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CYCLOPROPANONE DISELENOKETALS INTERESTING BUILDING BLOCKS IN ORGANIC SYNTHESIS [1]

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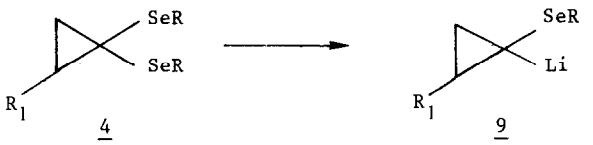
The formation of a cyclopropane ring and the direct introduction of a cyclopropyl moiety in organic molecules has attracted wide interest in synthetic organic chemistry. Both electrophilic [3] and nucleophilic [4-8] moieties have been used for the second problem and recently several new methods have appeared for the later case [4-8].

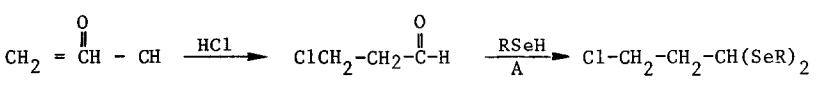
The aim of this report is to present new synthetic methods for the introduction of nucleophilic cyclopropyl moieties using the yet unknown 1-lithio 1-cyclopropyl selenides 9 and to propose new synthetic routes to such reagents from open chain derivatives.



4 9

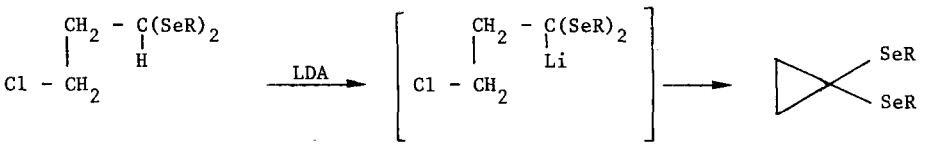
Selenoketals [9-14] have been recently introduced as potent precursors of α-selenocarbanions [9-13] However cyclopropanone selenoketals were unknown [2] and the classical routes [9-11] are not very efficient for such special case due to the unavailability of cyclopropanones.

The first route to such diselenoketals starts from easily available acroleine 1. Addition of excess of anhydrous hydrochloric acid to a CCl_4 solution of acroleine produces the 3-chloropropanal 2 which is directly transformed to 3-chloro 1,1-selenomethyl ketal 3a (65% yield) by addition of methyl selenol to the crude acidic mixture [10].
When selenophenol is used in place of methyl selenol, successful synthesis of 3-chloro 1,1-selenophenyl propane 3b (75% yield) requires the drastic removal of the excess of hydrochloric acid and the adjunction of zinc chloride catalyst to the crude solution [11].



1 2 R:CH_3 A: HCl 3a : 65%
R:C_6H_5 A: $ZnCl_2$ 3b : 75%

The synthesis of the desired cyclopropanone diselenoketals 4 requires in both cases the successful metalation α to the selenyl moiety and subsequent cyclization. Using lithium diisopropyl amide (LDA) as base, 3-chloro 1,1-selenophenyl propane 3b is cleanly transformed to the desired cyclic acetal 4b in 80% yield (LDA 1eq. - THF/-78°C 1hr., 20°C 2 hrs). But more drastic conditions are required for the selenomethyl case; the desired acetal 4a being obtained when 3 equivalents of LDA are used (THF/25°C, 1 hr .)[25]



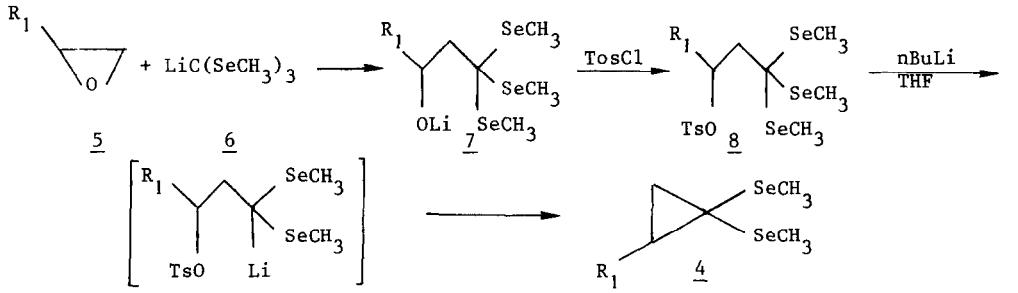
3a R : CH_3 77% 4a

3b R : C_6H_5 80% 4b

Another strategy for cyclopropanone diselenomethylketal synthesis was also used which takes advantage of the preparation of the desired α selenomethyl carbanion via the carbon selenium bond cleavage in α heterosubstituted selenomethyl orthoester [14,15].

The starting 3-tosyloxy 1,1,1-selenomethyl alcane 8 is prepared by reacting lithio selenomethyl orthoformiate 6 [14,15] with epoxides 5, and "in situ" tosylation of the resulting lithium alkoxides [* selenomethyl orthoformiate/LDA-THF/-78°C, 1.30 hr. - * epoxide 5/-78°C, 1-2 hrs. 20°, 1 hr * TosCl 1 eq./0°C, 15 hrs]. The THF solution containing the crude tosylate is then cooled at -78°C and directly reacted with 1 eq. of nBuLi for 1.5 hr. and at 20°C for 0.5 hr.
After hydrolysis and usual work up, the desired cyclopropanone selenomethyl acetal 4 is obtained after distillation or purification by preparative then layer chromatography [16,17,18]

Using this procedure, the ketals 4a, 4c, 4d and 4e are prepared 60,60,47 and 45% overall yield respectively from ethylene oxide;1,2-oxidopropane;1,2-oxidooctane and 1,2-oxidododecane.



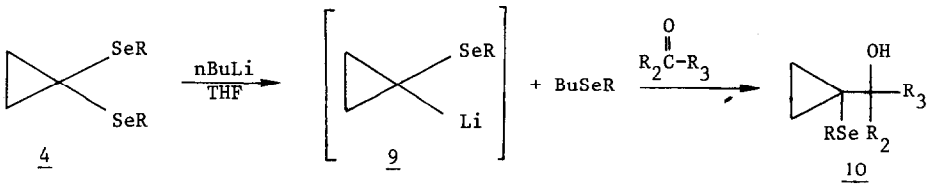
5 6 7 8 4

4a R_1 = H (60%)
4d R_1 = C_6H_3 (47%)

4c R_1 = CH_3 (60%)
4e R_1 = $C_{10}H_{21}$ (45%)

The second part of this report deals with the cleavage of the carbon selenium bond in cyclopropanone selenoacetals 4.

Preliminary results indicate that both diselenophenyl- and diselenomethylketals 4 are efficiently transformed to their corresponding α selenocarbanions when reacted with nBuLi in THF for 0.10 to 0.5 hr. using the conditions under which the other selenoacetals are cleaved (nBuLi-THF/ -78°C)[9,10,12,13]. These intermediates are trapped at -78°C with aldehydes and ketones producing the corresponding β-hydroxyselenides 10 in quite good yield.



4 9 10

R	R_2	R_3	Yield in 10 %
C_6H_5	H	C_6H_{13}	72
CH_3	H	CH_3	69
CH_3	H	C_6H_{13}	75
CH_3	H	$C_{10}H_{21}$	40
CH_3	CH_3	C_3H_7	64
CH_3	C_2H_5	C_2H_5	55

These last results merit some comments : B. Trost [8] recently reported that 1-lithio 1-thiophenyl cyclopropane enolises open chain ketones and thus acts as a base and surprisingly, there is no report in the case of aldehydes. From our experimental results, we can say that seleno analogs 9 are much more nucleophilic (see table), a tendancy already observed with others α-selenocarbanions [10,12,22]. However, the moderate yields uncountered in some examples (see table) lead us to admitt that they are more basic than other α selenocarbanions already described [10,12,13,22] β-hydroxycyclopropyl selenides 10 should be valuable intermediates in organic synthesis not only in relation with the previous work on β-hydroxyselenides [10,12,13,19-22] but also due to the presence of a cyclopropane ring bearing a potentially good leaving group directly branched [16;4,7] and also an hydroxyl group in β position [23,24].

Extensive work is in progress in our laboratories to know more about the reactivities of cyclopropanonediselenoketals, 1-lithio 1-selenyl cyclopropanes and also β-hydroxyselenides presented here.

References

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