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3-Methylseleno-2-[methylselenomethyl]-propene Valuable Precursor of Trimethylenemethane and Trimethylenemethane dianion.

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Abstract : 3-Methylseleno-2-[methylselenomethyl]-propene proved to be a valuable precursor of 3-lithio-2-[methylselenomethyl]-propene and 3-lithio-2-[lithiomethyl]-propene. These have been reacted with various electrophiles and have in turn be successfully transformed into functionalized cyclic ethers.

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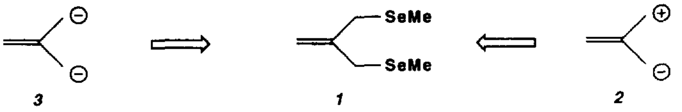
3-Methylseleno-2-[methylselenomethyl]-propene *1* proved to be a new versatile synthetic reagent able to transfer a four carbon unit as trimethylenemethane *2*[1] and isobutene dianion *3*[2] synthons (Scheme 1).

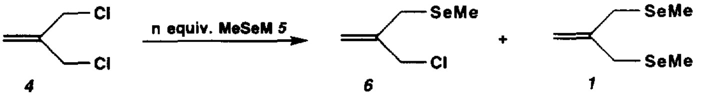
Scheme 1



Although a large number of related reagents bearing a variety of heteroatomic moieties have been disclosed for the same purpose over the past fifteen years, the new building block offers the advantage of being readily available and efficiently transformed to the desired synthons taking advantage of the known propensity of allylselenides[3] to produce allyllithiums on reaction with butyllithiums and to react with electrophilic species.

The starting material *1* has been readily synthesized from commercially available 3-chloro-2-[chloromethyl]-propene *4* and stoichiometric amounts of sodium methylselenolate *5a* in DMF (2 equiv. MeSeNa (from 1 equiv. MeSeSeMe, 2 equiv. NaH, DMF, 20°C, 1h) 20°C, 2h, 80% yield, Scheme 1; entry a). Selective formation of the mono-substituted derivative *6*, an intermediate in the synthesis of *1*, cannot be achieved under related conditions but occurs when potassium methylselenolate *5b* in THF is used instead (Scheme 2, entry c; compare entry c to b).

Scheme 2

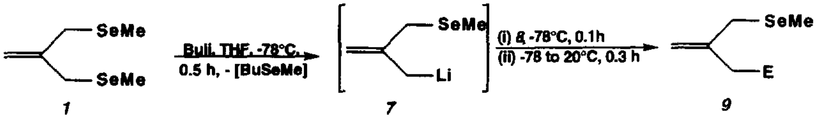


Entry	Conditions	*1*/*6* ratio	Yields[a] in *1* or *6*
a	2 equiv., MeSeNa, DMF, 20°C	100/0	80%
b	1 equiv. MeSeNa, DMF, 20°C	66/34[b]	
c	1 equiv. MeSeH, KOH, THF, 70°C, 1h	12/88	42%

(a) Refers to analytically pure compounds obtained by distillation (b) a 50/50 ratio is obtained if *5* is added very slowly to a solution of 4 in DMF.

3-Methylseleno-2-[methylselenomethyl]-propene *1* reacts readily with *n*-butyllithium (1 equiv.) in THF to produce, at -78°C, 3-lithio-2-[methylselenomethyl]-propene *7* in almost quantitative yield . This novel organometallic reacts at that temperature with a large array of electrophiles *8* including alkyl- and allyl bromides and carbonyl compounds to produce the corresponding adducts *9* in 34-72 % overall yield, Scheme 3.

Scheme 3

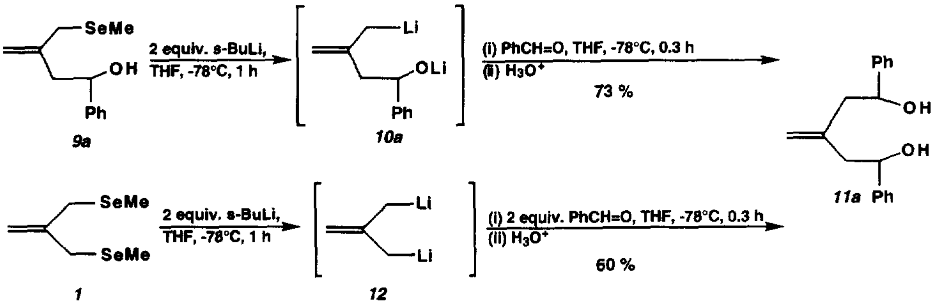


Entry	*8*	Product	E	Yield in *9* %
1	PhCH(=O)	*9a*	PhCH-OH	66
2	Ph(C=0)Me	*9b*	PhCMe-OH	72
3	$n\text{-}C_5H_{11}\text{-}Br$	*9c*	$n\text{-}C_5H_{11}$	65
4	$CH_2{=}CH\text{-}CH_2\text{-}Br$	*9d*	$CH_2{=}CH\text{-}CH_2$	34
5	$CH_2{=}CH\text{-}(CH_2)_2\text{-}CH_2\text{-}Br$	*9e*	$CH_2{=}CH\text{-}(CH_2)_2\text{-}CH_2$	70

The allyllithium *7* possesses a seleno moiety in γ-position susceptible to interaction with the carbanionic center. Although we cannot exclude rapid scrambling of the lithium and the methylseleno group from one to the other allylic sites, we have secured by a careful ^{77}Se NMR study [4] of this reaction that 3-lithio-2-[methylselenomethyl]-propene *7* is (i) already formed (+92 ppm) besides butyl methyl selenide (+ 155 ppm) at -78°C and (ii) quite stable between -78°C and - 50°C but very rapidly collapses around 0°C. No effort has been made to determine the nature of the resulting species.

The adducts *9* are functionalized allylic selenides susceptible to further reaction. Thus 4-phenyl-4-hydroxy-2-[methylselenomethyl]-butene *9a* is in turn cleaved by *sec*-butyllithium and produces, on further reaction with benzaldehyde *8a*, the diol *11a* in good yield ((i) 2 equiv. *s*-BuLi, THF, -78°C, (ii) 1 equiv. PhCH=O, (ii) H_3O^+, 73%, Scheme 4).

Scheme 4

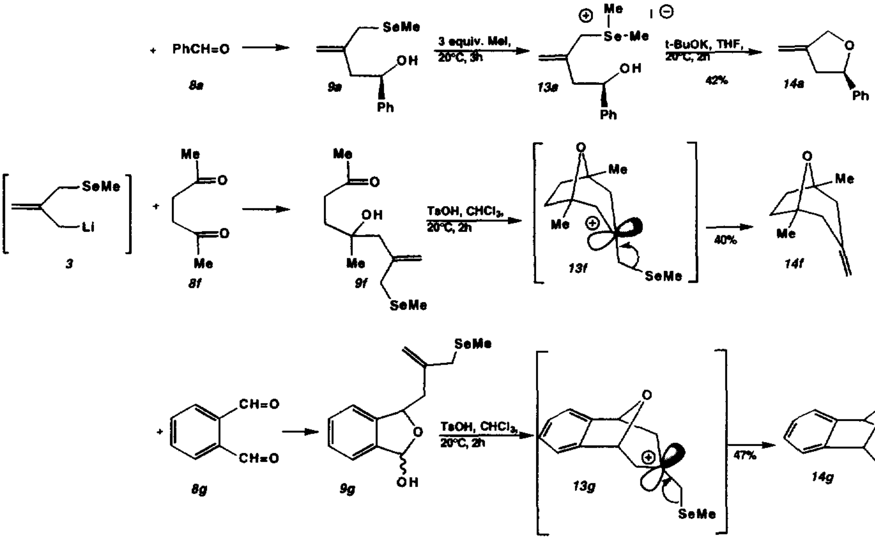


The synthesis of the same diol ***11a*** has been also achieved directly from ***1*** by sequential addition of two equivalents of *s*-BuLi (THF, -78°C, 1h) and of benzaldehyde (Scheme 4). This reaction involves the intermediary formation of 3-lithio-2-[lithiomethyl]-propene ***12*** which has been previously prepared$^{2a,d-f}$ from isobutene and *n*-butyllithium-TMEDA.

Although the later method seems by far more attractive, careful comparison performed in our laboratory, definitely shows the advantage of the method just disclosed : easy handling of the starting material, short reaction time and reproducible results.

3-Methylseleno-2-[methylselenomethyl]-propene ***1*** proved to be a valuable annelation reagent able to transfer a four carbon unit to various derivatives such as benzaldehyde ***8a***, 2,5-pentanedione ***8f*** and phthalaldehyde ***8g*** (Scheme 5). The first reaction provides functionalized alcohols, in about 60% yields, on which the methylseleno moiety can be transformed to a leaving group. This has been achieved by alkylation which produces a selenonium salt readily substituted by a hydroxyl group suitably positioned to give the 2-phenyl-4-methylidene tetrahydrofuran ***14a*** (Scheme 5),^{1f,1h,2j} or by taking advantage of the ability of the methylseleno moiety to stabilize a β-carbenium ion as in the transformation of ***9f*** to ***14f*** and of ***9g*** to ***14g***.

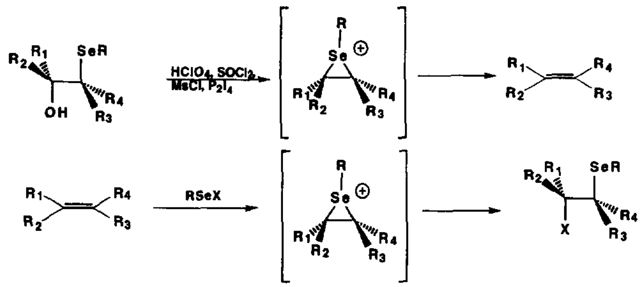
Scheme 5



Compounds ***14f*** and ***14g*** have been already very recently prepared by Molander^{2j} from the same carbonyl compounds and 3-iodomethyl-2-[(trimethylsilyl)methyl] propene ***15***. The yields described by this author are much better (66 and 91% respectively) than those reported in this paper which have not yet been optimized. Nevertheless our building block ***1*** is far more stable and more accessible than ***15***.

The reaction of the intermediate allylselenides ***9f*** and ***9g*** with cationic species leads us to suspect that this functional group might have a reactivity related to the one of allyl silanes and allyl stannanes. The formation of a seleniiranium ion, which has been already postulated as an intermediate in the stereospecific addition of selenium electrophiles to alkenes and in the stereospecific synthesis of alkenes from β-hydroxyalkylselenides, can be envisaged.^{5} We are working towards this end.

Scheme 6



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4. The NMR measurements have been carried out on a Jeol JNM 90 using the following settings : 19,93 MHz, 134 KHz, 5677 Hz and 20,000 Hz. The chemical shifts have been measured from the center of the window. Under these conditions the ^{77}Se NMR shift of *1* is : + 80.5 ppm (Me$_2$Se being used as external standart : 0 ppm).
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