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AN EFFICIENT GENERAL SYNTHESIS OF ω-OLEFINIC METHYL ESTERS

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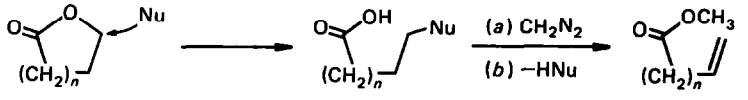
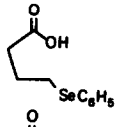
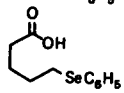
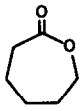
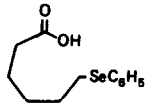
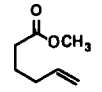
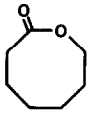
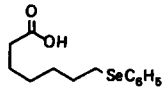
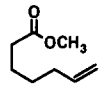
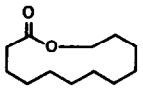
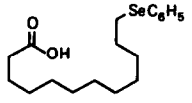
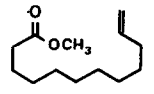
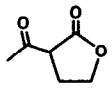
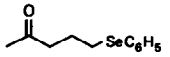
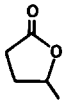
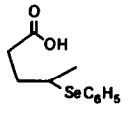
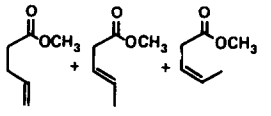
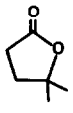
During the course of another investigation, we required an efficient approach to a number of simple ω-olefinic methyl esters. An attractive route to such systems appeared, as illustrated below, to be nucleophilic cleavage of the alkyl-oxygen bond of readily available, appropriately sized lactones, followed after esterification via elimination of the initially introduced nucleophile.[1,2,3] Sodium phenyl selenolate appeared to be the reagent of choice for the following reasons.



(1)

First, this reagent is conveniently prepared in a variety of solvents from commercially available diphenyl diselenide via $NaBH_4$ reduction.[4] Second, several selenium nucleophiles, including methyl,[5] phenyl[6] and benzyl[7] selenolate, have been shown to effect, at least in modest yields, cleavage of the alkyl carbon-oxygen bond of γ-and δ-lactones.[8] Finally, according to the recent work of Sharpless[9]

TABLE 1.[13] A GENERAL SYNTHESIS OF ω-OLEFINIC METHYL ESTERS

	Substrate	*Reaction time (hours)*	*Phenyl selenide*	*Yield (percent)*	*ω-Olefinic methyl ester*	*Yield (percent*
1		2		98		70
2		3		95		65
3		4		90		71
4		10		90		70.5
5		15		55		60.5
6		2		92		60
7		4		80		78
					3 : 3 : 1	
8		20	No reaction			
9		20	No reaction			

and Reich[10] oxidative elimination of the initially introduced ω-phenyl selenyl substituent should proceed efficiently under very mild conditions.

In this letter we document that sodium phenyl selenolate is indeed an efficient reagent for the conversion of simple lactones to the corresponding ω-olefinic methyl esters. Our results are illustrated in Table I.[11,12] Treatment of lactones 1-7 with a carefully deoxygenated DMF solution containing 1.1 eq. of sodium phenyl selenolate (diphenyl diselenide $NaBH_4$ under N_2) at 110-120°C for the periods indicated in Table I afforded the corresponding ω-phenylselenyl carboxylic acids in 55-98% yield.[13] Noteworthy here is the fact that larger lactones require somewhat longer reaction times for complete ring cleavage, while lactones 8 and 9 were quantitatively recovered even when subjected to prolonged reaction times (i.e. 20 hr). The carboxylic acid derivatives were next esterified with ethereal diazomethane and for analytical purposes purified via preparative vapor phase chromatography.[13] Subsequent conversion to the respective selenoxide was then effected at -78° C through the agency of ozone in methylene chloride. After several preliminary trials, elimination of the selenoxide was found to be best effected in chloroform containing a trace of pyridine. To this end, the methylene chloride was removed *in vacuo*, chloroform containing several drops of pyridine added, and the resultant solution heated at reflux for 1 hr. Removal of the solvent *in vacuo* and kugelrohr distillation of the resultant oil yielded the ω-olefinic methyl ester[17] in 60-75%.[13]

Collectively the results depicted in Table I demonstrate that sodium phenyl selenolate is an exceedingly powerful non-basic nucleophile capable of effecting displacement of the carboxylate group in a wide variety of primary lactones. Secondary and tertiary lactones however, except for γ-valerolactone (7) were found to be completely unaffected. This chemoselectivity may prove synthetically advantageous when more complex lactones are examined. Finally, we note that 2-acetyl butyrolactone (6) yielded 5-phenylselenyl-2-pentanone with concommitant decarboxylation. This transformation is significant for two reasons. First, lactone 6 is a reasonably strong carbon acid ($pK_a \sim 10\text{-}11$)[14] which appears not to protonate sodium phenyl selenolate and thereby impede the cleavage reaction. Second, this transformation if general for related 2-acetyl lactones may provide an attractive route to ω-olefinic ketones.[15]

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References and Footnotes

1. Dealkylation of esters and aryl methyl ethers has been promoted by a wide variety of nucleophiles. For a review on ester cleavage via S_N2-type dealkylation see J. E. McMurry, Org. Reactions, 24, 187 (1976).

2. For specific examples wherein sulfur is the nucleophile see P. A. Bartlett and W. S. Johnson, Tetrahedron Letters 4459 (1970); G. I. Feutrill and R. N. Murington, Tetrahedron Letters, 1327 (1970), G. I. Feutrill and R. N. Murington, Austr. J. Chem., 25, 1719 and 1733 (1972).

3. During the course of this investigation Professor T. Ross Kelly informed us that lithium thiomethoxide in HMPA at room temperature is an effective reagent for alkyl-oxygen cleavage of lactones and aryl methyl ethers; T. R. Kelly, B. B. Dali and W.-G. Tsang, Tetrahedron Letters, in press.

4. B. Sjoberg and S. Herdevall, Acta. Chem. Scand., 12, 1347 (1958).

5. H. Plieninger, Chem. Ber., 83, 265 (1950).

6. W. H. H. Gunther, J. Org. Chem., 31, 1202 (1966); K. Sindelar, J. Metysova and M. Protiva, Coll. Czech. Chem. Comm., 34, 3801 (1969).

7. L.-B. Agenas, Arkiv for Kemi, 24, 415 and 573 (1965).

8. For an example of the demethylation of aryl methyl ethers with sodium benzyl selenolate see: R. Ahmad, J. M. Saá and M. P. Cava, J. Org. Chem., 42, 1228 (1976).

9. K. B. Sharpless and R. F. Lauer, J. Am. Chem. Soc., 95, 2697 (1973).

10. H. J. Reich, I. L. Reich and J. M. Renga, J. Am. Chem. Soc., 95, 5813 (1973).

11. Similar results have been obtained by Professor Dennis Liotta and associates (H. Santiesteban and W. Markiewicz) of Emory University; see accompanying articles. We wish to thank Professor Liotta for providing us with a preprint of their work prior to publication.

12. Treatment of butyrolactone with lithium phenyl selenolate in HMPA at 70°C also effects ring cleavage albeit in only 30% yield. This reagent, an air sensitive high melting solid (295-300°C with decomp.), was prepared by treating a benzene solution of phenyl selenol [W. G. Salmond, M. A. Barta A. M. Cain and M. C. Sobala, Tetrahedron Letters, 1683 (1977)] with 1.1 eq of methyl lithium. Removal of the solvent in vacuo and trituration with dry ether yields the reagent as an off white solid.

13. All yields recorded here were based on isolated material which was > 95% pure. Analytical samples of each new ester, obtained by preparative vapor phase chromatography (vpc), gave satisfactory ir (CCl_4) and 220 MHz nmr ($CDCl_3$) spectra as well as elemental analysis.

14. H. O. House, "Modern Synthetic Reactions" second edition, W. A. Benjamin, Inc. Menlo Park, Calif., p. 494, 1972.

15. In a related study we have demonstrated that sodium phenyl selenolate in DMF effects nucleophilic ring cleavage of such monoactivated cyclopropanes as 2-acetylcyclopropane and bicyclo[3.1.0]-2-hexanone. The results of this study will be forthcoming in the near future.