

NOVEL SYNTHESIS OF BENZYLITHIUMS FROM BENZYLSELENIDES

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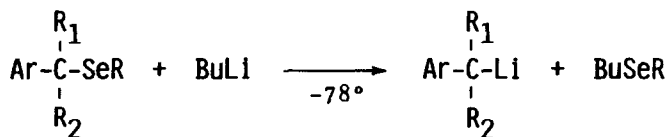
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*Benzylselenides are found to be valuable precursors of benzylolithiums.
The scope of the new method is disclosed.*

The synthesis of benzylolithiums is not straightforward since they cannot be prepared from benzylhalides by halogen-metal exchange¹⁻³ due to their propensity to react with the starting benzylhalides, nor from alkylbenzenes and bases due to competing ring metallation reaction.⁴ They are however available, although with some restriction on reaction of benzylmercury⁵ and benzyltin⁶⁻⁷ derivatives with alkylolithiums or by cleavage of the carbon-oxygen or carbon-sulfur bonds respectively of benzylethers⁸ with lithium and benzylsulfides with lithium naphthalenide.⁹

We report in this letter a new method, which allows the synthesis of various benzylolithiums from benzylselenides, and which takes advantage of the easy cleavage of the carbon selenium bond^{10,11} of these selenides by alkylolithiums.

Scheme 1



Best results are obtained when benzylphenyl- and benzylmethyl-selenides are added at -78° to n-butyllithium in THF-hexane (method A) or to t-butyllithium in THF (method B) or in ether-hexane (method C). Under these conditions a series of benzylolithiums bearing two hydrogens, one hydrogen and one alkyl groups and even two alkyl groups on the carbanionic center have been quite quantitatively obtained after 0.3h besides butylphenyl- or butylmethyl-selenides (scheme 1). It is interesting to notice that the C-Se bond cleavage occurs exclusively at the benzylic site. The other mode of cleavage leading to phenyl- or methylolithium was never observed.

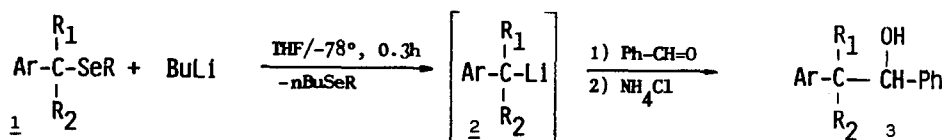
This new method offers several advantages over the other ones since:

1) It allows the synthesis of a wide range of benzylolithiums possessing even a highly hindered carbanionic center (table 1 entries g,h,m) or bearing an halogen⁸ or a methoxy group⁹ on the aromatic ring (table 1, entries i-l). It must be recalled that the later organometallics are not available from previous methods^{8,9}. — 2) The starting benzylselenides are readily available.¹²⁻¹⁴ — 3) The reaction medium is homogeneous. — 4) The butylselenides, formed as by products in these reactions, can be easily separated from the desired products.

The special case of cumylphenylselenide (table 1, entry c) deserves further comment since dicumyl (2,3-dimethyl-2,3-diphenylbutane) is formed in high yield (72 %) instead of the expected cumyllithium. This product probably arises from the substitution of the selenenyl moiety of the cumylselenide by the cumyllithium formed. This side reaction is minimized (20 % of dicumyl) if cumylmethylselenide is instead used as the starting material and can be completely suppressed if n-butyllithium is replaced by t-butyllithium (THF-hexane, -78°) (Table 1, entry m).

All the organometallics prepared during this study were reacted with benzaldehyde in order to get standardized results (Table) and have produced the corresponding alcohols in high yields. Unless otherwise stated, the reactions described in this study, were performed at -78° and were quenched with methanol at -78° prior to the usual work up.

Table



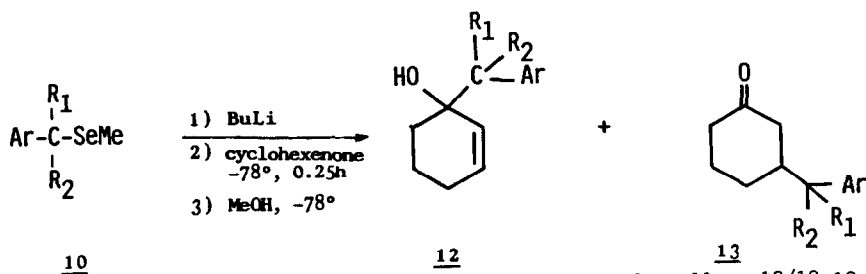
ENTRY	R	Ar	R ₁	R ₂	method	Yield in 3 (%)
a	Ph	Ph	H	H	A	86
b	Ph	Ph	H	Me	A	79*
c	Ph	Ph	Me	Me	A	0
d	Me	Ph	H	H	A	98
e	Me	Ph	H	Me	A	83
f	Me	Ph	Me	Me	A	72°
g	Me	Ph	Me	iPr	A	80
h	Me	Ph	nPr	iPr	A	78
i	Me	o-Cl-Ph	H	H	A	94
j	Me	p-Cl-Ph	H	H	A	91
k	Me	p-F-Ph	H	H	A	83
l	Me	p-MeO-Ph	H	Me	A	82
m	Me	Ph	Me	Me	B	81

* 1-phenyl-1 pentanol and bis cumyl are instead isolated in 43% and 74% yield

° bis cumyl is isolated in 20%.

In most of the cases, the order of addition of the reagents, has a great influence on the results. For example the reverse order of addition of the reagents (n-BuLi added to the benzylselenide) favors: — 1) in the case of cumylmethylselenide, the formation of dicumyl (38 % instead of 20%) (scheme 2a). — 2) in the case of benzylphenylselenide, its metallation, leading to 1-phenylselenobenzyl lithium (24 %) besides the desired benzyl lithium (61 %) (scheme 2b).

Scheme 4



Ar	R ₁	R ₂	Solvent	Overall yield %	13/12+13 ratio %
p-F-Ph	H	H	THF	68	60
p-F-Ph	H	H	THF/HMPT	67	100
p-F-Ph	H	H	ether	68	46
Ph	H	H	THF/HMPT	64	100
Ph	H	H	ether	-	56 +
Ph	H	Me	THF/HMPT	65	100
Ph	H	Me	ether	63	100
Ph	Me	Me	THF/HMPT	67	100
Ph	Me	Me	ether	66	100

+ by NMR.

We are at present looking at the limitation of this original method of synthesis of benzylolithiums and we are studying their reactivity towards other functional groups.

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