upon a racemic cobalt(III)-tetramine moiety can give excellent asymmetric yields of tetraminecobalt(III)-amino acid complex. Furthermore, under the same conditions, a reasonably high asymmetric yield may be obtained using a symmetric amino acid with only catalytic amounts of chiral material present in the original reaction mixture. Since **7** undergoes acid-catalyzed decarboxylation to give an asymmetric yield of an alanine complex,[14] this leads to an asymmetric amino acid synthesis using only catalytic amounts of chiral agents.

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Oxidation-Reduction Reactions of Organoselenium Compounds. 1. Mechanism of the Reaction between Seleninic Acids and Thiols[1]

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Abstract: In aqueous dioxane benzeneseleninic acid, $PhSeO_2H$, reacts with 3 mol of an alkanethiol, RSH, to yield 1 mol each of the corresponding selenenyl sulfide PhSeSR and disulfide RSSR. Over the pH range 0.2-10.0 and with the thiol present in large stoichiometric excess over the seleninic acid, the reaction takes place in two distinct stages, both of which exhibit a first-order dependence on thiol concentration. In the first stage the thiol and $PhSeO_2H$ react to form an intermediate having a λ_{max} at 265 nm, and which is believed to be the thiolseleninate PhSe(O)SR. In the second stage this intermediate then reacts with the thiol to initiate a reaction sequence leading to PhSeSR and RSSR as the final products. The pH-rate profiles associated with the two stages of the reaction are quite different. For the first stage at pH $\leq$2 the kinetically dominant pathway for formation of the intermediate is reaction of RSH with $PhSeO_2H_2^+$, from pH 2.5 to 4.5 it is reaction of RSH with $PhSeO_2H$, and above pH 5 it is reaction of RS^- with $PhSeO_2H$. The rates of all these processes are only slightly slower when the thiol is *t*-BuSH than they are when it is *n*-BuSH. The pH-rate profile for the second stage indicates that above pH 5 the kinetically important process is reaction of the intermediate with the thiolate ion RS^-, while below pH 2 it is reaction of RSH with a protonated form of the intermediate. For both these reactions the rate of reaction in the *t*-BuSH system is over 10^4 *slower* than in the *n*-BuSH system. This very large rate difference indicates that the rate-determining step of the reaction of the intermediate PhSe(O)SR with RS^- (or of the protonated intermediate with RSH) involves attack on the sulfur atom of the intermediate, the complete mechanism for the second stage being as shown in Scheme II. While the intermediate PhSe(O)SBu-*t* is quite stable thermally in dilute solution in aqueous dioxane, it decomposes rapidly at room temperature in concentrated solution in anhydrous acetone. Possible reasons for its surprising difference in stability under these different conditions are briefly discussed.

Research in recent years has shown that certain reactions of organoselenium compounds can be used to effect a number of valuable synthetic transformations.[2-8] These developments, plus the important physiological effects of selenium, either definitely established[9] or tentatively hypothesized,[10] have greatly heightened interest in organoselenium chemistry. With this increased interest it becomes highly desirable to learn much more about the detailed mechanisms of reactions of organoselenium compounds, a subject that has received only very limited attention in the past.

Aromatic seleninic acids, $ArSeO_2H$, are moderately strong oxidizing agents and can be reduced to diselenides, ArSeSeAr, by a variety of reagents,[11-14] including thiols. According to Rheinboldt and Giesbrecht[11] the stoichiometry of the thiol-seleninic acid reaction is as shown in the equation

$$2ArSeO_2H + 6RSH \rightarrow ArSeSeAr + 3RSSR + 4H_2O \quad (1)$$

Because of the current interest[10] in the physiological chemistry of selenium and the ubiquitous nature of thiol groups in biological systems investigation of the mechanism of the reduction

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of $ArSeO_2H$ by thiols seemed a particularly appropriate place to begin our studies of organoselenium mechanisms. The present paper reports our results.

Results

Stoichiometry of the Reaction. In dilute solution in aqueous dioxane with the thiol present in substantial excess over benzeneseleninic acid the stoichiometry of the reaction is, not that reported by Rheinboldt and Giesbrecht, but rather as shown in eq 2. The identity of the selenenyl sulfides PhSeSR was established by actual isolation and comparison with authentic samples. The same stoichiometry was observed at all pHs at which the reaction was studied.

$$PhSeO_2H + 3RSH \rightarrow PhSeSR + RSSR + 2H_2O \quad (2)$$

1a, R = *n*-Bu
b, R = *t*-Bu

Upon standing in solution the selenenyl sulfides, **1**, do slowly disproportionate into a mixture of diphenyl diselenide and the disulfide RSSR:

$$2PhSeSR \rightarrow PhSeSePh + RSSR$$

However, this disproportionation, a known reaction,[15] is very slow under our reaction conditions compared to the relatively rapid reaction between thiol and the seleninic acid leading to the formation of **1** (eq 2).

Evidence for the Formation of an Intermediate on the Reaction Coordinate. When followed spectrophotometrically the reaction of benzeneseleninic acid with excess 2-methyl-2-propanethiol exhibits well-defined biphasic character at all pHs studied. In the initial stage of the reaction the absorbance of the solution in the 260–290-nm region increases markedly and a species having a maximum at 265 nm is formed. In the second stage the absorption maximum at 265 nm then slowly disappears, and the final spectrum of the solution is that expected for PhSeSBu-*t* (**1b**).

With *t*-BuSH as the reacting thiol the rate of the second stage is at least 15 times slower at all pHs than the rate of the first, so that one has essentially complete conversion of the seleninic acid to the 265-nm intermediate before conversion of this intermediate to PhSeSBu-*t* becomes significant. On the other hand, when the thiol is *n*-BuSH the situation is different. Over a limited pH range (monochloroacetate or formate buffers) formation of an intermediate species having a maximum at 265 nm is detectable, but outside this pH range the rate of disappearance of the intermediate is enough faster than its rate of formation so that buildup of the intermediate is not detectable.

After outlining the kinetics and pH–rate profiles associated with the two stages of the reactions we will return to further consideration of the 265-nm intermediates and, in particular, to experiments designed to elucidate the structure of the intermediate formed in the *t*-BuSH–benzeneseleninic acid reaction.

Kinetics of the Thiol–Benzeneseleninic Acid Reactions. The kinetics of the reactions of the two thiols with $PhSeO_2H$ were studied spectrophotometrically at 25 °C in 60% dioxane (v/v) under conditions where the thiol was always present in large stoichiometric excess over the seleninic acid. The variation of rate with pH was examined over a range extending from 0.6 M $HClO_4$ (pH 0.2) to a phosphate buffer having a pH of 10.0 in 60% dioxane.

For the reaction of *t*-BuSH with the seleninic acid rates were followed by monitoring the change in optical density with time at 265 nm. As noted earlier the reaction of the thiol with the seleninic acid is kinetically biphasic (eq 3), with the rate of the

$$PhSeO_2H \xrightarrow[RSH]{k_a} \underset{(\lambda_{max}\ \text{at}\ 265\ \text{nm})}{\text{intermediate}} \xrightarrow[RSH]{k_b} PhSeSR \quad (3)$$

first stage being so much faster than the rate of the second that the rates of the two stages can be measured independently. Both stages are found to be first order in mercaptan. The rate data for the two stages of the benzeneseleninic acid–*t*-BuSH reaction at various pHs are collected in Table I.

The majority of the kinetic studies of the *n*-BuSH–$PhSeO_2H$ reaction were carried out by following the increase in the absorbance of the solution with time at 240 nm. At this wavelength ϵ for the intermediate and for PhSeSBu-*n* are virtually the same, so that plots of log $(A_\infty - A)$ at 240 nm vs. time are satisfactorily linear at all pHs, including those (pH 5–7) where the intermediate builds up to a significant concentration. Their slopes equal the experimental first-order rate constant for the first stage (step k_a) of the *n*-BuSH–$PhSeO_2H$ reaction; at any given pH they vary linearly with mercaptan concentration and are therefore equal to k_a[*n*-BuSH].

Rate constants for the second stage of the *n*-BuSH–seleninic acid reaction (step k_b) are only obtainable over that limited pH range (5–7) where the concentration of the intermediate builds up to a sufficient level so that the absorbance at 265 nm goes through a well-defined maximum during the course of the reaction. In that pH region the experimental first-order rate constants for the second stage, k_b[*n*-BuSH], were determined by following the absorbance at 265 nm, measuring the time, t_{max}, at which the absorbance reached a maximum value, and then using the relationship between t_{max} and the rate constants for two consecutive first-order reactions given by Wiberg,[16] plus the already known value of $k_i = k_a$[*n*-BuSH], to calculate k_b[*n*-BuSH].

The results of the kinetic studies on the first stage of the *n*-BuSH–benzeneseleninic acid reaction are collected in Table II. The kinetic data on t_{max} at 265 nm and the values of k_b calculated from t_{max} measurements are summarized in Table III.

pH–Rate Profile for the Two Stages of the Thiol–Benzeneseleninic Acid Reactions. Figure 1 shows the pH–rate profiles for the two stages (k_a and k_b) of the *t*-BuSH–$PhSeO_2H$ reaction. Figure 2 gives the pH–rate profile for k_a for the reaction of *n*-butyl mercaptan with the seleninic acid and k_b for the same system for the limited pH range over which it was measurable.

The pHs of the various carboxylate buffers in 60% dioxane were derived from the measured pHs for each of the buffers in water and previous measurements, either in this laboratory[17] or others,[18] of ΔpK_a for each of the carboxylic acids for transfer from water to 60% dioxane as solvent. The pHs of the two phosphate buffers in 60% dioxane were determined by measuring spectrophotometrically the degree of dissociation of thiophenol in each of the buffers in the manner described by Kice and Rogers,[17a] and then using the observed ratios of $[PhS^-]/[PhSH]$ and the previously measured[17a] pK_a of thiophenol in 60% dioxane to calculate the pH of each buffer.

As can be seen from the solid curves in Figures 1 and 2 the data for k_a for the reactions of the thiols with $PhSeO_2H$ seem to be fitted reasonably well by an equation of the form

$$k_a = \frac{k a_{H^+}^2 + k' a_{H^+} + k''}{K_a + a_{H^+}} \quad (4)$$

where K_a is the acid dissociation constant for $PhSeO_2H$ and was assumed to have a value of 6×10^{-8} M ($pK_a = 7.2$) in 60% dioxane.[19] The values of k, k', and k'' used to generate the curves for k_a shown in Figures 1 and 2 were as follows:

	k	k'	k''
for *t*-BuSH	$2.8\ M^{-2}\ s^{-1}$	$0.05\ M^{-1}\ s^{-1}$	$0.48 \times 10^{-6}\ s^{-1}$
for *n*-BuSH	$10\ M^{-2}\ s^{-1}$	$0.25\ M^{-1}\ s^{-1}$	$2.4 \times 10^{-6}\ s^{-1}$

The experimental data for k_b for the *t*-BuSH reaction in the pH region 0–2 are well fitted by assuming $k_b = 0.15 a_{H^+}$, while

Table I. Kinetics of the Reaction of Benzeneseleninic Acid with 2-Methyl-2-propanethiol in 60% Dioxane at 25 °C

reaction conditions	pH	10^4[PhSe-O_2H], M	10^3[RSH], M	10^3k_i, s^{-1} [a]	$k_a = k_i/$[RSH], $M^{-1}s^{-1}$	10^5k_{ii}, s^{-1} [b]	$k_b = k_{ii}/$[RSH], $M^{-1}s^{-1}$
0.6 M $HClO_4$	0.22	0.71	1.2	2.6	2.2	14	0.12
			1.8	3.6	2.0	18	0.10
0.4 M $HClO_4$	0.40	0.71	1.2	1.5	1.2	7.6	0.063
		0.94	1.8	2.0	1.1	11	0.061
0.2 M $HClO_4$	0.70	0.94	1.5	0.62	0.41	3.3	0.024
			1.8	0.90	0.50	5.1	0.029
0.1 M $HClO_4$	1.00	0.94	1.2	0.29	0.24	1.7	0.015
			1.5	0.34	0.23	2.1	0.015
0.012 M $HClO_4$	1.92	1.21	3.0	0.20	0.067	0.46	0.0015
			3.7	0.25	0.068	0.54	0.0015
0.5:1.0 CF_3CO_2H-$CF_3CO_2^-$ buffer [d]	3.1	1.13	3.0	0.17	0.056	[c]	
0.65:1.0 Cl_2CHCO_2H-$Cl_2CH_2CO_2^-$ buffer [d]	4.2	1.13	3.0	0.18	0.060	[c]	
3.5:1.0 $ClCH_2CO_2H$-	4.9	1.20	3.0	0.18	0.060	[c]	
$ClCH_2CO_2^-$ buffer [e]			3.7	0.24	0.065	[c]	
1.1:1.0 $ClCH_2COOH$-	5.4	1.20	3.0	0.43	0.14	[c]	
$ClCH_2CO_2^-$ buffer [f]			3.7	0.56	0.15	[c]	
1.3:1.0 $HCOOH$-$HCOO^-$	6.0	0.71	1.2	0.51	0.42	[c]	
buffer [f]		1.2	1.5	0.57	0.38	[c]	
			2.1	0.90	0.42	[c]	
0.28:1.0 $HCOOH$-	6.6	1.2	3.0	4.9	1.6	0.15	0.0005
$HCOO^-$ buffer [f]			3.7	6.3	1.7	0.18	0.0005
1.2:1.0 $AcOH$-AcO^-	7.36	1.2	3.0	10.0	3.3	0.40	0.0014
buffer [f]			3.7	12.9	3.5	0.55	0.0015
0.17:1.0 $AcOH$-AcO^-	8.2	1.2	3.0	15.8	5.3	2.6	0.0090
buffer [f]			3.7	21	5.6	3.4	0.0095
			4.4	24.5	5.6	3.8	0.0089
1:1 KH_2PO_4-K_2HPO_4	9.0	1.2	3.0	21	7.0	15	0.052
buffer, $[H_2PO_4^-] = 0.02$ M			3.7	27	7.3	18.5	0.052
0.12:1.0 KH_2PL_4-K_2HPO_4	10.0	0.91	3.7	30	8.1	73	0.27
buffer, $[HPO_4 =] = 0.03$ M		1.2	2.2	22	9.6	120	0.27
			3.0	27	9.0	93	0.28

[a] k_i is the experimental first-order rate constant for the first stage of the *t*-BuSH-$PhSeO_2H$ reaction. [b] k_{ii} is the experimental first-order rate constant for the second stage of the reaction. [c] Too small to measure accurately. [d] $[RCO_2^-] = 0.02$ M. [e] $[RCO_2^-] = 0.01$ M. [f] $[RCO_2^-] = 0.05$ M.

in the pH region 7–10 they are fitted by the relationship $k_b = 4.2 \times 10^{-11}\,(1/a_{H^+})$. In the pH region 5–7.5 for the *n*-BuSH reaction $k_b = 1.65 \times 10^{-6}\,(1/a_{H^+})$; in more acid media (pH <2) k_b for the *n*-BuSH–seleninic acid reaction was so much faster than k_a that no determination of k_b was possible.

Experiments Aimed at Elucidation of the Structure of the Intermediate in the *t*-BuSH–$PhSeO_2H$ Reaction. A number of otherwise plausible possibilities for the structure of the 265-nm intermediate in the *t*-BuSH–$PhSeO_2H$ reaction can be ruled out. First, one can show that the intermediate is not 2-methyl-2-propanesulfenic acid, *t*-BuSOH. This sulfenic acid can be generated[22] by pyrolysis of di-*tert*-butyl sulfoxide at moderate temperatures in a variety of solvents, with the concentration of the sulfenic acid building up in the solution to a level where its spectral characteristics are easily detected. We pyrolyzed di-*tert*-butyl sulfoxide in dioxane at 80 °C and monitored the course of the reaction by ultraviolet spectrophotometry. After 2 h the absorption of the sulfoxide at 223 nm had been replaced by an increase in the absorption of the solution at 215 nm, but there was *no detectable absorbance at 265 nm.* (Similar results were obtained when the pyrolysis was carried out in acetonitrile solution.) Longer heating of the pyrolysis reaction solutions led, as noted by Shelton and Davis,[22] to the conversion of the sulfenic acid to *tert*-butyl 2-methyl-2-propanethiolsulfinate, *t*-BuS(O)SBu-*t*. This thiolsulfinate, an authentic sample of which was also synthesized by an unambiguous, alternate route, exhibits a λ_{max} in 60% dioxane at 245 nm, but *not* one at 265 nm. Thus, one can also rule out *t*-BuS(O)SBu-*t* as a possible structure for the 265-nm intermediate.

A third possibility for the 265-nm intermediate that can be ruled out is benzeneselenenic acid PhSeOH. A dilute solution of benzeneselenenyl chloride,[2c] PhSeCl, in anhydrous dioxane was treated with a small amount of water in order to hydrolyze the selenenyl chloride to PhSeOH. Observation of the ultraviolet spectrum of the solution showed that upon addition of the water the λ_{max} at 244 nm due to PhSeCl disappeared almost instantaneously but without the development of any significant absorbance at 265 nm. This result indicates that the 265-nm intermediate is not PhSeOH.

The stability of the 265-nm intermediate from the reaction of *t*-BuSH with $PhSeO_2H$ in aqueous dioxane at pH 3–7 suggested that it might be possible to isolate this intermediate in relatively pure form by allowing $PhSeO_2H$ to react in 60% dioxane with a slight molar excess of *t*-BuSH until the solution showed maximum absorbance at 265 nm, then rapidly freezing the reaction solution and removing the solvent and any excess mercaptan by lyophilization. Since the intermediate is apparently much less thermally stable in concentrated form (vide infra) than in a dilute solution in aqueous dioxane, it was critical to keep the lyophilization flask cooled in ice during the latter stages of the lyophilization in order to prevent extensive decomposition of the intermediate. With this precaution, most of the 265-nm intermediate survived the lyophilization workup. This was demonstrated by redissolving a portion of the residue in 60% dioxane and examining the ultraviolet absorption spectrum of the solution.

In acetone-d_6 at −20 °C the NMR spectrum of the 265-nm intermediate shows an aromatic ring multiplet between δ 7.5 and 8.0, a sharp singlet for a *tert*-butyl group at δ 1.63, and

Table II. Kinetics of the First Stage of the Reaction of Benzeneseleninic Acid with 1-Butanethiol in 60% Dioxane at 25 °C

reaction conditions	pH	$10^4[PhSeO_2H]_0$, M	10^3[RSH], M	10^3k_i, s^{-1} [a]	$k_a = k_i/[RSH]$, M^{-1} s^{-1}
0.6 M $HClO_4$	0.22	0.67	1.3	9.2	7.1
			2.0	14.1	7.1
		1.00	2.0	14.1	7.1
0.4 M $HClO_4$	0.40	0.67	1.3	5.9	4.5
			2.0	9.1	4.6
		1.00	2.0	8.7	4.4
0.2 M $HClO_4$	0.70	0.67	2.0	4.5	2.3
		1.00	2.0	4.7	2.4
0.1 M $HClO_4$	1.00	0.67	1.3	1.7	1.3
			2.0	2.7	1.4
		1.00	2.0	2.4	1.2
			2.7	3.4	1.3
0.06 M $HClO_4$	1.22	0.67	2.2	1.4	0.64
			3.2	2.1	0.65
		1.00	3.2	2.0	0.63
0.01 M $HClO_4$	2.00	0.67	1.3	0.40	0.31
			2.0	0.57	0.29
		1.00	2.0	0.57	0.29
			2.7	0.81	0.30
1:1 CF_3COOH-CF_3COO^- buffer[b]	2.8	0.67	2.0	0.59	0.30
		1.00	2.0	0.62	0.31
			2.7	0.82	0.30
0.65:1.0 $Cl_2CHCOOH$-Cl_2CHCOO^- buffer[c]	4.2	0.67	2.0	0.72	0.36
		1.00	2.0	0.77	0.38
			2.7	1.00	0.37
3.5:1.0 $ClCH_2COOH$-$ClCH_2COO^-$ buffer	4.9	0.67	2.0	1.05	0.52
		1.00	2.0	1.07	0.53
			2.7	1.43	0.53
1.1:1.0 $ClCH_2COOH$-$ClCH_2COO^-$ buffer[d]	5.4	0.67	1.3	2.3	1.8
			2.0	3.4	1.7
		1.00	2.0	3.4	1.7
1.3:1.0 $HCOOH$-$HCOO^-$ buffer[d]	6.0	0.67	1.3	6.3	4.8
			2.0	9.6	4.8
		0.84	2.0	9.4	4.7
		1.00	2.0	9.5	4.8
0.28:1.0 $HCOOH$-$HCOO^-$ buffer[d]	6.6	0.67	1.3	15.2	12
			2.0	24	12
		0.84	2.0	24	12
1.2:1.0 $AcOH$-AcO^- buffer[d]	7.36	0.67	1.3	26	20
			2.0	39	20
		1.00	2.0	38	19
0.17:1.0 $AcOH$-AcO^- buffer[d]	8.2	0.67	1.3	36	28
			2.0	55	28
		0.84	2.0	54	27
1:1 KH_2PO_4-K_2HPO_4 buffer, $[H_2PO_4^-] = 0.02$ M	9.0	0.67	1.9	68	36
			2.2	76	35
		0.84	2.7	101	38
0.12:1.0 KH_2PO_4-K_2HPO_4 buffer, $[HPO_4^{2-}] = 0.03$ M	10.0	0.67	1.9	67	35
			2.2	85	39
		0.84	2.7	110	41

[a] k_i is the experimental first-order rate constant for the first stage of the *n*-BuSH-$PHSeO_2H$ reaction. [b] $[RCO_2^-] = 0.02$ M. [c] $[RCO_2^-] = 0.01$ M. [d] $[RCO_2^-] = 0.05$ M.

another sharp singlet at δ 3.7. Upon being warmed from −20 to 20 °C and kept at that temperature for 1 h, the NMR of the solution undergoes striking change: (1) the singlet at δ 1.63 vanishes, and is replaced by a singlet at δ 1.32 associated with the *tert*-butyl protons in PhSeSBu-*t* and *t*-BuSSBu-*t*; (2) the aromatic multiplet between δ 7.5 and 8.0 associated with the 265-nm intermediate disappears and is replaced by the kind of multiplet between δ 7.2 and 7.8 that one finds for the phenyl protons in both PhSeSBu-*t* and PhSeSePh; (3) the singlet originally present at δ 3.7 shifts to δ 4.2. That this peak at δ 4.2 is due to water is suggested by the fact that adding a small amount of water to the solution results in further enhancement of the peak at δ 4.2. The final NMR spectrum of the solution at 20 °C after the intermediate has undergone decomposition is thus identical with that of a mixture of water plus PhSeSBu-*t*, PhSeSePh, and *t*-BuSSBu-*t*, and each of the three organic products could be isolated by chromatography of the residue left after evaporation of the acetone-d_6. We could find no evidence for any other NMR signals that could be attributed to other products of the decomposition.

The marked instability of the intermediate at room temperature in a relatively concentrated solution in acetone-d_6 contrasts dramatically with its considerable stability in dilute (10^{-4} M) solution in 60% dioxane. Possible reasons for this dramatic difference in behavior will be considered in the Discussion. Warming the solid lyophilization residue to room temperature also led to a relatively rapid decomposition of the intermediate and to the production of a mixture of PhSeSBu-*t*, PhSeSePh, and *t*-BuSSBu-*t* as the apparently virtually exclusive organic products. This thermal instability of solid

Table III. Kinetics of the Second Stage of the Reaction of Benzeneseleninic Acid with 1-Butanethiol in 60% Dioxane at 25 °C

reaction conditions	pH	$10^4[PhSeO_2H]_0$, M	10^3[RSH], M	t_{max}, s[a]	(k_{ii}/k_i)[b]	$k_b = k_{ii}/$[RSH], $M^{-1}\ s^{-1}$
1.2:1.0 AcOH-AcO^- buffer, $[RCOO^-]$ = 0.05 M	7.36	1.21	1.2	30	1.9	38
		0.91	1.0	38	1.7	34
0.28:1.0 HCOOH-$HCOO^-$ buffer, $[RCOO^-]$ = 0.05 M	6.6	1.21	1.2	90	0.59	7.1
			1.6	57	0.82	9.8
1.5:1.0 HCOOH-$HCOO^-$ buffer, $[RCOO^-]$ = 0.05 M	5.9	0.91	1.2	320	0.29	1.3
			1.7	240	0.26	1.2
1.1:1.0 $ClCH_2COOH$-$ClCH_2COO^-$ buffer, $[RCOO^-]$ = 0.05 M	5.4	1.2	1.2	1080	0.155	0.26
			1.6	870	0.125	0.21
3.5:1.0 $ClCH_2COOH$-$ClCH_2COO^-$ buffer, $[RCOO^-]$ = 0.01 M	4.9	1.2	1.2	3000	0.23	0.12
			2.0	2040	0.161	0.085

[a] Time required for absorption at 265 nm to reach its maximum value. [b] Calculated from the relationship between t_{max} and the rate constants for two consecutive first-order reactions given in ref 16.

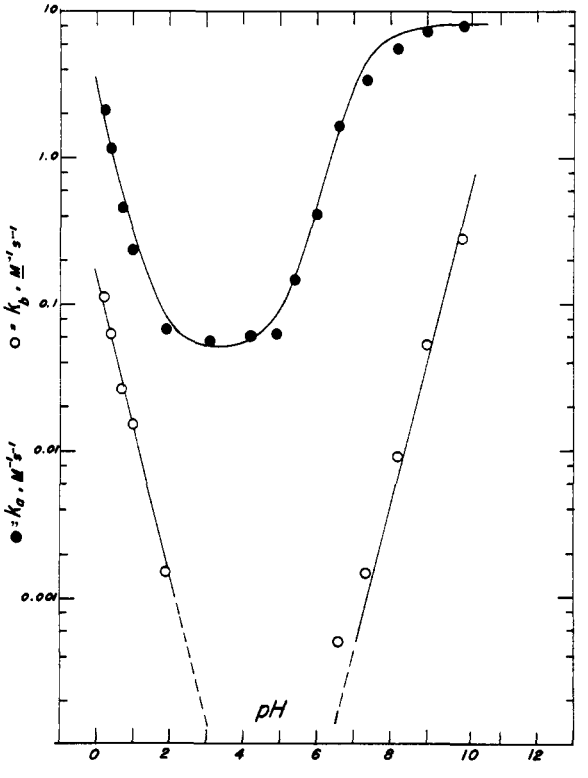


Figure 1. pH-rate profiles for the two stages of the reaction of *t*-BuSH with benzeneseleninic acid at 25 °C in 60% dioxane: ●, rate constants, k_a, for the first stage of reaction (solid curve calculated from eq 4 using K_a for $PhSeO_2H = 6 \times 10^{-8}$ M, $k = 2.8\ M^{-2}\ s^{-1}$, $k' = 0.05\ M^{-1}\ s^{-1}$, and $k'' = 0.48 \times 10^{-6}\ s^{-1}$); ○, rate constants, k_b, for second stage of reaction (solid lines are drawn with unit slope).

samples of the intermediate precluded obtaining reliable other types of spectral information (infrared, mass spectrum) about its structure.

Discussion

The reaction of benzeneseleninic acid, $PhSeO_2H$, with either excess 1-butanethiol (*n*-BuSH) or 2-methyl-2-propanethiol (*t*-BuSH) in aqueous dioxane leads to the formation of the appropriate selenenyl sulfide PhSeSR (eq 2), rather than to diphenyl diselenide as reported by Rheinboldt and Giesbrecht.[11] The eventual formation of diphenyl diselenide in such systems is the result of slow subsequent disproportionation of the selenenyl sulfide to PhSeSePh and RSSR.

The formation of the selenenyl sulfide involves the formation first from the thiol and $PhSeO_2H$ of an intermediate species having an absorption maximum at 265 nm via a reaction that is first order in the stoichiometric concentrations of both the thiol and the seleninic acid. The intermediate is then consumed in a reaction that is first order in intermediate and first order in thiol, and the end products of the reaction sequence initiated by this reaction are 1 mol each of the selenenyl sulfide PhSeSR and the disulfide RSSR. Without concern as yet for the ionization state of the various reactants in the different steps, the *kinetic* situation for the thiol-$PhSeO_2H$ reactions can thus be represented as

$$PhSeO_2H + RSH \xrightarrow{k_a} \text{intermediate (I)} \qquad (5a)$$

$$I + RSH \xrightarrow{k_b} PhSeSR + RSSR \qquad (5b)$$

For the reaction of *t*-BuSH with the seleninic acid one finds that at all pHs $k_b \ll k_a$, but for the reaction of the primary thiol, *n*-BuSH, $k_b < k_a$ only over a very limited pH range, and at most pHs $k_b > k_a$.

Figures 1 and 2 show that the pH-rate profiles for k_a and k_b are quite different. Consider first the pH-rate profile for k_a. Reaction of both thiols (*t*-BuSH or *n*-BuSH) with $PhSeO_2H$ shows the same type of U-shaped pH-rate profile for k_a, the rate constant for the tertiary thiol, *t*-BuSH, being somewhat slower (factor of 4 to 5) at all pHs than k_a for *n*-BuSH. The pH-rate profile for k_a in each case is given by an equation of the form shown in eq 4, using a value of K_a for $PhSeO_2H$ ($pK_a = 7.2$) within the range expected[19] for that acid in 60% dioxane. The three equations responsible for the different kinetic terms in the numerator of eq 4 *must each be capable of leading* (after either suitable rapid proton-transfer steps and/or dehydrations) *to the same 265-nm intermediate*, since the formation of this intermediate is observed at *all* pHs from 0 to 10 in the reaction of *t*-BuSH with $PhSeO_2H$.

Since both *t*-BuSOH and PhSeOH were shown to have ultraviolet spectra entirely different from that of the 265-nm intermediate one can rule out the possibility of step k_a involving an oxygen transfer from seleninic acid to thiol:

$$RSH + PhSeO_2H \rightarrow RSOH + PhSeOH \qquad (6)$$

and all the variations on this, such as

$$RS^- + PhSeO_2H \rightarrow RSO^- + PhSeOH \xrightarrow[\text{fast}]{H_2O} RSOH + PhSeOH$$

in which the initial reactants are in different ionization states.

The NMR spectrum of the 265-nm intermediate from the reaction of *t*-BuSH with $PhSeO_2H$ shows the presence of both

Scheme I. Mechanism of the First Stage of the Thiol–Benzeneseleninic Acid Reaction

$$PhSeO_2H + H^+ \underset{}{\overset{K_1}{\rightleftharpoons}} PhSeO_2H_2^+ \quad (7a)$$

$$PhSeO_2H \overset{K_a}{\rightleftharpoons} PhSeO_2^- + H^+ \quad (7b)$$

$$RSH + PhSeO_2H_2^+ \xrightarrow{k_H} PhSe(OH)(OH)-S^+(H)-R \xrightarrow[-H^+]{fast} \quad (8a)$$

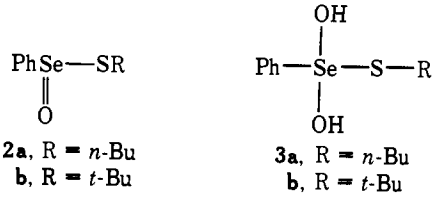
$$RSH + PhSeO_2H \xrightarrow{k_0} PhSe(OH)(OH)-SR \quad (8b)$$

$$\xrightarrow{-H_2O} PhSe(=O)-SR \quad \mathbf{2}$$

$$RS^- + PhSeO_2H \xrightarrow{k_{RS^-}} PhSe(O^-)(OH)-SR \xrightarrow[+H^+]{fast} \mathbf{3} \quad (8c)$$

$$RSH \overset{K_{RSH}}{\rightleftharpoons} RS^- + H^+ \quad (9)$$

a phenyl and a *tert*-butyl group. One reasonable structure for the intermediate is thiolseleninate **2b**, PhSe(O)SBu-*t*, with the third signal in the NMR (δ 3.7) being ascribed to water of hydration tenaciously held by the strongly dipolar seleninyl group of **2b**. A closely related alternative would be **3**, the covalent hydrate of **2**. However, since covalent hydrates are not observed with such seleninyl compounds as selenoxides,[23] despite their propensity to retain water of hydration tenaciously, formulation of the 265-nm intermediate as **2**, rather than **3**,



2a, R = *n*-Bu
b, R = *t*-Bu

3a, R = *n*-Bu
b, R = *t*-Bu

seems preferable at the present time.

We therefore propose the mechanism for the first stage (k_a step) of the thiol-seleninic acid reaction shown in Scheme I. This mechanistic scheme will give the following dependence of rate on pH for k_a:

$$k_a = \frac{k_H K_1 a_{H^+}^2 + k_0 a_{H^+} + k_{RS^-} K_{RSH}}{K_a + a_{H^+}} \quad (10)$$

This is of exactly the same form as eq 4. The mechanism in Scheme I does therefore correctly account for the observed pH-rate profile for k_a.

Different pathways for formation of intermediate **2** are kinetically dominant in different pH regions. Below pH 2 it is reaction of the undissociated thiol with the protonated seleninic acid, $PhSeO_2H_2^+$ (eq 8a). At these pHs $a_{H^+} \gg K_a$, and so in this pH region $k_a = k_H K_1 a_{H^+}$, thus accounting for the linear increase in k_a with a_{H^+} which is observed at pH < 2.

In the region (pH 2.5–4.5) where the rate is effectively independent of pH, the kinetically dominant path for formation of the intermediate is reaction of RSH with the undissociated seleninic acid $PhSeO_2H$ (eq 8b). Values for the rate constant, k_0, for this reaction are 5×10^{-2} M^{-1} s^{-1} for *t*-BuSH, and 2.5×10^{-1} M^{-1} s^{-1} for *n*-BuSH.

Above pH 5 the kinetically important pathway for formation of the intermediate becomes nucleophilic addition of the thiolate anion RS^- to the undissociated seleninic acid (eq 8c).[24] In the region where eq 8c is dominant k_a will be given by $k_{RS^-}K_{RSH}/(K_a + a_{H^+})$, so that above pH 5 the rate increases with increasing pH up to the point where $K_a \gg a_{H^+}$ and then levels off at a value equal to $k_{RS^-}K_{RSH}/K_a$. Given its pK_a in water,[25] the pK_a for *t*-BuSH in 60% dioxane is probably about 14. From this and K_a for $PhSeO_2H$ (6×10^{-8} M), k_{RS^-} is estimated to be 5×10^7 M^{-1} s^{-1} for the reaction of *t*-BuS^- with $PhSeO_2H$. While large, this is a perfectly reasonable value, well below the diffusion-controlled upper limit for rate constants of bimolecular reactions, and of the same order of magnitude as the rate constants (10^7–$10^{8.6}$ M^{-1} s^{-1}) that have been observed for nucleophilic attack by alkanethiolate ions on various other reactive substrates such as phenyl benzenethiolsulfonate[17a] and quinazoline.[26]

The ratio (k_{RS^-}/k_0) gives the reactivity toward $PhSeO_2H$ of the thiolate ion RS^-, as compared to thiol RSH. For both thiols this ratio has a very large value, ~10^9. However, since several other cases are known[17a,26] where (k_{RS^-}/k_{RSH}) for attack of thiolate ion vs. thiol on a given substrate is from $\geq 10^7$ to $\geq 2 \times 10^8$, we do not consider the very large value of k_{RS^-}/k_0 for the proposed mechanism of the thiol-seleninic acid reaction as any cause for concern about the correctness of the mechanism in Scheme I.

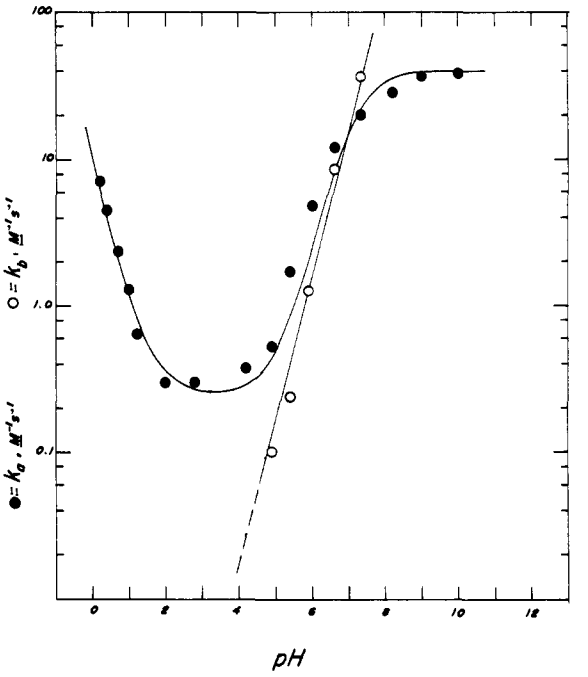
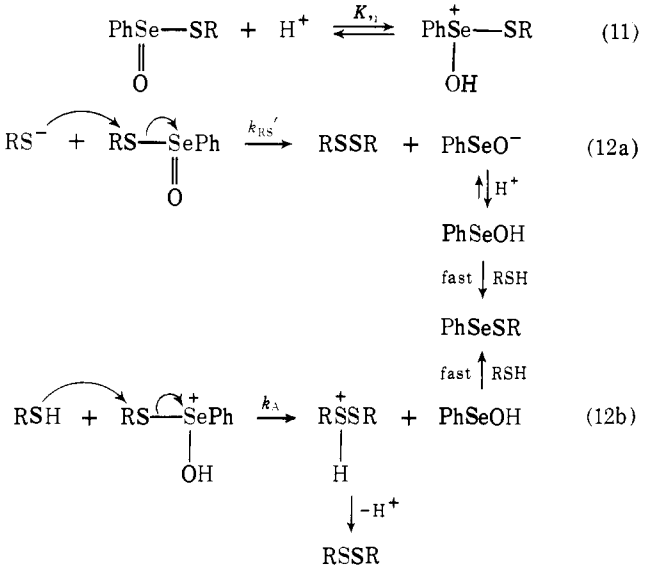


Figure 2. pH-rate profiles for the two stages of the reaction of *n*-BuSH with benzeneseleninic acid at 25 °C in 60% dioxane: ●, rate constants, k_a, for first stage of reaction (solid curve calculated from eq 4 using K_a for $PhSeO_2H = 6 \times 10^{-8}$ M, $k = 10$ M^{-2} s^{-1}, $k' = 0.25$ M^{-1} s^{-1}, and $k'' = 2.4 \times 10^{-6}$ s^{-1}); ○, rate constants, k_b, for second stage of reaction (solid line is drawn with unit slope).

Let us now consider the second stage of the thiol-seleninic acid reaction. As noted earlier, the rate-determining step (k_b) of this reaction sequence is first order in the intermediate and first order in the thiol.

The pH-rate profile for k_b for the *t*-BuSH–**2b** reaction, insofar as it could be determined,[27] is shown in Figure 1. Below pH 2 k_b increases linearly with increasing a_{H^+} in a fashion consistent with a rate expression of the type rate = k_A[*t*-BuSH][**2b**][H^+]. Reaction of the thiol with a protonated form of **2b** is apparently the kinetically significant process in this pH region. Above pH 6.5 k_b is *inversely* proportional to a_{H^+}, showing no signs of leveling off up to the highest pH (10.0) at which rate measurements were made. This is consistent with the kinetics being given in this pH region by rate =

Scheme II. Mechanism of the Second Stage of the Thiol–Benzeneseleninic Acid Reaction



$k'_{t\text{-BuS}}[t\text{-BuS}^-][\mathbf{2b}]$. Reaction of the intermediate with the thiolate ion is the kinetically important process under these conditions. The same is also true (Figure 2) for the reaction of *n*-BuSH with **2a** for the pH range (5–7.5) over which it was measurable.

In striking contrast to the situation for reaction 8c, where the rate constants for reaction of both *t*-BuS$^-$ and *n*-BuS$^-$ with $PhSeO_2H$ are about the same, the rate constant ($k'_{t\text{-BuS}}$) for the reaction of *t*-BuS$^-$ with intermediate **2b** is approximately $10^{4.5}$ *slower* than the rate constant ($k'_{n\text{-BuS}}$) for the reaction of *n*-BuS$^-$ with **2a.**

Reactions that involve nucleophilic attack on the sulfur of a *t*-BuS group are known[27] to be generally orders of magnitude slower than the analogous reaction involving attack on the sulfur of an *n*-BuS group. The fact that $(k'_{n\text{-BuS}}/k'_{t\text{-BuS}}) = 10^{4.5}$ therefore strongly suggests that reaction of the intermediate with the thiolate ion involves attack by the thiolate on the sulfur atom in **2,** a process that should be much faster with **2a** than with **2b** and its sterically hindered sulfur.

Accordingly we suggest that in the pH range where the rate-determining step of the second stage of the thiol–seleninic acid reaction is attack of RS$^-$ on **2** the mechanism is as shown in eq 12a in Scheme II. For the acid-catalyzed reaction of the thiol with the protonated intermediate that becomes the rate-determining step of the second stage in relatively acid solution (pH <2) we propose an analogous mechanism (eq 12b) involving attack of the undissociated thiol, RSH, on the sulfur of protonated **2.** In such a mechanism reaction of *t*-BuSH with protonated **2b** would again be expected to be *much* slower than attack of thiol on protonated **2a.** Although we cannot directly measure k_b for the *n*-BuSH–**2a** reaction in this pH region, we do know that, since it must be considerably larger than k_a for reaction of *n*-BuSH with $PhSeO_2H$, it is definitely *at the least* several orders of magnitude larger than k_b for the reaction of *t*-BuSH with **2b** at the same pH. The mechanisms for the second stage proposed in eq 12a and 12b also are attractive in that after the rate-determining step only one further simple and straightforward reaction, that of thiol with PhSeOH to give PhSeSR, is required in order to complete the scheme.

Except for its rather slow reaction with excess thiol, intermediate **2b** seems to be quite stable in dilute ($\sim 10^{-4}$ M) solution in aqueous dioxane. In dramatic contrast to this stability of **2b** in dilute solution in aqueous dioxane is its rapid decomposition at room temperature in relatively concentrated ($\sim$0.5 M) solution in acetone-d_6. The NMR of the acetone solution after the decomposition is complete reveals the presence of a mixture of PhSeSBu-*t*, PhSeSePh, and *t*-BuSSBu-*t* plus water. If any more highly oxidized organosulfur or organoselenium compounds are present they are not there in sufficient concentration to give detectable NMR signals.

How can one account for the striking difference in the stability of **2b** under these different conditions and for the products formed upon its decomposition in acetone? While **2b** is thermally quite stable in solvent media such as aqueous dioxane in which the seleninyl group is strongly hydrated and solvated, we tentatively suggest that the stability of the thiolseleninate may be much lower in media such as anhydrous acetone in which such solvation is absent and that in such solvents thiolseleninate **2b** decomposes rapidly to PhSeSBu-*t*, PhSeSePh, and *t*-BuSSBu-*t*, plus oxygen. The suggestion that oxygen is one of the products of decomposition of PhSe(O)SR is not unreasonable since Woodbridge[29] has reported that two major products of the thermal decomposition of dodecaneseleninic anhydride, $C_{12}H_{25}Se(O)OSe(O)C_{12}H_{25}$, in benzene are dodecyl diselenide and oxygen. Thermal decomposition of a seleninyl derivative to yield oxygen as one of the products thus has precedent.

Several possible mechanisms can be written for conversion of PhSe(O)SR to the decomposition products. The simplest would involve initial homolytic dissociation of PhSe(O)SR to PhSeO· and RS· radicals followed by the sequence of reactions shown below:

$$\mathrm{PhSe(O)SR} \rightarrow \mathrm{PhSeO\cdot} + \mathrm{RS\cdot}$$

$$2\mathrm{PhSeO\cdot} \rightarrow [\mathrm{PhSe\text{-}O\text{-}O\text{-}SePh}] \rightarrow 2\mathrm{PhSe\cdot} + \mathrm{O_2}$$

$$\mathrm{PhSe\cdot} + \mathrm{RS\cdot} \rightarrow \mathrm{PhSeSR}$$

$$2\mathrm{PhSe\cdot} \rightarrow \mathrm{PhSeSePh}$$

$$2\mathrm{RS\cdot} \rightarrow \mathrm{RSSR}$$

It is also possible to arrive at the same products by various schemes in which the PhSeO· and RS· radicals induce the decomposition of PhSe(O)SR.

Whatever emerges on further study to be the correct explanation for the contrasting behavior of **2b** in different media, it is clear that **2b** represents an interesting new type of selenium compound with apparently considerable unexpected and surprising chemistry. Its discovery in the course of what began as simply the study of the mechanism of the reaction between thiols and seleninic acids is hopefully indicative of the kind of interesting new dimensions in organoselenium chemistry that can result from study of the mechanism of reactions of organic selenium compounds.

Experimental Section

Preparation and Purification of Materials. 1-Butanethiol (Aldrich) and 2-methyl-2-propanethiol (Aldrich) were purified by fractional distillation and stored under nitrogen. Dioxane was purified by the procedure described by Fieser and Fieser;[30] freshly fractionally distilled dioxane was then frozen and stored at −20 °C to prevent the formation of peroxides prior to use. All water used in kinetic studies was doubly distilled from glass. The carboxylic acids used in the preparation of the various buffers employed were of the highest degree of purity available commercially.

Benzeneseleninic Acid. Diphenyl diselenide (Eastman), purified by recrystallization from hexane, was oxidized to benzeneseleninic acid using the procedure described by McCullough and Gould.[20] The purified seleninic acid, mp 120–121 °C (lit.[20] 121 °C), was stored in a desiccator until used.

Di-*tert*-butyl Sulfoxide. This was prepared from di-*tert*-butyl sulfide (Aldrich) in the manner outlined by Barnard and co-workers.[31] The sulfoxide was purified by recrystallization from pentane, mp 62–63 °C (lit.[31] 63.5–65 °C), UV (60% dioxane) λ_{max} 223 nm (ϵ 710).

tert-Butyl 2-Methyl-2-propanethiolsulfinate. To a solution of 5.35 g (0.03 mol) of di-*tert*-butyl disulfide (Aldrich) in 50 mL of glacial acetic acid was added dropwise 3.14 g of 30% hydrogen peroxide (0.03 mol of H_2O_2). The reaction mixture was stirred overnight at room temperature and then heated to 40 °C for 0.5 h. The solution was then poured into 100 mL of water, and the mixture was extracted twice with 50-mL portions of chloroform. The chloroform extracts were washed several times with water and dried over magnesium sulfate, and the chloroform was then removed under reduced pressure to afford the thiolsulfinate as a colorless oil, 7.45 g (93%). It was purified by vacuum distillation: bp 64 °C (0.1 mm), lit.[32] 55 °C (0.05 mm); UV (60% dioxane) λ_{max} 245 nm (ϵ 1280).

Benzeneselenenyl Chloride. This was prepared from diphenyl diselenide using the procedure described by Reich and co-workers.[2c] The selenenyl chloride, obtained as orange crystals, was further purified by recrystallization from hexane, mp 63–65 °C (lit.[2c] 63–64 °C), UV (dioxane) λ_{max} 244 nm (ϵ 1.01×10^4).

n-Butyl Benzeneselenenyl Sulfide (1a). Bromine (0.26 g, 1.6 mmol) was added dropwise to a solution of diphenyl diselenide (0.5 g, 1.6 mmol) in 8 mL of chloroform at 0 °C. The resulting dark-red solution of benzeneselenenyl bromide was then quickly mixed with 0.29 g (3.2 mmol) of 1-butanethiol. Within minutes the red color of the solution was discharged. The solvent was then evaporated to leave a yellow oil. Chromatography of the oil on silica gel using hexane as eluent gave three fractions: di-*n*-butyl disulfide (0.16 g), *n*-butyl benzeneselenenyl sulfide (**1a**, 0.36 g), and diphenyl diselenide (0.255 g). The selenenyl sulfide **1a** as isolated from the chromatography was analytically pure and exhibited the following characteristics: IR (neat) 3080 (m), 2970 (s), 2940 (s), 2880 (m), 1585 (m), 1482 (s), 1472 (m), 1445 (s), 1025 (m), 730 (s), and 685 cm^{-1} (m); NMR ($CDCl_3$) δ 0.66–1.0 (distorted triplet, 3 H), 1.06–1.80 (multiplet, 4 H), 2.70–2.96 (triplet, 2 H), and 7.18–7.80 (multiplet; 5 H); UV (60% dioxane) λ_{max} 242 nm (ϵ 6900) and 310 (ϵ 520). Anal. Calcd for $C_{10}H_{14}SSe$: C, 49.00; H, 5.71. Found: C, 49.08; H, 5.85.

tert-Butyl Benzeneselenenyl Sulfide (1b). Using the same procedure as for the synthesis of **1a**, reaction of 0.26 g of bromine with 0.5 g of diphenyl diselenide followed by addition of 0.29 g of 2-methyl-2-propanethiol gave upon evaporation of the solvent 0.76 g of oily residue. Chromatography of the residue on silica gel using hexane as eluent gave two fractions: *tert*-butyl benzeneselenenyl sulfide (**1b**, 0.35 g) and diphenyl diselenide (0.40 g). The selenenyl sulfide **1b** was further purified by vacuum distillation: bp 63 °C (0.15 mm); IR (neat) 3080 (m), 2980 (s), 2920 (m), 2880 (m), 1590 (m), 1485 (s), 1465 (m), 1448 (m), 1360 (s), 1165 (s), 1024 (m) 730 (s), and 685 cm^{-1} (m); NMR ($CDCl_3$) δ 1.32 (singlet, 9 H) and 7.18–7.80 (multiplet, 5 H); UV (60% dioxane) λ_{max} 245 nm (ϵ 7900) and 300 (ϵ 730). Anal. Calcd for $C_{10}H_{14}SSe$: C, 49.00; H, 5.71. Found: C, 49.09; H, 5.83.

Isolation of Selenenyl Sulfides 1a and 1b as Products of the Reaction of Benzeneseleninic Acid with Thiols. To 0.76 g (4 mmol) of benzeneseleninic acid dissolved in 40 mL of 60% dioxane were added 1.8 g (20 mmol) of 1-butanethiol and 4 mL of a 1 N solution of perchloric acid. The mixture was allowed to stir for 20 min at room temperature before the dioxane was evaporated under reduced pressure. The residue was mixed with 150 mL of water and the mixture extracted twice with 50-mL portions of chloroform. The chloroform extracts were washed several times with water and then dried over anhydrous magnesium sulfate. Removal of the chloroform left an oily residue which was subjected to chromatography on silica gel using hexane as eluent. From the chromatography was obtained 0.91 g (93%) of selenenyl sulfide **1a**, identical in all respects with the synthetic sample prepared by reaction of PhSeBr with *n*-BuSH (vide supra). No diphenyl diselenide was isolated from the chromatography.

Reaction of 1.8 g (20 mmol) of 2-methyl-2-propanethiol with 0.76 g (4.0 mmol) of benzeneseleninic acid in 40 mL of 60% dioxane to which had been added 4 mL of 1 N perchloric acid was carried out in the same manner except that the solution was allowed to stand at room temperature for 1 h before workup. Chromatography of the oily residue from evaporation of the chloroform extracts afforded 0.85 g (87%) of *tert*-butyl benzeneselenenyl sulfide (**1b**), identical in all respects with the synthetic sample of **1b** whose preparation has been outlined earlier. Again, no diphenyl diselenide was found upon chromatography of the oily residue.

Procedure for Kinetic Runs. A stock solution of benzeneseleninic acid in 60% dioxane (v/v) was prepared by dissolving a weighed amount of the acid in a known volume of the solvent. A stock solution of the appropriate thiol in the same solvent was also prepared immediately prior to use by dissolving a carefully weighed amount of the thiol in a known volume of 60% dioxane. To 3.5 mL of a 60% dioxane solution containing the proper amount of either perchloric acid or buffer, and contained in a 1-cm stoppered cell in the thermostated cell compartment of a Cary Model 17 spectrophotometer, was then added by microsyringe an amount of seleninic acid stock solution sufficient to give the desired initial concentration of benzeneseleninic acid. The reaction was then initiated by adding, using a second microsyringe, the proper amount of the stock solution of the thiol. In the case of the reactions involving benzeneseleninic acid and 2-methyl-2-propanethiol (*t*-BuSH) the change in the optical density of the solution with time at 265 nm was then followed. The absorbance at this wavelength first increases with time, reaches a maximum, and then very slowly declines to its final value. The rates of the two reactions are sufficiently different that they can be treated as two independent, consecutive processes for the purposes of kinetic analysis.

For most of the runs with 1-butanethiol the increase in absorbance with time at 240 nm was followed. In a small group of runs at pHs between 4.9 and 7.4 the change in absorbance at 265 nm with time was monitored, and the time required for the optical density at this wavelength to increase to its maximum value before starting to decline was determined.

Pyrolysis of Di-*tert*-butyl Sulfoxide. Shelton and Davis[22] have shown that pyrolysis of di-*tert*-butyl sulfoxide in a variety of solvents (including dioxane and acetonitrile) leads to the formation of 2-methyl-2-propanesulfenic acid, *t*-BuSOH, and isobutylene. To determine if this sulfenic acid could be the 265-nm intermediate observed in the *t*-BuSH–$PhSeO_2H$ reaction the following experiment was performed. Di-*tert*-butyl sulfoxide (0.054 g, 0.24 mmol) was dissolved in 5 mL of pure dioxane and the solution heated in a constant temperature bath at 80 °C. At fixed time intervals 0.05-mL aliquots of the solution were withdrawn with a microsyringe and added to 3.5 mL of 60% dioxane contained in a 1-cm spectrophotometer cell in a Cary Model 17 spectrophotometer, and the ultraviolet absorption spectrum of the resulting solution was determined.

A similar experiment was performed using acetonitrile rather than dioxane as the solvent. In neither case was any absorbance maximum at 265 nm detected.

Isolation and Spectral Study of the Intermediate in the *t*-BuSH–$PhSeO_2H$ Reaction. A solution of 0.13 g (1.4 mmol) of 2-methyl-2-propanethiol in 20 mL of 60% dioxane was mixed with a solution of 0.19 g (1.0 mmol) of benzeneseleninic acid in 5 mL of 60% dioxane. The formation of the 265-nm intermediate was monitored by removing 0.01-mL aliquots of this reaction solution, adding these to 3.5 mL of 60% dioxane in a 1-cm spectrophotometer cell, and determining the optical density at 265 nm. When the concentration of the intermediate reached its maximum value as evidenced by the maximum in absorbance at 265 nm (80–90 min) the reaction solution was quickly transferred to a lyophilization flask and frozen at −78 °C. The solvent was then removed by lyophilization. In order to prevent decomposition of the intermediate it is important that the lyophilization flask be cooled externally with an ice bath during the latter stages of the lyophilization. The white, powdery residue (0.16 g) remaining at the end of the lyophilization was then kept at dry ice temperature until use.

A sample of the lyophilization residue was redissolved in 60% dioxane and the ultraviolet spectrum of the solution was determined. It was found to still possess the maximum at 265 nm characteristic of the intermediate. At −20 °C in acetone-d_6 the NMR spectrum of the lyophilization residue exhibited the following signals: a relatively weak sharp singlet at δ 1.32 due to the protons of the *tert*-butyl groups in the PhSeSBu-*t* and *t*-BuSSBu-*t* impurities inevitably present to some extent in the residue; a strong sharp singlet at δ 1.63 (protons of the *tert*-butyl groups in the intermediate); a sharp singlet at δ 3.71; a pair of aromatic multiplets, the weaker at δ 7.2–7.8 (due to the PhSeSBu-*t* and PhSeSePh impurities present in the intermediate) and the stronger at δ 7.5–8.0 (due to the aromatic protons in the intermediate). When the acetone-d_6 solution was allowed to warm from −20 to 20 °C and stand for 1 h, the singlet at δ 1.63 disappeared completely, with a corresponding increase in the intensity of the singlet at δ 1.32, the singlet at δ 3.71 disappeared and was replaced by one of similar intensity at δ 4.2, and the aromatic multiplet at δ 7.5–8.0 disappeared with a corresponding increase in the strength of the multiplet at δ 7.2–7.8. The signal at δ 4.2 is throught to be due to water since addition of a small amount of water to the final solution led to an increase in the intensity of this singlet. Removal of acetone-d_6 and

chromatography of the residue on silica gel using hexane as eluent afforded three separate fractions shown to be *t*-BuSSBu-*t*, *t*-BuSSePh, and PhSeSePh, respectively, by examination of their spectral properties.

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Preparation and Crystal and Molecular Structure of Sodium [Bis(inosine 5′-monophosphate)(diethylenetriamine)-copper(II)] Decahydrate. Possible Implications for Intrastrand Cross-Linking of Polynucleotides by Copper(II) and Platinum(II) Complexes

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Abstract: The synthesis and crystal and molecular structure of sodium [bis(inosine 5′-monophosphate)(diethylenetriamine)-copper(II)] decahydrate, $Na_2[Cu(5'\text{-IMP})_2(dien)]\cdot 10H_2O$, are reported. The complex crystallizes in the orthorhombic system, space group $P2_12_12$, with a = 8.706 (4), b = 21.074 (12), and c = 12.171 (7) Å, Z = 2, d_{measd} = 1.60 (2) g/cm^3, and d_{calcd} = 1.61 g/cm^3. The structure was solved by direct methods. Full-matrix least-squares refinement, based on 2051 counter-collected F_o's, has led to a final R value of 0.08. The copper positions in the unit cell were found to be disordered such that the copper atom occupies each of two sites 50% of the time. The primary coordination sphere about the copper is (4 + 1+ 1) with the equatorial plane defined by the tridentate dien chelate and N(7) of a 5′-IMP ligand. The axial positions are occupied by a second N(7) atom of a symmetry-related 5′-IMP anion and a water molecule. Extensive intramolecular hydrogen bonding is observed. Comparison of the equatorial-axial binding mode of the two purine ligands in $[Cu(5'\text{-IMP})_2(dien)]^{2-}$ vs. the cis equatorial binding found in $[Pt(5'\text{-IMP})_2(NH_3)_2]^{2-}$ and $[Pt(5'\text{-IMP})_2(ethylenediamine)]^{2-}$ is explored in terms of the possible effect of intrastrand cross-linking of polynucleotides by Cu(II) and Pt(II) complexes.

Introduction

Rosenberg[1] observed that certain Pt(II) compounds are effective anticancer agents. Subsequent in vivo and in vitro studies implicate the binding of Pt(II) compounds to nucleic acids.[2] Numerous solution and solid-state studies aimed at elucidating the nature of the metal binding have been undertaken.[2] Beyond an accumulation of evidence that Pt(II) is readily bound to N(7) of guanosine and inosine and their nu-

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