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THE OXIDATION OF N-ACYLHYDRAZINES BY BENZENESELENINIC ACID - A NOVEL SYNTHESIS OF SELENOLESTERS

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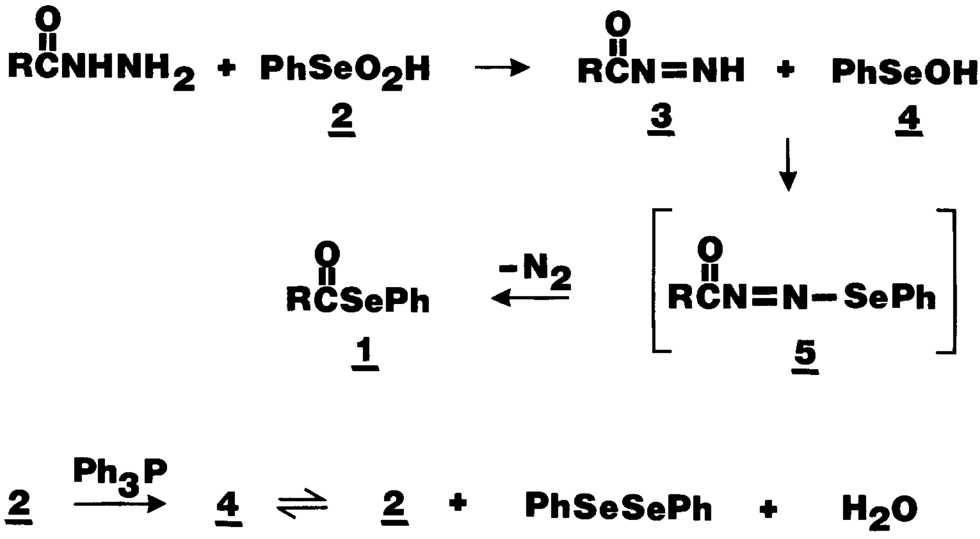
Abstract: The reaction of N-acylhydrazines with benzeneseleninic acid in the presence of triphenylphosphine affords high yields of diverse selenolesters.

Selenolesters (1) are of considerable current interest as acyl-transfer agents[1], particularly in the synthesis of antibiotic macrocyclic lactones[2]. Existing methods[1,3] for preparing compounds 1 are effective, but generally employ unpleasant or air-sensitive reagents.

We report that diverse selenolesters are obtained in high yield by the oxidation of N-acylhydrazines with benzeneseleninic acid (2) in the presence of triphenylphosphine. The seleninic acid is a commercially available, stable, odourless solid which oxidizes a variety of nitrogen nucleophiles under mild conditions[4,5].

We envisage the oxidation of N-acylhydrazines to proceed *via* initial formation of unstable diazenes 3[6]. Benzeneselenenic acid (4) is produced simultaneously and reacts with 3 to generate the desired selenolesters. Species 5 are possible intermediates[7]. However, selenenic acid 4 is unstable and disproportionates to 2 and diphenyl diselenide[8]. Thus, selenolester yields are low unless steps are taken to maintain a sufficient concentration of 4 throughout the reaction. Hypophosphorous acid and diethyl phosphite are known to reduce seleninic acids to selenenic acids *in situ*[9], and we reasoned that oxidation of N-acylhydrazines with excess 2 in the presence of triphenylphosphine would lead to simultaneous formation of 4 and enhanced yields of the desired products. Indeed, selenolester yields were typically 20-25% higher when the phosphine was present. Generation of 4 *in situ* by comproportionation[8] of diphenyl diselenide and 2 was less effective in achieving high yields of 1. These processes are depicted below:



Formation of unwanted N,N'-diacylhydrazines during the oxidation[4] was efficiently suppresse by slow addition of the hydrazine to 2. As expected, inverse addition produced the N,N'-diacyl derivatives in high yield.

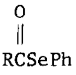
The selenolesters obtained by this method are listed in the accompanying Table. Alkyl, cycloalkyl, aryl and unsaturated derivatives were prepared without difficulty, even in the case of the highly hindered compounds 1b and 1i. The anomalous low yield of selenolester 1e stems from competing decarbonylation, as evidenced by the formation of a small amount of benzyl phenyl selenide.

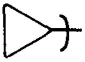
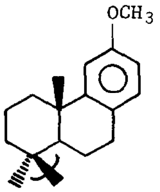
In a typical procedure, a dichloromethane solution of the N-acylhydrazine and an equimolar amount of triphenylphosphine was added over 30-60 min. to *ca.* 2.2 molar equivalents of 2 in dichloromethane at room temperature. The solution was concentrated and the selenolester isolated by preparative t.l.c. (silica-gel). All products were identified by their ir, nmr and mass spectra and were homogeneous (t.l.c. or g.c.). All new selenolesters gave correct elemental analyses. Diphenyl diselenide and triphenylphosphine oxide were obtained as byproducts.

Finally, we report that N-benzyolhydrazine reacted with benzeneselenenyl chloride in the presence of pyridine to furnish selenolester 1f in 47% yield.

Further studies of the reactions of N-acylhydrazines with seleninic acids and of the synthetic utility of selenolesters are in progress in this laboratory.

TABLE

Preparation of Selenolesters  $RC(=O)SePh$ (1)[a]

Entry	R	Isolated Yield (%)	Description
1a	CH_3	94	oil
1b	$t\text{-}C_4H_9$	83	oil
1c		81	oil
1d		86	oil
1e	$PhCH_2$	73	m.p. 41-43°
1f	Ph[b]	88	m.p. 35-37°[c]
1g	$CH_2{=}CH(CH_2)_8$	81	oil
1h	$TBDMS\text{-}O\text{-}(CH_2)_{14}$[d]	81	oil[e]
1i		84	m.p. 133-134°

a) All reactions were performed in dichloromethane at room temperature unless otherwise noted. b) The solvent was 1% methanol-dichloromethane. c) lit.[10] m.p. 40°. d) TBDMS = t-butyldimethylsilyl. e) Desilylation of 1h was effected quantitatively in 50% acetic acid at room temperature; the 15-hydroxy selenolester had m.p. 50-52°.

Acknowledgement

We thank the University of Calgary for financial assistance from the President's Fund.

References and Notes

1. Selenolesters function as acylating agents when activated by "selenophilic" metals such as Hg (II). See: (a) S. Masamune, Y. Hayase, W. Schilling, W. K. Chan and G. S. Bates, J. Am. Chem. Soc., 99, 6756, (1977). (b) A. P. Kozikowski and A. Ames, J. Org. Chem., 43, 2735, (1978).
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5. Benzeneseleninic anhydride also oxidizes nitrogen nucleophiles. See reference (4) and: (a) D. H. R. Barton, D. J. Lester and S. V. Ley, J.C.S. Chem. Comm., 445, (1977). (b) D. H. R. Barton, D. J. Lester and S. V. Ley, J.C.S. Chem. Comm., 276, (1978). (c) M. R. Czarny, J.C.S. Chem. Comm., 81, (1976).
6. By analogy, N,N'-disubstituted hydrazines are oxidized to azo compounds by 2 or the anhydride[4,5b].
7. The possibility that some selenolester formation occurs *via* the reaction of acyl radicals derived from decomposition of 3 with diphenyl diselenide (or other selenium containing species) cannot be excluded[4].
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