

# Synthesis of N,C-dilithio-2-allylpyrrole and its solvent-controlled reactions with electrophiles

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## Abstract

The N,C-dilithiated product **1** of 2-allylpyrrole was prepared and studied by  $^7\text{Li}$  NMR in THF/HMPTA. Compound **1** reacts selectively in THF with electrophiles ( $\text{H}_2\text{O}$ ,  $\text{MeI}$ ,  $\text{Me}_3\text{SiCl}$ ) to give the Z-isomers **2a–4a**. In diethylether, the analogous reactions lead selectively to the E-isomers **2b–4b**.

**Keywords:** Pyrrole; 2-Substituted; N,C-dilithiation;  $^7\text{Li}$  NMR

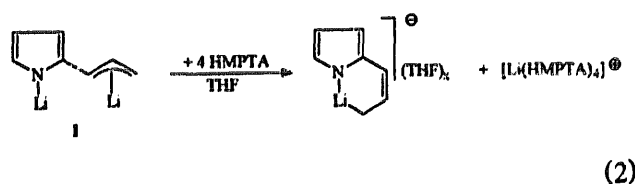
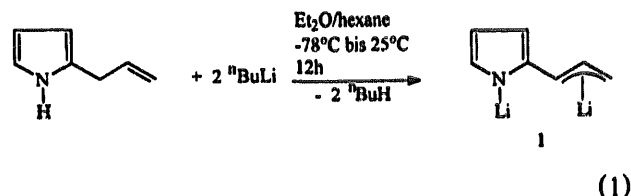
## 1. Introduction

N,C-dilithiated compounds are attractive starting materials in organic and organometallic synthesis, as has been shown in the case of allylamines [1–4] or *ortho*-toluidine derivatives [2,5]. Similarly, the dilithiated monobenzylamine *o*- $\text{LiC}_6\text{H}_4\text{CH}_2\text{N}(\text{Li})\text{CH}_2\text{CH}_2\text{NMe}_2$  has been studied in detail [6,7]. N,C-dilithiated pyrroles have not been described so far. Known C,C-dilithiated compounds containing a pyrrole ring have been described from N-substituted pyrroles such as 1-phenylpyrrole [8] and 1-ethynylpyrrole [9]. Although the N–H function and the C=C double bond in 2-allylpyrrole are further apart than in allylamines, 2-allylpyrrole is certainly a promising candidate for N,C-dilithiation. Here we report on the synthesis of N,C-dilithio-2-allylpyrrole and some of its solvent-controlled selective transformations.

## 2. Results and discussion

2-Allylpyrrole reacts with two equivalents of  $^n\text{BuLi}$  in hexane/ether to give the N,C-dilithio derivative **1** in high yield (Eq. (1)). The reaction proceeds stepwise, as expected, the N–H function being more reactive than the allyl group. Compound **1** is insoluble in hexane or

ether but soluble in THF. If 4.5 equivalents of HMPTA are added to a THF solution of **1**, a broad  $^7\text{Li}$  NMR signal is observed at room temperature, which changes below  $-80^\circ\text{C}$  to a quintet [ $^2J(^{31}\text{P}, ^7\text{Li}) = 6.9\text{ Hz}$ ] and several broad  $^7\text{Li}$  signals (see Fig. 1). The appearance of the quintet at low temperatures indicates that a lithium cation has been removed from **1** and is now coordinated by four HMPTA molecules. The surroundings of the  $^7\text{Li}$  nucleus in this cation must be highly symmetrical, otherwise the scalar  $^{31}\text{P}-\text{O}-^7\text{Li}$  coupling would not be resolved because of efficient quadrupolar relaxation of the  $^7\text{Li}$  nucleus. It is suggested that the broad  $^7\text{Li}$  resonance signals belong to various associated species of the anion shown in Eq. (2).



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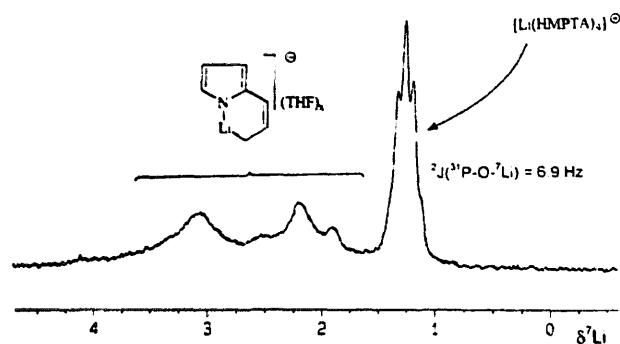
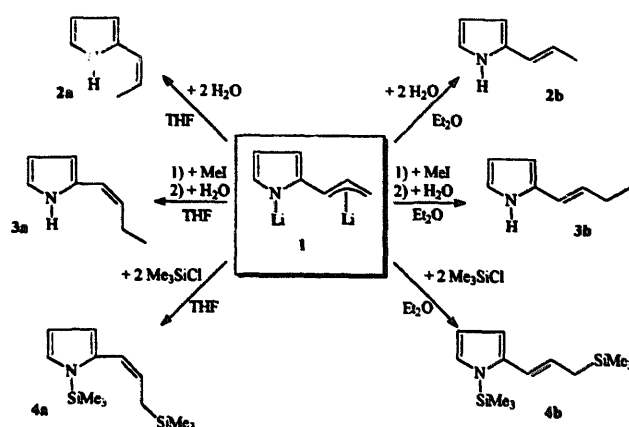


Fig. 1. 97.2 MHz  $^7\text{Li}$  NMR spectrum of **1** in THF at  $-80^\circ\text{C}$  in the presence of 4.3 equiv.  $(\text{Me}_2\text{N})_3\text{PO}$  (HMPTA).

The simplified structure of the anion in Eq. (2) indicates that reactions of electrophiles with **1** in donor solvents such as THF may afford selectively the products with *cis*-configuration at the  $\text{C}=\text{C}$  bond. In contrast, in non-polar or weaker donor solvents, these reactions might lead to mixtures of products with *cis*- and *trans*-configuration, or only to the *trans*-products. The results of the reactions of **1** with  $\text{H}_2\text{O}$ ,  $\text{MeI}$  and  $\text{Me}_3\text{SiCl}$  in THF or in diethylether are summarized in Scheme 1. In THF all products possess the *cis*-configuration at the  $\text{C}=\text{C}$  double bond, whereas in ether the *trans*-products are formed selectively. The respective stereochemistry is readily apparent from the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra (see Table 1), in particular from the vicinal coupling constants  $^3J(\text{H}, \text{H})$  across the  $\text{C}=\text{C}$  bond [10]. The compounds **2** [11] and **3** [12] were previously obtained as 1:1 mixtures of *E/Z*-isomers by other methods.



Scheme 1.

The *cis*-selectivity observed for reactions of **1** with electrophiles in THF is promising for the use of **1** as a versatile synthon in heterocyclic synthesis. The ease of N,C-dilithiation of 2-allylpyrrole suggests that N,C,C-trilithiation of 2,5-diallylpyrrole will also be feasible.

### 3. Experimental

All preparative work and handling of samples, except the organic products **2a/b** and **3a/b**, was carried out under an atmosphere of dry  $\text{N}_2$ , using oven-dried glassware and dry solvents. Starting materials were commercial products or were prepared according to literature

Table 1  
NMR data for the pyrrole derivatives 1–4

	<b>1</b>	<b>2a</b> (Z)	<b>2b</b> (E)	<b>3a</b> (Z)	<b>3b</b> (E)	<b>4a</b> (Z)	<b>4b</b> (E)
N-R		H	H	$\text{CH}_3$	$\text{CH}_3$	$\text{SiMe}_3$	$\text{SiMe}_3$
3'-R'		H	H	H	H	$\text{SiMe}_3$	$\text{SiMe}_3$
$\delta^7\text{Li}$	0.9 <sup>a</sup>						
$\delta^{29}\text{Si}$	N-Si	—	—	—	—	11.2	11.1
	3'-Si	—	—	—	—	1.9	1.6
$\delta^{13}\text{C}$	C-2	132.8	129.9	129.6	130.5	134.4	137.7
$[J(^{29}\text{Si}, ^{13}\text{C})]$	C-3	98.7	108.6	108.2	106.1	109.6	107.6
	C-4	106.4	109.2	109.0	108.7	111.3	110.4
	C-5	123.2	117.2	117.7	117.4	122.7	123.2
	C-1'	76.3	120.1	121.5	118.2	118.3	120.1
	C-2'	146.8	121.8	121.5	129.8	127.3	125.9
	C-3'	45.3	14.5	18.1	22.3	25.6	19.6 [46.8]
	N-R	—	—	—	—	0.2 [58.0]	0.7 [58.1]
	3'-R'	—	—	13.7	13.5	-2.0 [51.0]	-1.9 [51.9]

<sup>a</sup> At room temperature.

procedures (2-allylpyrrole [13]). NMR spectra were recorded using Jeol EX270 and Bruker ARX 250 spectrometers equipped with multinuclear units. Chemical shifts are given with respect to Me<sub>4</sub>Si [ $\delta^1\text{H}(\text{CHCl}_3/\text{CDCl}_3) = 7.24$ , (THF) = 1.85;  $\delta^{13}\text{C}(\text{CDCl}_3) = 77$ , (THF) = 26.5; LiCl (1 M in D<sub>2</sub>O) ( $\delta^7\text{Li}$  with  $\Xi(^7\text{Li}) = 38.86377\text{MHz}$ ].

### 3.1. *N,C-dilithio-2-allylpyrrole 1*

A solution of <sup>n</sup>BuLi (187 mmol) in 120 ml of hexane and 100 ml of diethylether was added dropwise to a stirred solution of 10 g (93.4 mmol) of 2-allylpyrrole in 200 ml of ether at  $-78^\circ\text{C}$ . The mixture was stirred for 12 h and warmed to room temperature. After that the bright yellow reaction mixture was filtered, the yellow precipitate was washed with pentane, and 9.4 g (85%) of **1** were obtained as a yellow powder. <sup>1</sup>H NMR (THF; 250 MHz)  $\delta^1\text{H} = 6.68\text{ m}$ , C<sup>5</sup>-H; 6.17 m, C<sup>4</sup>-H; 5.84 m, C<sup>3</sup>-H; 4.54 d [9.5 Hz, <sup>3</sup>J] C<sup>1</sup>-H; 6.32 m, C<sup>2</sup>-H; 2.55 d [11.0 Hz, <sup>3</sup>J] (2H) C<sup>3</sup>.

### 3.2. Adduct of **1** with HMPTA

HMPTA (1.35 g; 7.5 mmol) was added to a solution of 0.2 g (1.7 mmol) **1** in 5 ml of THF at  $-78^\circ\text{C}$ . The colour changed from orange to dark red. The solution of the adduct must be stored at low temperatures ( $-78^\circ\text{C}$ ), otherwise slow decomposition takes place.

### 3.3. Reactions of **1** with electrophiles

#### 3.3.1. In THF

8.4 mmol of H<sub>2</sub>O, or Me<sub>3</sub>SiCl, or 4.2 mmol of MeI (followed by 4.2 mmol of H<sub>2</sub>O) respectively were added in one portion to a stirred solution of 0.5 g (4.2 mmol) of **1** in 20 ml of THF at  $-78^\circ\text{C}$ . The orange solution became colourless. After warming to room temperature the solvent was removed and the residue extracted with hexane.

**2a**. Removal of the hexane and sublimation gave 0.33 g (73%) of **2a** as colourless platelets (m.p.  $57^\circ\text{C}$ ). <sup>1</sup>H NMR (CDCl<sub>3</sub>; 250 MHz)  $\delta^1\text{H} = 8.09$  [br], NH; 6.81 m, C<sup>5</sup>-H; 6.43 m, C<sup>3</sup>-H/C<sup>4</sup>-H; 6.28 d [11.6 Hz, <sup>3</sup>J] C<sup>1</sup>-H; 5.72 m, C<sup>2</sup>-H; 2.06 d [7.3 Hz, <sup>3</sup>J] C<sup>3</sup>-H.

**3a**. Removal of the hexane and distillation gave 0.40 g (78%) of **3a** as a colourless liquid (b.p.  $43^\circ\text{C}/1\text{Torr}$ ). <sup>1</sup>H NMR (CDCl<sub>3</sub>; 250 MHz)  $\delta^1\text{H} = 8.00$  [br], NH; 6.91 m, C<sup>5</sup>-H; 6.65 m, C<sup>3</sup>-H; 6.61 t, C<sup>4</sup>-H; 6.38 d [11.6 Hz, <sup>3</sup>J] C<sup>1</sup>-H; 5.78 m, C<sup>2</sup>-H; 2.71 m, C<sup>3</sup>-H; 1.45 t, CH<sub>3</sub>.

**4a**. Removal of the hexane and distillation gave 0.70 g (73%) of **4a** as a colourless liquid (b.p.  $92^\circ\text{C}/0.1\text{Torr}$ ). <sup>1</sup>H NMR (CDCl<sub>3</sub>; 250 MHz)  $\delta^1\text{H} = 6.97\text{ m}$ , C<sup>5</sup>-H; 6.63 m, C<sup>3</sup>-H; 6.51 m, C<sup>4</sup>-H; 6.60 d [11.2 Hz, <sup>3</sup>J] C<sup>1</sup>-H; 5.87 m, C<sup>2</sup>-H; 2.15 d, C<sup>3</sup>-H; 0.70 s, N-SiCH<sub>3</sub>; 0.33 s, 3'-SiCH<sub>3</sub>.

#### 3.3.2. In diethylether

8.4 mmol of H<sub>2</sub>O or Me<sub>3</sub>SiCl were added to a stirred suspension of 0.5 g (4.2 mmol) of **1** in 20 ml of ether at  $0^\circ\text{C}$ . In the case of the reaction with 4.2 mmol MeI the mixture was stirred at room temperature for 1 h, and then 4.2 mmol of H<sub>2</sub>O were added. After the colour of the dispersion changed to white, the mixture was filtered.

**2b**. Removal of the solvent from the filtrate and sublimation gave 0.29 g (65%) of **2b** as a colourless powder (m.p.  $35^\circ\text{C}$ ). <sup>1</sup>H NMR (CDCl<sub>3</sub>; 250 MHz)  $\delta^1\text{H} = 8.01$  [br], NH; 6.82 m, C<sup>5</sup>-H; 6.51 t, C<sup>4</sup>-H; 6.48 m, C<sup>3</sup>-H; 6.47 d [15.9 Hz, <sup>3</sup>J] C<sup>1</sup>-H; 5.03 m, C<sup>2</sup>-H; 2.16 d, C<sup>3</sup>-H.

**3b**. Removal of the solvent from the filtrate and distillation gave 0.4 g (65%) of **3b** as a colourless liquid (b.p.  $43^\circ\text{C}/1\text{Torr}$ ). <sup>1</sup>H NMR (CDCl<sub>3</sub>; 250 MHz)  $\delta^1\text{H} = 8.04$  [br], NH; 6.84 m, C<sup>5</sup>-H; 6.53 m, C<sup>3</sup>-H; 6.50 m, C<sup>4</sup>-H; 6.48 d [16.2 Hz, <sup>3</sup>J] C<sup>1</sup>-H; 6.07 m, C<sup>2</sup>-H; 2.52 m, C<sup>3</sup>-H; 1.43 t, CH<sub>3</sub>.

**4b**. Removal of the solvent from the filtrate and distillation gave 0.57 g (60%) of **4b** as a colourless liquid (b.p.  $90^\circ\text{C}/0.1\text{Torr}$ ). <sup>1</sup>H NMR (CDCl<sub>3</sub>; 250 MHz)  $\delta^1\text{H} = 6.81\text{ m}$ , C<sup>5</sup>-H; 6.49 m, C<sup>3</sup>-H; 6.33 t, C<sup>4</sup>-H; 6.37 d [15.5 Hz, <sup>3</sup>J] C<sup>1</sup>-H; 6.16 m, C<sup>2</sup>-H; 1.75 d, C<sup>3</sup>-H; 0.59 s, N-SiCH<sub>3</sub>; 0.17 s, 3'-SiCH<sub>3</sub>.

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