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NEW METHOD FOR THE RING ENLARGEMENT OF CYCLIC KETONES

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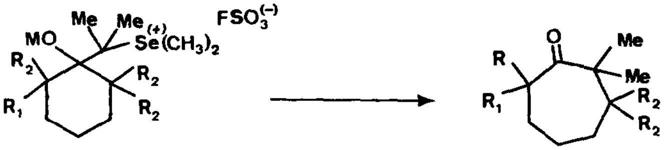
A simple two step procedure which allows thering enlargement of cyclic kktones is disclosed which takes advantage of the high nucleophilicity of α-selenoalkyllithiums towards carbonyl compounds and of a novel transposition reaction which occurs on the resulting β-hydroxyselenides.

The ring enlargement of cyclic ketones is a valuable synthetic transformation which formally requires the insertion of a carbene between the carbonyl group and one of the two adjacent carbon atoms [1].

During our work directed towards the synthesis of epoxides from hindered ketones [2], we had the opportunity to observe a new rearrangement which immediately(0 2hr) took place when β-hydroxy selenonium salts 4a and 4b were gently heated (∿ 40°) or dissolved in a chlorinated solvent (CH_2Cl_2, 20°) and which produces the cycloheptanones 5a and 5b innearly quantitative yield (Scheme I).

SCHEME I



4	a	$R_1=R_2=Me$	M = MgX/20°	94%	5
	b	$R_1=H$ R = Me	M = H/20°	90%	
	c	$R_1=R_2=H$	M = H/180°	trace	

This rearrangement should be valuable in organic synthesis if it could be generalized. We therefore tried to extend it to other β-hydroxyselenides 3 These were synthetized in good yield from 4-tbutyl cyclohexanone, cyclohexanone and cyclopentanone according to our published procedure [2] and were tested as candidates for the ring enlargement reaction.

We rapidly found that the presence of the two alkyl groups on the carbon bearing the selenonium salt (prepared from 3, FSO_3CH_3 in ether)[2] was essential for occurrence of the desired rearrangement which was limited to hindered derivatives. For example, the salt 4c derived from cyclohexanone was unaffected when dissolved in chlorinated solvents (20°C or 80°C) and produces only trace amount of 2,2-dimethyl cycloheptanone on heating under vacuum, even at 180°C.

The chance of generalization had become very low when we observed that the β-hydroxy-

selenide 3c (R =C_6H_5, scheme II) instantaneously reacts with silver tetrafluoroborate at 20°C in chloroform, and produces a yellow crystalline intermediate which slowly transforms to the desired 2,2-dimethylcycloheptanone 5c on heating at 50° for 2.5 hrs (method A).
This new reaction (method A) was found to occur on a wide range of β-hydroxyphenylselenides and β-hydroxymethylselenides 3 possessing two alkyl groups on the carbon [3] bearing the selenyl moiety (scheme II). The yields in rearranged ketones were however modest (40-60%) since olefins [4] were simultaneously formed.

The formation of these olefins can be easily rationalized from our previous work [5] The fluoroboric acid liberated during the ring enlargement is able to transform the β-hydroxyselenide to a tetrasubstituted olefin which is further isomerized in this highly acidic medium. In order to minimize this side reaction, we tried to avoid the acidic medium and we carried out the reaction in the presence of triethylamine ; we also reacted the silver tetrafluoroborate on a preformed solution of the lithio alcoholate derived from the β-hydroxyselenide. In none of these cases, the transposition occurred.

After several unsuccessful attempts [6,7], we found that the transformation could be readily achieved if basic alumina (Woelm 02072 , 8 mol eq) was present in the reaction mixture (method B, scheme II) and even better results were obtained if the β-hydroxyselenide is reacted in a chlorinated solvent, with a preformed $Al_2O_3/AgBF_4$ suspension prepared by stirring together silver tetrafluoroborate (1.4 mole/eq) the alumina (Woelm 02072 ; 8 eq) and anhydrous ether (3 ml/mmol) followed by removal of the solvent in vacuo (method C, scheme II). Typical experiment is shown on the final page. All the yields described in this paper refers to those of purified compounds whose spectroscopical data (IR, ^{1}H-NMR, MS) and microanalysis are in perfect agreement with the proposed structures

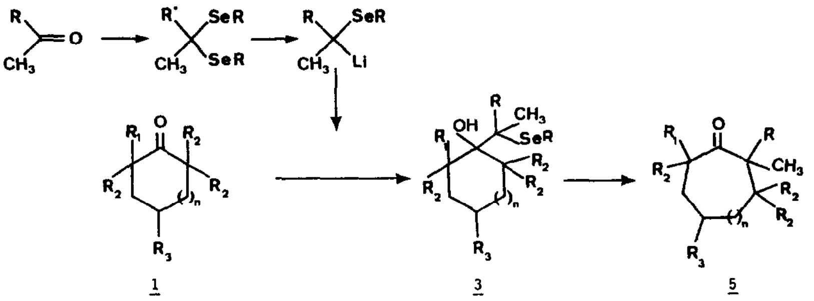
The set of reactions presented here should implement the methods already described [1] for ring enlargement of cyclic ketones, since most of those, to our knowledge, have not been so far described to insert one carbon bearing two alkylgroups α to the carbonyl of a ketone.
The other advantages of the method presented lie in

a) the absence of polyhomologation reactions often observed if both the new carbon-carbon bond formation and the ring enlargement occur nearly simultaneously (i.e. diazoalcane reaction) ,
b) the absence of epoxides (a by product often simultaneously formed in other methods) ,
c) the great availability of α-selenoalkyllithiums (from carbonyl compounds) and their high nucleophilicity towards carbonyl compounds [2] which permits the high yield syntheses of β-hydroxyselenides

Finally, the methodology disclosed is simple and unusual since it allows the formal insertion of one ketone (activated as a selenoacetal) into another one (scheme II).

Work is now in progress in order to determine the scope and limitation of this new transposition. We are also trying the reactivity of other metal salts on β-hydroxyselenides.

SCHEME II



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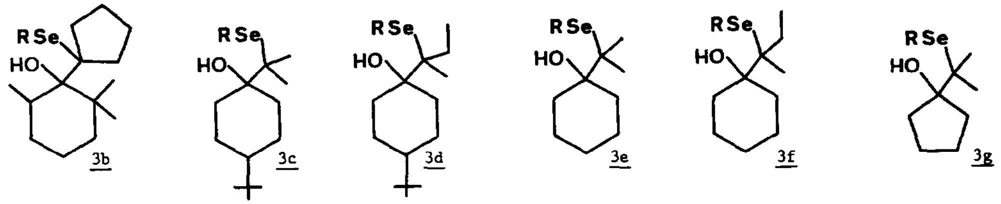

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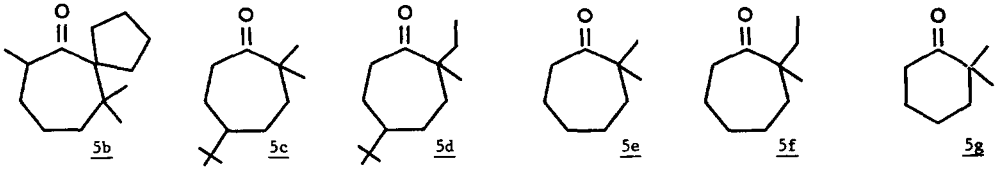

Yield in 3 %*	- , *63*	70, *75*	60, *75*	82**, *70***	79, *70*	- , *45*
Methods+						
A$_1$	50(20,5 3)					75(20,5)
A$_2$		61(20,8) *38(80,3)*	32(80,3) *38(80,3)*	39(40,2 5) *40(20,2 5)*	50(80,3)	
B		47(80,0 2) *74(80,1 5)*	45(80,16) *50(20,3)*	68(40,2 5) *85(20,2 5)*		
C		62(80,4) *89(20,1 5)*	65(20,3 5) *70(80,1 5)*			

* The preparation of these compounds has been done[2] in ether at -78°, except for ** , the yields refer to purified products
Normal character refers to R = CH$_3$, italic character R = C$_6$H$_5$

** Reaction performed in THF at -78°

\+ Method A$_1$ AgBF$_4$/CH$_2$Cl$_2$, Method A$_2$ AgBF$_4$/CHCl$_3$, Method B AgBF$_4$ + Al$_2$O$_3$, Method C AgBF$_4$ – Al$_2$O$_3$
The numbers refer respectively to the yield and between brackets to the temperature and the time of the 3 → 5 reaction

REFERENCES AND NOTES

1) a. Transformations using the Nitrogen atom as the leaving group

- C.D. Gutsche, Org. React., 8, 364 (1954)
- P.A.S. Smith and D.R. Baer, Org. React., 11, 157 (1960)
- A.E. Greene, J-P. Deprés, J. Amer. Chem. Soc., 101, 4003 (1979)
- W.L. Mock and M.E. Hartman, J. Org. Chem., 42, 459 (1977)
- W.L. Mock and M.E. Hartman, J. Amer. Chem. Soc., 92, 5767 (1970)
- R.K. Murray and T.M. Ford, J. Org. Chem., 44, 3504 (1979).

b. Transformations using Halogen as a leaving group

- A.J. Sisti, J. Org. Chem., 33, 453 (1968)
- A.J. Sisti, J. Org. Chem., 33, 3953 (1968)
- H. Taguchi, H. Yamamoto, H. Nozaki, J. Amer. Chem. Soc., 96, 6510 (1974)
- J. Villieras, P. Perriot, J.F. Normant, Synthesis, 968 (1979).

c. Transformations using Sulfur as a leaving group

- S. Knapp, A.F Trope and R.M. Ornaf, Tet. Lett., 4301 (1980).
- T. Cohen, D. Kuhn, J.R. Falck, J. Amer. Chem. Soc., 97, 4749 (1975).

2) D. Labar, A. Krief, unpublished results.

3) We are currently trying to apply this reaction on derivatives bearing two hydrogens or a hydrogen and an alkyl group on the carbanionic center of the α-selenoalkyllithium.

4) With some exception no attempt was made in this preliminary work to isolate these volatile olefins.

5) a. J. Remion, W. Dumont and A. Krief, Tet. Lett., 1385 (1976)

b. J. Remion and A. Krief, Tet. Lett., 3743 (1976) and references cited.

6) Unsuccessful attemps include the use of . Ag_2CO_3 ; $HgCl_2$; Φ_3CSbF_6 , $Tl(OCOCF_3)_3$, $Tl\ (C_5H_5)_2$ in various solvents.

7) Successful attemps include the use of $AgSbF_6$ and TlOEt. They are under careful study in our laboratory.

TYPICAL EXPERIMENTS.

Anhydrous Silver Tetrafluoroborate (280 mg, 1.4 mmol) and basic Alumina (woelm.02072, 808 mg, 8 mmol) are stirred at 20° in ether (anhydrous, 3 ml) for 0.3 hr. The solvent is then removed under vacuum (rotatory evaporator, 15 mm Hg, 0.3 hr). The residue is suspended in chloroform [1,5 ml for experiment conducted at 20°, 5,5 ml for those at 60°] and the β-hydroxyselenide 3c (R = C_6H_5) (354 mg, 1 mmol) in chloroform (0.5 ml) is then added. After stirring at 20° for 1.5 hr (reaction over by TLC), ether (20 cc) is added and the resulting suspension is filtered over flo.
The solvents are removed in vacuo and the crude mixture is purified on Preparative Layer chromatography (PLC, SiO_2 Merck, pentane-ether 85/15, rf 0.5). The cycloheptanone 5c (175 mg) is isolated in 89 % yield.

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