 6.06 (*br d*, 1H); ^{13}C nmr: 13.95, 14.02, 22.42, 22.90, 28.06, 31.60, 33.91, 36.68, 51.58, 61.19, 112.57, 115.09, 142.66, 146.80, 169.56, 172.15; IR (neat): 3280 (*s br*), 3080*w*, 2952*s*, 2928*s*, 2856*w*, 1744*s*, 1654*s*, 1594*w*, 1546*s*, 1466*m*, 1376*m*, 1298*w*, 1264*w*, 1188*s*, 1128*w*, 1028*m*, 896*s*; MS: 281 (M^+, 9%, calc. for $C_{16}H_{27}NO_3$: 281.1991, found: 281.1999), 238 (20), 207 (17), 166 (31), 149 (96), 102 (100), 93 (66), 43 (94).

Ethyl 2-acetamido-4-benzoylpent-4-enoate (3o) Reaction of **1** (100mg, 0.211mmol) and benzoyl chloride (37μl, 0.316mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 2h yielded after workup the title compound as a thick oil (42mg, 69%). ^{1}H nmr: 1.26 (*t*, *J*7.2Hz, 3H), 1.96 (*s*, 3H), 2.92 (*dd*, *J*7.9, 13.8Hz, 1H), 3.00 (*dd*, *J*5.1, 13.8Hz, 1H), 4.18 (*m*, 2H), 4.72 (*m*, 1H), 5.79 (*s*, 1H), 6.04 (*s*, 1H), 6.71 (*br d*, 1H), 7.45 (*m*, 2H), 7.56 (*m*, 1H), 7.73 (*d*, *J*7.4Hz, 2H); ^{13}C nmr: 14.02, 22.93, 34.26, 52.41, 61.47, 128.18, 129.63, 130.27, 132.41, 136.96, 143.03, 169.86, 171.47, 197.93; MS: 289 (M^+, 13%, calc. for $C_{16}H_{19}NO_4$: 289.1314, found: 289.1304), 245 (13), 229 (37), 215 (44), 183 (40), 173 (50), 155 (65), 105 (60), 102 (100), 77 (60), 43 (79).

Ethyl (*E*)-2-acetamido-4-methylene-7-phenyl-hept-6-enoate (3m) Reaction of **1** (100mg, 0.211mmol) and cinnamyl chloride (48mg, 0.316mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 6h yielded after workup the title compound as a thick oil (63mg, 99%). ^{1}H nmr: 1.26 (*t*, *J*7.2Hz, 3H), 2.03 (*s*, 3H), 2.46 (*dd*, *J*8.3, 14.1Hz, 1H), 2.62 (*dd*, *J*5.7, 14.1Hz, 1H), 2.97 (*d*, *J*7.0Hz, 2H), 4.20 (*q*, *J*7.2Hz, 2H), 4.77 (*dt*, *J*8.2, 5.8Hz, 1H), 4.91 (*s*, 1H), 4.98 (*s*, 1H), 6.21 (*dt*, *J*7.0, 15.8Hz, 1H), 6.34 (*br d*, 1H), 6.46 (*d*, *J*15.8Hz, 1H), 7.20-7.40 (*m*, 5H); ^{13}C nmr: 13.98, 22.82, 38.69, 38.88, 50.51, 61.27, 114.44, 125.94, 127.03 (with shoulder), 128.36, 131.98, 137.13, 142.98, 169.75, 172.25; IR ($CHCl_3$): 3444*m*, 2988*m*, 2932*w*, 1734*s*, 1674*s*, 1598*w*, 1508*s*, 1448*m*, 1396*s*, 1344*w*, 1224 (*br m*), 1184*m*, 1128*m*, 1022*m*, 970*m*, 908*m*; MS: 301 (M^+, 3%, calc. for $C_{18}H_{23}NO_3$: 301.1678, found: 301.1667), 242 (55), 169 (100), 157 (50), 140 (31), 129 (23), 105 (18), 102 (30), 91 (28), 43 (43).

Ethyl 2-acetamido-4-methylenehept-6-enoate (3n) Reaction of **1** (100mg, 0.211mmol) and allyl bromide (27μl, 0.316mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 15h yielded after workup the title compound as a thick oil (38mg, 80%). ^{1}H nmr: 1.20 (*t*, *J*7.2Hz, 3H), 1.93 (*s*, 3H), 2.32 (*dd*, *J*8.3, 14.1Hz, 1H), 2.48 (*dd*, *J*5.8, 14.1Hz, 1H), 2.70 (*d*, *J*6.9Hz, 2H), 4.10 (*q*, *J*7.2Hz, 2H), 4.62 (*dt*, *J*5.8, 8.1Hz, 1H), 4.76 (*br s*, 1H), 4.81 (*m*, 1H), 4.98 (*m*, 1H), 5.03 (*m*, 1H), 5.70 (*ddt*, *J*6.9, 9.4, 17.5Hz, 1H), 6.13 (*br d*, 1H); ^{13}C nmr: 14.01, 22.88, 38.56, 39.83, 50.52, 61.29, 114.27, 116.81, 135.35, 142.77, 169.72, 172.28; IR (neat): 3284*br*, 3076*m*, 2980*m*, 2928*w*, 1744*s*, 1656*s*, 1548*s*, 1438*m*, 1376*m*, 1300*w*, 1198*s*, 1132*w*, 1026*m*, 914*m*; MS: 225 (M^+, 100%, calc. for $C_{12}H_{19}NO_3$: 225.1365, found: 225.1357), 183 (4), 179 (4), 166 (6), 165 (7), 151 (14), 110 (18), 102 (16), 93 (20), 43 (26).

Ethyl 2-acetamido-4-methylene-5-phenylpentanoate (3p) Reaction of **1** (100mg, 0.211mmol) and benzyl bromide (38μl, 0.316mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 1h yielded after workup the title compound as a thick oil (58mg, 100%). ^{1}H nmr: 1.24 (*t*, *J*7.2Hz, 3H), 1.98 (*s*, 3H), 2.33 (*dd*, *J*8.3,

14.1Hz, 1H), 2.49 (*dd*, *J*5.6, 14.2Hz, 1H), 3.36 (*br s*, 2H), 4.16 (*m*, 2H), 4.74 (*dt*, *J*8.3, 5.6Hz, 1H), 4.85 (*s*, 1H), 4.89 (*s*, 1H), 6.25 (*br d*, 1H), 7.15-7.35 (*m*, 5H); ^{13}C nmr: 13.93, 22.77, 38.00, 42.01, 50.47, 61.22, 115.12, 126.17, 128.24, 128.88, 138.57, 143.68, 169.73, 172.23; IR (neat): 3284 (*br s*), 3060*w*, 3024*w*, 2980*w*, 2928*w*, 1742*s*, 1656*s*, 1600*w*, 1548*s*, 1440*m*, 1376*m*, 1196 (*s br*), 1028*m*, 904*m*, 740*m*, 702*m*; MS: 275 (M^+, 10%, calc. for $C_{16}H_{21}NO_3$: 275.1521, found: 275.1511), 215 (58), 143 (59), 142 (47), 131 (42), 102 (97), 91 (51), 43 (100).

Ethyl (*E*)-2-acetamido-5-phenylpent-4-enoate (*E*-4a) Reaction of ***E*-2** (100mg, 0.211 mmol) and iodobenzene (35µl, 0.316mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at 40° for 15h then at 60° for 1h yielded after workup an isomeric mixture of products consisting of the title compound and the 4-phenylallylglycinate (**3a**) as a thick oil (45.5mg, 83%, ratio 92:8). ^{1}H nmr: 1.25 (*t*, *J*7.2Hz, 3H), 1.99 (*s*, 3H), 2.68 (*m*, 2H), 4.19 (*m*, 2H), 4.72 (*br q*, *J*7.7Hz, 1H), 6.04 (*dt*, *J*7.4, 15.7Hz, 1H), 6.33 (*br d*, *J*7.6Hz, 1H), 6.37 (*d*, *J*15.7Hz, 1H), 7.20-7.35 (*m*, 5H); ^{13}C nmr: 14.12, 23.01, 35.75, 51.89, 61.43, 123.47, 126.08, 127.45, 128.44, 133.82, 136.65, 169.75, 171.77; IR ($CHCl_3$): 3436*m*, 2988*m*, 1736*s*, 1674*s*, 1604*w*, 1510*s*, 1448*w*, 1378*m*, 1344*w*, 1024*m*, 968*m*; MS: 261 (M^+, 6%, calc. for $C_{15}H_{19}NO_3$: 261.1365, found: 261.1356), 202 (77), 129 (100), 117 (60), 102 (60), 43 (89).

Ethyl (*E*)-2-acetamido-5-(thien-2-yl)pent-4-enoate (*E*-4c) Reaction of ***E*-2** (85mg, 0.179mmol) and 2-iodothiophene (30µl, 0.269mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 3h yielded after workup an isomeric mixture of products consisting of the title compound and the 4-thienylallylglycinate (**3c**) as a thick oil (36mg, 74%, ratio 93:7). ^{1}H nmr: 1.22 (*t*, *J*7.0Hz, 3H), 1.97 (*s*, 3H), 2.62 (*m*, 2H), 4.16 (*m*, 2H), 4.67 (*dt*, *J*5.7, 7.7Hz, 1H), 5.83 (*dt*, *J*7.4, 15.6Hz, 1H, C4-H), 6.27 (*br d*, *J*7.6Hz, 1H, NH), 6.52 (*d*, *J*15.6Hz, 1H, C5-H), 6.84 (*d*, *J*3.4Hz, 1H), 6.89 (*dd*, *J*3.5, 5.2Hz, 1H), 7.07 (*d*, *J*5.1Hz, 1H); ^{13}C nmr: 14.12, 22.05, 35.60, 51.89, 61.51, 123.13, 124.00, 125.26, 126.93, 127.20, 141.72, 169.75, 171.67; IR ($CHCl_3$) 3436*m*, 2988*m*, 1734*s*, 1672*s*, 1512*s*, 1438*w*, 1399*w*, 1378*m*, 1344*m*, 1024*m*, 958*m*, 856*m*; MS: 267 (M^+, 10%, calc. for $C_{13}H_{17}NO_3S$: 267.0929, found: 267.0918), 208 (100), 135 (68), 123 (58), 102 (29), 43 (39).

Ethyl (*E*)-2-acetamido-5-(naphth-2-yl)pent-4-enoate (*E*-4d) Reaction of ***E*-2** (40mg, 0.084mmol) and 2-naphthyl triflate (35mg, 0.127mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 4h yielded after workup the title compound as a white solid (20mg, 76%). Mp: 126-127° (CH_2Cl_2/light petroleum); ^{1}H nmr: 1.25 (*t*, *J*7.2Hz, 3H), 2.00 (*s*, 3H), 2.73 (*m*, 2H, C3-H's), 4.21 (*m*, 2H), 4.76 (*dt*, *J*5.8, 7.7Hz, 1H, a), 6.15 (*br*, 1H, NH, overlapping with *dt*, *J*7.4, 15.7Hz, 1H, C4-H), 6.57 (*d*, *J*15.7Hz, 1H), 7.41 (*m*, 2H, aromatic), 7.51 (*dd*, *J*1.6, 8.7Hz, 1H), 7.64 (*br s*, 1H), 7.75 (*m*, 3H); ^{13}C nmr: 14.20, 23.16, 36.02, 52.00, 61.57, 123.36, 123.89, 125.84, 126.00, 126.26, 127.60, 127.86, 128.17, 132.89, 134.06, 134.17, 145.37, 169.74, 171.83; IR (nujol mull): 3280*m*, 1746*s*, 1650*s*, 1552*s*, 1304*w*, 1266*w*, 1214*s*, 1182*m*, 1130*m*, 1024*m*, 960*m*, 896*w*, 860*m*, 808*m*, 746*m*, 720*w*; MS: 311 (M^+, 2%, calc. for $C_{19}H_{21}NO_3$: 311.1521, found: 311.1530), 252 (47), 223 (5), 179 (100), 167 (85), 165 (26), 152 (21), 102 (13), 43 (23); Calc. for $C_{19}H_{21}NO_3$: C 73.29, H 6.80, N 4.50; found: C 73.37, H 6.78, N 4.32.

Ethyl (*E,E*)-2-acetamido-7-phenylhepta-4,6-dienoate (*E*-4f) Reaction of ***E*-2** (100mg, 0.211mmol) and E-β-bromostyrene (41μl, 0.316mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 15h yielded after workup the title compound as a thick oil (45mg, 75%). ^1H nmr: 1.28 (*t*, *J*7.2Hz, 3H), 2.02 (*s*, 3H), 2.64 (*m*, 2H), 4.21 (*m*, 2H), 4.70 (*dt*, *J*5.8, 7.8Hz, 1H), 5.65 (*dt*, *J*7.5, 15.0Hz, 1H), 6.25 (*dd*, *J*10.4, 15.2Hz, 1H), 6.28 (*br*, 1H), 6.48 (*d*, *J*15.7Hz, 1H), 6.73 (*dd*, *J*10.2, 15.7Hz, 1H), 7.20-7.40 (*m*, 5H); ^{13}C nmr: 14.13, 23.04, 35.58, 51.87, 61.47, 126.17, 127.46, 127.53, 128.16, 128.50, 131.84, 134.44, 136.93, 169.76, 171.73; IR ($CHCl_3$) 3432 (*br m*), 3012*m*, 1736*s*, 1672*s*, 1510*m*, 1450*w*, 1378*m*, 1342*w*, 1236*m*, 1024*w*, 926*w*, 858*w*, 666*m*; MS: 287 (M^+, 1%, calc. for $C_{17}H_{21}NO_3$: 287.1521, found: 287.1509), 260 (4), 228 (18), 202 (4), 188 (7), 154 (22), 131 (36), 114 (51), 102 (43), 72 (100), 43 (43), 42 (96).

Ethyl (*E,Z*)-2-acetamido-7-(carboethoxy)hepta-4,6-dienoate (*E,Z*-4g) Reaction of ***E*-2** (85mg, 0.179mmol) and ethyl *Z*-3-iodoacrylate(49mg, 0.215mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at ambient temperature for 45h yielded after workup the title compound as a thick oil (43mg, 84%). ^1H nmr: 1.18 (*t*, *J*7.2Hz, 3H), 1.20 (*t*, *J*7.1Hz, 3H), 1.93 (*s*, 3H), 2.55 (*br dt*, *J*6.9, 14.4Hz, 1H), 2.64 (*br dt*, *J*6.2, 14.5Hz, 1H), 4.08 (*q*, *J*7.1Hz, 2H), 4.12 (*m*, 2H), 4.62 (*br dt*, 1H, a), 5.54 (*d*, *J*11.3Hz, 1H, C7-H), 5.83 (*dt*, *J*7.5, 15.3Hz, 1H, C4-H), 6.32 (*br d*, *J*7.8Hz, 1H), 6.43 (*t*, *J*11.3Hz, 1H, C6-H) 7.33 (*ddd*, *J*0.7, 11.3, 15.2Hz, 1H, C5-H); ^{13}C nmr: 14.01, 14.10, 22.92, 35.67, 51.51, 59.86, 61.53, 117.20, 130.15, 137.30, 143.75, 166.10, 169.83, 171.46; IR ($CHCl_3$): 3432 (*br m*), 2984*m*, 2932*w*, 1736*s*, 1666*s*, 1512*m*, 1378*m*, 1096*w*, 1022*w*, 858*w*; MS: 284 ($[M+H]^+$, 16%), 283 (M^+, 14, calc. for $C_{14}H_{21}NO_5$: 283.1419, found: 283.1408), 238 (22), 237 (19), 224 (51), 210 (11), 195 (86), 140 (43), 102 (56), 43 (100).

Ethyl (*E*)-2-acetamido-4-(cyclohex-1-en-1-yl)pent-4-enoate (4h) Reaction of ***E*-2** (80mg, 0.169mmol) and cyclohex-1-en-1-yl triflate (47mg, 0.202mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 4h yielded after workup the title compound as a white solid (21mg, 47%). Mp: 87-89°; ^1H nmr: 1.22 (*t*, *J*7.0Hz, 3H), 1.50-1.65 (*m*, 4H), 1.97 (*s*, 3H), 2.00-2.05 (*m*, 4H), 2.51 (*br t*, 2H, C3-H's), 4.15 (*m*, 2H), 4.60 (*br q*, 1H, a), 5.28 (*dt*, *J*7.3, 15.6Hz, 1H), 5.63 (*br s*, 1H, cyclohexenyl vinylic), 6.01 (*d*, *J*15.5Hz, 1H), 6.03 (*br*, 1H, NH); ^{13}C nmr: 14.16, 22.32, 22.41, 23.15, 24.42, 25.70, 35.63, 52.07, 61.37, 118.73, 129.16, 135.12 (quarternary olefinic), 137.73, 169.66, 171.40; IR (nujol mull): 3253*m*, 3068*w*, 1746*s*, 1638*s*, 1556*s*, 1464*s*, 1340*m*, 1194*s*, 1130*m*, 1100*w*, 1028*w*, 970*m*, 948*w*; MS: 265 (M^+, 1%, calc. for $C_{15}H_{23}NO_3$: 265.1678, found: 265.1668), 206 (7), 177 (3), 133 (12), 121 (4), 102 (5), 91 (7), 79 (5), 43 (7), 32 (100), 31 (28), 29 (64).

Ethyl (*E*)-2-acetamido-5-(3,4-dihydronaphth-1-yl)pent-4-enoate (4i) Reaction of ***E*-2** (88mg, 0.186mmol) and α-tetralenyl triflate (75mg, 0.269mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 12h yielded after workup the title compound as a thick oil (29.7mg, 53%). ^1H nmr: 1.21 (*t*, *J*7.1Hz, 3H), 1.96 (*s*, 3H), 2.21 (*m*, 2H), 2.50-2.70 (*m*, 4H), 4.14 (*q*, *J*7.0Hz, 2H), 4.65 (*dt*, *J*5.8, 7.8Hz, 1H), 5.75 (*dt*, *J*7.4, 15.5Hz, 1H), 6.02 (*br t*, *J*4.6Hz, 1H), 6.17 (*br d*, *J*7.7Hz, 1H), 6.27 (*br d*, *J*15.4Hz, 1H), 7.05-7.20 (*m*, 4H); ^{13}C nmr: 14.15, 23.07, 23.11, 28.04, 35.89, 52.02, 61.49, 123.60, 124.66, 126.20, 126.34, 126.94, 127.59, 132.43, 133.98, 135.47, 136.47, 169.63, 171.89; IR ($CHCl_3$) 3436 (*br m*), 2988*m*,

2932*w*, 1736*s*, 1674*s*, 1510*s*, 1446*w*, 1378*s*, 1344*w*, 1240*m*, 1180*w*, 1150*w*, 1022*m*, 910*w*; MS: 313 (M^+, 13%, calc.for $C_{19}H_{23}NO_3$: 313.1678, found 313.1669), 268 (10), 254 (13), 225 (15), 181 (85), 145 (35), 141 (40), 128 (35), 102 (65), 86 (55), 84 (90), 70 (45), 43 (100).

Ethyl (*E*)-2-acetamido-5-(2-[carboethoxy]cyclopent-1-en-1-yl)pent-4-enoate (4k). Reaction of ***E*-2** (87mg, 0.183mmol) and 2-(carboethoxy)cyclopent-1-en-1-yl triflate (77mg, 0.269 mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 12h yielded after workup the title compound as a thick oil (55mg, 93%). ^1H nmr: 1.19 (*t*, *J*7.2Hz, 3H), 1.21 (*t*, *J*7.2Hz, 3H), 1.76 (*br quin*, *J*7.6Hz, 2H), 1.94 (*s*, 3H), 2.45-2.70 (*m*, 6H), 4.05-4.20 (*m*, 4H), 4.61 (*br q*, 1H), 5.70 (*dt*, *J*7.4, 15.7Hz, 1H), 6.22 (*br d*, *J*7.8Hz, 1H), 7.24 (*d*, *J*15.8Hz, 1H); ^{13}C nmr: 14.02, 14.20, 21.06, 22.97, 33.96, 34.04, 36.05, 51.70, 59.76, 61.43, 128.92, 129.09, 130.95, 151.09, 165.68, 169.75, 171.57; IR ($CHCl_3$) 3432 (*m br*), 2984*m*, 1734*s*, 1674*s*, 1512*m*, 1468*w*, 1446*w*, 1376*m*, 1342*w*, 1258*s*, 1022*m*, 860*w*; MS: 323 (M^+, 4%, calc. for $C_{17}H_{25}NO_5$: 323.1733, found: 323.1723), 278 (9), 264 (20), 235 (32), 204 (12), 189 (23), 165 (15), 162 (17), 134 (20), 117 (17), 105 (20), 102 (34), 43 (100), 29 (46).

Ethyl (*E*)-2-acetamido-6-(methylene)undec-4-enoate (4l) Reaction of ***E*-2** (100mg, 0.211mmol) and hept-1-en-2-yl triflate (78mg, 0.316mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 2h yielded after workup the title compound as a thick oil (34.4mg, 58%). ^1H nmr: 0.85 (*t*, *J*6.7Hz, 3H), 1.15-1.45 (*m*, 9H), 1.97 (*s*, 3H), 2.09 (*br t*, *J*7.3Hz, 2H), 2.53 (*m*, 2H), 4.15 (*m*, 2H), 4.62 (*dt*, *J*5.7, 7.8Hz, 1H), 4.87 (*br s*, 2H, both vinylic H's), 5.47 (*dt*, *J*7.4, 15.7Hz, 1H), 6.05 (*d*, *J*15.7Hz, 1H), 6.06 (*br*, 1H, NH); ^{13}C nmr: 14.02, 14.14, 22.48, 23.13, 27.72, 31.70, 31.91, 35.76, 51.96, 61.44, 114.86, 122.48, 136.30, 145.70, 169.63, 171.84; IR (neat) 3288 (*m br*), 3072*w*, 2952*w*, 2928*m*, 2856*m*, 1744*s*, 1656*s*, 1544*s*, 1440*m*, 1376*s*, 1344*w*, 1300*w*, 1192*s*, 1132*m*, 1028*m*, 970*m*, 888*m*; MS: 281 (M^+, 10%, calc. for $C_{16}H_{27}NO_3$: 281.1991, found: 281.1980), 238 (7), 235 (11), 222 (21), 208 (16), 193 (17), 166 (86), 149 (26), 137 (29), 102 (100), 193 (62), 43 (67).

Ethyl (*E*,*E*)-2-acetamido-8-phenylocta-4,7-dienoate (4m) Reaction of ***E*-2** (85mg, 0.179mmol) and cinnamyl chloride (37µl, 0.269mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 6h yielded after workup the title compound as a thick oil (52mg, 96%). ^1H nmr: 1.25 (*t*, *J*7.1nmr, 3H), 2.00 (*s*, 3H), 2.52 (*m*, 2H), 2.90 (*br t*, *J*6.5Hz, 1H), 4.17 (*q*, *J*7.1Hz, 1H), 4.18 (*q*, *J*7.0Hz, 1H), 4.64 (*dt*, *J*5.8, 7.8Hz, 1H), 5.39 (*dt*, *J*7.0, 15.3Hz, 1H), 5.59 (*dt*, *J*6.5, 15.2Hz, 1H), 6.16 (*dt*, *J*6.4, 16.0Hz, 1H), 6.23 (*br d*, *J*7.7Hz, 1H), 6.37 (*d*, *J*15.9Hz, 1H), 7.15-7.35 (*m*, 5H); ^{13}C nmr: 14.06, 22.98, 35.28, 35.66, 51.88, 61.28, 124.84, 125.84, 126.94, 128.08, 128.37, 130.60, 132.52, 137.33, 169.58, 171.83; IR (neat) 3288 (*br m*), 3056*w*, 3024*w*, 2980*w*, 1736*s*, 1656*s*, 1598*w*, 1546*s*, 1496*w*, 1438*m*, 1376*m*, 1198*m*, 1132*m*, 1028*m*, 970*s*, 744*m*, 696*m*; MS: 301 (M^+, 9%, calc. for $C_{18}H_{23}NO_3$: 301.1678, found: 301.1667), 256 (3), 242 (7), 228 (4), 187 (9), 169 (17), 168 (19), 145 (29), 142 (23), 141 (26), 105 (40), 102 (49), 91 (49), 86 (71), 84 (100), 57 (57), 43 (83).

Ethyl (*E*)-2-acetamido-6-oxo-6-phenylpent-4-enoate (4n) Reaction of ***E*-2** (100mg, 0.211 mmol) and benzoyl chloride (37µl, 0.316mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at ambient temperature for 48h

yielded after workup the title compound as a thick oil (49mg, 80%). ^{1}H nmr: 1.20 (*t*, *J*7.1Hz, 3H), 1.96 (*s*, 3H), 2.74 (*dt*, *J*6.4, 14.8Hz, 1H), 2.80 (*dt*, *J*5.5, 14.7Hz, 1H), 4.14 (*q*, *J*7.2Hz, 2H), 4.74 (*br q*, 1H), 6.61 (*br d*, *J*7.6Hz, 1H), 6.85 (*dt*, *J*6.3, 15.7Hz, 1H), 6.88 (*d*, *J*15.8Hz, 1H), 7.40 (*br t*, *J*7.4Hz, 2H), 7.50 (*br t*, *J*7.3Hz, 1H), 7.84 (*d*, *J*8.2Hz, 2H); ^{13}C nmr: 14.02, 22.90, 35.14, 51.25, 61.70, 128.42, 128.46, 128.74, 132.85, 137.16, 142.39, 169.92, 171.18, 189.95; IR (neat) 3292 (*m br*), 3060*w*, 2980*w*, 1736*s*, 1666*s*, 1624*w*, 1596*w*, 1578*w*, 1546*m*, 1450*m*, 1376*m*, 1292*w*, 1226*m*, 1134*m*, 1096*w*, 1022*m*, 860*w*, 762*w*, 696*m*; MS: 289 (M^+, 6%, calc. for $C_{16}H_{19}NO_4$: 289.1314, found: 289.1310), 288 (3), 245 (13), 242 (22), 173 (19), 156 (69), 146 (94), 145 (41), 105 (100), 102 (63), 77 (59), 43 (97).

Ethyl (*E*)-2-acetamido-6-phenylhex-4-enoate (4o) Reaction of ***E*-2** (85mg, 0.179mmol) and benzyl bromide (32μl, 0.269mmol) with 5mol% $Pd(AsPh_3)_4$ in THF at reflux for 95min yielded after workup the title compound as a thick oil (34mg, 68%). ^{1}H nmr: 1.23 (*t*, *J*7.2Hz, 3H), 1.97 (*s*, 3H), 2.48 (*br dt*, *J*6.8, 14.1Hz, 1H, C3-H), 2.54 (*br dt*, *J*6.1, 14.1Hz, 1H, C3-H), 3.32 (*d*, *J*6.7Hz, 2H, C6-H's), 4.15 (*q*, *J*7.2Hz, 2H), 4.63 (*br dt*, *J*5.8, 7.7Hz, 1H, a-H), 5.40 (*dt*, *J*7.3, 15.1Hz, 1H, C4-H), 5.67 (*dt*, *J*6.8, 15.1Hz, 1H, C5-H), 6.15 (*br d*, *J*7.2Hz, 1H), 7.10-7.35 (*m*, 5H); ^{13}C nmr: 14.04, 22.96, 35.23, 38.92, 51.86, 61.32, 124.77, 126.00, 128.32, 133.87, 140.07, 169.55, 171.85; IR (neat) 3284 (*br s*), 3064*w*, 3024*w*, 2984*w*, 2932*w*, 1736*s*, 1656*s*, 1548*s*, 1498*m*, 1378*m*, 1344*w*, 1198*m*, 1096*m*, 972*m*, 860*w*, 750*m*, 700*m*; MS: 275 (M^+, 6%, calc. for $C_{16}H_{21}NO_3$: 275.1521, found: 275.1513), 230 (3), 216 (73), 202 (15), 187 (9), 170 (10), 169 (8), 160 (52), 145 (54), 143 (30), 142 (69), 131 (24), 125 (52), 102 (80), 91 (76), 43 (100).

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