

Original Syntheses of Carbonyl Compounds and gem-Dihalocyclopropanes
from β -Hydroxyalkylselenides

A. Krief^{*}, J.L. Laboureur and W. Dumont

Department of Chemistry
Facultés Universitaires Notre-Dame de la Paix
B-5000 Namur, Belgium

*β -hydroxyalkylselenides possessing two alkyl substituents on the carbon bearing the selenenyl moiety react with dihalocarbenes generated from haloforms and thalious ethoxide or under phase transfer catalysis to produce ring enlarged ketones as the sole product in the first case, as the main product in the second. The reaction takes another course when the dihalocarbenes generated from haloforms and tBuOK or from trihalomethylphenylmercury are employed and leads *inter alia* to dihalocyclopropanes.*

β -Hydroxyalkylselenides, easily prepared for example from two carbonyl compounds, are particularly valuable intermediates in organic synthesis¹. They resemble pinacols in reactivity but the presence of two heteroatomic moieties with different hardness allows incomparable chemoselectivity unattainable with pinacols.

Thus whereas acids, mesyl chloride, thionyl chloride, phosphorous triiodide, diphosphorous tetraiodide and trimethylsilyl iodide selectively react on the hydroxyl moiety and finally lead to olefins¹, tin hydrides, hydrogen peroxide, methyl iodide or magic methyl and silver tetrafluoroborate selectively react on the selenium atom producing alcohols¹, allyl alcohols¹, β -hydroxyalkylmethylselenonium salts¹, and ketones^{1c,d} respectively.

Recently, it was reported^{3,4} that dichlorocarbene smoothly generated from chloroform and thalious ethoxide selectively reacts on the selenium atom of β -hydroxyalkylselenides producing dichloroselenenylmethanes and either epoxides³ ($R_1 = H$, $R_2 = H$, or alkyl), or carbonyl compounds⁴ ($R_1 = R_2 = \text{alkyl}$) depending upon the number of substituents present on the carbon bearing the selenenyl moiety (Scheme, method A).

We report in this letter novel results concerning the reaction of β -hydroxyalkylselenides 3 possessing two alkyl groups on the carbon bearing the selenium atom with dihalocarbenes, generated in a more conventional way from haloforms under phase transfer catalysis⁵ [(50 % aqueous sol. of KOH, 0.44 mol. equiv. benzyltriethylammonium chloride, 5 mol. equiv. haloform in methylene dichloride (Scheme, method B)] or on reaction of potassium t-butoxide (10 mol. equiv.) with the haloform⁶ (20 mol. equiv.) in pentane at reflux (Scheme, method C).

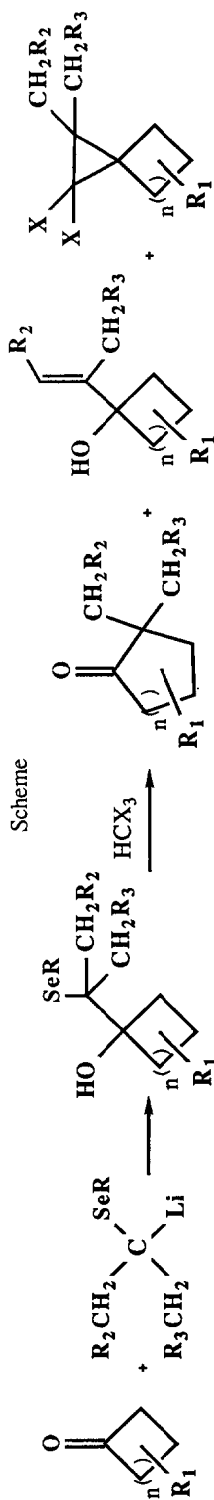
Under conditions involving phase transfer catalysis (method B) the reaction proceeds much faster (1 to 2 hr at 20°C) than the one using thallos ethoxide (8 to 24 hr at 20°C, method A) but produces, besides of the ring enlarged ketone 4 (63-80%), a small percentage (usually 0 to 15%) of an allyl alcohol formally resulting from the elimination of the selenenyl moiety and one of the hydrogen attached to a β -carbon. This side reaction, which was only rarely observed ⁷ under conditions A, is much more important

- i. when bromoform is used instead of chloroform (Scheme, compare entries Bg and Bh)
- ii. when the β -hydroxyalkylselenide is derived from large membered (> 6) cyclic ketones (Scheme, compare entry Bl to entries Ba, Bb, Bc, Bg and Bk) or from 1-lithio 1-(cycloalkyl)-methyl- or phenyl-selenides (Scheme, compare entries Be or Bf to entry Bc).

Reaction conditions B offer however over the previously published ones ^{4a} (method A) the advantages of : i. inexpensive reagents, ii. enhanced speed, iii. ease of separation for low boiling ketones (such as 2,2-dimethyl cyclopentanone, Scheme, entry Ba) from the solvent.

In the course of this work we have also reacted some β -hydroxyalkylselenides with the carbenes expected to be formed from haloforms and potassium t-butoxide. We found, at least for the cases studied, a great difference of reactivity between methylseleno and phenylseleno derivatives. Thus phenylseleno compounds lead to several unidentified products if the temperature of this exothermic reaction is allowed to increase, whereas rearranged ketones are produced in moderate yields besides dihalocyclopropanes generated in small amounts when the reactions are performed at -40° (Scheme, entries Ci, Cm). The reaction takes another course with methylseleno analogues and usually produces, regardless of the conditions used, dihalocyclopropanes in 20-50 % yields (Scheme, entries Cc, Cd, Cd, Cg, Ch and Cl). Ketones are often observed in trace or small amounts but in some cases these become the major component (Scheme, compare entries Cj to Cg). We have not yet a reasonable explanation for such discrepancies.

The cyclopropane derivatives are probably formed by addition of excess dihalocarbenes on olefins, probably transiently produced by reaction of the carbene on the oxygen rather than on the selenium atom of the β -hydroxyalkylselenides. Another alternative pathway would have been the intermediary formation of epoxides ³ and their deoxygenation by the



	2			R	Yield (%) in 3	X	Method A		Method B		Method C	
	R ₁	R ₂	R ₃				Yield (%)	4	Yield (%)	5	6	
a	H	H	H	Me	75	Cl	--	--	63	00	--	--
b	H	H	H	Me	45	Cl	56	00	70	00	--	--
c	H	H	H	Me	82	Cl	71	07	61	07	01	02
d	H	H	H	Me	82	Br	--	--	--	--	02	02
e	H	CH ₂	CH ₂	Me	80	Cl	71	22	67	22	19	08
f	H	CH ₂	CH ₂	Ph	75	Cl	87	20	71	20	--	--
g	4-tBu	H	H	Me	70	Cl	99	05	75 ^a	05	08	04
h	4-tBu	H	H	Me	70	Br	--	23	35 ^a	23	01	00
i	4-tBu	H	H	Ph	75	Cl	96	05	79 ^a	05	73	00
j	4-tBu	Me	Me	Me	35	Cl	80 ^a	03	76 ^a	03	78	01
k	H	H	H	Me	64	Cl	90	04	74	04	05	00
l	H	H	H	Me	76	Cl	79	13	73	13	01	00
m	H	H	H	Ph	70	Cl	--	--	--	--	45	00

Method A: 5.6 eq. TiOEt/CHCl₃, 20°C, 8h.

Method B: 50% aq. KOH/CHCl₃ - CH₂Cl₂, PhCH₂NEt₃Cl, 20°C/1h -

Method C: 10 eq. tBuOK/20 eq. CHX₃, pentane, exothermic.

Method C': 20 eq. tBuOK/40 eq. CHCl₃, pentane -40°C.

a) The epoxide formed by elimination between the hydrogen of the hydroxyl group and the selenenyl moiety is present in trace amounts in the medium.

b) As a 80/20 ratio of stereoisomers.

c) This reaction has been performed at low temperature under conditions C'.

carbenes. This process, which has few precedents in the literature ^{5,8} can be discarded in our case since oxidoisopropylidene cyclohexane is recovered unchanged under the conditions of the above mentioned reaction (method C).

Similarly, dihalocyclopropanes are obtained when the β -hydroxyalkylselenides are reacted with trihalogenomethylphenyl-mercury under conditions in which dihalocarbenes are expected to be formed ^{6,9}.

Some of these dihalocyclopropanes have also been prepared in better yields from β -hydroxyalkylselenides by a two steps sequence involving first the synthesis of the olefin ¹⁰ (PI_3/NEt_3 , CH_2Cl_2 , 20°) and then its cyclopropanation by the dihalocarbene generated from potassium t-butoxide and haloforms.

From the results now available it is clear that the conditions under which the dihalocarbenes are produced have a dramatic effect on the site of attack of the β -hydroxyalkylselenides and on the nature of the resulting product. The reaction involving thallos ethoxide in chloroform, although often slow and involving an exotic reagent is without doubt the most suitable (generality, high yield, no side reaction) for the ring enlargement of β -hydroxyalkylselenides derived from cyclic ketones (Scheme, compare column A to B and C).

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