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NUCLEOPHILIC RING OPENING OF LACTONES VIA S_N2-TYPE REACTION WITH UNCOMPLEXED PHENYL SELENIDE ANION

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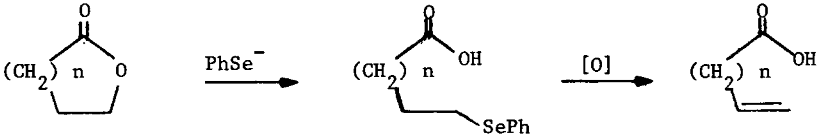
Recently, we have been interested in using phenyl selenide anion as the key reagent for the conversion of lactones to ω-vinylcarboxylic acids.[1] Conceptually, our approach to this problem is shown in Scheme I.

Scheme I



The choice of phenyl selenide anion as the ring-opening reagent seemed particularly attractive for two reasons. First, a simple lactone possesses two sites which are potentially reactive to nucleophiles, the carbonyl carbon and the carbinolic carbon. Based on Hard Soft Acid Base Theory, a soft nucleophile, such as phenyl selenide anion, should show a preference for S_N2-type attack at the carbinolic carbon and thus produce an ω-phenylselenylcarboxylic acid.[2] Second, the conversion of the ω-phenylselenylcarboxylic acid to the corresponding ω-vinylcarboxylic acid via an oxidation/elimination sequence should prove to be a facile, high yield process.[3]

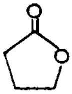
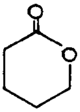
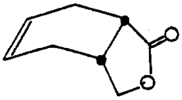
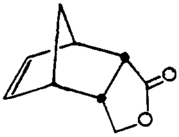
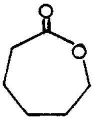
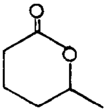
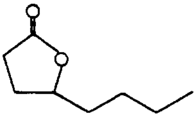
As reported in the previous communication we have developed a new method for generating uncomplexed phenyl selenide anion, 1 (see Scheme II).

Scheme II

$$\underset{2}{\text{PhSeSePh}} + \text{Na}^{o} \xrightarrow{\text{THF}} \underset{1}{\text{Na}^{+}\,{}^{-}\text{SePh}} \xleftarrow{\text{THF}} \underset{3}{\text{PhSeH}} + \text{NaH}$$

If 1 is solubilized by the addition of either 1-2 ml of hexamethylphosphoramide (HMPA) or 0.05 molar equivalents of 18-Crown-6, nucleophilic ring opening of a variety of primary lactones can be effected in high yield under very mild conditions. A listing of the lactones studied is

Table I. The Reaction of Uncomplexed Phenyl Selenide Anion with Lactones.

Substrate	Compound Number	Cation Solvator	Temp. (°C)	Time[a] (hrs.)	Yield[b]
	4	HMPA	67°	3	79%
		18-Crown-6	25°	3	85%
	5	HMPA	67°	3	85%
		18-Crown-6	25°	3	85%
	6	HMPA	67°	4	75%
	7	HMPA	67°	4	80%
	8	HMPA	67°	6	20%
		18-Crown-6	25%	6	0%
	9	HMPA	67°	20	0%
		18-Crown-6	25°	20	0%
	10	HMPA	67°	20	0%
		18-Crown-6	25°	20	0%

[a] % yields refer to isolated yields.

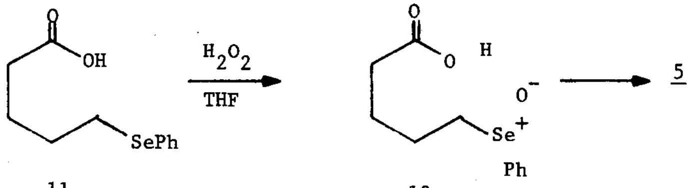
[b] Reaction times have not been optimized.

given in Table I. The experimental procedure for this process is the same as the procedure given in the previous communication for the alkyl-oxygen cleavage of esters and thus will not be repeated here.

With the exception of 8, all of the substrates yielded essentially equivalent results regardless of whether HMPA in refluxing THF or 18-Crown-6 in ambient THF was employed as the cation solubilizer. The differences observed with 8 probably result because the preferred conformations of the seven-membered ring lactone are less suitable for S_N2-type displacement than their six- and five-membered ring counterparts. The higher reaction temperature (67^o vs. 25^o) could increasingly populate the less stable conformation required for efficient displacement and thus increase the reaction rate. Consistent with this, Scarborough and Smith have cleaved 8 with phenyl selenide anion in 90% yield at 110^o-120^oC.[5]

It is also of interest to note that both 9 and 10 can be recovered unchanged even after exposure to the reaction conditions for periods as long as 20 hours. This was somewhat surprising in that, as the reaction proceeds, a copious precipitate is formed. This may be interpreted in terms of an initial acyl-oxygen cleavage by phenyl selenide anion forming a ω-hydroxyphenylselenyl ester, followed by subsequent reclosure to the lactone during work-up.[6]

Our initial attempts at converting 5-phenylselenylvaleric acid, 11, to 4-pentenoic acid, 12, via oxidative elimination with hydrogen peroxide provided us with an interesting result. The only product isolated from the oxidation of 11 was valerolactone, 5. Thus, hydrogen peroxide apparently oxidizes 11 to an intermediate selenoxide, 13, which does not rapidly undergo cis elimination.[7]



11

13

Instead selenoxide 13 undergoes a type of [2,3]-sigmatropic rearrangement to yield 2.[8] However, if the ω-phenylselenyl carboxylic acid is esterified either with boron trifluoride etherate in refluxing methanol or ethereal diazomethane, oxidation to the corresponding selenoxide proceeds in a straightforward fashion.[9] Although many different experimental procedures for effecting the thermal elimination of these selenoxides have been investigated, the best results were achieved using the method described by Scarborough and Smith.[4] Utilizing this method, yields of 60-75% could be consistently obtained for the ω-vinylcarboxylic esters derived from 4, 5, 6, 7 and 8.

In summary, uncomplexed phenyl selenide anion has been shown to be an effective reagent for opening five- and six-membered ring primary lactones via an S_N2-type cleavage. Further studies involving the use of uncomplexed phenyl selenide anion, as well as other highly-reactive selenium anions, will be the subject of future reports.

References

(1) There is some literature precedent for effecting lactone ring openings with a number of selenium anions. For some examples, see: L. -B. Agenas, Arkiv. fur Kemi, 24, 415 (1965); ibid., 573 (1965); W. H. H. Gunther, J. Org. Chem., 31, 1202 (1966); K. Sindelar, J. Metysova and M. Protiva, Coll. Czech. Chem. Commun., 34, 3801 (1969).

(2) T. S. Ho, Chem. Rev., 75, 1 (1975).

(3) K. B. Sharpless and R. F. Lauer, J. Amer. Chem. Soc., 95, 2697 (1973); H. J. Reich, I. L. Reich and J. M. Renga, J. Amer. Chem. Soc., 95, 5813 (1973).

(4) All compounds gave satisfactory i.r., n.m.r., m.s. and C, H analysis.

(5) See accompanying paper. We sincerely thank Prof. Amos Smith for providing us with a preprint of his work prior to publication.

(6) The cleavage of isopropyl benzoate by phenyl selenide anion may also proceed by acyl-oxygen cleavage. See previous communication.

(7) The oxidation state of 13 is uncertain.

(8) An alternative mechanism could involve a proton shift from the acid to the selenoxide oxygen followed by an S_N2 displacement.

(9) This process is most conveniently accomplished via ozonolysis at -78°C in dichloromethane solution. See: G. Ayrey, D. Barnard and D. T. Woodbridge, J. Chem. Soc., 2089 (1962).