One-pot Synthesis of Azasilocine and Azagermocine Derivatives from Diallyl Amines

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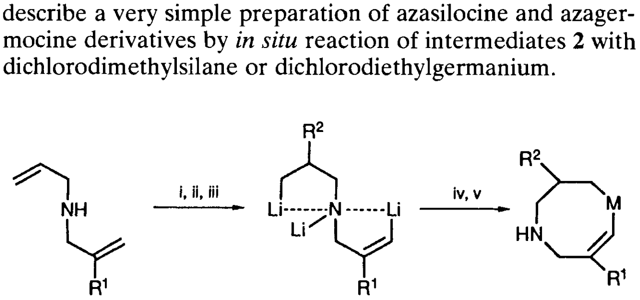
The successive reaction of diallyl amines **1** with several alkyllithium reagents and dichlorodimethylsilane or dichlorodiethylgermanium leads, after hydrolysis, to the corresponding azasilocine and azagermocine derivatives **3** and **4**.

We have recently reported[1] the regio- and stereo-selective lithiation of diallyl amines of the type **1**, which affords the corresponding lithiated intermediates **2**. These new synthons react with diethyl carbonate yielding pyrrolizidine derivatives.[2] The formation of these systems can be understood by assuming the formation of either a butyrolactam or an eight-membered ring.[2] In the present communication we describe a very simple preparation of azasilocine and azagermocine derivatives by *in situ* reaction of intermediates **2** with dichlorodimethylsilane or dichlorodiethylgermanium.



1a; R^1 = H
b; R^1 = Me

2

3; M = SiMe$_2$
4; M = GeEt$_2$

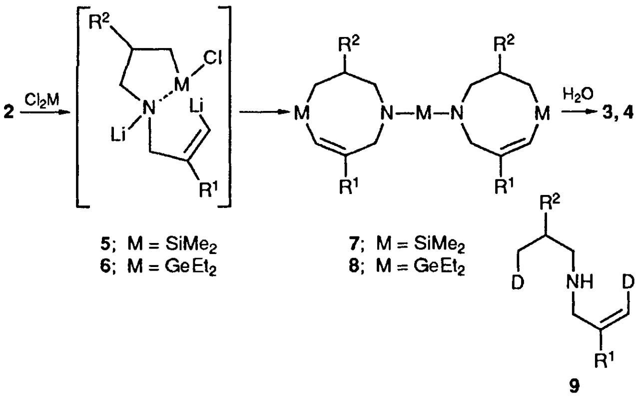
Scheme 1 *Reagents and conditions*: i, Bu^{n}Li, −50 to −30 °C; ii, Bu^{t}Li, −30 to 20 °C; iii, R^{2}Li/TMEDA (R^2 = Et, Bu^n), 20 °C; iv, Cl$_2$M (M = SiMe$_2$, GeEt$_2$), −78 to 20 °C; v, H$_2$O

The successive treatment of diallyl amines **1** with n-butyllithium at −50 to −30 °C, *tert*-butyllithium at temperatures between −30 and 20 °C, and n-butyllithium in the presence of *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) at 20 °C led to intermediates **2**;[1] the *in situ* reaction of these trianionic species with dichlorodimethylsilane or dichlorodiethylger-

Table 1 Preparation of azasilocine and azagermocine derivatives **3** and **4** from diallyl amines **1**

Starting amine	Electrophile	Product[a]	Yield[b] (%)	R_F (hexane : diethyl ether)
1a	Me$_2$SiCl$_2$	**3a** (R^2 = Et)	69	0.23 (9 : 1)
1a		**3a** (R^2 = Bu^n)	72	0.27 (9 : 1)
1b		**3b** (R^2 = Et)	62	0.37 (9 : 1)
1b		**3b** (R^2 = Bu^n)	67	0.44 (9 : 1)
1a	Et$_2$GeCl$_2$	**4a** (R^2 = Et)	63	0.25 (4 : 1)
1a		**4a** (R^2 = Bu^n)	71	0.28 (4 : 1)
1b		**4b** (R^2 = Et)	64	0.33 (4 : 1)
1b		**4b** (R^2 = Bu^n)	68	0.38 (4 : 1)

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



Scheme 2

manium at −78 to 20 °C afforded after hydrolysis the corresponding azasilocine and azagermocine derivatives **3** and **4** (Scheme 1 and Table 1).

The reaction of the trianion **2** with the dichlorometalloid presumably involves the formation of the species **5** and **6**, which favour the cyclization to the eight-membered ring compounds. These intermediates **5** and **6** yield the compounds **7** and **8**, which after hydrolysis afforded the corresponding azasilocine and azagermocine derivatives **3** and **4**. Related to this we have observed that an excess of dichlorometalloid is necessary. When one equivalent is used the yields are lower; so, the reaction leads after deuteriolysis (D_2O) to a mixture of the corresponding compounds **3** or **4** and the deuteriated derivatives **9**, which arise from the unreacted intermediates **2** (Scheme 2).

The proposed structures for **7** and **8** are supported by the ^{29}Si NMR data. The compound **7a** (R^2 = Bu^n) shows two signals at δ 11.8 and −16.5 for the silicon atoms, whereas the product **3a** (R^2 = Bu^n) presents one signal at −26.9 in the spectrum (both referenced to hexamethyldisiloxane).

A typical reaction was performed as follows. A solution of n-butyllithium (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 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. A solution of n-butyllithium (5 mmol) in hexane and TMEDA (5 mmol) was added at the same temperature and stirring was continued for 2 h at 20 °C. After cooling to −78 °C, dichlorodimethylsilane (7.5 mmol) 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 (see Table 1).

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References

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