Pergamon

Tetrahedron Letters, Vol. 37, No. 31, pp. 5435-5436, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)01142-2

Isomerization of 2-(2-Propenoxy)phenyllithium: Tandem Anionic Cyclization – γ-Elimination

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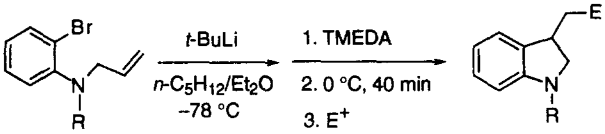
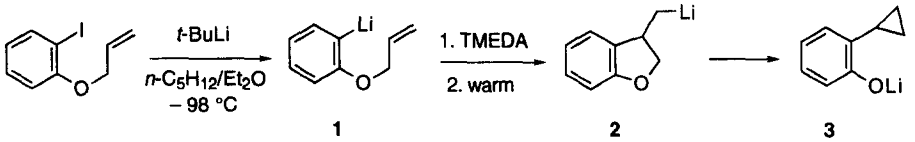
Abstract: 2-(2-Propenoxy)phenyllithium (**1**), which may be prepared from the corresponding iodide by low-temperature lithium–iodine exchange, rearranges on warming in the presence of TMEDA via 5-exo cyclization to (2,3-dihydrobenzofuranyl)methyllithium (**2**) followed by γ-elimination to give variable amounts of the lithium salt of 2-(cyclopropyl)phenol (**3**). Copyright © 1996 Elsevier Science Ltd

While the facile ring-closure of unsaturated alkyllithiums has been shown to be a convenient route to a variety of functionalized carbocyclic products,[2] less information is available on the utility of such cyclizations for the preparation of heterocycles.[3] Both we and the Liebeskind group recently disclosed that 5-exo closure of the organolithium derived from a 2-bromo-N-allylaniline provides a high-yield route to C(3)-substituted indolines.[4] In light of the ease with which indolines are produced by closure of a 2-(N-allylamino)phenyllithium, we were prompted to investigate the possibility of preparing 3-substituted 2,3-dihydrobenzofurans by cyclization of the analogous oxygen-containing system, 2-(2-propenoxy)phenyllithium (**1**). As detailed below, cyclization of **1** gives (2,3-dihydrobenzofuranyl)methyllithium (**2**) but the process does not provide a synthetically viable route to the heterocycle: rather, isomerization of **1** in the presence of TMEDA proceeds via a novel domino cyclization–elimination sequence to give the lithium salt of 2-(cyclopropyl)phenol (**3**).



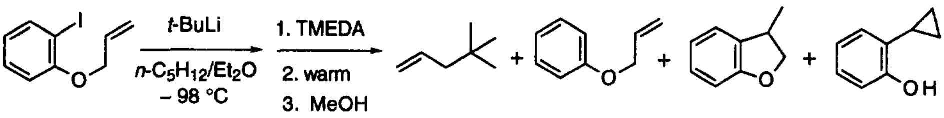


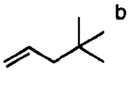
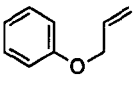
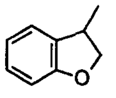
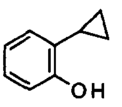
1 **2** **3**

Solutions of **1** were prepared at –98 °C in *n*-pentane–diethyl ether (3:2 by vol) by treatment of the corresponding iodide[5] with 2 molar equiv. of *t*-BuLi.[6] Quench of such reaction mixtures at –98 °C with MeOH delivered the expected allyl phenyl ether along with variable amounts of an equimolar mixture of 4,4-dimethyl-1-pentene and phenol produced by S_N' addition of excess *t*-BuLi to **1**. The aryllithium is unexpectedly resistant to isomerization at elevated temperatures in *n*-pentane–diethyl ether solution (no cyclization results when solutions of **1** are held at +23 °C for 1 h) but the isomerization of **1** is significantly more facile when 2 equiv of TMEDA are added to the reaction mixture prior to warming.

When solutions of **1** are warmed to temperatures above ~ –10 °C in the presence of TMEDA, a sequential cyclization–elimination sequence ensues (**1** → **2** → **3**) accompanied by the formation of significant quantities of 4,4-dimethyl-1-pentene and phenol from attack of excess *t*-BuLi on the allyl ether moiety of **1** (Table 1). The unwanted S_N' cleavage of **1** may be minimized by conducting the exchange reaction with less than 2 molar equiv of *t*-BuLi; however, the residual *t*-BuI remaining in solution then serves as an efficient proton source and results in inadvertent quench of **1** prior to cyclization. Given that the S_N' cleavage effectively removes a quantity of **1** from the reaction mixture, the novel two-step rearrangement of **1** to **3** is a surprisingly efficient process: the 46 % yield of 2-(cyclopropyl)phenol (Table 1, entry 5) corresponds to an ~ 80 % conversion of **1** to **3**.

Table 1. Isomerization of 2-(2-Propenoxy)phenyllithium **1**



entry	temp, °C	time, h	products, % yield [a]			
			 [b]			
1	-78	0.1	9	91		
2	-2	1	60	25	15	
3	-2	2	58	15	15	13
4	22	1	40	1	32	27
5	23	2	43	1	10	46[c]

[a] Yields were determined by capillary GC and are corrected for detector response. [b] An equimolar quantity of phenol was also produced. [c] Isolated yield of 40 %; the physical and spectroscopic properties of 2-(cyclopropyl)phenol were fully in accord with those reported for this material.[7]

Acknowledgment. This work was supported by the Connecticut Department of Economic Development.

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(*Received in USA* 6 *May* 1996; *revised* 4 *June* 1996; *accepted* 5 *June* 1996)