Prop-2-ynyl- and Propadienyl-lithium Reagents. Regiocontrolled Synthesis of Allenic Compounds

Chanh Huynh and Gérard Linstrumelle

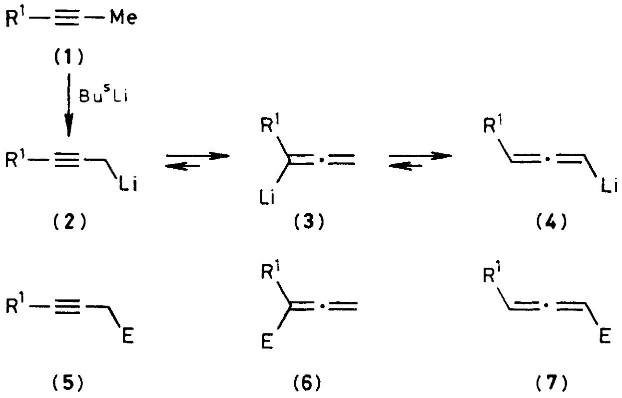
E.R. 12 du C.N.R.S., Laboratoire de Chimie, Ecole Normale Supérieure, 24, rue Lhomond, 75231 Paris Cédex 05, France

Direct proof for the rearrangement of the prop-2-ynyl-lithium (**2**) into the propadienyl-lithium (**4**) is provided by the formation of the 1,3-disubstituted allenic compounds (**7**).

The interest in prop-2-ynylmetals in organic synthesis has increased. Although a mixture of acetylenic and allenic isomers is often formed owing to the rearrangement of the prop-2-ynyl group,[1] much effort has been devoted to the control of the regioselectivity of these ambident species. In connection with previous reports on propadienyl-lithium reagents,[2] we have studied the reactivity of the prop-2-ynyl-lithium (**2**).

We report here the regioselective reaction of 1-lithioalk-2-ynes with epoxides to give the 1,1-disubstituted allenic alcohols (**6**) and the transformation of the lithioderivative (**2**) [or (**3**)] into the 1,3-disubstituted propadienyl-lithium compound (**4**) which is characterized by its derivatives (**7**).

The lithioderivative (**2**) was easily prepared by the treatment of alk-2-ynes (**1**) with s-butyl-lithium† in tetrahydrofuran (THF)–cyclohexane at 0 °C for 1.5 h; its structure has been confirmed by n.m.r. spectroscopy.[3] Addition of various



a; $R^1 = Pr^n$, $E = CH_2CH(OH)Me$
b; $R^1 = Pr^n$, $E = CH_2CH_2OH$
c; $R^1 = n\text{-}C_8H_{17}$, $E = CH_2CH(OH)Me$
d; $R^1 = Pr^n$, $E = Bu^n$
e; $R^1 = n\text{-}C_8H_{17}$, $E = Me$
f; $R^1 = Me$, $E = CH_2CH(OH)Me$
g; $R^1 = Me$, $E = n\text{-}C_8H_{17}$

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† n-Butyl-lithium in hexane gave the same results for the preparation of the 1,1-disubstituted allenic alcohols (**6**). However, n-butyl-lithium containing residual base (20—30%) gave a high proportion of acetylides derived from 1-lithioalk-1-ynes.

Table 1

Entry	Substituents	HMPA/equiv.	Time[a]	Electrophile	Products[b] (5)	: (6)	: (7)	Total yield,[b] %
1	**a**	0	—	Propylene oxide	45	55	0	85
2	**a**	0.5	0.5 min	"	12	87	1	86
3	**a**	1	2 h	"	12	87	1	84
4	**a**	1.5	2 h	"	7	48	35	77
5	**a**	5	2 h	"	5	19	71	80
6	**b**	0.5	0.5 min	Ethylene oxide	19	80	1	88
7	**b**	1	2 h	"	11	79	4	80
8	**b**	5	2 h	"	6	36	53	86
9	**c**	5	2 h	Propylene oxide	1	25	72	73
10	**d**	1	2 h	Butyl iodide	52	46	2	60
11	**d**	5	2 h	"	15	0	65	60
12	**e**	5	2 h	Methyl iodide	15	1	80	85

[a] Time before addition of the electrophile, at −78 °C. After addition of the electrophile, the reaction mixture was maintained at −78 °C for 1 h, allowed to rise to 0 °C, and hydrolysed. [b] Distilled compounds. When **(5)** + **(6)** + **(7)** is not equal to 100, a minor product derived from lithioacetylide has been formed.

Table 2

Entry[a]	Substituents	Starting material	HMPA/equiv.	Time[b]	Electrophile	Products[c] (5)	: (6)	: (7)	Total yield,[c] %
13	**a**	$R^1-CH=C=CH_2$	1	1 min	Propylene oxide	2	20	78	91
14	**a**	$R^1-CH=C=CH_2$	5	2 h	"	2	16	70	80
15	**f**	$R^1-CH=C=CHBr$	1	1 min	"	0	5	95	50
16	**f**	$R^1-CH=C=CHBr$	5	2 h	"	0	22	78	51
17	**d**	$R^1-CH=C=CH_2$	1	2 h	Butyl iodide	0	5	95	55
18	**d**	$R^1-CH=C=CH_2$	5	2 h	"	0	0	95	45
19	**e**	$R^1-CH=C=CH_2$	1	2 h	Methyl iodide	0	5	95	62
20	**g**	$R^1-CH=C=CHBr$	1	2 h	Octyl iodide	0	0	100	67

[a] Entries 13, 14, and 17—19: the allenic hydrocarbons were treated with s-butyl-lithium in THF at −80 °C (ref. 2). Entries 15, 16, and 20: the halide was treated with lithium metal in diethyl ether (ref. 2) then THF and HMPA were added at −80 °C. [b] The temperature of the reaction mixture was −78 °C; after addition of the electrophile the reaction mixture was maintained at −78 °C for 1 h and then allowed to rise to 0 °C and hydrolysed. [c] Distilled compounds. When **(5)** + **(6)** + **(7)** is not equal to 100, a minor product derived from lithioacetylide has been formed.

electrophiles gave a mixture of the acetylenic and allenic compounds **(5)** and **(6)**. Thus, addition of epoxides gave a mixture (45:55) of alcohols **(5)** and **(6)** in 80% yield [E = $CH_2CH(OH)R'$]. However, in the presence of 0.5 equiv. (or 1 equiv.) of hexamethylphosphoramide (HMPA),[4]‡ the 1,1-disubstituted allenic alcohols **(6)** [E = $CH_2CH(OH)R'$] were obtained in good yields (Table 1, entries 2, 3, and 6).[5]

Furthermore, when the lithiospecies **(2)** was maintained at −75 °C for 2 h in the presence of a larger quantity of HMPA (5 equiv.), it was transformed into the propadienyl-lithium compound **(4)** which was characterized by alkylation (Table 1, entries 11 and 12) and hydroxyalkylation (Table 1, entries 5, 8, and 9).

It may be assumed that with 1 equiv. of HMPA, **(2)** exists as an ion pair. However, this ion pair does not rearrange significantly into **(4)** (Table 1, entries 3, 7, and 10). With a larger amount of HMPA, a more dissociated ion pair is formed which is easily converted into the more thermodynamically stable allenic species **(4)**. Under these conditions, the species **(4)** and **(3)** are in equilibrium and react at different rates which vary with the electrophile added. With epoxides, they give a mixture of alcohols **(6)** and **(7)** and with alkyl iodides, **(4)** reacts faster than **(3)** [or **(3)** follows another reaction pathway] since the formation of the 1,1-disubstituted alkylated products **(6d)** and **(6e)** (Table 1, entries 11 and 12) is not observed ($\leqslant$1%). Similar results were obtained for the hydroxyalkylation (Table 2, entries 13—16) and alkylation (Table 2, entries 17—20) of propadienyl-lithium reagents.

The propadienyl-lithium compound **(4)** has been implicated as a possible intermediate in the intramolecular rearrangement of 1-lithioalk-2-ynes into lithioacetylides in THF at room temperature (20 h).[3]§ However, under our conditions, acetylenic derivatives were formed in less than 5% yield and the allenic derivatives **(7)** were isolated in significant yields.

The authors gratefully acknowledge financial support from the Centre National de la Recherche Scientifique.

Received, 18th May 1983; Com. 641

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‡ Under these conditions, alkylation was not selective and gave a mixture (30:70) of **(5d)** and **(6d)**. The ambident reactivity of the prop-2-ynyl-lithium **(2)** is thus dependent on the nature of the electrophile.

§ An intermolecular mechanism would fit our results more accurately since addition of undeca-1,2-diene to the prop-2-ynyl-lithium **(2)** ($R^1 = Pr^n$) gives, after trapping with electrophiles (propylene oxide, methyl iodide), the derivatives **(7c)** and **(7e)**, respectively, of undeca-1,2-dienyl-lithium **(4)** (R^1 = n-C_8H_{17}).