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Lithiated Butyrolactams from Dianions Derived from Allyl Amines and Hexacarbonylchromium or Tungsten

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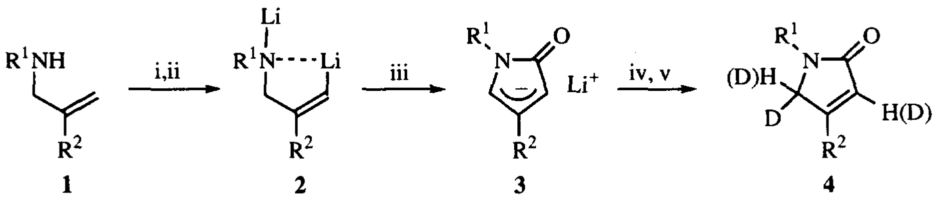
Abstracts: *Dilithiated dianions **2**, derived from secondary allyl amines **1**, react with hexacarbonylchromium or tungsten to give lithiated butyrolactams **3**, which have been characterized by reaction with different electrophiles (deuterium oxide, allyl bromide, carbon dioxide, and benzaldehyde) to give the corresponding substituted butyrolactams **4**, **7**, **8**, **9**, and **10**.*

Fischer pentacarbonyl chromium carbene complexes are nowadays being extensively used as reagents in organic synthesis;[1] among them alkoxycarbene complexes are the most developed and are usually prepared by reaction of an organolithium reagent with hexacarbonylchromium and further alkylation.[2] The direct reaction of carbonyl transition metal carbenes with organolithium compounds to give biscarbene complexes is very unusual,[3] but biscarbene complexes have been obtained by reaction of β-dilithiocompounds with metal carbonyls.[4] Moreover, γ-lithioalkoxides have been employed in the synthesis of cyclic pentacarbonyl chromium carbene complexes.[5] On the other hand, we have reported the direct regio- and stereo-selective lithiation of secondary allyl and methylallyl amines to the corresponding vinylic dianions,[6] which could act as useful intermediates in the preparation of cyclic Fischer biscarbene complexes. However, in the reaction of these dianions with hexacarbonylchromium or tungsten we did not observed this behaviour, but instead we describe in the present communication the preparation of lithiated butyrolactams and their subsequent functionalization with several electrophilic reagents.

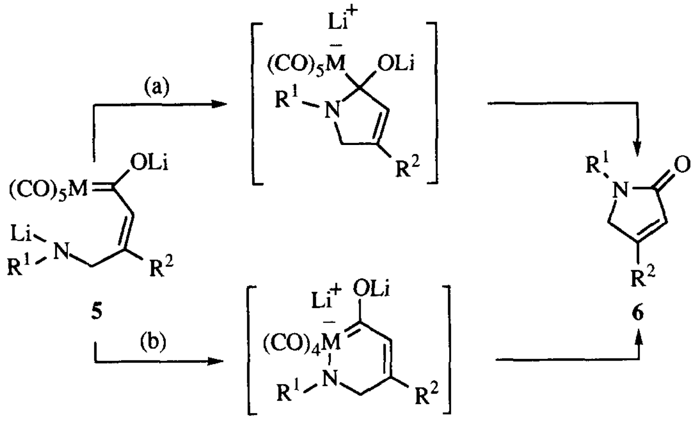
Successive treatment of different allyl amines **1** with n-butyllithium at -50 to -30°C, and *tert*-butyllithium at temperatures ranging between -30 and 20°C in ether as solvent led to the vinylic lithiated dianions **2** in a regio and stereo-selective way. The reaction of these dianionic species with hexacarbonylchromium in ether as solvent at temperatures ranging between 0 and 20°C afforded the lithiated butyrolactams **3**. These intermediates were characterized by treatment with deuterium oxide to yield the deuteriated butyrolactams **4**. Mass spectra of compounds **4** showed the presence of three isotopic isomers corresponding to the mono-, di-, and trideuteriated butyrolactams (Scheme 1 and Table 1). It is worth noting that undeuteriated starting amines **1** were found along with the corresponding butyrolactams **4**. On the other hand, treatment of dianions **2** with hexacarbonyl tungsten under the same reaction conditions afforded, after deuterolysis, the corresponding deuteriated butyrolactams **4** (Scheme 1 and Table 1).



a; $R^1 = Ph, R^2 = H$
b; $R^1 = Ph, R^2 = Me$
c; $R^1 = 4\text{-}MeOC_6H_4, R^2 = H$
d; $R^1 = 4\text{-}MeOC_6H_4, R^2 = Me$

Scheme 1. *Reagents and conditions:* i, ${}^{n}BuLi$, -50 to -30°C; ${}^{t}BuLi$, -30 to 20°C; iii, $M(CO)_6$ (M= Cr, W), 0 to 20°C; iv, D_2O, 20°C; v, H_2O

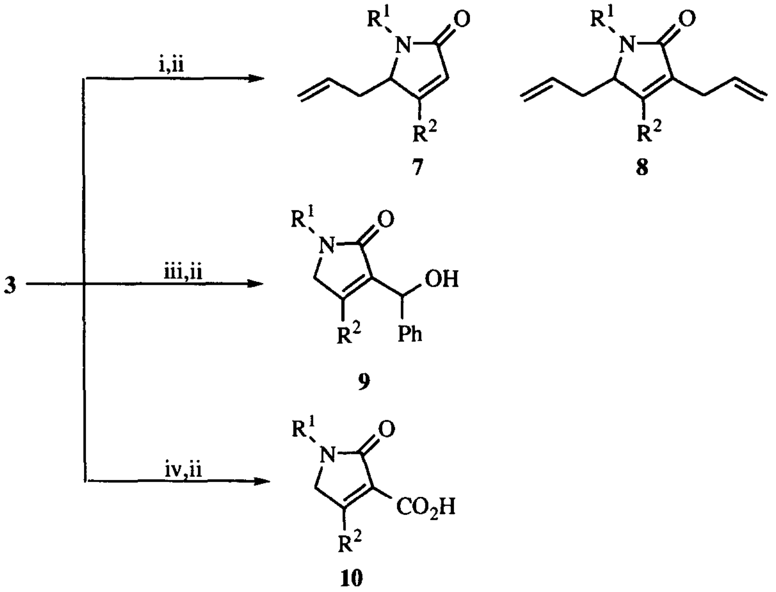
The formation of the butyrolactams can be accounted for most consistently by assuming the external attack of the dianion **2** at the coordinated carbonyl of $M(CO)_6$ to give the anionic carbene complex **5**, which subsequently experiments either the intramolecular attack of the amide nitrogen at the carbene carbon atom and β-elimination[7] (way a) or the displacement of a coordinated carbonyl by the nitrogen atom and further reductive elimination (way b), leading to the butyrolactams **6** (Scheme 2).



Scheme 2

The low yields obtained in the reaction can be understood by assuming that unreacted dianions **2** can act as lithiation agents. So, the butyrolactams generated in the reaction react with the dianions **2** leading to the lithiated butyrolactams **3**. In order to verify this observation, butyrolactam **6b** was treated with an excess of the dianionic intermediate **2b** and a mixture of the corresponding mono-, di-, and trideuteriated butyrolactam **4b** was obtained after deuterolysis. In this context, it is worth noting that treatment of **6b** with other lithiation reagents did not lead to the same results, and so, when *tert*-butyllithium was used as lithiation reagent, 2-*tert*-butyl-4-methyl-1-phenylpyrrol was obtained instead the lithiated butyrolactam **3b**.

On the other hand, treatment of lithiated butyrolactams **3** with several electrophiles (allyl bromide, benzaldehyde, and carbon dioxide) led, after hydrolysis, to the corresponding functionalized butyrolactams **7**, **8**, **9**, and **10** (Scheme 3 and Table 1).



Scheme 3. *Reagents and conditions:* i, $CH_2{=}CHCH_2Br$, -78 to 20°C; ii, H_2O; iii, PhCHO, -78 to 20°C; iv, CO_2, -78 to 20°C.

Table 1. Preparation of Intermediates **3** from Allyl Amines **1** and Reaction with Electrophiles to give Products **4**, and **7**, **8**, **9**, and **10**.

Starting amine	Intermediate	R^1	R^2	M	Electrophile	Product[a]	% Yield[b]	m.p./°C(hexane/$CHCl_3$) or R_F(hexane:AcOEt)
1a	**3a**	Ph	H	Cr	D_2O	**4a**	12	90-92
1b	**3b**	Ph	Me	Cr	D_2O	**4b**	36	87-88
1b	**3b**	Ph	Me	W	D_2O	**4b**	43	87-88
1c	**3c**	$4\text{-}MeOC_6H_4$	H	Cr	D_2O	**4c**	10	97-99
1d	**3d**	$4\text{-}MeOC_6H_4$	Me	Cr	D_2O	**4d**	22	105-108
1b	**3b**	Ph	Me	Cr	$CH_2{=}CHCH_2Br$	**7**	25	0.27(2:1)
1b	**3b**	Ph	Me	Cr	$CH_2{=}CHCH_2Br$	**8**	12	0.37(3:1)
1b	**3b**	Ph	Me	Cr	PhCHO	**9**	32	145-147
1b	**3b**	Ph	Me	Cr	CO_2	**10**	30	0.24(2:1)

[a] All products were fully characterized by spectroscopic methods (IR, ^1H and ^{13}C NMR, and mass spectrometry). [b] Isolated yield based on the starting amine **1**.

A typical reaction was performed as follows. A solution of n-butyllithium (5 mmol) in hexane was added to a solution of the corresponding amine **1** (5 mmol) in diethyl ether (25 ml) at -50°C under argon and stirred for 20 min at temperatures ranging between -50 and -30°C. A solution of *tert*-butyllithium (5 mmol) in pentane was added to the resulting mixture at -30°C with further stirring for 2 h while the temperature was allowed to rise to 20°C. The mixture was added to a suspension of hexacarbonylchromium (5 mmol) in diethyl ether (40 ml) at 0°C and stirring was continued for 1 h at temperatures ranging between 0 and 20°C. After cooling to -78°C, an excess of deuterium oxide (or the corresponding electrophile) was added, and stirring was continued while the temperature was allowed to rise to 20°C. The resulting mixture was then hydrolysed with water and extracted with diethyl ether. The organic layer was dried (Na_2SO_4), the solvents were removed (15 mmHg), and the residue was purified by flash column chromatography or recrystallization (see Table 1).

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