DOI: 10.1002/ejoc.200600540

α-Amino-α-vinyl-γ-butyrolactone Derivatives from α-{[(Trimethylsilyl)-methyl]alkylidene}-γ-butyrolactones

Marinella Capuzzi,[a,b] Augusto Gambacorta,[c] Tecla Gasperi,[a,b] M. Antonietta Loreto,*[a,b] and P. Antonio Tardella[a]

Keywords: α-Amino lactones / Aza-Michael reactions / Allylsilanes / Vinyl triflates / Cross-coupling / Palladium

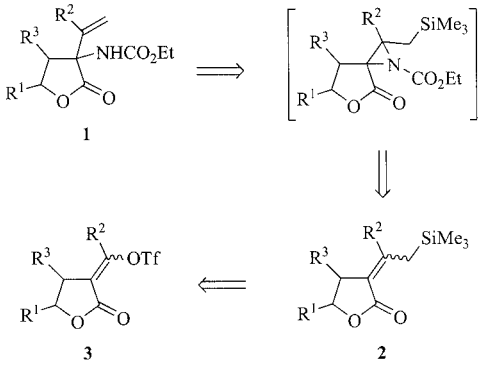
N-Protected α-amino-α-vinyl-γ-butyrolactones **1** are obtained by the aza-Michael-type addition of $NsONHCO_2Et$ to novel silylated α-ylidene-γ-butyrolactones **2**, through ring opening of the intermediate aziridine and loss of the trimethylsilyl group. The stereoselective synthesis of compounds **2**, by cross-coupling reactions between α-[(triflyloxy)ylidene]-γ-butyrolactones **3** and tris[(trimethylsilyl)methyl]aluminum, is also described.

Introduction

In the past years, significant attention has been focused on the synthesis of α-amino-γ-butyrolactone derivatives.[1] The biological interest in this class of compounds is linked to the presence of the α-amino-γ-lactone skeleton in several compounds with antiallergic and antineoplastic properties.[2] Furthermore, *N*-acylhomoserine lactones control the transcription of specific genes in Gram-negative bacteria and have been used as quorum-sensing autoinducers.[3] From the synthetic point of view, α-amino-γ-lactone derivatives constitute valuable precursors for the synthesis of biologically important compounds. In particular, α-amino-α-vinyl-γ-lactones have been successfully used by Berkowitz et al. as intermediates in the preparation of α-vinyl amino acids,[4] which are mechanism-based inhibitors for enzymes of the amino acid decarboxylase class. Recently, Smith et al. have published an interesting synthetic route to obtain polypyrrolinone nonpeptidomimetics starting from α-alkyl-α-aminolactones.[5]

For several years, our research group has been interested in studying the reactivity of electron-poor olefins towards ethyl *N*-{[(4-nitrobenzyl)sulfonyl]oxy}carbamate ($NsONHCO_2Et$) in order to obtain *N*-(ethoxycarbonyl)-aziridines, which can be opened to obtain new amino derivatives.[6,7] In the presence of a base, the anion of $NsONHCO_2Et$ carries out a nucleophilic attack at the olefinic β-carbon atom by an aza-Michael-type reaction, followed by ring closure and the expulsion of the NsO^- group. Particularly, this reaction sequence on α-ylidene-γ-butyrolactones afforded spiroaziridines, precursors of α-amino-γ-butyrolactone derivatives,[6] while the same aminating reagent, when allowed to react with α,β-unsaturated esters and ketones, carrying a (trimethylsilyl)methyl group at the double bond, gave α-amino-α-vinyl derivatives through aziridination and subsequent loss of the trialkylsilyl group.[7]

On these grounds, faced with the synthesis of both α-amino-γ-butyrolactone derivatives and α-vinyl amino acids, we planned the preparation of the novel α-{[*N*-(ethoxycarbonyl)]amino}-α-vinyl-γ-butyrolactones **1** according to the retrosynthetic analysis depicted in Scheme 1. Thus, the novel α-{[(trimethylsilyl)methyl]alkylidene}-γ-butyrolactones **2**, obtained in turn from the triflates **3**, could undergo an aza-Michael-type addition of $NsONHCO_2Et$ to afford intermediate aziridines. Subsequent loss of the trialkylsilyl group and concomitant aziridine ring opening, could give the expected α-{[*N*-(ethoxycarbonyl)]amino}-α-vinyl-γ-bu-



Scheme 1. Retrosynthetic analysis for the synthesis of α-{[*N*-(ethoxycarbonyl)]amino}-α-vinyl-γ-butyrolactones **1**.

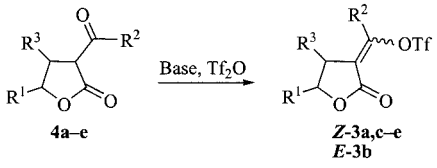
[a] Dipartimento di Chimica, Università "La Sapienza", Piazzale Aldo Moro 5, Rome 00185, Italy
Fax: +39-06-490631
E-mail: mariaantonietta.loreto@uniroma1.it
[b] Istituto C.N.R. di Chimica Biomolecolare, Dipartimento di Chimica, Università "La Sapienza", Piazzale Aldo Moro 5, Rome 00185, Italy
[c] CISDiC, Dipartimento di Ingegneria Meccanica e Industriale, Università "Roma Tre", Via della Vasca Navale 79, Rome 00146, Italy

tyrolactones **1**. We report here the synthesis of triflates **3**, their conversion into the allylsilanes **2** and the amination of the latter to afford the α-{[*N*-(ethoxycarbonyl)]amino}-α-vinyl-γ-butyrolactones **1**.

Results and Discussion

Allylsilanes with a carbonyl group at the β- or γ-position, or their equivalents, represent a powerful synthetic tool in organic synthesis, since they can formally react either as nucleophiles or as electrophiles.[8] Though several preparations of this class of functionalized allylsilanes are known in the literature,[9] to the best of our knowledge, no examples of allylsilanes carrying a γ-butyrolactone moiety at the double bond, as in **2**, have been reported. In order to obtain these challenging substrates, we have chosen to perform a Pd-catalyzed cross-coupling reaction between α-[(triflyloxy)ylidene]-γ-butyrolactones **3** and tris[(trimethylsilyl)methyl]aluminum, according to the route previously described for the synthesis of [γ-(methoxycarbonyl)allyl]silanes.[7c] Actually, cross-coupling reactions provide one of the most useful synthetic ways for stereoselective carbon–carbon bond formation.[10]

The α-[(triflyloxy)ylidene]-γ-butyrolactones **3a**–**e** were synthesized from the corresponding and previously described α-acyl-γ-butyrolactones **4a**–**e** (Scheme 2), obtained in turn either by cross-Claisen acylation of commercial γ-butyrolactones[11] or by the enolate-promoted ring-opening reaction of styrene oxide followed by intramolecular transesterification.[12]



Scheme 2. Synthesis of α-[(triflyloxy)ylidene]-γ-butyrolactones **3a**–**e**.

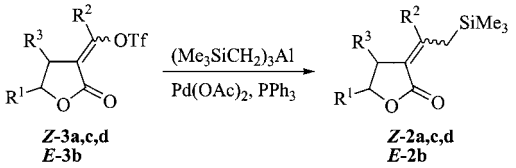
According to the procedure reported for the preparation of **3a**,[13] we treated the α-acyl-γ-butyrolactones **4a**–**e** with trifluoromethanesulfonic anhydride in the presence of a suitable base to afford the corresponding triflates in the yields and under the conditions reported in Table 1. In the case of substrate **4b**, isolated as the sodium salt, the corresponding known vinyl triflate **3b** was directly obtained without employing any additional base.[14] It is noteworthy that vinyl triflates **3a**–**e** were easily purified by crystallization from diethyl ether.[15] The (*Z*) selectivity for the novel compounds **3c**–**e** is consistent with the behaviour reported by Jacobi et al.[13] for the vinyl triflate **3a**. Presumably, Li^+ coordination with both the exocyclic and endocyclic carbonyl groups forces the enolate into the less stable (*Z*) configuration. Accordingly, the use of the sodium enolate in the case of **4b** results in the more stable (*E*)-enolate and affords (*E*) selectivity for the vinyl triflate **3b**.[11a,16]

Table 1. Synthesis of triflates **3**.

Substrate	R^1	R^2	R^3	Base	Solvent	*T* [°C]/Time [h]	Product	Yield [%]
4a	H	CH_3	H	*n*BuLi	THF	–78/1	***Z*-3a**	68
4b	H	H	H	*n*BuLi	THF	–78/1	–[a]	–
4b	H	H	H	LDA	THF	–40/6	–[a]	–
4b	H	H	H	–[b]	DME	–40 to 25/7	***E*-3b**	50
4c	H	Ph	H	*n*BuLi	THF	–78/2	***Z*-3c**	75
4d	Ph	CH_3	H	*n*BuLi	THF	–78/3	***Z*-3d**	70
4e	H	CH_3	Ph	*n*BuLi	THF	–78/3	***Z*-3e**	62

[a] Unreacted substrate was recovered. [b] The sodium salt of **4b** was directly used without any additional base.

With the triflates **3** in hand, we performed the synthesis of the allylsilanes **2** (Scheme 3).



Scheme 3. Synthesis of α-{[(trimethylsilyl)methyl]alkylidene}-γ-butyrolactones **2a**–**d**.

The cross-coupling reaction was initially performed on **3a**, as a model substrate, according to the same procedure reported for the synthesis of [γ-(methoxycarbonyl)allyl]silanes,[7c] but initial results were quite disappointing. In fact, through the in situ generation of the catalytic species, $Pd(PPh_3)_4$, by reduction of $Pd(OAc)_2$ by the *n*BuLi/PPh_3 system, the addition of the vinyl triflate **3a** and transmetallation with $(Me_3SiCH_2)_3Al$, formed in situ from $AlCl_3$ and Me_3SiCH_2Li, we did not observe the formation of the expected allylsilane **2a**, even after 24 h at reflux. Only the addition of a second equiv. of $(Me_3SiCH_2)_3Al$ allowed us to isolate the product **2a** in 33% yield. In an effort to improve the reaction efficiency, several different combinations of solvents, bases and alkylating agent ratios were evaluated, but only low yields of product could be obtained.

Finally, the use of a large excess of $(Me_3SiCH_2)_3Al$ at 50 °C, in the absence of *n*BuLi, afforded the desired allylsilane **2a** in 95% yield with a (*Z*) configuration. Therefore, the cross coupling proceeds with retention of the double bond configuration, as confirmed by the deshielding of the CH_2-TMS protons compared to the methyl protons in the ^1H NMR spectrum.

Presumably, the excess of $(Me_3SiCH_2)_3Al$ or the triphenylphosphane itself[17] acts as a reducing agent towards the palladium acetate. The above optimized protocol for the vinyl triflate **3a** was successfully extended to the other triflates **3b**–**e** by adjusting the reaction time and the temperatures to enhance the reactivity on a case-by-case basis (Table 2).

In all experiments, the cross coupling proceeded with retention of the double bond configuration in the parent triflates, and the best results were obtained in the synthesis of allylsilanes **2a**–**c**, while minor conversion was observed with the allylsilane **2d**, substituted with a phenyl group on the

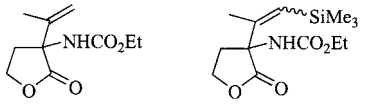
Table 2. Pd-cross-coupling reaction between compounds **3** and $(Me_3SiCH_2)_3Al$.

Substrate[a]	R^1	R^2	R^3	*T* [°C]/Time [h]	Product	Yield [%]
***Z*-3a**	H	CH_3	H	50/4	***Z*-2a**	95
***E*-3b**	H	H	H	50/5	***E*-2b**	71
***Z*-3c**	H	Ph	H	70/4	***Z*-2c**[b]	83
***Z*-3d**	Ph	CH_3	H	50/4	***Z*-2d**	62
***Z*-3e**	H	CH_3	Ph	50/4	–[c]	–
***Z*-3e**	H	CH_3	Ph	70/24	–[c]	–

[a] The molar ratio of **3a**–**e**/$(Me_3SiCH_2)_3Al$/$Pd(OAc)_2$/PPh_3 = 1:2.5:0.09:0.36. [b] In this case, a larger excess of $(Me_3SiCH_2)_3Al$ was used. [c] Unreacted substrate was recovered.

ring. The triflate **3e** did not react, possibly because steric hindrance of the phenyl group in the β-position made the transmetallation step in the catalytic cycle unfavourable.

With the α-{[(trimethylsilyl)methyl]alkylidene}-γ-butyrolactones **2** in hand, and on the basis of our previous results,[6,7] we extended the amination reaction to these compounds. First attempts were carried out on the substrate **2a** by adding to it 5 equiv. of an $NsONHCO_2Et$/CaO mixture (1:1 molar ratio) portionwise at room temperature. After the usual workup, it was not possible to find the expected spiroaziridine intermediate, but we obtained two new compounds. The major product was the desired unsaturated α-amino-γ-lactone **1a** (64% yield) (Figure 1), derived from the ring opening of the intermediate spiroaziridine with the concomitant loss of the silyl group (Scheme 4). The minor product was the unexpected compound **5a** (10% yield) (Figure 1), generated by the loss of a proton instead of the trimethylsilyl group.[18] Fortunately, it was possible to convert, almost quantitatively, **5a** into **1a** through the known acid-catalysed protodesilylation of vinylsilanes.[19] Therefore, direct treatment of the crude reaction mixture with acetic acid resulted in the formation of **1a** as the only product in higher yield.



1a **5a**

Figure 1. Products obtained by reaction of **2a** with $NsONHCO_2Et$ and CaO, without treatment with AcOH.

The above amination protocol, followed by treatment with acetic acid, was performed on the silylated compounds **2a**–**d** and provided the α-{[*N*-(ethoxycarbonyl)]amino}-γ-lactones **1a**–**d** (Scheme 4), in the yields and under the conditions reported in Table 3. Compounds **1a**–**d** were isolated and characterized by NMR and GC-MS analyses, and the spectroscopic data are in agreement with the reported structures.

Table 3. Amination reaction on allylsilanes **2**.

Substrate	R^1	R^2	**2**/$NsONHCO_2Et$/CaO	Time [h]	Product	Yield [%][a]
***Z*-2a**	H	CH_3	1:5:5	6	**1a**	73
***E*-2b**	H	H	1:5:5	6	**1b**	70
***Z*-2c**	H	Ph	1:8:8	9	**1c**	55
***Z*-2d**	Ph	CH_3	1:6:6	7	**1d**	52

[a] Isolated yields of the crude mixtures obtained after treatment with AcOH, as determined by HPLC chromatography.

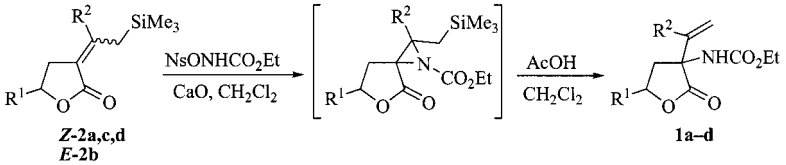
It is noteworthy that, starting from the allylsilane **2d**, substituted on the ring, we isolated the α-amino-α-vinyllactone **1d** as single diastereomer, as shown by HPLC analysis and the ^1H NMR spectrum. Probably, the bulky phenyl group in the γ-position of the lactone ring drives the aminating agent approach from the less hindered face of the double bond, *anti* to the substituent, affording diastereoselectively the formation of **1d**, analogous to the behaviour previously observed in the aziridination of α-ylidene-γ-butyrolactones.[6b]

Conclusions

In summary, we have described an efficient three-step synthesis of the novel α-{[*N*-(ethoxycarbonyl)]amino}-α-vinyl-γ-lactones **1a**–**d** by the aza-Michael-type aziridination of the new silylated α-ylidene-γ-butyrolactones **2a**–**d**. The latter, due to the versatility of both the allylsilane and enone systems, are valuable building blocks and have been stereoselectively obtained by Pd-catalyzed cross coupling between the easy accessible α-[(triflyloxy)ylidene]-γ-butyrolactones **3a**–**d** and tris[(trimethylsilyl)methyl]aluminum. Compounds **1a**–**d** are interesting intermediates in the preparation of α-vinyl amino acids and direct precursors of quaternary α-aminolactones having in the α-position all functionalities obtainable by chemical elaboration of the vinyl group.

Experimental Section

General: All reactions were performed under argon with standard air-free manipulation techniques. Solvents and common reagents were purchased from commercial sources and used without further purification. All reactions were monitored by GC-MS analysis and by thin layer chromatography (TLC) carried out on Merck F-254 silica glass plates and visualized with UV light and I_2. Chromatographic separations were performed on Merck silica gel 60 (230–



***Z*-2a,c,d** ***E*-2b** **1a–d**

Scheme 4. Amination reaction performed on **2a**–**d** with $NsONHCO_2Et$ and CaO, followed by treatment of the crude mixtures with AcOH.

400 mesh). Purifications by HPLC were performed with an instrument equipped with a differential refractometer and an analytical column (3.9 × 300 mm, flow rate 1.3 mL/min). ^{1}H (200 MHz) and ^{13}C NMR (50 MHz) spectra were recorded with a Varian Gemini 200 spectrometer; chemical shifts are expressed in ppm (δ) and are referenced to the carbon and residual proton signals of the solvent ($CHCl_3$: δ = 7.26 ppm for ^{1}H NMR, δ = 77.0 ppm for ^{13}C NMR), unless otherwise indicated. IR spectra were recorded in $CHCl_3$ with a Perkin–Elmer 1600 instrument (FT-IR); data are presented in wavenumbers (cm^{-1}). MS data were obtained by GC-MS coupling with an HP 5890 apparatus, equipped with a phenylmethylsilicon capillary column (15 m, 0.25 mm i.d.). HRMS data were recorded with a Micromass Q-TOF micro Mass Spectrometer (Waters). All melting points were determined with a Mel-Temp apparatus and are uncorrected.

Synthesis of α-Acyl-γ-butyrolactones 4b–e

Sodium (*E*)-(2-oxodihydrofuran-3-ylidene)methoxide (*E*-4b sodium salt):[11a] To a stirred suspension of NaH (580 mg, 14.5 mmol, 60% suspension in mineral oil) in anhydrous DME (60 mL), a mixture of commercial γ-butyrolactone (1.14 mL, 15 mmol) and ethyl formate (1.21 mL, 15 mmol) in anhydrous DME (8 mL) was added. After the addition of absolute ethanol (0.1 mL), the mixture was heated to 40 °C for 22 h. The reaction mixture was directly filtered through a Büchner funnel under vacuum and washed several times with anhydrous diethyl ether to obtain the ***E*-4b** sodium salt as a fine, powdery, white solid (1.990 g, 97% yield). M.p. 116–118 °C. ^{1}H NMR (D_2O, 200 MHz, 25 °C): δ = 2.60 (t, J = 8.4 Hz, 2 H, CH_2CH$_2$O), 4.16 (t, J = 8.4 Hz, 2 H, CH$_2$CH_2O), 8.26 (s, 1 H, C=CH) ppm. ^{13}C NMR (D_2O, 50 MHz): δ = 23.8 (*C*H$_2$CH$_2$O), 66.8 (CH$_2$O), 93.4 (*C*=CH), 172.2 (C=*C*H), 180.3 (C=O) ppm.

3-Benzoyldihydrofuran-2-one (4c):[11b] To a stirred suspension of NaH (1.309 g, 30 mmol, 60% suspension in mineral oil) in anhydrous DME (50 mL), methyl benzoate (3.73 mL, 30 mmol) was added. The reaction mixture was heated to 50 °C, and then a solution of γ-butyrolactone (1.280 g, 15 mmol) in anhydrous DME (7 mL) was added dropwise. After the addition of anhydrous methanol (0.1 mL), the resulting yellow solution was stirred at reflux for an additional 5 h. After cooling the mixture to room temp., the reaction was quenched by the cautious addition of H_2O (20 mL) followed by acidification with 1 N HCl to pH = 4. The organic layer was separated, and the aqueous layer was extracted with diethyl ether. The combined organic phases were dried (Na_2SO_4), concentrated under vacuum, and the crude mixture was purified by flash chromatography (hexane/AcOEt, 9:1) to obtain pure **4c** (2.052 g, 72% yield). ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 25.8 (*C*H$_2$CH$_2$O), 47.7 (*C*H-C=O), 67.5 (CH$_2$*C*H$_2$O), 128.5 (CH$_{arom.}$), 129.1 (CH$_{arom.}$), 133.8 (CH$_{arom.}$), 135.0 (C$_{arom.}$), 172.9 (O-C=O), 193.2 (Ph–C=O) ppm. R_f 0.49 (silica gel, hexane/AcOEt, 7:3). MS: m/z (%) = 190 (2.4) [M]$^+$, 105 (100). The ^{1}H NMR spectrum is in agreement with literature data.

***trans*- and *cis*-3-Acetyl-5-phenyldihydrofuran-2-one (4d) and *trans*-3-Acetyl-4-phenyldihydrofuran-2-one (4e):**[12] A solution of EtONa was prepared from absolute ethanol (28.8 mL, 494.6 mmol) and sodium (1.474 g, 64.1 mmol). The flask was then cooled with ice, and ethyl acetoacetate (9.8 mL, 76.9 mmol) was added rapidly. The reaction mixture was stirred at room temp. for 1 h, and styrene oxide (8.77 mL, 76.9 mmol) was added dropwise at 0 °C over a period of 30 min. The mixture was warmed to room temperature and stirred for an additional 72 h. The alcohol was removed under reduced pressure, below 50 °C, and glacial acetic acid (8.8 mL, 67.3 mmol) and ice were added to the syrupy residue. The excess of acetic acid was neutralized with $NaHCO_3$. The oily layer was separated, the aqueous layer was extracted with diethyl ether, and the combined organic phases were dried (Na_2SO_4). Solvent was removed under vacuum, and the crude residue was purified by flash chromatography (hexane/AcOEt, 9:1) to give **4d** (5.020 g, 32% yield, 1:1 *cis*/*trans* mixture) and **4e** as only the *trans* stereoisomer (9.098 g, 58% yield). The characterization data are in agreement with literature data.

Synthesis of α-[(Triflyloxy)alkylidene]-γ-butyrolactones 3a–e

(1*Z*)-1-(2-Oxodihydrofuran-3-ylidene)ethyl Trifluoromethanesulfonate (3a):[13] A solution of commercial α-acetyl-γ-butyrolactone (0.76 mL, 7.09 mmol) in anhydrous THF (30 mL) was cooled to –78 °C under argon. *n*BuLi (2.5 M solution in hexane, 2.84 mL, 7.09 mmol) was added dropwise, under efficient stirring, over a period of 10 min, and the resulting mixture was stirred at –78 °C for an additional 30 min. Trifluoromethanesulfonic anhydride (1.19 mL, 7.09 mmol) was added over a period of 5 min. The resulting solution was stirred at –78 °C for an additional 20 min, quenched by the careful addition of ice-cold saturated $NaHCO_3$/brine (1:1) (24 mL) and extracted with diethyl ether. The combined organic extracts were dried (Na_2SO_4), concentrated under reduced pressure, and the residue was crystallized from diethyl ether to obtain **3a** as a white crystalline solid (1.253 g, 68% yield). M.p. 64–65 °C (ref.[13] 65–66 °C). MS: m/z (%) = 260 (24) [M]$^+$, 43 (100). Other spectroscopic data are in agreement with literature data.

(*E*)-(2-Oxodihydrofuran-3-ylidene)methyl Trifluoromethanesulfonate (3b):[14] A stirred suspension of the sodium salt of **4b** (1.900 g, 13.97 mmol) in anhydrous DME (28 mL) was cooled to –40 °C, and trifluoromethanesulfonic anhydride (2.35 mL, 13.97 mmol) was added dropwise. The reaction mixture was stirred at –40 °C for an additional 1 h and at room temp. for a further 3 h. The solvent was removed by evaporation under vacuum, and the residue was filtered and washed with diethyl ether. The organic phase was treated with a saturated solution of $NaHCO_3$, and the aqueous layer was extracted with diethyl ether. The combined organic phases were dried with Na_2SO_4, concentrated under vacuum, and the crude product was purified by flash chromatography (hexane/diethyl ether, 1:1) to give **3b** as a white crystalline solid (1.718 g, 50% yield). M.p. 41–42 °C (ref.[14] 41–42 °C). ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 24.2 (*C*H$_2$CH$_2$O), 65.9 (CH$_2$*C*H$_2$O), 117.0 (*C*=C-OTf), 118.4 (q, J = 321 Hz, CF_3), 142.6 (C=*C*-OTf), 168.5 (C=O) ppm. MS: m/z (%) = 246 (13.1) [M]$^+$, 69 (100). The ^{1}H NMR spectrum is in agreement with literature data.

(*Z*)-(2-Oxodihydrofuran-3-ylidene)(phenyl)methyl Trifluoromethanesulfonate (3c): This compound was prepared from **4c** (1.800 g, 9.47 mmol), according to the procedure described for **3a**. After the addition of trifluoromethanesulfonic anhydride, the resulting solution was stirred at –78 °C for an additional 3 h. The crude mixture was purified by crystallization from diethyl ether and by flash chromatography of the crystallization mother liquor to obtain **3c** (2.287 g, 75% total yield). M.p. 134–136 °C. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1750, 1685 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 3.21 (t, J = 7.1 Hz, 2 H, CH_2CH$_2$O), 4.38 (t, J = 7.1 Hz, 2 H, CH$_2$CH_2O), 7.40–7.62 (m, 5 H, CH$_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 29.3 (*C*H$_2$CH$_2$O), 64.7 (CH$_2$*C*H$_2$O), 118.1 (q, J = 309 Hz, CF_3), 118.6 (*C*=C-OTf), 127.8 (CH$_{arom.}$), 128.7 (CH$_{arom.}$), 131.2 (CH$_{arom.}$), 131.5 (C$_{arom.}$), 149.0 (C-OTf), 165.2 (C=O) ppm. R_f = 0.17 (silica gel, hexane/AcOEt, 8:2). MS: m/z (%) = 322 (0.8) [M]$^+$, 105 (100). HRMS: calcd. for $C_{12}H_9F_3NaO_5S$ [M] 345.0020; found 345.0029.

(1*Z*)-1-(2-Oxo-5-phenyldihydrofuran-3-ylidene)ethyl Trifluoromethanesulfonate (3d): This compound was prepared from **4d** (900 mg, 2.94 mmol), according to the procedure described for **3a**. After the

addition of trifluoromethanesulfonic anhydride, the resulting solution was stirred at –78 °C for an additional 3 h. The crude mixture was purified by crystallization from diethyl ether and by flash chromatography of the crystallization mother liquor to obtain **3d** as a white crystalline solid (691 mg, 70% yield). M.p. 86–88 °C. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1752, 1695 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 2.18 (dd, J = 1.9 Hz, J = 2.0 Hz, 3 H, CH_3), 2.96 (ddq, J = 16.9 Hz, J = 6.2 Hz, J = 2.0 Hz, 1 H, C*H*H-C=C), 3.46 (ddq, J = 16.9 Hz, J = 8.2 Hz, J = 1.9 Hz, 1 H, CH*H*-C=C), 5.55 (dd, J = 8.2 Hz, J = 6.2 Hz, 1 H, CHPh), 7.29–7.46 (m, 5 H, $CH_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 19.6 (CH_3), 35.5(CH_2), 77.2 (CHPh), 118.3 (*C*=C-OTf), 118.4 (q, J = 320 Hz, CF_3), 125.3 ($CH_{arom.}$), 128.9 ($CH_{arom.}$), 129.0 ($CH_{arom.}$), 139.1 ($C_{arom.}$), 149.5 (C-OTf), 165.1(C=O) ppm. R_f = 0.47 (silica gel, hexane/AcOEt, 7:3). MS: m/z (%) = 336 (0.3) $[M]^+$, 97 (100). HRMS: calcd. for $C_{13}H_{11}F_3NaO_5S$ [M] 359.0177; found 359.0183.

(1*Z*)-1-(2-Oxo-4-phenyldihydrofuran-3-ylidene)ethyl Trifluoromethanesulfonate (3e): This compound was prepared from **4e** (1.419 g, 6.96 mmol), according to the procedure described for **3a**. After the addition of trifluoromethanesulfonic anhydride, the resulting solution was stirred at –78 °C for an additional 3 h. The crude mixture was purified by crystallization from diethyl ether and by flash chromatography of the crystallization mother liquor to obtain **3e** as a white crystalline solid (1.450 g, 62% yield). M.p. 124–126 °C. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1751, 1692 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.90 (s, 3 H, CH_3), 4.19–4.30 (m, 2 H, CH_2), 4.72 (t, J = 8.5 Hz, 1 H, CHPh), 7.20–7.44 (m, 5 H, $CH_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 19.6 (*C*H_3), 44.6 (*C*HPh), 72.7 (CH_2O), 118.3 (q, J = 320 Hz, CF_3), 121.9 (*C*=C-OTf), 127.0 ($CH_{arom.}$), 128.2 ($CH_{arom.}$), 129.7 ($CH_{arom.}$), 139.5 ($C_{arom.}$), 152.8 (C-OTf), 165.6 (C=O) ppm. R_f = 0.25 (silica gel, hexane/AcOEt, 7:3). MS: m/z (%) = 336 (0.5) $[M]^+$, 43 (100). HRMS: calcd. for $C_{13}H_{11}F_3NaO_5S$ [M] 359.0177; found 359.0183.

Synthesis of α-{[(Trimethylsilyl)methyl]alkylidene}-γ-butyrolactones 2a–d

(*Z*)-3-[1-Methyl-2-(trimethylsilyl)ethylidene]dihydrofuran-2-one (2a): A solution of tris[(trimethylsilyl)methyl]aluminum was prepared by adding [(trimethylsilyl)methyl]lithium (1.0 M solution in pentane, 18.7 mL, 18.75 mmol) to a magnetically stirred suspension of $AlCl_3$ (834 mg, 6.25 mmol) in dry 1,2-dichloroethane (25 mL) under argon and at room temp. for 30 min. Triflate **3a** (650 mg, 2.5 mmol) in dry benzene (4 mL) was added under argon to a solution of $Pd(OAc)_2$ (50 mg, 0.22 mmol) and PPh_3 (236 mg, 0.90 mmol) in dry benzene (2 mL). The resulting mixture was immediately transferred by cannula into the tris[(trimethylsilyl)methyl]aluminum solution and stirred at 50 °C for 4 h. The workup consisted of dilution with CH_2Cl_2, washing with 0.2 M HCl, H_2O and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Purification by flash chromatography on silica gel afforded **2a** as a light yellow oil (471 mg, 95% yield). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1755, 1690 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 0.08 [s, 9 H, $Si(CH_3)_3$], 1.87 (t, J = 1.4 Hz, 3 H, C=C-CH_3), 2.54 (t, J = 1.4 Hz, 2 H, CH_2SiMe$_3$), 2.88 (m, 2 H, CH_2CH$_2$O), 4.29 (t, J = 7.7 Hz, 2 H, CH$_2$CH_2O) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = –1.0 [$Si(CH_3)_3$], 25.0 (C=C-*C*H_3), 27.1 (CH_2SiMe_3), 27.7 (*C*H_2CH_2O), 63.9 (CH_2CH_2O), 114.2 (*C*-C=O), 154.1 (*C*-CH_2SiMe_3), 167.1 (C=O) ppm. R_f = 0.52 (silica gel, hexane/AcOEt, 8:2). MS: m/z (%) = 198 (18.3) $[M]^+$, 73 (100). HRMS: calcd. for $C_{10}H_{18}NaO_2Si$ [M] 221.0974; found 221.0980.

(*E*)-3-[2-(Trimethylsilyl)ethylidene]dihydrofuran-2-one (2b): This compound was prepared from **3b** (140 mg, 0.57 mmol), according to the procedure described for **2a**. After the addition of the triflate lactone **3b** solution to the Pd^0 catalyst, the reaction mixture was stirred at 50 °C for 5 h. Purification by flash chromatography on silica gel (hexane/AcOEt, 9:1) afforded **2b** as a light yellow oil (74 mg, 71% yield). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1755, 1690 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 0.08 [s, 9 H, $Si(CH_3)_3$], 1.73 (dt, J = 9.3 Hz, J = 1.4 Hz, 2 H, CH_2SiMe_3), 2.75–2.85 (m, 2 H, CH_2CH$_2$O), 4.36 (t, J = 7.5 Hz, 2 H, CH_2O), 6.89 (dt, J = 9.3 Hz, J = 2.8 Hz, 1 H, C=CH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = –1.4 [$Si(CH_3)_3$], 23.7 (CH_2SiMe_3), 25.3 (*C*H_2CH_2O), 65.1 (CH_2O), 122.1 (*C*-C=O), 139.7 (C=*C*H), 171.4 (C=O) ppm. R_f = 0.45 (silica gel, hexane/AcOEt, 8:2). MS: m/z (%) = 184 (13.3) $[M]^+$, 73 (100). HRMS: calcd for $C_9H_{16}NaO_2Si$ [M] 207.0817; found 207.0825.

(*Z*)-3-[1-Phenyl-2-(trimethylsilyl)ethylidene]dihydrofuran-2-one (2c): This compound was prepared from **3b** (322 mg, 1 mmol), according to the procedure described for **2a**. An excess of 4 equiv. of $(Me_3SiCH_2)_3Al$, generated in situ, was required for a good conversion. After the addition of the triflate lactone **3c** solution to the Pd^0 catalyst, the reaction mixture was stirred at 70 °C for 3 h. Purification by flash chromatography on silica gel (hexane/AcOEt, 9:1) afforded **2c** as a colourless oil (216 mg, 83% yield). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1750, 1685 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 0.00 [s, 9 H, $Si(CH_3)_3$], 2.77–3.09 (m, 4 H, CH_2CH$_2$O, CH_2SiMe$_3$), 4.16–4.46 (m, 2 H, CH_2O), 7.27–7.64 (m, 5 H, $CH_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = –1.2 [$Si(CH_3)_3$], 26.9 (CH_2SiMe_3), 29.6 (*C*H_2CH_2O), 64.6 (*C*H_2O), 116.1 (*C*=CPh), 127.1 (*C*$H_{arom.}$), 128.1(*C*$H_{arom.}$), 128.3 (*C*$H_{arom.}$), 142.8 ($C_{arom.}$), 155.9 (C=*C*Ph), 171.2 (C=O) ppm. R_f = 0.70 (silica gel, hexane/AcOEt, 8:2). MS: m/z (%) = 260 (36) $[M]^+$, 130 (100). HRMS: calcd. for $C_{15}H_{20}NaO_2Si$ [M] 283.1130; found 283.1140.

(*Z*)-3-[1-Methyl-2-(trimethylsilyl)ethylidene]-5-phenyldihydrofuran-2-one (2d): This compound was prepared from **3d** (202 mg, 0.6 mmol), according to the procedure described for **2a**. Purification by flash chromatography on silica gel (hexane/AcOEt, 9:1) afforded **2d** as a light yellow oil (102 mg, 62% yield). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1748, 1688 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 0.08 [s, 9 H, $Si(CH_3)_3$], 1.84 (t, J = 1.4 Hz 3 H, C=C-CH_3), 2.53 (dt, J = 11.2 Hz, J = 1.4 Hz, 1 H, C*H*HSiMe$_3$), 2.61 (dt, J = 11.2 Hz, J = 1.4 Hz, 1 H, CH*H*SiMe$_3$), 2.77 (m, 1 H, C*H*H), 3.31 (m, 1 H, CH*H*), 5.42 (dd, J = 8.6 Hz, J = 6.4 Hz, 1 H, C*H*Ph), 7.30–7.41 (m, 5 H, $CH_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = –0.9 [$Si(CH_3)_3$], 25.0 (C=C-*C*H_3), 27.4 (CH_2SiMe_3), 36.7 (*C*H_2CH_2O), 76.3 (CHPh), 114.7 (*C*=C-CH_3), 125.3 ($CH_{arom.}$), 128.0 ($CH_{arom.}$), 128.6 ($CH_{arom.}$), 141.3 ($C_{arom.}$), 154.7 (C=*C*-CH_3), 170.3 (C=O) ppm. R_f = 0.59 (silica gel, hexane/AcOEt, 8:2). MS: m/z (%) = 274 (4.7) $[M]^+$, 73 (100). HRMS: calcd. for $C_{16}H_{22}NaO_2Si$ [M] 297.1287; found 297.1292.

Representative Amination Procedures

Method A: To a stirred solution of the silylated α-ylidene-γ-butyrolactone **2** (1 mmol) in CH_2Cl_2 (1 mL), $NsONHCO_2Et$ (290 mg, 1 mmol) and CaO (56 mg, 1 mmol) were added portionwise at room temp. every hour, until the molar ratio of substrate/$NsONHCO_2Et$/CaO reported in Table 3 was reached. As the reaction was exothermic, during every addition the flask was cooled in an H_2O bath to avoid overheating. After the time reported in Table 3, the reaction was quenched by adding a pentane/CH_2Cl_2 solution (8:2). The resulting solid by-product was filtered and washed with the same solution. The organic phase was concentrated under reduced pressure and dried (Na_2SO_4). The crude mixture was purified by HPLC chromatography (hexane/AcOEt, 8:2).

Method B: To a stirred solution of the silylated α-ylidene-γ-butyrolactone **2** (1 mmol) in CH_2Cl_2 (1 mL), $NsONHCO_2Et$ (290 mg,

1 mmol) and CaO (56 mg, 1 mmol) were added portionwise at room temp. every hour, until the molar ratio of substrate/$NsONHCO_2Et$/CaO reported in Table 3 was reached. As the reaction was exothermic, during every addition the flask was cooled in an H_2O bath to avoid overheating. After the time reported in Table 3, the reaction was quenched by adding a pentane/CH_2Cl_2 solution (8:2). The resulting solid by-product was filtered and washed with the same solution. The organic phase was concentrated under reduced pressure and stirred with AcOH (0.56 mL, 10 mmol) for 48 h at room temp. The mixture was washed with saturated $NaHCO_3$, extracted with CH_2Cl_2, and the combined organic phases were dried (Na_2SO_4) and concentrated under reduced pressure. Reaction products were isolated by HPLC chromatography (hexane/AcOEt, 8:2).

Ethyl (3-Isopropenyl-2-oxotetrahydrofuran-3yl)carbamate (1a) and Ethyl {3-[1-Methyl-2-(trimethylsilyl)vinyl]-2-oxotetrahydrofuran-3-yl}carbamate (5a): These compounds were prepared from **2a** (198 mg, 1 mmol), according to amination method A. HPLC purification (hexane/AcOEt, 8:2) afforded **1a** (136 mg, 64% yield) and **5a** (29 mg, 10%) as colourless oils. **1a**: IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3430, 1774, 1723 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.24 (t, J = 7.1 Hz, 3 H, CH_3CH_2), 1.87 (s, 3 H, CH_3C=C), 2.69–2.93 (m, 2 H, CH_2CH_2O), 4.11 (q, J = 7.1 Hz, 2 H, CH_3CH_2), 4.17–4.25 (m, 1 H, CH_2CHHO), 4.40–4.50 (m, 1 H, CH_2CHHO), 5.12–5.16 (m, 2 H, C=CH_2), 5.34 (br. s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 14.4 (CH_3CH_2), 18.5 (CH_3C=C), 33.2 (CH_2CH_2O), 61.3 (C-NH), 63.1 (CH_3CH_2), 65.8 (CH_2O), 114.9 (C=CH_2), 139.7 (C=CH_2), 155.2 (CO_2Et), 175.0 (lactone C=O) ppm. R_f = 0.09 (silica gel, hexane/AcOEt, 8:2). MS: m/z (%) = 213 (2.3) $[M]^+$, 96 (100). HRMS: calcd. for $C_{10}H_{15}NNaO_4$ [M] 236.0899; found 236.0904. **5a**: IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3430, 1772, 1719 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 0.13 [s, 9 H, $Si(CH_3)_3$], 1.24 (t, J = 7.1 Hz, 3 H, CH_3CH_2), 1.92 (s, 3 H, CH_3C=C), 2.61–2.97 (m, 2 H, CH_2CH_2O), 4.11 (q, J = 7.1 Hz, 2 H, CH_3CH_2), 4.16 (t, J = 8.8 Hz, 1 H, $CHHO$), 4.43 (t, J = 8.9 Hz, 1 H, $CHHO$), 5.28 (s, 1 H, NH), 5.61 (s, 1 H, C=CH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = –0.3 [$Si(CH_3)_3$], 14.6 (CH_3CH_2), 17.4 (CH_3C=C), 33.1 (CH_2CH_2O), 61.2 (CH_3CH_2), 65.6 (CH_2O), 98.0 (C-NH), 128.3 (C=CH), 146.8 (C=CH), 155.2 (CO_2Et), 175.4 (lactone C=O) ppm. R_f = 0.16 (silica gel, hexane/AcOEt, 8:2). MS: m/z (%) = 285 (2.6) $[M]^+$, 73 (100). HRMS: calcd. for $C_{13}H_{23}NNaO_4Si$ [M] 308.1294; found 308.1290. Compound **1a** was also prepared from **2a** (198 mg, 1 mmol), according to amination method B. Purification by HPLC chromatography (hexane/AcOEt, 8:2) afforded **1a** as a colourless oil (155 mg, 73% yield).

Ethyl (2-Oxo-3-vinyltetrahydrofuran-3-yl)carbamate (1b): This compound was prepared from **2b** (74 mg, 0.4 mmol), according to amination method B and purified by HPLC chromatography (hexane/AcOEt, 8:2) to give **1b** as a colourless oil (56 mg, 70% yield). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3430, 1774, 1720 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.25 (t, J = 7.1 Hz, 3 H, CH_3CH_2), 2.63–2.88 (m, 2 H, CH_2CH_2O), 4.12 (q, J = 7.1 Hz, 2 H, CH_3CH_2), 4.22 (t, J = 8.5 Hz, 1 H, $CHHO$), 4.48 (t, J = 8.5 Hz, 1 H, $CHHO$), 5.25 (br. s, 1 H, NH), 5.40 (d, J = 10.4 Hz, 1 H, CH=CHH), 5.40 (d, J = 17.4 Hz, 1 H, CH=CHH), 5.97 (dd, J = 10.4 Hz, J = 17.4 Hz, 1 H, CH=CHH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 14.4 (CH_3CH_2), 34.3 (CH_2CH_2O), 60.7 (C-NH), 61.3 (CH_3CH_2), 65.5 (CH_2O), 118.1 (CH=CH_2), 133.6 (CH=CH_2), 155.1 (CO_2Et), 175.1 (lactone C=O) ppm. R_f = 0.32 (silica gel, hexane/AcOEt, 7:3). MS: m/z (%) = 199 (2.3) $[M]^+$, 82 (100). HRMS: calcd. for $C_9H_{13}NNaO_4$ [M] 222.0742; found 222.0746.

Ethyl [2-Oxo-3-(1-phenylvinyl)tetrahydrofuran-3-yl]carbamate (1c): This compound was prepared from **2c** (208 mg, 0.8 mmol), according to amination method B and purified by HPLC chromatography (hexane/AcOEt, 8:2) to afford **1c** as a colourless oil (159 mg, 55% yield). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3430, 1770, 1722 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.23 (t, J = 7.1 Hz, 3 H, CH_3CH_2), 2.61–2.80 (m, 1 H, $CHHCH_2O$), 2.89–3.16 (m, 1 H, $CHHCH_2O$), 3.80–4.00 (m, 1 H, CH_2CHHO), 4.11 (q, J = 7.1 Hz, 2 H, CH_3CH_2), 4.40 (m, 1 H, CH_2CHHO), 5.34 (br. s, 1 H, NH), 5.43 (s, 1 H, CH=CHH), 5.50 (s, 1 H, CH=CHH), 7.28–7.51 (m, 5 H, $CH_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 14.4 (CH_3CH_2), 33.7 (CH_2CH_2O), 61.4 (C-NH), 63.3 (CH_3CH_2), 65.5 (CH_2O), 118.2 (C=CH_2), 128.3($CH_{arom.}$), 128.4 ($CH_{arom.}$), 128.5 ($CH_{arom.}$), 137.7 ($C_{arom.}$), 145.6 (C=CH_2), 155.1 (CO_2Et), 175.3 (lactone C=O) ppm. R_f = 0.25 (silica gel, hexane/AcOEt, 7:3). MS: m/z (%) = 275 (0.6) $[M]^+$, 202 (100). HRMS: calcd. for $C_{15}H_{17}NNaO_4$ [M] 298.1055; found 298.1060.

Ethyl (3-Isopropenyl-2-oxo-5-phenyltetrahydrofuran-3-yl)carbamate (1d): This compound was prepared from **2d** (96 mg, 0.35 mmol), according to amination method B. Purification by HPLC chromatography (hexane/AcOEt, 8:2) afforded **1d** as a single diastereomer (colourless oil, 52 mg, 52% yield). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3430, 1771, 1723 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz, 25 °C): δ = 1.25 (t, J = 7.1 Hz, 3 H, CH_3CH_2), 1.80 (dd, J = 1.4 Hz, J = 0.7 Hz, 3 H, CH_3C=C), 2.57 (dd, J = 14.0 Hz, J = 6.1 Hz, 1 H, $CHHCHPh$), 3.31 (dd, J = 14.0 Hz, J = 8.6 Hz, 1 H, $CHHCHPh$), 4.12 (q, J = 7.1 Hz, 2 H, CH_3CH_2), 5.04 (q, J = 1.4 Hz, 1 H, CHH=C), 5.09 (br. s, 1 H, CHH=C), 5.25 (br. s, 1 H, NH), 5.81 (dd, J = 8.6 Hz, J = 6.1 Hz, 1 H, CHPh), 7.31–7.42 (m, 5 H, $CH_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz, 25 °C): δ = 14.5 (CH_3CH_2), 19.0 (CH_2=CCH_3), 40.8 (CH_2CH_2O), 61.6 (CH_3CH_2), 64.4 (CH_2CH_2O), 78.2 (CHPh), 115.2 (C=CH_2), 125.2 ($CH_{arom.}$), 128.2 ($CH_{arom.}$), 128.7 ($CH_{arom.}$), 139.7 ($C_{arom.}$), 141.3 (C=CH_2), 155.7 (CO_2Et), 174.9 (lactone C=O.) ppm. R_f = 0.19 (silica gel, hexane/AcOEt, 7:3). MS: m/z (%) = 289 (0.9) $[M]^+$, 216 (100). HRMS: calcd. for $C_{16}H_{19}NNaO_4$ [M] 312.1212; found 312.1220.

Acknowledgments

We thank the Italian Ministero dell'Istruzione dell'Università e della Ricerca (MIUR), and the University "La Sapienza" of Rome (National Project "Stereoselezione in Sintesi Organica. Metodologie ed Applicazioni") for financial support.

[1] a) D. Ma, W. Zhu, *J. Org. Chem.* **2001**, *66*, 348–350; b) R. Cannella, F. Clerici, M. L. Gelmi, M. Penso, D. Pocar, *J. Org. Chem.* **1996**, *61*, 1854–1856; c) U. Kazmaier, *Tetrahedron Lett.* **1996**, *37*, 5351–5354.

[2] S. J. deSolms, E. A. Giuliani, S. L. Graham, K. S. Koblan, N. E. Kohl, S. D. Mosser, A. I. Oliff, D. L. Pompiliano, E. Rands, T. H. Scholz, C. M. Wiscount, J. B. Gibbs, R. L. Smith, *J. Med. Chem.* **1998**, *41*, 2651–2656.

[3] a) Z.-Q. Luo, S. Su, S. K. Farrand, *J. Bacteriol.* **2003**, *185*, 5665–5672; b) J. A. Olsen, R. Severinsen, T. B. Rasmussen, M. Hentzer, M. Givskov, J. Nielsen, *Bioorg. Med. Chem. Lett.* **2002**, *12*, 325–328.

[4] M. L. Pedersen, D. B. Berkowitz, *J. Org. Chem.* **1993**, *58*, 6966–6975.

[5] A. B. Smith, III, H. Liu, R. Hirschmann, *Org. Lett.* **2000**, *2*, 2037–2040.

[6] a) T. Gasperi, M. A. Loreto, P. A. Tardella, E. Veri, *Tetrahedron Lett.* **2003**, *44*, 4953–4956; b) T. Gasperi, M. A. Loreto, A. Migliorini, P. A. Tardella, *Heterocycles* **2005**, *65*, 1447–1454.

[7] a) S. Fioravanti, M. A. Loreto, L. Pellacani, S. Raimondi, P. A. Tardella, *Tetrahedron Lett.* **1993**, *34*, 4101–4104; b) M. A. Loreto, P. A. Tardella, D. Tofani, *Tetrahedron Lett.* **1995**, *36*, 8295–

8298; c) F. Pompei, M. A. Loreto, P. A. Tardella, *Tetrahedron* **1997**, *53*, 15853–15858; d) M. A. Loreto, C. Pompili, P. A. Tardella, *Tetrahedron* **2001**, *57*, 4423–4427; e) T. Gasperi, M. A. Loreto, P. A. Tardella, A. Gambacorta, *Tetrahedron Lett.* **2002**, *43*, 3017–3020; f) T. Gasperi, M. A. Loreto, P. A. Tardella, *Tetrahedron Lett.* **2003**, *44*, 8467–8470.

[8] a) V. K. Aggarwal, B. A. Bethel, R. Giles, *Chem. Commun.* **1999**, 325–326; b) I. Fleming, P. Maiti, C. Ramarao, *Org. Biomol. Chem.* **2003**, *1*, 3989–4004.

[9] a) L. Chabaud, P. James, Y. Landais, *Eur. J. Org. Chem.* **2004**, 3173–3199; b) T. K. Sarkar, *Synthesis* **1990**, 969–983; c) S. BouzBouz, E. De Lemos, J. Cossy, *Adv. Synth. Catal.* **2002**, *344*, 627–630; d) J.-H. Pi, X. Huang, *Synlett* **2003**, 2413–2415; e) S. Streiff, N. Ribeiro, L. Désaubry, *J. Org. Chem.* **2004**, *69*, 7592–7598.

[10] Inter alia: a) L. F. Tietze, I. Hiriyakkanavar, H. P. Bell, *Chem. Rev.* **2004**, *104*, 3453–3516; b) P. Espinet, A. M. Echavarren, *Angew. Chem.* **2004**, *116*, 4808–4839; *Angew. Chem. Int. Ed.* **2004**, *43*, 4704–4734 and references cited therein; c) R. R. Tykwinski, *Angew. Chem.* **2003**, *115*, 1604–1606; *Angew. Chem. Int. Ed.* **2003**, *42*, 1566–1568; d) W. A. Herrmann, K. Öfele, D. Preysing, S. K. Schneider, *J. Organomet. Chem.* **2003**, *687*, 229–248; e) A. C. Hillier, G. A. Grasa, M. S. Viciu, H. M. Lee, C. Yang, S. P. Nolan, *J. Organomet. Chem.* **2002**, *653*, 69–82.

[11] a) G. A. Howie, I. K. Stamos, J. M. Cassady, *J. Med. Chem.* **1976**, *19*, 309–313; b) J. R. Blanton, R. E. Salley, *J. Org. Chem.* **1989**, *54*, 723–726; c) R. C. D. Brown, C. J. R. Bataille, G. Bruton, J. D. Hinks, N. A. Swain, *J. Org. Chem.* **2001**, *66*, 6719–6728.

[12] D. B. Reitz, *J. Org. Chem.* **1979**, *44*, 4707–4709.

[13] P. A. Jacobi, R. W. DeSimone, I. Ghosh, J. Guo, S. H. Leung, D. Pippin, *J. Org. Chem.* **2000**, *65*, 8478–8489.

[14] P. J. Stang, W. L. Treptow, *J. Med. Chem.* **1981**, *24*, 468–472.

[15] Attempts at purification by chromatography on silica gel only were pursued, but lower yields were obtained.

[16] J. Jonas, *Collect. Czech. Chem. Commun.* **1984**, *49*, 1907–1913.

[17] C. Amatore, A. Jutand, M. A. M'Barki, *Organometallics* **1992**, *11*, 3009–3013.

[18] We have previously observed a similar behaviour in the aziridination of a cyclic γ-silylated α,β-unsaturated ester (see ref.[7c]).

[19] I. Fleming, J. Dunoguès, R. Smithers, *Org. React.* **1989**, *37*, 57–575.

Received: June 21, 2006
Published Online: September 7, 2006

