

Regio- and Stereo-selective Lithiation of Diallyl Amines: an Easy Entry to Trianionic Intermediates

José Barluenga,*^a Francisco Foubelo,^a Rosario González,^a Francisco J. Fañanás,^a and Miguel Yus^b

^a Departamento de Química Organometálica, Facultad de Química, Universidad de Oviedo, 33071 Oviedo, Spain

^b División de Química Orgánica, Facultad de Ciencias, Universidad de Alicante, 03690 Alicante, Spain

The successive treatment of diallyl amine (**1a**) with an alkyl-lithium reagent leads to several trianionic derivatives (**4a**) in a regio- and stereo-selective manner; in the case of *N*-allyl-*N*-(methylallyl) amine (**1b**), the lithiation step is only observed in the methylallyl moiety of the amine; these trianions are characterized by reaction with deuterium oxide to yield the corresponding deuteriated products (**5**).

Recently we have described the direct regio- and stereo-selective lithiation of several secondary allyl and methylallyl amines by successive treatment with *n*-butyl-lithium and *t*-butyl-lithium and the reactions of the obtained intermediates with several electrophiles.¹ In the present communication we report the behaviour of diallyl amines towards different alkyl-lithium reagents.

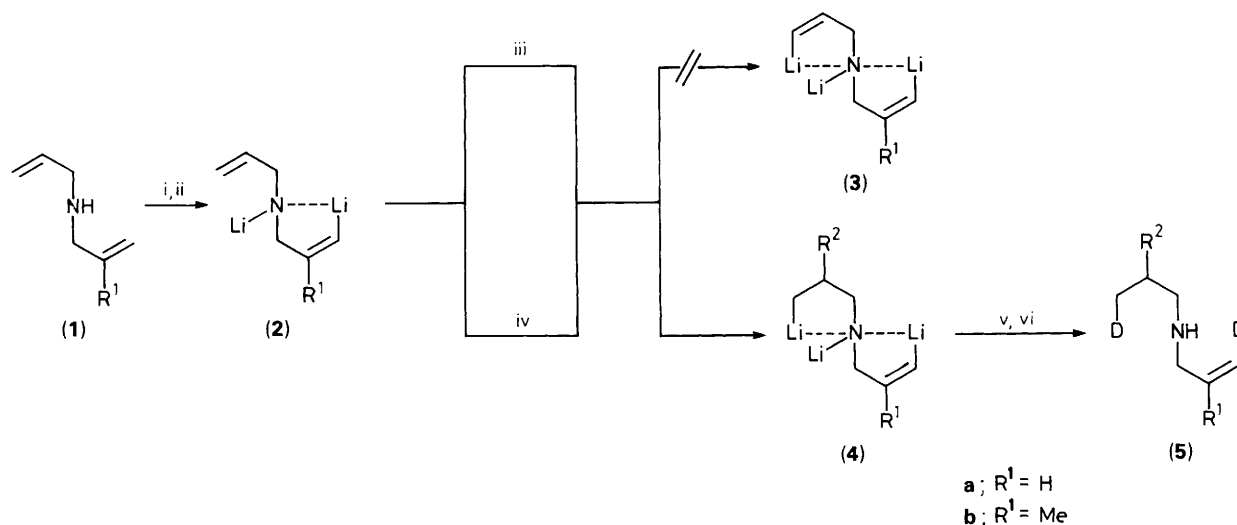
Successive treatment of diallyl amine [(**1a**) R¹ = H] with *n*-butyl-lithium and *t*-butyl-lithium at temperatures ranging between -50 and 20 °C led to the expected dianion (**2a**) by removal of the vinylic hydrogen.² Treatment of this intermediate (**2a**) with an equimolar amount of *t*-butyl-lithium at temperatures ranging between -20 and 20 °C did not lead to an abstraction of the vinylic hydrogen of the other allyl group to afford the dilithiated diallyl amines (**3a**), but quantitative addition of the *t*-butyl-lithium to the double bond led to formation of the corresponding trianion (**4a**).³ When *s*-butyl-lithium was used instead of *t*-butyl-lithium the corresponding addition product was again formed. The addition of *n*-butyl-lithium occurs in a similar manner, but the presence of *N,N,N',N'*-tetramethylethylenediamine (TMEDA) is necessary in order to increase the reactivity of the organolithium derivative. Further reactions of these trianions with deuterium oxide yield, after hydrolysis, the corresponding deuteriated product (**5a**) (Scheme 1 and Table 1).

The direct lithiation of the first allyl group can be understood by assuming that the nitrogen atom of the lithium amide, formed in the first step, can co-ordinate to the lithium

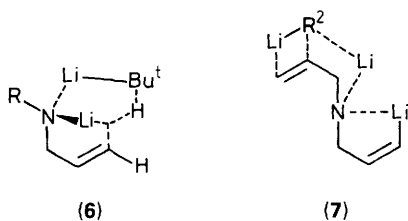
atom of *t*-butyl-lithium, increasing its reactivity and inducing a proximity effect⁴ [see (**6**)]. The other lithium atom interacts with the double bond fixing the *s-cis* geometry and allowing the vinyl hydrogen atom placed at the *cis* position relative to the nitrogen substituent to be removed. In contrast, there is no reaction when the amine lacks *cis* hydrogen atoms. The model outlined [see (**7**)] accounts well for the addition step. The interaction of the lithium atom of the amide with the alkyl group of the organolithium reagent, which would result in an increase in its reactivity, together with the simultaneous proximity effect, would allow the co-ordination of the carbon-carbon double bond to the lithium atom.

In this context it is worth noting the high regioselectivity shown by *N*-allyl-*N*-(methylallyl)amine [(**1b**) R¹ = Me], which under the same reaction conditions gives the trianionic intermediate [(**4b**) R² = Bu^t]. This trianion has been fully characterized by treatment with deuterium oxide to yield the corresponding dideuteriated product [(**5b**) R² = Bu^t]. The synthetic utility of these new synthons is currently under study.

A typical reaction was performed as follows. A solution of *n*-butyl-lithium (5 mmol) in hexane was added to a solution of the 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 *t*-butyl-lithium (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 then cooled to



Scheme 1. Reagents and conditions: i, BuⁿLi, -50 to -30 °C; ii, Bu^tLi, -30 to 20 °C; iii, RLi (R = Bu^s, Bu^t), -20 to 20 °C; iv, BuⁿLi/TMEDA, 20 °C; v, D₂O, 20 °C; vi, H₂O.



$-20\text{ }^{\circ}\text{C}$ and the corresponding alkyl-lithium reagent (5 mmol)[†] was added and stirring was continued for 2 h at temperatures ranging between -20 and $20\text{ }^{\circ}\text{C}$. The mixture was again cooled to $-20\text{ }^{\circ}\text{C}$, deuterium oxide (*ca.* 100 mmol) was added, and the reaction was stirred while the temperature was allowed to rise to $20\text{ }^{\circ}\text{C}$. 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 distillation (see Table 1).

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[†] When *n*-butyl-lithium was used, TMEDA (5 mmol) was added and the addition temperature was $20\text{ }^{\circ}\text{C}$.

Table 1. Preparation of intermediates (4) from amines (1) and characterization with deuterium oxide to give products (5).

Starting amine (1)	Inter-mediate (4)	Product (5) ^a	% Yield ^b	B.p./ $^{\circ}\text{C}$ (0.1 mmHg)
a	a	a ; $\text{R}^2 = \text{Bu}^n$	87	42–44
a	a	a ; $\text{R}^2 = \text{Bu}^s$ ^c	91	41–43
a	a	a ; $\text{R}^2 = \text{Bu}^t$	93	38–40
b	b	b ; $\text{R}^2 = \text{Bu}^t$	86	50–52

^a All products (5) were fully characterized by spectroscopic methods (IR, ^1H and ^{13}C NMR, and mass spectrometry). ^b Isolated yield based on the starting amine (1). ^c Equimolecular mixture of diastereoisomers.

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