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Synthesis and *C*-Alkylation of *C*-Protected β-Enamino Acid Derivatives from Oxa- Thia- and Imidazolines

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Abstract: Various heterocycles **3a-h** can be readily metallated and condensed with a variety of organic nitriles to afford *C*-protected β-enamino acid derivatives **1** (or **2**). Procedures for alkylation of compounds **1** to obtain **2** as well as a *"one-pot"* preparation of **2** from **3** are also described.

Keywords: Oxazolines; Thiazolines; Enamines; Alkylation; Theoretical studies.

Introduction

The chemistry of β-amino acids and their derivatives has received increasing attention during the last few years [1]. This is partly due to the fact that β-amino acids are components of a variety of metabolites [2] [3]. On the other hand, β-peptides are an emerging class of unnatural biopolymers with surprising secondary structural propensities [4] [5]; for example, self-assembling cyclic β^3-peptide nanotubes can act as artificial transmembrane ion channels [6]. Moreover, β-amino α,β-unsaturated acid derivatives, particularly esters, have also found widespread use in the synthesis of naturally occurring compounds such as alkaloids [7] and antibiotics [8], and as important building blocks for the synthesis of biomolecules. They have also been employed as synthons in stereoselective synthesis [9] as well as precursors to primary amines with pharmacological properties [10].

Several different strategies have been developed for the synthesis of β-amino α,β-unsaturated esters: a) condensation reactions between β-ketoesters and amines [11], including aza-Wittig type reactions [12]; b) addition of ester enolates to nitriles (the Blaise reaction [13], strongly dependant on the metal employed to generate the enolate [14]) or to *N*-substituted amide derivatives, such as tosylimines [15] or imidoyl halides [16]; c) conjugate addition of amines to alkyne carboxylate derivatives [17] (esters or amides) and d) addition of imines to activated carbonic acid derivatives [18], although in the latter case the formation of the *N*-alkoxycarbonyl compound is sometimes a competing side reaction [19].

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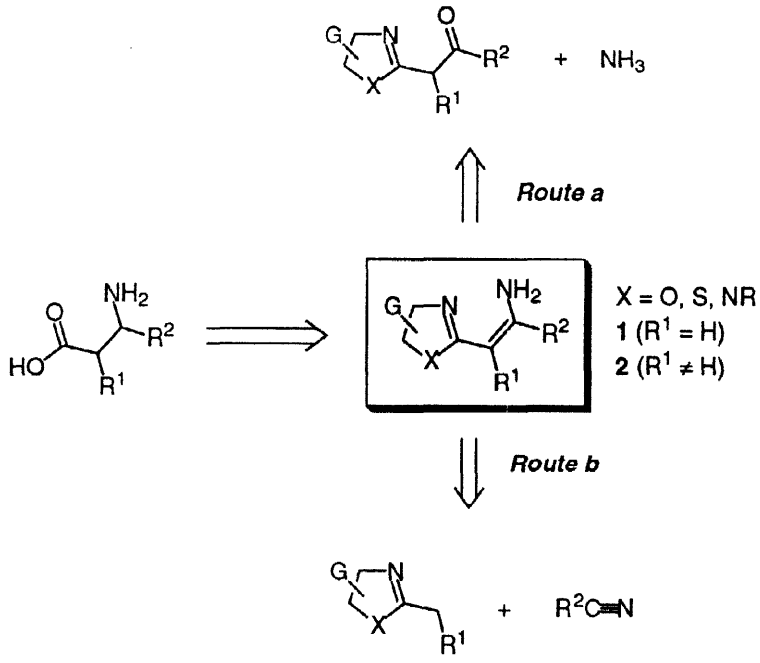
We have focused our research interest on the synthesis of *C*-protected β-enamino acids which are potential precursors to β-amino acids (Scheme 1), and we have considered the employment of heterocyclic systems as protecting groups for the carboxyl functional group. Among the several options presented in the literature [20], we have centred our efforts in the Δ^2-oxazoline moiety. The chemistry of this heterocyclic functionality has been widely developed by Meyers [21] and it has been commonly adopted mainly due to the ease of its synthesis, its stability and the smooth conditions required to transform it into other functional groups or heterocycles [21], [22].



Scheme 1

In this paper we present our studies on the metalation and further treatment with nitriles not only of Δ^2-oxazolines but also of Δ^2-thia- and imidazolines **3a-h** (Figure 1). We also describe the alkylation in the α-position of the β-enamino acid derivatives obtained [23].

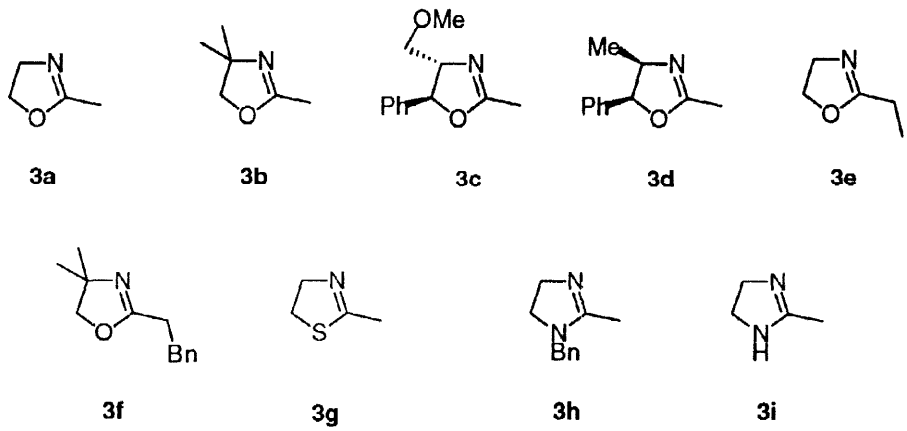
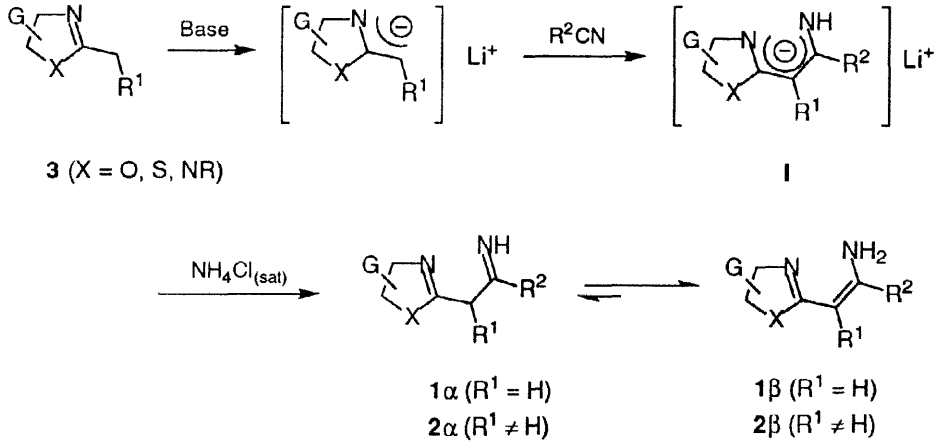


Figure 1

Results and Discussion

i) **Synthesis of β-amino α,β-unsaturated Δ^2-oxa-, thia- and imidazoline derivatives 1 (or 2).** Two routes, shown in Scheme 1 (*Route a* and *Route b*), are possible for the preparation of *C*-protected β-enamino acid derivatives **1** (or **2**). The β-oxoderivatives employed as starting material in *Route a* can be easily prepared [24]; however, earlier reports indicated that their aminolysis under different conditions do not yield compounds **1** (or **2**) [25].

Route b seems to be, *a priori*, a more attractive and direct route to compounds **1** (or **2**). It represents a modified Blaise reaction that consists of the addition of a nitrile to an azaenolate. The addition of different nitriles to the heterocyclic azaenolate derived from **3a-h** (base/heterocycle/nitrile ratio: 1.25/1.1/1.0) in dry THF usually at low temperature (– 78 °C to – 50 °C or – 78 °C to r.t.,) gave the anionic intermediate **I** in relatively short reaction times (2-5 h) (Scheme 2). After quenching with aqueous saturated NH_4Cl, intermediate **I** evolved to a single reaction product **1** (or **2**), that was isolated in the β tautomeric form, probably due to the additional stabilisation resulting for the possibility of intramolecular hydrogen bonding [26]. Tautomer α was never detected by NMR, independently of the nature of the substituents of both heterocycle and nitrile.



Scheme 2

Compounds **1** (or **2**) prepared are listed in Table 1 and were obtained in good yields, except in some cases when aliphatic nitriles (entries 8-12) or thiazoline **3g** (entries 30-31) were employed.

The reaction presents two important features: the base used to generate the azaenolate and the stability, both thermal and temporal, of the azaenolate. Regarding the base, slightly better results were obtained when *n*-BuLi rather than LDA was employed (Table 1, entries 16, 20, 23 and 27 *vs.* 2 and 29); in other words, *n*-BuLi is a more efficient deprotonating reagent than LDA for the formation of alkyl-Δ^2-oxa-, thia- and imidazolidine enolates. Related to the thermal stability, it should be pointed out that when *n*-BuLi was employed, it was necessary to keep the temperature in the range between – 78 °C and – 50 °C while the LDA generated azaenolate was stable to higher temperatures (up to r. t.) and longer reaction times [27].

Table 1. *C*-Protected *N*-unsubstituted β-enaminoacids 1 and 2 from 3 and nitriles.

Entry	3	R^1	R^2	1 or 2	Yield (%)[a]	
					Method A[b]	Method B[b]
1	**3a**	H	Ph	**1a**		85 (72)
2	**3a**	H	*p*-MeC_6H_4	**1b**	84	88 (75)
3	**3a**	H	*p*-$MeOC_6H_4$	**1c**		95 (80)
4	**3a**	H	2-Furyl	**1d**	82 (57)	
5	**3a**	H	2-Pyridyl	**1e**	60 (54)	
6	**3a**	H	4-Pyridyl	**1f**		89 (73)
7	**3a**	H	2-Thiophenyl	**1g**		85 (80)
8	**3a**	H	*c*-C_3H_5	**1h**	78 (68)	
9	**3a**	H	*c*-C_6H_{11}	**1i**	70 (53)	
10	**3a**	H	*i*-Pr	**1j**	78 (60)	
11	**3a**	H	Et	**1k**	76 (56)	
12	**3a**	H	CH_3OCH_2	**1l**	74 (67)	
13	**3a**	H	*p*-FC_6H_4	**1m**	83 (70)	
14	**3a**	H	*o*-$MeSC_6H_4$	**1n**		85(71)
15	**3b**	H	Ph	**1o**	90 (75)	
16	**3b**	H	*p*-MeC_6H_4	**1p**	89 (72)	72
17	**3b**	H	*p*-$MeOC_6H_4$	**1q**		76 (54)
18	**3b**	H	2-Furyl	**1r**		95 (78)
19	**3b**	H	2-Naphtyl	**1s**		92 (80)
20	**3c**	H	*p*-MeC_6H_4	**1t**	78 (60)	68
21	**3d**	H	4-Pyridyl	**1u**		93 (81)
22	**3e**	Me	Ph	**2a**		98 (85)
23	**3e**	Me	*p*-MeC_6H_4	**2b**	77 (65)	66
24	**3e**	Me	*p*-$MeOC_6H_4$	**2c**		85 (70)
25	**3e**	Me	2-Furyl	**2d**	74 (62)	
26	**3f**	Bn	4-Pyridyl	**2e**	82 (69)	
27	**3g**	H	Ph	**1v**	95 (52)[c]	67
28	**3g**	H	*p*-MeC_6H_4	**1w**	95 (86)	
29	**3g**	H	*p*-$MeOC_6H_4$	**1x**	76	80 (68)
30	**3g**	H	2-Furyl	**1y**		35 (24)
31	**3g**	H	*c*-C_3H_5	**1z**	62 (48)	
32	**3h**	H	*p*-MeC_6H_4	**1ρ**		87 (64)

[a] Crude yield. In parenthesis isolated yield.
[b] Method A = *n*-BuLi. Method B = LDA.
[c] During chromatographic purification partial hydrolysis to the corresponding β-ketoderivative was observed.

This methodology is of wide application regarding both the nitrile and the heterocyclic compound. In the case of imidazoline derivatives [28], starting material was recovered unchanged when the free amino imidazoline **3i** was treated with two equivalents of base (LDA) and subsequent addition of nitrile; however, the employment of sp^3-NH protected imidazoline **3h** resulted in an 87% yield of compound **1ρ** (Table 1, entry 32).
Also, the excellent yields obtained when chiral non-racemic oxazolines **3c,d** were employed (Table 1, entries 20-21) identify this reaction as a potential tool for the stereoselective synthesis of enantiomerically pure β-amino acids.
Compounds **1** (or **2**) were characterised by ^{1}H and ^{13}C-NMR and MS. The configuration of the double bond was found to be *Z* by NOE experiments performed on compound **1a**. This configuration allows the afore mentioned possibility of formation of stabilising hydrogen bonding in a similar manner as has been observed for related systems [29].
In order to confirm the experimental results, a theoretical study was performed with both semiempirical (AM1) and *ab initio* (Hartree-Fock) calculations. Geometries were fully optimised with the standard basis set 3-21G at the Hartree-Fock level and energies were evaluated at the HF/6-31G* level over the previously optimised structures by using the GAUSSIAN 94 program package [30]. Total (Hartree) and relative (Kcal/mol) energies of optimised structures corresponding to compounds **1a**, **1h**, **1k** and **1ω** are given in Table 2. Some of the possible geometries for compounds **1** are showed in Figure 2.

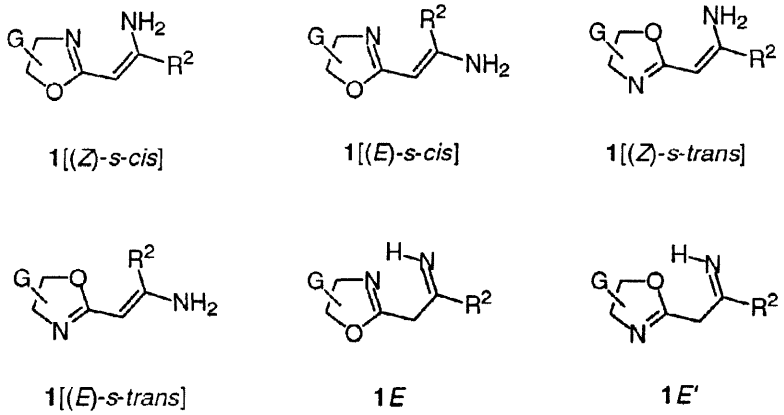


Figure 2

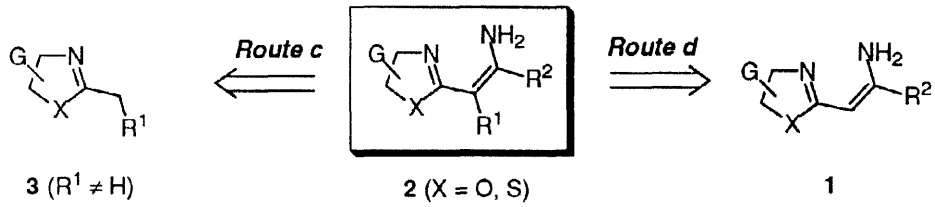
Structures $\mathbf{1a}_1$, $\mathbf{1h}_1$, $\mathbf{1k}_1$ and $\mathbf{1\omega}_1$ corresponding to *(Z)-s-cis* isomers are 10.6, 6.3, 6.8 and 12.2 Kcal/mol respectively more stable than the corresponding *(E)-s-cis* isomers $\mathbf{1a}_2$, $\mathbf{1h}_2$, $\mathbf{1k}_2$, and $\mathbf{1\omega}_2$. These results are in complete agreement with the NMR experiments commented before. Also, structures $\mathbf{1a}_1$, $\mathbf{1h}_1$, $\mathbf{1k}_1$, and $\mathbf{1\omega}_1$ were 3.9, 4.0, 4.3 and 7.1 Kcal/mol more stable than the *(Z)-s-trans* isomers $\mathbf{1a}_3$, $\mathbf{1h}_3$, $\mathbf{1k}_3$, and $\mathbf{1\omega}_3$, even though the intramolecular interaction between *N*-H(7) and N(6)-H(7) in all the calculated structures is weaker than the interaction between *N*-H(7) and O(5)-H(7) (for example 1.957 Å in $\mathbf{1h}_1$ *vs* 1.919 Å in $\mathbf{1h}_3$) (Figure 3). In a similar way, iminic structures *E* and *E'* are, in all cases, less stable than the corresponding *(Z)-s-cis*. This fact is also in accordance with the experimental results as the iminic tautomers **1α** were not detected by NMR spectroscopy (see Table 2).

Table 2. Total (Hartree) and relative (Kcal/mol) energies of optimised structures corresponding to compounds 1a, 1h, 1k and 1ω

		E_{Tot}			E_{Rel}		
	Structure	AM1	HF/3-21G //3-21G	HF/6-31G*[a]	AM1	HF/3-21G //3-21G	HF/6-31G*[a]
1a	**1a$_1$[(*Z*)-*s*-*cis*]**	0.03288	-603.90145	-607.28338	0.0	0.0	0.0
	1a$_2$[(*E*)-*s*-*cis*]	0.04159	-603.88108	-607.26646	5.5	12.8	10.6
	1a$_3$[(*Z*)-*s*-*trans*]	0.03529	-603.89655	-607.27720	1.5	3.1	3.9
1h	**1h$_1$[(*Z*)-*s*-*cis*]**	0.02635	-490.88571	-493.63743	0.0	0.0	0.0
	1h$_2$[(*E*)-*s*-*cis*]	0.03452	-490.87434	-493.62654	5.1	7.1	6.8
	1h$_3$[(*Z*)-*s*-*trans*]	0.02930	-490.88017	-493.63063	1.8	3.5	4.3
	1h$_4$[(*E*)]	0.03313	-490.86792	-493.63401	4.2	11.2	2.1
	1h$_5$[(*E'*)]	0.03293	-490.86533	-493.63190	4.1	12.8	3.5
1k	**1k$_1$[(*Z*)-*s*-*cis*]**	-0.03078	-453.27418	-455.80573	0.0	0.0	0.0
	1k$_2$[(*E*)-*s*-*cis*]	-0.02331	-453.26291	-455.79574	4.7	7.1	6.3
	1k$_3$[(*Z*)-*s*-*trans*]	-0.02834	-453.26912	-455.79940	1.5	3.2	4.0
	1k$_4$[(*E*)]	-0.02156	-453.26016	-455.79303	5.8	8.8	8.0
1ω[b]	**1ω$_1$[(*Z*)-*s*-*cis*]**	0.03220	-774.39188	-778.45412	0.0	0.0	0.0
	1ω$_2$[(*E*)-*s*-*cis*]	0.03758	-774.36771	-778.43466	3.4	15.2	12.2
	1ω$_3$[(*Z*)-*s*-*trans*]	0.03911	-774.37729	-778.44276	4.3	9.2	7.1
	1ω$_4$[(*E*)]	0.03786	-774.37636	-778.44085	3.4	9.7	8.3

[a] *Single point* energies at HF/6-31G*//3-21G level.
[b] 3ω: 2-(4,5-dihydro-1,3-thiazol-2-yl)-1-buten-2-amine; model compound (not synthesised).

***ii)* Alkylation reaction of *C*-protected *N*-unsubstituted β-enamino acids 1.** Compounds **2** can be prepared using two different strategies (*Route c* and *Route d*, Scheme 3). *Route c* implies the reaction of a 2-alkyl-Δ^2-oxa- or thiazoline **3** with a nitrile and requires the availability of the appropriate heterocycle **3**. A limited number of alkylated heterocycles **3** are commercially available and some others can be obtained by heterocyclization reactions or by lengthening the heterocycle side chain [31]. In fact *Route c* ($R^1 \neq H$) is a particular case of the previously described methodology (*Route b*, $R^1 = H$), but in this case stronger deprotonating conditions are required and lower reaction yields are obtained due to the lower acidity of the α hydrogen of the 2-alkyl-Δ^2-oxa- or thiazolines **3** (see entries 22-26, Table 1).



3 ($R^1 \neq H$) **2** (X = O, S) **1**

Scheme 3

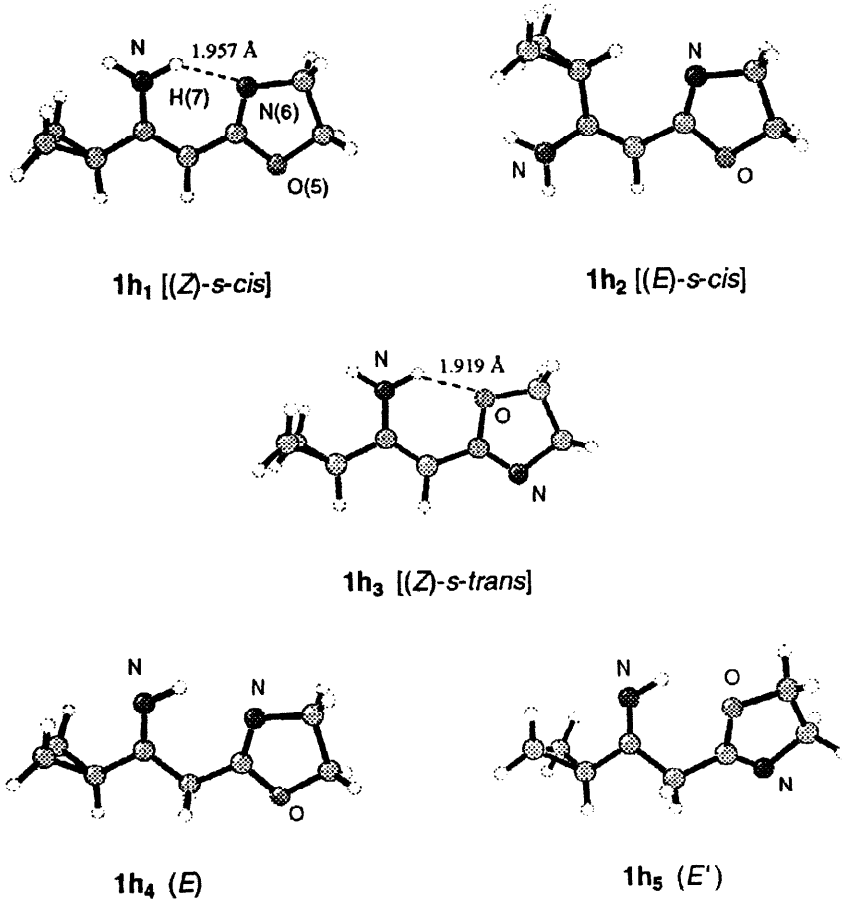
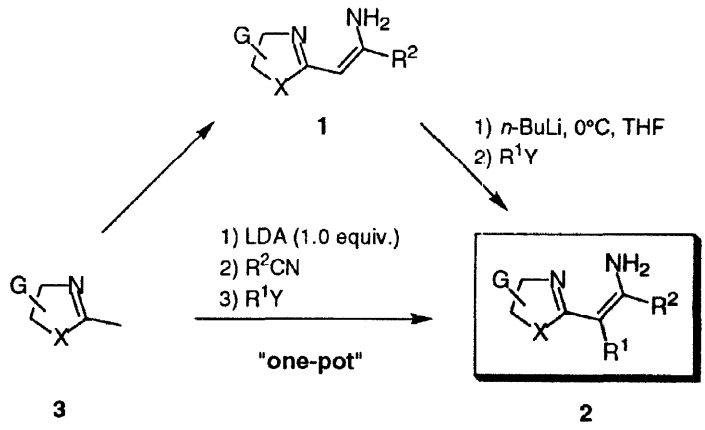


Figure 3

On the other hand, *Route d* consists of the alkylation of β-amino α, β-unsaturated oxa- and thiazolines **1** with alkyl halides and represents the first example of the reactivity of compounds **1**. Alkylation of related systems such as β-enamino esters [32] and 4-amino-1-azadienes [33] is already well documented.

Thus, treatment of compounds **1** with *n*-BuLi at 0 °C in THF generated anion **I** (Scheme 2). After approximately one hour, a solution of alkyl halide (ratio *n*-BuLi/**1**/R^1Y: 1.1/1.0/1.2) in THF was added and stirring was continued at room temperature until disappearance of the starting material was confirmed by TLC (Scheme 4). After quenching and working-up of the reaction, compounds **2** were obtained in good to moderate yields (Table 3).

In several cases some unreacted starting material was detected in less than 10%. On the other hand, the reaction was completely regioselective and no *N*-alkylated or *C*-dialkylated products were observed. Regarding the organic halide, the bulk of substituent R^1 is not a decisive factor as substituents with different sizes such as methyl, *i*-propyl, *n*-propyl and *n*-butyl (entries 2, 4, 6, 8, Table 3) or *n*-propyl, benzyl and allyl (see entries 7, 9, 11, Table 3) gave similar results. However, the halogen atom plays a major role in the reaction as higher yields were obtained when better leaving groups were employed (entries 7 *vs.* 6, 10 *vs.* 9). The reaction conditions also tolerate sulphur or selenium electrophiles (entries 12, 13).



Scheme 4

Table 3. α-Alkylated *C*-protected *N*-unsubstituted β-enaminoacids 2 from 1.

Entry	1	R^1	R^2	Y	2[a]	Yield (%)[b]	One-pot Yield (%)[b]
1	**1a**	Me	Ph	I	**2a**	76	
2	**1b**	Me	*p*-MeC_6H_4	I	**2b**	80	96
3	**1c**	Me	*p*-$MeOC_6H_4$	I	**2c**	68	
4	**1a**	*i*-Pr	Ph	Br	**2f**	70	
5	**1a**	Allyl	Ph	Br	**2g**	83	
6	**1b**	*n*-Pr	*p*-MeC_6H_4	I	**2h**	78 (81)[c]	94
7	**1b**	*n*-Pr	*p*-MeC_6H_4	Br	**2h**	75	
8	**1b**	*n*-Bu	*p*-MeC_6H_4	I	**2i**	70 (79)[c]	96
9	**1b**	Bn	*p*-MeC_6H_4	Br	**2j**	70 (75)[c]	92
10	**1b**	Bn	*p*-MeC_6H_4	Cl	**2j**	53	
11	**1b**	Allyl	*p*-MeC_6H_4	Br	**2k**	70	84
12	**1b**	PhS	*p*-MeC_6H_4	PhS	**2l**	90	
13	**1b**	PhSe	*p*-MeC_6H_4	PhSe	**2m**	65	
14	**1b**	CH_2CO_2Et	*p*-MeC_6H_4	Br	**2n**	95	
15	**1c**	Allyl	*p*-$MeOC_6H_4$	Br	**2o**	75	
16	**1f**	Me	4-Pyridyl	I	**2p**	85	
17	**1o**	Me	Ph	I	**2q**	84	
18	**1p**	*n*-Pr	*p*-MeC_6H_4	I	**2r**	83	
19	**1t**	Me	*p*-MeC_6H_4	I	**2s**	95	
20	**1w**	*n*-Pr	*p*-MeC_6H_4	I	**2t**	78	82
21	**1w**	Allyl	*p*-MeC_6H_4	Br	**2u**	70	
22	**1x**	*n*-Pr	*p*-$MeOC_6H_4$	I	**2v**	95	

[a] For compounds **2d** and **2e** see Table 1.
[b] Yields after purification.
[c] Reaction carried out with TMEDA as co-solvent.

Several variations were performed to improve the results indicated that: a) the addition of TMEDA as co-solvent resulted in slightly higher reaction yields (see entries 6, 8, 9) and b) a slight excess of alkyl halide should be used; when the reaction was carried out in an equimolecular way lower yields were obtained, while dialkylated products were observed when two or more equivalents of R^1Y were employed, also lowering the reaction yield.
Once the reaction conditions were perfectly established we decided to perform a "*one-pot*" nitrile addition-alkylation reaction in order to obtain alkylated compounds **2** directly from **3**. Thus, for example, *p*-toluonitrile was added to the oxa- or thiazoline azaenolate (base/heterocycle/nitrile ratio: 1.25/1.1/1.0) in THF at low temperature (in the range – 78 °C to – 50 °C); after 2-5 h, a slight excess of the electrophile (electrophile/heterocycle ratio: 1.5/1.0) was added and the reaction stirred at room temperature for an additional 3-5 h. Alkylated compounds **2** were isolated after hydrolysis and work-up (Scheme 4).
The results in Table 3 (entries 2, 6, 8, 9, 11, 20) indicate that the "*one-pot*" procedure is more efficient than the two steps method, avoiding time of purification and isolation of intermediates **1** and improving the overall yield.
In conclusion, 2-alkyl-Δ^2-oxazoline, 2-methyl-Δ^2-thia- and imidazoline azaenolate addition to nitriles constitutes a simple and efficient procedure to prepare *C*-protected *N*-unsubstituted β-enamino acid derivatives **1** (or **2**) in high yield and with complete regioselectivity. The stereochemistry of the obtained compounds was found to be *Z* (*E* for **2l** and **2m**) by NMR and by theoretical (*ab initio*) calculations. Compounds **1** can be easily *C*-alkylated in high yields and with complete regioselectivity. Finally an alternative "*one*-pot" method to synthesise *C*-alkylated compounds **2** from 2-methyl-Δ^2-oxa- or thiazolines has been developed, avoiding isolation and purification of intermediates **1** and producing higher yields of compounds **2**.

Experimental Section

General. THF was distilled under argon from sodium/benzophenone ketyl as drying agent. Diisopropylamine, used to generate LDA, was refluxed over KOH, distilled, and stored under argon at 4 °C. Solvents used in extractions and in chromatographic columns were distilled prior to use. All other reagents were commercially available and were used without further purification. (4*R*,5*S*)-*cis*-2,4-Dimethyl-5-phenyloxazoline (**3d**) was prepared according to methods described in the literature [31]. Compounds were visualised on analytical thin layer chromatograms (TLC) by UV light (254 nm). Silica gel (60 Å) for flash chromatography and basic aluminium oxide (70-290 mesh) were purchased from Scharlau or Merck (200-450 mesh). Mass spectral data, low-resolution mass spectroscopy (LRMS) and high-resolution mass spectroscopy (HRMS) were measured by electron impact at 70 eV in a VG AUTOSPEC spectrometer. Infrared spectra (cm^{-1}) were obtained on a FT IR spectrometer. Elemental analysis were performed at CID-CSIC (Barcelona) and Facultad de Ciencias (Universidad de Zaragoza) microanalysis service.
All reactions which required an inert atmosphere were conducted under dry argon, and the glassware was oven dried (120 °C), evacuated, and purged with argon. Temperatures are reported as bath temperatures. Melting points are reported uncorrected and were measured on a Cambridge Instruments apparatus using open capillary tubes. ^{1}H NMR spectra were recorded with a Bruker AC-250 or a Varian Gemini-300 instrument, with tetramethylsilane as the internal standard. ^{1}H NMR: splitting pattern abbreviations are: s, singlet; bs, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet. ^{13}C NMR: multiplicities were determined by DEPT, abbreviations are: q, CH_3; t, CH_2; d, CH; s, C, except for compound

1m where a C signal appears as a doublet due to C-F coupling. Compounds **1k** and **1o** have been previously described [25].

Computational Methods. Computational calculations were performed with the GAUSSIAN 94 program package [30]. Structures were optimised at HF/3-21G level of theory and energies were evaluated at HF/6-31G* level of theory. All the calculations were performed on a Silicon Graphics Indigo-Iris, Indigo or Cray XMP-Unicos supercomputer.

Preparation of β-amino α,β-unsaturated Δ^2-oxazoline, Δ^2-thiazoline and Δ^2-imidazoline derivatives 1 (or 2) by alkylation of compounds 3a-h.

General Procedure. Method A. *n*-BuLi (17.5 mmol, 2.5 M in hexane) was added dropwise to a solution of **3a-h** (15.4 mmol) in THF (25 mL) at – 78 °C under inert atmosphere. The reaction was turned yellow/orange, depending on the starting material, as the azaenolate was formed. After 45 min to 1 h at – 78 °C a solution of nitrile (14.0 mmol) in THF (10 mL) was added and the colour of the reaction rapidly changed. The reaction was monitored by TLC, and in most cases proceeded cleanly at low temperature; however, for some aliphatic nitriles, it was necessary to allow the reaction mixture to reach room temperature. In any case, after 2-4 h an aqueous saturated NH_4Cl solution was added and the mixture was extracted with CH_2Cl_2 (3 x 40 mL). The combined organic layer was washed several times with saturated brine (20 mL, each time) and dried over anhydrous Na_2SO_4. Solvents were evaporated under reduced pressure to give a solid or oily residue. Solid residues were rinsed with a hexane/ethanol mixture, filtered and recrystallized. Oily residues were purified by flash chromatography or by distillation under reduced pressure. Thus compounds **1** (or **2**) were prepared in the yields reported in Table 1.

General Procedure. Method B. LDA was generated by dropwise adding *n*-BuLi (17.5 mmol, 2.5 M in hexane) to a solution of diisopropylamine (17.5 mmol) in dry THF (10 mL) at – 20 °C and stirring for 30 min. The reaction flask was cooled to – 78 °C, a solution of compound **3a-h** (15.4 mmol) in dry THF (10 mL) was added dropwise and the reaction mixture was kept at – 78 °C for 45 min-1 h. A solution of nitrile (14.0 mmol) in dry THF (10 mL) was then added at that temperature and stirring was maintained for 2-4 h as the reaction flask was allowed to reach room temperature. Changes of colour were observed, and work-up and purification were carried out, as has been described for method A.

(Z)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-phenyl-1-ethen-1-amine (1a). White solid. Mp 56-8 °C; ^{1}H NMR (250 MHz) δ 7.52-7.36 (m, 5 H), 6.50 (bs, 2 H, NH_2), 4.94 (s, 1 H), 4.16 (t, *J* = 8.4, 2 H), 3.97 (t, *J* = 8.4, 2 H); ^{13}C NMR (62.8 MHz) δ 164.0 (s), 155.5 (s), 137.9 (s), 129.4 (d), 128.6 (d), 126.9 (d), 81.1 (d), 65.4 (t), 54.3 (t); IR (KBr) 3428, 3176, 1627, 1608. MS (*m/z*) 188 (M^+), 187 (100%). Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.21; H, 6.38; N, 14.89. Found: C, 69.97; H, 6.41; N, 14.81.

(Z)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methylphenyl)-1-ethen-1-amine (1b). White solid. Mp 85-7 °C; ^{1}H NMR (250 MHz) δ 7.45 (d, *J* = 8.5, 2 H), 7.20 (d, *J* = 8.5, 2 H), 6.8 (bs, 2 H, NH_2), 4.95 (s, 1 H), 4.22 (t, *J* = 8.8, 2 H), 4.00 (t, *J* = 8.8, 2 H), 2.37 (s, 3 H); ^{13}C NMR (62.8 MHz) δ 166.4 (s), 155.5 (s), 139.2 (s), 134.3 (s), 128.8 (d), 125.3 (d), 79.7 (d), 65.1 (t), 53.7 (t), 20.6 (q); IR (KBr) 3383, 3204, 1631, 1593. MS (*m/z*) 202 (M^+), 201 (100%). Anal. Calcd for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.93; N, 13.86. Found: C, 71.25; H, 6.96; N, 13.90.

(Z)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methoxyphenyl)-1-ethen-1-amine (1c). White solid. Mp 66-8 °C; ^{1}H NMR (250 MHz) δ 7.49 (d, *J* = 9.0, 2 H), 6.91 (d, *J* = 9.0,

2 H), 6.5 (bs, 2 H, NH_2), 4.89 (s, 1 H), 4.18 (t, J = 7.2, 2 H), 3.98 (t, J = 7.2, 2 H), 3.82 (s, 3 H); ^{13}C NMR (62.8 MHz) δ 166.7 (s), 160.5 (s), 155.2 (s), 130.1 (s), 127.1 (d), 113.8 (d), 80.2 (d), 65.3 (t), 55.1 (t), 54.1 (q); IR (KBr) 3379, 3182, 1632, 1574. MS (*m/z*) 218 (M^+), 217 (100%). Anal. Calcd for $C_{12}H_{14}N_2O_2$: C, 66.05; H, 6.42; N, 12.84. Found: C, 66.21; H, 6.31; N, 12.91.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(2-furyl)-1-ethen-1-amine (1d). White solid. Mp 105-7 °C; ^{1}H NMR (250 MHz) δ 7.45 (d, J = 1.6, 1 H), 6.68 (d, J = 3.4, 1 H), 6.46 (bs, 2 H, NH_2), 6.45 (dd, J = 3.4, 1.6, 1 H), 5.17 (s, 1 H), 4.25 (t, J = 8.8, 2 H), 4.01 (t, J = 8.8 H); ^{13}C NMR (62.8 MHz) δ 166.6 (s), 149.9 (s), 144.4 (s), 142.9 (d), 111.7 (d), 107.8 (d), 78.7 (d), 65.5 (t), 54.4 (t); MS (*m/z*) 178 (M^+, 100%). Anal. Calcd for $C_9H_{10}N_2O_2$: C, 60.67; H, 5.62; N, 15.73. Found: C, 60.72; H, 5.61; N, 15.79.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(2-pyridyl)-1-ethen-1-amine (1e). Brown solid. Mp 118-20 °C; ^{1}H NMR (250 MHz) δ 8.6 (d, 1 H), 7.74-7.66 (m, 2 H), 7.31-7.24 (m, 2 H), 7.7-7.2 (bs, 2 H, NH_2), 5.33 (s, 1 H), 4.21 (t, J = 8.4, 2 H), 4.04 (t, J = 8.4, 2 H); ^{13}C NMR (62.8 MHz) δ 166.8 (s), 151.9 (s), 151.2 (s), 148.5 (d), 136.4 (d), 123.8 (d), 119.6 (d), 79.5 (d), 65.6 (t), 54.5 (t); IR (KBr) 3374, 3269, 1628, 1589. MS (*m/z*) 189 (M^+), 188 (100%). Anal. Calcd for $C_{10}H_{11}N_3O$: C, 63.49; H, 5.82; N, 22.22. Found: C, 63.39; H, 5.89; N, 22.17.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-pyridyl)-1-ethen-1-amine (1f). Brown solid. Mp 112-5 °C; ^{1}H NMR (250 MHz) δ 8.66 (d, J = 6.0, 2 H), 7.43 (d, J = 6.0, 2 H), 6.5 (bs, 2 H, NH_2), 5.06 (s, 1 H), 4.20 (t, J = 8.4, 2 H), 4.03 (t, J = 8.4, 2 H); ^{13}C NMR (62.8 MHz) δ 166.5 (s), 152.6 (s), 150.6 (s), 145.5 (d), 120.5 (d), 83.6 (d), 66.0 (t), 54.6 (t); IR (KBr) 3380, 3245, 1625, 1617. HRMS calcd for $C_{10}H_{11}N_3O$ 189.0902, found 189.0896.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(2-thienyl)-1-ethen-1-amine (1g). Yelow solid. Mp 88-91 °C; ^{1}H NMR (250 MHz) δ 7.19 (m, 2 H), 6.96 (m, 1 H), 6.50 (bs, 2 H, NH_2), 4.98 (s, 1 H), 4.08 (t, J = 8.3, 2 H), 3.87 (t, J = 8.3, 2 H); ^{13}C NMR (62.8 MHz) δ 166.6 (s), 148.7 (s), 141.0 (s), 127.8 (s), 126.5 (d), 125.0 (d), 81.8 (d), 65.8 (t), 54.7 (t); IR (KBr) 3397, 3282, 1628, 1576. HRMS calcd for $C_9H_{10}N_2OS$ 194.0513, found 193.9971. Anal. Calcd for $C_9H_{10}N_2OS$: C, 55.67; H, 5.15; N, 14.43. Found: C, 55.57; H, 5.12; N, 14.49.

(*Z*)-1-Cyclopropyl-2-(4,5-dihydro-1,3-oxazol-2-yl)-1-ethen-1-amine (1h). White solid. Mp 72-4 °C; ^{1}H NMR (250 MHz) δ 6.20 (bs, 2 H, NH_2), 4.45 (s, 1 H), 4.11 (t, J = 8.6, 2 H), 3.87 (t, J = 8.6, 2 H), 1.45 (m, 1 H), 0.80 (m, 2 H), 0.68 (m, 2 H); ^{13}C NMR (62.8 MHz) δ 166.6 (s), 159.2 (s), 77.4 (d), 65.1 (d), 54.0 (t), 15.4 (t), 6.3 (t); IR (KBr) 3447, 3352, 1629, 1565. MS (*m/z*) 152 (M^+), 151 (100%). HRMS calcd for $C_8H_{12}N_2O$ 152.0949, found 152.0955. Anal. Calcd for $C_8H_{12}N_2O$: C, 63.15; H, 7.89; N, 18.42. Found: C, 63.27; H, 7.64; N, 18.51.

(*Z*)-1-Cyclohexyl-2-(4,5-dihydro-1,3-oxazol-2-yl)-1-ethen-1-amine (1i). Pale yelow oil, purified by flash chromatography on basic Al_2O_3 (hexane/AcOEt: 3/1); ^{1}H NMR (250 MHz) δ 4.54 (s, 1 H), 4.01 (t, J = 8.3, 2 H), 3.90 (t, J = 8.3, 2 H), 2.12-1.61 (m, 6 H), 1.43-1.10 (m, 5 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 167.0 (s), 163.1 (s), 77.5 (d), 65.1 (t), 54.1 (t), 44.7 (d), 32.9 (t), 31.6 (t), 25.7 (t); MS (*m/z*) 194 (M^+), 111 (100%). Anal. Calcd for $C_{11}H_{18}N_2O$: C, 68.04; H, 9.28; N, 14.43. Found: C, 67.83; H, 9.04; N, 14.21.

(*Z*)-1-(4,5-Dihydro-1,3-oxazol-2-yl)-3-methyl-1-buten-2-amine (1j). Pale yelow oil. Bp 150-2 °C (10^{-2} Torr.); ^{1}H NMR (250 MHz) δ 4.47 (s, 1 H), 4.10 (t, J = 7.8, 2 H), 3.86 (t, J = 7.8, 2 H), 2.34 (m, 1 H), 1.13 (d, J = 6.6, 6 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 166.9 (s), 163.8 (s), 77.1 (d), 65.1

(t), 54.2 (t), 34.3 (d), 21.1 (q); IR (neat) 3432, 3325, 1621, 1578. MS (*m/z*) 154 (M^+), 111 (100%). Anal. Calcd for $C_8H_{14}N_2O$: C, 62.34; H, 9.09; N, 18.18. Found: C, 62.06; H, 8.86; N, 17.94.

(Z)-1-(4,5-Dihydro-1,3-oxazol-2-yl)-3-methoxy-1-propen-2-amine (1l). Pale yelow oil. Bp 76-9 °C (10^{-3} Torr.); ^{1}H NMR (250 MHz) δ 6.20 (bs, 2 H, NH_2), 4.56 (s, 1 H), 4.21 (s, 2 H), 4.05 (t, *J* = 8.8, 2 H), 3.92 (t, *J* = 8.8, 2 H), 3.30 (3 H, s); ^{13}C NMR (62.8 MHz) δ 166.0 (s), 153.3 (s), 79.3 (d), 72.5 (t), 65.3 (t), 57.7 (t), 54.1 (q); MS (*m/z*) 156 (M^+), 111 (100%). Anal. Calcd for $C_7H_{12}N_2O_2$: C, 53.84; H, 7.69; N, 17.94. Found: C, 53.68; H, 7.60; N, 17.98.

(Z)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-fluorophenyl)-1-ethen-1-amine (1m). Yelow solid. Mp 79-81 °C; ^{1}H NMR (300 MHz) δ 7.53 (m, 2 H), 7.06 (m, 2 H), 6.53 (bs, 2 H, NH_2), 4.86 (s, 1 H), 4.22 (t, *J* = 7.7, 2 H), 3.96 (t, *J* = 7.7, 2 H); ^{13}C NMR (62.8 MHz) δ 165.0 (s), 161.7 (s), 160.5 (d, $J_{C\text{-}F}$ = 452.0 Hz), 134.0 (s), 127.7 (d), 115.6 (d), 81.4 (d), 65.4 (t), 54.2 (t); IR (KBr) 3391, 3265, 1621, 1601. MS (*m/z*) 206 (M^+), 205 (100%). Anal. Calcd for $C_{11}H_{11}FN_2O$: C, 64.07; H, 5.34; N, 13.50. Found: C, 64.11; H, 5.39; N, 13.65.

(Z)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(2-thiamethylphenyl)-1-ethen-1-amine (1n). Yelow solid. Mp 59-60 °C; ^{1}H NMR (250 MHz) δ 7.34-7.15 (m, 4 H), 4.70 (s, 1 H), 4.22 (t, *J* = 8.3, 2 H), 4.02 (t, *J* = 8.3, 2 H), 2.44 (s, 3 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 166.7 (s), 154.9 (s), 137.5 (s), 137.0 (s), 129.5 (d), 129.0 (d), 125.9 (d), 125.0 (d), 83.8 (d), 65.7 (t), 54.6 (t), 16.2 (q); IR (KBr) 3357, 3264, 1619, 1570. HRMS calcd for $C_{12}H_{14}N_2OS$ 234.0827, found 234.0827.

(Z)-2-(4,5-Dihydro-4,4-dimethyl-1,3-oxazol-2-yl)-1-(4-methylphenyl)-1-ethen-1-amine (1p). White solid. Mp 58-60 °C; ^{1}H NMR (250 MHz) δ 7.40 (d, *J* = 8.5, 2 H), 7.15 (d, *J* = 8.5, 2 H), (6.50 (bs, 2 H, NH_2), 4.78 (s, 1 H), 3.79 (s, 2 H), 2.29 (s, 3 H), 1.25 (s, 6 H); ^{13}C NMR (62.8 MHz) δ 164.9 (s), 155.3 (s), 139.4 (s), 135.1 (s), 129.2 (d), 125.7 (d), 80.8 (d), 77.1 (t), 66.7 (s), 28.8 (q), 21.1 (q); IR (KBr) 3397, 3206, 1628, 1573. HRMS calcd for $C_{14}H_{18}N_2O$ 230.1419, found 230.1410.

(Z)-2-(4,5-Dihydro-4,4-dimethyl-1,3-oxazol-2-yl)-1-(4-methoxyphenyl)-1-ethen-1-amine (1q). White solid. Mp 65-7 °C; ^{1}H NMR (250 MHz) δ 7.46 (d, *J* = 9.0, 2 H), 6.78 (d, *J* = 9.0, 2 H), 6.50 (bs, 2 H, NH_2), 4.74 (s, 1 H), 3.77 (s, 2 H), 3.71 (s, 3 H), 1.23 (s, 6 H); ^{13}C NMR (62.8 MHz) δ 164.1 (s), 160.3 (s), 154.8 (s), 133.7 (s), 130.2 (d), 127.0 (d), 113.7 (d), 80.3 (d), 76.9 (t), 66.5 (s), 55.0 (q), 28.7 (q); IR (KBr) 3392, 3283, 1632, 1604. HRMS calcd for $C_{14}H_{18}N_2O_2$ 246.1368, found 246.1365.

(Z)-2-(4,5-Dihydro-4,4-dimethyl-1,3-oxazol-2-yl)-1-(2-furyl)-1-ethen-1-amine (1r). White solid. Mp 49-51 °C; ^{1}H NMR (250 MHz) δ 7.40 (d, *J* = 1.8, 1 H), 6.64 (d, *J* = 3.3, 1 H), 6.50 (bs, 2 H, NH_2), 6.43 (dd, *J* = 3.3, 1.8 1 H), 5.06 (s, 1 H), 3.85 (s, 2 H), 1.30 (s, 6 H); ^{13}C NMR (62.8 MHz) δ 164.0 (s), 160.3 (s), 150.2 (s), 144.2 (s), 142.9 (d), 111.7 (d), 107.6 (d), 79.1 (d), 77.2 (t), 66.4 (s), 28.9 (q); IR (KBr) 3388, 3227, 1639, 1595. HRMS calcd for $C_{11}H_{14}N_2O_2$ 206.1055, found 206.1058.

(Z)-2-(4,5-Dihydro-4,4-dimethyl-1,3-oxazol-2-yl)-1-(1-naphtyl)-1-ethen-1-amine (1s). Yelow oil, purified by flash chromatography on basic Al_2O_3 (hexane/AcOEt: 3/1); ^{1}H NMR (250 MHz) δ 8.25 (m, 1 H), 7.71 (m, 1 H), 7.45-7.35 (m, 7 H, 5 H_{arom} + NH_2), 4.65 (s, 1 H), 3.78 (s, 2 H), 1.27 (s, 6 H); ^{13}C NMR (62.8 MHz) δ 164.7 (s), 155.6 (s), 137.4 (s), 134.2 (s), 131.2 (s), 128.8 (d), 127.0 (d), 126.7 (d), 126.3 (d), 125.8 (d), 84.7 (d), 77.4 (t), 67.6 (s), 26.7 (q). Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.69; H, 6.77; N, 10.52. Found: C, 76.37; H, 6.44; N, 10.29.

(*Z*)-2-[(4*S*,5*S*)-4,5-Dihydro-4-methoxymethyl-5-phenyl-1,3-oxazol-2-yl)]-1-(4-methylphenyl)-1-ethen-1-amine (1t). Pale yelow oil, purified by flash chromatography on basic Al_2O_3 (hexane/AcOEt: 3/1); ^{1}H NMR (250 MHz) δ 7.50-7.10 (m, 9 H), 5.18 (d, *J* = 7.5, 1 H), 4.93 (s, 1 H), 4.20 (m, 1 H), 3.59 (dd, *J* = 9.2, 4.4, 1 H), 3.43 (dd, *J* = 9.2, 7.3, 1 H), 3.39 (s, 3 H), 2.33 (s, 3 H), the signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 166.3 (s), 156.1 (s), 141.4 (s), 139.4 (s), 134.7 (s), 129.1 (d), 128.3 (d), 127.5 (d), 125.7 (d), 125.6 (d), 125.3 (d), 81.4 (d), 80.0 (d), 75.2 (t), 74.2 (d), 58.8 (q), 20.9 (q); IR (neat) 3463, 3268, 1626, 1601; $[\alpha]^{25}_D$ + 57.1 (*c* 1.5, $CHCl_3$); MS (*m/z*) 322 (M^+), 277 (100%). Anal. Calcd for $C_{20}H_{22}N_2O_2$: C, 74.53; H, 6.83; N, 8.69. Found: C, 74.37; H, 6.62; N, 8.50.

(*Z*)-2-[(4*R*,5*S*)-4,5-Dihydro-4-methyl-5-phenyl-1,3-oxazol-2-yl)]-1-(4-pyridyl)-1-ethen-1-amine (1u). Clear brown oil, purified by flash chromatography on basic Al_2O_3 (hexane/ AcOEt: 3/1); ^{1}H NMR (250 MHz) δ 8.69-8.66 (m, 2 H), 7.49-7.47 (m, 2 H), 7.40-7.25 (m, 5 H), 6.72 (bs, 2 H, NH_2), 5.57 (d, *J* = 9.5, 1 H), 5.17 (s, 1 H), 4.61 (m, 1 H), 0.85 (d, *J* = 6.8, 3 H); ^{13}C NMR (62.8 MHz) δ 165.2 (s), 152.8 (s), 150.5 (d), 145.4 (s), 137.4 (s), 128.3 (d), 127.8 (d), 126.3 (d), 120.5 (d), 83.2 (d), 82.3 (d), 65.1 (d), 18.5 (q); $[\alpha]^{25}_D$ + 62.88 (*c* 0.66, $CHCl_3$); IR (neat) 3467, 3367, 1638, 1545. HRMS calcd for $C_{17}H_{17}N_3O$ 279.1371, found 279.1360. Anal. Calcd for $C_{17}H_{17}N_3O$: C, 73.11; H, 6.09; N, 15.05. Found: C, 73.07; H, 6.13; N, 15.10.

(*Z*)-2-(4,5-Dihydro-1,3-thiazol-2-yl)-1-phenyl-1-ethen-1-amine (1v). Yelow solid. Mp 26-8 °C; ^{1}H NMR (250 MHz) δ 7.43 (m, 2 H), 7.29 (m, 3 H), 6.80 (bs, 2 H, NH_2), 5.06 (s, 1 H), 4.25 (t, *J* = 8.5, 2 H), 3.12 (t, *J* = 8.5, 2 H); ^{13}C NMR (62.8 MHz) δ 167.1 (s), 153.7 (s), 138.0 (s), 129.0 (d), 126.3 (d), 125.9 (d), 89.0 (d), 64.5 (t), 32.8 (t); IR (KBr) 3417, 3206, 1618, 1583. MS (*m/z*) 204 (M^+, 100%). Anal. Calcd for $C_{11}H_{12}N_2S$: C, 64.70; H, 5.88; N, 13.72. Found: C, 64.81; H, 5.79; N, 13.78.

(*Z*)-2-(4,5-Dihydro-1,3-thiazol-2-yl)-1-(4-methylphenyl)-1-ethen-1-amine (1w). Yelow solid. Mp 70-2 °C; ^{1}H NMR (250 MHz) δ 7.41 (d, *J* = 9.0, 2 H), 7.16 (d, *J* = 9.0, 2 H), 6.85 (bs, 2 H, NH_2), 5.13 (s, 1 H), 4.33 (t, *J* = 8.5, 2 H), 3.20 (t, *J* = 8.5, 2 H), 2.36 (s, 3 H); ^{13}C NMR (62.8 MHz) δ 167.3 (s), 153.8 (s), 139.9 (s), 135.2 (s), 129.6 (d), 126.2 (d), 88.5 (d), 64.7 (t), 33.0 (t), 21.5 (q); IR (KBr) 3458, 3159, 1609, 1544. MS (*m/z*) 218 (M^+), 217 (100%); Anal. Calcd for $C_{12}H_{14}N_2S$: C, 66.05; H, 6.42; N, 12.84. Found: C, 66.11; H, 6.35; N, 12.78.

(*Z*)-2-(4,5-Dihydro-1,3-thiazol-2-yl)-1-(4-methoxyphenyl)-1-ethen-1-amine (1x). Yelow solid. Mp 42-5 °C; ^{1}H NMR (250 MHz) δ 7.45 (d, *J* = 9.0, 2 H), 6.87 (d, *J* = 9.0, 2 H), 6.73 (bs, 2 H, NH_2), 5.10 (s, 1 H), 4.32 (t, *J* = 8.4, 2 H), 3.80 (s, 3 H), 3.20 (t, *J* = 8.4, 2 H); ^{13}C NMR (62.8 MHz) δ 166.9 (s), 160.6 (s), 153.3 (s), 130.1 (s), 127.3 (d), 113.9 (d), 87.8 (d), 64.3 (t), 55.2 (q), 32.7 (t); MS (*m/z*) 234 (M^+), 233 (100%); Anal. Calcd for $C_{12}H_{14}N_2OS$: C, 61.53; H, 5.98; N, 11.96. Found: C, 61.37; H, 5.89; N, 11.92.

(*Z*)-2-(4,5-Dihydro-1,3-thiazol-2-yl)-1-(2-furyl)-1-ethen-1-amine (1y). Yelow solid. Mp 37-9 °C; ^{1}H NMR (250 MHz) δ 7.44 (d, *J* = 1.5, 1 H), 6.70 (bs, 2 H, NH_2), 6.64 (d, *J* = 3.2, 1 H), 6.43 (dd, *J* = 3.2, 1.5 1 H), 5.34 (s, 1 H), 4.32 (t, *J* = 7.5, 2 H), 3.20 (t, *J* = 7.5, 2 H); ^{13}C NMR (62.8 MHz) δ 167.0 (s), 150.2 (s), 143.4 (d), 143.0 (s), 112.1 (d), 108.3 (d), 86.5 (d), 64.9 (t), 35.6 (t); IR (KBr) 3369, 3274, 1626, 1590. MS (*m/z*) 218 (M^+), 217 (100%); HRMS calcd for $C_9H_{10}N_2OS$ 194.0513, found 194.0508.

(*Z*)-1-Cyclopropyl-2-(4,5-dihydro-1,3-thiazol-2-yl)-1-ethen-1-amine (1z). White solid. Mp 50-2 °C; ^{1}H NMR (250 MHz) δ 6.52 (bs, 2 H, NH_2), 4.69 (s, 1 H), 4.25 (t, *J* = 8.2, 2 H), 3.18 (t, *J* = 8.2, 2 H), 1.45 (m, 1 H), 0.82 (m, 2 H), 0.71 (m, 2 H); ^{13}C NMR (62.8

MHz) δ 166.6 (s), 157.3 (s), 85.5 (d), 64.3 (t), 32.6 (t), 15.4 (t), 6.50 (t); IR (KBr) 3446, 3248, 1600, 1546. HRMS calcd for $C_8H_{12}N_2S$ 168.0721, found 168.0718.

(*Z*)-2-(1-Benzyl-4,5-dihydro-1*H*-2-imidazolyl)-1-(4-methylphenyl)-1-ethen-1-amine (1ρ). Yelow solid. Mp 66-9 °C; ^{1}H NMR (250 MHz) δ 7.44-7.16 (m, 9 H), 4.95 (s, 1 H), 4.37 (s, 2 H), 3.85 (t, *J* = 9.1, 2 H), 3.20 (t, *J* = 9.1, 2 H), 2.35 (s, 3 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 166.0 (s), 155.1 (s), 139.1 (s), 138.3 (s), 136.1 (s), 129.1 (d), 128.3 (d), 127.3 (d), 126.9 (d), 125.8 (d), 80.6 (d), 51.9 (t), 50.9 (t), 49.5 (t), 21.1 (q); IR (KBr) 3457, 3378, 1618, 1548. Anal. Calcd for $C_{19}H_{21}N_3$: C, 78.35; H, 7.21; N, 14.43. Found: C, 78.27; H, 7.12; N, 14.37.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-phenyl-1-propen-1-amine (2a). White solid. Mp 74-6 °C; ^{1}H NMR (250 MHz) δ 7.27 (m, 5 H), 6.50 (bs, 2 H, NH_2), 4.11 (t, *J* = 8.8, 2 H), 3.93 (t, *J* = 8.8, 2 H), 1.61 (s, 3 H); ^{13}C NMR (62.8 MHz) δ 168.6 (s), 152.8 (s), 139.0 (s), 128.34 (d), 128.28 (d), 128.17 (d), 87.7 (s), 65.5 (t), 54.5 (t), 14.3 (q); IR (KBr) 3439, 3252, 1626, 1596. HRMS calcd for $C_{12}H_{14}N_2O$ 202.1106, found 202.1104. Anal. Calcd for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.93; N, 13.86. Found: C, 71.18; H, 6.81; N, 14.01.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methylphenyl)-1-propen-1-amine (2b). White solid. Mp 125-7 °C; ^{1}H NMR (250 MHz) δ 7.27 (m, 4 H), 6.53 (bs, 2 H, NH_2), 4.11 (t, *J* = 8.8, 2 H), 3.93 (t, *J* = 8.8, 2 H), 2.10 (s, 3 H), 1.61 (s, 3 H); ^{13}C NMR (62.8 MHz) δ 168.5 (s), 152.8 (s), 138.1 (s), 136.0 (s), 128.8 (d), 127.9 (d), 87.3 (s), 65.4 (t), 53.4 (t), 21.1 (q), 14.3 (q); IR (KBr) 3343, 3278, 1625, 1583. MS (*m/z*) 216 (M^+), 215 (100%). Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.22; H, 7.41; N, 12.96. Found: C, 72.23; H, 7.44; N, 12.98.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methoxyphenyl)-1-propen-1-amine (2c). White solid. Mp 81-4 °C; ^{1}H NMR (250 MHz) δ 7.22 (d, *J* = 8.8, 2 H), 6.82 (d, *J* = 8.8, 2 H), 6.30 (bs, 2 H, NH_2), 4.12 (t, *J* = 7.7, 2 H), 3.96 (t, *J* = 7.7, 2 H), 3.70 (s, 3 H), 1.64 (s, 3 H); ^{13}C NMR (62.8 MHz) δ 168.0 (s), 159.5 (s), 152.6 (s), 132.0 (s), 129.4 (d), 113.5 (d), 86.0 (s), 65.4 (t), 55.1 (t), 54.4 (q), 14.4 (q); IR (KBr) 3451, 3281, 1631, 1591. HRMS calcd for $C_{13}H_{16}N_2O_2$ 232.1211, found 232.1217.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(2-furyl)-1-propen-1-amine (2d). Yelow solid. Mp 57-9 °C; ^{1}H NMR (250 MHz) δ 7.50 (d, *J* = 1.5, 1 H), 6.70 (bs, 2 H, NH_2), 6.59 (d, *J* = 3.1, 1 H), 6.48 (dd, *J* = 3.1, 1.5, 1 H), 4.19 (t, *J* = 7.8, 2 H), 4.05 (t, *J* = 7.8, 2 H), 1.98 (s, 3 H); ^{13}C NMR (62.8 MHz) δ 168.8 (s), 150.0 (s), 141.7 (d), 141.1 (s), 111.7 (d), 111.5 (d), 88.2 (s), 65.5 (t), 54.7 (t), 14.4 (q); IR (KBr) 3355 (br), 1676, 1565. HRMS calcd for $C_{10}H_{12}N_2O_2$ 192.0898, found 192.0898. Anal. Calcd for $C_{10}H_{12}N_2O_2$: C, 62.50; H, 6.25; N, 14.58. Found: C, 62.48; H, 6.32; N, 14.62.

(*Z*)-2-(4,5-Dihydro-4,4-dimethyl-1,3-oxazol-2-yl)-3-phenyl-1-(4-pyridyl)-1-propen-1-amine (2e). Yelow solid. Mp 160-3 °C; ^{1}H NMR (250 MHz) δ 8.56 (m, 2 H), 7.22-7.00 (m, 7 H), 3.80 (s, 2 H), 3.44 (s, 2 H), 1.33 (s, 6 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 165.5 (s), 151.4 (s), 150.2 (d), 146.4 (s), 142.8 (s), 128.3 (d), 127.7 (d), 125.6 (d), 122.9 (d), 92.0 (s), 77.3 (t), 67.2 (s), 33.7 (t), 29.1 (q); IR (KBr) 3410, 3270, 1634, 1601. HRMS calcd for $C_{19}H_{21}N_3O$ 307.1684, found 307.1686. Anal. Calcd for $C_{19}H_{21}N_3O$: C, 74.26; H, 6.84; N, 13.68. Found: C, 74.31; H, 6.79; N, 13.60.

α-Alkylation of β-amino α,β-unsaturated Δ^2-oxazoline and Δ^2-thiazoline derivatives 1. General Procedure. *n*-BuLi (2.92 mmol, 2.5 M in hexane) was added dropwise to a solution of the corresponding oxa or thiazoline derivative **1** (2.65 mmol) in

THF (10 mL) at 0 °C under inert atmosphere. After stirring the reaction for 15 min. at room temperature, a solution of TMEDA (3.90 mmol) in THF (10 mL) was added and stirring was maintained for 1-1.5 h (Table 3, entries 6, 8 and 9). The reaction mixture was cooled down to 0 °C and a solution of the corresponding alkyl halide (3.18 mmol) in THF (10 mL) was added and allowed to react for 10-14 h at room temperature. After quenching with aqueous saturated NH_4Cl solution, the reaction mixture was extracted with CH_2Cl_2 (3 x 40 mL). The combined organic layer was washed several times with saturated brine (20 mL, each time) and dried over anhydrous Na_2SO_4. Solvents were evaporated under reduced pressure to give a solid or oily residue. Solid residues were rinsed with a hexane/ethanol mixture, filtered and recrystallized. Oily residues were purified by flash chromatography or by distillation under reduced pressure. Thus compounds **2** were prepared in the yields reported in Table 3. Compounds **2a-e** have already been synthesised from heterocycles **3**.

Synthesis of compounds 2 by *"one-pot"* nitrile addition-alkylation from heterocycles 3a or 3g. General Procedure. LDA was prepared by adding *n*-BuLi (17.5 mmol, 2.5 M in hexane) dropwise to a solution of diisopropylamine (17.5 mmol) in dry THF (10 mL) at – 20 °C and stirring for 30 min. After cooling the reaction flask to – 78 °C, a solution of compound **3a** or **3g** (15.4 mmol) in dry THF (10 mL) was introduced dropwise via an addition funnel and the reaction mixture was kept at – 78 °C for 45 min-1 h. A solution of nitrile (14.0 mmol) in dry THF (10 mL) was then added and stirring was maintained for 2 h at that temperature. The corresponding alkyl halide (23.1 mmol) was dissolved in THF (10 mL) and added and stirring was continued for 3 h at room temperature or until TLC evidenced consumption of intermediate **I** (R^1 = H) (Scheme 2). Work-up and purification as described before (*vide supra*) yielded compounds **2** as reported in Table 3.

(Z)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-3-methyl-1-phenyl-1-buten-1-amine (2f). Pale yelow oil, purified by flash chromatography on basic Al_2O_3 (hexane/AcOEt: 3/1); ^1H NMR (250 MHz) δ 7.28-7.24 (m, 5 H), 6.50 (bs, 2 H, NH_2), 4.17 (t, *J* = 9.0, 2 H), 3.83 (t, *J* = 9.0, 2 H), 2.31 (m, 1 H), 0.99 (d, *J* = 7.0, 6 H); ^{13}C NMR (62.8 MHz) δ 169.5 (s), 153.4 (s), 140.3 (s), 128.8 (d), 128.7 (d), 128.3 (d), 99.1 (s), 65.8 (t), 54.0 (t), 29.7 (d), 22.7 (q); IR (neat) 3443, 3356, 1613, 1537. HRMS calcd for $C_{14}H_{18}N_2O$ 230.1419, found 230.1416.

(Z)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-phenyl-1,4-pentadien-1-amine (2g). White solid. Mp 89-91 °C; ^1H NMR (250 MHz) δ 7.29 (s, 5 H), 5.90-5.70 (m, 1 H), 4.83 (m, 2 H), 4.10 (t, *J* = 8.8, 2 H), 3.98 (t, *J* = 8.8, 2 H), 2.71 (d, *J* = 5.7, 2 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 168.9 (s), 155.0 (s), 139.8 (d), 139.3 (s), 129.1 (d), 128.9 (d), 128.5 (d), 114.1 (t), 90.8 (s), 66.2 (t), 55.1 (t), 33.14 (t); IR (KBr) 3447, 3154, 1621, 1596. MS (*m/z*) 227 (M^+–1, 100%). Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.68; H, 7.01; N, 12.28. Found: C, 73.85; H, 7.10; N, 12.30.

(Z)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methylphenyl)-1-penten-1-amine (2h). White solid. Mp 108-111 °C; ^1H NMR (250 MHz) δ 7.30-7.10 (m, 4 H), 4.21 (t, *J* = 8.5, 2 H), 4.03 (t, *J* = 8.5, 2 H), 2.39 (s, 3 H), 2.07 (t, 2 H), 1.35 (m, 2 H), 0.72 (t, 3 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 168.7 (s), 153.6 (s), 138.1 (s), 136.2 (s), 128.9 (d), 127.9 (d), 93.3 (s), 65.4 (t), 54.3 (t), 30.6 (t), 24.5 (t), 21.2 (q), 13.9 (q); IR (KBr) 3355, 3246, 1622, 1554. HRMS calcd for $C_{15}H_{20}N_2O$ 244.1575, found 244.1579.

(Z)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methylphenyl)-1-hexen-1-amine (2i). Pale yelow oil, purified by flash chromatography on basic Al_2O_3 (hexane/AcOEt: 3/1); ^1H NMR (250 MHz) δ 7.30-6.60 (m, 4 H), 6.50 (bs, 2 H, NH_2), 4.16 (t, *J* = 8.3, 2 H), 4.04 (t, *J* =

8.3, 2 H), 2.37 (s, 3 H), 2.03 (t, 2 H), 1.28 (m, 2 H), 1.12 (m, 2 H), 0.73 (t, 3 H); ^{13}C NMR (62.8 MHz) δ 168.8 (s), 153.6 (s), 138.2 (s), 136.3 (s), 129.0 (d), 128.0 (d), 93.5 (s), 65.6 (t), 54.5 (t), 33.7 (t), 28.3 (t), 22.6 (q), 21.4 (t), 14.0 (q); IR (neat) 3298 (br), 1647, 1610. HRMS calcd for $C_{16}H_{22}N_2O$ 258.1732, found 258.1732.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methylphenyl)-3-phenyl-1-propen-1-amine (2j). White solid. Mp 59-62 °C; ^{1}H NMR (250 MHz) δ 7.40-6.90 (m, 9 H), 4.20-3.90 (m, 6 H), 3.50 (s, 2 H), 2.39 (s, 3 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 168.5 (s), 154.9 (s), 143.3 (s), 138.5 (s), 135.7 (s), 129.0 (d), 127.9 (d), 127.75 (d), 127.73 (d), 125.1(d), 90.8 (s), 65.6 (t), 54.4 (t), 34.0 (t), 21.2 (q); IR (KBr) 3470, 3397, 1619, 1582. HRMS calcd for $C_{19}H_{20}N_2O$ 292.1575, found 292.1576.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methylphenyl)-1,4-pentadien-1-amine (2k). White solid. Mp 102-5 °C; ^{1}H NMR (250 MHz) δ 7.27 (d, J = 7.8, 2 H), 7.18 (d, J = 7.8, 2 H), 6.60 (bs, 2 H, NH_2), 5.88-5.80 (m, 1 H), 4.95-4.85 (m, 2 H), 4.20 (t, J = 8.5, 2 H), 4.05 (t, J = 8.5, 2 H), 2.82 (d, J = 5,7, 2 H), 2.37 (s, 3 H); ^{13}C NMR (62.8 MHz) δ 168.3 (s), 154.5 (s), 139.3 (s), 138.3 (s), 135.7 (d), 128.8 (d), 127.7 (d), 113.4 (t), 90.1 (s), 65.5 (t), 54.3 (t), 32.5 (t), 21.2 (q); IR (KBr) 3354, 3298, 3075, 1684, 1642, 1608. HRMS calcd for $C_{15}H_{18}N_2O$ 242.1419, found 242.1392. Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.38; H, 7.44; N, 11.57. Found: C, 74.17; H, 7.31; N, 11.32.

(*E*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methylphenyl)-2-phenylsulfanyl-1-ethen-1-amine (2l). White solid. Mp 146-8 °C; ^{1}H NMR (250 MHz) δ 7.30-7.00 (m, 9 H), 5.20 (bs, 2 H, NH_2), 4.20 (t, J = 7.5, 2 H), 4.09 (t, J = 7.5, 2 H), 2.32 (s, 3 H); ^{13}C NMR (62.8 MHz) δ 169.0 (s), 165.6 (s), 142.3 (s), 140.0 (s), 135.9 (s), 129.4 (d), 129.2 (d), 128.0 (d), 125.2 (d), 124.7 (d), 81.3 (s), 66.9 (t), 55.6 (t), 22.0 (q); IR (KBr) 3476, 3414, 1594, 1493. HRMS calcd for $C_{18}H_{18}N_2OS$ 310.1139, found 310.1131. Anal. Calcd for $C_{18}H_{18}N_2OS$: C, 69.67; H, 5.80; N, 9.03. Found: C, 69.55; H, 5.81; N, 9.10.

(*E*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methylphenyl)-2-phenylselanyl-1-ethen-1-amine (2m). White solid. Mp 110-2 °C; ^{1}H NMR (250 MHz) δ 7.30-7.08 (m, 9 H), 4.30-4.08 (m, 4 H), 2.33 (s, 3 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 168.4 (s), 164.6 (s), 139.0 (s), 136.6 (s), 136.3 (s), 134.8 (s), 128.9 (d), 128.6 (d), 128.5 (d), 127.43 (d), 127.38 (d), 124.8 (d), 66.1 (t), 55.1 (t), 21.2 (q); IR (KBr) 3448, 2869, 1596, 1576. HRMS calcd for $C_{18}H_{18}N_2OSe$ 356.9808, found 356.9699.

Ethyl (*Z*)-4-amino-3-(4,5-Dihydro-1,3-oxazol-2-yl)-4-(4-methylphenyl)-3-butenoate (2n). White solid. Mp 50-3 °C; ^{1}H NMR (250 MHz) δ 7.27 (d, J = 8.6, 2 H), 7.16 (d, J = 8.6, 2 H), 4.20-3.99 (m, 6 H), 3.06 (s, 3 H), 2.35 (s, 3 H), 1.20 (t, 3 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 174.2 (s), 168.2 (s), 156.3 (s), 139.4 (s), 135.8 (s), 129.8 (d), 128.4 (d), 86.9 (s), 66.4 (t), 60.9 (t), 55.2 (t), 35.4 (t), 22.0 (q), 14.9 (q); IR (KBr) 3402, 3228, 1732, 1626. HRMS calcd for $C_{16}H_{20}N_2O_3$ 288.1473, found 288.1484. Anal. Calcd for $C_{16}H_{20}N_2O_3$: C, 66.66; H, 6.94; N, 9.72. Found: C, 66.27; H, 6.78; N, 9.75.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methoxyphenyl)-1,4-pentadien-1-amine (2o). White solid. Mp 81-3 °C; ^{1}H NMR (250 MHz) δ 7.27 (d, J = 8.8, 2 H), 6.85 (d, J = 8.8, 2 H), 5.90-5.80 (m, 1 H), 4.95-4.84 (m, 2 H), 4.19 (t, J = 8.5, 2 H), 4.16 (t, J = 8.5, 2 H), 3.97 (s, 3 H), 2.80 (d, J = 5.7, 2 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 167.8 (s), 159.1 (s), 153.7 (s), 138.8 (d),

130.5 (s), 128.5 (d), 112.8 (d), 112.9 (t), 89.4 (s), 65.0 (t), 54.7 (t), 53.8 (q), 32.0 (t); IR (KBr) 3451, 3379, 1618, 1547. HRMS calcd for $C_{15}H_{18}N_2O_2$ 258.1368, found 258.1359.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-pyridyl)-1-propen-1-amine (2p). Brown solid. Mp 113-4 °C; ^{1}H NMR (250 MHz) δ 8.64 (d, *J* = 4.4, 2 H), 7.28 (d, *J* = 4.4, 2 H), 6.50 (bs, 2 H, NH_2), 4.22 (t, *J* = 8.5, 2 H), 4.06 (t, *J* = 8.5, 2 H), 1.69 (s, 3 H); ^{13}C NMR (62.8 MHz) δ 168.1 (s), 150.1 (s), 149.6 (s), 146.6 (d), 123.0 (d), 89.0 (s), 65.6 (t), 54.5 (t), 14.2 (q); IR (KBr) 3336, 3164, 1627, 1599. HRMS calcd for $C_{11}H_{13}N_3O$ 203.1058, found 203.1052.

(*Z*)-2-(4,5-Dihydro-4,4-dimethyl-1,3-oxazol-2-yl)-1-phenyl-1-propen-1-amine (2q). White solid. Mp 58-61 °C; ^{1}H NMR (250 MHz) δ 7.36 (s, 5 H), 6.50 (bs, 2 H, NH_2), 3.88 (s, 3 H), 1.68 (s, 3 H), 1.34 (s, 6 H); ^{13}C NMR (62.8 MHz) δ 166.1 (s), 152.7 (s), 139.3 (s), 128.4 (d), 87.8 (s), 77.3 (t), 67.1 (s), 29.2 (q), 14.4 (q); IR (KBr) 3419, 3158, 1623, 1555. HRMS calcd for $C_{14}H_{18}N_2O$ 230.1419, found 230.1420.

(*Z*)-2-(4,5-Dihydro-4,4-dimethyl-1,3-oxazol-2-yl)-1-(4-methylphenyl)-1-penten-1-amine (2r). White solid. Mp 63-6 °C; ^{1}H NMR (250 MHz) δ 7.21-7.00 (m, 4 H), 3.79 (s, 2 H), 2.29 (s, 3 H), 1.91 (t, 2 H), 1.26 (s, 6 H), 1.25 (m, 2 H), 0.66 (t, 3 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 166.1 (s), 153.2 (s), 138.0 (s), 136.4 (s), 128.9 (d), 128.0 (d), 93.4 (s), 76.5 (t), 66.7 (s), 30.5 (t), 28.0 (t), 24.6 (t), 21.3 (q), 14.0 (q); HRMS calcd for $C_{17}H_{24}N_2O$ 272.1888, found 272.1897.

(*Z*)-2-[(4*S*,5*S*)-4,5-Dihydro-4-methoxymethyl-5-phenyl-1,3-oxazol-2-yl)]-1-(4-methylphenyl)-1-propen-1-amine (2s). Pale yelow oil, purified by flash chromatography on basic Al_2O_3 (hexane/AcOEt: 3/1); ^{1}H NMR (250 MHz) δ 7.53-7.18 (m, 9 H), 5.25 (d, *J* = 7.5, 1 H), 4.26 (m, 1 H), 3.65 (dd, *J* = 9.1, 4.3, 1 H), 3.58 (dd, *J* = 9.1, 7.3 1 H), 3.43 (s, 3 H), 2.33 (s, 3 H), 1.80 (s, 3 H), a bs signal corresponding to the 2 H of the NH_2 group was not observed; ^{13}C NMR (62.8 MHz) δ 168.4 (s), 153.9 (s), 141.8 (s), 138.5 (s), 136.2 (s), 129.2 (d), 128.7 (d), 128.3 (d), 127.9 (d), 125.6 (d), 87.2 (s), 81.8 (d), 75.6 (t), 74.7 (d), 59.5 (q), 21.5 (q), 14.6 (q); $[\alpha]^{25}_D$ + 28.3 (*c* 0.54, $CHCl_3$); IR (neat) 3451, 3273, 1625, 1604. HRMS calcd for $C_{21}H_{24}N_2O_2$ 336.1837, found 336.1828. Anal. Calcd for $C_{21}H_{24}N_2O_2$: C, 75.00; H, 7.14; N, 8.33. Found: C, 74.68; H, 7.18; N, 8.25.

(*Z*)-2-(4,5-Dihydro-1,3-thiazol-2-yl)-1-(4-methylphenyl)-1-penten-1-amine (2t). Pale yelow oil, purified by flash chromatography on basic Al_2O_3 (hexane/AcOEt: 3/1); ^{1}H NMR (250 MHz) δ 7.30-7.15 (m, 4 H), 6.80 (bs, 2 H, NH_2), 4.36 (t, *J* = 8.8, 2 H), 3.16 (t, *J* = 8.8, 2 H), 2.37 (s, 3 H), 2.04 (t, 2 H), 1.36 (m, 2 H), 0.70 (t, *J* = 6.8, 3 H); ^{13}C NMR (62.8 MHz) δ 172.4 (s), 152.9 (s), 139.0 (s), 137.2 (s), 129.8 (d), 128.9 (d), 100.4 (s), 65.0 (t), 34.5 (t), 32.7 (t), 25.9 (t), 21.5 (q), 14.7 (q). Anal. Calcd for $C_{15}H_{20}N_2S$: C, 69.23; H, 7.69; N, 10.27. Found: C, 69.55; H, 7.51; N, 10.83.

(*Z*)-2-(4,5-Dihydro-1,3-thiazol-2-yl)-1-(4-methylphenyl)-1,4-pentadien-1-amine (2u). White solid. Mp 54-6 °C; ^{1}H NMR (250 MHz) δ 7.28-7.10 (m, 4 H), 6.91 (bs, 2 H, NH_2), 5.79 (m, 1 H), 4.90 (m, 2 H), 4.32 (t, *J* = 8.8, 2 H), 3.15 (t, *J* = 8.8, 2 H), 2.80 (d, *J* = 5.7, 2 H), 2.32 (s, 3 H); ^{13}C NMR (62.8 MHz) δ 171.5 (s), 153.2 (s), 138.9 (d), 138.4 (s), 135.9 (s), 128.9 (d), 127.6 (d), 114.4 (t), 96.1 (s), 64.2 (t), 36.0 (t), 32.1 (t), 21.2 (q); IR (KBr) 3451, 3293, 1592, 1559. HRMS calcd for $C_{15}H_{18}N_2S$ 258.1190, found 258.1196.

(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methoxyphenyl)-1-penten-1-amine (2v). Pale yelow oil, purified by flash chromatography on basic Al_2O_3 (hexane/AcOEt: 3/1); ^{1}H NMR (250 MHz) δ 7.28 (d, *J* = 8.6, 2 H), 6.90 (d, *J* = 8.6, 2 H), 6.87 (bs, 2 H, NH_2), 4.36 (t, 2 H), 3.82 (s, 3 H), 3.16 (t, *J* = 8.1, 2 H), 2.05 (t, *J* = 8.1, 2 H), 1.36 (m, 2 H), 0.71 (t, *J* =

7.3, 3 H); ^{13}C NMR (62.8 MHz) δ 171.8 (s), 159.6 (s), 152.0 (s), 131.8 (s), 129.4 (d), 113.8 (d), 99.8 (s), 64.4 (t), 55.4 (q), 34.6 (t), 32.1 (t), 25.3 (t), 14.1 (q); HRMS calcd for $C_{15}H_{20}N_2OS$ 276.1296, found 276.1306.

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References

[1] For a recent monograph on β-amino acids, see: Juaristi, E. in Enantioselective Synthesis of β-Amino Acids. Wiley-VCH: New York, 1997.
[2] See, for example: *Theopalauamide*, Schimdt EW, Bewley CA, Faulkner DJ, J. Org. Chem. 1998; 63: 1254-1258.
[3] *Taxol*, Nicolau KC, Sorensen EJ, in Classics in Total Synthesis. VCH, Weinheim, 1996, pp 655-672 and references cited therein.
[4] Applequist J, Bode KA, Appella DH, Christianson LA, Gellman SH, J. Am. Chem. Soc. 1998; 120: 4891-4892.
[5] Gellman SH, Acc. Chem. Res. 1998; 31: 173-180.
[6] Clark TD, Buehler LK, Ghadiri MR, J. Am. Chem. Soc. 1998; 120: 651-656.
[7] Dufour M, Gramain J-C, Husson H-P, Sinibaldi M-E, Troin Y, J. Org. Chem. 1990; 55: 5483-5490.
[8] Hashiguchi S, Kawada A, Natsugari H, J. Chem. Soc., Perkin Trans 1, 1991; 2435-2444.
[9] Cardillo G, Gentilucci L, Tolomelli A, Tomasini C, J. Org. Chem. 1998; 63: 3458-3462.
[10] Naringrekar VH, Stella V, J. J. Pharm. Sci. 1990; 79: 138-144.
[11] Ferraz HMC, Oliveira EO, Payret-Arrua ME, Brandt CA, J. Org. Chem. 1995; 60: 7357-7359.
[12] Kloek JA, Leschinsky KL, J. Org. Chem. 1978; 43: 1460-1462.
[13] Lee ASY, Cheng R-Y, Tetrahedron Lett. 1997; 38: 443-446.
[14] Hiyama T, Kobayashi K, Tetrahedron Lett. 1982; 23: 1597-1600.
[15] Fukuyama T, Yung YM, Tetrahedron Lett. 1981; 22: 3759-3760.
[16] Fustero S, Pina B, Simón-Fuentes A, Tetrahedron Lett. 1997; 38: 6771-6774.
[17] Beholz LG, Benovxky P, Ward DL, Barta NS, Stille JR, J. Org. Chem. 1997; 62: 1033-1042.
[18] Fustero S, Díaz MD, Pérez-Carlón R, Tetrahedron Lett. 1993; 34: 725-728.
[19] Eckert H, Forster B, Angew. Chem. Int. Ed. Engl. 1987; 26: 894-895.
[20] See, for example: Kocienski PJ, in Protecting Groups. Georg Thieme Verlag, Stuttgart, 1994; pp 118-154.
[21] Meyers AI, Gant TG, Tetrahedron 1994; 50: 2297-2360.
[22] For leading references regarding the employment of oxazoline derivatives as chiral ligands in asymmetric catalysis see: End N, Macko L, Zehnder M, Pfaltz A, Chem. Eur. J. 1998; 4: 818-824.
[23] For a preliminary communication see: Fustero S, Díaz MD, Barluenga J, Aguilar E, Tetrahedron Lett. 1992; 33: 3801-3804.
[24] Tohda Y, Morikawa M, Kawashima T, Ariga M, Mori Y, Chem. Lett. 1986; 273-274.
[25] Poindexter G, Catt JD, Sasse PA, Kercher MA, Heterocycles 1993; 36: 295-305.
[26] Fustero S, Navarro A, Díaz MD, García de la Torre M, Asensio A, Sanz F, Liu M, J. Org. Chem. 1996; 61: 8849-8859 and references cited therein.
[27] Lutomski KA, Meyers AI, in Asymmetric Synthesis. Morrison JD, Ed. Academic Press, Orlando, 1984; 13: pp 213-274.
[28] See, for example: Jones CF, Anderson MW, Smallridge HJ, Tetrahedron Lett. 1988; 29: 5001-5004.
[29] Chowdry MM, Burrows AD, Mingos MP, White AJP, Williams DJ, J. Chem. Soc., Chem. Commun. 1995; 1521-1522.
[30] Frisch MJ, Schlegel HB, Gill PMW, Johnson BG, Robb MA, Cheeseman JR, Keith T, Petersson GA, Montgomery JA, Raghavachari K, Al-Laham MA, Zakrzewski VG, Ortiz JV, Foresman JB, Ciolowski J, Stefanov BB, Nanayakkara A, Challacombe N, Peng CY, Ayala PY, Chen W, Wong MW, Andrés JL, Replogle ES, Gomperts R, Martin RL, Fox DJ, Binkley JS, DeFrees DJ, Baker J, Stewart JJP, Head-Gordon M, González C, Pople JA, *GAUSSIAN 94*, Revision C.3; Gaussian Inc.; Pittsburgh, PA, 1995.
[31] Meyers AI, Knaus G, Kamata K, Ford ME, J. Am. Chem. Soc. 1976; 98: 567-576.
[32] Ando K, Takemasa Y, Tomioka K, Koga K, Tetrahedron 1993; 49: 1579-1588.
[33] Barluenga J, Jardón J, Gotor V, J. Org. Chem. 1985; 50: 802-804.