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ORIGINAL METHOD FOR THE RING ENLARGEMENT OF CYCLIC KETONES

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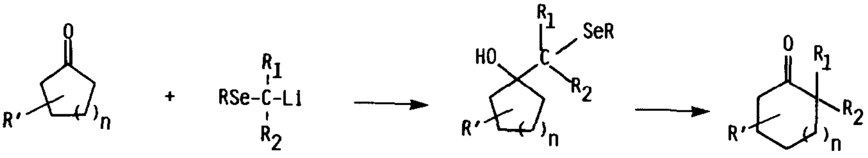
Thallium ethoxide in chloroform was found to be a particularly valuable combination for the rearrangement of β-hydroxyselenides to ketones.

We recently found [1] that α-selenoalkyllithiums bearing two alkyl groups on the carbanionic center are valuable reagents for the ring enlargement of cyclic ketones [2-4] (Scheme 1). The key step of this transformation is without contest the rearrangement of the β-hydroxyselenides which takes place with silver tetrafluoroborate at reflux of chloroform.

Scheme 1



Best results were obtained if the reaction was performed under experimental conditions which avoid the acidic medium propitious to the concomitant formation of olefins . However, except when the reactions are run in the presence of basic alumina [1], ketones are not formed if silver tetrafluoroborate is reacted in the presence of a base.

We have tried several metal salts in order to increase the yield of rearranged ketone and thought to use a salt possessing a soft metal able to coordinate to the soft selenium atom and a basic counter ion able to transform at the same time the hydroxyl group to the corresponding alcoholate.

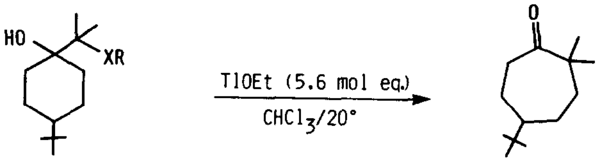
In the course of that systematic work we found that thallium ethoxide in chloroform fulfil our requirement. Thus β-hydroxyselenides possessing two alkyl residues on the carbon bearing the selenenyl group rearrange smoothly to the desired ketone on reaction with thallium ethoxide (5 mol.eq) in chloroform .

The reactions are usually conducted at room temperature for 3 to 12 hrs, are much more rapid (∿ 1 hr) if performed at +70° and provide particularly high yield of ketones (Table).

These experimental conditions have been successfully applied to phenylthio derivatives which have been for the first time rearranged to ketones [5] (Table, Scheme 2).

Methylseleno derivatives were found to be more reactive than their phenylseleno analogues themselves more reactive than the phenylthio compounds (Scheme 2).

Scheme 2



1 → 2

X	R	(2 / 1 ratio , time in hrs)
Se	Me	(88 /12, 2) (95 / 4, 4)
Se	Ph	(80 /20, 4) (90 /10, 6)
S	Ph	(46 /54, 7)

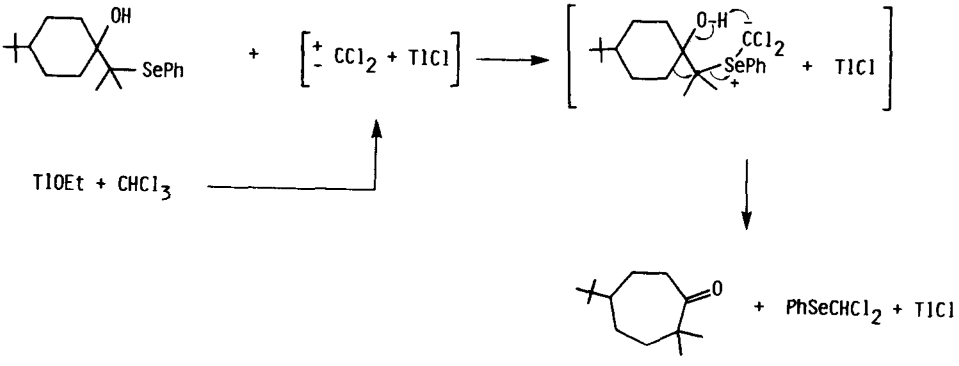
The reaction does not occur in ether, or THF, pentane, benzene and more surprising in methylene dichloride or carbon tetrachloride. It however takes place in bromoform but in the later case the reaction is much faster and produces olefins (15-20 %) besides the ketone.

The rearrangement also takes place in ether and methylene dichloride but provided that two or three equivalents of chloroform are present in the medium.

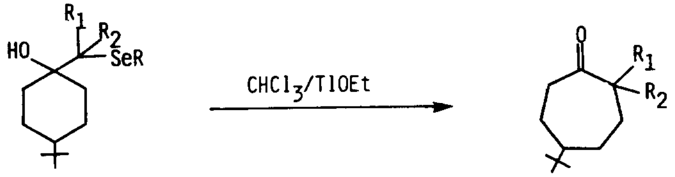
This lead us to suspect that thallium ethoxide does not react directly on the β-hydroxyselenide but that dihalogeno carbenes are involved in these transformations.

The concomitant formation of thallium chloride [6] and phenylseleno dichloromethane in the reaction of thallium ethoxide in chloroform with β-hydroxyphenylselenides tends to support the proposal (Scheme 3).

Scheme 3

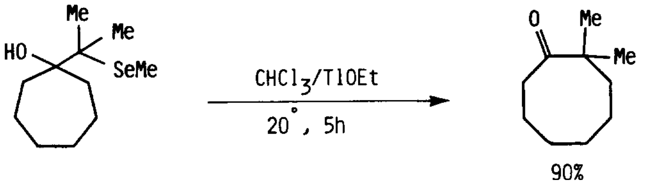


TABLE



	R_1	R_2	R	Yield %. (temperature, time).	
a	Me	Me	Me	100 (20, 8)	96 (60, 2)
b	Me	Me	Ph	96 (20, 8)	95 (60, 2)
c	Me	Et	Me	98 (20, 7)	
d	Me	Et	Ph	83 (20, 8)	
e	Ph	Me	Me	74 (20, 3)	

f



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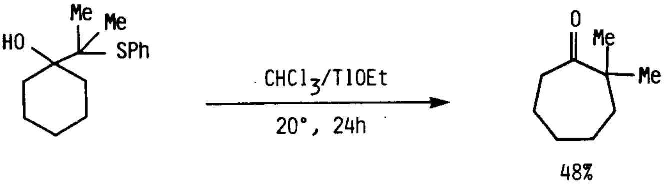

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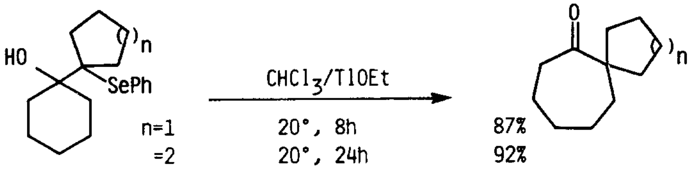
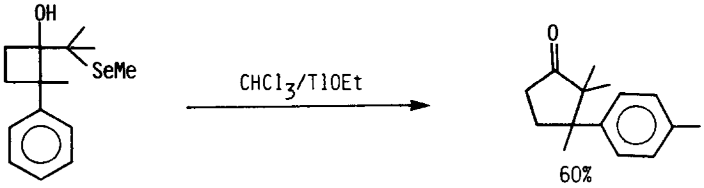


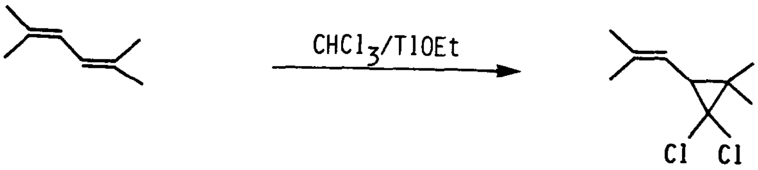
i



* Obtained as a 73/27 mixture of stereoisomers which have been separated

Another support arises from the formation of the dichlorocyclopropane if 2,5-dimethylhexadiene is reacted in place of the β-hydroxyselenide under the conditions reported above (Scheme 4). This compound presumably results from the addition of dichlorocarbene to the diene.

Scheme 4



It is not the only example since other authors [7,8,9] have reported that cyclopropanation of olefins can occur on reaction of thallium derivatives and chloroform.

We are currently investigating the scope and limitation of this new method of homologization of ketones which was already applied to the synthesis of cuparenone [4b] (Table entry i). We are also trying to perform the rearrangement using carbenes prepared by more conventional routes.

Références and Notes

1) D. Labar, J.L. Laboureur, A. Krief, Tet. Lett., 983 (1982).
2) For other methods implying the rearrangement of β-hydroxy diazoniums to carbonyl compounds :
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3) For other methods implying the rearrangement of β-hydroxy halides to carbonyl compounds :
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   d. R.C. Gadwood, J. Org. Chem., 48, 2098 (1983)
   e. H. Nishuyama, T. Kitajima, A. Yamamoto, K. Itho, J.C.S. Chem. Comm., 1232 (1982).
5) β-hydroxy thioacetals [a] and β-hydroxy orthothioesters [b] rearrange however to α-thio and α-dithioketones respectively, see for example :
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   b. S. Knapp, A.F. Trope, R.M. Ornaf, Tet. Lett., 4301 (1980).
6) That Thallium chloride is formed during the process has been confirmed by analysis of the precipitate by neutron activation. We thank Prof. Demortier, Facultés Universitaires Notre-Dame de la Paix, Namur, for this analysis.
7) C.M. Hull, Synth. Comm., 2, 121 (1972).
8) A. McKillop unpublished results. We thank Prof. McKillop for providing us at the beginning of the work, with his result on the cyclopropanation of olefins with Thallium ethoxide in chloroform.
9) V.I. Shcherbakov, S.F. Zhil'tsov. Zhur, Obsch. Khim., 40, 2046 (1970).

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