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ß-ARYL AND ß-VINYL-α,ß-DIDEHYDRO-α-AMINOACID DERIVATIVES THROUGH THE PALLADIUM-CATALYSED REACTION OF ARYL AND VINYL TRIFLATES WITH METHYL α-ACETAMIDOACRYLATE

A. Arcadi,[a] S. Cacchi,[b]* F. Marinelli,[a] E. Morera,[c] G. Ortar[c]

a) Dipartimento di Chimica, Ingegneria Chimica e Materiali, via Assergi 4, 67100 L'Aquila (Italy)
b) Dip. di Studi di Chimica e Tecnologia delle Sostanze Biologicamente Attive, Università degli Studi "La Sapienza", P.le A. Moro 5, 00185 Roma (Italy)
c) Dip. di Studi Farmaceutici, Università degli Studi "La Sapienza", P.le A. Moro 5, 00185 Roma (Italy)

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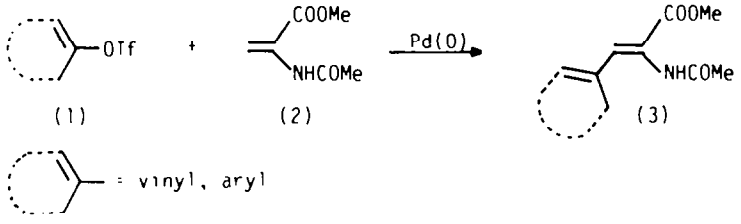
Summary - Vinyl and aryl triflates react with methyl α-acetamidoacrylate in the presence of catalytic amounts of palladium to give ß-vinyl and ß-aryl-α,ß-didehydro-α-aminoacid derivatives in good to high yields. A variety of reaction conditions were examined. Vinyl triflates give good results in the presence of both $Pd(OAc)_2(PPh_3)_2$/n-Bu_3N and $Pd(OAc)_2$/$NaHCO_3$/n-Bu_4NCl. In most cases, however, because of simplicity, high yields, and reaction rate, the $Pd(OAc)_2$/AcOK combination appears to be the system of choice. The behaviour of aryl triflates is less homogeneous. Best results were obtained in the presence of the $Pd(OAc)_2$/n-Bu_3N/DPPF/LiCl and $Pd(OAc)_2$/$NaHCO_3$/n-Bu_4NCl systems.

Introduction

The widespread use of proteogenic and non proteogenic[1] α-aminoacids in physical and life sciences as well as the demand for uncommon α-aminoacids[2] in organic and biorganic chemistry make these compounds a synthetic target of great interest. To this end, a variety of procedures have been developed in recent years and some of them deal with palladium-catalysed reactions. These syntheses rely upon two of the most important applications of palladium chemistry: vinylic substitution and allylation reactions. Namely, aryl bromides and iodides were reacted with α-acetamido acrylic acid[3] and α-acylamino acrylates[4,5] to give ß-aryl-α,ß-didehydro-α-aminoacid (DDAA) derivatives (their conversion into optically active α-aminoacids can be performed via the well-established catalytic reduction using a rhodium-chiral phosphine catalyst[6]), allyl[7] and allenyl[8] esters were reacted with methyl N-(diphenylmethylene) glycinate producing precursors of α-allyl- or α-allenyl-α-aminoacids, and allenes were treated with vinyl or aryl halides and carbonucleophiles to give dienic or styryl α-aminoacid derivatives through a sequential two-step process.[9] An intramolecular palladium-catalysed rearrangement of allyl ester of Schiff bases derived from glycine to α-allyl-α-aminoacids has also been described.[10]

Fairly recently, vinyl[11] and aryl[12] triflates were introduced as suitable precursors of σ-vinyl and σ-aryl palladium intermediates. In a few years time a large number of applications has been reported and it became apparent that widely diffused ketones and phenols can be looked at as easily available $C(sp^2)$-moieties in palladium-catalysed carbon-carbon bond forming reactions.[13]

Since vinyl[11a,14] and aryl[12a] triflates were reported to give palladium-catalysed vinylic substitution reactions in the presence of olefinic systems, we decided to explore their utilization in the preparation of the DDAA derivatives (3) according to the following scheme.



Scheme 1

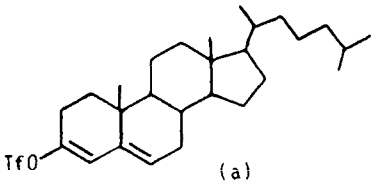
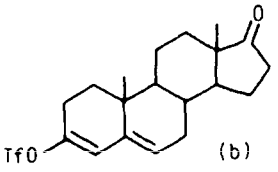
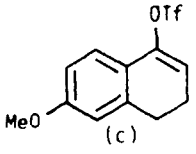
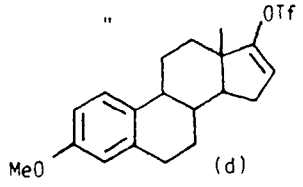
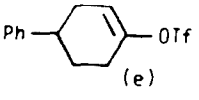
These compounds are interesting targets not only as precursors of α-aminoacids but also on their own.[15] DDAA residues are structural units of several natural peptides which show biological activity such as antrimycins[16] and cirratiomycins,[17] tuberculostatic peptides, and lavendomycin,[18] active against gram-positive bacteria. Furthermore, since substitution of DDAA for α-aminoacids produces changes in the secondary structures of peptides, several authors have investigated their incorporation into peptides.[19] The presence of a dienic system in ß-vinyl-α,ß-didehydro-α-aminoacids could eventually show biological properties.

The results of this study are reported hereafter.

Results and Discussion

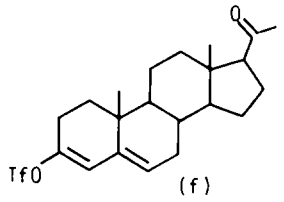
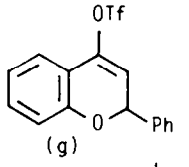
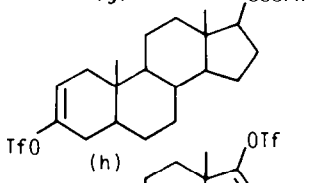
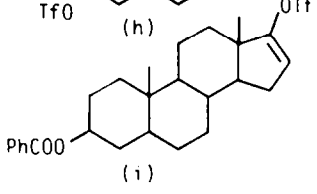
Initially, we examined the reaction of cholesta-3,5-dien-3-yl triflate (1a) with methyl α-acetamidoacrylate (2) and found that the reaction can be successfully performed under traditional Heck conditions. In the presence of $Pd(OAc)_2(PPh_3)_2$ and $n\text{-}Bu_3N$ as the base (Procedure A) the corresponding DDAA derivative was obtained in 64 % yield (Table 1, entry 1). The use of the $Pd(OAc)_2/NaHCO_3/n\text{-}Bu_4NCl$ system[20,14c] (Procedure B), however, led to the formation of (3a) in higher yield with higher reaction rate (Table 1, entry 2). Then a variety of vinyl triflates were successfully reacted with (2) according to this procedure (Table 1, entries 4,5,7,9). Results comparable to those obtained under Jeffery conditions with respect to yields and better with respect to reaction rate were obtained

Table 1 - Palladium-Catalysed Reaction of Vinyl Triflates with Methyl α-Acetamidoacrylate.[a]

Entry	Vinyl triflate (1)	Procedure[b]	Reaction time (h)	Yield of (3) (%)[c]
1	 (a)	A	24	64
2	"	B	3	76
3	"	C	2	80
4	 (b)	B	4	79
5	 (c)	B	2	68[d]
6	"	C	2	74[e]
7	 (d)	B	7	60
8	"	C	2	58
9	 (e)	B	15	76
10	"	C	1	74

(continued)

Table 1 - (continued)

Entry	Vinyl triflate (1)	Procedure [b]	Reaction time (h)	Yield of (3) (%)[c]
11	 (f)	C	2	71
12	 (g)	C	1.5	63[f]
13	 (h)	C	1.5	90
14	 (i)	C	5	64

a) All the reactions are carried out by using a (1):(2) = 1:2 molar ratio in DMF at 80°C under conditions A,B, or C. b) Procedure A: $Pd(OAc)_2(PPh_3)_2$/n-Bu_3N = 0.05 eq/5 eq; Procedure B:$Pd(OAc)_2$/$NaHCO_3$/n-Bu_4NCl = 0.05 eq/4 eq/1 eq; Procedure C: $Pd(OAc)_2$/AcOK = 0.05 eq/4 eq. c) Yields refer to single runs and are given for pure isolated products. d) Obtained as a 90/10 Z/E mixture. e) Obtained as a 65/35 Z/E mixture. f) Obtained as a 68/32 Z/E mixture.

in the presence of $Pd(OAc)_2$ and AcOK as the base (without the addition of the ammonium salt; Procedure C) (Table 1, entries 3,6,8,10-14).

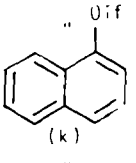
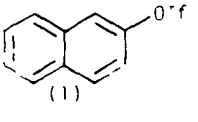
The study was next extended to aryl triflates and the reaction of 4-methoxyphenyl triflate (1j) with (2) in the presence of $Pd(OAc)_2(PPh_3)_2$ and n-Bu_3N (procedure A) was initially examined. These conditions, however, were found unsatisfactory and the starting triflate was recovered in almost quantitative yield (Table 2, entry 1). Disappointing results were also obtained substituting 1,1'-bis(diphenylphosphino)ferrocene (DPPF) or 1,3-bis(diphenylphosphino)propane (DPPP) for PPh_3 (Table 2, note d) and the addition of an excess of LiCl to $Pd(OAc)_2(PPh_3)_2$/n-Bu_3N and $Pd(OAc)_2$/DPPP/n-Bu_3N has proved to be

unsuccessfull as well (Table 2, note g). In the presence of the $Pd(OAc)_2/n\text{-}Bu_3N/DPPF/LiCl$ system (procedure D), however, the vinylic substitution product was isolated in satisfactory yield (Table 2, entry 3). This procedure was applied to other aryl triflates (Table 2, entries 9,12,13).

The use of the $Pd(OAc)_2/NaHCO_3/n\text{-}Bu_4NCl$ system (procedure B) met with failure (Table 2, entry 2). These conditions, however, were found effective in promoting vinylation of α- and ß-naphthyl triflates (Table 2, entries 4,6). The $Pd(OAc)_2/AcOK$ system (procedure C), found to give the best results with vinyl triflates, is not so efficient with the aryl triflates we examined. For example, α- and ß-naphthyl triflates gave higher yields of (3) under Jeffery conditions (Table 2, compare entry 4 with 5 and 6 with 7) and phenyl triflate produced only traces of (3) (Table 2, entry 11).

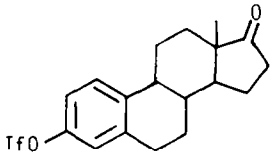
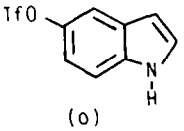
In what concerns the stereochemistry, the reaction proceeds with high stereoselectivity and usually one stereoisomer was isolated as the sole or the main product. Its stereochemistry was assigned on the ground of NMR analysis and was found to be Z in agreement with the results reported by Naso et al.,[3] Hegedus et al.,[4] and Frejd et al.[5] for related palladium-catalysed reactions of aryl halides with α-acylamino acrylate derivatives.

Table 2 - Palladium-Catalysed Reaction of Aryl Triflates with Methyl α-Acetamidoacrylate.[a]

Entry	Aryl triflate (1)	Procedure[b]	Reaction time (h)	Yield of (3) (%)[c]
1	4-MeO-C_6H_4OTf (j)	A[d]	24	--[e]
2	"	B	"	--[f]
3	 (k)	D[g]	"	42
4		B	14	61
5	"	C	20	47
6	 (l)	B	3	70
7	"	C	8	20

(continued)

Table 2 - (continued)

Entry	Aryl triflate (1)	Procedure[b]	Reaction time (h)	Yield of (3) (%)[c]
8	 (m)	B	20	14
9	"	D	20	62
10	Ph-OTf	B	20	14
11	"	C	20	-
12	"	D	20	75
13	 (o)	D	48	38

a) All the reactions are carried out by using a (1):(2) = 1:2 molar ratio in DMF at 80°C under conditions A,B,C, or D. b) Procedure A: $Pd(OAc)_2(PPh_3)_2$ /n-Bu_3N = 0.05 eq/5 eq; Procedure B:$Pd(OAc)_2$ /$NaHCO_3$/n-Bu_4NCl = 0.05 eq/4 eq/1 eq; Procedure C: $Pd(OAc)_2$ /AcOK = 0.05 eq/4 eq; Procedure D: $Pd(OAc)_2$/n-Bu_3N/DPPF/LiCl = 0.05 eq/5 eq/0.1 eq/ 3 eq. c) Yields refer to single runs and are given for pure isolated products. d) No traces of the vinylic substitution product were detected (TLC analysis) substituting DPPF or DPPP for PPh_3. The starting material was recovered in 68 % and 30 % yield in the presence of DPPF and DPPP, respectively. When the reaction was carried out at 100°C (8h) in the presence of DPPF as the ligand, the starting material was recovered in 92 % yield. e) Starting material recovered in 95 % yield. f) Starting material recovered in 93 % yield. g) The starting material was recovered in 78% and 73 % yield, respectively, by using $Pd(OAc)_2(PPh_3)_2$/n-Bu_3N and $Pd(OAc)_2$/DPPP/n-Bu_3N in the presence of an excess of LiCl.

Compound (3n) had ^1H- and ^{13}C-NMR spectra well in agreement with those observed for Z-ß-phenyl-α-acetamido acrylic acid methyl ester prepared from phenyl iodide and methyl α-acetamido acrylate[5] and from phenyl iodide and α-acetamido acrylic acid[3] and subsequent esterification of the resulting coupling product. Upon N-methylation* of (3a), (3d), and

* N-methylation was carried under PTC conditions.[22] N-methyl derivatives of (3a), (3d), and (3j) were isolated in 65, 68, and 60 % yield, respectively. Control experiments carried out with (3a) revealed that no apparent isomerization takes place under the methylation conditions. NMR analysis of (3a), recovered upon treatment under usual PTC conditions omitting MeI, revealed that its configuration remained unchanged.

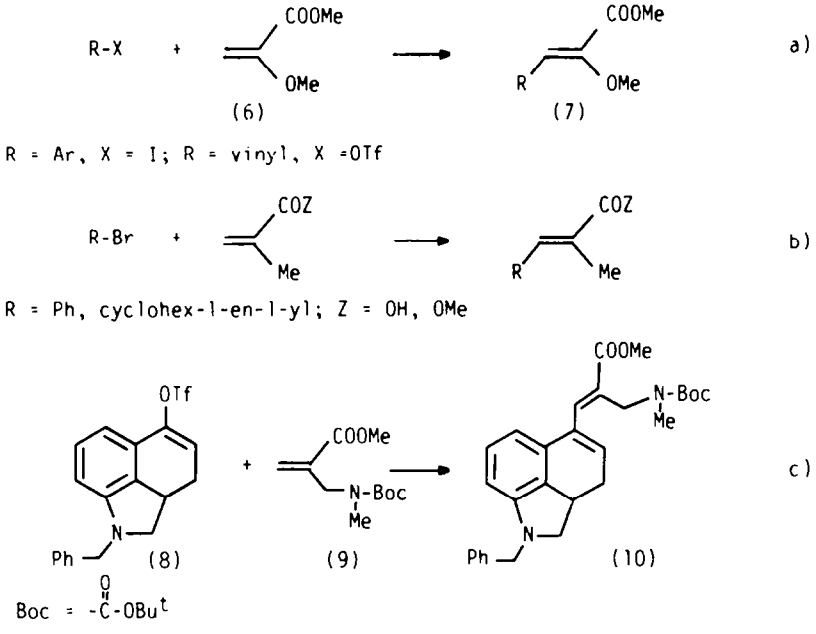
(3j) ß-vinyl protons were found to undergo downfield shifts (0.12 ppm, 0.20 ppm, and 0.31 ppm, respectively). Similarly, the N-methyl derivative of (3n), obtained as a by product from the esterification of ß-phenyl-α-acetamido acrylic acid,[3] showed the vinyl proton signal at δ 7.66 while (3n) had the vinyl proton concealed within the aromatic envelope (δ 7.46-7.31). Since methylation of the E-isomer has been reported to produce a large upfield shift of the vinyl proton,[21] this result has been taken to point to the Z configuration. Furthermore, the N-methyl derivative of (3n) gave a ^{1}H-NMR spectrum identical with that reported by Frejd et al.[5]

The Nuclear Overhauser Enhancement (NOE) technique, reported to be a good method for differentiating between the E- and Z-isomers of DDAA,[23] also confirmed the Z configuration. Irradiation of the amide proton signal of (3j) produced no enhancement of the vinyl proton signal. For example, with ethyl ß-phenyl-α-(benzyloxycarbonylamino) acrylate a large negative enhancement (ca. 30%) for the E-isomer and no enhancement for the Z-isomer have been reported.[5]

Only with vinyl triflates (1c) and (1g) considerable amounts of isomeric vinylic substitution products were obtained. This lack of stereoselectivity was found to be dependent on the nature of the added base. For example, (3c) was obtained as an about 90:10 Z/E mixture in the presence of $NaHCO_3$ and as an about 65/35 Z/E-mixture in the presence of AcOK. This result could reflect the presence of different organopalladium intermediates derived from replacement of the poorly coordinating triflate anion with better ligands. Formation of various organopalladium halides from organopalladium triflates and external halides has been reported and, particularly, the regio- and stereochemical outcome of Heck reaction of electron-rich olefins with aryl triflates has been found to be controlled through addition of halide salts.[14f] We have found that the reactivity of aryl halides containing strongly electron-withdrawing groups with ß-substituted-α,ß-unsaturated carbonyl compounds is strongly affected by the presence of the acetate anion, most likely through the formation of organopalladium acetates.[24] Therefore, it is conceivable that with the $NaHCO_3$/n-Bu_4NCl combination DDAA derivatives arise from decomposition of addition σ-alkylpalladium chlorides while in the presence of AcOK σ-alkylpalladium acetates are involved along the reaction pathway. The stereoselectivity of the vinylic substitution reaction could be dependent on the different reactivity of these organopalladium intermediates. Clearly, further work is to be done to gain insight into this point.

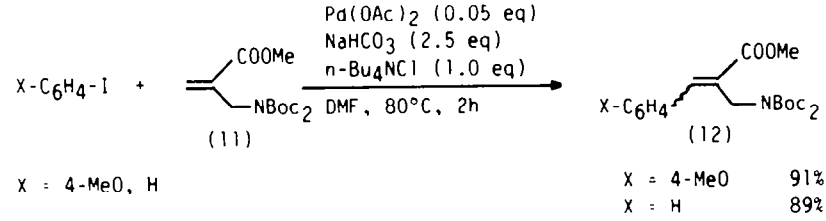
It should be stressed that the same stereochemical trend observed with α-acetamido acrylic acid derivatives was observed in the palladium-catalysed reactions of a variety of

α-substituted acrylates. Formation of vinylic substitution products with the added vinyl or aryl unit on the opposite side of the carboxylic group was strongly favoured in the reaction of aryl iodides and vinyl triflates with methyl α-methoxyacrylate (6)[14c] (Scheme 2a), in the reaction of phenyl[25] and vinyl[26] halides with α-methyl acrylic acid derivatives (Scheme 2b), and in the reaction of the vinyl triflate (8) with (9) (a key step in a concise approach to (±)-lysergic acid)[27] (Scheme 2c).



Scheme 2

Interestingly, the reaction of aryl iodides (2 eq) with (11), a compound related to (9), produced an about 60/40 mixture of isomeric vinylic substitution products (12) in high yield.



Scheme 3

The reasons of the stereochemical outcome of the reaction of α-acetamido acrylate derivatives with organopalladium complexes were not investigated by us nor by the other authors concerned with palladium-catalysed preparation of ß-aryl-DDAA derivatives. Nevertheless, it seems unlikely that the usually observed high stereoselectivity is related to differences in the steric demand of the acetamido and ester groups. Accordingly, Frejd et al. reported that methyl α-acetamido acrylate and methyl α-(N-methyl)-acetamido acrylate, the latter containing a more crowded nitrogen center, react with phenyl iodide producing the corresponding Z-ß-phenyl-DDAA derivatives in 73 and 79 % yield, respectively.[5]

With respect to the reactivity of aryl and vinyl triflates, it seems apparent that not always they give the best results under the same reaction conditions. Furthermore, aryl triflates showed a behaviour less homogeneous than vinyl triflates. Procedure D [$Pd(OAc)_2$/n-Bu_3N/DPPF/LiCl] was found to be more convenient with some of the aryl triflates we examined. In most cases good results were obtained by using Procedure B [$Pd(OAc)_2$/$NaHCO_3$/n-Bu_4NCl] while Procedure C [$Pd(OAc)_2$/AcOK] appeared usually unsatisfactory.

Vinyl triflates gave good results under Heck and Jeffery conditions. However, because of high yields, reaction rate, and simplicity of reaction conditions, AcOK appeared the base of choice. Neither amines nor expensive n-Bu_4NCl are required. Less expensive ammonium salts could be conceivably used with $NaHCO_3$ and we indeed obtained good results with TEBA. For example, the reaction of cholesta-3,5-dien-3-yl triflate with (2) according to the procedure B but substituting TEBA for n-Bu_4NCl, produced the corresponding vinylic substitution product in 80 % yield (80°C, 5 h). Even so, however, still remains that omitting the ammonium salt cheaper and simpler reaction conditions can be used.

In conclusion, this palladium-catalysed reaction of vinyl and aryl triflates widens further the potential of these easily available intermediates as useful $C(sp^2)$-moieties in carbon-carbon bond forming reactions. It seems of particular interest the possibility, now at hand, to "introduce" the functionality of DDAA into widely diffused compounds containing ketonic and phenolic functionalities.

Experimental

Melting points were determined with a Büchi 510 apparatus and are uncorrected. All starting materials, catalysts, solvents, and amines are commercially available and were used without further purification. Methyl 2-acetamidoacrylate was prepared by PTC esterification of 2-acetamido acrylic acid.[22] Preparation of aryl and vinyl triflates was

carried out according to ref. 28.

Reactions were carried out on a 0.5-3 mmol scale. The products were purified by flash chromatography on silica gel 40-63 μ (Merck) eluting with n-hexane/AcOEt mixtures. NMR spectra ($CDCl_3$; TMS as the internal standard) were recorded with a Varian XL-300 spectrometer. IR spectra (KBr, unless otherwise indicated) were recorded on a Perkin-Elmer 683 spectrometer and a Nicolet SDXFT/IR spectrometer. All the isolated products gave satisfactory microanalyses.

General Procedures of Reaction of Methyl 2-Acetamidoacrylate with Aryl and Vinyl Triflates

Procedure A - This is exemplified by the reaction of methyl 2-acetamidoacrylate with cholesta-3,5-dien-3-yl triflate (1a) (Table 1, entry 1). A mixture of methyl 2-acetamidoacrylate (0.17 g, 1.16 mmol), (1a) (0.30 g, 0.58 mmol), $n\text{-}Bu_3N$ (0.69 ml, 2.9 mmol), and $Pd(OAc)_2(PPh_3)_2$ (0.022 g, 0.029 mmol) in DMF (4 ml) was stirred at 80°C for 24 h under a nitrogen atmosphere. Et_2O and HCl 0.1M were added, the organic layer was washed with a saturated $NaHCO_3$ solution, water, dried (Na_2SO_4), and concentrated at reduced pressure. The residue was purified by flash chromatography eluting with a 60/40 n-hexane/AcOEt mixture to give (3a) (0.189 g, 64% yield).

Procedure B - This is exemplified by the reaction of methyl 2-acetamidoacrylate with cholesta-3,5-dien-3-yl triflate (1a) (Table 1, entry 2). A mixture of methyl 2-acetamidoacrylate (0.25 g, 1.75 mmol), (1a) (0.44 g, 0.87 mmol), $Pd(OAc)_2$ (0.010 g, 0.043 mmol), $n\text{-}Bu_4NCl$ (0.243 g, 0.87 mmol), and $NaHCO_3$ (0.293 g, 3.49 mmol) in DMF (5 ml) was stirred at 80°C for 3h under a nitrogen atmosphere. AcOEt and a saturated NH_4Cl solution were added, the organic layer was washed with water, dried (Na_2SO_4), and concentrated at reduced pressure. The residue was purified by flash chromatography eluting with a 60/40 n-hexane/AcOEt mixture to give (3a) (0.330 g, 76% yield).

Procedure C - This is exemplified by the reaction of methyl 2-acetamidoacrylate with 17β-benzoyloxy-5α-androst-2-en-3-yl triflate (1h) (Table 1, entry 13). A mixture of methyl 2-acetamidoacrylate (0.190 g, 1.33 mmol), (1h) (0.351 g, 0.66 mmol), $Pd(OAc)_2$ (0.007 g, 0.03 mmol), and AcOK (0.261 g, 2.66 mmol) in DMF (3 ml) was stirred at 80°C for 1.5 h under a nitrogen atmosphere. CH_2Cl_2 and a saturated $NaHCO_3$ solution were added, the organic layer was washed with water, dried (Na_2SO_4), and concentrated at reduced pressure. The residue was purified by flash chromatography eluting with a 40/60 n-hexane/AcOEt mixture to give (3h) (0.309 g, 90% yield).

Procedure D - This is exemplified by the reaction of methyl 2-acetamidoacrylate with 4-methoxyphenyl triflate (1j) (Table 2, entry 3). A mixture of methyl 2-acetamidoacrylate

(0.457 g, 3.2 mmol), (1j) (0.408 g, 1.6 mmol), n-Bu_3N (1.9 ml, 7.9 mmol), LiCl (0.204 g, 4.8 mmol), $Pd(OAc)_2$ (0.018 g, 0.08 mmol),and DPPF (0.089 g, 0.16 mmol) in DMF (3 ml) was stirred at 80°C for 24 h under a nitrogen atmosphere. Et_2O and HCl 0.1M were added, the organic layer was washed with a saturated $NaHCO_3$ solution, water, dried (Na_2SO_4), and concentrated at reduced pressure. The residue was purified by flash chromatography eluting with a 50/50 n-hexane/AcOEt mixture to give (3j) (0.232 g, 58% yield).

General Procedure of N-Methylation of α,ß-Didehydro-α-aminoacid Methyl Esters - This is exemplified by the N-methylation of (3d). A mixture of (3d) (0.100 g, 0.24 mmol), n-Bu_4NCl (0.068 g, 0.24 mmol), and methyl iodide (0.34 g, 2.4 mmol) in a two phase CH_2Cl_2 (3 ml)/NaOH 2N (3 ml) system was stirred at 40°C overnight. CH_2Cl_2 was added, the organic layer was washed with water, dried (Na_2SO_4), and concentrated at reduced pressure. The residue was purified by flash chromatography eluting with a 50/50 n-hexane/AcOEt mixture to give the corresponding N-methyl derivative (0.069 g, 68% yield); mp = 160-161°C. IR 1720, 1670, 1615 cm^{-1}. ^1H NMR δ 7.19 (d, J = 8.8 Hz, 1H), 7.10 (brs, 1H), 6.72 (dd, J = 8.8 Hz, J = 2.2 Hz, 1H), 6.64 (d, J = 2.2 Hz, 1H), 6.32 (m, 0.5H), 6.29 (m, 0.5H), 3.84 (s, 3H), 3.78 (s, 3H), 3.01 (s, 1.5H), 2.98 (s, 1.5H), 1.91 (s, 1.5H), 1.89 (s, 1.5H), 0.87 (s, 3H). ^{13}C NMR δ 170.9, 170.5, 165.2.

3a. mp 223-224°C. IR 3200, 1720, 1645, 1600 cm^{-1}. ^1H NMR δ 7.13 (brs, 1H), 6.94 (brs, 1H), 6.29 (brs, 1H), 5.66 (m, 1H), 3.76 (s, 3H), 2.13 (s, 3H). ^{13}C NMR δ 170.0, 166.2.

3b. mp 120-121°C. IR 3245, 1740, 1665, 1620 cm^{-1}. ^1H NMR δ 7.34 (brs, 1H), 7.11 (brs, 1H), 6.29 (brs, 1H), 5.67 (m, 1H), 3.76 (s, 3H), 2.12 (s, 3H) 0.95 (s, 3H), 0.91 (s, 3H). ^{13}C NMR δ 173.4, 170.2, 166.2.

3c. Z-isomer: mp 118-120°C. IR 3250, 1730, 1660, 1250 cm^{-1}. ^1H NMR δ 7.09 (brs, 1H), 6.99 (d, J = 8.4 Hz, 1H), 6.88 (brs, 1H), 6.73-6.67 (m, 2H), 6.20 (m, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 2.74 (m, 2H), 2.33 (m, 2H), 1.84 (s, 3H). ^{13}C NMR δ 165.5, 158.9.
E-isomer: mp 95-97°C. IR 3470, 1695, 1640, 1235 cm^{-1}. ^1H NMR δ 7.63 (brs, 1H), 7.55 (d, J = 1.8 Hz, 1H), 7.06 (d, J = 8.1 Hz, 1H), 6.72-6.65 (m, 2H), 5.82 (m, 1H), 3.79 (s, 3H), 3.53 (s, 3H), 2.74 (m, 2H), 2.28 (m, 2H), 2.14 (s, 3H). ^{13}C NMR δ 165.8, 158.6.

3d. mp 258-260°C. IR 3200, 1715, 1645 cm^{-1}. ^1H NMR δ 7.19 (d, J = 8.7 Hz, 1H), 6.90 (brs, 1H), 6.73-6.64 (m, 4H), 6.14 (m, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 2.12 (s, 3H), 0.85 (s, 3H). ^{13}C NMR δ 165.4, 157,5.

3e. mp 139°C (dec.). IR 3200, 1700, 1640 cm^{-1}. ^1H NMR δ 7.89 (brs, 1H), 7.57 (brs, 1H),

7.30-7.09 (m, 5H), 6.19 (m, 1H), 3.72 (s, 3H), 2.07 (s, 3H). ^{13}C NMR δ 170.7, 166.2.

3f. mp 208-210°C. IR 3230, 1720, 1700, 1650 cm^{-1}. ^{1}H NMR δ 7.14 (brs, 1H), 7.11 (brs, 1H), 6.28 (brs, 1H), 5.65 (m, 1H), 3.76 (s, 3H), 2.13 (s, 3H), 0.92 (s, 3H), 0.66 (s, 3H). ^{13}C NMR δ 209.5, 170.1, 166.2.

3g. obtained as a 68/32 Z/E mixture. IR (liquid film) 3260, 1720, 1670 cm^{-1}. ^{1}H NMR* δ (Z-isomer) 5.87 (d, J = 3.6 Hz, 0.7H), 3.82 (s, 2.1H), 1.85 (s, 2.1H); (E-isomer) 5.66 (d, J = 3.9 Hz, 0.3H), 3.43 (s, 0.9H), 2.10 (s, 0.9H). ^{13}C NMR δ 165.2, 165.0, 153.2, 153.1.

3h. mp 159-160°C. IR 3240, 1725, 1660 cm^{-1}. ^{1}H NMR δ 8.03 (d, J = 7.08 Hz, 2H), 7.55-7.41 (m, 3H), 7.06 (brs, 1H), 6.73 (brs, 1H), 6.09 (m, 1H), 4.84 (m, 1H), 3.77 (s, 3H), 2.11 (s, 3H), 0.94 (s, 3H), 0.76 (s, 3H). ^{13}C NMR δ 169.8, 166.6, 166.2.

3i. mp 198-200°C. IR 3200, 1720, 1700, 1645 cm^{-1}. ^{1}H NMR δ 8.03 (d, J = 6.9 Hz, 2H), 7.57-7.40 (m, 3H), 7.06 (brs, 1H), 6.69 (brs, 1H), 6.12 (m, 1H), 4.95 (m, 1H), 3.79 (s, 3H), 2.11 (s, 3H), 0.91 (s, 3H), 0.82 (s, 3H). ^{13}C NMR δ 166.1, 165.4, 148.4.

3j. mp 134-135°C. IR 3260, 1740, 1260, 845, 760 cm^{-1}. ^{1}H NMR δ 7.96 (brs, 1H), 7.41 (d, J = 8.2 Hz, 2H), 7.29 (s, 1H), 6.81 (d, J = 8.2 Hz, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 2.02 (s, 3H). ^{13}C NMR δ 169.9, 166.0.

3k. mp 170-172°C. IR 3200, 1715, 1655 cm^{-1}. ^{1}H NMR δ 7.93-7.41 (m, 8H), 7.12 (brs, 1H), 3.86 (s, 3H), 1.86 (s, 3H). ^{13}C NMR δ 169.1, 165.4.

3l. mp 147-148°C. IR 3260, 1725, 1665 cm^{-1}. ^{1}H NMR δ 7.82-7.45 (m, 9H), 3.79 (s, 3H), 2.03 (s, 3H). ^{13}C NMR δ 169.4, 165.8.

3m. mp 166-167°C. IR 3260, 1730 cm^{-1}. ^{1}H NMR δ 7.98 (brs, 1H), 7.60 (brs, 1H), 7.34-7.20 (m, 3H), 3.82 (s, 3H), 2.13 (s, 3H), 0.90 (s, 3H). ^{13}C NMR δ 169.28, 165.9, 162.6.

3n. mp 121-122°C (lit.[29] mp 125-127°C). ^{13}C NMR δ 169.0, 165.8.

3o. mp 122-123°C. IR 3250, 1720, 1645 cm^{-1}. ^{1}H NMR δ 7.85 (d, J = 8.7 Hz, 1H), 7.71 (brs, 1H), 7.53-7.49 (m, 2H), 7.37 (d, J = 3.6 Hz, 1H), 7.32 (brs, 1H), 6.80 (d, J = 3.6 Hz, 1H), 3.85 (s, 3H), 2.13 (s, 3H). ^{13}C NMR δ 168.9, 165.7.

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* Only signals unambiguously assigned to Z- and E-isomers are reported.

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