



Lithiation of Allyl Chlorides and Reactions with Electrophiles.

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Abstract: Deprotonation of allyl chlorides **1** and **8** with lithium diisopropylamide (LDA) gives chlorocinnamyl lithium **2** and benzothiazolylchloroallyllithium **9**. Both **2** and **9** react with unenolizable carbonyl compounds with the *in situ* quench procedure furnishing styryl oxiranes **7** and benzothiazolylvinyl oxiranes **10**. In the absence of an external electrophile, **2** undergoes a homocoupling reaction leading to the enyne **5**. Lithiation of **1**, followed by the addition of the carbonyl compound, provides propargylic alcohols **6**. Copyright © 1996 Elsevier Science Ltd

α -Halogenocarbanions constitute an important part of carbanion chemistry. Indeed, since the pioneering work by Kobrich,^{1a} such carbanions have become increasingly useful in synthetic organic chemistry.¹ Studies concerning their structural features have also been carried out.²

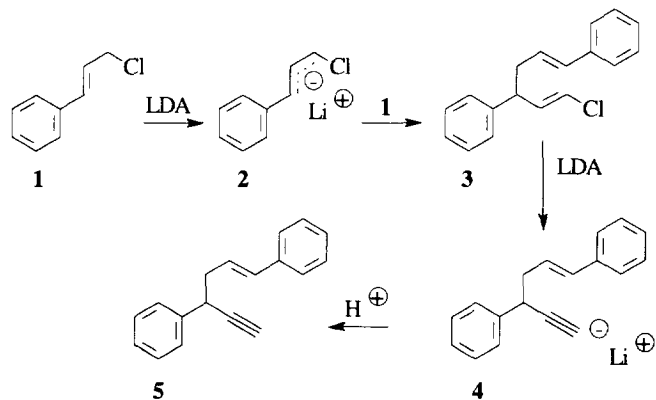
Among the α -halogenocarbanions α -halogenoallylcarbanions have been much less studied and applied in synthesis due to their bias to undergo "self-consumption".³ There have been published only a few reports on the generation and trapping reactions of α -halogenoallyl carbanions.⁴ Only α,α -dihaloallyllithium had witnessed broad synthetic utility,⁵ till the development of an *in situ* generation procedure of α -halogenoallylcarbanions.⁶

α -Halogenoallylcarbanions are ambident nucleophiles: indeed, they may react with an electrophile to give the α - or the γ -product depending upon the counterion.⁷ Chloroallyllithium, generated by deprotonation of allylchloride with LDA, reacts with aldehydes to give predominantly γ -products. In contrast, lithiation of allylchloride with LDA in the presence of $ZnCl_2$ and reaction with carbonyl compounds lead mainly to α -products.^{7,8}

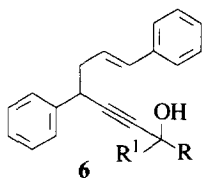
To our surprise α -halogenocarbanions from aryl and heteroaryl substituted allylchlorides have not been studied so far. In this paper, as part of our recent work on the generation and synthetic applications of heteroaryl halogenoallyllithiums,⁹ we report on the lithiation of two such allyl chlorides and their reactions with electrophiles.

Treatment of *trans*-cinnamyl chloride **1** with LDA (THF/-80 °C) followed by quenching with aq. NH_4Cl gave almost a quantitative yield of the enyne **5**.¹⁰ Its formation can be explained by assuming that chlorocinnamyl lithium **2** reacts, in a γ -regioselective way, with **1** to give the homocoupling product **3**. HCl elimination and deprotonation of the acetylenic hydrogen would furnish the acetylide ion **4** and then the *trans* enyne **5**.

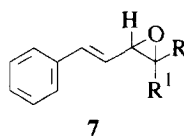
Lithiation of **1** followed by the immediate addition of cyclohexanone, gave an excellent yield of the propargylic alcohol **6a**. Comparable results were obtained when **2** was treated with other carbonyl compounds to give propargylic alcohols **6b-d**, all adopting the *trans* configuration. In all probability, the propargylic alcohols **6** arise from the coupling of the acetylide ion **4**, resulting from the homocoupling reaction of **2**, with the carbonyl compound.



Propargylic alcohols **6a** and **6b** also formed when lithiation of **1** was carried out in the presence of cyclohexanone or acetophenone (an *in situ* quench procedure). A small percentage of **5** was also observed. Under the same experimental conditions, **2** reacted with isobutyraldehyde yielding the alcohol **6e**. From these results it is evident that **2** undergoes "self-consumption" faster than the addition to the carbonyl compound.



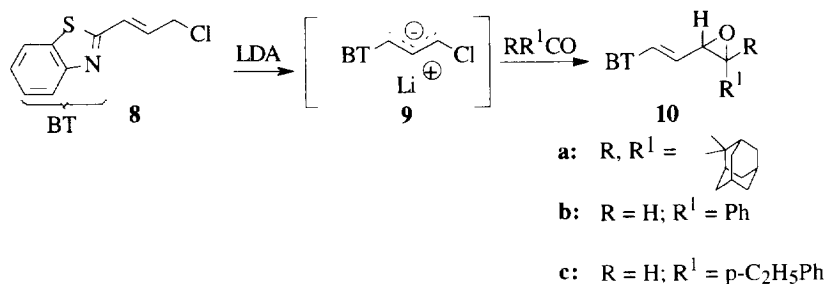
- a:** $\text{R}, \text{R}' =$
- b:** $\text{R} = \text{CH}_3; \text{R}' =$
- c:** $\text{R} = \text{H}; \text{R}' =$
- d:** $\text{R} = \text{H}; \text{R}' =$
- e:** $\text{R} = \text{H}; \text{R}' = \text{CH}(\text{CH}_3)_2$



- a:** $\text{R}, \text{R}' =$
- b:** $\text{R} = \text{R}' =$
- c:** $\text{R}, \text{R}' =$
- d:** $\text{R} = \text{H}; \text{R}' =$
- e:** $\text{R} = \text{H}; \text{R}' =$

In contrast, the addition of a solution of cinnamyl chloride **1** and an unenolizable carbonyl compound such as adamantanone, benzophenone or fluorenone to a solution of LDA gave in a complete α -regioselection very high yields of the *trans* styryl epoxides **7a**, **7b** and **7c**, respectively. Under the same experimental conditions, **2** reacted with *p*-ethylbenzaldehyde and *p*-chlorobenzaldehyde to give acceptable yields of the styryl epoxides **7d** and **7e** respectively, together with propargylic alcohols **6d** and **6e**. The epoxides **7d** and **7e** were assigned the *trans* configuration at the C-C double bond and at the oxirane functionality on the basis of the coupling constants ($J = 16$

Hz between the vinylic hydrogens and $J = 2$ Hz between the oxirane ring hydrogens). It is worthy pointing out that other α -halogenoallyllithiums add to carbonyl compounds with γ -regioselection.^{7,8}



Lithiation of benzothiazolylallyl chloride **8**¹¹ (LDA/THF/ -80°C) in the presence of adamantanone led regioselectively to the benzothiazolylvinyl epoxide **10a**. Vinylic oxiranes **10b** and **10c** formed in the reaction of the putative lithiated intermediate **9** with benzaldehyde and *p*-ethylbenzaldehyde, respectively.

Table. Lithiation of cinnamylchloride **1** and benzothiazolylallylchloride **8** with LDA in THF at -80°C and reactions with electrophiles

Allyl chloride	Carbonyl Compound	Method	Reaction product (% yield)
1	-	-	5 (>95%)
"	cyclohexanone	A	6a (95)
"	"	B	6a (90) + 1 (10)
"	acetophenone	A	6b (90)
"	"	B	6b (70) + 1 (20)
"	<i>p</i> -C ₂ H ₅ C ₆ H ₄ CHO	A	6c (90)
"	"	B	6c (55) + 7d (25)
"	<i>p</i> -ClC ₆ H ₄ CHO	A	6d (90)
"	"	B	6d (48) + 7e (32)
"	(CH ₃)CHCHO	A	6e (80) + 1 (10)
"	adamantanone	B	7a (94)
"	benzophenone	B	7b (85)
"	fluorenone	B	7c (80)
8	adamantanone		10a (80)
"	PhCHO	B	10b (75)
"	<i>p</i> -C ₂ H ₅ C ₆ H ₄ CHO	B	10c (75)

Method A: the allyl halide (1 eq.) was first added to LDA (1.2 eq.). After a few min. the carbonyl compound (1.2 eq.) was added. **Method B:** the solution of the allylic halide (1 eq.) and the carbonyl compound (1.2 eq.) was added to the LDA solution (1.2 eq.). Yields were calculated on isolated, purified compounds.

General Procedure, Method B: the reaction of **2** with adamantanone is described as an example. A solution of **1** (0.304 g, 2 mmol) and adamantanone (0.360 g, 2.4 mmol) in THF (3 mL) was added dropwise at -78°C under nitrogen atmosphere to the LDA solution (2.4 mmol), prepared from diisopropylamine (0.245 g, 2.4 mmol) in THF (10 mL) and *n*-BuLi (2.4 mmol). The reaction mixture was allowed to warm to rt, kept there for 2h and then quenched with aqueous sat. NH_4Cl . Extraction with ether (3 x 25 mL), drying over Na_2SO_4 and evaporation of the solvent under reduced pressure gave almost quantitatively **7a**.¹²

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10. The enyne **5** was assigned the *trans* configuration on the basis of the coupling constants between the vinylic hydrogens ($J = 15.7$ Hz).
11. The allyl chloride **8** was prepared from 1-(2-benzothiazolyl)-2-propen-1-ol and MeSO_2Cl . The propenol was prepared by treating 2-formylbenzothiazole with vinylmagnesium bromide.
12. All the new compounds showed satisfactory microanalytical data and consistent NMR and GC MS data.

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