over the range pH 5 to 8.2, using MOPS, citrate, and phosphate buffers where appropriate. The binding of pure apo A-I to the egg lecithin single bilayer vesicles was measured under the same experimental conditions as the binding of I, but the free and bound protein were separated by rapid gel permeation chromatography using Sepharose 6B. A simple Langmuir isotherm is again sufficient to interpret the data, and it yields $K_D = (9.4 \pm 1.7) \times 10^{-7}$ M with a maximum of six apo A-I molecules per vesicle. Rapid gel permeation chromatography using Sepharose CL-4B showed that both the vesicle-peptide and vesicle-apo A-I complexes have the same hydrodynamic properties (d = 250 Å) as the pure vesicle, indicating the absence of any major reorganization of the lipid structure such as disk formation or fusion into large liposomes.

At the air-water interface insoluble monolayers of I form spontaneously by adsorption from dilute solutions or by spreading of concentrated solutions. The monolayers are stable for at least several hours at a variety of surface pressures, even after repeated compression and expansion. Analysis of the force area curve shows that the surface behavior of the monolayers can be described by the same equation as the one observed for apo HDL and apo A-I monolayers:[5,6,14] $\pi[A - A_{00}(1 - K\pi)] = C$, where K is the surface compressibility and A_{00} is the limiting molecular area extrapolated to zero surface pressure. The compressibility seen for peptide I is $K = 2.1 \times 10^{-2}$ cm/dyn, the same as found for apo HDL, $K = 1.8 \times 10^{-2}$ cm/dyn. Most importantly, the collapse pressure (π = 22 dyn/cm) of the peptide and protein monolayers appear to be indistinguishable. We find that the limiting area of the peptide extrapolated to zero surface pressure is equal to 23 Å^2 per amino acid residue, whereas A_{00} = 16.3 Å^2/amino acid for apo HDL.[6] These values suggest that the stable form of the peptide at the air-water interface is a relatively compact folded conformation, presumably a helix. Peptide I is also able to penetrate phospholipid monolayers at the air-water interface to the same extent as apo A-I does; addition of peptide I to the subphase of a π = 14 dyn/cm egg lecithin monolayer results in an increase of the surface pressure to 24 dyn/cm.

Our results show that a docosapeptide of high amphiphilic helix potential does behave in solution, at phospholipid-water interfaces, and at the air-water interface in a manner similar to that of apo A-I. Since peptide I epitomizes apo A-I in its tendency to form an amphiphilic helix and yet reproduces the essential surface properties of the intact apolipoprotein, we conclude that the structural role of apolipoprotein A-I is fulfilled by its helical segments, and it is not necessary to invoke a highly organized tertiary structure thereof. The synthesis of amphiphilic helical oligopeptides of simple sequence and well-defined surface properties opens the way to the systematic study of the structure-function relationship of lipid-associated proteins and to the construction of water-soluble lipid-peptide complexes of desirable and useful physical and physiological properties.

Acknowledgments. The work presented in this paper was supported by USPHS Program Project HL-18577, USPHS Medical Scientist Traineeship 5TGM-07281, and USPHS HL-15062 (SRC). The authors thank Dr. R. L. Heinrikson for the sequence analysis of the peptide and Dr. A. M. Scanu for providing a sample of apo A-I.

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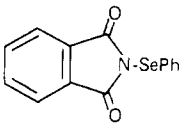
Daikichi Fukushima, Josh P. Kupferberg
Shinji Yokoyama, Daniel J. Kroon
E. T. Kaiser,* F. J. Kézdy*
Departments of Chemistry and Biochemistry
University of Chicago, Chicago, Illinois 60637
Received February 8, 1979

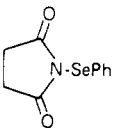
N-Phenylselenophthalimide (N-PSP) and *N*-Phenylselenosuccinimide (N-PSS). Two Versatile Carriers of the Phenylseleno Group. Oxyselenation of Olefins and a Selenium-Based Macrolide Synthesis

Sir:

In recent years the phenylseleno group became a very powerful tool in organic synthesis owing to its fertile and easily manipulated nature.[1-3] The most useful transformations of this group are its oxidative and reductive removal to introduce unsaturation and saturation respectively. In these organoselenium-based operations, the first and most crucial stratagem is the introduction of the phenylseleno (PhSe) group into the organic molecule. In this communication we report on the reactions of *N*-phenylselenophthalimide (N-PSP) and *N*-phenylselenosuccinimide (N-PSS), two new, versatile and useful carriers of the PhSe group. These readily available and



N-PSP



N-PSS

relatively stable reagents are highly effective for introducing the PhSe group into unsaturated substrates. Of particular importance is their utility in the oxyselenenation of olefins and cyclization reactions including the formation of cyclopropanes and macrolides. This new method of macrolide formation from long, open-chain, unsaturated carboxylic acids constitutes a new concept for the synthesis of these biologically important compounds.[4-6]

N-PSP[7] is readily prepared from potassium phthalimide and phenylselenenyl chloride and is a perfectly stable colorless crystalline solid. N-PSS is conveniently obtained from allylphenylselenide and *N*-chlorosuccinimide by the method of Sharpless and Hori[8] as a white crystalline solid. This substance is stable at −20 °C under argon for long periods of time although in the air and at 25 °C it slowly decomposes turning increasingly yellow. The following reactions of N-PSP and N-PSS illustrate the versatility and effectiveness of these newly introduced organoselenium reagents in organic synthesis.

I. Oxyselenation of Olefins. *N*-Phenylselenophthalimide and *N*-phenylselenosuccinimide react readily with olefins at 25 °C in methylene chloride in the presence of 2-3 equiv of water and acid catalyst (0.05-0.1 equiv, e.g., *p*-toluenesulfonic, pyridinium *p*-toluenesulfonate, camphorsulfonic) to afford *hy-*

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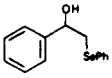
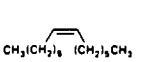
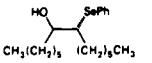
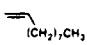
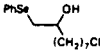
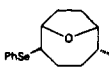
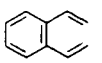
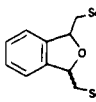
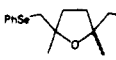
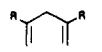
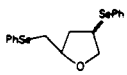
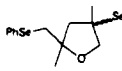
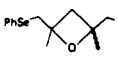
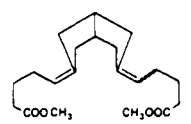
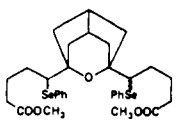
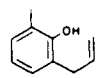
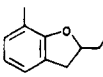
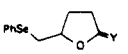
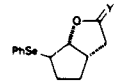
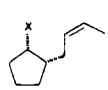
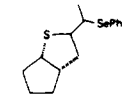
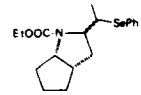
Table I. Reactions of *N*-Phenylselenophthalimide (N-PSP) and *N*-Phenylselenosuccinimide (N-PSS) with Unsaturated Substrates[a]

Entry	Substrate	Product	Reagent	Yield (%)
	Enes:			
1			N-PSP N-PSS	90 92
2			N-PSP N-PSS	89 84
3			N-PSP N-PSS	80 82
4			N-PSP N-PSS	93 94
5			N-PSP N-PSS	68 64
			N-PSP N-PSS	25 23
	Dienes:			
6			N-PSP N-PSS	97 95
7			N-PSP N-PSS	71 70
8			N-PSS	63
9, R = H			N-PSP	55
10, R = CH_3			N-PSS	24
			N-PSS	53
11			N-PSP	22
	Enes containing internal nucleophiles:			
12			N-PSP N-PSS	80 90
13, X = COOH		 Y = O	N-PSP N-PSS	100 98
14, X = CH_2OH		Y = H_2	N-PSP N-PSS	90 95
15, X = COOH		 Y = O	N-PSP N-PSS	100 98
16, X = CH_2OH		Y = H_2	N-PSP N-PSS	83 86
17, X = SAc			N-PSP N-PSS	70 72
18, X = NHCOOEt			N-PSP	90

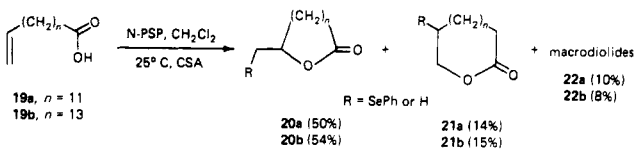
[a] Reactions were carried out in methylene chloride on a 0.1–1.0-mmol scale and the products were isolated chromatographically (silica, column or plate). Reaction times varied from 1 to 24 h; TLC was used to follow the course of the reactions.

droxyselenides in excellent yields as indicated in Table I. Considerable regioselectivity is observed in these reactions as evidenced by entries 2, 3, and 5. Hydroxyselenides are useful intermediates for the synthesis of a variety of products, including allylic alcohols.[10] The strategic utilization of dienes in this oxyselenation reaction (1.25 equiv of N-PSP or N-PSS + 0.75 equiv of H_2O per double bond) leads to *oxygen heterocycles* with the simultaneous introduction into the product of two PhSe groups.[11] As shown in Table I, tetrahydropyran, tetrahydrofuran, and oxetane systems can be readily formed in good to excellent yields by this method. High regioselectivity is again observed in these reactions leading selectively to various ring sizes. This size selectivity is dictated not only by the double-bond substitution but also by the relative thermodynamic stabilities of the rings formed.

II. Cyclization of Unsaturated Substrates Containing Internal Nucleophiles. Both N-PSP and N-PSS were proven to be superior reagents to phenylselenenyl halides[12] for carrying out organoselenium-induced ring closures of unsaturated substrates. Unsaturated carboxylic acids, phenols, alcohols, thioacetates,[12b] and urethanes[12g] cyclize smoothly with these reagents (1.1–1.3 equiv) in methylene chloride in the presence of an acid catalyst (vide supra) at −78–25 °C. In all cases studied, excellent yields of cyclic products containing the PhSe group were obtained. The results are shown in Table I. The reluctance of these new reagents to react with unsaturated centers in the absence of external or favorably located internal nucleophiles and the inert nature of the phthalimide and succinimide byproducts make them excellent and selective initiators of ring-closure reactions.

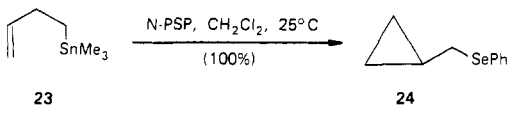
III. Macrolide Formation.[4-6,13] A remarkable property of *N*-phenylselenophthalimide and *N*-phenylselenosuccinimide is their ability to initiate *macrolide* formation from long-chain unsaturated carboxylic acids at ambient temperatures (Scheme I). Because a large body of naturally occurring and medicinally used macrolide antibiotics contain 14- or 16-membered rings,[4-6] we chose to examine the formation of these particular ring sizes. Specifically, exposure of the carboxylic acids **19a,b** to excess N-PSP in the presence of camphorsulfonic acid (CSA) as catalyst in methylene chloride (0.01 M) at 25 °C under anhydrous conditions resulted in the formation of the macrocyclic lactones **20a,b** (R = SePh) and their regioisomers **21a,b** (R = SePh) in good yields (Scheme I) as major products. Macrodiolide (isomeric mixtures) formation was also observed in these reactions, the yields of these products increasing with concentration to the expense of monomeric lactones.[14] It should be emphasized that other electrophilic organoselenium reagents such as phenylselenenyl halides and phenylselenenic acid[10] do not lead to macrolides under similar circumstances, addition of PhSeX across the double bond being the main pathway.[15] Reductive removal of the PhSe group from the phenylselenomacrolides **20a,b** with tri-*n*-butyltin hydride (*n*-Bu_3SnH) in the presence of azobisisobutyronitrile (AIBN) (toluene, 110 °C) resulted in the formation of the corresponding macrolactones (**20a,b** and **21a,b**, R = H) in excellent yields (95–100%). Two naturally occurring macrolides, exaltolide (**21c**, R = H, n = 12)[16] and 9-decanolide (**20a**, R = H, n = 7)[13b,17] have been synthesized by this new methodology.

Scheme I. Macrolide Synthesis



IV. Carbon–Carbon Bond Formation. Finally the potential

Scheme II. Cyclopropane Synthesis



23 24

of these new organoselenium compounds (N-PSP and N-PSS) in the construction of carbon–carbon bonds was demonstrated by the efficient formation of *cyclopropanes* (Scheme II). For example, the unsaturated organotin derivative **23** on treatment with N-PSP (1.1 equiv) in methylene chloride at 25 °C under acid catalysis (vide supra) is quantitatively converted to the phenylselenocyclopropane **24.**

The ready access, relative stability of the described selenium reagents (N-PSP and N-PSS), and the demonstration of their versatile nature as carriers of the PhSe group should make them useful and selective reagents for a number of selenium-based synthetic operations. The design, synthesis, and chemistry of novel organoselenium reagents and their application to the synthesis of natural and "unnatural" products is continuing in these laboratories.[18]

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(4) (a) Nicolaou, K. C. *Tetrahedron* **1977,** *33,* 683 and references cited therein. (b) Masamune, S., Bates, G. S.; Corcoran, J. W. *Angew. Chem., Int. Ed. Engl.* **1977,** *16,* 585 and references cited therein. (c) Back, T. G. *Tetrahedron* **1977,** *33,* 3041 and references cited therein.
(5) For a Pd(0)-initiated macrolide synthesis by C–C bond formation, see ref 13a.
(6) After our initial reports[12c,d] of the phenylselenocycloetherification reaction, a macrolide synthesis based on this cyclization principle appeared: Petrzilka, M. *Helv. Chim. Acta* **1978,** *61,* 3075.
(7) *N*-Phenylselenophthalimide was prepared as follows. A 250-mL round-bottom three-necked flask fitted with an Ar inlet was charged with potassium phthalimide (3.00 g, 16.2 mmol) and phenylselenenyl chloride (2.87 g, 15 mmol). After several evacuations and purges with Ar, dry and degassed hexane (15 mL, distilled from CaH_2 under Ar) was added and the mixture was vigorously stirred for 2 h at 25 °C (all PhSeCl dissolves). Dry methylene chloride (100 mL, distilled from CaH_2 under Ar) was added and the solution was filtered to remove solid materials. The solution was concentrated on the rotary evaporator to ~20 mL and dry hexane (80 mL) was added. The crystalline solid was collected by filtration and washed thoroughly with dry hexane: yield, 3.92 g (88%); colorless crystals; mp 171–175 °C dec. This product is sufficiently pure for use. An analytical sample was obtained by recrystallization from methylene chloride–ether (or hexane) as colorless crystals: mp 171–175 °C dec; IR (KBr) ν_{max} 1720 (vs) cm^{-1}; NMR (60 MHz, $CDCl_3$) τ 2.0–2.8 (m); exact mass calcd for $C_{14}H_9O_2NSe$ *m/e* 302.9798, found 302.9798; Anal. ($C_{14}H_9O_2NSe$) C, H, N, Se.
(8) *N*-Phenylselenosuccinimide, the first member of this general class of reagents, was first mentioned by Sharpless and Frejd (Frejd, T.; Sharpless, K. B. *Tetrahedron Lett.* **1978,** 2239. We thank Professor K. B. Sharpless and Dr. T. Hori for the experimental procedure for the preparation of this compound. For details of the synthesis and some other aspects of the chemistry of this reagent, see Sharpless, K. B.; Hori, T. *J. Org. Chem.*, in press.
(9) All new compounds showed satisfactory spectral and analytical data.
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K. C. Nicolaou,*[19] D. A. Claremon
W. E. Barnette, S. P. Seitz
Department of Chemistry, University of Pennsylvania
Philadelphia, Pennsylvania 19104

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Additions and Corrections

Steric and Electronic Effects on ^{15}N Chemical Shifts of Saturated Aliphatic Amines and Their Hydrochlorides [*J. Am. Chem. Soc.*, **100,** 3889 (1978)]. By RUDOLPH O. DUTHALER and JOHN D. ROBERTS,* Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California 91125.

Page 3892, column 2; second sentence in the third paragraph (line 26) should read: "Thus, the shifts of the tertiary amine hydrochlorides of **29–41,** like those of the secondary amine hydrochlorides, **21, 23,** and **24,** are downfield of those predicted."

Structures and Energetics of Planar and Tetrahedral Dilithiomethane. A Near Degeneracy of Singlet and Triplet Electronic States [*J. Am. Chem. Soc.*, **100,** 5972 (1978)]. By WILLIAM D. LAIDIG and HENRY F. SCHAEFER,* Department of Chemistry and Lawrence Berkeley Laboratory, University of California, Berkeley, California 94720.

Several corrections must be made in Table II. The table in corrected form follows:

Table II. Relative Energy Predictions for Dilithiomethane. The Absolute Energies for the Tetrahedral Singlet are −53.8362 hartrees (SCF) and −54.0277 hartrees (CI)

	E (SCF), kcal	μ (SCF), D	*E* (CI), kcal	*E* (CI),[a] kcal
planar singlet	3.2	4.85	4.0	4.2
planar triplet	−15.8	−1.22	2.4	5.9
tetrahedral singlet	0.0	5.42	0.0	0.0
tetrahedral triplet	−16.6	−0.76	1.3	4.7

[a] Corrected for unlinked clusters.

Reactivity in Methyl Transfer Reactions. 3. Equilibria and Rates in Transfers between Substituted Thiophenoxides [*J. Am. Chem. Soc.*, **101,** 417 (1979)]. By EDWARD S. LEWIS* and SEMYON KUKES, Department of Chemistry, Rice University, P.O. Box 1892, Houston, Texas 77001.