1,4-Reductive Addition of Hydrazoic Acid to γ-Oxo-α,β-unsaturated δ-Lactones and -Lactams: A Convenient Route to α-Amino-γ-oxo-α,β-unsaturated δ-Lactones and -Lactams

Sofia D. Koulocheri,[a] Serkos A. Haroutounian,*[a] Costas D. Apostolopoulos,[a] Raj K. Chada,[b] and Elias A. Couladouros*[a,c]

Keywords: Oxo enamines / Reductive addition / Hydrazoic acid / δ-Lactones / δ-Lactams

γ-Oxo-α,β-unsaturated δ-lactones and lactams, which are easily accessible from their corresponding 2-furylcarbinols, were used as substrates for the 1,4-reductive addition of hydrazoic acid. The outcome of the reaction is the formation, in high yields, of the corresponding α-amino-γ-oxo-α,β-unsaturated δ-lactones and -lactams, compounds of great biological and synthetic interest.

Introduction

Derivatives of α,β-unsaturated δ-lactones and -lactams are often found as structural subunits of a wide variety of natural products and analogues[1] which exhibit valuable biological activities.[2] These compounds have been used as substrates for the addition of various nucleophiles and 1,2-binuclophiles, leading to the formation of biologically active compounds, such as diazepinones and thiazepinones.[3]

In the course of the authors' long-standing research work in the synthesis of novel biologically interesting polyfunctionalized heterocycles (e.g. amino sugars, amino azasugars, and unnatural amino acids), the conjugate addition of hydrazoic acid to α,β-unsaturated heterocyclic ketones[4] and quinones[5] has been studied. Currently, the research interest is focused on the addition of hydrazoic acid to γ-oxo-α,β-unsaturated δ-lactones and -lactams of general formulae **3**, which are easily accessible from 2-furylcarbinols **1**, according to previous research findings.[6] These compounds represent an intriguing case, since their enhanced reactivity toward nucleophiles suggests that they are perfectly fitted for use as substrates in the conjugate addition of hydrazoic acid. Such has proven to be the case and herein is presented the synthesis of δ-lactones and -lactams containing the oxo enamine moiety. The latter constitute an unusual structural backbone which is often crucial for biological activity[7] or for their use as valuable intermediates in organic synthesis as "push-pull" alkenes.[8]

Literature reports on the synthesis of oxo enamine derivatives by replacement of a vinylic hydrogen atom in α,β-unsaturated ketones are scarce, and none refer to the direct introduction of an unsubstituted amino group.[9] Most of the methods reported hitherto of oxo enamine preparation are limited either to the palladium-catalyzed arylamination,[10] or amidation,[11] or to a base-induced two-step β-elimination.[12] All these syntheses require vigorous reaction conditions,[9] and the course of the reaction depends strongly on the applicable substrates.[13] Thus, the reported reaction represents a useful straightforward route to synthetically important oxo enamine derivatives under mild experimental conditions which are tolerable for various functional groups.

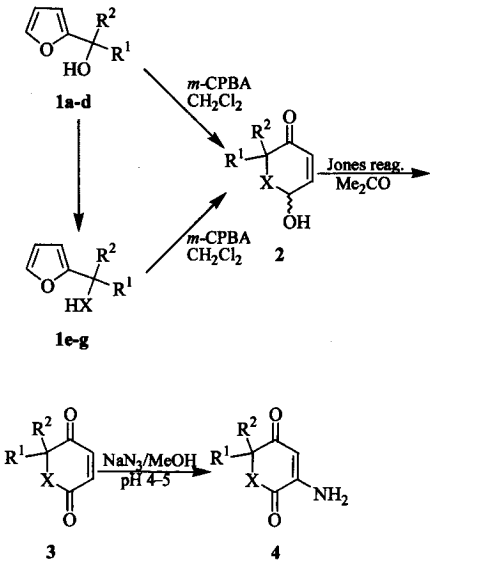
Results and Discussion

The starting compounds, 2-furylcarbinols **1a–d**[6] (Scheme 1) were obtained by treating the corresponding carbonyl compounds with 2-furyllithium, while *N*-tosylfurfurylamines **1e–g** were prepared by the reaction of 2-furylcarbinols with hydrazoic acid, followed by hydrogenation in the presence of palladium and tosylation of the resulting amine. These compounds underwent an oxidative rearrangement sequence on their furan part upon treatment with 3-chloroperbenzoic acid (*m*-CPBA),[14] furnishing the fairly stable pyranones **2a–c**[6] and azapyranones **2f,g**. In the case of tosylamine **1e**, however, reaction with *m*-CPBA under diverse reaction conditions and stoichiometry produced only the spirolactam **3e** and no trace of the expected azapyranone **2e** was detected. Furthermore, the use of a larger excess of *m*-CPBA for prolonged reaction times resulted in the subsequent transformation of azapyranones **2f,g** to δ-lactams **3f,g**. Similar behavior was not observed for the 2-furylcarbinols, whose reaction was ended at the 2*H*-pyranone formation stage **2a–c**. Nevertheless, all intermediates **2a–g** were converted by Jones oxidation to their corresponding δ-lactones and -lactams **3a–g** in high yields.

Treatment of the substrates **3a–g** with hydrazoic acid under various reaction conditions gave no trace of the expected standard Michael addition product (azide). On the contrary, a product identified as the corresponding aminoenyl derivative **4** was obtained in high yield. The structure

[a] Chemistry Laboratory, Agricultural University of Athens, Iera odos 75, Athens 11855, Greece
Fax: (internat.) + 30-1/5294265
E-mail: sehar@aua.gr
[b] Department of Chemistry, The Scripps Research Institute, 10666 North Torrey Pines Rd., La Jolla, CA 92037, USA
[c] Organic and Bioorganic Chemistry Laboratory, NCSR Democritos, P. O. Box 60228, Ag. Paraskevi 15310, Greece

 © WILEY-VCH Verlag GmbH, D-69451 Weinheim, 1999 1434–193X/99/0606–1449 $ 17.50+.50/0



Entry	X	R¹	R²	Yield (%) 2	3	4
a	O			79	98	94
b	O		Me	81	93	88
c	O		Me	85	95	85
d	O		H	-	-	-
e	NTs			-	65	83
f	NTs		H	67	96	77
g	NTs	$CH_2OTBDPS$	H	80	93	75

Scheme 1. Synthetic route to oxo enamines **1**–**4**

of this unexpected and rather peculiar product was established by spectroscopic and analytical data, while the structure of the compound **4c** was unequivocally established by X-ray crystallographic analysis. To our knowledge there are no examples of a similar behavior in the literature, apart from reports concerning the 1,4-reductive addition of azide anion to naphthoquinones,[5][15] indicating that there are electronical and structural similarities between these two classes of compounds (Scheme 2).

Intending to determine the optimal reaction conditions, we have used a variety of solvents and experimental conditions, concluding that the use of a protic and rather polar solvent (e.g. methanol, ethanol, THF/H_2O, DMF/H_2O) is a prerequisite for the reaction, since no reaction occurred in their absence. The best results, however, were obtained when the reaction was performed in methanol. We have also found that in order to obtain high yields and avoid the formation of by-products, it is essential to perform the reaction in a moderately acidic (buffered, pH = 4–5) environment. At high pH values, solvolysis is the competitive reaction which gradually predominates, while in stronger acidic environment the reaction time is prolonged substantially, with a consequent sharp decrease in the yield. It is further noticeable that at high pH values the disubstituted substrates

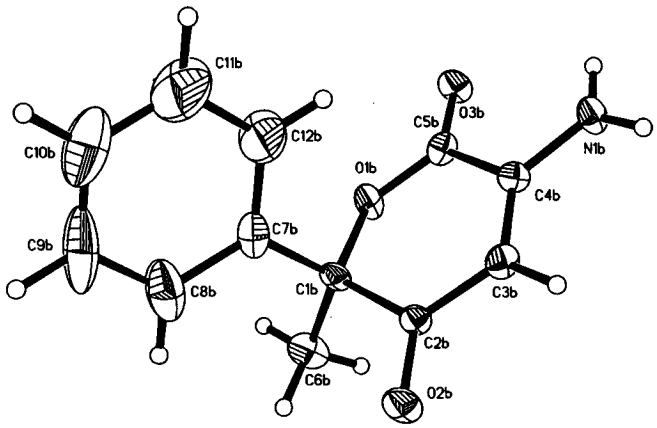
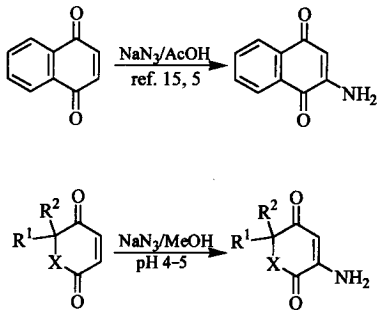
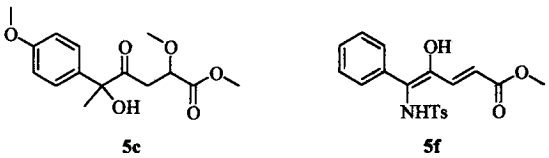


Figure 1. ORTEP drawing of compound **4c** (ellipsoids at 30% probability)



Scheme 2. Hydrazoic acid addition to naphthoquinone and γ-oxo-α,β-unsaturated δ-lactones and -lactams

(lactones **3a**–**c** and lactam **3e**) behave in a different fashion compared to the monosubstituted ones (lactams **3f**,**g**). More specifically, reaction of monosubstituted lactam **3f** with hydrazoic acid in the presence of a strong base furnishes the highly conjugated anionic form of compound **5f** (Scheme 3), thus precluding the possibility of any reductive addition. On the contrary, a similar enolization process is not possible for the disubstituted δ-lactone **3c** and methanolysis is followed by the conjugate addition of a methoxy ion yielding compound **5c**.

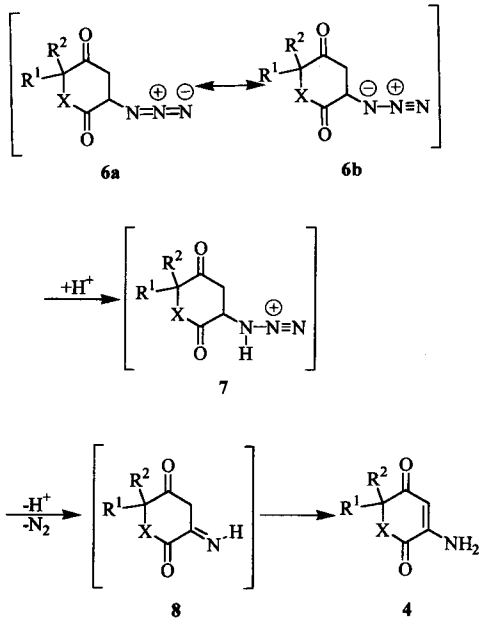


Scheme 3. Byproducts formed in strong basic environment

The reported reaction provides high yields for substrates having diverse substituents, in contrast to literature methods which report that the yields depend strongly on the substitution.[10] In the case of substrate **3d**, however, the reaction leads rapidly to a complex mixture of products, presumably because the facile enolization of the carbonyl group gives rise to several condensation products, precluding the possibility of isolating a single major product derived through 1,4-azide addition to the unsaturated system.

The above pathway is not favored when tosylated azaheterocycles are used as substrates and their aminoenyl derivatives were always obtained in relatively good yields. For the purposes of comparison the synthesis of the azaheterocyclic analogues of disubstituted phenyl derivatives **3b,c** was also attempted. However, conversion of the phenyl-2-furylcarbinols to their corresponding 2-furfurylamines failed, because under the reaction conditions the labile conjugated tertiary hydroxy group was eliminated. Thus, by ejection of a water molecule the very stable allylic hydrocarbon was formed making the synthesis of disubstituted phenyl-δ-lactams impossible by this pathway.

The mechanism proposed to explain the outcome of this reaction is described in Scheme 4 and suggests that the addition of the azide moiety produces tautomers **6a,b**, which under acidic conditions are converted into the imino intermediate **8**, by loss of dinitrogen. The latter is readily transformed to its stable aminoenyl tautomer **4**. These findings and the proposed mechanism are reminiscent of the previously known conversion of 2-azido ketones to 2-amino-α,β-unsaturated ketones and the addition of hydrazoic acid to naphthoquinones.[5,15,16]



Scheme 4. Mechanism of azide anion addition to γ-oxo-α,β-unsaturated δ-lactones and -lactams

In summary, the 1,4-reductive addition of hydrazoic acid to γ-oxo-α,β-unsaturated δ-lactones and -lactams presented provides a simple and efficient route for the synthesis of their corresponding α-aminoenyl derivatives, compounds of synthetic and biological interest. Further studies on synthetic applications and biological activity of these compounds are currently in progress.

Experimental Section

General: M.p. (uncorrected): Büchi melting-point apparatus. – FT IR: Nicolet Magna 750, series II. Samples were recorded as KBr pellets, unless otherwise stated. – ^{1}H NMR: Bruker AC 200 in $CDCl_3$ using TMS as internal standard. – Elemental analyses: Microanalytical Service, Laboratory of the University of Illinois. – Flash chromatography: 32–63-mm silica-gel packing (Merck). All reactions were carried out under argon and anhydrous conditions. They were monitored by thin-layer chromatography using TLC sheets coated with silica gel 60 F_{254} (Merck). – All starting materials were purchased from Aldrich (analytical reagent grades) and used without further purification. Solvents were dried by distillation prior to use. The following compounds were prepared according to literature procedures: 2-(*tert*-Butyldiphenylsilyloxy)-1-(furan-2-yl)ethanol (**1g**),[4b] 2-furylcarbinols **1b–d**, 2*H*-pyran-3-ones **2a–d** and δ-lactones **3a–d**.[6]

General Procedure for the Synthesis of *N*-Tosylfurfurylamines from 2-Furylcarbinols (3 Steps): 2-Furylcarbinol (6 mmol) was dissolved in an ice-cold solution of hydrazoic acid (30 mL, 0.27 N)[17] in benzene, and concd. H_2SO_4 (0.2 mL) added. After 1 h of stirring at that temp., the reaction was quenched with an ice-cold solution of ammonia (15 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (20 mL). The combined organic layers were washed with NH_4Cl and concentrated under reduced pressure yielding a slurry which was chromatographed using hexane as eluent to give 5.4 mmol of the desired azide. The latter was dissolved in ethyl acetate (8 mL) and hydrogenated in the presence of Pd/C (0.1 g, 10%) under 1 bar pressure for 40 min. The reaction mixture was filtered through Celite and dichloromethane (10 mL) and triethylamine (6.8 mmol) were added to the filtrate. The resulting solution was cooled to 0°C and *p*-toluenesulfonyl chloride (6.8 mmol) was added in portions under stirring. The reaction was allowed to reach room temp. and stirred for additional 3 h. Then, the mixture was extracted successively with $NaHCO_3$ and brine, the solvent removed by means of a rotary evaporator and chromatographed using ethyl acetate/hexane (1:4) as eluent yielding the desired product in pure crystalline form.

2-(1-Azidocyclohexyl)furan: Yield 1.068 g (93%). – IR (neat): $\tilde{\nu}$ = 2103 cm^{-1} (N_3), 1012, 745 (furan). – ^{1}H NMR: δ = 1.21–1.79 (m, 6 H, CH_2), 1.96 (m, 4 H, CH_2), 6.27 (d, *J* = 3.2 Hz, 3-H), 6.34 (dd, *J* = 3.2, 1.8 Hz, 4-H), 7.4 (d, *J* = 1.8 Hz, 5-H).

2-(2-Furyl)cyclohexyl-*N*-(4-tolylsulfonyl)amine (1e): Yield 1.35 g (81%). – M.p. 145–146°C. – IR: $\tilde{\nu}$ = 3261 cm^{-1} (N–H). – ^{1}H NMR: δ = 1.40 (m, 4 H, CH_2), 1.68 (m, 2 H, CH_2), 2.10 (m, 4 H, CH_2), 2.33 (s, 3 H, CH_3), 5.02 (s, NH), 6.05 (m, 2 H, 3-,4-H), 6.88 (m, 1 H, 5-H), 7.10 (d, *J* = 8.2 Hz, 2 H, Ph–H), 7.45 (d, *J* = 8.2 Hz, 2 H, Ph–H). – $C_{17}H_{21}NO_3S$ (319.4): calcd. C 63.92, H 6.63, N 4.39; found C 63.88, H 6.51, N 4.50.

2-[Azido(phenyl)methyl]furan: Yield 0.86 g (72%). – IR (neat): $\tilde{\nu}$ = 2100 cm^{-1} (N_3), 1010, 740 (furan). – ^{1}H NMR: δ = 5.65 (s, 1 H, CH), 6.20 (d, *J* = 3.1 Hz, 1 H, 3-H), 6.34 (dd, *J* = 3.1, 1.9 Hz, 1 H, 4-H), 7.39 (m, 6 H, 5-H, Ph–H).

***N*-Phenyl-*N*-[(4-tolylsulfonyl)methyl](2-furyl)amine (1f):** Yield 1.04 g (74%). – M.p. 132–133°C. – IR: $\tilde{\nu}$ = 3276 cm^{-1} (N–H). – ^{1}H NMR: δ = 2.37 (s, 3 H, CH_3), 5.20 (d, *J* = 7.6 Hz, 1 H, NH), 5.60 (d, *J* = 7.6 Hz, 1 H, CH), 5.99 (d, *J* = 3.1 Hz, 1 H, 3-H), 6.18 (dd, *J* = 3.1, 1.9 Hz, 1 H, 4-H), 7.19 (m, 8 H, 5-H, Ph–H), 7.58 (d, *J* = 8.3 Hz, 2 H, Ph–H). – $C_{18}H_{27}NO_3S$ (327.1): calcd. C 66.03, H 5.23, N 4.28; found C 66.21, H 5.05, N 4.39.

(2-Azido-2-furan-2-yl)ethoxy-*tert*-butyldiphenylsilane. – Preparation via the Corresponding Unisolated Mesylate and Subsequent Reaction with Sodium Azide:[18] Yield 1.928 g (82%). – IR (neat): $\tilde{\nu}$ = 2110 cm^{-1} (N_3), 1020, 740 (furan). – ^1H NMR: δ = 1.05 (s, 9 H, C–CH_3), 3.95 (d, *J* = 5.4 Hz, 2 H, CH_2), 4.57 (t, *J* = 5.4 Hz, 1 H, CH), 6.30 (m, 2 H, 3-H,4), 7.25–7.70 (m, 11 H, 5-H, Ph–H).

***N*-(4-Tolylsulfonyl)-2-(*tert*-butyldiphenylsilyloxy)-1-(2-furyl)ethylamine (1g):** Yield 2.215 g (87%). – M.p. 102–103°C. – IR: $\tilde{\nu}$ = 3281 cm^{-1} (N–H). – ^1H NMR: δ = 1.02 (s, 9 H, C–CH_3), 2.41 (s, 3 H, CH_3), 3.81 (m, 2 H, CH_2), 4.55 (m, 1 H, CH), 5.24 (d, *J* = 7.9 Hz, 1 H, NH), 6.12 (d, *J* = 3.1 Hz, 1 H, 3-H), 6.22 (dd, *J* = 3.1, 1.8 Hz, 1 H, 4-H), 7.20 (d, *J* = 8.6 Hz, 2 H, Ph–H), 7.45 (m, 11 H, 5-H, Ph–H), 7.64 (d, *J* = 8.6 Hz, 2 H, Ph–H). – $C_{29}H_{33}NO_4SSi$ (519.7): calcd. C 67.02, H 6.40, N 2.70; found C 66.89, H 6.26, N 2.61.

General Procedure for the Synthesis of δ-Lactams from *N*-Tosylfurfurylamines (2 Steps): m-Chloroperbenzoic acid (3.3 mmol, 70%) was added in portions to a stirred solution of *N*-tosylfurfurylamine (2.2 mmol) in chloroform (10 mL), while the temperature was maintained below 10°C. The reaction mixture was allowed to reach room temp. and stirred for an additional 3 h. Then the reaction mixture was washed successively with 20% KI, 30% $Na_2S_2O_3$, concd. $NaHCO_3$, water, brine and concentrated to a yellowish solid which was chromatographed (ethyl acetate/hexane, 3:7) to give the desired azapyranone as solid which was recrystallized from diethyl ether/hexane. 0.5 mL of Jones reagent[19] was added dropwise to an ice-cold solution of the product (1.5 mmol) in acetone(10 mL). After stirring for an additional 15 min, the solid inorganic byproducts were removed by decantation, the liquid layer was concentrated under reduced pressure and the resulting residue was partitioned between ethyl acetate (20 mL) and water (10 mL). The organic layer was separated, washed with brine, dried with $MgSO_4$, and concentrated in vacuo yielding a residue which was crystallized from cold diethyl ether.

1-(4-Tolylsulfonyl)-1-azaspiro[5.5]undec-3-ene-2,5-dione (3e): Yield 0.477 g (65%). – M.p. 124–125°C. – IR: $\tilde{\nu}$ = 1710 cm^{-1} (C=O), 1680 (N–C=O). – ^1H NMR: δ = 1.80 (m, 10 H, H-7,8,9,10,11), 2.43 (s, 3 H, CH_3), 6.53 (d, *J* = 10.1 Hz, 1 H, 3-H), 6.61 (d, *J* = 10.1 Hz, 1 H, 4-H), 7.35 (d, *J* = 8 Hz, 2 H, Ph–H), 7.89 (d, *J* = 8 Hz, 2 H, Ph–H). – $C_{17}H_{19}NO_4S$ (333.4): calcd. C 61.24, H 5.74, N 4.20; found C 61.33, H 5.59, N 4.01.

6-Hydroxy-2-phenyl-1-(4-tolylsulfonyl)-1,6-dihydro-2*H*-pyridin-3-one (2f): Yield 0.5 g (67%). – M.p. 110–112°C. – IR: $\tilde{\nu}$ = 3350 cm^{-1} (OH), 1696 (C=O). –^1H NMR: δ = 2.37 (s, 3 H, CH_3), 3.45 (s, 1 H, OH), 5.45 (s, 1 H, 2-H), 5.95 (m, 1 H, 6-H), 6.15 (d, *J* = 10.6 Hz, 1 H, 4-H), 6.85 (m, 1 H, 5-H), 7.15 (d, *J* = 8.3 Hz, 2 H, Ph–H), 7.30 (m, 5 H, Ph–H), 7.61 (d, *J* = 8.3 Hz, 2 H, Ph–H). – $C_{18}H_{17}NO_4S$ (343.4): calcd. C 62.96, H 4.99, N 4.08; found C 63.01, H 4.78, N 4.14.

6-Phenyl-1-(4-tolylsulfonyl)-1,6-dihydropyridine-2,5-dione (3f): Yield 0.492 g (96%). – M.p. 165–166°C (dec). – IR: $\tilde{\nu}$ = 1739 cm^{-1} (C=O), 1697 (N–C=O). – ^1H NMR: δ = 2.37 (s, 3 H, CH_3), 6.05 (s, 1 H, 6-H), 6.64 (d, *J* = 10.2 Hz, 1 H, 3-H), 6.84 (d, *J* = 10.2 Hz, 1 H, 4-H), 7.15 (d, *J* = 8.3 Hz, 2 H, Ph–H), 7.28 (m, 5 H, Ph–H), 7.50 (d, *J* = 8.3 Hz, 2 H, Ph–H). – $C_{18}H_{15}NO_4S$ (341.4): calcd. C 63.33, H 4.43, N 4.10; found C 6.14, H 4.30, N 4.08.

2-(*tert*-Butyldiphenylsilyloxymethyl)-6-hydroxy-1-(4-tolylsulfonyl)-1,6-dihydro-2*H*-pyridin-3-one (2g): Yield 0.943 g (80%). – M.p. 118–119°C. – IR: $\tilde{\nu}$ = 3360 cm^{-1} (OH), 1700 (C=O). – ^1H NMR: δ = 0.91 (s, 9 H, C–CH_3), 2.43 (s, 3 H, CH_3), 3.60 (dd, *J* = 10.6, 2.4 Hz, 1 H, CH_{2a}), 3.89 (dd, *J* = 10.6, 2.4 Hz, 1 H, CH_{2b}), 4.54 (m, 1 H, 2-H), 4.90 (br., 1 H, OH), 6.09 (m, 1 H, 6-H), 6.19 (d, *J* = 10.4 Hz, 1 H, 4-H), 7.07 (dd, *J* = 10.4, 4.8 Hz, 1 H, 5-H), 7.32 (m, 12 H, Ph–H), 7.78 (d, *J* = 8 Hz, 2 H, Ph–H). – $C_{29}H_{33}NO_5SSi$ (535.7): calcd. C 65.02, H 6.21, N 2.61; found C 64.78, H 6.02, N 2.79.

6-(*tert*-Butyldiphenylsilyloxymethyl)-1-(4-tolylsulfonyl)-1,6-dihydropyridine-2,5-dione (3g): Yield 0.745 g (93%). – M.p. 200–201°C (dec.). – IR: $\tilde{\nu}$ = 1725 cm^{-1} (C=O), 1690 (N–C=O). – ^1H NMR: δ = 0.89 (s, 9 H, C–CH_3), 2.44 (s, 3 H, CH_3), 4.15 (m, 2 H, CH_2), 5.01 (m, 1 H, 6-H), 6.68 (d, *J* = 10.2 Hz, 1 H, 3-H), 6.73 (d, *J* = 10.2 Hz, 1 H, 4-H), 7.25 (d, *J* = 8.6 Hz, 2 H, Ph–H), 7.41 (m, 10 H, Ph–H), 7.91 (d, *J* = 8.6 Hz, 2 H, Ph–H). – $C_{29}H_{31}NO_5SSi$ (533.7): calcd. C 65.26, H 5.85, N 2.62; found C 65.39, H 6.01, N 2.71.

General Procedure for the Synthesis of Enamines from α,β-Unsaturated δ-Lactones and -Lactams: A stirred solution of dione **3** (1 mmol) in methanol (20 mL) was buffered with the addition of a 1:1 mixture of AcOH/AcONa. Then a seven-fold excess (7 mmol) of sodium azide was added portionwise and the reaction was run for 6–12 h. The reaction mixture was partitioned in ethyl acetate/water (40 mL, 3:1) and the organic layer washed with water, brine, dried with $MgSO_4$ and concentrated under vacuum. Chromatographic purification (ethyl acetate/hexane, 1:2) furnished the desired product as white solid.

3-Amino-1-oxaspiro[5.5]undec-3-ene-2,5-dione (4a): Yield 0.183 g (94%). – M.p. 209–210.5°C. – IR: $\tilde{\nu}$ = 1740 cm^{-1} (O–C=O), 3430, 3260 (NH_2), 1660 (=C–C=O). – ^1H NMR: δ = 1.36–2.08 (m, 10 H, 7-,8-,9-,10-11-H), 5.32 (s, 2 H, NH_2), 5.73 (s, 1 H, 4-H). – $C_{10}H_{13}NO_3$ (195.2): calcd. C 61.53, H 6.71, N 7.17; found C 61.61, H 6.66, N 7.19.

3-Amino-6-methyl-6-phenyl-2*H*-pyran-2,5(6*H*)-dione (4b): Yield 0.19 g (88%). – M.p. 127–129°C. – IR: $\tilde{\nu}$ = 1730 cm^{-1} (O–C=O), 3430, 3330 (NH_2), 1670 (=C–C=O). – ^1H NMR: δ = 1.95 (s, 3 H, CH_3), 5.50 (br., 2 H, NH_2), 5.70 (s, 1 H, 4-H), 7.25–7.45 (m, 5 H, Ph–H). – $C_{12}H_{11}NO_3$: calcd. 217.0739; found 217.0741.

3-Amino-6-methoxyphenyl-6-methyl-2*H*-pyran-2,5(6*H*)-dione (4c): Yield 0.21 g (85%). – M.p. 165–167°C . – IR: $\tilde{\nu}$ = 1730 cm^{-1} (O–C=O), 3420, 3310 (NH_2), 1660 (=C–C=O). – ^1H NMR: δ = 1.93 (s, 3 H, CH_3), 3.81 (s, 3 H, CH_3O), 5.34 (s, 2 H, NH_2), 5.72 (s, 1 H, 4-H), 6.85 (d, *J* = 8.8 Hz, 2 H, Ph–H), 7.40 (d, *J* = 8.8 Hz, 2 H, Ph–H). – $C_{13}H_{13}NO_4$ (247.3): calcd. C 63.15, H 5.30, N 5.66; found C 63.35, H 5.19, N 5.69.

3-Amino-1-(4-tolylsulfonyl)-1-azaspiro[5.5]undec-3-ene-2,5-dione (4e): Yield 0.289 g (83%). – M.p. 211–213°C. – IR: $\tilde{\nu}$ = 1700 cm^{-1} (C=O), 3440, 3320 (NH_2), 1635 (N–C=O). – ^1H NMR: δ = 1.42–2.04 (m, 10 H, 7-,8-,9,-10-,11-H), 2.44 (s, 3 H, CH_3), 5.19 (br., 2 H, NH_2), 5.63 (s, 1 H, 4-H), 7.45 (d, *J* = 8.2 Hz, 2 H, Ph–H), 7.81 (d, *J* = 8.2 Hz, 2 H, Ph–H). – $C_{17}H_{20}N_2O_4S$ (348.4): calcd. C 58.60, H 5.79, N 8.04; found C 58.89, H 5.61, N 8.11.

3-Amino-6-phenyl-1-(4-tolylsulfonyl)-1,6-dihydropyridine-2,5-dione (4f): Yield 0.275 g (77%). – M.p. 226–227 (dec)°C. – IR: $\tilde{\nu}$ = 3430, 3290 cm^{-1} (NH_2), 1705 (C=O), 1630 (N–C=O). – ^1H NMR: δ = 2.37 (s, 3 H, CH_3), 5.42 (s, 2 H, NH_2), 5.78 (s, 1 H, 4-H), 6.15 (s, 1 H, 6-H), 7.22 (d, *J* = 8.3 Hz, 2 H, Ph–H), 7.31–7.52 (m, 5 H, Ph–H), 7.61 (d, *J* = 8.3 Hz, 2 H, Ph–H). – $C_{18}H_{16}N_2O_4S$ (356.4): calcd. C 60.66, H 4.53, N 7.86; found C 60.88, H 4.61, N 7.55.

3-Amino-6-(*tert*-butyldiphenylsilyloxymethyl)-1-(4-tolylsulfonyl)-1,6-dihydropyridine-2,5-dione (4g): Yield 0.410 g (75%). – M.p. 239–241 (dec)°C. – IR: $\tilde{\nu}$ = 1700 cm^{-1} (C=O),3465, 3310 (NH_2),