of the selenenic anhydride in anhydrous dioxane, and the progress of the hydrolysis was monitored by following the decrease in the absorbance of the solution at the appropriate wavelength (440 nm for **2a**, 425 nm for **2b**).

For the runs followed by stopped-flow spectrophotometry an aliquot of the solution of **2b** in dioxane was diluted 70-fold with 60% dioxane to prepare a solution of **2b** (7×10^{-5} M) in 60% dioxane that was then placed in one of the reservoir syringes of a Durrum-Gibson stopped-flow spectrophotometer. A 60% dioxane solution containing the desired buffer (or dilute HCl or $HClO_4$), plus any lithium perchlorate needed to maintain constant ionic strength, was placed in the other reservoir syringe. The hydrolysis of **2b** was initiated by mixing the two solutions, and the decrease in absorbance with time at 425 nm was recorded on a storage oscilloscope.

Registry No. **1a**, 56790-60-4; **1b**, 84250-81-7; **2a**, 84250-76-0; **2b**, 84250-80-6; **3b**, 90990-68-4.

Mechanism of the Reaction of Thiols with *o*-Nitro- and *o*-Benzoylbenzeneselenenic Acids and Anhydrides[1]

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The kinetics of the reaction of an alkanethiol (*n*-BuSH) with *o*-nitro- (**1a**) and *o*-benzoylbenzeneselenenic (**1b**) acids (eq 3) and with the corresponding selenenic anhydrides (eq 4, **2a** and **2b**) have been investigated over a range of pH in a series of buffers in 60% dioxane. The pH–rate profiles show that acid catalysis is not important for the reaction of either anhydride with the thiol, and a mechanism (eq 12) is proposed in which replacement of the stabilizing ortho substituent as a ligand by either *n*-BuSH or $n\text{-BuS}^-$ is followed by loss of $ArSeO^-$ from the resulting reactive intermediate ($I^{\pm}$). On the other hand, reaction of the *o*-nitro acid (**1a**) with the thiol requires acid catalysis, presumably because OH is enough poorer a leaving group than ArSeO that its departure must be assisted by a proton transfer. Acid catalysis is also important at pH < 6 for the reaction of the *o*-benzoyl acid (**1b**) with *n*-BuSH. In this case, however, the mechanism of the acid-catalyzed reaction involves reversible formation of hemithioketal **7** by acid- and buffer-catalyzed addition of the thiol to the carbonyl group of **1b**, followed by specific-H^+ catalyzed intramolecular decomposition of **7**. The *o*-benzoyl acid also reacts much more readily than expected with $n\text{-BuS}^-$; a mechanism involving reaction of the thiolate ion with an intermediate (**8**) formed by reversible intramolecular addition of the SeOH to the >C=O group in **1b** is suggested.

Ganther[2] has proposed that reaction of a selenenic acid functional group with the thiol group of glutathione (GSH) to afford a selenenyl sulfide (eq 1) is one of the important

$$\text{E-SeOH} + \text{GSH} \rightarrow \text{E-SeSG} + H_2O \qquad (1)$$

steps in the reaction cycle for the action of the essential mammalian enzyme, glutathione peroxidase. We therefore felt that a study, using a simple model system, of the mechanism of the reaction between a thiol and a selenenic acid should be valuable, in that information about the behavior (formal kinetics, pH–rate profile, etc.) of this reaction could be helpful in suggesting factors likely to be important for the occurrence of the process in the glutathione peroxidase reaction cycle.

Most selenenic acids are, of course, too unstable to be isolated and purified. However, Rheinboldt and Giesbrecht[3] reported some years ago what they believed was the successful isolation and purification of two selenenic acids, *o*-nitrobenzeneselenenic acid (**1a**) and *o*-benzoylbenzeneselenenic acid (**1b**). Since **1a** and **1b** represented the only reported examples of isolable selenenic acids of relatively uncomplicated structure, they were selected as substrates for the contemplated study.

When we repeated the preparation and isolation of the compounds described by Rheinboldt and Giesbrecht,[3] we discovered[4] that the compounds isolated are actually the selenenic anhydrides (**2a** and **2b**), rather than the selenenic acids.[5] *Stable* dilute *solutions* of **1a** and **1b** in aqueous organic solvents can, however, be easily prepared from **2a** and **2b** by hydrolysis (eq 2).[4,6]

$$\begin{array}{lcl} \text{ArSeOSeAr} + H_2O & \xrightarrow{H^+} & 2\text{ArSeOH} \qquad (2) \\ \mathbf{2a},\ \text{Ar} = o\text{-}O_2NC_6H_4 & & \mathbf{1b},\ \text{Ar} = o\text{-PhC(O)}C_6H_4 \\ \mathbf{2b},\ \text{Ar} = o\text{-PhC(O)}C_6H_4 & & \mathbf{1a},\ \text{Ar} = o\text{-}O_2NC_6H_4 \end{array}$$

The present paper reports the results of a study of the kinetics of the reaction of a simple thiol (eq 3, R = *n*-Bu) with **1a** and **1b** over a range of pH in 60% dioxane as solvent.

$$\text{ArSeOH} + \text{RSH} \xrightarrow{k_{\text{RSH}}} \text{ArSeSR} + H_2O \qquad (3)$$

In addition, since hydrolysis of **2a** and **2b** (eq 2) is usually slower than their rate of reaction with *n*-BuSH (eq 4, R = *n*-Bu) we have also been able to study the kinetic behavior of eq 4 independently under most of the same

$$\text{ArSeOSeAr} + \text{RSH} \xrightarrow{k_{\text{RSH}}'} \text{ArSeSR} + \text{ArSeOH} \qquad (4)$$

reaction conditions for which kinetic data were obtained on eq 3. The two reactions, eq 3 and 4, exhibit marked differences in pH–rate profile and in the influence of the Ar group on rate. The reaction of the *o*-nitro acid (**1a**) also shows significantly different mechanistic behavior than is found for the *o*-benzoyl acid (**1b**).

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(1) This research supported by the National Science Foundation, Grant CHE-79-18877.

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(3) (a) Rheinboldt, H.; Giesbrecht, E. *Chem. Ber.* **1955**, *88*, 666. (b) Rheinboldt, H.; Giesbrecht, E. *Ibid.* **1956**, *89*, 631.

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(5) Reich, H. J.; Willis, W. W., Jr.; Wollowitz, S. *Tetrahedron Lett.* **1982**, *23*, 3319.

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Table I. Rate Constants for the Reaction of *o*-Nitrobenzeneselenenic Anhydride (2a) with 1-Butanethiol at 25 °C in 60% Dioxane[a]

reactn conditions	pH[d]	[HA], M	[A$^-$], M	k_{RSH}', M^{-1} s^{-1} [b]	k_{buf}, M^{-2} s^{-1} [c]	k_{RSH}^0, M^{-1} s^{-1} [c]
1:10 AcOH–AcO$^-$ buffer	8.44	0.0020	0.020	1.12	14.9	0.79
		0.0015	0.015	1.04		
		0.0010	0.010	0.96		
		0.0005	0.005	0.88		
1:4 AcOH–AcO$^-$ buffer	8.04	0.0050	0.020	0.95	13.6	0.65
		0.0038	0.015	0.84		
		0.0025	0.010	0.77		
		0.0013	0.005	0.70		
1:1 AcOH–AcO$^-$ buffer	7.44	0.020	0.020	0.71	7.4	0.42
		0.015	0.015	0.64		
		0.010	0.010	0.57		
		0.005	0.005	0.50		
4:1 AcOH–AcO$^-$ buffer	6.84	0.020	0.0050	0.61	7.8	0.41
		0.015	0.0038	0.55		
		0.010	0.0025	0.51		
		0.005	0.0013	0.46		
10:1 AcOH–AcO$^-$ buffer	6.44	0.020	0.0020	0.57	5.5	0.45
		0.015	0.0015	0.54		
		0.010	0.0010	0.52		
		0.005	0.0005	0.48		
1:1 HCO_2H–HCO_2^- buffer	6.10	0.020	0.020	0.61	4.3	0.42
		0.010	0.010	0.48		
		0.005	0.005	0.47		
5:1 HCO_2H–HCO_2^- buffer	5.40	0.020	0.0040	0.48	3.5	0.39
		0.010	0.0020	0.43		
		0.005	0.0010	0.41		
1:2 H_3PO_4–$H_2PO_4^-$ buffer	5.10	0.010	0.020	0.45	2.5	0.37
		0.0050	0.010	0.41		
		0.0025	0.005	0.39		
1:1 H_3PO_4–$H_2PO_4^-$ buffer	4.80	0.020	0.020	0.41	1.5	0.35
		0.015	0.015	0.40		
		0.010	0.010	0.37		
		0.005	0.005	0.37		
5:1 H_3PO_4–$H_2PO_4^-$ buffer	4.10	0.020	0.004	0.43	2.0	0.38
		0.010	0.002	0.41		
		0.005	0.001	0.39		
1:2 CF_3CO_2H–$CF_3CO_2^-$ buffer	3.1	0.010	0.020	0.55	3.6	0.45
		0.005	0.010	0.52		
		0.0025	0.005	0.47		
0.002 N $HClO_4$	2.7			0.37		0.37
0.005 N $HClO_4$	2.3			0.41		0.41

[a] All data at ionic strength = 0.02. [b] Slope of plot of k_1 vs. [*n*-BuSH] for runs for each buffer solution (Table V). [c] Obtained from k_{RSH}' using plot according to eq 5. [d] pH's calculated from known pK_a's in 60% dioxane of acids used for buffers (see Table III of ref 6).

Results

Kinetics of the Reaction of 2a with 1-Butanethiol. The kinetics of the reaction of *o*-nitrobenzeneselenenic anhydride (**2a**) with *n*-BuSH were studied at 25 °C in 60% dioxane (v/v) as solvent at constant ionic strength (0.02) in a series of buffers and dilute perchloric acid solutions covering a pH range from 2.3 (0.005 N $HClO_4$) to 8.44 (1:10 AcOH:AcO$^-$ buffer). The reaction was followed by monitoring the decrease in the absorbance of the solution at 440 nm. Under the reaction conditions employed the rate of reaction of *n*-BuSH with **2a** (eq 4) was at least 10 times faster than the rate of reaction of **1a** (eq 3), so that there was no difficulty in determining the absorbance (A_∞^i) corresponding to the completion of eq 4. The reactions were carried out with the thiol present in large stoichiometric excess over **2a** and at thiol concentrations high enough that the rate of reaction 4 was at least 5 times faster than the rate of hydrolysis[6] of **2a** (eq 2) under the same conditions. Plots of log ($A - A_\infty^i$) vs. time showed excellent linearity in all cases. The experimental first-order rate constants, k_1, for the various runs are tabulated in Table V[7] (see supplementary material).

A plot of k_1 vs. [*n*-BuSH] was made for the data for each buffer solution. The slope, k_{RSH}', is the second-order rate constant for eq 4 (Ar = *o*-$O_2NC_6H_4$). The values of k_{RSH}' (Table I) indicate that with all buffers there is some increase in k_{RSH}' with increase in buffer concentration. Plots of k_{RSH}' vs. $[\text{buffer}]_{\text{total}}$ (eq 5) are linear and provide both k_{RSH}^0, the buffer-independent rate constant for eq 4 for each pH, and k_{buf} for the buffer; these are listed in Table I.

$$k_{RSH}' = k_{RSH}^0 + k_{buf}[\text{buffer}]_{\text{total}} \qquad (5)$$

Curve A of Figure 1 shows the pH–rate profile for k_{RSH}^0 for the reaction of **2a** with *n*-BuSH and corresponds to eq 6. It is apparent that the pH-independent term in eq 6

$$k_{RSH}^0 \text{ (for } \mathbf{2a}\text{)} = 0.38 \text{ M}^{-1} \text{ s}^{-1} + 1.5 \times 10^{-9} (1/a_{H^+}) \text{ M}^{-1} \text{ s}^{-1} \qquad (6)$$

is either the exclusive, or the dominant, contributor to k_{RSH}^0 over practically the entire pH range studied.

Kinetics of the Reaction of 2b with 1-Butanethiol. The kinetics of this reaction (eq 4, Ar = *o*-PhC(O)C_6H_4) can be studied only at pH > 6, because below pH 6 the rate of H_3O^+-catalyzed hydrolysis of **2b** (eq 2) becomes considerably faster[6] than the rate of reaction of **2b** with *n*-BuSH, even at thiol concentrations as large as 0.04 M. Even at pH's above 6 there is the additional problem that the rate of reaction of **2b** with the thiol (eq 4) is only from 2.5 to 4 times faster than the rate of reaction of **1b** with

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[7] See paragraph at end of paper regarding supplementary material.

Table II. Rate Constants for the Reaction of *o*-Benzoylbenzeneselenenic Anhydride (2b) with 1-Butanethiol at 25 °C in 60% Dioxane[a]

reactn conditions	pH[d]	[HA], M	[A$^-$], M	k_{RSH}', M^{-1} s^{-1} [b]	k_{buf}, M^{-2} s^{-1} [c]	k_{RSH}^0, M^{-1} s^{-1} [c]
1:10 AcOH–AcO$^-$ buffer	8.44	0.0020	0.020	0.93	*e*	0.93
1:4 AcOH–AcO$^-$ buffer	8.04	0.0050	0.020	0.47	*e*	0.47
1:2 AcOH–AcO$^-$ buffer	7.74	0.010	0.020	0.29	*e*	0.29
1:1 AcOH–AcO$^-$ buffer	7.44	0.020	0.020	0.16	*e*	0.16
		0.010	0.010	0.16		
2:1 AcOH–AcO$^-$ buffer	7.14	0.020	0.010	0.124		
		0.015	0.0075	0.10	3.1	0.060
		0.005	0.0025	0.067		
4:1 AcOH–AcO$^-$ buffer	6.84	0.020	0.0050	0.13		
		0.010	0.0025	0.092	3.3	0.048
		0.005	0.0013	0.065		
10:1 AcOH–AcO$^-$ buffer	6.44	0.020	0.0020	0.108		
		0.010	0.0010	0.072	3.1	0.04
		0.005	0.0005	0.055		
1:1 HCO_2H–HCO_2^- buffer	6.10	0.020	0.020	0.082		
		0.010	0.010	0.053	2.7	0.027
		0.005	0.005	0.037		

[a] All data at ionic strength = 0.02. [b] Slope of plot of k_1 vs. [*n*-BuSH] for runs for each buffer solution (Table VI). [c] Obtained from k_{RSH}' using plot according to eq 5. [d] pH's calculated from known pK_a's for acids used for buffers (see Table III of ref 6). [e] Not large enough relative to k_{RSH}^0 to be measurable.

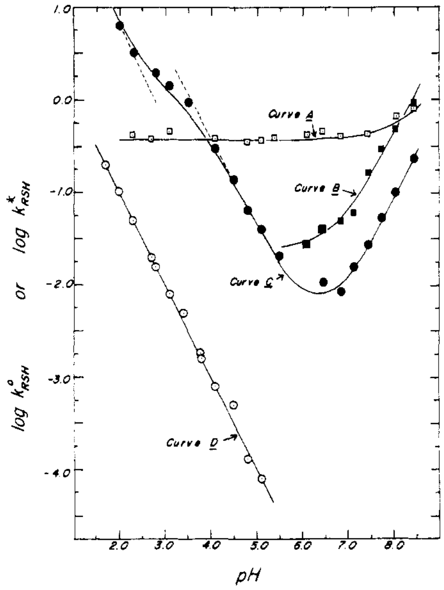


Figure 1. pH–rate profiles for reactions of *n*-BuSH with selenenic anhydrides and acids: curve A (⊡) reaction with anhydride **2a**; curve B (■) reaction with anhydride **2b**; curve C (●) reaction with selenenic acid **1b**; curve D (○) reaction with selenenic acid **1a**. All data at 25 °C in 60% dioxane (v/v) at ionic strength = 0.02.

the same species (eq 3), so that with **2b** (in contrast to the situation with **2a**) reaction 4 is not complete before reaction 3 begins to be significant. However, by following the reaction at 425 nm, where the extinction coefficient for **2b** is large compared to those for either **1b** or ArSeSBu-*n*, it was possible to operate under conditions where the absorbance change observed was that due only to reaction 4 and an absorbance (A_∞^i) corresponding to the completion of reaction 4 could be determined experimentally. Plots of log ($A - A_\infty^i$) vs. time for this wavelength showed excellent linearity (thiol was present in large stoichiometric excess over **2b** in all runs).

The first-order rate constants, k_1, for the *n*-BuSH–**2b** reactions (all carried out at 25 °C at constant ionic strength, 0.02) are collected in Table VI[7] (supplementary material). Values of k_{RSH}', the slope of a plot of k_1 vs. [RSH] for the different buffers, are collected in Table II. In acetate buffers having pH ≥ 7.44 k_{RSH}' is independent of $[\text{buffer}]_{\text{total}}$; in the remaining buffers it is not, and the value of k_{RSH}^0 must be determined from the intercept at $[\text{buffer}]_{\text{total}} = 0.00$ of a plot of k_{RSH}' vs. $[\text{buffer}]_{\text{total}}$.

The values of k_{RSH}^0 for the reaction of **2b** with *n*-BuSH at different pH's are listed in Table II and plotted in Figure 1 (curve B). Curve B corresponds to eq 7. Although this equation is of the same general form as that (eq 6) for the reaction of the thiol with **2a**, the pH-independent term for **2b** is 15 times smaller than the one for **2a**, while the rate term dependent on $1/a_{H^+}$ is about 3 times larger than the one for **2a**.

$$k_{RSH}^0 \text{ (for } \mathbf{2b}) = 0.025 \text{ M}^{-1}\text{ s}^{-1} + 4.0 \times 10^{-9}(1/a_{H^+}) \text{ M}^{-1}\text{ s}^{-1} \quad (7)$$

Kinetics of the Reaction of 1b with 1-Butanethiol. Dilute (10^{-4} M) solutions of **1b** in 60% dioxane were prepared immediately before use by hydrolyzing **2b** in the presence of 0.001 N $HClO_4$ ($t_{1/2} < 2$ s). After adjusting their pH to the desired value and addition of *n*-BuSH (0.002–0.04 M), the kinetics of the reaction of **1b** with the thiol (eq 3) at 25 °C were followed at 410 nm, and the first-order rate constant, k_1, was determined from the slope of a plot of log ($A - A_\infty$) vs. time.

The data for acetate, dihydrogen phosphate, and trifluoroacetate buffers and for 0.005–0.01 N $HClO_4$ solutions are collected in Table VII[7] (supplementary material). In all of these solutions there is a linear dependence of k_1 on [*n*-BuSH], and values of k_{RSH} for eq 3 (equal to the slope of a plot of k_1 vs. [*n*-BuSH]) are shown in Table III. In the acetate and dihydrogen phosphate buffers k_{RSH} is independent of $[\text{buffer}]_{\text{total}}$; in the trifluoroacetate buffers k_{RSH} exhibits a dependence on $[\text{buffer}]_{\text{total}}$ of the type in eq 5 and k_{RSH}^*, the [buffer]-independent rate constant for eq 3 at a given pH, was determined from a plot of k_{RSH} vs. $[\text{buffer}]_{\text{total}}$.

Curve C of Figure 1 is the pH–rate profile for k_{RSH}^* for the reaction of **1b** with *n*-BuSH; it corresponds to eq 8.

$$k_{RSH}^* \text{ (for } \mathbf{1b}),\ \text{M}^{-1}\text{ s}^{-1} = \left[\frac{4300a_{H^+} + 2.6 \times 10^6 a_{H^+}^2}{1 + 4200a_{H^+}}\right] + 0.004 + 8.2 \times 10^{-10}(1/a_{H^+}) \quad (8)$$

In formate or chloroacetate buffers the **1b**-*n*-BuSH system exhibits markedly different behavior than the straightforward reaction of **1b** with *n*-BuSH outlined above. Although k_1 (which is much faster than in acetate or dihydrogen phosphate buffers of equivalent pH) is proportional to [*n*-BuSH] at *very low* thiol concentrations,

Table III. Rate Constants for the Reaction of *o*-Benzoylbenzeneselenenic Acid (1b) with 1-Butanethiol at 25 °C in 60% Dioxane[a]

reactn conditions	pH[d]	[HA], M	[A$^-$], M	k_{RSH}, M^{-1} s^{-1} [b]	k_{buf}, M^{-2} s^{-1} [c]	k_{RSH}*, M^{-1} s^{-1} [c]
1:10 AcOH–AcO$^-$ buffer	8.44	0.002	0.020	0.23	*e*	0.23
1:4 AcOH–AcO$^-$ buffer	8.04	0.005	0.020	0.10	*e*	0.10
1:2 AcOH–AcO$^-$ buffer	7.74	0.010	0.020	0.053	*e*	0.053
		0.005	0.010	0.053		
1:1 AcOH–AcO$^-$ buffer	7.44	0.020	0.020	0.027	*e*	0.027
2:1 AcOH–AcO$^-$ buffer	7.14	0.020	0.010	0.016	*e*	0.016
4:1 AcOH–AcO$^-$ buffer	6.84	0.020	0.005	0.0086	*e*	0.0086
10:1 AcOH–AcO$^-$ buffer	6.44	0.020	0.002	0.011	*e*	0.011
1:5 H_3PO_4–$H_2PO_4^-$ buffer	5.5	0.002	0.010	0.021	*e*	0.021
1:2 H_3PO_4–$H_2PO_4^-$ buffer	5.1	0.005	0.01	0.041	*e*	0.041
1:1 H_3PO_4–$H_2PO_4^-$ buffer	4.8	0.010	0.010	0.060	*e*	0.064
		0.005	0.005	0.068		
2:1 H_3PO_4–$H_2PO_4^-$ buffer	4.5	0.010	0.005	0.14	*e*	0.14
5:1 H_3PO_4–$H_2PO_4^-$ buffer	4.1	0.010	0.002	0.30	*e*	0.30
1:5 CF_3CO_2H–$CF_3CO_2^-$ buffer	3.5	0.004	0.020	1.8		
		0.002	0.010	1.5	38	0.95
		0.001	0.005	1.1		
1:2 CF_3CO_2H–$CF_3CO_2^-$ buffer	3.1	0.010	0.020	2.8		
		0.0075	0.015	2.4	46	1.4
		0.0025	0.005	1.8		
1:1 CF_3CO_2H–$CF_3CO_2^-$ buffer	2.8	0.020	0.020	6.7		
		0.010	0.010	4.3	1.2×10^2	1.95
		0.005	0.005	3.1		
0.005 N $HClO_4$	2.3	0.005		3.2		3.2
0.010 N $HClO_4$	2.0	0.010		6.6		6.6

[a] All data at ionic strength = 0.02. [b] Slope of plot of k_1 vs. [*n*-BuSH] for runs for each buffer (Table VII). [c] Plot of k_{RSH} vs. $[\text{buffer}]_{total}$; k_{RSH}* = intercept, k_{buf} = slope. [d] pH's calculated from known pK_a's in 60% dioxane of acids used as buffers. [e] Buffer catalysis not detectable.

it becomes *independent* of [*n*-BuSH] and reaches a limiting value, k_{lim}, at [*n*-BuSH] $\simeq$ 0.01 M. For a given buffer acid (RCO_2H) k_{lim} is independent of buffer ratio but proportional to [RCO_2H]. The observed behavior is what would be expected for the mechanism shown in eq 9 if

$$\mathrm{ArSeOH} + \mathrm{RCO_2H} \underset{k_{-a}}{\overset{k_a}{\rightleftharpoons}} \mathrm{H_2O} + \underset{\mathbf{3}}{\mathrm{ArSeOC(O)R}} \xrightarrow{k_b[\mathrm{RSH}]} \text{products} \quad (9)$$

k_b[RSH] > k_{-a}[H_2O] for [RSH] ≥ 0.01 M. As the "normal" behavior in acetate and trifluoroacetate buffers demonstrates, only for certain carboxylic acids are k_a, k_{-a}, and k_b each of the correct magnitude for eq 9 to become a kinetically more important route to products than the direct reaction of **1b** with *n*-BuSH.

Kinetics of the Reaction of 1a with 1-Butanethiol. Reaction of solutions of **1a** (prepared by hydrolysis of **2a**) with *n*-BuSH was studied in the same manner as for the *n*-BuSH-**1b** reaction; the kinetics were followed at 440 nm, and the rate constants, k_1, for runs in dihydrogen phosphate and trifluoroacetate buffers and in 0.002–0.02 N $HClO_4$ are listed in Table VIII[7] (supplementary material). In these solutions k_1 exhibits a linear dependence on [RSH]; data for k_{RSH} for eq 3 (the slope of a plot of k_1 vs. [*n*-BuSH]) are collected in Table IV.

In the buffer solutions catalysis of the reaction by both H_3O^+ and buffer is observed. Consequently, k_{RSH}* at each pH was determined from the intercept at $[\text{buffer}]_{total}$ = 0.0 of a plot of k_{RSH} vs. $[\text{buffer}]_{total}$; the slope equals k_{buf}. Data for both k_{RSH}* and k_{buf} are given in Table IV. Experimental problems, discussed below, prevented measurement of accurate rates for the reaction of *n*-BuSH with **1a** at pH's above 5.1. The pH-rate profile for k_{RSH}* in the pH range 1.7 to 5.1 (shown as curve D in Figure 1) corresponds to eq 10.

$$k_{RSH}^* \text{ (for } \mathbf{1a}\text{, pH = 1.7–5.1), M}^{-1}\text{ s}^{-1} = 10a_{H^+} \quad (10)$$

In chloroacetate, formate, and also acetate buffers k_1 showed the same type of behavior—$k_1 \sim$ [*n*-BuSH] at low thiol concentrations, k_1 independent of [*n*-BuSH] at higher thiol concentrations—noted with the *n*-BuSH-**1b** system in chloroacetate and formate buffers. This precluded measurement of the rate of the direct reaction of *n*-BuSH with **1a** in such media.

An experiment in which **2a** (0.03 M) was allowed to react with *t*-BuSH (0.06 M) in 0.01 N $HClO_4$ and the reaction product (*o*-$O_2NC_6H_4SeSBu$-*t*, 94%) was isolated and identified demonstrated that a selenenyl sulfide is indeed the product of the reaction of a thiol with both **2a** and **1a**.

Discussion

The pH-rate profiles (curves A and B of Figure 1) show that acid catalysis is not important for the reaction (eq 4) of an alkanethiol (*n*-BuSH) with either selenenic anhydride. This contrasts with the hydrolysis (eq 2) of the same anhydrides,[6] where acid catalysis is required for the reaction to proceed at a measurable rate. These pH-rate profiles also show that a reaction of the anhydride with thiolate ion (*n*-BuS$^-$) becomes kinetically significant relative to the reaction with undissociated thiol (*n*-BuSH) at higher pH's, particularly for **2b**. In these reactions with *n*-BuSH and *n*-BuS$^-$ the reactivity of **2a** relative to **2b** is very different from that found[6] in the hydrolysis of the two anhydrides, or in the reaction of the corresponding selenenic acids (**1a** and **1b**) with the thiol. In both of the latter cases the *o*-benzoyl derivative reacts orders of magnitude faster than the *o*-nitro compound. In contrast, in the reaction of anhydrides **2a** and **2b** with the thiol the *o*-nitro compound reacts either only slightly slower (reaction with *n*-BuS$^-$), or about 15 times faster (reaction with *n*-BuSH) than the *o*-benzoyl anhydride.

The pH-rate profiles (curves C and D of Figure 1) for the reaction of the selenenic acids (**1a** and **1b**) with the thiol (eq 3) show that an acid-catalyzed reaction is dominant kinetically for both substrates at pH < 5. The rate constant for this H_3O^+-catalyzed reaction of the thiol with selenenic acid is much larger for **1b** than for **1a**. This is similar to the behavior of the acid-catalyzed hydrolysis of **2a** and **2b**.[6] It is also significant that the pH-rate profile for the H_3O^+-catalyzed reaction of **1b** with *n*-BuSH has

Table IV. Rate Constants for the Reaction of *o*-Nitrobenzeneselenenic Acid (1a) with 1-Butanethiol at 25 °C in 60% Dioxane[a]

reactn conditions	pH[d]	[HA], M	[A$^-$], M	k_{RSH}, M^{-1} s^{-1} [b]	k_{buf}, M^{-2} s^{-1} [c]	k_{RSH}*, M^{-1} s^{-1} [c]
1:2 H_3PO_4–$H_2PO_4^-$ buffer	5.1	0.010	0.020	0.0011	0.034	0.00008
		0.0075	0.015	0.00078		
		0.0050	0.010	0.00059		
1:1 H_3PO_4–$H_2PO_4^-$ buffer	4.8	0.020	0.020	0.0021	0.053	0.00013
		0.015	0.015	0.0016		
		0.010	0.010	0.0012		
		0.0075	0.0075	0.00094		
2:1 H_3PO_4–$H_2PO_4^-$ buffer	4.5	0.040	0.020	0.0046	0.07	0.0005
		0.024	0.012	0.0031		
		0.020	0.010	0.0027		
5:1 H_3PO_4–$H_2PO_4^-$ buffer	4.1	0.020	0.004	0.0050	0.19	0.0008
		0.015	0.003	0.0044		
		0.010	0.010	0.0033		
10:1 H_3PO_4–$H_2PO_4^-$ buffer	3.8	0.020	0.0020	0.0088	0.32	0.0016
		0.015	0.0015	0.0067		
		0.010	0.010	0.0051		
1:10 CF_3CO_2H–$CF_3CO_2^-$ buffer	3.8	0.0020	0.020	0.0118	0.47	0.0018
		0.00175	0.0175	0.0106		
		0.0015	0.015	0.0097		
		0.0010	0.010	0.0069		
1:4 CF_3CO_2H–$CF_3CO_2^-$ buffer	3.4	0.0050	0.020	0.031	1.05	0.005
		0.0025	0.010	0.018		
1:2 CF_3CO_2H–$CF_3CO_2^-$ buffer	3.1	0.0050	0.010	0.034	1.7	0.008
		0.0025	0.005	0.019		
1:1 CF_3CO_2H–$CF_3CO_2^-$ buffer	2.8	0.010	0.010	0.065	2.4	0.016
		0.005	0.005	0.040		
0.002 N $HClO_4$	2.7	0.002		0.020		0.020
0.005 N $HClO_4$	2.3	0.005		0.050		0.050
0.010 N $HClO_4$	2.0	0.010		0.105		0.105
0.020 N $HClO_4$	1.7	0.020		0.20		0.20

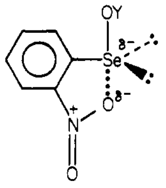
[a] All data at ionic strength = 0.02. [b] Slope of plot of k_1 vs. [*n*-BuSH] for runs for each buffer solution (Table VIII). [c] Plot of k_{RSH} vs. $[\text{buffer}]_{\text{total}}$; k_{buf} = slope, k_{RSH}* = intercept. [d] pH's calculated from known pK_a's in 60% dioxane of acids used as buffers.

an inflection between pH 2.5 and 4 of the same type as is seen[6] in the pH–rate profile for the H_3O^+-catalyzed hydrolysis of **2b**. No inflection is observed in the pH–rate profile for the reaction of the thiol with **1a**.

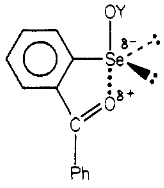
The acid-catalyzed reaction of **1a** with the thiol, like the hydrolysis of anhydride **2a**, exhibits general-acid catalysis. Unfortunately, the incursion of eq 9 as a complicating reaction restricted the number of acids for which catalytic constants (k_{HA}) could be determined to three—H_3O^+ (10 M^{-2} s^{-1}), CF_3CO_2H (5 M^{-2} s^{-1}), and H_3PO_4 (~0.1 M^{-2} s^{-1}). From these limited data it is not possible to determine whether the **1a**–BuSH reaction does, or does not, show a *nonlinear* Brønsted plot of log k_{HA} vs. pK_a of HA like the general-acid catalyzed hydrolysis of **2a**.[6]

Curve C of Figure 1 shows that at pH ≥ 7 the important kinetic pathway (rate ~ $1/a_{H^+}$) for the reaction of the thiol with **1b** is reaction with *n*-BuS$^-$ and that the rate constant for this process is but 5 times smaller than the rate constant for the reaction of *n*-BuS$^-$ with the corresponding anhydride (**2b**). In contrast, no reaction of *n*-BuS$^-$ with the *o*-nitro selenenic acid that has a rate comparable to the rate of reaction of *n*-BuS$^-$ with **2a** is detectable.[8] There must therefore be some factor or feature that enables selenenic acid **1b** to react much, much faster than selenenic acid **1a** with *n*-BuS$^-$. Any viable explanation for the much greater reactivity toward thiolate of the *o*-benzoyl (**1b**) relative to the *o*-nitro (**1a**) acid must be consistent with the fact that such markedly enhanced reactivity for the *o*-benzoyl derivative is not found in the reaction of *n*-BuS$^-$ with the corresponding anhydrides (**2a** and **2b**).

Selenenic acids **1a** and **1b** are much more stable than ordinary areneselenenic acids (such as PhSeOH). Similarly, the two selenenic anhydrides (**2a** and **2b**) are more stable than most areneselenenic anhydrides. X-ray crystallographic studies of other stabilized ortho-substituted benzeneselenenyl derivatives[9] show that a direct interaction of the *o*-NO_2 or PhC(O) group with selenium, as shown in **4a** and **4b**, is responsible for this enhanced stability and



4a, Y = H or *o*-$O_2NC_6H_4Se$



4b, Y = H or *o*-PhC(O)C_6H_4Se

that the most stable conformation for **4a** and **4b** is (as depicted) a trigonal bipyramid where the oxygen attached to selenium and the coordinating oxygen of the ortho substituent occupy the two apical positions.

For *o*-nitrobenzeneselenenyl halides coordination of the nitro group to selenium has been shown by Austad[10] to decrease the rate at which they undergo nucleophilic substitution by >10^6. This occurs because the oxygen of the nitro group, by occupying one apical position, prevents facile, one-step displacement (eq 11a) of X$^-$ from the other apical position. Direct, one-step displacement (eq 11b) of the group OY in **4a** and **4b** by a nucleophile is therefore not expected to be possible. As a result, substitution reactions of nucleophiles with either selenenic anhydrides **2a** and **2b** or selenenic acids **1a** and **1b** have to proceed by other mechanisms.

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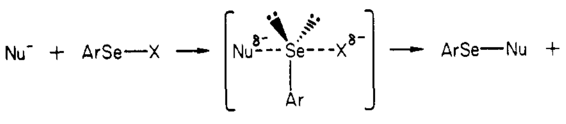
[8] The kinetic dominance of the reaction process shown in eq 9 in acetate buffers prevents accurate measurement of the rate of reaction of *n*-BuS$^-$ with **1a** in such media. Only a rough *upper* limit for the rate of the direct reaction of the thiol with **1a** at pH's ≥7.4 can be estimated. However, from this the rate constant for the reaction of *n*-BuS$^-$ with **1a** must be *at least 10^8 smaller* than the rate constant for the reaction of *n*-BuS$^-$ with **2a**.

[9] Eriksen, R.; Hauge, S. *Acta Chem. Scand.* **1972**, *26*, 3152.

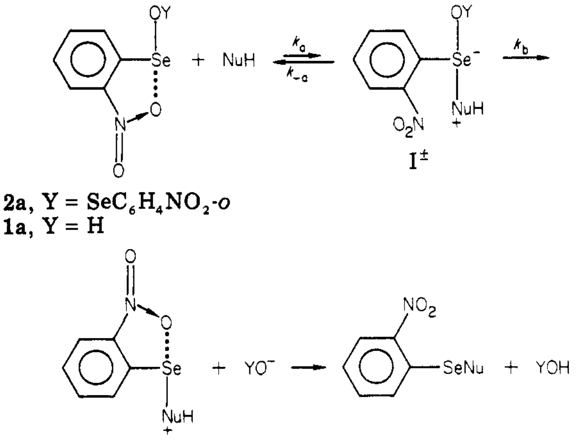
[10] (a) Austad, T. *Acta Chem. Scand. Ser. A.* **1975**, *29A*, 895. (b) Austad, T. *Ibid.* **1977**, *31A*, 93.



(11a)

(11b)

Mechanism for the Reaction of 2a with an Alkanethiol. The first step in the reaction of any nucleophile (NuH) with **2a** or **1a** should be replacement of the o-NO_2 as a ligand by the nucleophile (step k_a, eq 12), giving intermediate I±. Expulsion of YO^- (step k_b) from I± leads to products; expulsion of NuH (step k_{-a}) regenerates the reactants. In the hydrolysis of **2a**,[6] where NuH = H_2O, k_{-a} is so rapid, and so much faster than step k_b (i.e., $k_b <<<< k_{-a}$), that (k_b/k_{-a}) is too small for eq 12 to be able to serve as a kinetically effective route to products; acid catalysis of the departure of the ArSeO group is therefore required in the hydrolysis of **2a**. On the other hand, in the reaction of **2a** with the thiol, where NuH equals n-BuSH, the rate of step k_{-a} should be much smaller than when NuH is H_2O, and, even though $k_b < k_{-a}$, (k_b/k_{-a}) is large enough so that eq 12 ($k_{exp} = k_a k_b/k_{-a}$) provides a kinetically satisfactory path to products. The same will naturally also be true for **2a** when the nucleophile is n-BuS^-; in fact, in that case one might expect $k_b > k_{-a}$. Thus in the reaction of **2a** with either n-BuSH or n-BuS^- the mechanism followed is that shown in eq 12.



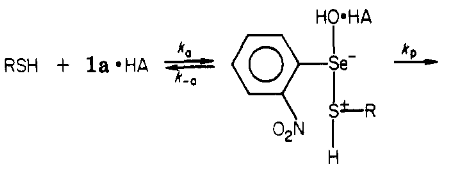
2a, Y = $SeC_6H_4NO_2$-o
1a, Y = H

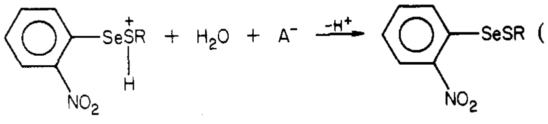
I±

(12)

Mechanism for the Reaction of 1a with an Alkanethiol. When the substrate reacting with n-BuSH is the selenenic acid (**1a**), rather than the anhydride (**2a**), YO^- is not o-$O_2NC_6H_4SeO^-$ but the *much* poorer leaving group, OH^-, and k_b for loss of OH^- from I± should be orders of magnitude smaller than k_b for loss of o-$O_2NC_6H_4SeO^-$. Because k_b is so much smaller, we again encounter a situation, as in the hydrolysis of **2a**,[6] where $k_b <<<< k_{-a}$ that k_b/k_{-a} is too small for the mechanism in eq 12 to be kinetically effective. Acid catalysis of the depature of the OH group is therefore necessary in order for its loss to be adequately competitive in rate with step k_{-a}. The observation of general-acid rather than specific-H^+ catalysis indicates that this proton transfer to the OH group is not an equilibrium process. By analogy with the mechanism[6] for the acid-catalyzed hydrolysis of **2a**, the "preassociation" mechanism in eq 13 and 14 is suggested for the reaction of **1a** with n-BuSH.[11]

$$\mathbf{1a} + HA \underset{}{\overset{K_{assoc}}{\rightleftharpoons}} \mathbf{1a}\cdot HA \qquad (13)$$

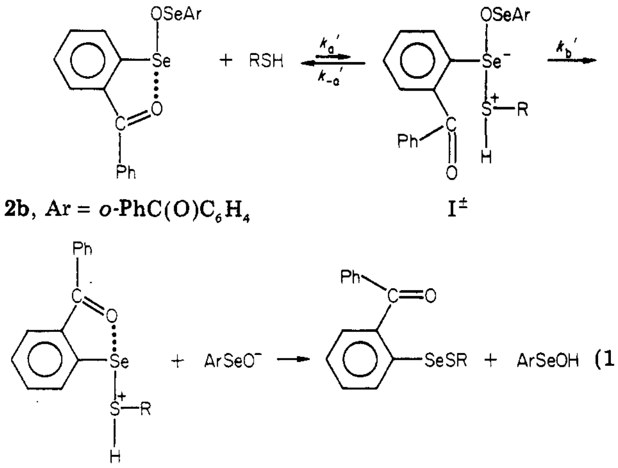




(14)

The important difference in the reactions of the thiol with the selenenic anhydride (**2a**) and the selenenic acid (**1a**) is that in the former case there is a good enough leaving group (o-$O_2NC_6H_4SeO$) that acid catalysis of its departure is not needed, whereas in the latter case, where there is a much poorer leaving group (OH), acid catalysis of its departure is required in order for the reaction to proceed at a reasonable rate.

Mechanism for the Reaction of 2b with an Alkanethiol. Reaction of **2b** with either n-BuSH or n-BuS^- is believed to take place via the same type of mechanism (shown for n-BuSH in eq 15) outlined earlier for the reaction of **2a** with these nucleophiles.



2b, Ar = o-$PhC(O)C_6H_4$

I±

(15)

As previously noted, **2b** reacts with n-BuSH about 15 times slower than does anhydride This requires that $k_b'(k_a'/k_{-a}')$ in eq 15 be fifteen times smaller than $k_b(k_a/k_{-a})$ in eq 12 (Y = o-$O_2NC_6H_4Se$). Factors that could be responsible for this difference include the following. First, the greater the electron-withdrawing character of the substituent in the aryl group of ArSeO, the faster should be the rate of loss of $ArSeO^-$ from I± (step k_b or k_b'). Since PhC(O) is a weaker electron-withdrawing group than NO_2 (σ_p for PhC(O) = +0.46, σ_p for NO_2 = +0.78), k_b' should be smaller than k_b. Second, given that formation of I± from the selenenic anhydride presumably results in some increase of electron density on the selenium attacked by the thiol, the weaker electron-withdrawing character of PhC(O) could also cause k_a'/k_{-a}' to be smaller than (k_a/k_{-a}). The greater steric bulk of PhC(O) relative to NO_2 might also contribute to k_a'/k_{-a}' being smaller than k_a/k_{-a}. Another factor will be the relative strength of the coordinative interaction of the two ortho substituents with Se, but whether this is stronger for PhC(O) than for NO_2 (as would be required for it to work toward k_a'/k_{-a}' being smaller than k_a/k_{-a}) is not known.

In the reaction with n-BuS^-, where attack of the thiolate ion on the anhydride (for **2a**, step k_a of eq 12, NuH = RS^-), rather than loss of $ArSeO^-$, is thought to be rate determining, **2b** reacts, not slower, but slightly faster than **2a**.

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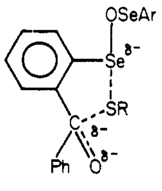
(11) The limited data on the variation of log k_{HA} with pK_a suggest that the Brønsted plot for the acid-catalyzed reaction of **1a** with n-BuSH may be nonlinear. This can be accomodated by the mechanism in eq 13 and 14 ($\alpha = 0$ for acids where $k_p > k_{-a}$, $\alpha > 0$ for acids where $k_p < k_{-a}$, K_{assoc} independent of the pK_a of HA).[6]

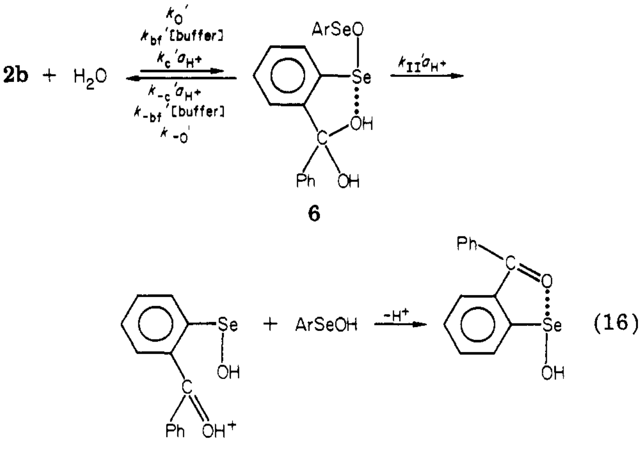
One explanation, which has the advantage of being compatible with that just given for the behavior of the n-BuSH reaction, is that, while k_a'/k_{-a}' is smaller for **2b** than k_a/k_{-a} for **2a**, both k_a' and k_{-a}' are larger than k_a and k_{-a}, respectively, a possible reason being stabilization of the transition state (**5**) by the ortho carbonyl group in a manner reminiscent of the fashion[12] in which an adjacent C=O stabilizes the transition state for S_N2 reactions of α-halo carbonyl compounds.



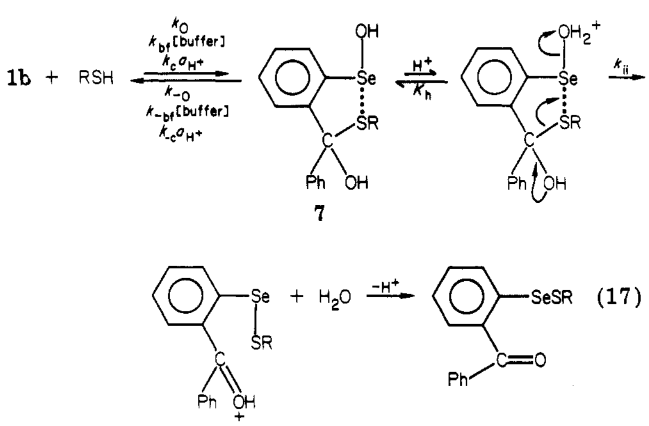
5

Mechanisms for the Reaction of 1b with an Alkanethiol. Although both selenenic anhydrides react with a thiol by the same mechanism, the mechanism for the reaction of selenenic acid **1b** with n-BuSH is quite different than that outlined earlier for the reaction of **1a** with this thiol.

Let us consider first the acid-catalyzed reaction of **1b**. Curves C and D of Figure 1 show that the H_3O^+-catalyzed reaction of **1b** with n-BuSH is 60–350 times faster than the H_3O^+-catalyzed reaction of **1a**, and that there is the same kind of inflection in the pH–rate profile for the H_3O^+-catalyzed reaction of **1b** as was seen[6] in the pH–rate profile for the H_3O^+-catalyzed hydrolysis of **2b**. In the hydrolysis of **2b** this inflection results from the fact that in the mechanism shown in eq 16 step k_{II}' is rate determining in buffers with pH ≥ 4 ($k_{hyd} = k_{II}'K_{eq}'a_{H^+}C_{H_2O}$), while in dilute HCl or $HClO_4$ solutions (low pH and no buffer) H_3O^+-catalyzed formation of **6** is rate determining ($k_{hyd} = k_{II}'K_{eq}'a_{H^+}C_{H_2O}/(1 + k_{II}'/k_{-c}')$).[6] We suggest an analogous mechanism (eq 17), with hemithioketal **7** as an intermediate, for the acid-catalyzed reaction of **1b** with n-BuSH. In buffers of pH ≥ 4 establishment of the equilibrium between **1b** and the hemithioketal is rapid compared to the conversion of **7** to products, and $k_{RSH}^* = k_{II}K_{eq}a_{H^+}$. On the other hand, in dilute hydrochloric or perchloric acid solutions (low pH, no buffer) k_{bf}[buffer] $= 0$ and $k_c a_{H^+} > k_0$ and since $k_{II} > k_{-c}$, $k_{RSH}^* = k_{II}K_{eq}a_{H^+}/(1 + k_{II}/k_{-c})$. From curve C in Figure 1 $k_{II}/k_{-c} = 6$.



$k_{II}' > k_{-c}'$
$K_{eq}' = (k_0'/k_{-0}') = (k_{bf}'/k_{-bf}') = (k_c'/k_{-c}')$



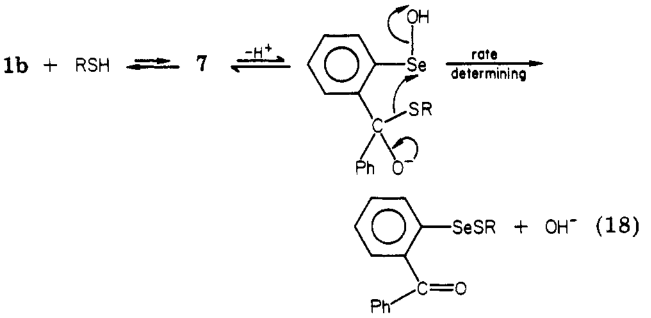
$K_{eq} = (k_0/k_{-0}) = (k_{bf}/k_{-bf}) = (k_c/k_{-c})$
$k_{II} = k_{ii}K_h$

Rate constant k_c for the H_3O^+-catalyzed addition of n-BuSH to **1b** can be calculated from the k_{RSH}^* values for dilute HCl and $HClO_4$ solutions, since for those reaction conditions:

$$k_c = \left[\frac{k_{RSH}^*(\text{dilute H}^+)}{a_{H^+}}\right]\left[1 + \frac{k_{-c}}{k_{II}}\right] = 620\ M^{-2}\ s^{-1}(1 + 0.16) = 7.2 \times 10^2\ M^{-2}\ s^{-1}$$

This value of k_c may be compared with k_c' (55 $M^{-2}\ s^{-1}$)[6] for the formation of **6** from **2b** in eq 16. Recent work by Burkey and Fahey[13] has demonstrated that with ketones R′R″C=O where R′ and R″ are, as in the present case, relatively bulky groups K_{RSH} for formation of the hemithioketal R′R″C(OH)SR may be no more than 40 times larger than K_{H_2O} for formation of the carbonyl hydrate $R'R''C(OH)_2$. That being the case, it is acceptable for k_c to be only 13 times larger than k_c'.

Let us now turn to consideration of the mechanism of the reaction of **1b** with n-BuS⁻ that dominates the pH–rate profile in curve C at pH ≥ 7. The rate of this reaction is suprisingly rapid, being *at least* 10^3 faster than any reaction of the thiolate with the o-nitro selenenic acid (**1a**) and only 5 times slower than the rate of reaction of n-BuS⁻ with anhydride **2b**. Initially we considered that the mechanism might be as shown in eq 18, with the anion of the hemithioketal as the key intermediate. There are two reasons, however, why this mechanism does not appear to be satisfactory. First, if it were correct, an analogous reaction (eq 19) involving the conjugate base of carbonyl hydrate **6** might be expected to be kinetically significant in the hydrolysis of **2b** at similar pH's; yet the pH–rate profile for that reaction[6] under such conditions shows no evidence of any process with rate $\sim 1/a_{H^+}$. Second, if the rapid reaction of **1b** with n-BuS⁻ were due to eq 18, then reaction



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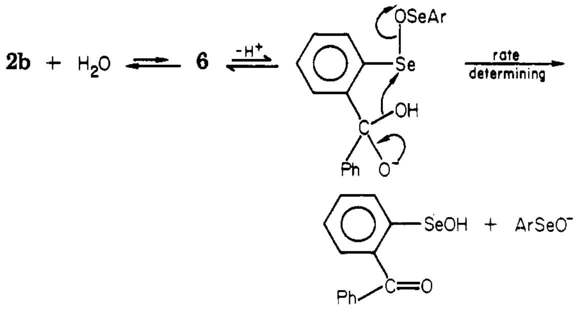
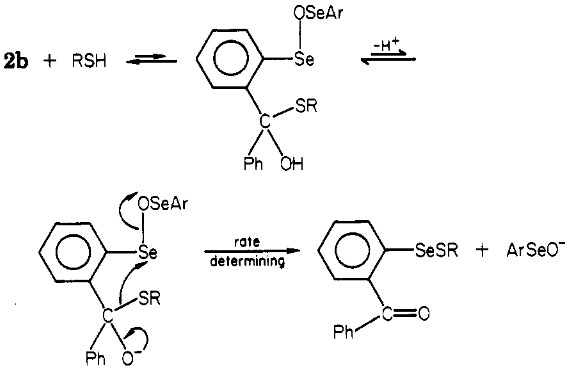
[12] Bartlett, P. D.; Trachtenberg, E. N. J. Am. Chem. Soc. 1958, 80, 5808.

[13] Burkey, T. J.; Fahey, R. C. J. Am. Chem. Soc. 1983, 105, 868.



(19)

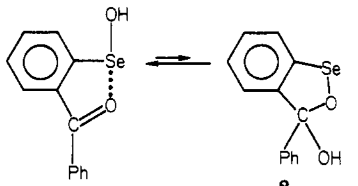
of **2b** with n-BuS$^-$ ought to occur via eq 20 and with a rate



(20)

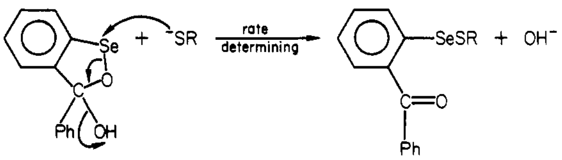
that would presumably be much faster than the rate of reaction of the thiolate with either **1b** (OH$^-$ much poorer leaving group than ArSeO$^-$) or **2a** (similar reactivity difference to that for **1a** vs. **1b**). This, of course, is contrary to the reactivity pattern actually observed for reaction of n-BuS$^-$ with these three substrates.

A satisfactory alternative to eq 18 for the mechanism of the reaction between n-BuS$^-$ and **1b**, and one that is compatible with the observed relative reactivity toward the thiolate of **1a**, **1b**, and **2b**, is shown in eq 21. In this



1b **8**

(21a)



8

(21b)

mechanism the reactive intermediate is **8**, which is in equilibrium with **1b** and is formed from it by the intramolecular addition of the SeOH function across the C=O group. We believe that the PhC(OH)O group in **8** should be a somewhat better leaving group than the OH group in **1b**. More important, since there is no ortho substituent coordinated to Se in **8**, a direct, one-step displacement (of the general type shown in eq 11a) of this group by n-BuS$^-$ (eq 21b) is possible; Austad[10a] using areneselenenyl halides as substrates, has shown that the rate for such a process can be $>10^6$ faster than the rate of reaction of the same nucleophile with the equivalent ortho-stabilized areneselenenyl compound.

While reversible additions of reagents Z–OH to carbonyl groups (to give ZOCOH) are common in organic chemistry, equivalent additions to nitro groups are not. A reaction pathway analogous to eq 21 is therefore not expected to be feasible for the reaction of **1a** with n-BuS$^-$. Neither would one be expected for the reaction of **2b** with the thiolate, since a selenenic anhydride function should have no tendency to add across a C=O group. Selenenic acid **1b** is accordingly the only one of the three substrates for which this type of mechanism should be possible, and this provides a satisfactory rationale for the greater than expected relative reactivity of **1b** toward the thiolate.

Comparison of the pH-independent rate terms in eq 7 ($0.025\ M^{-1}\ s^{-1}$) and eq 9 ($0.004\ M^{-1}\ s^{-1}$) indicates that the reaction of the undissociated thiol with **1b** also proceeds at a rate only about 5 times slower than the rate of reaction of **2b** with the same species. We suggest that this reaction of **1b** probably also involves **8** as an intermediate, with the rate-determining step being attack of n-BuSH, rather than n-BuS$^-$ on **8**.[14]

Relevance of Current Results to the Mechanism for Eq 1. A relatively stable selenenic acid group has been postulated[2] to be present at the active site in the oxidized form of the enzyme glutathione peroxidase, and reaction of this SeOH group with the thiol group in glutathione (eq 1) has been suggested[2] to be one of the key steps in the reaction cycle for this enzyme. At the outset of this research we had hoped that determination of the mechanism of reaction of a thiol with "stable" selenenic acids **1a** and **1b** might provide information indicative of the probable mechanism for eq 1.

The present results, however, indicate that modest changes in the nature of the substituent responsible for stabilizing a selenenic acid can lead to a marked change in the mechanism that operates for the reaction. The present results also show that reaction of a thiol with either **1a** or **1b** (eq 3), a simple and straightforward process chemically, is far more complex mechanistically than had been expected a priori. These several considerations suggest that, until there is knowledge of what structural factor(s) is responsible for stabilization of the SeOH group at the active site in glutathione peroxidase, no attempt should be made to extrapolate the mechanistic behavior of reaction 3 for either **1a** or **1b** as indicative of what is likely to be involved for the corresponding reaction (eq 1) of the enzyme.

Experimental Section

Preparation and Purification of Materials. The preparation and purification of **2a** and **2b** is outlined in an accompanying paper,[6] as if the purification of the dioxane used. 1-Butanethiol (Aldrich) was purified by fractional distillation. All water used in kinetic runs was doubly distilled from glass. All other reagents used were of the highest purity commercially available and were used without further purification.

Procedure for Kinetic Runs. Reaction of 2a with Thiol. Stock solutions of **2a** (5×10^{-3} M) and 1-butanethiol (1 M or 4 M) in anhydrous dioxane were prepared immediately prior to use. A 60% dioxane solution (3.5 mL) containing the desired concentrations of buffer (or dilute $HClO_4$) and lithium perchlorate was placed in a 1-cm spectrophotometer cell in the thermostatted cell compartment of a Cary Model 17 spectrophotometer. To this was then added by microsyringe 35 μL of the stock solution of **2a**. The reaction was then initiated by adding, via a second microsyringe, the appropriate amount of one of the stock solutions of the thiol, and the progress of the reaction was monitored by

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[14] Although the behavior of the acid-catalyzed reaction of the thiol with **1b** is satisfactorily accommodated by the mechanism shown in eq 17, the possibility of an alternate mechanism, involving reaction of n-BuSH with protonated **8** (**8**–H$^+$) cannot be excluded. In such a mechanism, in order to have the observed inflection in the pH-rate profile, the **1b** $\rightleftharpoons$ **8** equilibrium would have to be subject to acid and buffer catalysis in the same manner as the equilibrium between **1b** and **7** in eq 17.

following the decrease in the absorbance of the solution with time at 440 nm.

Reaction of 2b with Thiol. The reaction of **2b** with the thiol was studied by using the same general procedure as just described for the reaction of *n*-BuSH with **2a**. The progress of the reaction was followed by monitoring the decrease in the absorbance of the solution with time at 425 nm.

Reaction of 1b with Thiol. To 3.5 mL of 60% dioxane in a 1-cm spectrophotometer cell thermostated at 25 °C was added 35 μL of a freshly prepared stock solution of **2b** (5×10^{-3} M) in dioxane, followed by 3.5 μL of a 1 M solution of perchloric acid. The solution was allowed to stand for 5 min to ensure that hydrolysis of **2b** to **1b** was complete. Then the proper amounts of buffer (or perchloric acid) and lithium perchlorate solutions to afford the desired reaction conditions were added by microsyringe. This was followed by the initiation of the reaction by the addition of the proper amount of a stock solution of the thiol in dioxane via another microsyringe. The reaction of **1b** with the thiol was followed by observing the decrease in the absorbance of the solution with time at 410 nm.

Reaction of 1a with Thiol. For the runs in dilute perchloric acid, or in trifluoroacetate buffers, the procedure was as follows. To a 60% dioxane solution (3.5 mL) containing the desired concentrations of perchloric acid (or buffer) and lithium perchlorate was added 35 μL of a stock solution of **2a** (5×10^{-3} M) in dioxane. The absorbance of the solution at 440 nm was then monitored in order to determine when the hydrolysis of **2a** to **1a** was complete (for some reaction conditions several hours were required). At that point the desired amount of a stock solution of *n*-BuSH in dioxane was added by microsyringe, and the decrease in the absorbance of the solution at 440 nm, due to the reaction of **1a** with the thiol, was followed.

For the runs in H_3PO_4–$H_2PO_4^-$ buffers the procedure was slightly different. A stock solution of **1a** (0.01 M) in 90% dioxane was prepared by dissolving **2a** (5×10^{-3} M) in 90% dioxane containing 0.01 N $HClO_4$ and allowing the hydrolysis of the selenenic anhydride to proceed to completion. (The progress of the hydrolysis was monitored by removing aliquots, and, after appropriate dilution, measuring the absorbance at 440 nm.) A portion (35 μL) of this stock solution of **1a** was added to 3.5 mL of a 60% dioxane solution containing the proper concentrations of buffer and lithium perchlorate, and the reaction of **1a** with the thiol was then initiated by the addition via microsyringe of the correct amount of a stock solution of *n*-BuSH in dioxane.

Products of the Reaction of 2a and 1a with 2-Methyl-2-propanethiol. Selenenic anhydride **2a** (0.29 g, 0.70 mmol) was dissolved in 15 mL of dioxane. To this was then added 0.5 mL of a 3 M solution of 2-methyl-2-propanethiol (1.40 mmol) in dioxane and 0.515 mL of 0.97 M aqueous perchloric acid, followed by enough water to bring the final volume of the solution to 25 mL. The solution was allowed to stand at room temperature. Periodically 2.5-μL aliquots were removed and diluted to 3.0 mL with 60% dioxane, and their ultraviolet spectrum was scanned between 320 and 460 nm. When the scan indicated that the reaction was complete, the solution was poured into 100 mL of water and extracted three times with 10-mL portions of chloroform. The chloroform was dried (Na_2SO_4), the solvent was removed under reduced pressure at room temperature, and the residue was subjected to an oil pump vacuum for several hours to remove the last traces of solvent and dioxane. The residue, a yellow oil, was shown by TLC to consist of a single compound that was identified as *tert*-butyl *o*-nitrobenzeneselenenyl sulfide, *t*-$BuSSeC_6H_4NO_2$-*o*, 0.39 g (94%): NMR ($CDCl_3$) δ 7.2–8.5 (m, 4 H), 1.38 (s, 9 H); mass spectrum, *m/e* 291 (M^+, ^{80}Se), 289 (M^+, ^{78}Se), 235 ($M^+ - C_4H_8$), 202 ($M^+ - C_4H_9S$), 186, 154, 106, 88, 57, 41.

Registry No. 1a, 56790-60-4; **1b**, 84250-81-7; **2b**, 84250-80-6; 7 (R = Bu), 90941-71-2; 8, 90941-72-3; *t*-$BuSSeC_6H_4NO_2$-*o*, 90941-75-6; (*o*-$NO_2C_6H_4Se)_2O$, 84250-76-0; BuS^-, 20733-16-8; BuSH, 109-79-5; $CH_3C(CH_3)_2SH$, 75-66-1.

Supplementary Material Available: Tabulation of results of individual kinetic runs for **2a** (Table V), **2b** (Table VI), **1b** (Table VII), and **1a** (Table VIII) (13 pages). Ordering information is given on any current masthead page.

Solution and Flash Vacuum Pyrolyses of 3-Arylpropanesulfonyl and 2-(Aryloxy)ethanesulfonyl Azides. Synthesis of 7-Membered Sultams

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The solution and flash vacuum pyrolyses of 3-arylpropanesulfonyl azides have been studied and the results compared with those of the corresponding 2-arylethanesulfonyl azides. The best yields of 7-membered ring sultams are formed on solution decomposition in Freon 113. Hydrogen abstraction and solvent insertion products are obtained mainly in hydrocarbon solvents. The structures of the 7-membered sultams have been established unambiguously and an authentic sample of the parent 2,3,4,5-tetrahydro[*c*]-1,2-thiazepine 1,1-dioxide prepared. Decomposition of 3-(2,6-dichlorophenyl)propanesulfonyl azide (**22**) leads to a 6,9-dichloro sultam (**33c**) via a 1,2-chlorine shift. FVP of 3-(2-mesityl)propanesulfonyl azide (**20**) gave a good yield of the 7-membered ring sultam (**34**) (1,2-methyl shift). FVP of 3-phenyl-1-propanesulfonyl azide (**16**) at 995 °C (0.05 mm) gave, among other products, a 6.2% yield of 5,6,7,8-tetrahydroquinoline (**39**). The formation of these products is discussed. Thermolysis of 2-(aryloxy)ethanesulfonyl azides gave the corresponding 7-membered ring sultams **27** as well.

The thermal decomposition of sulfonyl azides in solution in saturated or aromatic hydrocarbons is a unimolecular process[1] leading to sulfonylnitrenes[2] which can then undergo inter- or intramolecular reactions. Thus, the solution decomposition of 2-phenylethanesulfonyl azides in hydrocarbon solvents was found to yield small amounts of intramolecular cyclization products together with products of intermolecular reactions, namely C–H insertion and

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