ONE-POT SYNTHESIS OF α , β -UNSATURATED BUTYROLACTAMS FROM ALLYL AMINES José Barluenga, ^{*} Francisco J. Fañanás, Francisco Foubelo, and Miguel Yus Departamento de Química Organometálica, Facultad de Química, Universidad de Oviedo, 33071 Oviedo, Spain

<u>Summary</u>: The successive reaction of different allylamines 1 with <u>n</u>-butyl-lithium, <u>t</u>-butyl-lithium, and diethyl carbonate at temperatures ranging between ~50 and 20°C leads after hydrolysis to the corresponding α , β -unsaturated butyrolactams 3 in an one-pot process.

Although a wide methodology has been developed for the construction of the α,β -butenolide ring,¹ only a few examples are reported for the preparation of their nitrogen analogues,² the most important being the oxidation of pyrrole derivatives. α,β -Unsaturated butyrolactams, which can in part isomerize to the corresponding β,γ -systems,³ are important intermediates in the synthesis of different natural products,⁴ or pyrrolic skeletons⁵ such as pyrrole pigments.⁶ On the other hand, we have very recently reported⁷ the direct lithiation of allyl amines of the type 1, which takes place in a regio and stereoselective manner yielding the corresponding γ -functionalized organolithium intermediates 2. We describe here the direct preparation of α,β -unsaturated butyrolactams by in situ reaction of intermediates 2 with diethyl carbonate.

The successive treatment of allylamines 1 with <u>n</u>-butyl-lithium at -50 to -30°C and <u>t</u>-butyl-lithium at temperatures ranging between -30 and 20°C led to the intermediates 2;⁷ the in situ reaction of these dianionic species with diethyl carbonate at -50 to 20°C afforded after hydrolysis the corresponding α,β -unsaturated butyrolactams 3 (Scheme 1 and Table 1).



Scheme 1. Reagents and conditions: i, $Bu^{n}Li$, -50 to -30°C; ii, $Bu^{t}Li$, -30 to 20°C; iii 0=C(OEt)₂, -50 to 20°C. In the case of starting from methallylaniline (1d) the corresponding allylic lithiation took place exclusively affording the intermediate 4d;⁷ the same reaction of 4d with diethyl carbonate as above yielded directly the unexpected product 3d, arisen from the expected butyrolactam 5d by an isomerization process in the basic reaction conditions (Scheme 2 and Table 1, entry 4).



Scheme 2.

Entry	Starting allyl amines			1 Inter-		Butyrolactam 3		
	No.	R ¹	R ²	R ³	mediate 2 ~	No.	Yield (%) ^b	M.p./°C ^c
1	1a ~~	Pr ⁱ	Ме	н	2a ~~	3a ~~	88	oil ^d
2	1b ~~	Ph	Н	н	2b ~~	3b ~~	71	90-92
3	1c ~~	Ph	н	Me	2c	3c ~~	78	97-98
4	1d ~~	Ph	Ме	н	4d	3d ~~	74	87-88
5	1e ~~	Су	н	н	2e ~~	3e ~~	68	oil ^e
6	1f ~~	Су	н	Me	2f ~~	3f ~~	69	$\texttt{oil}^{\mathbf{f}}$
7	1g ~~	Су	Me	н	2g ~~	3g ~~	77	68-70

Table 1. Preparation of α,β -unsaturated butyrolactams 3 from allylamines 1

^a All products 3 gave satisfactory spectral data (IR, ¹H and ¹³C NMR, and mass spectra). [•]^b Isolated yield based on the starting allyl amine 1. [•] From hexane-CH₂Cl₂. ^d \underline{R}_{F} 0.41 (silica gel, THF:hexane 3:1). ^e \underline{R}_{F} 0.41 (silica gel, THF:hexane 3:1).

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The use of diethyl carbonate is essential in the carbonation step, since the reaction with other agents such as ethyl chloroformate or carbon dioxide did not lead to the expected lactams 3. Thus, with ethyl chloroformate a mixture of products of <u>C</u>- and/or <u>N</u>-carbonation took place. The reaction of intermediates 2 with carbon dioxide occurred without further cyclization; so, in the case of the intermediate 2e the corresponding aminoacid salt 6e was formed, which did not undergo cyclization and in the subsequent esterification with anhydrous ethanol and hydrogen chloride suffers isomerization to give the corresponding <u>E</u>-aminoester 7e as the reaction product (Scheme 3).⁸



In conclusion, we think that the methodology described in this paper represents a new approach to the α, β -unsaturated butyrolactam moiety from allyl amines and an one-carbon atom fragment (Scheme 4).



In a typical reaction, to a stirred solution of the corresponding amine 1 (5 mmol) in diethyl ether (25 ml) was added an ethereal solution of <u>n</u>-butyllithium (5 mmol) at -50°C under argon and stirring was continued for 20 min at temperatures ranging between -50 and -30°C. To the resulting mixture was added a pentane solution of <u>t</u>-butyl-lithium (6 mmol) at -30°C and it was stirred for 2-4 h allowing the temperature to rise to 20°C. The resulting mixture was then 4862

treated with diethyl carbonate (5 mmol) at -50°C and it was stirred overnight allowing the temperature to rise to 20°C. The resulting mixture was hydrolyzed with water, extracted with diethyl ether, the organic layer dried (Na_2SO_4) and evaporated (15 Torr). The resulting residue was purified by flash chromatography (silica gel, diethyl ether) and/or recrystallization (see Table 1) to afford the lactam 3.

References and Notes

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- 6 A. H. Jackson and K. M. Smith in 'The Total Synthesis of Natural Products,' J. ApSimon (Ed.), Vol 6, J. Wiley & Sons, New York, 1984, p 237.
- 7 J. Barluenga, F. J. Fañanás, F. Foubelo, and M. Yus, <u>J. Chem. Soc., Chem.</u> <u>Commun.</u>, in the press.
- 8 Isolated yield: 54%, based on the starting amine 1e; m.p. 174-176°C (from hexane-CHCl₃).

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